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Focus Session:
AI in Biomedical Engineering

Practice of domain knowledge in trustworthy deep learning for CT-free PET imaging

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Introduction

Artificial intelligence (AI) -based methods have been proposed to substitute CT-based PET attenuation correction to achieve CT-free PET imaging. A critical bottleneck for these AI-based methods is their limited capability in the application in heterogenous domain of PET imaging, i.e. a variety of scanners and tracers.

Methods

This study employs a simple way to integrate domain knowledge in deep learning for CT-free PET imaging. In contrast to conventional direct deep learning methods, we decomposed the complex end-to-end generation into two components, anatomy-independent textures (relating to tracers and diseases) and anatomy-dependent correction. Compared to direct approaches, estimation of only low-frequency anatomy-dependent correction using 3D deep neural network can be more efficient and robust, which is verified in tests of external imaging tracers on different scanners. Whole body PET images of 829 patients using ^{18}F-FDG, ^{18}F-PSMA, ^{68}Ga-DOTA-TOC, ^{68}Ga-DOTA-TATE, ^{68}Ga-FAPI, acquired using clinical PET scanners, including Biograph Vision (Siemens Healthineers), United Imaging uMI 780 (United Imaging), Discovery MI (General Electric Healthcare) in Shanghai and Bern, were included for the development and testing of the proposed method.

Results

Although the method was developed using one tracer (^{18}F-FDG) and one scanner, it achieved average whole-body normalized root mean squared error (NRMSE) and peak signal-to-noise ratio (PSNR) of 0.3%±0.2% and 51.5±6.4 respectively for different scanners, and 0.6%±0.4% and 47.5±7.4 for different tracers, which have significantly improved over conventional deep learning methods.

Conclusion

The proposed decomposition-based method provides a simple approach to incorporate domain knowledge in deep learning, which can significantly improve the performance and robustness of CT-free PET correction. The trustworthy AI development may enhance the potential of clinical translation.

Generative-Adversarial-Network-Based Data Augmentation for the Classification of Craniosynostosis

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Introduction

Craniosynostosis is a congenital disease characterized by the premature closure of one or multiple sutures of the infant's skull. For diagnosis, 3D photogrammetric scans are a radiation-free alternative to computed tomography. However, data is only sparsely available and the role of data augmentation for the classification of craniosynostosis has not yet been analyzed.

Methods

In this work, we use a 2D distance map representation of the infants' heads with a convolutional-neural-network-based classifier and employ a generative adversarial network (GAN) for data augmentation. We simulate two data scarcity scenarios with 15 % and 10 % training data and test the influence of different degrees of added synthetic data and balancing underrepresented classes. We used total accuracy and F1-score as a metric to evaluate the final classifier.

Results

For 15 % training data, the GAN-augmented dataset showed an increased F1-score up to 0.1 and classification accuracy up to 3 %. For 10 % training data, both metrics decreased.

Conclusion

We present a deep convolutional GAN capable of creating synthetic data for the classification of craniosynostosis. Using a moderate amount of synthetic data using a GAN showed slightly better performance, but had little effect overall. The simulated scarcity scenario of 10 % training data may have limited the model's ability to learn the underlying data distribution.

Determine the Electrode Position in DBS via Multimodal Image Fusion Using Artificial Intelligence Techniques

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Introduction

Deep Brain Stimulation (DBS) is a neurosurgical procedure that involves the placement of a medical device referred to as a neurostimulator. It consists of a lead, a subcutaneous extension, an electrode, and a pulse generator. DBS is capable of directly altering brain activity in a controlled manner. DBS is used to treat many conditions with movement disorders such as Parkinson's disease, dystonia, tremor, etc.

Methods

During the planning of DBS therapy and interventional surgery, various imaging modalities such as computed tomography (CT), angiography, and magnetic resonance imaging (MRI) are often used. Combining different images is therefore challenging and requires image fusion strategies. While manual approaches to image fusion are often tedious and error-prone process steps, deep learning techniques seem to be a promising alternative. Our goal is to determine the precise orientation of electrodes utilizing deep learning algorithms. Our methodology involves spatial tracking of electrodes in CT and DynaCT images by identifying a region of interest (ROI), i.e., the region of similarity, by establishing a ground truth, and applying an image segmentation model using U-Net. The multimodal image fusion approach combines the advantages of CT imaging with a wider scan range with the high-resolution properties of DynaCT imaging.

Results

A comprehensive workflow consisting of image analysis, pre-processing, segmentation by Convolutional Neural Networks using supervised learning, Image registration to cope with misalignment, similarity measurement using Structural Similarity Index (SSIM), and image fusion using bit processes to fuse CT and DynaCT slices was developed and tested on selected brain image datasets.

Conclusion

Determining the exact electrode position based on deep learning will help reduce the risk of complications caused by unwanted stimulation-related side effects. Therefore, this work is crucial for patient-specific clinical imaging workflows and improves therapeutic outcomes by detecting misplaced electrodes, identifying target regions in the brain, or assessing complications.

Segmentation of Living and ablated Tumor parts in CT images Using ResLU-Net

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Abstract

Computed tomography (CT) is widely used as the imaging modality for the treatment of tumors in Microwave Ablation (MWA) therapy. In order to accurately perform ablation of liver tumors and prevent tumor recurrence, it is necessary to segment both the living tumor and the ablated tissue on the CT images. The U-Net model has outperformed other methods in biomedical image segmentation. However, because of the low contrast between tumor and liver tissue texture, the traditional U-net network cannot perform an accurate segmentation of the CT images of liver during MWA therapy. The aim of this study is to improve the U-net model network to achieve a higher segmentation performance on the CT images of liver tumor in MWA therapy. To achieve this, the residual block is added in the first steps of up-sampling to deepen the network depth and enhance the segmentation result. We compare the proposed method named as 'ResLU-Net' with a conventional U-Net model. The results show that the ResLU-Net method has a good performance in tumor segmentation with a structure similarity index (SSIM) value of 0.97. This new method can help physicians in the MWA therapy process.

Transparent Processing of Reflux Data by Artificial Intelligence

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Introduction

While digitization and automated processes are omnipresent in many areas of everyday life, medicine is undergoing a radical change. Artificial intelligence methods offer new perspectives for processing the ever-increasing volume of data. When it comes to medical contexts, there is a strict expectation towards self-learning algorithms from patients and doctors, as methods of artificial intelligence or machine learning are usually black-box models. Evidence-based medicine, however, works in a contrary way, as every decision made by a doctor is based on experience and rules.

Methods

A trend is emerging that describes the shift in the healthcare system towards data-driven systems. An intelligent machine that takes over or accompanies this process must also be able to formulate an explainable decision. Furthermore, data is often available in an unstructured form, which must first be processed in elaborate preliminary analyses. This paper picks up on the importance of the described topic and presents an analysis of methods such as deep learning, support vector machines, and decision trees, incorporating three specifically defined criteria.

Results

The methods are evaluated based on three criteria. One criterion involves the prediction quality of the trained models, another assesses the scalability to big data for use in the cloud. The third criterion deals with the evaluation of a transparent presentation of the different approaches. Thus, an explanatory value can be assessed for the result, according to which rule-based methods can be presented more transparently compared to deep learning models.

Conclusion

The algorithms are trained and evaluated using a data set on reflux disease. In this way, specific characteristics and medical peculiarities for the use of artificial intelligence will be explained in more detail. The algorithms use data from the reflux database, which was provided by the Reflux Centre Siegerland.

A participatory approach to redesign a tube connecting system for home parenteral nutrition

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Introduction

Patients undergoing home parenteral nutrition suffer a lower quality of life due to continuous daily therapy for up to 16 hours. Interruption of nutrition therapy for daily routine activities is not possible, as any interruption poses a health risk to the patient. Therefore, an outpatient care service comes twice a day for both connecting and disconnecting. The dependency of the care system disturbs patients way of life. The project focusses on challenges of self-determined interruption of the nutrition therapy to figure out designing parameters for a new tube connecting system.

Methods

To analyze the handling of connecting and disconnecting for patients, an ergonomics study in cooperation of engineers and health care scientists was conducted using the experimental design method. Nineteen probands were selected with respect to age, finger strength, frequency and experience with common closure systems. Clamping and the time required for dis-/connecting were measured for three common closure systems. The full factorial experiment plan with center points runs three times for each system. In addition, probands were questioned about their feeling during the connection process. Results gave hints for designing a tube connecting system for home parenteral nutrition pump system. The opening process of the system was virtually simulated by minimum and maximum finger force gained by the probands. This should always assure a safe connection and disconnection.

Results

In sum, using this participatory approach to design the closure system, fears and wishes from patients were taken in account. New tube connecting system has to always assure a safe connection and disconnection, regardless of patients‘ skillfulness and finger strength.

Conclusion

Next step should be to detect optimal flushing parameters to program and constructively integrate necessary components into a mobile feeding pump. Overall, an automatic flushing and the special closure system should enable patient self-determination in spite of home parenteral nutrition.

Multiple parallel hidden layers autoencoder for denoising ECG signal

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Introduction

Single/multiple hidden layers denoising autoencoders (S/MHL-DAE) have shown good denoising performance of biosignals, e.g., electrocardiogram (ECG). Here, we propose a DAE model with multiple parallel hidden layers (MPHL-DAE) employing activation function $f = tanh(cj)$ with various scale c to improve denoising performance.

Methods

An S/MHL-DAE consist of a single or multiple cascaded hidden layers between input and output layer, which have length l, to process input signal $\hat{\mathbf{x}} \in R^{1\times l}$. A DAE encodes the corrupted signal to a latent represention by k hidden neurons (HN) denoted coding layer, $\mathbf{h} = \mathbf{f}(\mathbf{W}\hat{\mathbf{x}} + \mathbf{b})$, and then decoded back to the reconstructed signal, $\mathbf{y} = (\hat{\mathbf{W}}\mathbf{h} + \hat{\mathbf{b}})$. We defined a MPHL-DAE with three hidden layers consisting of two intermediate hidden layers $\mathbf{h}_1$ and $\mathbf{h}_3$ (#HN: $l/2$), and a middle hidden layer $\mathbf{h}_2$ (#HN: k) as a coding layer. The three hidden layers of the MPHL-DAE consist of $P = 4$ parallel hidden streams, $\mathbf{h}_{kp},\ k = 1, \ldots, 3,\ p = 1, \ldots, P,\ c = 1,\ 0.5,\ 0.3,\ 0.1$, to enable a better matching to the different ECG features, e.g., QRS-complex of ECG. The parallel hidden processing streams are combined by a merging layer to compute the output.

Results

Apnea-ECG database is used to create 4,800 ECG segments ($f_{sampling} = 100$ Hz, $l = 80$ samples) from 48 records. The data were splitted to training, validation and testing set with 3,024, 816 and 960 ECG segments, respectively. Gaussian white noise was used to generate noisy data of noise level 5%, 10%, 50% $\sigma(x)$. The MHL-DAE with $c = 1\,\&\,0.1$ achieved signal-to-noise ratio $\mathbf{SNR}_{imp} = 10\&\,6.3\,dB$ respectively, in case of $50\%\ \sigma(x)\&\ k = 6$, while the MPHL-DAE achieved $\mathbf{SNR}_{imp} = 10\ dB$. However, in case of $5\%\,\sigma(x)\&\ k = 16$, the MPHL-DAE achieved excellent $\mathbf{SNR}_{imp} = 4.5\ dB$ in contrast to S/MHL-DAE, which achieved $\mathbf{SNR}_{imp} = -0.2\ \&\ 0.5\ dB$ respectively.

Conclusion

The MPHL-DAE model is a new promising tool for signal denoising, even though when the number of hidden neurons per hidden layer is small, and, in addition, for various noise levels.

Development of an AI-supported exercise therapy for advanced cancer patients

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Introduction

The onset of fatigue symptoms is a major barrier in physical exercise therapy for oncological palliative patients. The daily varying symptom severity complicates the adjustment of an optimal exercise load and represents, a major barrier for the participation in exercise therapy interventions. However, exercise is known to significantly reduce severity of prevalent symptoms. Therefore, the aim of this study was to analyse the feasibility of artificial intelligence in the classification of training states based on electrocardiogram (ECG).

Methods

An ECG is recorded via a Polar H10 chest strap and cardiac and pulmonary features are extracted. A classification into three intensity levels is performed using neural networks. Therefore, a sequential backward floating feature selection is applied with a consecutive hyperparameter optimization. In addition to the regular measurement, an input baseline measurement is considered.

Results

For AI-driven training in five locally advanced or metastatic patients during supervised exercise therapy as part of routine care, a very high classification quality is achieved with an F1 score of 0.95 ± 0.05 with the union of pulmonary and cardiac vital signs. This combination achieves more accurate classification results than the individual data sets for cardiac parameters (0.93 ± 0.06) and pulmonary parameters (0.72 ± 0.06). Overall, it shows that considering a baseline measurement has a positive effect on classification accuracy. 5-fold cross-validation is used to evaluate the results.

Conclusion

This study represents the first investigation into the use of artificial intelligence to classify exercise science content in palliative oncology patients. This vulnerable group of patients may benefit from objective assessment of exercise level using cardiovascular system parameters. The inaccuracy of pulmonary parameters is due to speech and motion artifacts. In the future, additional parameters such as subjective perception, age, height and gender will further improve the classification.

Automated anatomical quantification of the scapula for the management of shoulder disorders

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Introduction

Assessing the bone morphometry by imaging is useful for diagnosis and treatment of bone and joint disorders, including those in the shoulder. However, manual bone segmentation and quantification of morphological parameters is time consuming, and reliability is influenced by the subjective assessment and experience of the expert. Deep learning-based architectures has been proven successful for problems such as image segmentation and landmark detection. Therefore, we developed deep learning-based image analysis approaches for automatic quantification of scapular morphological markers from CT scans.

Methods

First, scapula and humerus were segmented from shoulder CT scans using nnU-Net, trained with 60 healthy and 56 osteoarthritic shoulder CT scans. In a second step, six landmarks allowing the quantification of scapular morphology were positioned on the scapula by four clinical experts. A unique reference position was determined for each landmark using a weighted average, and an algorithm was developed to automatically position these landmarks based on U-Net architecture. Finally, these landmarks were combined with segmented glenoid surface to automatically calculate morphological markers of the scapula such as inclination and version. Validation was performed using 5-fold cross-validation over the entire dataset.

Results

Validation showed excellent segmentation accuracy (Dice$\geq$0.97), and automatic landmark detection achieved equal or better accuracy than clinical experts, with an average prediction error <3 mm from landmarks' reference positions. Morphological markers quantified by clinical experts and those predicted automatically also agreed well: regression between manual and automatic measurements yielded slopes around 0.95 and R2>0.90.

Conclusion

These results demonstrate the feasibility of accurate morphometric quantification of the scapula based on CT scans using deep learning. Future work will focus on automating the segmentation of the glenoid surface from the scapula surface and applying this analysis to a large cohort of patients with glenohumeral osteoarthritis to evaluate the predictive power of these markers on clinical outcomes.

Improving transparency and performance of biomedical patent text classifications with explanation methods

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Introduction

Especially in biomedicine, automated data-driven approaches must provide transparency and traceability according to legal requirements. This is particularly difficult for applying artificial intelligence (AI) in medicine. Although e.g., machine learning classifiers help to master data deluge in healthcare towards even ground-breaking improvements in treatment, their black-box nature poses a crucial explainability problem.
However, research on this topic is lagging. Thus, we investigated the explainability of a text mining use case by implementing an explanation method for a patent classifier working on a biomedical domain model. Subsequently, knowledge gained from explanations for individual predictions was compared with knowledge of domain experts.

Methods

Patent texts from the Worldwide Patent Statistical Database PATSTAT were classified into six biomedical innovation fields from our previously published domain model using a support vector machine. The contributions of the features, i.e., pre-processed terms, to the prediction were computed via Shapley Additive exPlanations and aggregated for each class. Features that contributed positively to correct classification were contrasted with keywords extracted from expert knowledge. Moreover, we analysed the potential of improving classification performance regarding the F1 score by excluding features with low distinctiveness from the model.

Results

Feature analysis revealed a 56% match of identical features between the classifier's explanations and keywords extracted from expert knowledge. Lower match of features contributing to correct classifications compared to innovation field keywords correlates with higher performance on average, suggesting that semantically non-significant features can contribute to correct predictions. Using class-specific feature boosting to modify the classification process based on newly gained insights, achieved an overall improvement of the F1 score of up to 2%.

Conclusion

Our findings show that computing explanations for classifications provides transparency and the potential to reveal shortcomings and make improvements. Understanding how the classifier makes predictions could improve confidence in AI, i.e., in clinical decision support systems, in the future.

Supervised Machine Learning for Predicting Carbohydrate Malabsorptions Using Hydrogen Breath Tests

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Abstract

Carbohydrate malabsorptions symptoms include intestinal fluid retention, causing diarrhea and abdominal distention. The aim of this work is to create a machine learning model that predicts carbohydrate malabsorption using H_2 measurements from lactose and fructose tolerance tests. We compare the predictive ability of popular classifiers with classifiers that are specifically designed for time series data. Our approach was implemented using sklearn and sktime Python machine learning libraries. The highest predictive ability for the fructose dataset was achieved using a Random Forest Classifier (balanced accuracy = 0.91). In contrast, the highest predictive ability (balanced accuracy = 0.81) for the lactose dataset was obtained using an IndividualTDE time classifier. Our results indicate a high predictive ability for distinguishing between carbohydrate malabsorptions. However, the detection of SIBO is challenging but adapted time classifier models could reach higher performances compared to standard methods. Our results could establish the basis of an expert system for diagnosing carbohydrate malabsorptions and SIBO, respectively.

Annotation Efforts in Image Segmentation can be Reduced by Neural Network Bootstrapping

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Introduction

Modern medical technology offers potential for the automatic generation of datasets that can be deployed into deep learning systems. However, even though raw data for supporting diagnostics can be obtained with manageable effort, generating annotations is burdensome and time-consuming. Since annotating images for localization and delineation (semantic segmentation) is particularly exhausting, methods to reduce the human effort are especially valuable. We propose a combined framework that utilizes thresholding methods and unsupervised deep learning to automatically generate segmentation masks.

Methods

The interaction of those simple thresholding methods (Otsu thresholding / k-means clustering) and the U-Net architecture is used and investigated. The U-Net employs the erroneous annotations generated by the thresholding methods to generalize beyond the noise and thus obtains much better segmentation masks.

Results

It is shown through two experiments with biomedical data that our framework is capable of generating useful annotations. The segmentation masks are not flawless but could speed up a potential annotation process noticeably.

Conclusion

We show that extending the generation of pre-annotations with the help of deep neural networks can reduce the work of annotating without requiring additional effort since CNNs like U-Net are capable of learning associations that simple processes like thresholding cannot depict. Using our framework, unannotated datasets can be provided with pre-annotations fully unsupervised thus reducing the human effort to a minimum.

Automatic detection of subviral particles in fluorescence microscopy images of Marburg virus infected cells using a convolutional neural network

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Introduction

In this work, we have shown that a neural network can be trained to detect difficult data with high object density and minimal object size using synthetic data. This offers new possibilities in the field of detection and tracking, since a successfully trained network requires comparativley little time for predictions and could enable evaluations and analyses in real time. In the future, it could be interesting to investigate and compare other target sizes and network architectures.

Methods

A convolutional-neural-network (CNN) was trained to predict only a delta-peak for the particle position. For training, synthetic data were generated by randomly placing previously selected particle image sections on particle-free image backgrounds distributed around cell structures. In parallel a mask containing only one delta-peak at the centre of mass of the respective particle was created. 250 images with corresponding masks were generated synthetically. 200 images were choosen for training and validation, while 50 images have been used for testing the network performance on the synthetic images.

Results

In general, the network is able to localise up to 90% of the particles. However, particles are often marked by more than one delta-peak. The particle detection rate depends on the choice of threshold for the sigmoid output. For low thresholds, the particle detection rate increases, but so does the number of multiple detections per particle. This can be solved by post-processing and combining several delta-peaks, which are generally directly adjacent, into a single one.

Conclusion

In this work, we have shown that a neural-network can be trained to process difficult data successfully, i.e., images with high object density and small object size, using synthetic data. This offers new possibilities and could enable evaluations and analyses of true data in real time. It could be interesting to investigate and compare other target sizes and network architectures in the future.

Stochastic variational deep kernel learning based diabetic retinopathy severity grading

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Introduction

Diabetic retinopathy (DR) is a disease of the retina causing an alteration of vascular tissue and is one of the most probable causes of blindness. Due to the rising trend of diabetes, the early detection and severity classification of DR is crucial for choosing the most successful therapy and preventing vision loss. Automatic detection of DR on fundus images of the eye is mostly done by convolutional neural networks (CNNs). However, CNNs do not provide well-calibrated uncertainty estimates, which are essential for a thoughtful diagnosis.

Methods

This study in contrast uses stochastic variational deep kernel learning (SVDKL) for DR classification, which combines a deep CNN with Gaussian processes (GPs) into a single scalable end-to-end trainable model, which promises to provide predictions with reliable uncertainty estimates by exploiting approximate Bayesian inference. The experiments in this study aimed to estimate the benefit of SVDKL compared to the plain CNN, regarding uncertainty calibration as well as diagnostic performance for the task of DR severity grading.

Results

Training on the Kaggle DR dataset shows promising results.
We observed a naturally enhanced uncertainty calibration for the SVDKL models, more robust predictions, and an improved overall diagnostic performance over regular CNNs concerning the measured QWK score. Despite the SVDKL achieving a slightly reduced accuracy, the incorrect predictions were in closer proximity to the target stages, which is beneficial for clinical diagnosis as it minimizes the cost related to severe misclassifications.

Conclusion

From these preliminary results, we reason that using SVDKL can indeed be beneficial for clinical diagnoses and improve the quality of uncertainty estimates over using plain CNNs. However, further research has to be conducted on improving model performance and a more detailed evaluation of the uncertainty calibration is required.

Robustness evaluation on different training state of a CNN model

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Introduction

Convolutional neural networks have proved to be successful in many applications such as image processing. However, even imperceptible perturbations applied to the images can make the neural network performance unreliable. To guarantee an accurate performance in safety critical fields, it is necessary to assess the robustness of CNN solutions before launching. Adversarial attack is a machine learning approach to generate perturbations on real samples to detect the vulnerability of CNN. In this paper, we will use gradient method as an adversarial attack technique to evaluate the CNN robustness and training states.

Methods

A fine-tuned Alexnet model was trained with laparoscopic video images for surgical tool classification. About 25,000 training images from the Cholec80 database were used to train the model. A snapshot of the model was recorded when the training accuracy first reached 75%, 85%, 95%, and 99%. The gradient method was applied on a legitimate image to modify it from its original classification to a wrong classification. The difference between original image and the final adversarial image can be developed into a robust index.

Results

The results showed the adversarial image have larger difference with the original image at a better training state. That means the model gained more robustness in the training process. However, the results highly relied on the parameter setting. For instance, to evaluate the minimum perturbation could be generated by gradient method, the further experiments to determine the parameter α will be required. Furthermore, the number of samples evaluated is too small to get the generalized conclusion, the wrongly classified images need to be considered too.

Conclusion

The experiments demonstrate the relation between training states and robustness, i.e. the robustness improved at higher training states, especially for some particular classes. In future work, additional training with generated adversarial images may improve the robustness of the model.

Towards Identification of Biometric Properties in Blood Flow Sounds Using Neural Networks and Saliency Maps

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Introduction

A biometric identification system provides security to information and property, since biometric data is unique to an individual. The state-of-art biometric sensing technologies suffer from limitations such as forgery, lifelong persistence and effects of external conditions. Therefore, further research in this area is needed. In previous work, we demonstrated the potential of blood flow sounds for biometric authentication acquired by a custom-built auscultation device. For this purpose, we calculated the frequency spectrum for each cardiac cycle represented within the measurements based on continuous wavelet transform. The resulting spectral images were used to train a convolutional neural network based on measurements from seven users.

Methods

In this work, we investigate which areas of those images are relevant for the network to correctly identify a user. Since they describe the frequencies' energy within a cardiac cycle, this information can be used to gain knowledge on biometric properties within the signal. Therefore, we calculate the saliency maps for each input image and investigate their mean for each user.

Results

The obtained results indicate a strong relevance of the S2 segment of the cardiac cycle, especially the first half of this segment. The (first half of) S1 seems to be of relevance as well, while the diastole and systole seem not to include as much information relevant to the CNN's decision for the correct user. While the frequency bands of interest differ between the users in the dataset, no frequencies below 13 Hz or above 109 Hz seem to be of high relevance.

Conclusion

Those first results provide a starting point for further investigations, e.g. adressing the variance for samples from the same user and and validating the results with data from more different users.

Deep-learning based segmentation of lung parenchyma in translational research and clinical application

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Introduction

Precise identification of the lung parenchym is the basis of quantitative computer tomographic (CT) data analysis that requires morphological information about the lung tissue especially in injured lungs. Therefor segmentation is performed semi-automatically by consensus of trained radiologists in clinical context (ground truth - GT). Thereto we describe the development of a deep-learning based algorithm for automatic pathologic lung segmentation and discuss relevant quality metrics for algorithm comparison.

Methods

Two sequential convolutional U-networks working on different dimensionality were implemented using Matlab Deep Learning Toolbox and trained on 180 CT scans acquired in two past experimental studies of our group on a model of ARDS and on lung healthy pigs ($u2Net_{pig}$). Similarly, the algorithm has been trained and evaluated on a clinical data set containing 150 CT scans ($u2Net_{human}$). Finally, the $u2Net_{pig}$ algorithm was taken and transfer learned on the clinical data set ($u2Net_{trans}$). Compared to GT, similarity was assessed by Jaccard index (JI), contour agreement with average symmetric surface distance (ASSD), as well as linear dependence on each CT scan relative non-aerated compartment size of JI and ASSD (S_{JI} and S_{ASSD}). Effective end-expiratory lung volume (EELV) and change of non- and poorly aerated lung compartments (ΔNA) were compared with regression analysis.

Results

Lung segmentation with $u2Net_{pig}$ resulted in generally good median JI=0.91 and ASSD=0.89, respectively. On clinical data $u2Net_{human}$ performed segmentation with decreased JI=0.88 and ASSD=1.7mm. Dependence on non-aerated compartment size was S_{JI} =-0.20 and S_{ASSD}=4.0. $u2Net_{trans}$ improved JI=0.92 as well as ASSD=1.5mm, but decreased S_{JI}=-0.34 and S_{ASSD}=6.3. R^2 for EELV and ΔNA was 0.99 and 0.98, respectively.

Conclusion

Efficient automated segmentation of physiologic and pathologic lung parenchym is possible using uNets. Segmentation quality should be evaluated with respect to similarity, contour agreement and non-aerated lung compartment size. Clinically relevant measures can be derive using automatic lung segmentation.

Thyroid Nodule Region Estimation using Auto-Regressive Modelling and Machine Learning

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Introduction

Ultrasound (US) imaging is used for the diagnosis and also evaluation of thyroid nodules. A Thyroid Imaging Reporting and Data System (TIRADS) is used for the risk stratification of thyroid nodules through US images. The composition of thyroid nodules plays an important role in the risk-stratification process. The percentages of cystic and solid components in a thyroid nodule are one of the features that are can be indicative of the risk of malignancy.

Methods

In this work, we attempt to classify and estimate solid and cystic regions within nodules. 20x20 texture patches were extracted from solid and cystic regions and converted into signals. These signals are decomposed into low, mid, and high-frequency bands using Continuous Wavelet Transform (CWT). A total of 36 features were extracted from the decomposed signals using Auto-Regressive Modeling. The features were fed into three different Machine Learning (ML) algorithms (Artificial Neural Networks, K-Nearest Neighbors, and Random Forest Classifier) to provide us with a classification of solid versus cystic regions in thyroid nodule US images. Bispectrum features were also extracted from the texture patch database and fed into the same models solely for the purpose of comparison.

Results

The Random Forest Classifier obtained an Accuracy, Sensitivity, and Specificity of 90.41%, 99% and 91% respectively which was the highest among the three chosen ML algorithms and the bispectrum features. The output from the classification phase could also be used to determine the percentage of cystic and solid regions with a given thyroid nodule US image.

Conclusion

This work is aimed at reducing subjectivity between physicians and hence improving the risk stratification of thyroid nodules with US images. Additionally, this will also help in better calculating the dose for radioiodine therapy. The proposed approach works well with limited data because of the patch approach compared to whole images.

Saliency-assisted multi-label classification for explainable deep learning applications in endoscopic ENT navigation

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Introduction

In endoscopic procedures of the nasal sinuses, a critical issue for classification tasks is the ambiguous anatomical representations due to their complex composition. We investigated the potential of multi-label image-based classifications of sinus landmark combinations together with explainability methods for machine learning in an assistance function at the application level. By combining image classification and pixel attribution in a navigation function, we provide the surgeon with label predictions and additional localization cues of important pixels relevant to the model output with regard to the input image.

Methods

We used 3500 label annotated video sequences from 30 recorded sinus surgeries to fine-tune a pretrained ResNet50 as the feature extractor and a classification head using binary cross-entropy on one-hot encoded target vectors of landmark classes with a RAdam optimizer over 28-32 epochs. Image augmentation and a focal loss function were added to counter over-fitting. An explainability function then used the trained model to produce pixel attribution maps for predicted classes. These gradient maps were summed over all classes, and pixel values above 0.20 were clustered using weighted k-means based on the gradient value of each pixel coordinate. The resulting cluster centroids were then overlayed into the endoscopic image together with the predicted landmark classes. Three surgeons investigated three different overlay scenarios in a validation study.

Results

The top-1 class predictions reached a mean f1-score of 0.47 with a range of 0.71 and 0.28. Prediction results were largely dependent on over- and underrepresented classes. The provided explainability function at the application level showed the strong potential of providing visual cues from prediction results to surgeons at runtime to support human-machine interaction.

Conclusion

The classification task remains challenging due to ambiguous and imbalanced class representations. Provided explanations of classification results support surgeon-machine interaction and may improve the perceived model performance.

Denoising of ECG with single and multiple hidden layer autoencoders

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Introduction

Single/multiple hidden layers denoising autoencoders (S/MHL-DAE) have shown encouraging results in denoising electrocardiogram (ECG) signals. Here, we investigate the performance of S/MHL-DAE with scalable activation function (AF), e.g., tanh($c\theta$) with scale c .

Methods

A denoising autoencoder is a neural network with a single hidden layer or multiple hidden layers between input and output layer. It is trained with corrupted signals $\tilde{\mathbf{x}} \in \mathbb{R}^{L\times 1}$, which is, in case of SHL-DAE, encoded to the hidden layer, $\mathbf{h} = \mathbf{f}(\mathbf{W}\tilde{\mathbf{x}} + \mathbf{b})$, with N hidden neurons, and then decoded to denoised signals, i.e., $\mathbf{y} = \mathbf{f}(\widehat{\mathbf{W}}\mathbf{h} + \mathbf{b})$. We proposed MHL-DAE with three hidden layers: two intermediate hidden layers h_1 & h_3 and one hidden layer h_2 called coding layer. The performance of S/MHL-DAE with scaled AF, e.g., tanh($c\theta$) with $c = 0.1\,\&\,1$, is evaluated by signal-to-noise-ratio improvement SNR_{imp} and Pearson correlation coefficient $\sigma(\mathbf{x}, \mathbf{y})$. Assessment of MHL-DAE is also considered for different AF.

Results

The PTB-XL database was considered to create 500 QRS-aligned ECG segments from 50 healthy subjects with ten segments each ($f_{sampling} = 100\ Hz$, $L = 80$ samples). These segments are corrupted with Gaussian white noise of different levels, e.g., $\sigma_n = 0.03, 0.1, \& \, 0.3$. We created training, testing, and validation datasets from 300, 100 and 100 ECG segments. In case of $\sigma_n = 0.03$, the SHL-DAE with $N = 8\,\&\,32$ achieved $SNR_{imp} = -1.54\,\&\,3.64\,dB$ respectively, while MHL-DAE achieved $-3.64\,\&\,1.07\,dB$. However, having $\sigma_n = 0.3$, SHL-DAE achieved $SNR_{imp} = 13.97\,\&\,14.00\,dB$, while MHL-DAE, in contrast, achieved $14.76\,\&\,16.01\,dB$. Scaled AF, e.g., tanh($c\theta$) with $c = 1$ showed the best performance among other AF.

Conclusion

MHL-DAE is more suitable for ECG denoising. Low-noise signals generally require a higher number of hidden neurons than high-noise signals. The model parameters, e.g., the number of hidden neurons and the activation function, must be chosen carefully. For clinical applications, this has to be done automatically and reliably.

Interpretation of ResNet50 model for MI related cardiac events using Explainable Grad-CAM approach

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Introduction

Myocardial infarction (MI) occurring due to blockage in the coronary artery presents itself as alterations in the heart rhythmicity. etection of MI within the stipulated golden hour is essential to prevent fatality. Electrocardiogram (ECG) is an important tool that aids in capturing the rhythmicity of the heart. Deep Neural Network (DNN) provides an efficient way to detect the minute variations in the ECG waveform. In addition, the interpretability of the DNN using explainable AI techniques could highlight the intricate details in the ECG signal.

Methods

In this work, Residual Neural Network (ResNet), a DNN is trained and tested for its efficacy in extracting the features within ECG waveform to identify MI-related cardiac events. The interpretability of the ResNet model is studied using Gradient-weighted Class Activation Mapping (Grad-CAM). For this purpose, a public dataset containing 12- lead ECG records of 10 seconds duration is collected and utilized. It is inputted into ResNet50 model that contains 48 convolutional layers along with an Average Pooling layer and a Max pooling layer. The fully connected layer takes the extracted features as input from the pooling layer. The model is trained for 50 epochs and the evaluation metrics are obtained.

Results

The results indicate that the trained ResNet50 model can distinguish the ECG records as normal and MI. It is seen that the model accuracy increases as the number of epochs increases and reaches 92.86% at the 50th epoch. Grad-CAM reveals that the QRS segment in the ECG signal aids in the positive prediction of MI.

Conclusion

The adopted ResNet50 model can be effectively used to develop a computer-aided wearable system that monitors the QRS complex of heartbeat to monitor and categorize MI-related cardiac events using ECG.

Using deepMTJ for Accelerated Muscle-Tendon Junction Analyses

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Introduction

Biomechanical researchers observe muscles and tendons to study their behaviour. To distinguish between contributions of muscles and tendons, the muscle-tendon junctions' movement is usually recorded and tracked in ultrasound images. It has been shown that manual labelling is time demanding and can be prone to errors even when experts annotate datasets. Therefore, we recently introduced deepMTJ, an automatic muscle-tendon junction tracking tool based on deep learning. This contribution provides an overview of the open-source repository, the free-to-use online service, and the available dataset accessible via: https://deepmtj.org/.

Methods

The code repository of deepMTJ is accessible via: GitHub: https://github.com/luuleitner/deepMTJ. The provided functions allow users to extend our networks, retrain our model or predict muscle-tendon junctions in ultrasound images. Moreover, we have open-sourced the complete test dataset (1344 images, including ground truth labels) to benchmark future models (accessible via https://osf.io/wgy4d/). Our proposed method has a similar performance in identifying muscle-tendon junctions as four human specialists and is approximately one hundred times faster than manual labelling.

Results

To increase the accessibility and reduce the amount of code knowledge necessary to operate deepMTJ, we implemented deepMTJ as a software-as-a-service via a web application running in the google cloud. Moreover, we provide the complete deepMTJ package as executable cell code via a google Colab Notebook.

Conclusion

Recent user feedback has demonstrated the proposed generalizability of our method by applying the deepMTJ model to previously unseen data from an Ultrasonix ultrasound system.

Audio signal Differentiation of Alzheimer's induced Dementic condition using Gammatone Frequency Cepstral Coefficients and Random forest approach

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Introduction

Dementia occurs due to irreversible neurodegeneration of brain tissue primarily affecting the person's memory, cognition, and movement skills. Accessible, cost-effective, and non-invasive approaches for the automatic identification of Alzheimer's disease (AD) induced dementia have been the subject of extensive research. Recent studies show that the speech and language centers of the brain are affected in the early stages of the disease condition. Speech data collected can be utilized to discriminate between healthy and dementic subjects.

Methods

In this work, audio signals from normal ad AD are collected from a public source database. These signals are pre-processed for voice activity detection to identify the speaker of interest. Targeted features such as Gammatone Frequency Cepstral Coefficients (GFCC), Linear Predictive Codes, ad Perceptual Linear Prediction are extracted from the pre-processed signals. These features are tested for statistical significance ad ae validated using Random Forest classifier.

Results

Results indicate that pre-processed signals effectively contain the audio information from the subject in concern. Among the considered features, the GFCC showed high statistical significance. The speaker information is embodied through different energy levels and extraction of the GFCC aids in extracting the significant speaker information. Random forest classifier attained an accuracy of 77% in differentiating dementic subjects.

Conclusion

The utility of the GFCC in the refinement of necessary relative features aided in improving the accuracy and hence artificial intelligence systems defined based on the human auditory system could enhance the diagnosis of dementic condition.

Computation of flow through TAVI device by means of physics informed neural networks

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Introduction

Cardiovascular diseases are among the most common diseases with high mortality, including aortic valve stenosis and insufficiency. Minimally invasive implantation of transcatheter aortic valve prosthesis (TAVI) has become the standard procedure for patients with increased risk for open surgery. It is commonly accepted that the long-term outcome of aortic valve replacement depends on hemodynamic performance. This motivates the analysis of the velocity field in the vicinity of the TAVI. Computational fluid dynamics (CFD) methods have been established in the past, but show limitations in terms of computational effort when rapid design optimization or patient-specific decision making in real time is required.

Methods

In this study we show the usage of PINNs for predicting fluid flow through a TAVI device. We also show a method of enforcing boundary conditions for this specific problem. Due to the physics involved in the training process, this principle does in theory not require additional training data. To validate the method, we performed CFD simulations that solved the Navier-Stokes equations by means of finite volume methods.

Results

Besides the good estimation of the main flow components, discrepancies between CFD and PINN results are present.

Conclusion

Nevertheless, the flow structures have certain similarities in the coarse spatial localization of the vortex patterns occurring in flow through the TAVI device.

Thrilling AI - A novel, signal-based digital biomarker for diagnosing canine heart diseases

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Introduction

Auscultation methods enable non-invasive diagnosis of diseases, e.g. of the heart, based on heartbeat sounds. Regular, early examinations using machine learning techniques could help to detect diseases at an early stage to prevent serious health conditions and then provide optimal therapy through continuous monitoring. There is already a lot of work on human data using AI algorithms to detect patterns in signals or images. However, there is hardly no work on detecting heart murmurs with digital such as Myxomatous Mitral Valve Disease (MMVD).

Methods

In this paper, we present a canine auscultation project that aims to provide a tool to establish a baseline of classification parameters from audio signals that could be used to monitor canine health status by analyzing deviations from this baseline.

Results

The recorded signals are processed and analyzed using continuous wavelet transform, which provides spectral information about the recorded audio signals. Based on the audio signal and its spectrum, it is clear that in non-pathological heart sounds, the two heart sounds S1 and S2 are detected. In dogs with severe myxomatic mitral valve disease, the S2 sound is no longer detectable.

Conclusion

These preliminary observations suggest that the acquired signals not only contain significant heart sounds but also characterize biomarkers such as MMVD detection, which can also be detected with AI algorithms.

An End-to-End Deep Leaning Approach for Sleep-Wake Classification Using Single Channel EEG Signals

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Introduction

Sleep quality has a significant impact on human physical and mental health. The detection of sleep-wake states is thus of significant importance in the study of sleep. The performance of classical machine learning models for automated sleep detection depends on the signals considered and feature Extraction methods. Moreover, hand-crafted features are highly dependent on the experts and their prior knowledge about different physiological signals and conditions of the subjects.

Methods

To overcome this limitation, this paper develops an end-to-end deep learning approach for automated feature extraction and detection of sleep-wake states using single channel raw EEG signals. Moreover, we leverage transfer learning to train and fine tune the proposed model to avoid the complexities associated with building a deep learning model from scratch.

Results

Using polysomnography (PSG) data of 20 patients, our results demonstrate the effectiveness of the proposed deep learning pipeline, achieving an excellent test performance in detecting sleep events with an overall sensitivity and precision of 92.7% and 92.1% respectively.

Conclusion

The results demonstrate that the proposed approach can achieve superior performance compared to state-of-the-art studies on Sleep-Wake classification. Furthermore, it can attain reliable results as an alternative to classical methods that heavily rely on expert defined features.

Quality Assurance in Denture Production using Convolutional Neural Networks

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Introduction

The production of dentures is a complex process where layer is added onto layer under pressure. Therefore, various visually notable errors such as discolorations or cavities can occur. While quality control is at present performed manually, it is feasible to automate this process by using computer vision and convolutional neural networks (CNNs). This work proposes proof of concept for the image-based classification of produced dentures into defect-free products and rejections.

Methods

During generation of the dataset, challenges such as reflections and shadows were addressed using a diffuse light as well as a diffusion screen. For this work, merely staining error rejections were included. The 154 defect-free and 219 rejected dentures were photographed, giving a resulting dataset of 614 defect-free images while 609 images showed rejections. The percentages of training and test set are 82,4% and 17.6%, respectively. Data augmentation was employed to prevent overfitting. The best CNN setup is comprised of three convolutional layers with kernels of different sizes.

Results

The F1-score achieved for the classification of defect-free dentures is at 80.29%. When employing transfer learning, the score improved up to 92.61%.

Conclusion

In conclusion, this work demonstrates that CNNs have the potential to classify produced dentures accurately. In contrast to classical image analysis, the CNNs show a robustness against rotations. While the current performance is not yet sufficient for industrial utilization, future work should address shortcomings by improving the training set, including transfer learning and testing other network architectures. Furthermore, additional error types should be included.

Multi-class extension of common spatial pattern for motor imagery brain computer interfaces

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Introduction

The motor imagery (MI) based brain-computer interface (BCI) provides the possibility for people to control external devices by translating brain signals to external commands. Due to its low cost and high temporal resolution, multichannel electroencephalogram (EEG) is widely used as the control signal in MI-BCIs. Common spatial pattern (CSP) is the most powerful approach for feature extraction in MI-BCIs. Despite its efficiency, CSP is still suffering drawbacks such as outlier sensitivity and limitation to binary classification. In this work, we proposed a novel multi-class extension framework of CSP which is applicable for all general single-trial settings that require discrimination of brain states from EEG based on modulations of brain rhythms.

Methods

We proved that the proposed framework is equivalent to CSP in the binary case. For multi-class classification, the method was evaluated on BCI competition IV Dataset-2a (4 MI classes) against two common multi-class extension strategies using pair-wise and one-versus-rest techniques which separate the original multi-class problem into several binary ones. The competing methods were applied for the EEG signals bandpass-filtered between 8-30 Hz. After spatial filtering, the variances of signals are computed and concentrated into a feature vector set, which is finally fed into a linear discriminant analysis classifier for classification.

Results

The experimental results demonstrated the effectiveness of the proposed framework for computing spatial filters in multi-class classification to improve the classification accuracy compared to conventional pair-wise and one-versus-rest strategies for multi-class extension of CSP.

Conclusion

The proposed method is a promising approach to provide reliable EEG signal decoding results for MI-based BCIs. In future work, the framework will be implemented into MNE-Scan, an open-source and cross-platform application allowing for the real-time processing of EEG/MEG signals. In combination with MagCPP, which provides the external control of Magstim TMS device, a MI-based closed-loop TMS-EEG paradigm will be future evaluated.

Focus Session: Advances in Diagnostic, Interventional and Therapeutic Ultrasound (supported by EUFUS)

First-cycle oscillation excursions of Pickering-stabilised microbubbles subjected to a high-amplitude ultrasound pulse

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Introduction

Pickering stabilisation is a manufacturing process involving the adsorption of colloidal particles at gas-liquid interfaces. It is used to create the shells of stable, long-lived ultrasound contrast agent microbubbles. The purpose of the present study is to determine whether high-amplitude sonication influences the integrity of Pickering-stabilised shells.

Methods

Microbubbles, Pickering-stabilised with hydrophobised silica, were reconstructed from freeze-dried material by dissolving 5 mg in 5 mL distilled water. The microbubbles were measured to have radii of less than 10 μm. Quantities of 200 μL were observed with a high-speed camera operating at 10 million frames per second whilst being subjected to 3-cycle, 1-MHz, 1-MPa focussed ultrasound pulses. Radial bubble excursions were extracted from the video footage. In addition, radial excursions as a function of time were simulated using the Rayleigh-Plesset equation for free gas microbubbles and microbubbles encapsulated by 7.6-N/m shells.

Results

Some 40% of the microbubbles had expanded to excursions computed for encapsulated microbubbles. The remaining microbubbles had expanded to greater excursions, with only three microbubbles reaching free-gas bubble excursions. Microbubbles of the same initial radius were observed to expand to different maxima. Gas release from these disrupted microbubbles was not observed.

Lack of gas release might indicate that the particle structuring remained on the interface during radial oscillation. While these high-amplitude results indicate that optically identical microbubbles may have different shell properties, outcomes from low-amplitude experiments show consistent oscillation expansion for microbubbles of the same size.

Conclusion

We thus conclude that optically identical microbubbles may undergo shell disruption of different severity. Furthermore, we conclude that the disruption occurs during sonication and not prior to it. These findings may aid in the developement of pickering-stabilised agents that facilitate ultrasound-triggered release.

32 channel mobile ultrasound research system for bladder monitoring and muscle activity tracking

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Introduction

Ultrasound research systems need to fulfil specific requirements since the development of new approaches mostly relies on the availability of special data formats. For instance, research on beamforming algorithms requires the availability of pre-beamformed channel data, which is not provided by clinical sonography machines. Topics involving longterm monitoring furthermore introduce new requirements such as portability. Finally, not all scientific questions can be tackled with typical clinical sonographic probes, such that customized application-specific transducers are needed.

Methods

We developed a new portable low-cost 32 channel ultrasound research system with full access to the transmit and receive pipeline. Transmit signals are generated, transmitted, received and digitized on a 18 x 12 cm^2 PCB prior to USB transfer to a laptop/tablet. Different ultrasound transducers optimized for applications such as post-operative bladder monitoring and muscle activity tracking have as well been developed.

Results

The system allows acquisition and USB transfer of 300 frames/s of channel data. The receive bandwidth ranges from 100 kHz to 10 MHz (50 MSPS, 12bit). For bladder monitoring, we developed a 3 MHz 1,2 λ pitched 32 element phased array probe. In phantom experiments, a depth dependent resolution between 300 and 2000 µm was achieved. The system was evaluated with respect to AI-powered bladder segmentation on 20 probands, showing a mean underestimation of the bladder by 30% and less than 2% of tissue erroneously recognized as bladder. For muscle tracking, a bracelet with 32 single element 1 MHz transducers was developed and a custom software for acquisition of A-scan sequences has been implemented.

Conclusion

A new flexible ultrasound research system usable in settings with high demands towards mobility has been developed. Together with application-specific transducers, it can be very easily adapted for a wide range of mobile ultrasound applications. It has shown its potential for autonomous bladder monitoring and muscle activity tracking.

A concept to combine a gamma probe with ultrasound imaging for improved localization of sentinel lymph nodes: a feasibility study of the concept

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Introduction

This paper presents the proof-of-concept study of an adaptor, allowing the combination of a gamma probe with ultrasound (US) imaging, intending to improve the detectability of sentinel lymph nodes (SLNs).

Methods

The performance of the adaptor in US imaging, in terms of depth of penetration and distance accuracy, and gamma scanning, in terms of sensitivity and spatial resolution, was investigated.

Results

We observed that the quality of the US imaging through the adaptor was promising and close to that of normal US imaging. However, the performance of the gamma probe through the adaptor was fairly poor, necessitating the improvement in the design of the adaptor for better gamma scanning.

Conclusion

This study shall provide a basis for the development of a handheld gamma-US scanner for interventional procedures and small field-of-view (FOV) imaging in the future.

Investigation of Inertial Cavitation Induced by Modulated Focused Ultrasound Stimuli

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Introduction

Drug delivery can be achieved by a variety of different approaches. In our case, local drug release (LDR) is supposed to be triggered with a focused ultrasound stimulus via the effect of inertial cavitation (IC). In previous work, we typically transmitted a monofrequency sinusoidal burst (MFB) signal to generate IC. In this study, additional frequency (FMB) and amplitude modulated (AMB) ultrasound stimuli - within a harmless pressure range - are applied to investigate their capability of generating inertial cavitation.

Methods

As known from IC investigations of drug delivery concepts, we also employ a passive cavitation detection (PCD) setup in order to explore IC. For simulating realistic conditions, we utilize a flow through tissue-mimicking phantom representing tissue of a thickness of 30 mm that contains a thin canal of 1 mm in diameter. IC is excited via various burst signals by modulating the frequency and peak rarefaction pressure amplitude. At this point, one has to mention that we did not exceed a maximum mechanical index MI = 1.9, which is approved by the FDA for diagnostic applications. Normally, we use nanocapsules (NCs) for IC investigations, but this time, we employed a talcum-water mixture showing a similar cavitation effect compared to the NCs. In order to prove the excitation of IC, we performed control measurements with degassed, pure water.

Results

With respect to the modulated signals, the obtained results demonstrate that these also trigger IC, but no significant improvement could be achieved. The cavitation activity was weakest for the AMP; MFB and FMB signals generate IC in a similar range.

Conclusion

Since no significant improvement could be recognized, the MFB and AMB signals prove to be effective and most suitable.

Focus Session: Advances in Monitoring - Mobile and Stationary

Hemodynamic monitoring with impedance cardiography and blood pressure measurement with biomechanical stimulation of the leg muscles

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Abstract

Impedance cardiography (ICG) is a noninvasive method that helps to monitor many hemodynamic parameters such as stroke volume, cardiac output. On the other hand, biomechanical stimulation (BMS) helps to improve the body's health, especially the muscles. The aim of this study is the measurement of non-invasive hemodynamic parameters during a BMS to observe the changes of thim. In this study, the legs were biomechanically stimulated with a frequency of 12 Hz. Meanwhile, the impedance and continuous arterial blood pressure (CNAP) were measured. Several positions were taken. The calf, sole of the foot, thigh and buttock were biomechanically stimulated as well as the monitoring of the hemodynamic parameters in Rest before and after the BMS. Altogether more than 30 hemodynamic parameters are measured. The mean stroke volume of the first subjects is 99.90 $\pm$ 1.24 ml in Rest before stimulation and 99.76 $\pm$ 1.59 ml in Rest after the stimulation. The mean cardiac output is 7.96 $\pm$ 0.53 l/min in Rest before stimulation and 7.49 $\pm$ 0.38 l/min after the stimulation. Thus shows that the parameters differed before, during and after stimulation. In Addition, the Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were reduced by about 6.82 %.

Acquisition and Processing of Biomedical Data for Outpatient Care in Rural Areas

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Introduction

The declining number of physicians in rural areas is more and more affecting public medical services. Maintaining the quality and the availability of care therefore becomes a crucial issue. At the same time, the average age of the rural population is increasing, which means that more medical care is needed. These challenges could be addressed by providing telemedicine support to existing physicians. The focus of this paper is especially the home monitoring of vital data.

Methods

This paper describes a technical infrastructure for patients (and doctors) to measure their biomedical vital data themselves and make it available to their physician by transferring the data to cloud servers. The patient uses commercially available devices with Bluetooth connectivity and applies smartphone apps to check the data as well as to deliver it via gateway to the cloud. The general practitioner can then assess and evaluate data for diagnoses using a web application with cloud access.

Results

The approach is currently carried out in the project "DataHealth" which is located in Germany in Burbach in rural southern Westphalia. The digital medical platform as shown in this paper was implemented allowing involvement of patients for measuring vital signs. This considerably relieves doctors in their daily practice. Medical indications according to the measuring devices are e.g. arterial hypertension, diabetes mellitus II, pneumonia, cardiac failures, and atrial fibrillation. The patient group of two doctor's offices in the village consists of more than 40 people.

Conclusion

This paper focuses the technical infrastructure and concentrates on software and hardware issues of the outlined project. With this setting the authors contribute to an improvement of outpatient medical care quality through permanent health monitoring and faster application of treatment process steps in diagnostics.

Merging vital signs from different diagnostic devices to improve oxygenation with a high-frequency jet ventilator in children with meconium aspiration syndrome

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Introduction

Long-term monitoring of vital signs (pO2, pCO2, ECG, ...) during neonatal ventilation is essential and must be ensured continuously especially for neonates with meconium aspiration syndrome (MAS). Within the development of a new high-frequency jet ventilator (HFJV), an approach was made to merge data from different diagnostic devices to combine them to eventually optimize oxygenation indirectly by operating the HFJV. To overcome the problem of different time axes of the devices, a user interface was developed that allows to start a data recording for all devices simultaneously to make it comparable on a time axis.

Methods

To improve the treatment of MAS, the functions of the new device will be evaluated in an animal study. Two ventilators (conventional and HFJV), a transcutaneous blood gas monitor and a vital signs monitor will be connected to 48 newborn piglets. Each device is connected to the central monitoring unit, which contains the user interface and reads the data from the serial ports. The recordings should run for 72 hours per piglet. The system time of the monitoring unit is used as reference time for all recordings. The acquired data is stored in European Data Format, which is a validated and well-established tool in sleep medicine.

Results

The user interface for central data acquisition has been developed. The next step is to acquire data from the animal study. By pressing a single button on the user interface, data from the serial ports can be read simultaneously.

Conclusion

Time-synchronous data acquisition can improve the development of a new HFJV to provide the best possible oxygenation for neonates. A direct comparison of diagnostic parameters from different devices will allow a better understanding of the patients' cardiorespiratory reaction to changing device input (e.g. altering ventilation). The results of the study are intended to be transferred to human medicine.

Development and evaluation of a prototype for contactless respiration detection in infants and young children

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Introduction

There is no established procedure to objectively assess respiratory impairment in children with airway diseases. There is a large diagnostic gap, especially during sleep. Polysomnography is reserved for certain indications due to the resource requirements and can hardly be performed in a home setting. Our purpose is to develop a mobile and contactless audio-visual monitoring system that enables the recording of essential respiratory parameters. The aim of the first sub-project described here was the technical construction and clinical evaluation of a prototype for contactless recording of respiratory rate during sleep.

Methods

The prototype, mounted next to the bed, uses a 3D-camera to detect the position of the child by sending and receiving a laser signal and recording the excursions of the upper body. An evaluation of the respiratory rate detection was carried out in a preclinical feasibility study using a ventilated toddler simulator around which a breathing belt was placed as a reference. The data were recorded, analyzed and compared with the data from the breathing belt.

Results

In the preclinical study, it was evaluated that the respiratory patterns recognized by the prototype and the respiratory rates derived from them at different frequencies and volume settings matched those of the simulator and the breathing belt in almost all cases. Furthermore, various environmental conditions and interferences on the breathing pattern signal were examined, and the system was found to be highly robust.

Conclusion

With the development of the prototype, we have succeeded in realizing a method for the contactless detection of breathing patterns and respiratory rate, which has proven to be precise and robust on the basis of the preclinical study. Based on this, a clinical feasibility study is now being carried out to evaluate the prototype under realistic conditions on patients in a children's sleep laboratory.

Methods of Contactless Blood Pressure Measurement

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Introduction

Contactless blood pressure monitoring displays a chance for detecting hypertension and increasing the awareness of cardiovascular diseases. Camera-based methods show high potential for replacing inconvenient cuff-based technology. Blood pressure estimation through pulse transit time and other parameters obtained from photoplethysmography (PPG) signal present a promising alternative to conventional blood pressure measurement.

Methods

In this paper, recent approaches for contactless blood pressure monitoring were reviewed.

Results

All of the articles implemented systems based on PPG, whereas most of them used pulse transit time (PTT) as measuring parameter.

Conclusion

The results are reviewed and summarized while pinpointing key challenges and discussing expectations for future research.

Intelligent Garment based ECG Monitoring with AI support for Elderly

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Abstract

Smart underwear was designed to meet the demands of elderly people be monitored in outpatient environments. Especially the demands of elderly women have been addressed, who have heart failure but who still want to live in their home.
The smart bra comprises textile embroidered electrodes and an ECG event recorder. The recorder transmits the data to an attending physician if a trained artificial intelligence algorithm (AI) has discovered critical events in ECG signals. An implemented convolutional neural network, which uses the wavelet transformation of the ECG as input and to determine an interference index for this ECG signal is implemented. The AI was trained by 200 event recordings of 60 seconds. The interference index of textile garment integrated electrode signals have been compared with adhesive electrodes as reference.
The embroidered textile electrodes show comparable interference index compared to reference electrodes. The durability of the electrodes in washing tests was more than 50 washes and is thus in the range of the durability of underwear.
The smart bra meets the needs of elderly women and can be part of new remote monitoring services such as e-consultation or as a home-based follow-up to ensure seamless patient care after hospital or rehabilitation stays. Healthcare personnel has better access to the patient´s digital ECG data without direct consultation, independently of where the patient lives and the patient can feel safer.

Focus Session: Biomedical Applications of Magnetic Nanoparticles - Imaging

Comparison of in vitro and in vivo biocompatibility and MRI imaging performance for different iron oxide based contrast agents

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Introduction

Gadolinium-containing formulations, the current gold standard as contrast agent in magnetic resonance imaging (MRI), have been criticized for various depositions in the body, including the brain. That is why alternatives are being sought, particularly in the area of contrast agents containing superparamagnetic iron oxide nanoparticles (SPION).

Methods

We developed such a system named $\text{SPION}^{\text{Dex}}$, a SPION variant coated with cross-linked dextran. First, this system was compared with commercially available ferumoxytol and resovist concerning their toxicological particle profiles by testing colloidal stability in blood, the oxidative stress and the cytotoxicity. These were supplemented by further immunological assays including thrombocyte activation, plasmacoagulation and in vitro complement activation. In order to address concerns related to hypersensitivity reactions, we investigated complement activation-related pseudoallergy (CARPA) reactions following intravenous administration in a porcine model. Subsequently, MRI imaging performance was investigated in vitro as well as in vivo during liver imaging in mice.

Results

While on the cytotoxic level hardly any differences between the three particle types can be detected, the differences on the immunological side are all the more pronounced. In in vitro studies, Resovist showed abnormalities in platelet activation and, like ferumoxytol, an increase in plasma coagulation, albeit exploiting a different pathway. The most dramatic difference is seen in the CARPA assay. Here, both ferumoxytol and resovist showed very pronounced CARPA responses in the porcine model even at low concentrations (0.5 mg/kg bw). In contrast, $\text{SPION}^{\text{Dex}}$ did not elicit any CARPA responses, even at ten times higher concentrations. In vitro, $\text{SPION}^{\text{Dex}}$ was shown to have similar imaging performance compared to Ferumoxytol and better compared to Resovist, but in vivo experiments indicate that $\text{SPION}^{\text{Dex}}$ is excreted from the liver more rapidly.

Conclusion

Overall, our results indicate that $\text{SPION}^{\text{Dex}}$ is an extremely biocompatible and non-immunogenic SPION-based system that can lead to a more comfortable diagnostic treatment for the patients.

Dynamic bolus phantoms for the evaluation of the spatio-temporal resolution of MPI scanners

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Introduction

For a consistent assessment of results obtained from different MPI scanners, reference objects with well-defined imaging properties are mandatory. Mostly, static phantoms are realized for this purpose by filling a defined volume with a liquid tracer of known MNP concentration. Since such phantoms do not offer the possibility to assess time dependent properties of MPI signal acquisition and data analysis, we developed dynamic bolus phantoms, which provide movable liquid objects of variable size, tracer concentration, and velocity.

Methods

The dynamic phantoms are based on segmented flow of cylindrically shaped liquid tracer boluses. A hydrophobic carrier (silicon oil) is filled into a flexible tube system with different diameters, into which boluses of an aqueous MNP dispersion (perimag) are added. Each single tracer bolus is separated within the carrier and can be moved accurately through the tube system by pumping the hydrophobic carrier liquid. Different trajectories of the moving boluses were realized by mounting the tube into different 3D-printed tube holders. The velocity of moving boluses was adjusted to be 1 cm/s up to 40 cm/s, which represents realistic blood flow velocities within the body. The moving boluses were imaged by two different MPI scanner types (MPI 25/20FF, Bruker BioSpin operated at Charité University Medicine and TWMPI prototype V1, operated at Würzburg).

Results

Both scanners successfully imaged all moving boluses, showing an increasing blurring with increasing bolus velocity. We found that the obtained temporal imaging resolution is determined by the dimensions of the bolusesas well as the achievable spatial resolution.

Conclusion

We conclude, our phantoms are capable to assess the correlation of spatial and temporal resolution for moving objects of different size and velocity and are suited to evaluate and compare the performance of different MPI scanner architectures under different imaging parameters such as field modulation frequencies and acquisition times.

Dynamical imaging of a 3D printed patient-specific cerebral aneurysm phan-tom by MPI

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Introduction

Undetected, asymptomatic brain aneurysms include the high risk of progressive expansion, followed by rupture, hemorrhage and finally death in approximately 80% of the cases. Therefore, imaging techniques to assess the state of aneurysms are of high relevance. Magnetic Particle Imaging (MPI) is an ambitious biomedical imaging modality with high temporal and spatial resolution that is capable to detect and quantify aneurysms using magnetic nanoparticles (MNP) as tracer.

Methods

By MPI, we studied the flow characteristics of MNP in a vessel structure phantom made by 3D silicon printing using a preclinical MPI system (MPI 25/20 FF, Bruker Biospin, GER) equipped with an additional gradiometric receive-only coil. The vessel structure phantom contains straight and curved sections as well as an aneurysm and was created using medical imaging data. In some measurements, the phantom was additionally used with a flow diverter stent inside the aneurysm. To provide different flow rates, the vascular phantom was connected to a syringe pump (LA-800, Landgraf Laborsysteme HLL, GER). For the experiments, the syringe, tubing and phantom were filled with either destilled deionised water (ddH2O) or a glycerine-water mixture (59.1% glycerine, 40.9% ddH2O) to mimic the viscosity of blood. During the MPI data acquisition an MNP bolus of 100 µL Perimag (Micromod, GER) at an iron concentration c(Fe)= 50 mmol/L was administered into the tube at the entry of the vascular phantom and pumped through it at different flow rates from 1 or 3 mL/min.

Results

By MPI, we were able to visualise the dynamics of transport and residence of the MNP in the different parts of the vessel structure phantom.

Conclusion

Our results provide valuable information about the capability and success perspective of MPI imaging of vessel structures and detection and quantification of aneurysms for future in vivo applications.

Tabletop setup based on Optically Pumped Magnetometers for characterization of magnetic nanoparticles using Thermal Noise Magnetometry

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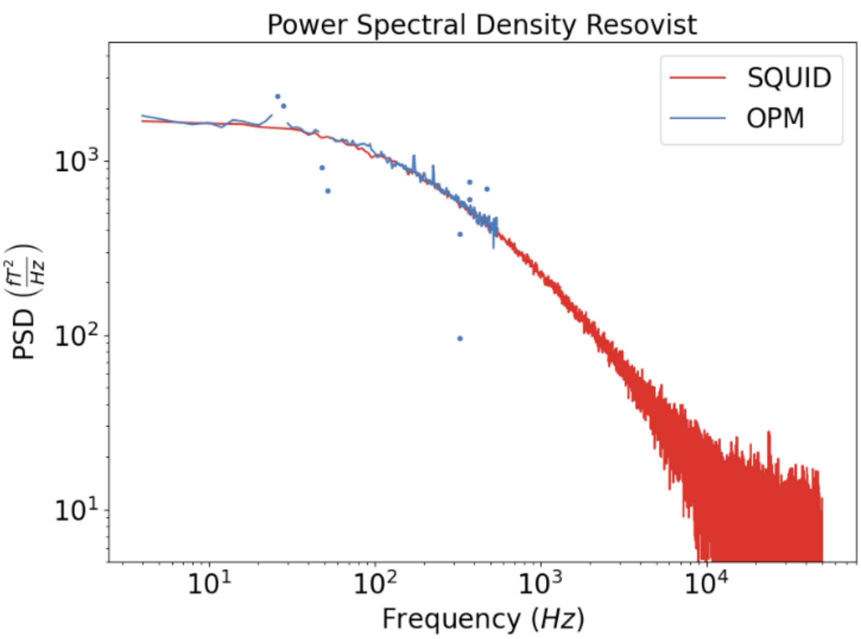
Abstract

Magnetic nanoparticles are very useful in biomedical applications, where they are employed in both diagnosis and therapy. To improve the performance of these applications, the particle properties need to be precisely characterized. All magnetic characterization methods have the disadvantage that they require the application of an external field to measure the magnetic response of the particles, which may change the magnetic state of the particles. The method of Thermal Noise Magnetometry (TNM) has been developed to characterize magnetic nanoparticle ensembles without any use of an external magnetic excitation[1]. The total switching rate of the thermal fluctuations on the magnetic signal of the sample depend on the physical and chemical properties of the particles. The characteristics of the nanoparticle ensemble thus greatly influences the magnetization dynamics, which can be mapped by measuring its thermal noise.

Until now, TNM measurements have been performed with SQUID sensors because of the small signals in the fT range [2]. Optically Pumped Magnetometers (OPMs) offer an alternative sensor system attractive for TNM. In this contribution, we present a tabletop TNM setup working with commercially available OPMs (QuSpin Gen-2 Zero-Field Magnetometers) in a laboratory magnetic shielding (Twinleaf MS-2).

Since our spectral measure is phase insensitive, we are able to use the OPMs above their bandwidth specified by the manufacturer by compensating for their frequency response profile in the power spectrum. The noise spectrum of a Resovist sample was measured in the OPM setup and compared with one measured in an in-house developed SQUID system. As is visible in the figure, we find a very good agreement. This means that the usage of the OPM setup is validated and that the OPM setup with high accessibility complements the SQUID setup with high sensitivity and bandwidth, thereby expanding the field of TNM to possible other magnetic noise related applications.



References

[1] J. Leliaert et al. Appl. Phys: Lett., 107(22):22401, 2015.

[2] K. Everaert et al. IEEE Access, 9:111505, 2021.

iMPI - Lightweight MPI scanner for human-sized intervention

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Introduction

Magnetic Particle Imaging (MPI) has become a promising tomographic method for multiple applications in biology, chemistry, medicine and physics, in in particular for cardiovascular medicine as an applicable radiation-free option for endovascular interventions supporting the common x-ray standard (digital subtraction angiography - DSA).

In this abstract, a first dedicated concept for a human-sized MPI scanner based on the Traveling Wave approach is presented, which is specifically designed to meet the requirements for cardiovascular interventions such as percutaneous transluminal angioplasty (PTA) and stenting.

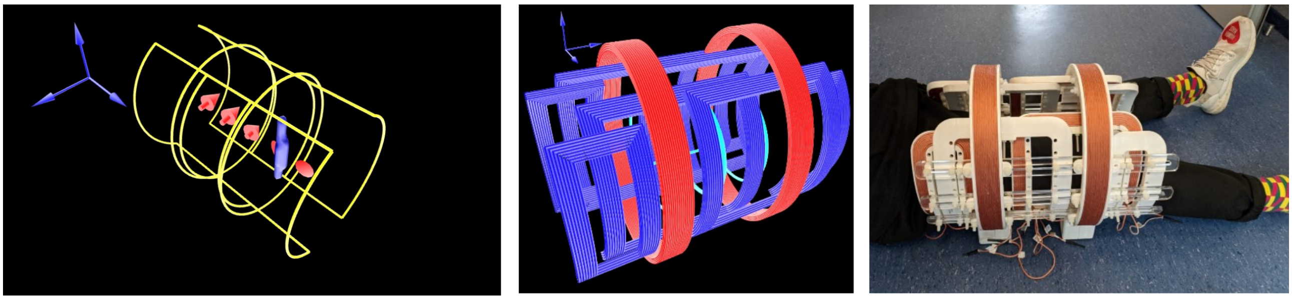
Methods

The aim of the interventional MPI scanner (iMPI) is to provide a radiation-free system comparable to the clinical gold-standard DSA. This requires spatial resolution in the range of millimeters, high temporal resolution, near real-time visualization, and an open design that provides a comfortable and flexible environment for patients and medical staff, as well as sufficient space for interventional instrumentation and its operation. Additionally, the open design allows for simultaneous conventional DSA, which is especially important in the trial and testing phase.

To provide a sufficient magnetic field gradient, which is required for a high spatial resolution in MPI, a novel hardware approach is used to generate and move dynamically a field-free line (FFL) within a specific region along specific trajectories. The result is projection display comparable to DSA, e.g., of vascular structures and stent positioning.

Results

To guarantee a strong magnetic field gradient of about 0.7 T/m, currents of about 200 Ampere driving the main electromagnets are required. This results in a power dissipation of about 50-60 Kilowatts in continuous mode, which requires a sophisticated cooling management. The figure shows the first prototype of the iMPI system.



Conclusion

A first human-sized projection MPI scanner for interventional treatment of human-sized legs has been designed and built providing promising results to pave the way to clinical routine.

Human-Head-Sized Quantitative Imaging of Magnetic Nanoparticles with Magnetorelaxometry and Optically Pumped Magnetometers

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Introduction

Magnetic nanoparticles~(MNP) enable exciting biomedical applications, e.g. magnetic hyperthermia. Quantitative imaging of MNP distributions is required for treatment planning and monitoring. MNP can be quantified by magnetorelaxometry (MRX), where the MNP's relaxation after previous magnetization is measured. Spatial information can be obtained by repeating the MRX procedure with different (inhomogeneous) magnetization fields and solving an ill-posed inverse problem. This so-called magnetorelaxometry imaging~(MRXI) has been successfully demonstrated with superconducting magnetometers~(SQUID) and optically pumped magnetometers~(OPM), e.g. for flat rabbit-sized regions of interest. Here, we theoretically and experimentally investigate and demonstrate the feasibility of upscaling MRXI to a human head sized setup.

Methods

Our setup is composed of 25 dual axis OPM from QuSpin and 72 excitation coils, which are mounted on a 3D-printed helmet. We exploit the possibility of flexible OPM sensor positioning and the combination of small and large magnetization coils for targeted magnetization for both superficial and deep regions possibly containing MNP. The phantom was a 3D-printed head, containing cubes of immobilized Berlin Heart MNP with an iron concentration of 3.7 mg/cm^3;. The setup was operated within a passively and actively magnetically shielded room~(Ak3b) at PTB Berlin.

Results

Preliminary reconstruction results demonstrate, that our OPM-MRXI setup allows for detecting point-like MNP located near the surface and/or at deeper brain regions with centimeter scale resolution. Like expected from our simulations, the eight large coils already allow for a coarse reconstruction of the MNP distribution. The sparse relaxation signal from the 64 small coils allows for improved reconstruction results for near-surface located MNP.

Conclusion

The proof of principle upscaling of MRXI to a human-head-sized region of interest was successfully demonstrated. Current work focuses on characterizing our setup.

Nonlinear Magnetorelaxometry Enabling Quantitative Imaging of Magnetic Nanoparticles in Large Body Regions

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Introduction

Magnetorelaxometry imaging (MRXI) enables the noninvasive quantitative detection of magnetic nanoparticles (MNPs). The state-of-the-art imaging process involves solving the inverse problem of the MRXI forward model, describing the MNP behaviour through simplified linear magnetic susceptibility. This model holds for weak magnetic excitation fields and small fields of view (FOVs) (<10 cm in diameter). However, larger FOVs (e.g., torso size) require larger excitation fields to adequately magnetize them which drives areas close to the electromagnetic coils into the nonlinear magnetization regime, thereby deteriorating MRXI results based on a linear model. Thus, we formulate a realistic nonlinear MRXI forward model. Furthermore, we exploit the introduced nonlinearity by using different magnetic field strengths, enabling more accurate imaging results than the standard approach.

Methods

The nonlinear model is tuned using real measurement data from MNPs magnetized with different magnetic field strengths. The proposed approach is tested in simulations on a $40\times20\times30$ cm^3; torso-shaped volume (3 cm voxel side length), using four large excitation coils and eight optical magnetic gradiometers (OMGs). MNP phantoms with 3.7 mgFe/ml MNP concentrations are reconstructed using the standard and the proposed approaches. Realistic model errors regarding FOV discretization and coil/sensor positioning and measurement noise (0.2 pT/rHz, appropriate for Twinleaf OMGs) are considered, yielding adequate MRXI signal-to-noise ratios of approximately 20 dB.

Results

All reconstructions produced by the nonlinear approach are up to 60% more accurate due to the nonlinear spatial encoding scheme. Specifically, this is useful since large coils (required for strong magnetization) hamper good spatial FOV encoding due to their more homogeneous magnetic fields compared to smaller coils. The proposed approach counteracts this disadvantage to some degree.

Conclusion

Combining the nonlinear MRXI model and the proposed spatial encoding scheme consistently outperforms the state-of-the-art MRXI approach throughout all simulations. These theoretical findings are currently being validated in experiments.

A multimodal phantom for Magnetic Resonance Imaging and Magnetic Particle Imaging

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Introduction

Magnetic particle imaging (MPI) is an emerging quantitative imaging technology visualizing the 3D distribution of MNP, in vivo. However, since MPI signal is generated by MNP only, the surrounding tissue cannot be imaged directly. Therefore, complementary imaging techniques, such as magnetic resonance imaging (MRI), are used to provide anatomical information. For experiment planning and quality assurance, multimodal phantoms are required that serve both imaging modalities simultaneously. Unfortunately, neither conventional MPI nor MRI phantoms are compatible for imaging with the other modality.

Methods

In this work, we present the development of a multimodal phantom using additive manufacturing (AM) and address the challenges in selecting appropriate materials for the fabrication of MPI/MRI phantoms. Physical parameters of six commercially available materials for AM were evaluated, including absorption (of MPI-tracer), shore hardness, aging, and printing accuracy. Time-domain Nuclear Magnetic Resonance (TD-NMR) was used to analyse the MRI performance of these materials. The materials were checked for potential magnetic contaminations and unwanted MPI tracer absorption by magnetic particle spectroscopy (MPS, i.e., 0-dimensional MPI).

Results

Of all investigated materials, silicone exhibited the best properties with a sufficient MR-signal performance (T2=26 ms, T1=397 ms) and the lowest absorption of MPI-tracer at the interface of AM materials (900 ng(Fe)/cm2). From this, a phantom consisting of MR-visible silicon material (BioTec, Dreve) was designed and fabricated by AM (i30+, Rapidshape) that contained cavities filled with an MPI-visible tracer (Synomag, Micromod Partikeltechnologie GmbH). The multimodal phantom was successfully imaged with MPI (preclinical MPI scanner, Bruker) and MRI (1T ICON, Bruker).

Conclusion

AM of silicone components that are MRI visible and compatible with MPI tracers enable flexible fabrication of MPI/MRI phantoms. In the future, composites made of silicone with embedded MNP will be developed that can be processed in multi-material AM systems. This would enable the fabrication of multimodal silicone phantoms with controllable magnetic properties within one single AM system.

Systematic approach of magnetic controlled cell labeling for magnetic particle imaging

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Introduction

Magnetic particle imaging (MPI) is a promising imaging technique determining the 3D distribution of magnetic nanoparticles (MNP). The capability of MPI cell tracking labeled with MNP, has successfully been shown. [1] The cell uptake is impacted by the selection of the MNP system (coating, size, zetapotential) and the type of biological medium. Presently, there is no magnetic quality control of cell labeling available including these aspects. Here, we will present a magnetic quality control procedure of MPI cell labeling.

Methods

The magnetic quality control procedure of MPI cell labeling will be presented by THP-1 cells labelled by two MNP systems Synomag and Synomag-D (Micromod, GER) in different biological media (e.g. Phosphate buffered saline (PBS), bovine serum albumin (BSA)). The basic characterization of the MNP is performed magnetically by magnetic particle spectroscopy (MPS-Bruker) and DC magnetometry (MPMS-XL-Quantum Design). In addition, the MNP are structurally characterized using small angle light scattering (SAXS-Anton Paar), dynamic light scattering (DLS-Malvern), asymmetric and centrifugal field flow fractionation (AF4, CF3-Postnova). The cell tracking takes place during magnetic particle imaging (MPI-Bruker). For this first MPI applicationand reconstruction of the loaded cells, five different system functions (SF) were recorded (Synomag liquid in water (c(Fe)=50 mmol/L), Synomag liquid in PBS (c(Fe)=50 mmol/L), Synomag freeze-dried (c(Fe)=50 mmol/L) and loaded cells (0.5 pg/cell and 15 pg/cell)).

Results

The magnetic quality control procedure of MPI cell labeling consists of three phases. First, we perform a magnetic and structural characterization of different MNP systems in the presence of biological media which often directly change their magnetic behavior. To this end, advanced separation techniques will be used to identify MNP-media-interaction. [2] As a result, PBS should be used as the medium for THP-1 cells in order to avoid/reduce aggregation already before cell uptake. Media like FCS causes strong aggregation between MNP and biological media and should be avoided.
In the second phase, signal changes during and after cell contact are quantified by magnetic measurements using MPS. From this THP-1 cells should be washed two times to reduce aggregations, also the iron volume and the incubation time should be sufficiently high (1 million THP-1 cells V_{FE}= 1000 uL, minimum t_{ink} = 10 min) so that the cells can be highly loaded (~10 pg/cell).
Finally, in the third step, the success perspective of MPI cell tracking for the selected MNP and media is estimated by analyzing of signal changes and resolution during and after cell uptake. Different loading states (m(Fe)= 0.1 to 10 pg/cell) were measured first at MPS and then at MPI. The five different SF are used for the reconstruction of the MPI-images. The SF with liquid Synomag shows a good reconstruction but does not reflect the condition of loaded cells.

Conclusion

The loaded cells were successfully quantified at the MPI. The selection of the system function (SF) is a key factor in the MPI reconstruction. Future studies will include the selection of an appropriate reference for loaded cells for measurement of the system function that ensures reliable MPI reconstruction.

Acknowledgements

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References

[1] Paysen, H., Löwa, N., Stach, A. et al. Cellular uptake of magnetic nanoparticles imaged and quantified by magnetic particle imaging. Sci Rep 10, 1922 (2020).
[2] Remmo, A., Löwa, N., Peter, J. and Wiekhorst, F. "Physical characterization of biomedical magnetic nanoparticles using multi-detector centrifugal field-flow fractionation" Curr. Dir. Biomed. Eng. vol. 7, no. 2, 2021, pp. 327-330.

MRI Investigation of Biodegradable Polymer Fibers with Incorporated Magnetic Nanoparticles

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Introduction

Magnetic nanoparticles (MNP) embedded in biodegradable fiber-based scaffolds can be used as sensors to non-invasively quantify the degradation state of the scaffold with magnetic resonance imaging (MRI). For a precise quantification of the degradation state, the influence of immobilized and agglomerated MNP in the scaffold material on the MRI signal must be considered. In this work, such influence is investigated.

Methods

Four polylactic-co-glycolic (PLGA) fibers with different diameters in the range of 120-300 µm each with up to 1 wt% MNP were melt-spun. Various degradation states were realized by exposing the fibers to both physiological and accelerated flow conditions using a self-designed test bench. The MNP inside the fibers were investigated via transmission electron microscopy. The fibers were measured with a T2 weighted sequence using a clinical 3 T MRI scanner. Model systems of MNP with different sizes and agglomeration states were embedded in ferrohydrogels mimicking the MNP states in the fiber to investigate their impact on MNP relaxivity. The local iron concentration was quantified with relaxometry measurements taking into account MNP immobilization and agglomeration.

Results

The degradation-induced changes, e.g. MNP concentration as well as their agglomeration and immobilization state, clearly influence T2 and T2* relaxation times of protons diffusing in the surroundings of the fibers. Relaxivity maps in the vicinity of the fibers show that the area of signal loss first increases and then decreases with higher fiber degradation sates. The relaxivities of the ferrohydrogels depend on MNP size and agglomeration state as well as on MNP immobilization. Taking into account these relaxivities for specific MNP degradation states, it was possible to precisely determine iron concentrations up to 0.2 mM.

Conclusion

The results demonstrate the feasibility of quantitative imaging of the degradation states of biodegradable fibers with MRI.

MPI tracer interactions and their effect on signal stability

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Introduction

Nanoparticles tend to agglomerate following their in vivo or in vitro application. This leads to particle interaction and, for magnetic particle imaging (MPI) tracers, to magnetic coupling phenomena.

Methods

Here, we investigate these effects and their influence on magnetic particle spectroscopy (MPS) and MPI signal stability. Highly magnetic flame-made Zn-ferrites with controlled interparticle distance are suggested as a stable MPI tracer system.

Results

Due to their pre-aggregated morphology, additional agglomeration does not substantially alter their magnetic response. This is in strong contrast to frequently investigated polymer-coated iron oxide nanoparticles, which show a massive MPS signal loss in a biologically relevant dispersion medium compared to water. This effect is also shown during MPI and renders these tracers inapplicable to further applications.

Conclusion

Our flame-made Zn-ferrites, on the other hand, show sufficient signal stability, which allows their detailed quantification via MPI.

Magnetic Particle Imaging using Toroidal and Poloidal Vortex Rotation of Halbach Rings

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Introduction

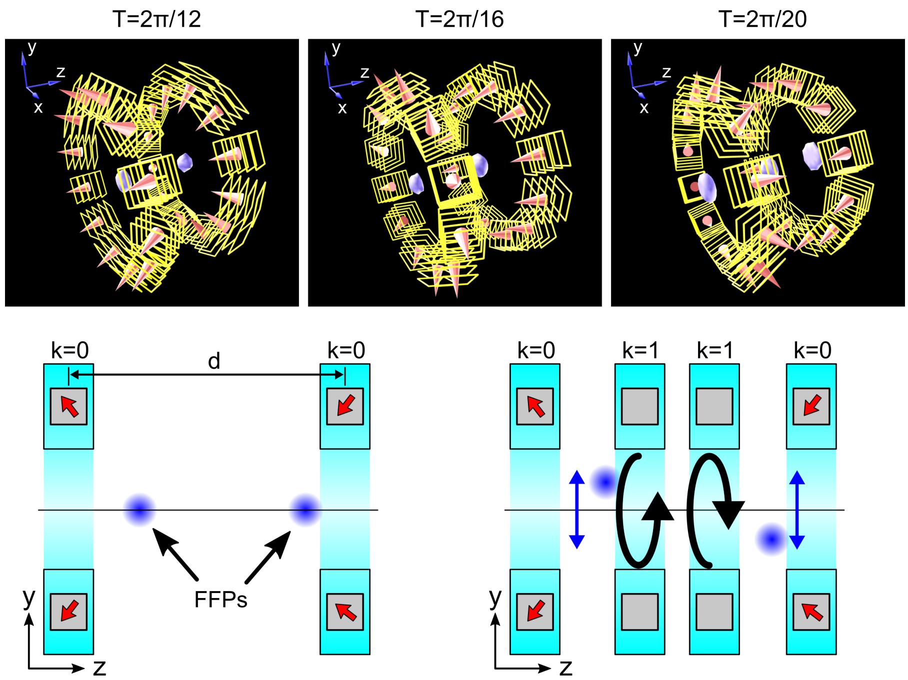
Magnetic Particle Imaging (MPI) is a promising imaging modality for direct visualization of superparamagnetic iron oxide nanoparticles (SPIONs). It relies on the nonlinear magnetization response of SPIONs on time-varying magnetic fields. For imaging and determining the SPION distribution, a strong gradient is steered through the field of view scanning the entire volume successively. Most MPI scanners are using electrical coils for the generation of fast-moving gradient fields, which requires sophisticated filter designs to reach a higher signal-to-noise ratio because of noise coming from the electrical equipment.
Alternative MPI scanner concepts using permanent magnets, such as Halbach rings, to generate strong gradients without the need of electrical power but with massive restrictions in flexibility.
In this abstract, a novel approach for MPI scanners using mechanically rotating Halbach rings is shown.

Methods

For a mechanical TWMPI scanner, two coaxial Halbach rings performing a synchronous vortex ring rotation with frequency f1 generating a field free point (FFP) moving along the symmetry axis of the scanner (Fig.1top).
Two additional Halbach rings with k=1 configuration, which counter-rotate along the z-axis with frequencies f2 and f3, are utilized to move the FFP along a spiral trajectory through the FOV (Fig.1bottom).

Results

A fully mechanically driven Traveling Wave MPI scanner approach covering a full 3D volume has been designed and built. Building all gradients of the MPI system from permanent magnets allow for high gradient fields combined with low energy consumption. In initial experiments the feasibility could be demonstrated.



Top: The time series shows the rotation of the Halbach rings at different times points with the direction of each magnet (red arrows) and the FFP position (blue). Bottom left: cut through the rings generating the traveling FFPs along the symmetry axis. Bottom right: additional Halbach rings rotating around the z-axis steer the FFPs along a spiral trajectory.

Towards Magnetorelaxometry Imaging for in vivo applications

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Introduction

Magnetic nanoparticles (MNPs) display a magnificent potential in cancer therapy such as hyperthermia and drug delivery. To improve therapy efficiency, it is necessary to quantify MNP distribution in the body before and after therapy. Magnetorelaxometry imaging (MRXI) is a noninvasive imaging modality providing this information. MRX is based on the measurement of the decaying net magnetic moment from an MNP ensemble. The MRX setup consists of: (1) the arrays of excitation coils to produce inhomogeneous magnetic field and aligning the MNP moments to the external field and (2) a very sensitive magnetometer to measure the decaying of the magnetic moment.

Methods

As a primary representative model for MRXI in humans, we positioned a head phantom simulating a glioblastoma multiforme (GBM) tumor. We developed a reference head phantom and measured MRXI using the 304-channel SQUID system with 55 excitation coils for magnetizing the MNP mimicking a GBM tumor of 12 cm3 volume (constituted 1 cm^3; cubes of EMG MNPs, iron concentration of 12 mg/ml and 20 mg/ml) (Figure 1).

Results

We report on our evaluation of the sensitivity of the MRXI when we placed the sample holder, filled with cubes of MNP, in different parts of the head (e.g., frontal, middle, and back part).

Conclusion

In this work, we want to empower our MRXI, which initially was developed for animal models, to provide the technology and structure required to establish MRXI for monitoring of MNPs in human cancer therapies.

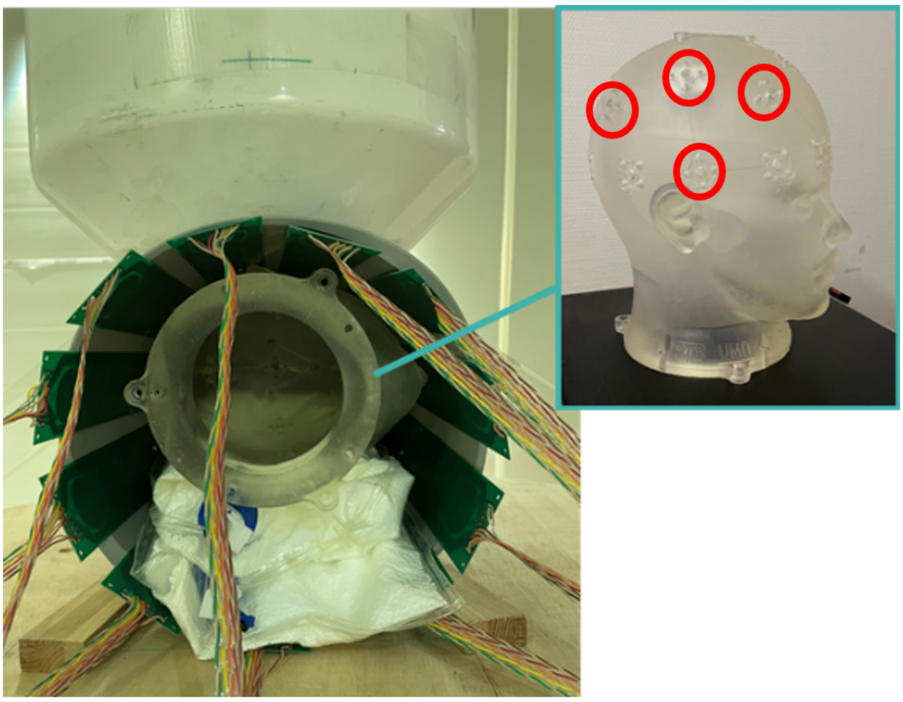

Figure 1: MRXI Setup for head phantom in different parts of the head.

Focus Session:
Biomedical Applications of Magnetic Nanoparticles - Therapies and Diagnostics

Adapting magnetic microspheres to several applications: hyperthermia, drug delivery and immunomagnetic separation

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Introduction

Polymeric magnetic microspheres (MMS) can be used for several medical and biotechnological applications, like drug delivery, hyperthermia or immunomagnetic separation. Depending on the application of interest, the MMS need to match specific requirements regarding their size, magnetic properties and antigen binding capacity. Therefore, we are working on size-controlled PLGA and PLA-MS with oleic acid coated MNP and conjugated antibodies.

Methods

Microspheres were produced by an emulsion-evaporation method, where an oil phase containing polymer, MNP and drug is homogenized in an aqueous PVA phase. The solvent evaporates out of the droplets and hardenend MS result. Synthesis parameters were varied to study the tunability of MS size. For incorporating hydrophobic MNP into the MMS, we established an oleic acid coating, characterizing resulting particles with VSM, DLS and TGA. Distribution of oleic acid coated MNP in MMS was investigated with SEM on focused ion beam cross-sections of MMS and VSM. Antibody conjugation was evaluated using click chemistry and the biotin-avidin adsorption mechanism. Release of Camptothecin out of MMS by magnetic heating to 43 °C compared to 37 °C was investigated.

Results

We found the MS size to depend mainly on homogenization speed and method (mechanical or ultrasonic) and PVA concentration, leading to diameters between 0.5 and 6 µm. Oleic acid coating enables monodisperse particles in organic solvents with a mean diameter of 190 nm, PDI of 0.12 and approx. 8 wt% oleic acid. MNP are distributed homogenously throughout the spheres while maintaining a spherical shape with MNP concentrations up to 33 wt%. Antibodies were immobilized on PLA microspheres, confirmed by optical measurements (ELISA). Drug release was increased by 30% with magnetic heating compared to passive release at body temperature.

Conclusion

We developed a toolbox of MMS that can be adapted to several applications by tuning their size, incorporating magnetic nanoparticles and conjugating antibodies to their surface.

Passage of magnetic nanoparticles through a differentiating blood-placenta barrier

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Introduction

The application of nanomaterials in a medical context is rapidly progressing. There is still the necessity to understand the interaction between nanomaterials and the human body in more detail, especially at cellular barriers. Since clinical trials on pregnant women are difficult to perform, physiologically appropriate models of the human placenta to study nanoparticle-placenta interactions in vitro are needed..
The aim of our investigations is to gain a better understanding of the interactions of magnetic nanoparticles (MNP), with the blood-placenta barrier [1]. In the present study, we investigated whether the fusion of cytotrophoblasts to syncytiotrophoblasts affects MNP passage through the barrier.

Methods

The in vitro BPB was established in a microfluidic chip by using the cytotrophoblast cell line BeWo on the apical (maternal) side and human primary placental pericytes on the basolateral (fetal) side. Differentiation of the BeWo cells was induced by a 24h-incubation with 20 µM forskolin. The morphological changes were confirmed by fluorescence microscopy (ZO-1) and qPCR (LGALS13, ZO-1). Citrate-coated MNP (hydrodynamic diameter 116 nm, z-potential -35 mV) were applied for 24 h. For quantification of the MNP content magnetic particle spectroscopy (MPS) was performed. Cytokine release was measured with the LEGENDplex human inflammation assay.

Results

After forskolin and MNP incubation the MNP distribution in the apical and basolateral compartment as well as in the cell layer was determined by MPS. The penetration rate of MNP was not affected by the formation of syncytiotrophoblasts. In the basolateral compartment, no significant difference in MNP content was measured between the untreated setting (2.3% $\pm$ 2.0%) and after cytotrophoblast fusion induced by forskolin (2.4% $\pm$ 1.6%). The IL-6 release is enhanced 2-fold after forskolin and MNP treatment.

Conclusion

We demonstrate that MNPs pass a cytotrophoblastic cell layer as well as a syncytiotrophoblast.

References

[1] Gresing, L., et al. J. Magn. Magn. Mater. 2021, 521, 167535

Biocompatibility studies and cellular interactions of biogenic magnetic nanoparticles

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Introduction

Biogenic nanoparticles are an intriguing example for a biomineralization process. Magnetotactic bacteria are capable of synthesizing magnetosomes, single-domain magnetite nanocrystals that are enveloped by a biological membrane. Strict genetic control on each step of biomineralization generates nanoparticles with extraordinary properties such as high crystallinity, strong magnetization and uniform shape and size. Moreover, the magnetosome membrane is accessible to genetic engineering, enabling the selective and highly controlled functionalization of the magnetosome surface with reactive moieties. Due to these characteristics, bacterial magnetosomes have the potential to yield promising agents for (bio)medical applications in diagnosis as well as magnetic imaging techniques or as drug carriers.[1]

Methods

In order to comprehensively evaluate the biocompatibility of isolated magnetosomes when administered to mammalian cells (cancer cell lines or primary cells), different cytotoxicity assays such as the PrestoBlue and SYTOX assay were performed. Furthermore, using microscopic and magnetic separation techniques, we in-depth assessed magnetosome - cell interactions.

Results

For the magnetosome-treated cell lines FaDu, BeWo, HCC78 and hPC-PL, concentration-dependent effects on cell viability were observed; however, we could demonstrate that even the highest tested particle concentration of ~400 µg mL^{-1} can be considered biocompatible. During incubation, the particles were internalized and accumulated in endolysosomal vesicles close to the nucleus. Remarkably, even upon short-term incubation magnetosomes - cell interactions were strong enough to allow for magnetic cell sorting, with ~60% of the treated FaDu cells being magnetically separated.[2]

Conclusion

In order to enhance these interactions and to address distinct cancer cell types, synthetic biology techniques are used for magnetosome display of specific anticancer peptides. Thereby we will generate a set of multifunctional magnetic nanoparticles that provide a flexible "tool" with potential in e.g. the targeting of circulating tumor cells.

References

[1] Vargas G., et al. Molecules 2018, 23, 2438
[2] Mickoleit F., et al. Nanoscale Adv. 2021, 3, 3799

Large single domain iron oxide nanoparticles as thermal markers for lateral flow assays

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Introduction

Using magnetic nanoparticles for extracorporeal heating applications, i.e. as thermal instead of colorimetric markers for lateral flow assays, enables the use of large external magnetic field amplitudes, since the restrictions concerning the field strength for patient safety don't apply, and particles with larger coercivities can be used. Therefore, we investigate the synthesis of large single domain particles with increased coercivity.

Methods

Particles were synthesized using the green rust method under oxygen free conditions at various synthesis temperatures between 5 and 85 °C. Particles were characterized using transmission electron microscopy (TEM), X-ray diffraction (XRD), Auger electron spectroscopy (AES), vibrating sample magnetometry (VSM), Mössbauer spectroscopy and calorimetric measurements for SAR evaluation.

Results

Particles show increasing mean sizes by XRD with increasing synthesis temperatures, ranging from 30 to 65 nm and at the same time increasing coercivity from 6 to 15 kA/m. For synthesis temperatures between 15 to 35 °C, high magnetization values around 85 Am^2/kg are obtained, whereas for temperatures above 45 °C, MS decreases, indicating the formation of a non- or weak magnetic phase apart from magnetite/maghemite. This parasitic phase was also confirmed by Mössbauer spectroscopy, showing an additional subspectrum for those samples indicating an antiferromagnetic Fe3+ bearing material. AES measurements confirmed the presence of Na in the sample synthesized at 75 °C whereas only Fe and O was found in the 35 °C sample. SAR measurements (H = 55 kA/m; f = 290 kHz) of immobilized particles showed promising values up to 600 W/g, while again samples synthesized above 45 °C showed lower SAR values due to their lower MS.

Conclusion

Our LSDP are promising candidates for heating applications due to their high HC and MS for synthesis temperatures below 45 °C. In ongoing work, we are investigating the parasitic non-magnetic phase in more detail and evaluate strategies to prevent its formation.

Sensitive and specific magnetic immunoassays using DNA nanotechnology

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Introduction

The sensitive and specific detection of nucleic acids such as cell-free DNA, microRNA, and pathogen RNA/DNA has gained enormous attention in the past few years due to their potential as disease biomarkers. Most relevantly, the ongoing COVID-19 pandemic strongly demonstrates the need for quick and reliable viral diagnostics. Magnetic nanoparticles (MNPs) with their unique magnetic properties open new opportunities in realizing fast and quantitative immunoassays. Binding of MNPs to analytes increases their hydrodynamic sizes, slowing down the magnetization relaxation process, which can be detected using Magnetic Particle Spectroscopy (MPS) [1]. Despite all technological advancements in instrumentation, the design of nanosensors and detection concepts is still in its infancy stage. For magnetic immunoassays to compete with other detection platforms, new detection schemes needed to be developed.

Methods

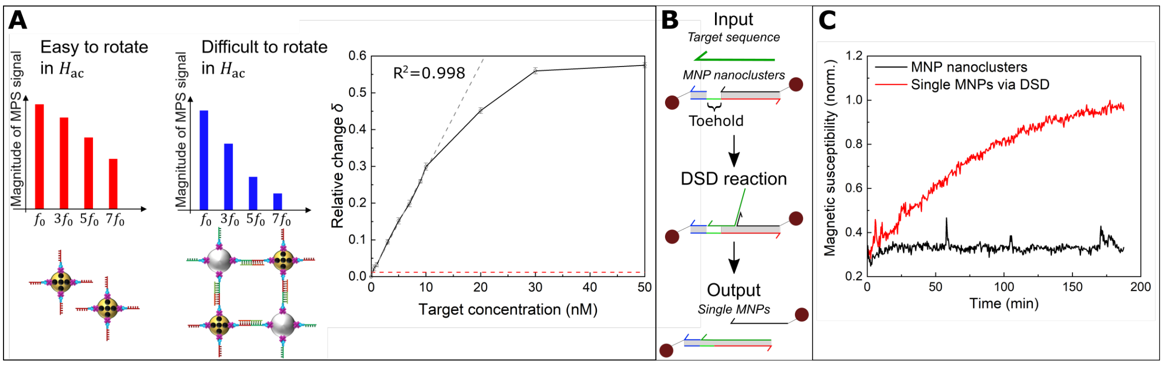
Here we combine novel DNA nanotechnology concepts and magnetic methods to establish specific and sensitive diagnostic tools for the detection of SARS-CoV-2 specific sequences. Our first assays are based on cross-linking MNPs with polystyrene beads upon adding the single-stranded (ss) target DNA, which changes the particle magnetic relaxation, being registered in the MPS harmonics spectrum (Fig. 1A). In our second approach, we exploit the toehold-mediated DNA strand displacement (TM-DSD) reaction for disassembly-based immunoassays. Therefore, we first tether DNA-MNPs into clusters by adding complimentary ssDNA that possesses unbound nucleotides, known as the toehold. A complimentary target sequence initiates branch migration, disassembling the clusters (Fig. 1B).

Results

Target DNA can be detected in a concentration-dependent manner with a limit of detection of 280 pM (Fig. 1A). Furthermore, we observe the disintegration of nanoclusters into single MNPs via TM-DSD upon adding target sequence, evidenced by magnetic susceptibility measurement (Fig. 1C).

Conclusion

We have shown that magnetic immunoassays provide rapid and quantitative results. Moreover, TM-DSD allows to design complex assay structures for high-sensitivity assays.



Acknowledgements

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References

[1] Kai Wu et al 2019 J. Phys. D: Appl. Phys. 52 173001

Simulating the magnetization dynamics of magnetic nanoparticles for biomedical applications

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Introduction

Magnetic nanoparticles are increasingly employed in biomedical applications such as disease detection and tumor treatment. To ensure a safe and efficient operation of these applications, a complete understanding of the particle dynamics is required. In this talk, I will present the results of two simulation studies in which we model the particles magnetization (and in one case also the rotational) dynamics.

Methods

Firstly, a magnetic characterization technique is presented in which the particles are excited by specific pulsed time-varying magnetic fields. Secondly, building on previous theoretical work, we present an equation to estimate the heat dissipation of individual, interacting particles at nonzero temperature that perform both field-induced and thermal switching. After validating this equation, we investigate a system of interacting particles with different anisotropies.

Results

We show that we can selectively excite nanoparticles of a given size so that the resulting measurement gives direct information on the size distribution without the need for any a priori assumptions or complex postprocessing procedures to decompose the measurement signal, which contrasts state-of-the-art magnetic characterization techniques. Next, we show that the generated heat becomes more homogeneously distributed at larger fields. We believe that this homogenization of the particle heating will help to achieve a more homogenized heating of tumours during hyperthermia treatments.

Conclusion

Our results open up possibilities to selectively excite certain particle types opens up perspectives in “multicolor” particle imaging, where different particle types need to be imaged independently within one sample. Furthermore, the use of the proposed equation would simplify the selection process of optimum nanoparticle distributions leading to optimal tumour heating.

References

[1] A. Coene, J. Leliaert, Sensors, 20, 3882 (2020)
[2] J. Leliaert, J. Ortega-Julia, D. Ortega, Nanoscale, 13, 14734-14744 (2021)

Towards a realistic 3D-model of tumor vascular networks

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Introduction

Realistic vascular tumor models are essential for in-silico or in-vitro investigations, e. g. in biosensing and drug delivery applications. For the development of such models, immunhistochemically stained tumor slices delineating the vessel walls are used. However, the preparation of such slices (e.g. slicing, staining, deposition of glass slides etc.) for the digital registration leads to misalignment artifacts. To counteract those artifacts, advanced image registration algorithms are necessary to re-align the slices. Here, we present the registration and reconstruction of a vessel network from a stack of tumor slices.

Methods

The developed registration algorithm proceeds in two steps. First, contiguous images were incrementally pre-aligned using feature- and area-based transformations and second, using the previous transformations, all serial images were registered at once. All computations were performed on the RWTH computation cluster and are designed highly parallelizable. Using image segmentation, vascular structures were identified in each image. Contiguous images were used as reference to be robust against noise and tissue ruptures. A combination of intensity and color-based thresholds along with heuristic analysis was used for the construction of binary images indicating vascular structures. Stacking binary images and interpolating between slices yielded the 3D model.

Results

The reconstructed model shows distinct vessels and their pathways within the tumor. The vessels have a rather straight trajectory. This effect is attributed to the fact that only a small part of a tumor (425 µm) was reconstructed. In areas of high structural density, a delineation of vessel structures was difficult.

Conclusion

The presented work shows promising results towards the reconstruction of a realistic model of a tumor from immunhistochemically stained tissue slices. For further optimization of the reconstruction algorithm, more image data as well as a more robust segmentation is needed. Using higher-resolution images and incorporating machine learning techniques will increase the segmentation algorithm's ability to differentiate between close-distance vascular structures.

Estimating the heating of complex aggregates of magnetic nanoparticles for hyperthermia

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Introduction

Clinical studies using magnetic nanoparticles must meet strict safety regulations that require knowledge and control of the particles[1]. Because the behaviour of nanoparticle aggregates are different from their unclustered counterparts, one of the challenges in magnetic hyperthermia is controlling the heat generated by nanoparticle clusters.
In silico approaches are often used to optimize treatment parameters, but these suffer from the drawback that methods that account for single particle dynamics are not capable of simulating the large number of particles used in therapy, whereas simulations at large scales require the use of effective parameters that are difficult to assess to correctly estimate the heating.
Our work closes the gap between both approaches by studying the heating of nanoparticle clusters, as found in biological tissues[3], allowing to translate results from small clusters to practical cases. Building on our previous work[4], we simulate magnetic nanoparticle clusters with different shapes and sizes.

Results

Our results suggest that starting from relatively small clusters of about 25 particles, the heat released per particle tends to converge to a value which depends on the shape of the clusters, where those clusters that are more elongated release more heat than the compact ones.

Conclusion

This work shows that it is possible to predict the outcome of large clusters of particles of any shape based on a simulation of a moderately sized cluster with the same geometrical and magnetic parameters. Our results can complement ongoing projects[4] to perform multi-scale simulations that to make accurate estimates of the heat released by magnetic nanoparticles during magnetic hyperthermia, leading to the optimization of the treatment.

References

[1] www.nocanther-project.eu
[2] Etheridge ML, et al. Technology (Singap World Sci). 2014 2(3):214-228
[3] Leliaert J, el al. Nanoscale, 2021 13, 14734-14744
[4] Rubia-Rodriguez I, et al. International Journal of Hyperthermia 38.1 (2021): 846-861

Optimization of the coprecipitation in the synthesis of SPIONs with rigorize control of process conditions

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Abstract

In this work, superparamagnetic iron oxide nanoparticles were synthesized using an alkaline coprecipitation. Two different bases (NaOH and NH_3) were used. Furthermore, the influence of temperature on the properties of the products was investigated. Three different Dextran derivates were used as shell material for the syntheses. The products of the different syntheses were investigated by Magnetic Particle Spectroscopy (MPS) and Photon Correlation Spectroscopy (PCS). The magnetic properties and the hydrodynamic diameter were used as quality criteria of the produced SPIONs. The results of this studies were evaluated and carefully compared.
Precipitation of iron salts ($FeCl_2$ und $FeCl_3$) in the presence of the coating material (Dextran with MW 20.000, 70.000 and Carboxymethyldextran) with a base (NH_3 or NaOH). molar ratio, the amount of coating material and the volumes of the bases used at the same concentration were used for the different syntheses. By using ammonia as a base, the pH value is increased slowly, which also has a positive effect on the controlled particle growth. However, the influence of the base also depends strongly on the coating material. With Dextran T70, larger particles are obtained with NH_3 than with NaOH In the study presented here, it was shown that the core diameter of the SPIONs produced is approximately constant even when different dextrans are used if the reaction conditions are maintained. Care was taken to ensure that the base drop-in time, the nucleation and crystallisation phases and the temperatures of the different reaction phases were the same. With the chosen parameters, SPIONs with a core diameter of 15-16 nm could always be obtained. However, if you use CMD instead of dextran, you get significantly different core diameters. This may be due to the changed structure of CMD due to the carboxymethly group.

Role of different kinetics factors on magnetic nanoparticle properties for their continuous synthesis in a millifluidic system

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Introduction

For optimized application of magnetic nanoparticles (MNP) in biomedicine, such as in hyperthermia tumor therapy and medical imaging, MNP with tailored properties (e.g. narrow size distribution, high magnetization, biocompatibility) and at large scale are necessary. Continuous manufacturing processes are reliable and scalable compared to batch processes, which have high technical variability and low throughput production. In this study, a versatile, reliable and scalable millifluidic continuous manufacturing process is presented and the role of kinetic factors for the synthesis on MNP properties is studied.

Methods

For the production of MNP with specific properties (core size diameter, hydrodynamic diameter, magnetization), a millifluidic and continuous synthesis setup was built. This consists of a reactor for mixture of liquids (MNP nucleation phase), i.e. base and iron salts, and a long tube in which gas and liquids are alternately pumped (MNP crystallization phase). Synthesis parameters were adjusted by suitable automations controls and the effects of ionic strength, different salts and base, the effect of temperature and concentration effects of ligand for MNP stabilization on the nucleation and crystallization phases were studied. The core and hydrodynamic size as well as the magnetic response to static and alternating magnetic fields of the synthesized MNP were analyzed. The iron concentration was determined based on complexation of Fe^{3+}.

Results

Depending on synthesis parameters, MNP with different properties were successfully synthesized. Different trends could be observed, such as bigger MNP sizes for lower reaction temperatures during the nucleation phase. The production system consisting of gas and liquid phases demonstrated to have a great influence on core size diameters and magnetic properties of MNP.

Conclusion

Using a millifluidic, continuous and partially automated synthesis system and adjusting the kinetic factors of the system, a reproducible and tunable production of MNP could be achieved.

Modified MPS: New benchtop approach in medical point-of-care diagnostics

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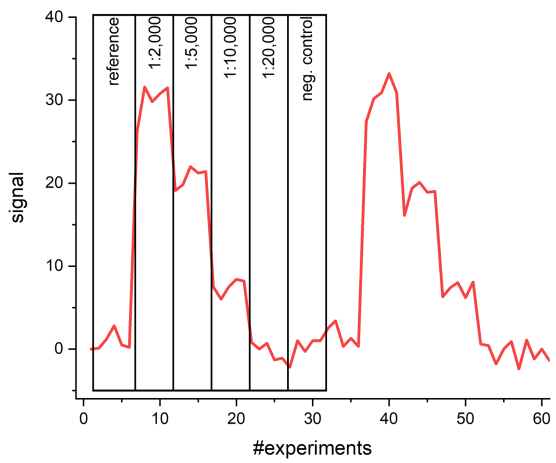
Introduction

By controlled engineering of a specific surface properties (functionalization), magnetic nanoparticles (MNPs) become special features for desired applications, e.g., bioassays for detection of binding compartments, e.g., antibodies. The characterization as well as a measurement of such binding states is of high interest and limited to highly specific techniques such as ELISA (Enzyme-linked Immunosorbent Assay) which are inflexible, expensive and time-consuming. Established as well as novel upcoming methods, such as ACS (AC-susceptometry) or MPS (Magnetic-Particle-Spectroscopy), exploit the magnetization response of functionalized MNP ensembles to assess specific information about the MNP mobility within their environment as well as the conjugations of chemical or biological compounds on their surface. Both methods have shown promising results in the past but cannot reach the sensitivity of above-mentioned techniques.

Methods

We used a novel method based on modified MPS method, that is sensitive to minimal changes in mobility of MNP ensembles outperforming the sensitivity of MPS and ACS by 6 and 5 orders of magnitude. This facilitates robust and easy-to-handle measurements of minimal changes in the diameter of MNPs, e.g., resulting from SARS-CoV-2 antibodies binding to the S1-antigen on the surface of functionalized MNPs. With a validated sensitivity of 8.5fM SARS-CoV-2-S1 antibodies (Figure), the proposed technique is competitive with the sensitivity of commonly used ELISA methods but provides more flexibility, robustness and rapid measurement times of milliseconds. Our method thus paves the way for deep insights into complex and rapid binding dynamics of functionalization chemistry and will revolutionize not only the point-of-care diagnostics but also impacts other fields in research and industries.



Results

The single experiments of the measuring sequence (ref, 1:2,000, 1:5,000, 1:10,000, 1:20,000 (equalling 8.5fM), neg. control) show a clear trend in signal of the 7th higher harmonics. Each sample was measured 5times without any averaging (acquisition time 10ms each).

Reduced Steering Performance in Magnetic Drug Targeting Induced by Shielding Arising from Accumulation of Particles

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Introduction

Magnetic Drug Targeting is a new approach in cancer therapy, where magnetic nanoparticles are used as carriers for cancer drugs. Commonly, external magnets are employed for steering the particles inside the blood vessels towards a desired direction. However, an unwanted side effect of the steering is the accumulation of the particles underneath the steering magnet. Many researchers address the number of accumulated particles, but, to the best of the authors' knowledge, the retroaction of the accumulation profile on the generated magnetic field and, therefore, on the magnetic steering force, has not been investigated so far. Thus, in the proposed study, the influence of the accumulation profile on the magnetic force was numerically investigated.

Methods

Therefore, a 2D model of a blood vessel with particles assumed as an accumulation profile and a nearby magnet was examined. Moreover, the length, thickness, and effective susceptibility of the approximated accumulation profile and the magnet size were varied.

Results

The results reveal that the field distribution is significantly affected, especially for high effective susceptibilities. The initially applied profile amplified the magnetic force; however, when the profile accumulated, it reduced the force up to 50 %.

Conclusion

Overall, the results reveal that the retroaction of the particle distribution on the magnetic field must be considered in a simulation model.

Ultrasound-Mediated Cavitation of Magnetic Nanoparticles for Drug Delivery Applications

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Introduction

Superparamagnetic iron-oxide nanoparticles (SPIONs) can serve as drug carriers for drug delivery purposes. They allow chemotherapy with reduced side effects by particle accumulation in the tumor area. The accumulation is stimulated by magnetic fields applied from outside the body. After transportation to the target tissue area (tumor) via the bloodstream, the particles penetrate the malignant tissue utilizing the EPR (Enhanced Permeability and Retention) effect. Further relevant drug delivery concept features are therapy process monitoring by nanoparticle density mapping and locally triggered drug release.

For monitoring SPIONs, their magnetic properties are utilized in special ("magnetomotive") ultrasound modalities. This method does not trigger local drug release. So-called "sonosensitive" non-magnetic polymer-based nanoparticles generate inertial cavitation in a focused ultrasound wave field. By exploiting this effect, ("passive" or "active") monitoring of these particles and their respective local drug release is possible. Exploiting cavitation with SPIONs would also allow monitoring and local drug release. However, little is known to date about the sonosensitivity of SPIONs with respect to ultrasound-induced cavitation in the context of monitoring and local drug release.

Methods

We have investigated the cavitation behavior of SPIONs under the influence of focused ultrasound at a frequency of 750 kHz with power used in diagnostic ultrasound. Broadband cavitation noise was detected and evaluated in an ultrasonic frequency range of 6 to 6.5 MHz by determining the voltage spectral noise density as a measure of cavitation level. Water (low cavitation) and talcum (high cavitation) served as comparison media.

Results

We were able to identify some particle types (compact nanoclusters, approx. 50 nm, lauric acid surface layer) that exhibit a high degree of cavitation allowing therapy monitoring.

Conclusion

Some types of SPIONs are suitable for drug delivery process monitoring utilizing cavitation. The use of cavitation in terms of local drug release enhancement will be investigated next.

Magnetic extraction of calcium oxalate crystals with iron oxide nanoparticles

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Abstract

Residual fragments can remain after kidney stone extraction which may necessitate another intervention. Magnetic nanoparticles (MNP) can be applied due to their properties of being able to bind to residual fragments and to be extracted by an external magnetic field. Calcium oxalate crystals and magnetic nanoparticles have been synthesized, characterized and used for binding and magnetic separation studies. The separation is validated by simulation and experimentally. MNP bind covalently to the fractals and a magnetic extraction of calcium oxalate fractals is possible. The agglomeration of MNP can be induced with the addition of salt which improves the extraction process. This proof-of-concept study is the fundament for a new way of stone extraction and can pave the way for new procedures in urology.

Focus Session:
Biomedical Control Systems

The Kv10.1 voltage-gated ion channel modeling based on control system theory

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Introduction

This work presents a control system theory-based modeling approach for the voltage-gated ion-channel Kv10.1 at different temperatures. Kv10.1 is commonly expressed in cells of the central nervous system and brain, but also in non-excitable cells, with aberrant expression and activity associated with various types of cancer cells that promote proliferation and thus tumor progression. According to systems and control theory, it was assumed that the voltage-gated channel Kv10.1 is a linear time-invariant system and, as such, exhibits dynamic behavior. The experimental results show that Kv10.1 operates as a first-order model based on the input voltage step protocol and the measured macroscopic ion current output.

Methods

To construct the model, we used the so-called system identification method. System identification is carried out to develop a mathematical system model from the input and acquired output data. The model can be estimated when the equations and correlations are unknown, but measure input and output values can be measured.

Results

The different behavior of the selected ion channel Kv10.1 at different temperatures is shown. We assumed that all initial conditions were equal to zero. Therefore, we estimated the transfer function in the period from 0.1-0.6s for the three models at 15 °C, 25 °C, and 35 °C. The models are given by equations and converted into the general form of first-order systems. The two main parameters of the models gain (K) and time constant (t) are developed and discussed.

Conclusion

As shown in this work, control system theory and system identification methodology can be used in mathematically modeling of the dynamic behavior of voltage-gated ion channels. The behavior of the studied models of the voltage-gated ion channel strongly depends on temperature. The models are also controllable and observable, so that classical, robust, or fuzzy control algorithms can be applied.

Microfluidic device using rapid drug gradient formation for bacterial resistance prediction

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Introduction

Antibiotic resistance is one of the leading global health issues, predicted to kill more people in 2050 than cancer. Current measures to tackle antibiotic resistance include prudent use, new drug development, and rapid diagnostics. While these are all necessary, they are not sufficient. In contrast, the proposed microfluidic device uses rapid antibiotic gradient formation to predict the dynamics of resistance evolution before antibiotics are used.

Methods

Bacterial resistance evolves much faster when the bacterial population is exposed to a concentration gradient, and resistance can evolve even at very low doses due to high selection pressure.

The microfluidic system utilizes convective and diffusive mass transfer mechanisms for the rapid formation of antibiotic gradients. Within a convection unit, antibiotics, nutrient media and diluents are mixed in a porous medium, and thus steady-state gradients can be formed within minutes. The diffusion unit above consists of an agar culture medium. Antibiotic gradients diffuse into the culture medium through a contact surface. This causes exposure of the bacterial population to all possible antibiotic concentration gradations or even combinations of two antibiotics. Evolutionary adaptation is continuously observed and allows immediate assessment of the sustainability of an antibiotic strategy.

Results

The microfluidic approach allows the generation of stable antibiotic gradients in a culture medium within hours. Gradient formation is numerically simulated with computational fluid dynamics and visualized and validated by fluorescent fluids. Experiments demonstrated that resistance evolution of E. coli MG1655 against Ampicillin within the microfluidic. The detected minimal inhibitory concentration rose from 2 µg/ml to 4 µg/ml of Ampicillin.

Conclusion

While the proposed method showed promising results in preliminary experiments using model organisms, further validation experiments using different bacterial strains and antibiotics need to be performed. In addition, it is planned to dynamically change the gradients within the microfluidics, to allow in-vitro simulation of pharmacokinetics within the human body.

Feedback Linearization of a Blower in an Anesthesia Workstation

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Introduction

Radial compressors, Blowers, which are often used in modern devices for medical ventilation, are known to have nonlinear dynamics regarding the generated pressure. To make them accessible for linear control theory their model needs to be linearized, which is usually done using Jacobian linearization. Such a linearization is only valid close to a fixed equilibrium point, which is impractical for applications, where the system is to follow a reference. Therefore, a controller to control the blower's output pressure is designed by using feedback linearization in this paper.

Methods

This paper uses a nonlinear gray box model of a blower driven by a brushless direct current (BLDC) motor to design a controller based on feedback linearization. The model consists of a state space model with two states, for the BLDC and a nonlinear output equation for the pressure at the blower's outlet considering rotation speed and flow through the blower. The controller is designed using input-output feedback linearization to approximate linear closed loop behavior of a first order system. The system is linearized based on the Lie-derivatives of the proposed model and state feedback. Pole placement is used for tuning the closed loop performance.

Results

The controller is evaluated regarding reference tracking and disturbance rejection in simulation and on a demonstration device using a predefined test sequence in an experimental setup. The obtained time constants are compared to the system behavior targeted in the design process. The evaluation showed that an approximate linear closed loop behavior was achieved and that feedback linearization is a valid choice for controlling the blower in medical devices.

Conclusion

Feedback linearization is generally capable to ensure reference tracking and to approximate the desired closed loop behavior of a first order system. Thus, it is a promising approach for the control of the ventilation unit's blower.

Real-time system for physiologically controlled closed-loop neurostimulation

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Introduction

Neuronal oscillations are physiological processes that can be pathologically disturbed. Scientific or therapeutic modulations of these oscillations require locking to endogenous frequency and phase conditions.
We introduce an integrated modular system capable to measure, analyze and modulate electro-physiological processes in real-time.

Methods

Our system records ExG data, e.g. EEG, EMG, from modules with eight channels with a sampling rate of 1 ksps and a resolution of 24 bit. We recorded bipolar EEG between positions F3 and P3. Data were processed after every sample, analyzing a selected frequency with a resolution of 2 Hz using the Goertzel algorithm on the samples of the last 500 ms, returning the current phase. When the target phase was detected, a four-channel digital input / output module connected to a TMS stimulator via BNC-TTL released a trigger. The rising edge of the trigger signal initiated a TMS impulse at a DuoMAG XT-100 (DEYMED Diagnostic GmbH, Weimar, Germany) at 120% RMT over position C3 with 45° tilt in anterior-posterior direction. The resulting motor evoked potential was recorded at the Abductor Pollicis Brevis with surface electrodes in bipolar montage by the ExG module.

Results

Our integrated modular system ensured a 2 ms hardware round-trip-time from data recording to trigger release. The frequency dependent phase shift was below 10°degrees. The recorded MEPs were modulated by the TMS dependent on the targeted frequency and phase.

Conclusion

This work presents the feasibility of real-time data analysis and release of neuro-modulatory stimulation. The integrated system enables physiological closed-loop control experiments on a stable real-time regime.

Evaluating the Normalized Excretion Rate of Intensive Care Patients Using a Quasi-Dynamic Transfer Function

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Introduction

Fluid overload in intensive care patients is associated with increased mortality and comorbidities. Hence, adequate fluid management remains challenging in daily clinical practice. We aim to explore the relationship of our novel concept coined normalized excretion rate with therapeutic parameters of fluid management in critically ill patients.

Methods

We present a retrospective study from a subgroup of elective cardiac surgery patients admitted to the ICU (Fluidatex study) using a system theory-based algorithm to evaluate the patient's response to treatment. Our approach estimates the patient's response to fluid administration and/or diuretic treatment with a transfer function based on the relationship between fluid intake and fluid loss. Time dependent parameters including dynamic gain and time constants are computed using a sliding window approach. The dynamic gain of the transfer function represents the excretion rate for a constant intake of one litre and is used as a digital biomarker.

Results

A total of 614 patients with a minimum duration of 24 hours of the evacuation phase according to the ROSE model by Malbrain were included. In total, 90% showed an average dynamic gain greater than 1 during the entire evacuation phase, indicating usability of the parameter. We analysed 1071 events of diuretic medication based on the entirely available medical records data. The normalized excretion rate increased after treatment in 88% of all events. 12% continued to have a gain of less than 1 for different medical reasons. Time constant and drug administration proofed not to be correlated.

Conclusion

The results of our concept of a modelled normalized excretion rate in critically ill patients indicate an association of patient response to diuretic treatment. Thus it may serve as novel biomarker to support intensivists in fluid management. Further studies should focus on assessing its performance in a larger, prospective, case-control-based patient cohort.

Clinical Pilot Trial with a Physiologic Control Algorithms for Left Ventricular Assist Devices

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Introduction

Left ventricular assist devices (LVAD) are implanted in late-stage heart failure patients. Currently, LVAD therapy is adapted to the patient by setting a constant pump speed (CS). However, this strategy does not adequately adapt to changing physiological demands. This results in periods of excessive support, potentially leading to inflow cannula suction, and periods of insufficient support, leading to worse therapy outcome. Automated physiological control (PhC) algorithms may increase pump support when it is needed and decrease support when it would otherwise be excessive.

Methods

In a clinical pilot trial investigating a novel control algorithm, six patients implanted with a centrifugal LVAD (HVAD, Medtronic plc, MN, USA) underwent a standardized protocol consisting of postural transition from supine to standing position, Valsalva maneuver and submaximal ergometry for a total of 13 trial days. The patients completed this protocol in CS and with activated PhC in an outpatient setting or at the intermediate care facility. Pump data was collected and suction burden as well as pump flowrate compared.

Results

Lower speeds in PhC mode compared to CS during suction-prone scenarios such as Valsalva maneuver straining (median: -90 [interquartile Range: -153,61] rpm) or during standing up (-112 [-155,51] rpm) reduced suction burden in most patients for a median difference of (-2 [-6,0] suction events/minute) and (0 [-10,2] suction events/minute) respectively.

In the late phase of submaximal bicycle ergometry pump speed was increased compared to CS by 86 [31,193] rpm resulting in an increased pump flowrate of 0.2 [0.0,0.5] L/min. However, in two patients speed could not be increased more than 100 rpm compared to CS without triggering suction.

Conclusion

The PhC allows additional adaptability to patient hemodynamics. Pump speed decreases during rest and increases during exercise resulted in less time spent in inadequate support levels. However, patient specific differences have to be taken into account.

Blood Glucose Control in Critically Ill Patients

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Introduction

Hyperglycemia and high glycemic variability are common in critically ill patients and can be caused as a secondary reaction to trauma, surgery, or diseases. Several studies associate stress-induced hyperglycemia with increased mortality and duration of stay in the hospital. Insulin therapy can reduce the risk of hyperglycemia and thereby improve patient recovery. The proper blood glucose target is discussed controversially as an overtreatment with insulin can lead to life-threatening hypoglycemia. The development of models and control algorithms for automatized insulin therapy can assist clinical staff and improve the quality of treatment. Different types of control strategies are compared for an optimal glucose therapy in this work.

Methods

A model describing the blood glucose metabolism in critically ill patients was used to study the performance of different control strategies for an automatized insulin therapy. A PID controller, state feedback controller, and model predictive controller were designed. A Kalman filter was used to estimate necessary states. The test scenario comprised nutrition and changes in insulin sensitivity. The performance of the controllers was compared with established clinical protocols.

Results

All control algorithms show a good control performance without steady-state state deviation from the blood glucose target value. However, the PID controller showed high blood glucose values after nutrition. Furthermore, after nutrition, already infused insulin could lead to hypoglycemic events. The state feedback controller showed an improved performance. As expected, the MPC showed the best performance. Disturbances such as nutrition could be accounted for in advance. Thus, hypoglycemic events due to the prolonged effect of applied insulin could be prevented.

Conclusion

The comparison of controllers gives a good overview of the strengths of different control strategies. Current protocols and PID controllers profit from their easy implementation. However, more elaborate control strategies yield better performance but require a better understanding of the underlying dynamics.

Control of a blower-based lung simulator for testing of mechanical ventilators

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Introduction

Automated functions are becoming increasingly important in mechanical ventilation, which react to patient behavior during ventilation and improve lung- and diaphragm protective ventilation therapy largely independent of the operator's experience. These functions must be extensively tested for a wide range of parameter combinations representing the lung mechanics to ensure patient safety. Therefore, this paper presents a first approach of an experimental setup with an underlying control concept for a lung simulator without volume limitation, which is capable of reproducing simulated patient behavior in the form of the occurring airflow and airway pressure at the system's outlet.

Methods

The general design of the lung simulator setup is based on the work of F. Bautsch et al. [1] and is modified slightly with regard to the underlying control concept. To illustrate this concept, a single-compartment model is used to simulate the virtual patient behavior. The lung model calculates the reference airflow of the patient that will occur due to the induced pressure difference created by the virtual patient or through a device under test at the system's outlet representing the conditions at the airways of the virtual patient.

Results

The first experimental setup, generating breathing cycles of one virtual patient for mandatory and assisted ventilation for pressure-controlled and volume-controlled modes, shows that the system can generate a quite realistic behavior of the simulated patient at the system's outlet with regard to the desired airflow.

Conclusion

The simulation results for the ventilation show that the presented system with the underlying control concept is capable of creating the desired behavior of a virtual patient for all tested ventilation modes at the system's outlet during ventilation through a device under test. Further development of this system can lead to a lung simulator that provides an automated way of testing mechanical ventilators.

Investigation of energy configuration in thermal ablation of malignant liver tumors

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Introduction

Percutaneous thermal ablation is an efficient treatment option for patients suffering from unresectable malignant liver tumors. However, due to unequal clinical context, the treatment is largely unstandardized and intended only as palliative care. For instance, tumors that are larger in size (> 3 cm) or irregular in shape, and those in vicinity to critical structures, are difficult to treat safely and efficiently with conventional ablative techniques. Thus, to account for this shortfall, we aim to regulate ablation energy with respect to a robotically driven needle position, and based on the shape of the tumor. Hereby, we describe a planning model for configuring the energy based on the tumor shape and investigate its applicability.

Methods

The model is based on the heat transfer equation. Ablation energy is calculated depending on the thermal properties of the patient model (tissue/phantom), temperature change, and the shape of the tumor. The model does not compensate for heat dissipation, absorption nor transfer by convection. To evaluate its applicability, the model was initially validated on a dataset of volumes ablated in a polymer phantom with predefined energies.

Results

There is a strong correlation between the energy proposed and the width of the ablated volumes (r2 = 0.98); however, lengthwise, it shows a weak dependance (r2 = 0.39). When compared to the energy used versus energy proposed, the model results in good correlation, but a wide confidence interval (r2 = 0.78, RSE = 6.97 kJ).

Conclusion

We describe a model for configuration of ablation energy based on the tumor shape. The model could serve as an initial step into a confluent ablation treatment, where we are able to treat even more complex ablation cases with reproducible clinical results, ultimately thriving to boarder patient inclusion and treatment standardization.

Mathematical modeling and control of the pituitary-thyroid feedback loop: Optimal hormone replacement therapies in hypothyroidism

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Introduction

One major disease associated with the pituitary-thyroid feedback loop is Hashimoto's thyroiditis, which goes along with hypothyroidism. This disease is usually treated with thyroid replacement hormones resulting in a so called levothyroxine (L-T4) monotherapy, or, if liothyronine (L-T3) is additionally prescribed, in an L-T3/L-T4 combined therapy. However, several problems with the current therapeutic approaches occur. First, a trial-and-error approach is employed to determine the correct dosages of a patient which leads to a long time until the correct dosages are found. Second, inadequately high dosages can generate symptoms of hyperthyroidism. Third, clinical studies report conflicting results concerning the benefit of an L-T3/L-T4 combined therapy compared to the L-T4 monotherapy to treat hypothyroidism.

Methods

To tackle these issues, we develop a mathematical model of the pituitary-thyroid feedback loop, including an oral intake of L-T4 and L-T3. Subsequently, we develop optimal thyroid hormone replacement strategies by implementing a model predictive controller (MPC) for the L-T4 monotherapy and the L-T3/L-T4 combined therapy, considering different genetic variants as well as different frequencies of medication intake.

Results

The application of MPC allows to find the correct dosage much earlier and inhibits hyperthyroid hormone concentrations. Additionally, the results suggest that an L-T3/L-T4 combined therapy yields slightly better hormone concentrations than the L-T4 monotherapy. In case of specific genetic variants, the differences between both types of therapy can become substantial. Two daily intakes of L-T3 could be the best trade-off between stable hormone concentrations and inconveniences for the patient.

Conclusion

The application of MPC is a very promising approach to determine optimal thyroid hormone replacement strategies. The dependence of the success of the therapy on genetic variants could explain the conflicting results from clinical studies.

Unprecedented Accuracy and Robustness in IMU-based Orientation State Estimation Through Nonlinear Filtering and Recurrent Neural Networks

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Introduction

Introduction Inertial orientation estimation (IOE) is a crucial and recurring step in inertial motion tracking applications for joint angle estimation, velocity and position estimation, and visualization. The accuracy of state-of-the-art IOE algorithms highly vary depending on environment, motions, and hardware. Tuning IOE algorithms for specific application contexts requires ground truth data that is almost never available. In practice, state-of-the-art IOE algorithms are applied with default parameterization and root mean squared errors that range from 5.3° to 16.7°. Robust and out-of-the-box IOE is thus still not achieved.

Methods

We present VQF and RIANN, a nonlinear filtering approach and a recurrent neural network-based (RNN) approach, which are publicly available and allow for real-time capable and plug-and-play IOE. RIANN incorporates IOE domain-specific advances in RNNs and is trained on publicly available datasets to obtain robust parameter-free 6D orientation estimation. VQF exploits a nonlinear and decoupled filter design for simultaneous 6D and 9D IOE with a novel inclination update step. We thoroughly validate the performance of both IOE methods on a broad set of benchmark datasets, and with respect to many highly competitive and online available IOE algorithms.

Results

RIANN outperforms all state-of-the-art IOE algorithms with average inclination errors of 1.32°, where existing methods yield average inclination errors up to 6.3°. VQF even outperforms RIANN and yields on average double the accuracy for 9D IOE, with respect to all state-of-the-art IOE algorithms. In stark contrast to existing algorithms, both methods show excellent generalizability across different hardware, sampling rates, motion characteristics, and application contexts without the need for retraining or adjusting hyperparameters.

Conclusion

We presented two methods that achieve robust and out-of-the-box IOE with unprecedented accuracy. Due to their true plug-and-play usability and significant improvements in IOE accuracy, RIANN and VQF have the potential to become easy-to-use tools that will lead to many advances in existing and unexplored inertial motion tracking applications.

Focus Session:
Biomedical Data Analytics

Explaining Predictions of Decision Support Systems in Healthcare

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Introduction

Artificial Intelligence (AI) methods, which are often based on Machine Learning (ML) algorithms, are also applied in the healthcare domain to provide predictions to physicians and patients based on electronic health records (EHRs), such as history of laboratory values, applied procedures and diagnoses. The question about these predictions "Why Should I Trust You?" encapsulates the issue with ML black boxes. Therefore, explaining the reasons for these ML predictions to physicians and patients is crucial to allow them to decide whether the prediction is applicable or not. In this paper, we explained and evaluated two prediction explanation methods for healthcare professionals (physicians and nurses).

Methods

We compared two model-agnostic explanation methods based on global feature importance and local feature importance. We evaluated the user trust and reliance (UTR) for the explanation results of each method in a user study based on real patients' electronic health records (EHR) and the feedback of healthcare professionals.

Results

Based on the user study, we observed that both methods have strengths and weaknesses according to the patients' data, especially based on the data size of the patient. When the amount of data is small, global feature importance is enough to use. However, when the patient's data size is big, using a local feature importance method makes more sense.

Conclusion

As future work, we will develop a hybrid explanation method (by combining these methods automatically with a smart setting) to obtain higher and more stable performance results in terms of user trust and reliance.

Different montages and dimension reduction methods for EEG signal analysis of Interictal Epileptic Discharges

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Introduction

In clinical applications, different montages of the recorded electroencephalography (EEG) signals are used. A mathematical analysis of the data raises the question of which montage is most suitable. Here, we investigate the impact of different montages and dimensionality reduction methods on EEG signal analysis of Interictal Epileptic Discharges (IED). Dimensionality reduction is performed to detect low-dimensional mathematical structures in the data and use them as an additional feature for detecting IEDs.

Methods

In our study three different dimensionality reduction methods are used: Dynamical Component Analysis (DyCA), Principal Component Analysis (PCA) and Uniform Manifold Approximation and Projection (UMAP). Both, DyCA and PCA factorize the input data matrix. DyCA leads to a generalized eigenvalue problem focusing on the dynamical components of the signal. PCA relates the data matrix to algorithms such as singular value decomposition (SVD). In contrast, UMAP is based on the t-distributed stochastic neighbor embedding algorithm (t-SNE). In this work, publicly available EEG data of IEDs and non-epileptiform control events such as background from the Temple University Hospital is investigated. The raw data is processed with different montages and filtered using a bandpass filter. The bipolar, the average and the reference montage are examined.

Results

Our investigation shows that in the case of IEDs significant patterns in the three-dimensional PCA and DyCA representations of the signals can be visually detected. On the other hand, the different montages of the EEG signal generally have only a minor influence on the observed three-dimensional structures.

Conclusion

These visual findings will be further investigated in a data-driven analysis framework. The impact of montages and dimensionality reduction methods on the resulting trajectories in phase space and classification accuracy of IEDs will be studied in more detail on a quantitative basis with e.g., topological based data analysis (TDA).

Revealing hidden information: Lipid ω-double-bond position detection in complex biological LC-MS/MS data

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Abstract

Lipids are central components of life: they constitute biological membranes, act as signaling molecules, and are used as energy sources. Enzymatic activity and signaling features of these molecules depend on the attached fatty acids, which are characterized by their carbon chain length, the number of carbon-carbon double bonds (DB), and the positions thereof. While established mass spectrometry (MS) based analytical methods are able to identify the former two structural aspects, the detection of DB positions remains a challenge. State-of-the-art analytical techniques capable of resolving lipid species on the DB position level have several drawbacks, such as decreased ion yield and undesired side products due to reliance on derivatization reactions or the need for invasive changes to the instrument, to mention a few. Moreover, all existing methods highly increase the complexity of MS spectra, subsequently impeding the computational analysis in complex mixtures by standard workflows.

Here we introduce a method, which - in contrast to existing analytical workflows - is able to detect the ω-DB position on a standard liquid chromatography tandem-MS (LC-MS/MS) instrument without the need for prior DB-derivatization. Integrated in the Lipid Data Analyzer (LDA) software, this new approach facilitates the automated identification of lipid molecular species ω-DB positions based on accurate calculation of expected retention times, calibrated by cell-produced isotopically labeled lipids featuring defined ω-positions.

We demonstrate the feasibility of our method by correctly identifying ω-3, ω-6, ω-7, ω-9 and ω-10 lipid molecular species in RAW264.7 cells and in NIST SRM 1950 human plasma.

By facilitating the characterization of complex lipid species on the ω-DB position level, our method is capable of increasing the structural details acquired on established LC-MS/MS setups without increasing complexity, thus allowing for an easy intergration with currently used high-throughput systems in food industry, pharmacy and medicine.

KneTex - Improvements to classification methods for a sensor system for rehabilitation after ACL surgery

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Introduction

Injuries and the associated surgery to the anterior cruciate ligament (ACL) can often trigger unpredictable effects, such as the so-called giving way effect, which is an uncontrolled buckling of the knee joint. For this purpose, the KneTex project has developed a smart textile-integrated sensor and actuator bandage system to record the movement of such patients and to monitor and support the rehabilitation process.

Methods

Long-term monitoring and analysis of the movement data will identify patterns or gait types that can lead to a giving way effect. This paper describes the recent developments of the random forest model-based motion classification system developed within the project.

Results

Improvements have been achieved by reducing the number of features needed by 25% using feature importance analysis, speeding up the computation time by 14%, and increasing the classification efficiency.

Conclusion

Feature elimination is an useful tool to improve classification systems in settings where feature count is high and feature importance analysis contributed by improving our understanding which sensors of our system are important for the motion classification task.

A systematic review of recorded technical settings used in bipolar and monopolar transurethral resection of bladder tumors

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Introduction

High-frequency (HF) surgery (both monopolar and bipolar application) has been established in medicine for decades and is very popular in transurethral (minimally invasive) surgery. However, the technical settings of generators are almost exclusively based on empirical data. So far, making a well-founded statement about a possible impact of technical parameters in HF surgery is nearly impossible.

Methods

Therefore, the aim of this research was to systematically review the published data for monopolar and bipolar transurethral resection of bladder tumor (mTURBT/bTURBT) to find out, whether the publications consider both sufficiently, technical parameters and physical parameters.

Results

Since most publications report technical parameters, it can be assumed that other authors also attach importance to these. Additionally, recent developments in HF generator technology show that manufacturers also seem to know about a minimization of tissue damage when adapting energy transfers dynamically. Nevertheless, it is shown that although technical parameters are reported, they have been insufficiently considered in analyses so far.

Conclusion

It is shown that although technical parameters are reported in publications, they have been insufficiently considered in analyses. Therefore, an analysis not only considering physiological parameters but also including technical parameters must be performed. The two technologies (monopolar and bipolar) should be considered separately, since the reported differences are always based on the application technique and not on technical (generator) settings.

Inference runtime of a neural network to detect atrial fibrillation on customized RISC-V-based hardware

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Abstract

As a common heart arrhythmia, atrial fibrillation (AF) is considered to be responsible for up to 15 % of all strokes. For the diagnosis of AF, long term electrocardiogram (ECG) recordings are widely used. These recordings are obtained by Holter monitors or state-of-the-art patch ECG devices. Energy efficiency is of critical importance to enable the use of the patch ECG devices for several days without changing batteries or patches, while maintaining a small and lightweight design. Energy consumption of microcontrollers strongly depends on their operating frequency. Hence they benefit from a minimal software run time in clock cycles. In this work the impact of customized hardware in combination with structural optimization on inference runtime of a neural network (NN), for the detection of AF and embedded in a patch ECG device, is investigated. The combination of optimized NN structure with the optimized hardware requires only 13% of the runtime compared to the original NN, while the accuracy is increased by 0.5 percent points.

Scaling Methods of the Pelvis without Distortion for the Analysis of Bone Defects

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Introduction

For the development of new types of hip implants for acetabulum revision, it is beneficial to analyse the acetabular defects of the indication group in advance. In order to be able to specially compare the bone defects with each other, a normalisation and accompanying scaling of the pelvis is necessary. Uniform scaling is required so that the bone structures are not distorted

Methods

In the following study, three scaling methods based on the minimal bounding box and sphere principle are compared with a method using 14 landmarks on the pelvis.The landmark method is applied to determine the true scaling factor. For the comparison of the different methods, 40 female pelvic models with an acetabular defect are analysed.

Results

In the comparison of the scaling methods, the method using minimal bounding spheres shows the least deviation from the landmark method (mean difference 3.30 +/- 2.17 %).

Conclusion

Due to the fact that no preprocessing (definition of the landmarks) is required and the fast implementation of the algorithm, the minimal bounding sphere is to be preferred to the landmark method for a fast size estimation.

Focus Session: Biomedical Engineering Beyond Borders

On the set up of a double degree programme in the field of biomedical engineering in northern Iraq

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Introduction

Global challenges such as climate change, food supply or medical care do not stop at national borders. Sustainable solutions require cooperation and progress in internationalization. Here we report on DAAD funded projects started to foster the cooperation between the University of Duhok (UoD), Autonomous Region of Kurdistan, Iraq, and the Technische Hochschule Mittelhessen (THM) in the field of biomedical engineering (BME) about 10 years ago.

Methods

To promote understanding, cultural and scientific exchange, mutual visits, lecturer stays and conferences were held several times a year. In addition, two summer schools were organised for a targeted exchange between Iraqi and German students and teachers. Due to the global corona pandemic, face to face events were replaced by Video conferences. To ensure a sustainable cooperation not only in the field of research but also in teaching, a contract for a double degree programme was worked out and ratified.

Results

As a result of the ongoing cooperation and to implement the ratified double degree programme, the department of BME was set up at the UoD. With the support of the Kurdish government in Erbil, the BME course could be started in 2018/19 winter semester. The total number of students is 92. 21 Iraqi students came to Giessen in March 2022 to prepare for their practical phases, i.e., professional internships, and their bachelor theses, which they want to carry out nationwide in industry, clinics or research institutions.

Conclusion

To implement the goal of internationalization set by the German government, everyone must be aware of a whole series of stumbling blocks, e.g., legal framework, bureaucratic hurdles, financing, language barriers and cultural differences. All these challenges can be solved if both sides are willing and persistent, so that both partners benefit from sustainable solutions that can form the basis for further cooperation.

Health Care facilities in Tanzania lack professional hospital engineers

Hermann Gilly

Introduction

In strategic plan 2014-2019 the Tanzanian Ministry of Health and Social Welfare identified “Human Resource for Health” to be the key component for “delivery of quality health and social welfare services, with the ultimate goal of having effective health services in a dispensary at every village, a health center at every ward and a district hospital at every district”. The 2016 development plan announced the construction of 67 new health facilities, in part improving existing district hospitals. In these strategic plans there is little notice in respect to maintenance of biomedical equipment.

Methods

The present investigation focuses on major health facilities (university hospitals) and district hospitals. The analysis is based both on documents released by MoHCDEC (Ministry of Health, Community Development, Gender, Elderly and Children) and on personal experience in selected hospitals.

Results

According to the governmental specifications district hospitals are supposed to have a minimal total staff (approx. 200) including few (biomedical) technologists. The lack of human resources for health, particularly doctors, is nothing new: district hospitals hardly find the recommended number of doctors. 75% Tanzanians live but only 26% of doctors serve in rural areas. This situation mirrors in respect to clinical and hospital engineers. In 2017 the Tanzanian minister of education reported a shortage of 7000 biomedical engineers. A substantial relief is hardly to be expected in the near future as in the major center for biomedical engineering education in Dar Es Salaam, the Institute of Technology, about 150 students per year finish their study. Thus the gap between the governmental efforts and reality remains evident.

Conclusion

In respect to biomedical engineering, extensive knowledge transfer, supervision and training to increase the provider’s skills will become more important than financially supporting the installment of technologically most advanced medical equipment in an inadequate infrastructure of district hospitals as well as in university health centers.

Ukraine Digital - Virtual Cryomicroscopy Research and teaching video tools with Kharkiv National University of Radioelectronics (NURE)

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Abstract

Our joint DAAD-project "Virtual Cryomicroscopy" started 2 years ago. Due to the war situation, we successfully applied for the project "Ukraine Digital - Securing Study Success in Times of Crisis", where we will provide teaching materials es-pecially experimental videos with Ukrainian subtitles in areas of Biomedical Engineering.
Virtual laboratories (VL) can solve many problems associated with laboratory workshops through the implementation of a virtual surface. VL are replacing real devices with computer models, endowing future engineers with necessary practical skills and knowledge. They allow to work with lab equipment without exposing it to any damage. The student observes a normal workflow and has the opportunity to study its structure. Additionaly, the use of VL's contributes to the quality of educa-tion. It becomes possible to increase the amount of theoretical knowledge obtained at lectures by repeating it in a more con-venient form outside the educational institution.
The VL is a software-simulated enviroment that allows experiments without direct contact with the device. It is a 3D-model of a digitized laboratory with software for user interaction. A training mode is implemented, where a tasks must be complet-ed. The user clicks on the element of interest and a pop-up window appears that contains information about this object, video information and detailed datasheet of the item. After the user studied all the elements, a window will pop up to con-firm the successful completion of the training mode and the next task can be completed.
Moreover, we start with digital seminars, where videos of our devices and experimental studies will give further understanding in practical lab work. Students at NURE subtitle the videos into Ukrainian language. The videos will be post-processed by our partners at "Leibniz Joint Lab: Data Science & Open Knowledge" at LUH.

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Focus Session:
Biomedical Optics & Photonics

Data-informed imaging: How radiography and shape models support endoscopic OCT imaging of the middle ear

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Introduction

Optical coherence tomography (OCT) is an interferometric imaging technique based on near-infrared light, that provides volumetric information of tissues with up to micron resolution. Using dedicated endoscopic optics in the sample arm, OCT enables the assessment of the eardrum and middle ear in vivo. However, revealing the ossicles is often limited due shadowing effects of preceding structures and, thus, the 3D impression is rather incomplete and difficult to interpret.

Methods

Using a custom endoscopic OCT system with a wide field of view, we acquired volumetric data sets of temporal bone specimens which had been previously examined with micro-computed tomography (µCT). Based on both manual and automatic segmentation including labels of the identified structures, the OCT and µCT volumes were spatially registered for comparison. Furthermore, we used a statistical shape model (SSM) that was derived from the µCT data sets and fitted the model to the OCT volumes based on the available degrees of freedom.
Additionally, we preoperatively performed OCT imaging of a patient receiving a cochlea implant and compared the results with a postoperative cone beam CT, as µCT imaging is not feasible in vivo.

Results

Assuming distortion-free µCT volumes as reference, the distortion-corrected endoscopic OCT volumes proved to be suitable for the 3D assessment of the ossicles. Due to the wavefront distortion and refraction of light passing the tympanic membrane, the visible parts of the ossicular chain appear in the correct position with slight deviations, blurring and reduced signal. Uncertain allocations, e.g. identifying the long process of the incus, are significantly improved by additional shape information.

Conclusion

Endoscopic OCT shows a high potential for clinical middle ear diagnostics. Shortcomings due to the limited optical penetration can be compensated to some extent by a priori knowledge of the anatomy and augmentation with other imaging data, e.g. regularly performed radiography.

A long-range common-path optical coherence tomography system for distance sensing in minimally invasive retinal surgery

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Introduction

For minimally invasive fiber-based applications the approach of common-path optical coherence tomography (CP-OCT) is frequently used due to its robustness and independence of fiber length. Here, the back reflection originating from the end surface of the measurement fiber acts as reference signal. However, in some applications - e.g., in a forceps for membrane peeling - the measurement fiber cannot be mounted directly at the distal end of the instrument, resulting in a reduced OCT measurement range. In this work, a long-range CP-OCT setup is presented which enables shifting the measurement range to an arbitrary position, for example to the tip of an instrument.

Methods

A setup was developed for introducing a pathway difference between two beams entering the OCT fiber coupler, employing a beam splitter, two mirrors mounted at different distances from the beam splitter, and two fiber collimators. The pathway difference between the two mirrors is adjusted to achieve the desired shift of the measurement range. The measurement fiber is polished and gold-coated to obtain a back reflection that can be used as reference signal for OCT independent of the surrounding medium.

Results

In-vitro distance measurements were successfully performed using gold-coated measurement fibers in a water-filled model eye serving as phantom for the human eye. Although the signal-to-noise ratio is reduced due to splitting the beams, it is still sufficient for distance measurement between instrument tip and retina and the obtained measurement accuracy is comparable to the same CP-OCT system without range-extension.

Conclusion

The available measurement range is one of the biggest challenges when adding fiber-based CP-OCT distance sensing features to certain ophthalmic instruments. Here, we present an approach that overcomes this limitation by shifting the measurement range to an arbitrary position using a relatively simple setup. First tests show high measurement accuracy in the ‘shifted’ OCT measurement range.

Opto-electro characterization of neural implants

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Introduction

Over the past years, neural implants have proven to be pivotal elements within any neural prosthetic system as they interface between the neurons and the electronic processing backend. However, using neural implants to restore complex functions such as vision requires the stimulation of numerous neural tissue areas within the visual cortex; such scaling of the number of electrodes per probe also scales drastically the amount of time, effort, and accuracy needed for electrochemical characterization of many individual electrodes' sites/probe. Herein, we introduce a state-of-the-art optoelectrical testing technique that paves the way to instantly check the functionality of a dense number of electrode sites simultaneously.

Methods

The working principle is to utilize a thin layer of Liquid crystals (LCs) sandwiched between the working electrodes and a transparent counter electrode. The LCs layer which opto-electrically switch when triggered by applied voltage difference facilitate the differentiation between functional/dysfunctional electrodes by comparing the absence/presence of switching in the liquid crystal layer, directly impacting the amount of reflected light off the electrode surface. This effect is visualized under the microscope by adding a polarization filter and can be resembled as if the electrode matrix acts similarly to a pixel matrix within LCDs.

Results

We tested this technique on a large number of available neural probes with 20 electrode sites of either 500 or 35 µm per probe, the electrodes are shorted at the connector base, and when applying voltage between the electrode surfaces and the ITO counter electrode; the functional electrode surfaces appeared dark as the LCs molecules has changed their orientation and obstructed the incident light from reflecting off the electrode surface, simultaneously the surfaces of dysfunctional electrodes remained distinguishably bright. This technique is extremely efficient for testing numerous electrode sites compared to one-by-one electrochemical characterization. In which a potentiostat, multiplexer, calibrated reference, and 4-5 minutes per electrode for characterization are needed.

Conclusion

In conclusion, we show the possibility for simultaneous, instant and efficient functionality screening of numerous electrodes. This technique needs to be further investigated for wafer-scale implementation..

Current Advances in the Optical Characterization of Intraocular Lenses

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Introduction

Cataract surgery, the replacement of the clouded eye lens by an artificial Intraocular Lens (IOL), is one of the most frequent surgical interventions. The quality of IOLs is ensured by international standards, where the ISO 11979-2 deals with the characterization of optical properties. As IOL designs advance over time (e.g. extended depth of focus, multifocal and simultaneous vision lens) also the test procedures must be refined.

Methods

Clinical outcomes indicate that advanced IOL designs tend to be more sensitive to postoperative IOL displacements (rotation, tilt and shift). In our work we present a novel measurement setup capable to assess IOL performance of modern IOL designs in the presence of lens tilt and decentration. Beyond the current specifications given by ISO 11979-2, the experimental setup also allows to quantify high order aberrations (up to 5th order).

Results

Results experimentally reveal findings in accordance to observations from clinical outcomes. Thus the setup proves useful for preclinical assessment of IOL designs. Additionally, by the measurement of Zernike wave front aberrations, more insight on the loss of optical quality can be gained, e.g. visual tolerability of different aberration types or possibility of spectacles correction.

Conclusion

We demonstrate that the presented measurement procedure adds value beyond the current requirements given by international standards. Thus such developments should be kept in mind for future modifications on the standard but also considering the technical feasibility of test procedures.

YOLO networks for polyp detection: A human-in-the-loop training approach

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Introduction

Early detection of adenomas and polyps is one central goal of colonoscopic screening programs. As the adenoma detection rate (ADR) depends on the experience of the endoscopist, AI-based polyp detection systems can be used for real-time assistance. Hence, to support the physicians such AI-based systems using deep-convolutional neural networks (DCNNS) have been introduced in the past years. One disadvantage of these techniques is the need of a huge amount of labeled training data.

Methods

We investigate a "human-in-the-loop approach" to minimize the required time to generate labeled training data. The approach is evaluated within the training a YOLOv4 neural network to detect polyps in colonoscopic image data. The performance metrics of the neural network are evaluated on three public datasets.

Results

The performance of the YOLO network increased from a precision of 0.88, recall of 0.83,

Tissue-simulating phantom for routine check of hyperspectral imaging systems

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Introduction

An imaging system needs a regular checkup to ensure accurate output and reveal potential malfunctions. Especially medical imaging systems claim for high standards of accuracy and stability. A common system test is accomplished by an imaging standard with known optical properties. We present 3D-printed phantoms that serve as a test system for a hyperspectral camera. To this end, a material with scattering properties close to human tissue was chosen and the amount of color pigments was adjusted to mimic the range of absorption coefficients of human tissue in the spectral range from 500 to 1000 nm.

Methods

3D-printed phantoms were fabricated, using the "color base" resin with added color pigments and low force stereolithography. For spectral characterization, a halogen light source and a spectrometer with 0.24 nm resolution were used. To determine absorption and scattering coefficients of the printed samples, the local diffuse reflectance and the total diffuse reflectance were measured. The suitability for system check was tested with a hyperspectral camera.

Results

A series of phantoms were printed and precisely measured, with a variety of shapes and optical properties. With optical parameters adjusted close to parameters in human tissue, the phantoms can be used as reference standards. For this purpose, the remission spectrum was recorded with a hyperspectral camera and the derived absorption spectra were compared to known parameters.

Conclusion

We demonstrate an additive manufacturing process to generate optical phantoms with absorption properties which cover the range of values found in human tissue between 500 to 1000 nm. The resulting phantoms are robust, reproducible and long-term stable. The high geometric accuracy in the µm range allows to implement small features that can be combined mosaic-like to complex phantoms. In addition, different thin layers can be combined to mimic absorption changes in the volume, addressing depth resolution issues.

Automatic detection of foreign objects and contaminants in colonoscopic video data using deep learning

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Introduction

In the field of colonoscopy results of automated or supporting procedures using medical image processing are often compromised by contaminants such as blood or stool, but also due to medical instruments. Such objects or contaminations often obscure relevant areas or cause disturbances in various algorithms and also prevent physicians from recognizing relevant information in the video-stream. Hence, automatic detection and segmentation of such contaminations is desirable, by obtaining proper segmentation masksto an algorithm yields the possibility to exclude such areas from analysis.

Methods

We created a training and validation dataset by collecting (and annotating, where necessary) endoscopic video sequences from various public available datasets and a privat collection. An encoder-decoder deep convolutional neural network was trained with this data to predict segmentation masks for blood, stool, medical instruments and other objects.

Results

Depending on the class (blood, stool, ...), we were able to obtain a mean Dice score in the range between 0.88 to 0.93 on the evaluation dataset.

Conclusion

The proposed approach hence allows us providing segmentation masks that are able to reduce problems in the subsequent image analysis and also find regions that were not properly observed.

Pressure sensor catheter based on Fiber Tip Fabry-Pérot-Interferometer and Fiber Bragg Grating for temperature compensation

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Introduction

Fiber-optic sensors provide a large scope of advantages. When applying these sensors in medical fields, signal linearity, small size or electromagnetic compatibility are benefits. This paper introduces a pressure sensor catheter which includes two different optical measurement principles, a Fiber Tip Fabry-Pérot-Interferometer for pressure sensing and a Fiber Bragg Grating for additional temperature sensing.

Methods

The Fabry-Pérot-Interferometer at the fiber tip is formed by a reflective multilayer membrane of a pressure sensor chip. The cavity provides absolute pressure sensing. 20 millimeter before the fiber tip a Fiber Bragg Grating is integrated for temperature sensing. The sensing components are completely coated with a silicone mantle of 2 mm diameter. The signal evaluation is both done with a Fiber Bragg Grating interrogation device. First, mechanical structure aspects of the manufactured fiber-optic hybrid sensor as well as the sensing principle is described. Then, experimental results, including quantification and separation of pressure and temperature sensitivity are presented.

Results

The Fiber Tip Fabry-Pérot-Interferometer shows a linear pressure as well as temperature sensitivity. The Fiber Bragg Grating has a very low pressure sensitivity but is highly temperature sensitive. Out of these characteristics the possibility for absolute pressure sensing with temperature compensation for the application as a pressure sensor catheter is confirmed. Different sensitivity factors ensure signal separation of pressure and temperature.

Conclusion

The pressure sensor catheter presents a hybrid sensor concept, consisting of two different fiber-optic sensing principles. With calibration the probe can be used as absolute pressure sensor, realized with a Fiber Tip Fabry-Pérot-Interferometer and a Fiber Bragg Grating providing necessary temperature compensation. Evaluation of the signals within the same readout unit is a promising approach for catheter designs with multiple sensing points.

Image registration for a mobile hyperspectral camera with integrated RGB camera

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Introduction

Wound assessment is a daily business in medical and care facilities, yet tools for a routinely standardized wound documentation are lacking. Hyperspectral imaging has the potential to monitor the wound healing process objectively by giving access to physiological parameters like oxygenation and perfusion status. The resulting parameter maps can be linked to the surrounding anatomy if incorporated into a common RGB-photo with higher resolution. In this work, we demonstrate image registration for such multi-modal images, aiming at facilitating the wound documentation process.

Methods

Two different RGB-images from one scene were taken using the same mobile device (TIVITA®, Diaspective Vision GmbH). The first pseudo-RGB-image (640x480 pixel) was generated from a hyperspectral measurement (500-1000 nm) with white-LED illumination. Target optics assure a constant recording distance of 50 cm. The second RGB-image (3840x2160 pixel) is a photography taken with the same LED lightning, but variable distance and object orientation. The registration approach is a feature-based matching procedure. Different established algorithms (SIFT, SURF, ORB, BRISK, KAZE, AKAZE) were tested for feature detection, with brute-force matching and RANSAC outlier removal applied.

Results

Image registration was successfully conducted with SIFT and SURF, evaluated on our test dataset. Similar illumination conditions are thereby essential for a successful alignment. An adapted contrast enhancement procedure is also required as an image pre-processing step.

Conclusion

SIFT and SURF can be used for fast multi-modal image registration, where both images differ in resolution and slightly in perspective, but where a similar illumination situation is guaranteed. This way, parameter maps derived from hyperspectral imaging can be superimposed upon a higher-resolution photography, resulting in an extended functionality of a mobile hyperspectral camera.

Bone Ablation Using a Ho:YAG Laser

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Introduction

Lasers have been widely investigated for use in soft-tissue surgery but also for osteotomy. Contactless interventions enabled by laser light are associated with low tissue loss, faster tissue healing, and high precision. This study aimed to optimize the ablation depth and duration at a fixed energy using a Ho:YAG laser, considering fiber delivery applications. Due to high absorption coefficient of water (one of the main constituents of bone) Ho:YAG lasers at 2.1 µm can be used in bone surgery applications.

Methods

In this study, we investigated the efficiency of ablation with Ho:YAG lasers in a free-space settings. We used a 2.1 µm Ho:YAG laser producing up to 4 J/pulse. We used a waterjet irrigation system to keep the tissue temperature under the critical temperature and a pressurized air nozzle to clear the debris in the laser path.

Results

We optimized the ablation process with only ~500 mJ/pulse for 60 s duration (corresponding to 50 pulses/point) along a 1cm cut. If the laser was applied for a longer time, deeper ablation would be possible, however, as the ablation depth increases, ablation efficiency decreases dramatically. Since longer pulse application may also induce some unwanted side effects, we kept the ablation duration to be 60 s. With around 50 pulses per position, 1.4 mm depth was achieved with an ablation efficiency (in z-direction) of ~28 µm/pulse.

Conclusion

Efficient porcine bone ablation was performed with a 10 Hz repetition rate by a Ho:YAG laser without any visible carbonization. The maximum depth measured was 1.4 (1.5) mm with an ablation efficiency of 28 (30) µm/pulse in z-direction with only ~500 (600) mJ/pulse of applied energy. All the craters were visualized using our OCT system, and these OCT images showed no evidence of damage around the laser-induced craters.

Blood vessel detection using hyperspectral imaging

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Introduction

For medical and biometric uses, blood vessel imaging and analysis are important, therefore developing a precise imaging system and image processing algorithms is essential. The hyperspectral imaging has piqued the interest of biomedical imaging experts, particularly in cases where typical imaging approaches fail to deliver the required results.

Methods

The hyperspectral image acquisition system TIVITA® has been used. In this work, to detect blood vessels based on the spectral properties of blood, all spectra in the wavelength range 750 nm - 950 nm were averaged. Due to disturbing factors (skin tone, fat), the resulting Mean NIR image is not able to detect the blood vessels completely. To extend this method, the spectra were standardised using SNV transformation. In the wavelength range 625 nm - 720 nm the slope of the spectra is not influenced by different melanin content but by oxygenation. Accordingly, the melanin effect can be eliminated by calculating BVI (Blood Vessel Index) in this spectral range. The combination of the two methods Mean NIR Image and BVI provides the final results of blood vessel detection.

Results

To ensure the stability of the algorithm against the disturbing factors that occur in blood vessel detection, images of dark skin and fatty body parts were used. The experimental results show that the algorithm can detect the vessel structure deep into the tissue and in body parts with subcutaneous fat. The blood vessels under dark skin can also be detected thanks to the selected spectral range for the calculation of BVI.

Conclusion

Hyperspectral approaches for blood vessel imaging are investigated in this research. This study used hyperspectral analysis to determine the optimal spectral range for enhanced image quality and higher blood vessel localization contrast. Taking sample images of different skin complexities, the desired image output was successfully obtained.

On model-based hyperspectral imaging

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Introduction

A common problem in hyperspectral imaging is due to the relatively large amount of spectral data to be handled during analysis of concerned images. The restriction to simple spectroscopic methods, a high demand on the used hardware, or the uses of storage-intense lookup tables may occur. This paper provides several contributions on model-based analyses of hyperspectral images, intended to overcome the aforementioned restriction or demands.

Methods

The algorithms are described by means of the perfusion of human skin and a corresponding two-layer tissue model whose optical properties are studied by Monte Carlo simulations. The particular role of the mean photon path length within the medium is studied and statistically characteristics are exploited to reduce the number of Monte Carlo simulations eventually needed to solve the inverse problem. That is, individual tissue concentrations are determined from measured remission spectra to ultimately estimate relevant tissue perfusion parameters, such as the oxygen saturation. Two strategies are presented to approximately solve the inverse problem. They are referred to as linear fitting and direct solving.

Results

As preliminary step towards a direct solver of the inverse problem, the scaling of Monte Carlo simulations combined with multi-dimensional histogram representations of path length distributions is validated. Furthermore, hyperspectral images of resolution 640 x 480 pixel, each with 100 wavelengths are analyzed by a spectral fitting method. A particular Fortran implementation of the bounded value least square algorithm allows to evaluate the aforementioned images in few seconds still without parallelization.

Conclusion

Various promising methods have been elaborated to aid the evaluation of hyperspectral images. Though, strategies are generally applicable, the accuracy eventually depends on the model's capability to reflect real measurements. Provided implementations are suitable for real-time applications in hyperspectral cameras.

FTIR spectroscopy as a powerful tool for detecting changes in skeletal muscle composition due to metabolic disorders

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Introduction

In addition to its primary function of supporting and moving the body, skeletal muscle plays an important role in many physiological processes, including thermogenesis, metabolism, and secretion of peptides to communicate with other tissues. The different skeletal muscle fibre types are critically involved in the modulation of carbohydrate, lipid, and protein metabolism. Therefore, they undergo a range of structural and functional changes related to metabolic disorders such as diabetes mellitus (DM), obesity, and the metabolic syndrome, which are among the leading causes of morbidity and mortality worldwide.

Methods

The need for efficient methods to distinguish between normal and pathological tissue is increasing with the growing knowledge of disease and the identification of newer diseases. Versatile, robust, and objective techniques are sought that allow qualitative and quantitative characterization of complex biological tissues in a time- and cost-effective manner. In response, alternative techniques, such as various spectroscopic approaches used primarily in other fields, are finding increasing application in biomedicine. The synergy of different spectroscopic and appropriate chemometric methods can provide very effective and powerful tools for studying the effects of pathological conditions closely related to modifications in tissue morphology and molecular composition.

Results

In this work, we report Fourier Transform Infrared (FTIR) spectroscopy results revealing changes in the macromolecular composition of weight-bearing and non-weight-bearing skeletal muscle in mouse models of obesity with insulin resistance and STZ-induced diabetes. Using FTIR spectroscopy independently of histochemical analysis, we found that the most pronounced effects on skeletal muscle composition occurred in the young STZ-induced diabetic group.

Conclusion

Our results suggest that FTIR spectroscopy has great potential to complement or even replace various complex histochemical techniques for early detection of metabolic abnormalities in skeletal muscle, phenotypic classification, and monitoring of disease progression associated with impaired insulin function.

In vivo determination of the collagen layer in the human tympanic membrane using polarization-sensitive endoscopic OCT

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Introduction

Optical coherence tomography (OCT) is a non-invasive interferometric imaging technique, which has been demonstrated for morphologic and functional examinations of the human tympanic membrane (TM) in vivo using endoscopic probes. While intensity-based OCT is limited in distinguishing different tissues, the polarization of the backscattered light provides a tissue-specific contrast, e.g. of birefringent tissue as collagen fibers. As the acoustic and mechanical properties and thus the hearing ability depend on the layer of collagen fibers in the TM, determining the collagen content is of interest. First in vivo measurements using polarization-sensitive OCT (PSOCT) are presented.

Methods

To extend the existing approach, an endoscopic swept-source OCT system was redesigned. Sample induced backreflected light superimposed with diagonally polarized reference light was detected by a custom-built polarization-diverse balanced photoreceiver. From the detected polarization-diverse signals, local retardation was calculated differentially based on successive Stokes polarization states. The system had an axial resolution of around 15 µm and 45 µm in lateral direction. Measurements were done on a healthy volunteer.

Results

Based on the local retardation, the collagen layer of the TM is distinguishable in the thickest regions of the membrane close to the umbo and the annulus. Resolving the layers in the thinner central regions is impeded by steep slopes of the TM, resulting in an incident beam almost parallel to the surface as well as vanishing birefringence contrast for aligned optic axis and incidence. Further evaluation, particularly of the fiber network, requires an improved resolution for precise detection.

Conclusion

PSOCT is suitable to assess the TM's collagen layer in vivo. Nevertheless, the nature of the tympanic membrane as well as the system's resolution limit the imaging. Further investigations will path the way to identify the collagen content of the TM. Eventually, this might improve the engineering of artificial materials used for TM reconstructions.

Focus Session:
BMBF-Twenty20 coordinated research project "RESPONSE - Partnership for Innovation in Implant Technology"

Long-term in vivo Test of a Nitinol Stent for the Eustachian Tube

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Introduction

Chronic Eustachian tube dysfunction (ETD) is widespread in the population and occurs from children to elderly people. Malfunction of the ET can lead to feelings of severe pressure in the middle ear, pain and incapability of pressure equalisation. ETD and its symptoms can become chronic and even lead to hearing loss. Current interventions lack long-term efficiency and sometimes need to be repeated. Thus, a newly designed self-expanding nitinol stent was examined as a permanent treatment option for ETD.

Methods

Nitinol stents (3-5 mm x 14 mm) were inserted unilaterally into physiological ETs of 24 healthy, adult blackface sheep. The animals were divided in groups of n=8 with an observation period of 3, 6 and 12 months after stent placement. All animals underwent weekly tympanometric measurements to observe the middle ear health status. Endoscopic imaging of the pharyngeal ET opening was performed during controls under general anesthesia. Finally, ex vivo examinations using cone beam computed tomography and histology were conducted.

Results

The stents remained at their place and showed no dislocation, even if the insertion was not deep enough. In few animals, endoscopy showed mild secretion from the pharyngeal ET opening and visible stent struts due to incorrect placement. In 19/23 middle ears, sporadic or ongoing changes in the tympanograms were detected, but also in 14/23 controls. Generally, the stents were well tolerated by the animals and first histology data show mild tissue reactions. Histological findings so far are good epithelisation of the stent but also mild or severe granulation tissue in some cases.

Conclusion

Results indicate that the in vivo performance could benefit from small modifications in size and shape. Furthermore, correct placement of the stent is crucial for the outcome. Overall, nitinol stents seem suitable as a prospective treatment option for ETD and further examinations are suggested.

Novel approaches for cochlear implant-based drug delivery

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Introduction

Cochlear implantation is a surgical procedure serving patients with severe to profound sensorineural hearing loss. In this intervention, the electrode array of a cochlear implant (CI) is inserted into the scala tympani (ST) of the cochlea. CIs are the most effective treatment for hearing loss. However, the potential electrode insertion trauma (EIT) and foreign body response (FBR) may lead to injury and fibrous tissue growth in the cochlea, which lower the CIs effectiveness and negatively influence the patient's hearing outcome. To reduce EIT and FBR, local drug delivery is among the most effective strategies. Various novel approaches of cochlear implant-based drug delivery are investigated.

Methods

Investigated drug delivery approaches are: An intracochlear catheter for acute drug delivery, drug-loaded polymer coatings on the electrode providing long term release, and a drug depot featuring on-demand signal induced drug release. Furthermore, topological structures of the electrode silicone body, that could modulate the release profile of embedded drug compounds incorporated in the silicone carrier matrix, and additionally steer the attachment or movement of fibroblasts to the electrode, are incorporated in the project.

Results

These drug delivery methods are studied considering the technical feasibility, as well as their effectiveness in vitro and in an animal model. Preliminary animal study results, including impedance measurements of drug-loaded polymer coated electrodes, as well as micro-structured electrodes, are presented. Additionally, the designs of these animal electrodes are transferred to the human electrode array CI-design, involving comprehensive bench testing to characterize the coated electrode specimens. Parameters such as the insertion force, friction, pressure built-up during insertion, and pharmaceutical properties are successfully characterized.

Conclusion

All investigated approaches for cochlear implant-based drug delivery are technically feasible but need further development. Moreover, a comprehensive evaluation of the conducted animal study is needed, to decide over next technical development steps.

Recommendations for the Development of CFD Model to Assess the Thrombogenic Potential of Stents

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Introduction

Computational fluid dynamics (CFD) has enormous potential for the development of novel cardiovascular implants. In particular, the evaluation of the thrombogenic potential of implants is gaining importance. For this purpose, the numerical model must represent the essential properties of the real system, i.e., an implant in the human blood circulation, in a suitable form. Due to its complexity, the model building process is crucial for the successful application of the model. Currently, there is no structured guideline for the application of numerical flow simulation to which model developers can refer. Based on NASA and ASTM, we present key aspects of the model building process using CFD for stent flow as an example.

Methods

Based on the NASA documentation the process of model development in order to perform CFD simulation for risk assessment regarding stent thrombosis was performed. The proposed steps of the NASA technical handbook were supplemented by information of ASME V&V40-2018 [4] and the applicability analysis framework.

Results

The four phases of model development proposed by NASA could be applied to the biomedical example of flow simulation in stent. Essential steps of the modelling process are defining the Question of Interest (QOU), the Context of Use (COU) and the intended use in an early stage. Validation and verification (V&V) activities are extensive challenges and require consideration even for the modelling process.

Conclusion

A systematic step-by-step guideline on how to perform the modelling process could help to accelerate the bench-to-bedside process. Furthermore, the technical documentation of the model development can be seen as a communication tool, which leads to increased understanding in interdisciplinary teams.

Microstent for minimally invasive treatment of Fallopian tube occlusions - porcine implantation ex vivo

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Introduction

Proximal impairments of the Fallopian tube causes female infertility in 35 % of cases. Current treatment options, such as in vitro fertilisation or tubal reconstruction, gain pregnancy rates of approximately 50 %. Recently, catheterization, which is associated with high re-occlusion rates could potentially be extended by implantation of a novel biodegradable microstent. The current work presents first results of ex vivo microstent implantation into porcine Fallopian tube samples using a novel application system.

Methods

For in vitro testing, radial force was measured as a function of the diameter of six microstent prototypes. Additionally, one microstent was implanted ex vivo in the porcine Fallopian tube sample using a novel application system. Micro-computed tomography images of the control group without stent and the stent group were analyzed regarding lumen opening area and feret diameter within six cross-sectional images, respectively.

Results

After crimping to a minimum crimping diameter of 0.8 mm and consecutive microstent release, a diameter recovery of (82.86 ± 1.01) % was measured. Based on imaging data, a clear increase in opening area after ex vivo microstent implantation was found compared with the control group. Feret diameter analysis showed an approximately constant Fallopian tube lumen along longitudinal axis in the stent group.

Conclusion

The current study demonstrates that the microstent applies the necessary radial forces to keep the Fallopian tube open. The opening diameter corresponds to the diameters given in the literature. Furthermore, the study proofs that the open cell microstent design allows an adaption to the anatomical path of the Fallopian tube, which leads to a low risk of an impaired Fallopian tube functionality. Further investigations will be focused on human Fallopian tube samples.

Surface Characterization for Combination Products using X-Ray Photoelectron Spectroscopy

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Introduction

X-Ray Photoelectron Spectroscopy (XPS), also referred to as Electron Spectroscopy for Chemicals Analysis (ESCA), has long been established as a powerful tool for studying the electronic structure and nature of chemical bonding in surface chemistry and physics- making use of either the excitation by tunable synchrotron radiation sources or laboratory light sources with fixed photon energy. Electron escape depth is typically limited to below 10 atomic layers, yielding an unsurpassed surface sensitivity of this technique.
Due to sensitivity of sample materials to ultra-high-vacuum environments, x-ray illumination and also charging, application to polymeric biomaterials remained limited, but became more and more feasible and therefore attracted rising interest during the last years.

Methods

In this study, a K-Alpha XPS System, Thermo Fisher Scientific, equipped with an aluminum Kα x-ray source and photon energy of 1486.6 eV, high efficiency electron transfer lens and 180° hemispherical analyzer has been used. Compensation of charge loss due to electron emission is allowed by an ultra-low energy co-axial electron source, being of particular importance when applied to the large group of non-conducting polymeric materials. Depth profiles, e.g. in case of layer-by-layer systems, are accessible either in a non-destructive way by compucentric sample rotation or by well defined Ar^+ ion surface sputtering.

Results

Recent experimental findings regarding the characterization of surface modifications and functionalizations of biomaterials and combination products will be discussed.

Conclusion

The contribution highlights the benefits of recent developments of commercially available state-of-the-art XPS devices especially for the analysis of polymeric biomaterials and their surface modifications. Earlier limitations of XPS with respect to sample materials could be gradually overcome by new experimental features concerning e.g. advanced detectors, charge neutralization and depth profiling, but also user friendliness, space-saving design and possibilities for automated software and remote control.

Cardiovascular, ophthalmologic and otolaryngologic medical device innovations - Progress report 2022 from the Twenty20 consortium RESPONSE

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Introduction

The coordinated research project “RESPONSE - Partnership for Innovation in Implant Technology” is one of ten research consortia within the BMBF program “Twenty20 - Partnership for Innovation”. Starting in 2014, RESPONSE has established a network of 33 partners from science, medicine and industry in order to jointly foster contributions to the field of implantable medical devices in cardiovascular medicine, ophthalmology and otolaryngology. As part of its strategy process, RESPONSE has integrated the topic of smart implants, as well as stent-based gynecologic and gastroenterologic implants.

Methods

RESPONSE is following its own guidance framework for medical device innovation strategies, which has been published in 2021. The consortium’s approach is aiming at participative technology development, integrating perspectives of developers and medical professionals, as well as systems and innovation researchers. In silico methods and smart implant concepts are being applied towards novel diagnostic and therapeutic functions.

Results

RESPONSE is currently in its transfer phase towards subsequent product development and alternative pathways of utilization of scientific results. This involves a portfolio of key innovations for novel medical devices, technologies and processes, aiming beyond the completion of the funding period in 2022: (i) covered stents and absorbable scaffolds, (ii) electrospun nonwovens for transcatheter heart valves and other medical devices, (iii) glaucoma microstents for ophthalmic application, and (iv) Eustachian tube stents for otolaryngologic application. Technological innovations cover local drug delivery systems and surface modifications for responsive functionalized implants.

Conclusion

RESPONSE keeps continuing its efforts in tackling the adverse effects of the corona pandemic on the collaborative work within a distributed network of clinical, non-clinical and industry partners. Although progression of practical R&D work has largely been resumed, particular challenges are still arising from the management of re-prioritization and rescheduling of joint project roadmaps. As intermittent clinical shutdown effects are persisting, market participants remain highly affected.

Bio-responsive drug delivery systems for blood-contacting medical devices

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Introduction

Biomaterials that contact blood elicit various defense reactions at their surface, which are currently treated by systemic drug administration. A promising alternative approach is based on activation-dependent coatings that release anticoagulant and immunomodulatory drugs in a localized dose adapted to the actual need. Such release systems reduce systemic drug exposure and prevent local over- or under-dosing and premature decay of the release.

Methods

A hydrogel system of four-armed poly(ethylene glycol) (starPEG) and heparin was equipped with linker peptides that are specifically cleaved by procoagulant or inflammatory proteases. The cleavage of the peptides degrades the hydrogel and releases the covalently bound bioactive molecules. This principle has been used to form anticoagulant hydrogels that release heparin as a bioactive molecule in response to activated coagulation factors. Transfer of this principle to an immunomodulatory platform was achieved by using elastase-cleavable peptides and conjugating anti-inflammatory drugs to the hydrogel matrix via the cleavable linker peptides.

Results

The efficacy of the systems has been demonstrated in applied in vitro experiments, and the hydrogels have been used as coatings for vascular stents.
Also, adsorptive binding of selectively cleavable peptide-drug conjugates using appropriate polymer anchors allows adaptive release of drugs from surfaces. This approach is attractive for the functionalization of medical devices where hydrogel coating could limit functionality, such as dialysis or oxygenator membranes.

Conclusion

We envision that such feedback-controlled release systems have the potential to endow biomedical implants with combinations of anticoagulant, anti-inflammatory, and antiseptic properties while minimizing patient exposure to potentially harmful drugs to the greatest extent possible.

Focus Session: Computational Modeling of Cardiac Function

Electrode modelling and simulation of diagnostic and pulmonary vein isolation in atrial fibrillation

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Abstract

Atrial fibrillation (AFib) is a quivering or irregular heartbeat that is usually not life-threatening but it can lead to blood clots, stroke, heart failure and other heart-related complications. The most commonly used treatment of AFib is the pulmonary vein isolation (PVI). The aim of the study was to model diagnostic catheters, ablation catheters and to integrate them into the Offenburg heart rhythm model for a static and dynamic simulation. The Modelling and simulation of electrical and thermal fields were accomplished with the software CST® (Computer Simulation Technology) from Dessault Systèms. Two PentaRays and one Lasso diagnostic catheter were modelled based on the technical manuals of the manufacturers as well as two Pentaspline Pulsed Field Ablation (PFA) catheter and HELIOSTAR™ ablation balloon. In addition a focus model to present and diagnose AFib, was accomplished. Both diagnostic electrode types were made of platinum. The HF ablation procedures were performed with a 8 mm platinum tip electrode, with an application duration of 45 seconds and a power output of 20 watts by Right Superior Pulmonary Vein and 30 watts by Left Superior Pulmonary Vein. The PVI using HF energy produced a maximum temperature of 72°C by 30 watt. The pulse field ablation procedures were performed by Pentaspline basket pose with the 20 poles of platinum, with an application duration of 12 seconds and a power output of 15 watts and frequency of 700 kHz by Right Inferior Pulmonary Vein and Left Inferior Pulmonary Vein. The maximum produced temperature was 46,7°C by 15 watt and 46,65°C by 20 watt. The HELIOSTAR ablation balloon with gold tip electrode produced a maximum temperature of 44,35°C by 15 watt with an application duration of 12 seconds. The 3D simulation of the temperature profile as well as diagnostic may be used to optimize the therapy of AFib.

Effects of Ventricular Myofiber Orientation on Mechanical Function in Human Heart Simulations

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Introduction

Currently, personalization of computational human heart models is often performed by combining a carefully designed patient-specific heart geometry with a generic myofiber orientation. This is due to a lack of accurate in vivo fiber orientation measuring techniques.
The goal of this study is to evaluate the effect of different myofiber orientations on selected biomarkers of mechanical heart function.

Methods

For a given heart geometry, we change endocardial and epicardial fiber angles in the ventricles independently from 0° to +/- 90° in equidistant steps of 30°. This results in 16 different fiber orientation combinations. We use these as input for our mechanical whole-heart model, which is coupled to a closed-loop model of the circulatory system.
To quantify the effect of the different fiber orientations, we evaluate clinically relevant biomarkers such as ejection fraction, wall thickening, twist and valve displacement.

Results

Horizontal fibers at endo- or epicardium led to reduced ejection fraction, mitral valve displacement and thickening of the myocardial wall. For some fiber orientations, the apex of the left ventricle rotated in the opposite direction leading to a negative twist. While all simulations yielded ejection fraction and wall thickening in the physiological range, maximum values of 59.95 % (ejection fraction) and 52.48 % (wall thickening) were observed for 60° at endocardium and -60° at epicardium, a combination often used in literature. Similar ejection fractions with lower maximum pressures in the left ventricle and still physiological results for all other biomarkers were observed when changing either epicardial fiber orientation to -30° or endocardial fiber orientation to 90°.

Conclusion

Mechanical function is strongly dependent on the fiber orientation throughout the myocardial wall of the ventricles. Achieving close to maximum ejection fraction with smaller maximum pressures for non-default fiber angles shows that it might be beneficial to refine the fiber orientations before tuning other model parameters.

Generation of Cardiac Digital Twins of Whole Heart Electrophysiology

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Introduction

Computer models of cardiac electrophysiology (EP), personalised to match both the anatomy and electrical activity of an individual patient, are termed Cardiac Digital Twins (CDTs). CDTs show high potential to aid in clinical diagnostics, treatment planning, prognostics, and device development. Challenges during anatomical and functional personalization, however, have limited clinical applicability. We aimed to overcome many of these challenges and report on a clinically-viable CDT of a single subject capable of simulating sinus rhythm and ventricular-based diseases with high fidelity.

Methods

Using an automated framework for the generation of the CDT from non-invasive clinical data, a whole heart model was built, personalised based on the 12-lead electrocardiogram (ECG) during sinus rhythm, and retrofit with a physiologically-detailed His-Purkinje system. Whole heart EP was accounted for by including atrial and atrio-ventricular conduction. Goodness of fit was assessed in the 12 lead ECG for sinus rhythm. Predictive capabilities of the mechanistic model were then probed by interrupting conduction in the left and right bundle branches, creating accessory paths, and pacing at the RV apex. Computed pathological ECGs were evaluated with clinical diagnostics. EP simulations were carried out with real-time performance.

Results

The personalised 12-lead ECG under normal sinus rhythm showed close correspondence with the measured 12-lead ECG. Pathological disease conditions resulted in 12 lead ECGs that manifested most of the expected morphological ECG features as assessed by diagnostic criteria. Minor discrepancies, however, were also observed.

Conclusion

The CDT of the single subject, with associated pathologies, could be generated within clinical time scales (<4 hours) and thus has great potential in patient-specific therapies. Minor discrepancies in both sinus rhythm and pathologies can be attributed to pathological factors that were not considered, such as dilation or slower cell-to-cell conduction. Broader validation with clinical data is needed to demonstrate agreement between models and physical reality.

Refining the Eikonal Model to Reproduce the Influence of Atrial Tissue Geometry on Conduction Velocity

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Introduction

Atrial fibrillation is responsible for a significant and steadily rising burden. Simultaneously, the treatment options for atrial fibrillation are far from optimal. Personalized simulations of cardiac electrophysiology could assist clinicians in the risk stratification and therapy planning for atrial fibrillation. However, the use of personalized simulations in clinics is currently not possible due to either too high computational costs or non-sufficient accuracy. Eikonal simulations come with low computational costs but cannot replicate the influence of cardiac tissue geometry on the conduction velocity of the wave propagation. Consequently, they currently lack the required accuracy to be applied in clinics. Biophysically detailed simulations on the other hand are accurate but associated with too high computational costs.

Methods

To tackle this issue, a regression model is created based on biophysically detailed bidomain simulation data. This regression formula calculates the conduction velocity dependent on the thickness and curvature of the heart wall. Afterwards the formula was implemented into the eikonal model with the goal to increase the accuracy of the eikonal model without losing its advantage of computational efficiency.

Results

The results of the modified eikonal simulations demonstrate that (i) the local activation times become significantly closer to those of the biophysically detailed bidomain simulations, (ii) the advantage of the eikonal model of a low sensitivity to the resolution of the mesh was reduced further, and (iii) the unrealistic occurrence of endo-epicardial dissociation in simulations was remedied.

Conclusion

The results suggest that the accuracy of the eikonal model was significantly increased. At the same time, the additional computational costs caused by the implementation of the regression formula are neglectable. In conclusion, a successful step towards a more accurate and fast computational model of cardiac electrophysiology was achieved.

Computational and Experimental Study of Controlling Cardiac Arrhythmia Using Optogenetics

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Introduction

Rotating spiral waves in the heart are associated with life-threatening cardiac arrhythmias. Today, strong, globally resetting electrical shocks are used to terminate cardiac fibrillation. Significant side effects have motivated the development of alternative low-energy approaches, (S.Luther, Nature (2011)). For this purpose a detailed understanding of the dynamics of spiral waves is required. Cardiac optogenetics opens novel paths to study the mechanisms underlying the onset, perpetuation, and control of cardiac arrhythmias. The termination of ventricular arrhythmias has been demonstrated in optogenetic Langendorff-perfused mouse hearts using global and structured illumination (R. Uribe, Front Physiol (2018), S. Hussaini, eLife (2021)). In this study, we use optogenetics as a tool to numerically and experimentally investigate the control method of resonant feedback pacing, in which global periodic illumination is applied to cardiac tissue.

Methods

We use a two-dimensional computational model to describe the spatiotemporal evolution of membrane voltage across an optogenetically modified murine cardiac monolayer . Additionally, we report the results of our ex vivo studies using 5 Langendorff-perfused hearts from αMHC-ChR2 transgenic mice.

Results

Our study shows a significant increase in termination efficiency of resonant feedback stimulation using periodic global illumination, compared to a single global optical pulse corresponding to conventional defibrillation. The dose-response curve demonstrates termination rates of more than 50% and 100% at the lowest and highest light intensity of 3.1 and 100 μW/mm2 for the resonant feedback case. In contrast, it shows a decrease in termination rate to 0 % and ≈45 % for the single optical pulse. Our simulations suggests that resonant drift is the underlying mechanism for termination of arrhythmia in mouse heart at very low LIs. Further experimental validation of these results is ongoing.

Conclusion

Resonant feedback pacing demonstrates effective low-energy defibrillation in numerical simulations and experimentally in intact mouse hearts (S. Hussaini, Ph.D. thesis, eDiss (2021)).

Physiologically valid 3D-0D models of cardiac electromechanics

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Introduction

Image-based computational models of cardiac electromechanics (EM) are a powerful tool to understand the mechanisms underlying physiological and pathological conditions in cardiac function and to improve diagnosis and therapy planning. To realize such advanced applications methodological key challenges must be addressed. First, enhanced computational efficiency and robustness is crucial to facilitate model personalization and the simulation of prolonged observation periods under a broad range of conditions. Second, physiological completeness encompassing therapy-relevant mechanisms is needed to endow models with predictive capabilities beyond the mere replication of observations.

Methods

In this talk, we report on a novel universal cardiac EM modeling framework that builds on a flexible method for coupling a 3D model of cardiac EM to the physiologically comprehensive 0D CircAdapt model representing closed-loop circulation. Additionally, we present recent advances in EM cardiac model personalization. In particular, we focus on the identification of passive cardiac properties. Here, we present a novel methodology to simultaneously perform an automated identification of in-vivo passive mechanical properties and an estimation of the unloaded reference configuration.

Results

We report on the efficiency, robustness, and accuracy of the numerical scheme and solver implementation and show the model's ability to replicate physiological behaviors by simulating the transient response to alterations in loading conditions and contractility, as induced by experimental protocols used for assessing systolic and diastolic ventricular properties. Further, we demonstrate the applicability of the framework to several clinically relevant problems.

Conclusion

The mechanistic completeness and efficiency of the framework renders advanced EM modeling applications feasible. The model facilitates the efficient and robust exploration of parameter spaces over prolonged observation periods which is pivotal for personalizing models to closely match observations. Moreover, the model can be trusted to provide predictions of the acute transient response to interventions or therapies altering loading conditions and contractility.

Using the Eikonal Model to Assess Anisotropic Conduction Velocity in Cardiac Tissue

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Introduction

Identification of cardiac tissue areas with heterogeneous or slow conduction velocity (CV) plays an important role in clinical practice. The radial basis function (RBF) method calculates CV from local activation times (LAT) obtained from electro-anatomical mapping. Validation of the RBF and similar methods in anisotropic propagation is challenging but relevant. This work modifies the fast iterative method (FIM) solving the Eikonal equation to provide ground truth values of CV to assess the RBF.

Methods

A 2D-patch and left atrium (LA) meshes were used to evaluate the RBF method with the FIM. Local speed was defined as 1000 mm/s everywhere. LATs are usually the only output of the FIM. However, calculating the CV magnitude (CVmag) and direction (CVdir) from the optimal trajectory is also possible. The obtained LATs were used as input for the RBF to estimate CVmag and CVdir values. Then, these predictions of the RBF were compared against the FIM ground truth. A regression model was used to improve the accuracy of the prediction of CVdir under the assumption of known fiber directions. In this regression model, the angle between fiber direction and gradient of the wave-front was the independent variable whereas CVdir error was the output of the regression model.

Results

CVmag mean absolute error was 116 mm/s and 235 mm/s in the 2D-patch and LA, respectively. The CVdir error was 25° and 29° in the 2D-patch and LA, respectively. The accuracy of the CVdir prediction improved to 7° and 5° in the 2D-patch and LA by implementing the regression model.

Conclusion

RBF and similar methods neglect anisotropy when calculating CV. Assessing RBF with FIM simulations at physiological ranges of anisotropy revealed significant errors in CV prediction. Therefore, the modified FIM can be a valuable tool to quantify these errors and provide new insights to improve the accuracy of RBF.

Focus Session: Development of a Direct Assistive Care Robot in a User-Centered Design Approach - BMBF-Project “PfleKoRo”

Implementing ethical aspects in the development of a robotic system for nursing care: a qualitative approach

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Introduction

As robotic systems in nursing are still in an early explorative research phase, potential long-term changes they can lead to are ambiguous. In line with the "Responsible Research and Innovation" approach, the multi-professional project "PfleKoRo" aims to anticipate and mitigate ethical risks that might be expected when starting a robot development. The robotic arm in question is intended as a hands-on support to nursing care. Therefore, the question is, which ethical risks and requirements must be taken into account when developing this robot?

Methods

Guided by the British Standard for the design of robotic systems, online focus groups with professional nurses and presence individual interviews with patients and their/or other patients' relatives were conducted in May and June 2021 to identify in an initial step ethical risks related to the robot's use and in a subsequent step, the requirements to minimize those risks. Sixteen professional nurses participated in three focus groups. Interviews were held with eight patients and relatives. The results were analysed using content analysis. Evidence from the literature and expert guidance were considered in both steps. Validation and verification methods were assigned appropriately.

Results

Ethical risks and requirements could be defined in the scopes of dignity, autonomy, privacy, human relationships and safety. Nurses feared that the robot would increase workload, whereas patients and relatives had concerns about the robot being considered a caregiver rather than a support for nurses. Despite the focus on possible negative consequences, participants also made optimistic comments regarding the future robot use.

Conclusion

The methodological approach contributed favourably to linking ethical implications to the work of engineers and thus influencing the development of the system. Focus groups and single interviews appeared appropriate for involving users to anticipate ethical risks early on during a robot's development, in accordance with the "Responsible Research and Innovation" approach.

Systematic Design of a Robotic End Effector for Physical Human-Robot Interaction during Caregiving Tasks

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Introduction

PfleKoRo aims to develop a robotic care assistance system, which allows caregivers to have patient lifting and holding tasks taken over by a robot. Physical interaction of robotic systems with patients and caregivers shows multiple challenges, which are hardly present in cooperative robotic systems used in industrial settings. To reach a high level of acceptance of patients and caregivers, a deep integration of these relevant stakeholders into the system's design process is needed. However, there are currently no guidelines available for the development of such an innovative system that considers the relevant stakeholders.

Methods

In this work, established guidelines and methods for identifying and prioritizing requirements were tested in collaboration with nursing professionals. The identified requirements were transformed into end effector concepts with the ability to lift and hold a patient's leg. Using prototypes, the concepts were evaluated and discussed with caregivers in a mock-up.

Results

While user integration into the design process proved to be necessary, the results of collaborative creative design methods were inconsistent and limited to analogies to existing lifters or the human hand. To encourage the innovation potential, solution-neutral methods were more adequate in the early development stages. The methods used resulted in a determination of possible areas on the leg that are suitable to be touched by a robot in the given task. First demands regarding the preferred contact area of the end effector could be stated, but appeared not to be sufficient. The end effector needed to be thin to be able to reach under the patient's leg in a supine position and lightweight to minimally reduce the robot's load capacity.

Conclusion

An end effector based on carbon fibre made shells showed to be most suitable. Pneumatic cushions were added to adapt the leg's surface. In the mock-up first tests with caregivers were successfully made.

PfleKoRo: Facilitation of care through cooperative robotics

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Abstract

"Good care" means responding individually to the needs of those in need of care and to respect their wishes. Bedridden persons, who are badly or extremely in need of care, pose a particular challenge because they are particularly vulnerable. Additionally, care of such persons places a great physical strain on the attending nurse or may demand a second caregiver when carrying out nursing activities. This ties up resources that could be better used to meet the demand for "good care". The aim of the PfleKoRo Project is to relieve as far as possible the physical and temporal burden on nursing staff in the care of bedridden persons. For this purpose, a cooperative robotic system is being developed, based on a user-centered design, which supports nursing duties as required, integrates itself smoothly into nursing routine and takes over physically stressful patient holding and repositioning tasks. The scientific-technical challenges here are to reconcile robotic assistance and human interaction and to anchor the situation-dependent needs of caregivers and persons requiring care in the technical implementation. These challenges are met by an iterative development process consisting of design, model creation, testing and evaluation, carried out jointly by care professionals, care recipients and system developers, which culminates in the robotic PfleKoRo system.
The PfleKoRo consortium comprises the key stakeholders required for integrated research and subsequent implementation. By supporting nursing duties for bedridden people, the PfleKoRo system will create more scope for "good care", from which care professionals and care recipients will benefit.

Development of a hand-guided cart concept with integrated holonomic drivetrain for ergonomic manoeuvring of a robotic care assistance system

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Introduction

The transportation or manoeuvring of heavy objects or devices takes up a large portion of the workday in many health professions. The manual moving of heavy loads can imply a biomechanical risk and moving tasks that require very high forces or torques necessitate the use of assistive devices as widely used in industrial settings. Introducing the robotic care assistance system PfleKoRo to hospitals and care homes, considering the system's dimensions and weight mobility is one key to the acceptance of the technology. Having the overall objective of relieving caregivers brings along a whole catalogue of new requirements arising from the healthcare setting, the users and the tasks performed with the system.

Methods

A mobility concept for PfleKoRo was developed by running multiple iterations of focus groups, co-creation workshops and evaluation sessions with caregivers from the University Hospital Aachen and the St. Gereon care home to ensure the assessment and addressing of all requirements. Initially the care environments were inspected to determine relevant constraints. Additionally daily nursing routines were analysed in cooperation with caregivers and nursing scientists. In interview sessions, the user demands which were expedient for guiding a usability focused design process were identified. Notably the resulting requirements specification illuminates the need for precise manoeuvrability in small spaces, lateral movement and compactness of the mobile robotic system while permitting physiological relief and safe and easy handling.

Results

The concept development eventuates in a hand-guided cart with an integrated holonomic drivetrain. Employing a first prototype, control parameters defining the cart dynamics that are essential for the usability of the system were optimised in cooperation with caregivers.

Conclusion

First prototype tests were successfull. The prototype's controls were intuitive and easy to use while proving good manoeuvrability when moving high loads.

User involvement in the development of a robotic assistance system for nursing care: a research project based on User-Centered Design

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Introduction

Various studies have shown that the development of products without user involvement leads to lower acceptance and usability. Our interdisciplinary project PfleKoRo aims to develop a robotic assistance system to support nurses in care interventions with patients. During the development phases of the robotic system, users, i.e. nurses, care recipients and informal caregivers, were involved.

Methodological steps of the study are carried out taking a User-Centered Design (UCD) into account. To date, there is no agreement about the most appropriate method to engage users. Therefore, we reflect our experiences with the UCD from different interdisciplinary perspectives, i.e. nursing, nursing science and engineering.

Methods

To implement the methodological steps of UCD, Co-creation sessions were prepared in interdisciplinary workshops; interviews and focus groups were conducted with patients (n=4), relatives (n=4) and nurses (n=30) to determine needs and user wishes, concerns and ethical aspects. Self-recordings of daily routines, video recordings of nursing activities and observations were further methods. Additionally, two nurses were constantly involved in the project in order to work and interact with the engineers throughout the development process.

Results

Due to the COVID-19 pandemic, not all initially selected methods could be implemented. Creative solutions were employed to replace the observations of daily nursing practices. Video recordings could illustrate but not fully replace self-experience. Focus groups and interviews proved to be rich in terms of end users´ needs and requirements. Since the majority of meetings took place as digital meetings, the communication and demonstration of technical parts were challenging.

Conclusion

From today's viewpoint, the methodological steps used seem practicable and purposeful for involving users. Especially for finding a common base for communication, extra time should be scheduled in interdisciplinary teams.

Concept for the automation of a direct caretaking robot

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Introduction

With the advance of developments in cooperative robotics, more and more systems are finding application in hospitals. Active caretaking robots, which support the nurse in direct human-machine contact during physically demanding tasks, have not been able to benefit from this evolution so far. This work presents a concept for automating such a robot to solve one of the significant technical challenges of direct robot patient interaction. The robot is enabled to approach specified positions on the patient, grip them and interact as defined.

Methods

The widely-used open-source framework ROS integrates the components, robot, camera, and gripper and enables communication. As a result, the components are connected via defined and standardized interfaces and can be easily exchanged. A depth camera is located above the robot and has a suitable view of the nursing bed. The real-time human keypoint detection framework OpenPose provides the current 3D pose of the patient. The camera's depth map is the basis for an occupancy grid map in which obstacles are stored. The motion planning framework MoveIt thus solves the inverse kinematics and plans a collision-free path for the robot. The relative position between the camera and the robot is calibrated using ChArUco markers and the OpenCV computer vision library and thus makes it possible to position the robot with centimeter accuracy. A state machine approach controls the robot with the transitions approach patient, grasp, and interaction.

Results

In the current state of development, defined positions described relative to the patient's keypoints could be successfully approached automatically. Likewise, the robot could perform linear and circular interaction movements around predefined joints.

Conclusion

Preliminary laboratory experiments show that the presented concept provides promising results and is suitable for automating a caretaking robot. The successive steps are the integration of the gripper and the practice evaluation by nursing staff.

Focus Session:
Digital Biomarkers for Clinical Management of Inherited Neurological Movement Disorders

A movement and tremor identification algorithm for evaluations during deep brain stimulation

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Introduction

Deep Brain Stimulation (DBS) has become one of the most important neurostimulation therapies for movement disorders. During intraoperative microelectrode recording (MER) the influence of active or passive movements on the neuronal activity is evaluated but the evaluation remains mostly subjective. Previous works have shown that quantitative objective tremor analysis can support neurosurgeons and neurologists and generate more precise and continuous data. The objective of this paper is to investigate the potential of a previously developed Weighted-frequency Fourier Linear combiner and Kalman filter-based recursive algorithm to identify tremor phases and to separate tremor from voluntary movements for the quantification of changes in tremor. The approach is tested on data from a clinical study where patients were asked to perform motor tasks while partially exhibiting tremor.

Methods

Ten accelerometer recordings from eight patients were acquired during MER from which 186 phases were manually annotated into: rest, postural and kinetic phase without tremor, and rest, postural and kinetic phase with tremor. The method first estimates the instantaneous tremor frequency and then decomposes the motion signal into voluntary and tremorous parts. The tremorous part is used to quantify tremor and the voluntary part to differentiate rest, postural and kinetic phases.

Results

Instantaneous tremor frequency and amplitude are successfully tracked online. When only analyzing tremorous phases an accuracy of 89.1% is reached. The performance drops to 76.3% when non-tremorous phases are also considered. Two main misclassifications were identified: postural phase without tremor being estimated as rest phase without tremor and kinetic phase without tremor as kinetic phase with tremor.

Conclusion

The results demonstrate the potential of the developed algorithm as an online tremorous movement classifier. It would benefit from a more advanced tremor detector but nevertheless the obtained digital biomarkers offer an evidence-based analysis and could optimize the efficacy of DBS treatment.

Sensor-based gait recordings at patients' home: first evidence of diurnal variability of gait parameters in hereditary spastic paraplegia

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Introduction

Hereditary Spastic Paraplegias (HSPs) are a heterogeneous group of progressive neurodegenerative disorders leading to increasing leg spasticity and consecutive gait impairments. Previous studies showed that instrumented gait analysis objectively quantifies gait impairment in HSP. This allows ubiquitous analysis of gait parameters in flexible environments to complement the clinical assessment. In this pilot study we assess changes of gait parameters during home recordings.

Methods

From a cross-sectional study with 112 ambulatory HSP patients, we recruited three patients (61, 63, and 72 years). Disease severity based on the Spastic Paraplegia Rating Scale was rated at 32, 26, and 17. Patients performed standardized gait tests in the morning, at noon, and in the evening over a period of two weeks resulting in more than 500 hours of recordings including more than 120 gait tests. During these gait tests, two inertial measurement units attached to the shoes recorded acceleration and gyroscopic rate. Sensor signals were processed using a previously developed algorithm for gait analysis in HSP. Consequently, temporal parameters were extracted by the algorithm.

Results

Gait parameters were significantly different between daytimes. Swing duration (% of gait cycle) was highest at noon. However, one patient showed the lowest in the morning while for a second patient it was lowest in the evening. For the third patient, no significant difference between morning and evening was observed.

Conclusion

This initial study indicates that daytime may affect gait parameters of HSP patients. Gait dysfunction based on swing duration varied individually, best performance was recorded around noon. The results of the present study suggest that daytime is a potential confounder for assessing gait in HSP. This is an important observation for standardized gait tests at the hospital and free-living gait recordings. Furthermore, these results must be confirmed in a larger HSP population.

Spectral Separation of Short Latency Tibial Nerve Evoked Potentials from Cortical Background Activity - Implications for Signal-To-Noise Management

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Introduction

Five decades ago, the diagnostic use of somatosensory evoked potentials (SEPs) pioneered clinical management of multiple sclerosis. Pilot studies and case reports indicate also a large diagnostic potential of SEPs for various types of inherited neurological movement disorders. However, time, effort, and technical restrictions of current recording systems hamper more widespread use. The identification of defined target frequency bands may promote significantly more robust signal-to-noise management (SNM) based signal processing.

Methods

We applied N-interval Fourier Transform (N-FTA) to signals from three healthy volunteers for investigating spectral components of evoked and background activity in individual recordings. From this spectral analysis, we identified target bands of high evoked-to-background ratio. We applied zero-phase target band filters in a SNM processing pipeline and performed response averaging for extracting SEPs. For comparison, we extracted SEPs also in a standard setting according to current guidelines.

Results

For nine recordings in all volunteers the largest cortical response was always obtained in derivation Cz'-Fz. Highest evoked activity and highest evoked-to-background ratio occurred between 30 and 40 Hz. Thus, the target band was set between 12 and 180 Hz. SNM provided comparable signal morphology to the standard setting as reflected by correlation coefficients $\geq$0.95 and mean deviations of P37 and N45 latencies of 0.1 ms (range -0.3 ms to 0.6 ms). For all recordings, signal-to-noise ratio was clearly better for SNM (range 6.0 to 14.9) as compared to the standard setting (ranging from "undetectable" to 10.7).

Conclusion

Based on individual well-defined diagnostic target bands, SNM allows for reliable assessment of cortical SEPs at improved quality. SNM may render evoked potential recordings less susceptible to artifacts and may allow for shorter recording times. This technique may allow for improving routine usability of SEP processing and will enhance diagnostic use for inherited movement disorders.

Biomarkers based on continuous non-invasive blood pressure - review and outlook

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Abstract

Stationary devices for continuous blood pressure (BP) with user-friendly finger sensors are getting common in various clinical fields and new wearable BP-monitors are about to enter the medical world. Apart from the commonly used parameters systolic and diastolic BP, beat-to-beat as well as pulse shape information of these devices is not easily accessible. This article is a review of existing pattern recognition analysis and an outlook to new biomarkers giving a deep insight into the cardiovascular system and its control.

Focus Session:
Engineering Approaches to Functional Health Assessments

Cross-spectral analysis quantifies the segmental coordination in unstable sitting

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Introduction

Low back pain (LBP) affects many individuals and is known to be associated with impaired trunk control. While LBP can be resolved by treating underlying trunk impairments, a better understanding of the mechanistic origin of the disorder is required. Trunk control has been commonly studied via an unstable sitting paradigm. Knowledge on how the base of support and body segments work together to complete the unstable sitting task, and how this is modified in individuals with LBP, could be utilized when designing interventions for this population. Our objective was to characterize the segmental coordination in non-impaired unstable sitting as elicited via a wobble board (WB) paradigm.

Methods

WB, pelvis, and trunk motion were recorded in fifteen non-disabled participants sitting on a wobble board. We used cross-spectral analysis to quantify the coordination of the anterior-posterior angular kinematics of the wobble board, pelvis, and trunk.

Results

During unstable sitting, the motion of the pelvis was followed by that of the trunk (one-eighth-cycle delay) and wobble board (half-cycle delay) at frequencies between 1 and 2 Hz.

Conclusion

Future work should utilize the knowledge gained in this study when creating rehabilitation interventions for individuals with LBP.

Clinical utility of gait stability measures: Selection and preliminary evaluation of the margin of stability

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Introduction

Gait-related falls account for most falls in the elderly. The identification of individuals at risk of falling due to unstable gait requires clinically feasible measures that can detect impairments in gait. Our objective was to: (1) assess the feasibility for clinical implementation of existing gait stability measures and select the most viable ones; and (2) evaluate the ability of the selected measures to detect gait impairments.

Methods

Nine measures were assessed for clinical feasibility, with only the margin of stability (MOS) being selected for evaluation. Ground reactions and motion of the lower body were recorded in fifteen non-disabled and three disabled participants during treadmill walking. Medial-lateral MOS was calculated and compared between the non-disabled and disabled participants to evaluate its ability to detect gait impairments.

Results

MOS values at heel strike (HS) and at the point between HS and contralateral toe-off with minimum MOS deviated between participants with lower limb impairments and non-disabled participants.

Conclusion

MOS at HS demonstrated the greatest potential to assess fall risk. Additional work is required before MOS can be recommended for clinical use.

Improved Global Navigation Satellite System filtering methods for the mobile six-minute walk test

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Introduction

Heart failure (HF) is a chronic disease with high hospitalizations rates and increased mortality.
The six-minute walk test (6MWT) is a standardized method to assess the functional health of HF patients by measuring the distance walked in six minutes.

Methods

The improved 6MWT with new filter algorithms, based on the development of smartphone application, can be used everywhere with a good global navigation satellite system (GNSS) signal.
This paper tests multiple filtering approaches to reduce the measured distance error in the application.

Results

We were able to decrease the average relative error of the application from 4.5% to 2.0%.
Additionally, the number of experiments with relative error over our chosen clinically significant difference of 5% is reduced by 90%.

Conclusion

Keeping these results in mind, the system can be considered clinically acceptable.

Home rehabilitation system for the upper extremity focusing on technology-aided assessment of spasticity

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Introduction

With the prevalence of stroke and other neurological diseases that cause deficiencies in sensory-motor function it is of utmost importance to have effective treatment modalities and assessment methods. This paper presents a robotic wrist rehabilitation device that facilitates both pronation/supination and flexion/extension movements. Further, it provides technology-aided assessment capabilities through measurement of joint stiffness, range of motion (ROM) and detection of the catch that is often associated with spasticity.

Methods

The mechanical and electrical system design, allowing for aforementioned training and assessment capabilities, is presented.
An indirect torque measurement via the actuator currents is proposed, which can determine the angle of catch, and compared to the already established methods of using inertial measurement units.
Based on this, and the already established methods of angle of catch assessment using data from inertial measurement units, a different approach of spasticity assessment is developed. The approach is tested using a simplified, mechanical model of the joint catch on the presented device.

Results

The established IMU based methods as well as the proposed torque measurement show similar performance with regard to assessment of the catch angle. This is the case independent of the movement velocity, where evaluations were carried out in the range of 40°/s to 90°/s.

Conclusion

Therefore, the presented device with its torque measurement approach shows a potential to assess not only joint stiffness but also the angle of catch without additional sensors. This has the benefit of potentially allowing for the implementation of technology-aided assessment capabilities in robotic rehabilitation devices like the one presented, without increasing the system complexity and cost.

Design of an experimental platform for gait analysis with ActiSense and StereoPi

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Introduction

Gait analysis is a systematic study of human movement. Combining wearable foot pressure sensors and machine learning (ML) solutions for a high-fidelity body pose tracking from RGB video frames could reveal more insights into gait abnormalities. However, accurate detection of heel strike (HS) and toe-off (TO) events is crucial to compute interpretable gait parameters.

Methods

In this work, we present an experimental platform to study the timing of gait events using a new wearable foot pressure sensor (ActiSense System, IEE S.A., Luxembourg), and Google's open-source ML solution MediaPipe Pose. For this purpose, two StereoPi systems were built to capture stereoscopic videos and images in real time. As a proof of concept, MediaPipe Pose was applied to one of the synchronised StereoPi cameras, and two algorithms (ALs) were developed to detect HS and TO events for gait analysis.

Results

Preliminary results from a healthy subject walking on a treadmill show a mean relative deviation across all time spans of less than 4 % for the ActiSense device and less than 16 % for AL2 (33% for AL1) employing MediaPipe Pose on StereoPi videos.

Conclusion

Finally, this work offers a platform for the development of sensor- and video-based ALs to automatically identify the timing of gait events in healthy individuals and those with gait disorders.

Modeling and Error Analysis in Camera-Based Jump Height Measurement

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Introduction

In this work, we use simulated data to quantify the different failure mechanisms of a previously presented low-cost jump height measurement system, based on widely available consumer smartphone technology.

Methods

In order to assess the importance of the different preconditions of the jump height measurement algorithm, we generate a synthetic dataset of 2000 random jump parabolas for 2000 randomly generated persons without real-world artifacts.
We then selectively add different perturbations to the parabolas and reconstruct the jump height using the evaluated algorithm.
The degree to which the manipulations influence the reconstructed jump height gives us insights into how critical each precondition is for the method's accuracy.

Results

For a subject-to-camera distance of 2.5 meters, we found the most important influences to be tracking inaccuracies and distance changes (non-vertical jumps).
These are also the most difficult factors to control.
Camera angle and lens distortion are easier to handle in practice and have a very low impact on the reconstructed jump height.
The intraclass correlation value ICC(3,1) between true jump height and the reconstruction from distorted data ranges between 0.999 for mild and 0.988 for more severe distortions.

Conclusion

Our results support the design of future studies and tools for accurate and affordable jump height measurement, which can be used in individual fitness, sports medicine, and rehabilitation applications.

Focus Session:
Extracorporeal-Based Perfusion

The use of cytokine adsorbers improves the contractile function of hearts after resuscitation

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Introduction

Cytokine adsorbers are used increasingly in cardiac surgery and cardiovascular perfusion. Some centers also report the use of cytokine adsorbers during extracorporeal cardiopulmonary resuscitation (ECPR). Nevertheless, the isolated effect of cytokine adsorption therapy on the contractile function of the heart after ischemia is unknown.

Methods

In a porcine model, we induced cardiac arrest by asphyxia. To investigate the effect of cytokine adsorption therapy (CytoSorb®, CytoSorbents) on the heart under controlled conditions, the hearts were explanted and resuscitated by reperfusion in Langendorff fashion with ((+)CS group, N=7) and without ((-)CS group, N=7) use of a cytokine adsorber. After 4 h, we measured left ventricular contractile function with a balloon catheter inserted through the mitral valve. Additionally, we performed pressure-contractility-matching (PCM) by measuring contractility at different coronary perfusion pressures.

Results

The (+)CS group showed a significantly improved endsystolic pressure (ESP; 160±13 vs. 103±15 mmHg; p=0.017), as well as significantly improved systolic pressure increment (dp/dtmax; 1941±164 vs. 854±139 mmHg/s; p<0.001) and diastolic pressure decrement (dp/dtmin; -1062±154 vs. -493±69 mmHg/s; p=0.005), compared to the (-)CS group. During PCM, the (+)CS group showed again a significantly improved ESP (107±6 vs. 70±14 mmHg; p=0.032), dp/dtmax (1399±109 vs. 632±106 mmHg/s; p<0.001) and dp/dtmin (-729±176 vs. -372±46 mmHg/s, p=0,091) at 20 mmHg of perfusion pressure, compared to the (+)CS group.

Conclusion

The use of CytoSorb® during isolated reperfusion and resuscitation of porcine hearts improves the contractile function of the left ventricle and could therefore also be beneficial during ECPR.

Effects of ECMO on hemostasis and the influence of COVID-19 on early thrombosis

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Introduction

COVID-19 can deteriorate pulmonary function to a degree that extracorporeal membrane oxygenation (ECMO) is needed as a life-saving intervention. COVID-19 as well as ECMO may cause severe coagulopathies which manifest themselves in micro and macro thrombosis. Previous studies established D-dimers as a marker for critical thrombosis of the ECMO system while increased D-dimers on admission are associated with a higher mortality in COIVD-19 patients. It is therefore crucial to determine if COVID-19 poses an increased risk of early thrombosis of the ECMO system.

Methods

40 patients who required ECMO support were enrolled in a retrospective analysis and assigned to two groups. The COVID group consisted of COVID-19 patients who required ECMO support (n=20), whereas ECMO patients without COVID-19 were assigned to the control group (n=20). D-dimers, fibrinogen, antithrombin III (ATIII), lactate dehydrogenase (LDH) and platelet count were qualitanalysed using locally weighted scatterplot smoothing and MANOVAs.

Results

In COVID-19 patients D-dimers reached their peak two days earlier than in the control group ($p=2{,}8115\cdot 10^{11}$). In COVID-19 fibrinogen decreased linearly while in the control group fibrinogen levels increased rapidly after ten days ($p=1{,}407\cdot 10^{3}$). In both groups a rapid increase in ATIII beyond 130 % at the start of ECMO was observable ($p=5{,}96\cdot 10^{15}$). In the COVID-19 group platelet count decreased from 210 giga/l to 130 giga/l after six days, while in the same time period platelets of the control group decreased from 180 giga/l to 100 giga/l ($p=1{,}1\cdot 10^{15}$). In both groups a marked increase in LDH beyond 5000 U/l occured ($p=3{,}0865\cdot 10^{15}$).

Conclusion

The early increase in D-dimers and decrease in fibrinogen suggests that COVID-19 patients bear an increased risk of early thrombosis of the ECMO system compared to other diseases. Additionally, the control group showed signs of severe inflammation ten days after the start of ECMO which were absent in COVID-19 patients.

On the effects of arterial vascular compliance on pulse wave velocity in a life-sized hydraulic mock circulation loop

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Introduction

Mock circulation loops are usually used to evaluate the interaction between ventricular assist devices and the native cardiovascular system. They consist of fluid reservoirs and connecting tubing pipes which could mimic instationary flow processes. Flow phenomena with counteracting extracorporeal life support systems may only be investigated if the built-in vascular models include anatomical features. Their similarity to physiological conditions would allow correctly representing circulatory parameters and transferability of simulation results to clinical practice. In this context pulse wave velocity is pivotal with its impact on pulse pressure and left ventricular afterload.

Methods

The agreement of the pulse wave velocity (PWV) to physiological values was examined in a recently developed pneumatically driven life-sized mock circulation loop with two compliant arterial and venous vascular silicone models. Two strain gauge sensors were positioned at the radial and femoral artery equivalent, the PWV was calculated with the time dependent pulse wave propagation speed of the systolic pressure between the two different vascular positions. Recording of the propagation speed was based on a MATLAB built software application with simultaneous recording of the strain gauge sensor output

Results

A technically predefined elastic modulus of the aortic silicone model around 3,1-3,4 N/mm^2 which is 10 times higher than in a healthy human aorta resulted in a systolic peak propagation time around 36 ms. The resultant PWV around 20,3 m/s was 3,6 times higher than a PWV around 5,6 m/s of a stratified age category of 50 to <60 years

Conclusion

Higher compliance values are practically required to increase durability and robustness for handling complex mock loops. A resultant higher PWV decreases the validity of circulatory models, suggesting a strong impact of PWV on wave propagation and counteracting instationary flow processes. This should be considered when results are transferred to clinical practice.

Promising AI-based approach to detect health risks by analysing blood values of patients undergoing ECMO

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Introduction

Extra Corporeal Membrane Oxygenation (ECMO) indications and usage has become an essential tool for patients with severe cardiac and pulmonary dysfunction refractory to conventional management. Its use can affect the blood in many complex and poorly understood ways, leading to excessive bleeding or clotting. Patients who are to weak to undergo open heart surgery use the less invasive procedure called Transcatheter Aortic Valve Implantation (TAVI). In this paper, a multiparametric analysis is performed regarding to platelets, hemoglobin, hematocrit, thromboplastin time and fibrinogens while using ECMO and TAVI.

Methods

The dataset consists of 30 patients, in which 15 patients were undergoing ECMO and the other 15 patients were undergoing TAVI. In the first analysis, the data history of all parameters is plotted and the structure investigated. In the second analysis, the parameters are investigated for their correlations.

Results

In the first analysis it became visible that the values of the platelets and fibrinogens fall down, before the organism reacts and the values increase again. The organism tries to level off the values. Investigating the correlation between these parameters results that hemoglobin and hematocrit correlate strongly with each other. However, in almost all cases the correlation between hemoglobin/hematocrit with platelets is low. In two cases, in which the platelets fall extremely down, the correlation between these parameters is high. A patient that didn't survive the ECMO procedure show the highest correlation between hemoglobin and platelets with 0.77 and hematocrit and platelets with 0.87.

Conclusion

The analysis of blood values after ECMO and TAVI show that patterns are available in the data history. It was also determined that the correlation between these parameters depends on the health state. Thus, a larger dataset provides the capability to monitor the health state with artificial intelligence and recognize risky states or anomalous patterns in the data history.

Investigation of the Drift Characteristics of Inline Blood Gas Sensors

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Introduction

During extracorporeal membrane oxygenation (ECMO), the status of blood gases is measured discretely every hour. To increase patient safety, online measurement of blood gases and pH-value is of great interest. Existing systems for online blood gas measurement have disadvantages e.g., complex calibration procedures or shunt mode operation. A measuring system with easy handling, high measurement accuracy and minimal drift is required. We present the evaluation of drift characteristics from a new optical online measurement system.

Methods

We used a new designed fluorescence optical measurement system with three dedicated sensor tips for blood gases (p_{CO2}/p_{O2}) and pH-value. An in vitro test setup consisting of blood pump, oxygenator, and silicone tubing was established to evaluate drift characteristics. Sensor tips were integrated inline via luer lock connection. A constant blood gas composition (p_{O2}=114 mmHg, p_{CO2}=48 mmHg, pH=7.3) was achieved by adjustment of the gas composition running through the oxygenator. Porcine blood was used, which was collected during slaughter process, heparinised and stored on ice for transport. Sensor characteristics were measured three times over a period of 6 hours. Reference measurements with a blood gas analyser ABL80 radiometer were realised at 30-minute intervals. To evaluate the sensor drift, the slope of the sensor characteristic curve was determined.

Results

The results show a maximum slope over 6 hours of 3,4 mmHg for p_{O2}, 1,26 mmHg for p_{CO2} and 0,11 for pH and demonstrate a smaller standard deviation (s_{PO2}=1,0mmHg, s_{PCO2}=1,0mmHg, s_{pH}=0,02) than the reference method (s_{PO2}=1,9mmHg, s_{PCO2}=1,8mmHg, s_{pH}=0,04).

Conclusion

All three sensors showed a slight drift over 6-hours period with a small standard deviation. Next steps will focus on studying blood gas changes during in vivo experiments to investigate the effect over a wide range of measurement parameters. In the future, it might be possible to monitor blood gases continuously throughout ECMO to improve patient safety.

Focus Session:
FWF doc.funds programme:
Image-Guided Diagnosis and Therapy

Augmenting microscopic navigated surgery with knowledge

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Abstract

The study of 3D object segmentation is one of the most challenging areas of research in computer vision especially in medical video analysis. The aim of this work is to identify 3D anatomical ear-nose-throat (ENT) structures in live video streams provided by a high-precision stereo-microscopic navigation system during ENT surgeries. The mentioned surgeries have been considered as the challenging procedure due to the deep cavities and subtle structures existed in the desired areas. The goal of 3D anatomical detection is to demonstrate structures in the external ear lobe and the ossicular chain in order to create automatic segmentation of anatomical structures and to augment microscopic navigated surgery for ENT surgeons. In addition, the oriented 3-dimensional bounding boxes around the mentioned areas in the 3D real world will be estimated. Most of the existing methods for the 3D object detection, are based on supervised machine learning techniques, considering that accurate 3D ground truth is provided in the training dataset. For this purpose, amanually created preliminary atlas of ENT structures created from CT data will serve as ground truth to extract the anatomic structures form the live video stream using computer vision and (un-) supervised machine learning approaches.As a proposed method, Convolutional Neural Network (CNN) will be applied to the trained datasets due to recent workswhich have been shown bright performances in various applications such as image classification, object detection, and semantic segmentation. Stereo cameras mounted on the microscope provide disparity images for detection, localizationand reconstruction of the structures in the surgical scene. Hence, based on the information obtained by a CNN and the disparity images, the exact 3D anatomical structures can be established. Due to the lack of a large-scale training dataset, transfer learning approach and data augmentation techniques will be checked using different deep learning algorithms. In this project different open-source libraries such as the Insight Registration and Segmentation Toolkit (ITK) and the Visualization Toolkit (VTK) which are written in C++ language will be utilized.

Preliminary data on a fully automated left ventricular late gadolinium enhancement detection by a convolutional neuronal network in chronic myocardial infarction

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Introduction

The aim of the study is to compare a fully automated segmentation of left ventricular late gadolinium enhancement (LGE) as evaluated by a convolutional neuronal network (CNN) with manual segmentation in chronic myocardial infarction.

Methods

Cardiac magnetic resonance imaging including two-dimensional LGE imaging was performed in 207 patients on a 1.5 T clinical scanner 12 months after ST-elevation myocardial infarction. LGE images were presented to a trained CNN for automated determination of left ventricular myocardium and consequently absolute LGE volume. Manual LGE segmentation according to the +5-SD method was used as reference standard. Image quality was assessed according to a 3-point Likert scale (2 = perfect image quality, 1 = some artifacts witout impaired LGE delineation, 0 = strong artifacts with impaired LGE delineation). Regression and Bland-Altman analysis were performed.

Results

In 207 included patients (177 male, mean age 57 years) LGE volume was 10.1 [IQR 3.8 to 17.0] ml according to manual segmentation and 8.9 [2.9 to 17.0] ml according to CNN segmentation. Bland-Altman analysis showed little average difference (0.6 ml, $p=0.37$), however, limits of agreement ranged from -13.8 ml to 15.0 ml. Linear correlation was fair (0.75, $p<0.001$). Subgroup analysis according to image quality showed comparable performance of CNN segmentation in all three groups.

Conclusion

Our fully automated LGE segmentation based on a CNN in two-dimensional data sets provides measurements with little average difference compared to very time-consuming manual segmentations. However, dispersion is substantially and limits the current application of this approach on a per-patient basis. Image quality does not affect CNN performance.

Machine learning in ENT

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Abstract

The presence of pathologic cervical lymph nodes for head and neck squamous cell carcinoma is regarded as an important prognostic factor. Lymph nodes are small, generally spherical or ellipsoidal shaped organs that filter disease from lymph fluid. When you have an infection, your lymph nodes swell in order to fight the infection. As a result, the primary radiologic criteria for lymph node classification in computed-tomography scans are based on shape.
Radiomics is a method that extracts a large number of quantitative data ("features") from medical images using data-characterisation algorithms. These radiomic features have the potential to reveal tumoral patterns and characteristics that the naked eye would not be able to detect; additionally, this technique is very useful for clinical prediction.
In this project we will use radiomics methodologies in order of helping and monitoring ENT oncology. To begin, radiomic features were extracted from segmented computer tomography scans using the open source PyRadiomics Library, then the data will be fed into feature selection algorithms, which will allow the lymph nodes to be classified.

Manipulation of biological samples in an acoustofluidic device for tomographic imaging

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Introduction

With the rise of in-vitro models as cell spheroids and organoids, it has been possible to narrow the gap to in-vivo studies. As fixation or labeling of such cell models and any contact to surfaces has been found to influence the cells, it is a desire to keep them in a natural environment to study them over time.

Methods

We have developed a microfluidic trapping platform with 3D acoustic trapping and optical tweezers to trap and non-invasively manipulate sub-mm samples in solution. We couple ultrasound into the chip from three orthogonal directions, where the top transducer is transparent to comply with optical imaging.

Results

In our device, we can keep a sample levitated and reorient it due to the acoustic radiation torque by tuning the relative strengths of the orthogonal acoustic transducers. We can also induce sustained rotations of a sample around one or two orthogonal object axes due to the arising acoustic viscous torque or in combination with optical tweezers. This sample rotation allows us to inspect the sample from all direction and to collect tomographic data while imaging from the top. We have adapted our trapping platform to be compatible with high-NA optical imaging, which in addition to higher image resolution opens up for the combination with illumination scanning.

Conclusion

Here we present our sono-optical manipulation platform and show results of reorientation and sustained rotations of biological samples. We will discuss our strategies for volumetric reconstruction and how our strategy aim to achieve an isotropic resolution of the object, which is a major challenge in 3D microscopy. Our technique opens up for long-term monitoring of live cell clusters, for example in development or oncology studies, towards personalized medicine and to reduce the need for animal-testing in biomedical research.

Deep learning approach for segmentation of cervical arteries in CTA images

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Introduction

The accurate segmentation of cervical arteries from computer tomography (CT) images is a difficult challenge in radiology. Its automation, however, will allow for a quantitative analysis of arterial geometrical structure for the use in large cohort patient studies. Although convolutional neural networks have achieved state-of-the-art results for numerous segmentation tasks in medical imaging, the large memory requirements for processing 3D CT angiography images as well as a lack of manually annotated training data prevent straightforward application.

Methods

We present a method to extract the region of interest (ROI) using intensity based gaussian windowing to highlight the arteries. Then, the ROI is extracted by using Radon transforms to find the parallelepiped that covers most of the remaining pixel intensity. The segmentation masks are created in three steps. First, we locate one artery on an axial slice and then use this information to extract a small 3D patch on which the artery is locally segmented using a 3D U-Net. Based on the predicted segmentation, we estimate the further course of the artery to push the small patch along. The local segmentation on the small patch as well as the estimation are repeated until the end of given artery.

Results

The networks were trained on the manually annotated segmentation masks of 10 patients. Images of 20 further patients were used for testing the method. First results look visually very promising and computational complexity is low.

Conclusion

The segmentation task can be executed very efficiently by relying on a mixture of prior knowledge, suitably exact definition of the ROI and learning. Such an approach is especially usefull in 3d due to the large memory requirements that come with more straightforward implementations of 3d convolutional networks.

Towards novel hybrid imaging probes by chelator scaffolding

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Introduction

The outcome of surgical tumor resection benefits from preoperative imaging and intraoperative real-time guidance. Dual-modality probes, combining positron emission tomography (PET) with fluorescence imaging (FI) capabilities in the same molecule, can be used for both applications and therefore are of high clinical relevance [1,2], in particular if the probes are specifically targeted towards the tumor.
In this project we aim to synthesize and evaluate the preclinical applicability of dual-modality probes based on different chelator scaffolds using a minigastrin peptide as a targeting sequence model.

Methods

Cyclic chelators, such as Fusarinine C, TRAP-Pr and DOTA, were selected as basis for synthesizing promising hybrid imaging probes. They serve as scaffold for attaching near-infrared (NIR) dyes and small peptides based on the Minigastrin sequence targeting the CCK2 receptor by using bioconjugation chemistry approaches. The compounds are initially characterized in vitro regarding their ^{68}Ga radiolabelling and stability properties, continuing with binding studies with target expressing cell lines. Finally, the most promising compounds will be investigated in normal animals regarding biodistribution and animal tumor models for targeting studies, imaging studies using both PET and optical imaging.

Results

As initial proof of principle, [Fe]Fusarinine C obtained from genetically modified fungal cultures was used as starting material. Its scaffold was conjugated to minigastrin5 peptide and Sulfo-cyanine5.5 dye to obtain a dual-modality imaging agent.
Further synthesis and preclinical evaluation of the studied compounds are currently ongoing.

Conclusion

Our preliminary results show that the preparation of dual-labeled imaging probes based on different chelating scaffolds is feasible.
Following studies will provide data about the applicability of the prepared compounds.

References

[1] Yuen R, et al. Dual Probes for Positron Emission Tomography (PET) and Fluorescence Imaging (FI) of Cancer. Pharmaceutics 2022, 14, 645.
[2] Summer D, et al. Developing Targeted Hybrid Imaging Probes by Chelator Scaffolding. Bioconjug Chem 2017, 28 (6), 1722-1733

Focus Session:
Hearing4All - Current Status and Future Options for Auditory Implants

Cochlear size assessment predicts scala tympani volume and electrode insertion force- Implications in robotic assisted cochlear implant surgery

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Introduction

The aim is to estimate the volume of scala tympani (ST) compartment of the cochlea from a linear measurement in micro-computer tomography (µCT) image of the human cochlea. The secondary aim is to measure the electrode insertion and explantation force in different sized cochlear models.

Methods

30 µCT datasets were used to segment the ST alone to measure its volume. Also the linear measurement, which is the cochlear basal turn diameter (A-value) was measured separately. Electrode insertion and explantation force was measured in two different sized ST models by inserting a 28mm long electrode at different insertion and explantation speeds.

Results

The mean A-value measured from 30 µCT datasets was 9.0 $\pm$ 0.5 mm. The mean ST volume was 34.2 $\pm$ 9 µL, with a range of 23-50 µL). We found that the ST volume increased linearly with an increase in A-value. The insertion and the explantation forces were higher in the smaller sized ST model compared to upscaled model.

Conclusion

The ST volume or the electrode insertion/explantation force correlates with the clinical cochlear parameter, which is the A-value.

A Fibre-based Neuronal Guidance Scaffold for Cochlear Implants

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Introduction

After insertion of a cochlear implant, the distance between the electrode and the spiral ganglion neurons (SGN) is relatively large. The idea is to design a neuronal guidance scaffold that bridges the gap between the implant and the SGN. This scaffold is made of biodegradable polymer fibres which are coated with components of the extracellular matrix (e.g. laminin and heparan sulphate (HS)) to offer growing neurites a favourable environment for their extension to the electrode. In addition, the fibres are decorated with different growth factors (e.g. brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3)) which are released from the fibres to ensure the survival of the SGN, stimulate the outgrowth of neurites and direct their growth to the electrode.

Methods

Firstly, the fibres were aminolysed to generate free amino groups on the surface. Then HS was attached to the fibres covalently. After this, the fibres with and without HS were incubated in a NT-3 solution. To test the release behaviour of the different fibre-types release experiments were carried out. In another experiment, laminin was attached to amino-modified fibres covalently. These fibres were used for cell culture investigations with cochleae of neonatal Sparague-Dawley rats.

Results

After the aminolysis, the fibres had a rough surface as shown by SEM images. FTIR measurements verified the amino modification. In release experiments with NT-3, it was observed that the release is more continuous when the fibres are coated with HS previously. The cell culture investigations demonstrated that explants with SGN can grow on laminin-coated fibres.

Conclusion

The characterisation of the polymer fibres proved the successful surface modification with amino groups. The release experiments revealed that it is possible to release NT-3 from the fibres. The cell culture investigations showed promising results concerning the use of these fibres as a neuronal guidance scaffold for SGN neurites.

Development of a Dual Porous Nanocomposite Coating for Neural Electrodes: Nanoporous Silica Nanoparticles Embedded in Nanoporous Platinum

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Introduction

Platinum is used as an electrode material in neural electrodes, e.g., the cochlear implant (CI). In addition to stimulating neurons through the electrode contacts, it is also important to restore and maintain healthy conditions in the cochlea. By provision of neuroprotective substances and neuronal growth factors, it is possible to restore the balance in the inner ear and thus stabilize the remaining spiral ganglion neurons. Furthermore, the outgrowth of neurites from these cells can be induced to improve the electrode-nerve contact and increase signal resolution. For optimal application, these drugs should be released locally, for example with an implant-associated local drug delivery system. Due to the inertness of the cochlea electrode materials (platinum and silicone), the development of such a system is not trivial.
Nevertheless, to achieve local implant-associated drug delivery, we devised a novel nanocomposite material of nanoporous silica nanoparticles (NPSNPs) embedded in the pores of nanoporous platinum (NPPt), which can be used as a coating on the platinum surfaces of the CI electrode. NPPt exhibits high conductivity and favorable electrochemical properties. NPSNPs provide large surface area, permanent porosity and great versatility in terms of easily tunable surface properties to achieve high drug loading.

Methods

To fabricate the NPSNP@NPPt material on the platinum surface, a hard-template method was employed, in which silica-polystyrene core-shell nanoparticles were used as templates. Platinum was electrolytically deposited between the particles and the polystyrene was removed by extraction.

Results

SEM investigations show the successful synthesis of the desired structure of the nanocomposite. The material exhibits good electrochemical properties and increased surface area due to the NPSNPs. Cell culture studies show good cytocompatibility.

Conclusion

The novel nanocomposite material combines the favorable properties of both NPPt and NPSNPs, especially the excellent electrochemical behaviour and high specific surface area, large pore volume and amenability to surface modifications.

Testing of different coating materials for surface functionalization of CI-electrodes

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Introduction

The cochlear implant (CI) electrically stimulates the auditory neurons of people suffering severely from sensorineural hearing loss by an electrode array (EA) inserted into the cochlea. For further functional improvements of the EA, efforts are made to optimize the implantation properties and to establish an inner ear drug treatment. Both aims could be achieved by a coating of the EA supporting a smooth implantation and allowing drug release.

Methods

Two hydrogels (alginate, chitosan) and two clinically used tissue adhesives (Tisseel®, Indermil®) were selected for testing their suitability for manual dip coating of silicone dummies of human CI-electrodes. The hydrogels differ in their characteristics but both consist of polysaccharides and need a crosslinking-step for gelation. Tisseel® is a two component (fibrinogen and thrombin) fibrin sealant and solidifies by mixing the components after thawing and warming to 37°C. Indermil® is based on an octyl blend cyanoacrylate formulation and polymerizes spontaneously after application. Coating was applied layer by layer by manually dipping the dummies and behavior during coating process, expenditure of time, and quality and robustness of the coating were compared.

Results

All tested coating materials can be applied in multiple layers. The hydrogels form a flexible, soft, and smooth coating, which is moderately robust to gripping with tools. The crosslinking is relatively time consuming and the coated dummies need to be stored in liquid medium before being processed further (e.g. implantation). Tisseel® requires alternating immersion in the two solutions and forms a smooth, flexible, and most robust coating. Indermil® needs dipping in one solution only but forms a solid crust on the silicone after polymerization.

Conclusion

All materials are suitability for manual dip coating of CI-electrode dummies but only the hydrogels and Tisseel® form a soft and flexible coating with a smooth surface, making them superior candidates for EA functionalization.

Evaluating performance of hearing implants - pupillometry as a measure beyond speech perception

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Abstract

With clinical and technological progress hearing rehabilitation with cochlear implants has achieved high levels, yet still there are a range of listening situations that are particularly challenging for implant users. Regardless of whether one considers clinical or technological advances, any attempt to further improve the system necessitates reliable and sensitive performance indicators. While traditionally speech perception is the predominantly used performance measure, several aspects of hearing performance are not adequately captured by speech perception alone. Furthermore, current audio processors for hearing implants contain signal processing stages which do not specifically aim at an improvement in speech perception and still improve the transmitted signal. Thus, the cognitive load required for understanding speech might vary while speech perception itself is unchanged. Measuring pupil dilation during auditory tasks has been shown to be a reliable indicator of listening effort and has been successfully applied to speech and non-speech related tasks.

This contribution will show how challenging listening situations like increased speaking speed or increased reverberation affect speech perception and listening effort in normal hearing listeners and how these findings apply to research in cochlear implants.

Focus Session: Implantable Assistance Systems and Rehabilitation Technology

Microelectrode Arrays for assesment of gastrointestinal motility - feasibility of minimally-invasive implantation

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Introduction

Disorders of gastrointestinal (GI) motility are common, show high inter-individual variety in symptoms and cause, and also lack structured therapeutic principles due to paucity of comprehensive neuro-anatomical assessment. The NEPTUN (BMBF 13GW0271D) research project aimed to develop a microelectrode array (MEA) for implantation onto the superior hypogastric plexus and its strands to create a neuro-electronic-interface for analysis and stimulation of the lower GI motility. While the dictum in lower GI surgery demands distinct protection of pelvic nerve structures, feasibility of a minimally-invasive implantation has to be demonstrated, yet. We present results and a video of a first MEA implementation onto the superior hypogastric plexus in a porcine model.

Methods

In preliminary studies open surgical approach to the superior hypogastric plexus was established in porcine and human cadavers. Using the established techniques from laparoscopic pelvic surgery, the presacral plane was accessed and the plexus was visualized with caution. A custom-built MEA was implanted trans-abdominally and the wires were externalized posterior to the ureter and iliac vessels into the subcutis using a single transcutaneous access to the retroperitoneum. Wireless connection to the device was established after closure of the abdominal cavity.

Results

Laparoscopic access to the superior hypogastric plexus and implantation of a MEA is feasible. Externalization of wires can be established by retroperitoneal guidance in humans and porcine models.

Conclusion

This work might extend the range of intraabdominal MEA device application by demonstrating feasibility of the implantation technique.

Impact of alternating current stimulation on osteoblasts' ROS production - direct contact AC-stimulation vs. AC-conditioned liquids

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Introduction

Electrical stimulation of bone has been used in experimental treatments since Fukada and Yasuda first described the piezoelectrical properties of bone [Fukada,Yasuda 1957]. Many studies described beneficial effects of electrical stimulation in fracture healing and in vitro studies have reported enhanced cell proliferation and collagen production [Griffin 2011][Pettersen 2021]. During electrical stimulation via direct contact electrodes, faradic byproducts like H2O2 can be produced. H2O2 belongs to reactive oxygen species (ROS), which influence osteoblasts' fate [Tao 2020]. The focus of our AC-stimulation study was on intracellular ROS production and the question whether AC-stimulated medium alone can influence cellular behavior.

Methods

Human osteoblastic MG-63 cells (ATCC) were cultured in DMEM (10% FCS) without phenolred and pyruvate. Electrical stimulation was applied to cells or medium for 2 h at 20 Hz, 10 ms rectangular pulses using L-shaped platinum electrodes [Mobini 2016] under standard culture conditions. Stimulation was current driven at 6 mA. Cellular ROS was detected by DCFDA Assay (Abcam) by incubation with 20 µM DCFDA for 30 min at 37°C. H2O2 was quantified by fluorimetric hydrogen peroxide assay kit (Sigma-Aldrich).

Results

Cellular ROS levels were significantly elevated up to 24 h in AC-stimulated cells compared to the control. The H2O2 concentration in the media was significantly increased directly after electrical stimulation and declined nearly to basic level over time. When cells were seeded in AC-stimulated liquid, ROS levels also increased within 24 h, even though the effect was not as strong as in directly stimulated cells.

Conclusion

AC stimulation with our chosen parameters leads to an increase of H2O2 in the cell culture medium. This affects cellular ROS production i.e. AC-stimulated medium alone influences cell fate.

A Versatile Neuromodulator Platform based on an Integrated Circuit

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Abstract

Closed-loop neuromodulation has shown tremendous potential in the treatment of various neurological ailments, including Alzheimer's disease, epilepsy and Parkinson's disease. The neuromodulator System-on-Chip developed by the University of Ulm realizes a fully-digital interface to the brain on an area of roughly 5x5mm^2, while consuming approximately 6mW. It includes 32 bidirectional channels, each with a low-noise recording front-end featuring various programmable gain and bandwidth options resulting in local field potential, action potential or full-band configurations. Each channel further includes a highly flexible stimulator, providing high voltage compliance ($\pm$9V), a large dynamic range of stimulation currents (32µA to 10mA), almost arbitrary waveform generation and constant current or constant voltage stimulation modes in a very efficient implementation. Additionally, the system includes safety features such as an electrode impedance estimation ($\pm$10% accuracy, [Reich et a., JSSC 2021]) which allows monitoring of the electrode condition while implanted by utilizing both the recorder and the stimulator unit. Blanking switches, passive charge balancing via discharge switches and tunable high-pass corners allow for a very fast recovery of the recorder after stimulation. The application specific integrated circuit is controlled by a digital interface and includes a second data interface where the recorded data, digitized by two on-chip 16-bit incremental Delta-Sigma ADCs, is combined into a single data stream transmitting at 10.24Mbit/s. The system has been successfully validated in-vitro, using phosphate buffered saline solution and PtIr-electrodes, and in-vivo using a rodent model with shaft electrodes. In the latter experiment, spike data was successfully recorded at an input-referred spike amplitude of approximately 30 µV. Possible future applications include the restoration of lost motor function in paralyzed patients and treatment of chronic pain, e.g., after stroke.

C-Fibre stimulation and recording of abdominal, autonomic nerves

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Introduction

Electric stimulation of and recording from peripheral nerves is a common approach in different medical applications. However, in general this means stimulation and recording A-fibres, as these fibres are stimulated with lower thresholds resulting in higher signal amplitudes. Apart from this abdominal, autonomic nerves have been shown to contain mainly thin, unmyelinated C-fibres which require different stimulation parameters and result in rather low signal amplitudes. This experimental work focuses on these specialties.

Methods

Evoked C-fibre activity was recorded from abdominal, autonomic nerves in an animal model using a neuromonitoring device.

Results

C-fibre activity could be shown with distance dependend stimulation thresholds between 7.5 to 40 mA and pulse widths of 0.3 to 1.5 ms.

Conclusion

C-fibre stimulation needs specialised stimulation and recording technology which will be a challange for implant development.

Real-time optimization of the position of an epidural spinal cord electrode for restoration of walking in people with spinal cord injury

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Introduction

Epidural electrical stimulation of the lumbar spinal cord represents a promising technique for restoration of standing and walking in people with spinal cord injury (SCI). With a gait-phase-adapted, targeted activation of specific dorsal afferent nerve roots the best outcome can be achieved. Because the correct positioning of the electrode is essential, the Eurostars-funded CONFIRM project aimed at developing and validating a real-time algorithm to support the intraoperative electrode placement.

Methods

We developed an algorithm consisting of 4 sequential steps (gross rostrocaudal, mediolateral, fine rostrocaudal positioning and final manual check) and providing information whether the actual electrode position is in the right cord segments and is better, worse or comparable to the previous position. It basically analyzes the sequence of electromyographic (EMG) responses of lower limb muscles during stimulation of predefined electrodes within the array.
For algorithmic validation, EMG data was analyzed from 28 lower body/limb muscles collected during the surgical placement of an epidural electrode array in an individual with a chronic complete SCI (level of injury C4). The stimulation amplitude of each of the 16 electrodes of the array was increased in steps of 0.5 mA (pulsewidth 300 µs, frequency 1 Hz) until EMG responses of at least two muscles were detected for three times.

Results

The offline-analysis of the data with the CONFIRM algorithm shows a correct rostrocaudal position and a mediolateral shift with potential tilt of the array. Both results are in line with the clinical impression of two experts. The automated threshold-based detection of the presence of evoked EMG-responses by the real-time capable cross-correlation with a muscle-specific reference EMG-response seems to be feasible.

Conclusion

The CONFIRM-algorithm based on the stepwise increase of stimulation amplitudes until the first detection of evoked EMG-responses supports the optimal positioning of an epidural electrode with a minimal number of steps.

Focus Session: Mechanics of Musculuskeletal Tissues: From Experiments to Computer Simulations (Joint Session with Austrian Branch of the European Society of Biomechanics)

A new compression test set-up for measuring visco-elastic material properties of individual trabeculae in physiological conditions

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Introduction

Bone's strength is based on its structural and material properties. While the structural properties, such as density and micro-architecture are straightforwardly measured with modern X-ray techniques, measuring material properties however is highly resource intensive. Further studies especially on trabecular bone show incoherent results. To improve the situation we developed a methodology and setup to characterize the material properties of the trabecular bone at the level of individual trabeculae, loaded in compression in a physiological environment.

Methods

For proof of principle, three trabeculae were excised from a human femoral head (Male age 72, no osteoporosis) and their geometry was measured via micro-computed tomography (µCT100, SCANCO Medical, nominal resolution 3.3µm, voltage 70kVp, current 145µA). Compression tests were performed with a servo-electric load frame (SEL-mini, Thelkin), equipped with a 10 N load sensor (S2M-10, HBM), and a HBSS water bath. Speckle patterns sprayed onto the samples prior to testing were tracked with a video camera (Kitocam, Kitotec) for optical strain measurement.

Results

Determined mechanical parameters (n=3) are (mean$\pm$std) apparent compression modulus (4.53$\pm$2.46) GPa, maximum compression stress (36.8$\pm$24) MPa, maximum compression strain (10.12$\pm$6.62)%, transition strength (23.5$\pm$24) MPa and transition strain (0.61$\pm$0.39)%.

Conclusion

Literature reports tensile/compression moduli ranging from 0.75GPa to 16.85GPa. The large variation is linked to experimental challenges, limited reproducibility, low sample numbers, varying experimental conditions (dry/wet), different origin of samples, and different anatomical locations. Therefore, a systematic, and reliable characterization of individual trabeculae in compression remains to be conducted. Frank et. al [JBMR_Plus(2021)] have developed a setup for tensile experiments and reported studies testing over 300 samples. On this basis, we here present the next developmental step: reproducible compression test for individual human trabeculae, in wet conditions. We envision this to deliver material properties required to simulate physiological loading conditions.

Development and Application of a Robotic Testbench for the Investigation of Viscoelastic Parameters of the Human Hand

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Introduction

The hand is the central tool of humans to interact with their environment. The versatility of applications and the resulting structural complexity of the hand have long been recognized. Precise coordination of several muscles is required even when operating a single finger. A complete test rig of the human hand to stimulate complex movements and measure motion and loads have not been succesful implemented yet.

Methods

In this paper, we present a new test rig for studying the kinematic and viscoelastic properties of the human hand. The test rig consists of eight force-controlled motors that are connected to the muscle tendons of the hand and can thus stimulate a hand specimen. In addition, an optical tracking system captures the resulting movement of the hand and a force-torque sensor measures the resulting loads at the fingertip. The system is extended by video recording for evaluation.

Results

We present an initial study using the experimental setup, in which a cadaver hand was prepared and fixed in the test rig. By stimulating eight tendons, the tweezer grip was successfully performed with the cadaver hand and the muscle forces as well as the resulting grip force were measured.

Conclusion

The presented test rig is suitable for the application of complex biomechanical investigations and is characterized especially by its precise force control behavior of the motors. With the presented approaches, valuable dynamic data of the hand can be obtained. The measurements performed in this way can contribute decisively to the further development and validation of viscoelastic models of the human hand.

Differences in geometric characteristics and spatial correlations of mineralization between healthy and diseased human bone

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Introduction

Bone is a living tissue that is constantly remodeled. With time the newly formed bone gradually increases its mineral content. Thus, bone tissue is a mosaic of bone packets of different age and, consequently, of different degree of mineralization. Using quantitative backscattered electron imaging it is possible to quantify the local mineral content on a scale of approximately one micrometer [1].

Methods

We have analyzed quantitative backscattered electron images obtained from human iliac bone. The samples stem from a reference adult and children cohort, and from children suffering from osteogenesis imperfecta (OI). We calculated separately in trabecular and cortical compartments the distance of each bone pixel to the nearest surface and related it to the local calcium content. Furthermore, spatial correlations in the degree of mineralization were assessed.

Results

For cortical bone, the distance histograms for the three different cohorts were similar. In contrast, for trabecular bone, the histogram corresponding to the adult cohort had the largest distances, while trabecular OI bone had the smallest distances to the surface. This is consistent with the observations that trabeculae are thinner and the osteocyte lacunae density is high in OI bone. All investigated samples show an increase in calcium content with increasing distance from the surface, nevertheless the shape of the curve obtained from OI bone is remarkably different compared to the healthy cohorts. Spatial correlations revealed similar differences in curves from OI bone compared to the healthy reference cohorts.

Conclusion

Geometric analyses are able to spot differences in healthy and diseased bone tissue. It is promising trying to relate the found characteristics also to mechanical properties. This might shed new light on mechanical peculiarities observed in bone pathologies, e.g, the high fragility of bone observed in OI.

References

[1] Hartmann, M.A. et al., Calcif. Tissue. Int. 109, 190 (2021)

Femoral bone composition and porosity: “Variances” and “in-variances” across species (cow, horse, ostrich, emu, pig, rabbit, and frog)

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Introduction

Bone is a hierarchically organized material. It is produced and absorbed by biological cells residing in the fluid environments filling (larger) vascular pores and (smaller) lacunar pores. The extracellular material is made up of hydroxyapatite crystals, collagen type I molecules, and water with non-collageneous organics.

Methods

We here explore the variation of
the associated physical quantities (mineral, organic, and water concentrations; vascular, lacunar, and extracellular porosities) across species, organs, and ages; by means of light microscopy
and dehydration-demineralization tests on femoral shaft tissues from cow, horse, emu, frog, ostrich, pig, and rabbit; by means of light microscopy and dehydration-demineralization tests.

Results

The extracellular volume
fractions of organic matter turn out to be similar across all tested non-amphibian tissues; as do the extracellular volume fractions of hydroxyapatite across all tested mammals. Hence, the chemical composition of the femoral extracellular bone matrix is remarkably “invariant” across differently aged mammals; while the water content shows significant variations, as does the partitions of water between the different pore spaces. The latter exhibit strikingly varying morphologies as well.

Conclusion

Our finding [1] further evidences the “universal patterns” encountered in
evolutionary developmental biology [2,3]; also, it provides interesting design requirements for the development of novel biomimetic tissue engineering solutions.

References

[1] Mat Sci Eng C 117, 111234, 2020.
[2] J Theor Biol 287, 115-130, 2011.
[3] J Theor Biol 244, 597-620, 2007.

Does an additional anterolateral tenodesis protect the anterior cruciate ligament after reconstruction?

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Introduction

In ligamentous injuries of the knee, a lateral extra articular tenodesis (LET) can be performed additional to an anterior cruciate ligament reconstruction (ACLR). The LET is intended to prevent ACLR ruptures, unload the ACLR and restore knee kinematics. The aim of this study was the direct measurement of forces in the ACLR and LET in various knee flexion angles under external joint loading.

Methods

Six human knee specimens were used for testing in a knee joint test bench at 0°, 30°, 60° and 90° of flexion. Specimens were loaded with an anterior tibial translation force (ATF), internal tibial torque (IT) and combinations of both (ATF+IT), while graft forces of the ACLR and LET were measured with load cells and knee joint motion was analyzed with an optical camera system. The following conditions were investigated: (1)native, (2)resected ACL, (3)additional anterolateral instability, (4)isolated ACLR and (5)combined ACLR and LET.

Results

Subjected to an internal tibial torque ACLR graft forces were reduced up to 61% by an additional LET. Forces in the LET of up to 112N were measured. For an isolated anterior tibial translation force the effect of the LET on the forces in the ACLR was negligible. With an additional anterolateral instability, only the combination of ACLR+LET was able to restore the native internal rotation under internal tibial torque loading. For 30° of flexion a combination of ACLR+LET caused an non-physiological reduction of internal tibal rotation.

Conclusion

The study showed, that ACLR graft forces under internal tibial torque loading can be reduced with an additional LET and residual rotational laxity after isolated ACLR can be decreased. This might reduce the risk of ACLR ruptures, in particular for pivoting motions. Care should be taken not to overconstrain the internal tibial knee joint motion with an additional LET.

Focus Session:
Model-Based Control of Biohybrid Implant Maturation - DFG PAK 961-2

ProcessControl - Towards Closed-Loop Control of Biohybrid Implant Maturation

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Introduction

Biohybrid implants are a seminal approach to treat cardiovascular valve diseases, promising a comprehensive therapy method. While they consist of a textile scaffold providing mechanical strength and a cell-embedded hydrogel, a pre-maturation in vitro is required to stimulate the cells to synthesize an extracellular matrix which is biomechanically stable and biocompatible. Various external stimuli, including biochemical and biomechanical parameters, affect the neo-tissue formation. The object of this work was to develop a process-controlled conditioning setup which is capable of widely mastering the maturation process and addressing the cells' donor-specific behaviour by employing online non-destructive monitoring techniques.

Methods

The conditioning process of a tissue engineered heart valve (TEHV) is controlled by a central computation unit which combines the systems' actuators for stimulation and sensors to monitor the maturation process in a model-based control software. Feedback-controlled actuators and linear motors created pulsatile flow through the TEHV with adjustable resistances and compliance. This is supported by various sensors, including pressure transducers, flow meters and a gas and pH monitoring system. A sterility-preserving multiphoton endoscopic system was employed along with a highspeed-camera and ultrasound probe.

Results

With the presented setup, TEHVs were successfully conditioned for 21 days. Manual intervention was widely replaced by implementing actuators and sensors in the process control, which finally reduced contamination risks and conditioning time. Furthermore, the tissue maturation was traceable online through the different imaging techniques.

Conclusion

The process-controlled setup with widely feedback-controlled control schemes helped to meet the need of adapted protocols for the conditioning of TEHVs. In addition, model-based control assisted in the handling of an inherently very complex system. Moreover, the setup helps to gain a deeper understanding of the maturation process by providing a basis for iterative investigation of different process parameters. This opens new prospects not only for research on TEHVs, but all types of biohybrid implants.

Tuning mechanical properties of fibrin-dextran hydrogels for the application in tissue engineered heart valve implants

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Introduction

Heart valve disease have become a major cause of mortality worldwide. The most common treatment for this disease is surgical replacement with a mechanical or biological heart valve. However, these implants have significant drawbacks (e.g., limited lifetime, risk of thrombose, and inability to grow). Therefore, efforts are being made to fabricate tissue-engineered heart valve implants (TEHVIs), which consist of cells in hydrogels with high mechanical stability and biocompatibility. Here, fibrin hydrogels are auspicious, as their natural occurrence in the body promotes cell proliferation and growth. Furthermore, the mechanical stability of fibrin hydrogels can be increased through additives (e.g. copolymers, biopolymers, etc.). Biopolymers such as dextran represent a promising option, as they exhibit biocompatible and biodegradable properties combined with tunable molecular weights and affordable production cost.

Methods

In this work, we introduce a hydrogel composed from natural fibrin and dextran hydrogels for the application in TEHVI. Here, dextran is functionalized with glycidyl methyl ether, which allows for the formation of hydrogels with dithiol addition. By varying the concentration of the components, different compositions of fibrin-dextran hydrogels were obtained and analyzed with rheology, scanning electron microscopy (SEM) and confocal microscopy.

Results

The analysis of the gelation process via rheology showed that a higher storage modulus was obtained for fibrin-dextran hydrogels. Compared with pure fibrin or dextran hydrogel, which have only one gelation point, fibrin-dextran hydrogel blends have two independent gelation points. The images of fibrin-dextran hydrogels obtained by cryo-SEM exhibit a combined structure, which is found in typical fibrin and dextran hydrogels. The imaging of stained fibers by means of confocal microscopy was successful. First experiments on the cell viability of fibrin-dextran hydrogels are being conducted.

Conclusion

To conclude, we have developed a novel hydrogel composed of fibrin and dextran with excellent mechanical properties and biocompatibility, which shows promising behavior for application in TEHVI.

Modelling ECM formation in Tissue Engineered constructs; characterization of scaffold cell interaction

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Introduction

The challenge of Tissue Engineering is hydrogel contraction during tissue maturation. This leads to a changed 3D geometry and thus dysfunction of the target tissue. To minimize contraction and enable biomimetic loadbearing of the engineered tissue we want to develop a textile-reinforced structure tailored to specific needs of an aortic valve.

Methods

In order to analyze tissue contraction we established a novel method based on the work by Truskey et. al to evaluate tissue contraction in static and dynamic cultivation. To characterize scaffold cell interaction we incorporated multiple reinforcements with different mechanical properties and microscopic structures. The formation of the ECM is analyzed both quantitative and qualitative by two photon microscopy.
We utilized different methods of incorporating the reinforcements, which differed in how much load the reinforcement could bear. By doing so, we could analyze the how load distribution mediates the ECM formation.

Results

We found that an isometric force leads to an oriented ECM formation regardless of reinforcement. In Addition in statically cultivated samples, the reinforcement did not affect the measured ECM content when an isometric force was applied to both groups.

Conclusion

This is one of few systematic studies of how a scaffold influences the ECM formation in vitro. This novel data can vastly improve in silico growth models. By better modelling the development time of scaffolds can be shortened. Furthermore, this method can work as a platform technology for further characterizations due to its adaptability.

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Quantifying the Adhesion of Hydrogels to Polymers for the Fabrication of Hybrid Biomaterial Constructs

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Introduction

In tissue engineering, hydrogels represent a promising class of materials for the direct cell environment. To create complex, dimensionally stable structures that can withstand mechanical stress, hydrogels are reinforced with polymer scaffolds. From this arise two important research questions: How forms the hydrogel a stable bond with the polymer scaffold? How can this be quantified? We present a model system of a PVP-co-GMA-enhanced fibrin-based hydrogel and thiol-ene-based polymer scaffolds from 3D printing to investigate these questions. The epoxy function in the GMA portion of the copolymer is expected to enable covalent bonding to free thiol groups on the surface of the polymer scaffolds.

Methods

Thiol-ene-polymers and the accessibility of thiol groups were characterized by FTIR-, XPS-spectroscopy and fluorescence microscopy. To quantify the hydrogel bonding to the polymer scaffold, two polymer parts were bonded with a defined amount of hydrogel under different conditions and investigated by single-lap-shear-test. Dry and wet bonding, bonding time, surface pretreatment, and hydrogel composition were varied.

Results

Thiol-ene-polymers of various compositions were prepared and availability of free thiol groups was demonstrated. Methods for chemical bonding and bonding quantification of fibrin gels to the polymer surface were established. While dry bonding resulted in adhesion strengths between 9-42kPa, wet bondings achieved 2-33kPa depending on the combination and composition of the thiol-ene-polymer and hydrogel, with the highest values found for samples of intermediate thiol and GMA composition. Coating of the polymers with PVP-co-GMA increased adhesion strength by 60% over uncoated samples.

Conclusion

Knowledge of the bonding behavior is essential for the fabrication of hybrid constructs of hydrogels and polymer scaffolds. Optimal bonding is not necessarily achieved by maximum availability of surface groups and corresponding anchor groups in the hydrogel. Prior coating of the polymer scaffolds leads to stronger bonding and thus presumably to better integration of the hydrogel.

Substantially reduced production time and molecular imaging of a biohybrid tissue engineered vascular graft

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Introduction

The production of tissue-engineered vascular graft (TEVG) usually involves a prolonged bioreactor cultivation period of up to several weeks to achieve maturation of extracellular matrix and sufficient mechanical strength. Therefore, we aimed to substantially shorten this conditioning time by combining a TEVG textile scaffold with a recently developed copolymer reinforced fibrin gel as a cell carrier. We further implemented our grafts with magnetic resonance imaging (MRI) contrast agents to allow the in-vitro monitoring of the TEVG's remodeling process.

Methods

A non-degradable polyvinylidene fluoride (PVDF) scaffold and molded along with copolymer-reinforced fibrin hydrogel and human arterial cells. Mechanical tests on the TEVGs were performed both instantly after molding and 4 days of bioreactor conditioning. The non-invasive in vitro monitoring of the PLGA degradation and the novel imaging of fluorinated thermoplastic polyurethane (19F-TPU) were performed using 7T MRI.

Results

After 4 days of close loop bioreactor conditioning 617±85 mm Hg of burst pressure was achieved, and advanced maturation of extracellular matrix (ECM) was observed by immunohistology, especially in regards to collagen and smooth muscle actin. The suture retention strength (2.24±0.3 N) and axial tensile strength (2.45±0.58 Mpa) of the TEVGs achieved higher values than the native arteries used as control. The contrast agents labeling of the TEVGs allowed the monitorability of the PLGA degradation and enable the visibility of the non-degradable textile component.

Conclusion

Here, we present a concept for a novel textile-reinforced TEVG, which is successfully produced in 4 days of bioreactor conditioning, characterized by increased ECM maturation and sufficient mechanical strength. Additionally, the combination of our approach with non-invasive imaging provides further insights into TEVG's clinical application.

Feasibility Study of a Chip-based Device for Testing Calcification of Cardiovascular Implants

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Introduction

Calcification impedes the function of cardiovascular tissues including cardiovascular implants. Therefore, in-vitro testing of biomaterials used in cardiovascular applications is necessary to assess the calcification propensity. The cross-talk between vascular smooth muscle cells (vSMC) and endothelial cells (EC) in biohybrid implants must be enabled for in-vitro testing. To date, however, the cellular cross-talk has not been systematically studied in cell cultures, because suitable models are missing. Within this study, we investigated the calcification of different cell lines and scaffold materials of biohybrid implants in a flow chip-based testing device, overcoming numerous limitations.

Methods

The cellular cross-talk was facilitated by two monolayers of vSMCs and ECs separated by a membrane in the chip. Different cell lines of ECs and vSMCs showed varied cross-talk and behavior; therefore, variable combinations of several cell lines were tested. Calcification of cell layers, polymer scaffold, cell-seeded and cell-free fibrin-based hydrogels, as well as combinations proceeded for two weeks using calcification-inducing medium under pulsatile flow and at 37 °C temperature. The cells and different materials were dyed with fluorescence-labeled Fetuin-A, a protein with a high affinity for early calcification, and analyzed using epifluorescence microscopy.

Results

Fluorescence microscopy revealed increasing calcification lesions within the cell layer of the chip-based testing devices. Furthermore, the different combinations of cell lines showed a variable propensity for calcification. The tested materials without seeded cells showed no sign of calcification.

Conclusion

The chip-based device is sufficient to test the calcification propensity of a dual-cell model as well as cellularized and cell-free scaffold materials of biohybrid cardiovascular implants. It is suitable to apply homogenous shear stress across the entire material surface, essential for the cells and their calcification behavior. The next step is a scale-up of the design to enable testing of full-size implants under more physiological environment in terms of pressure and pulse rate.

Focus Session: Nanotechnologies for Safe & Sustainable Biomedical Applications

Iron oxide nanoparticles with supramolecular ureidopyrimidinone coating

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Abstract

Antimicrobial peptides (AMPs) are in the focus of research in the last years since they carry the opportunity to overcome antimicrobial resistance. The mode of action differs from common antibiotics as the AMPs can directly target the negatively charged bacterial cell envelope. Especially the α-helical pentadecapeptide lasioglossin III has a high potential as it shows high antimicrobial behavior at physiological salt concentrations and potency to kill various types of cancer.
Against the high antimicrobial activity of AMPs stands the possibility of protease degradation and toxicity to mammalian cells in higher concentrations. Conjugating AMPs to polymers or nanoparticles can improve their performance and overcome these issues. The covalent binding of lasioglossin to ureidopyrimidinone units (UPy) allow the formation of stable supramolecular nanostructures while keeping the bioactive α-helical structure. Combining superparamagnetic nanoparticles by imine binding allows generating a magnetically controlled drug delivery system. That has the opportunity to carry the drug directly to the target. A high local concentration can improve efficiency while avoiding toxicity.
For characterization, infrared spectroscopy, transmission electron microscopy, X-ray diffraction, dynamic light scattering, zeta potential measurements, and Nile Red assay are used. The transformed particles are stable and have hydrophobic pockets.
The research focuses on the combination of UPy-AMP and magnetic nanoparticles in antimicrobial experiments with Escherichia coli. The new drug delivery system also shows high cytocompatibility in growth experiments and live dead staining with HK-2 cells. In internalization experiments, the interaction with human cells from attachment to internalization can be followed.
The work shows a new effective, cytocompatible drug delivery system for antimicrobial peptides that can be magnetically guided to the target.

Nanoparticle-based delivery of cmRNA as a novel therapeutic for tendon regeneration

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Introduction

Osteoarthritis (OA) is the most common chronic joint condition, affecting >40 million Europeans. Chemically modified mRNAs (cmRNA) for drug development have received considerable attention, however effective transfer to cells and tissues is required for successful outcomes. The aim of this study was to develop a safe and effective cmRNA therapy for OA, using injectable polymer-based nanoparticle carriers, enabling the effective delivery of therapeutic cmRNAs to cartilage and tendons.

Methods

Increasing amounts of poly(amidoamine)s-based nanoparticles (NPs) loaded with tdTomato cmRNA were used to determine the optimal cmRNA delivery conditions for rat tendon derived cells in 2D culture and explanted rat tail tendon fascicles. Therapeutic cmRNAs (i.e. Pdgfß, Il1ra) were tested for their translation efficiency by Western blot analysis 24, 48 and 72h after NP-based delivery. Gene and protein expression of several pro-inflammatory cytokines (i.e. Il1ß, Il6, Cox2, Tnfa) were investigated to demonstrate the anti-inflammatory effect conferred by Il1ra cmRNA, while cell proliferation and migration were determined for Pdgfß treated cells. Lastly, the functional efficacy of target cmRNAs was tested in vivo using an established rat patellar tendon window defect model.

Results

The strongest increase of Il1ra and Pdgfß protein in in tendon cells and cell culture supernatants was observed 24h and 48h after NP-based delivery of the respective cmRNAs. Treatment with Il1ra cmRNA repressed the expression of several pro-inflammatory cytokines (i.e. Il1ß, Il6, Cox2, Tnfa) in a tendinopathic organotypic tissue explant model, while Pdgfß cmRNA significantly increased tendon cell proliferation and cell migration in vitro. The in vivo rat model further emphasized the therapeutic effects of the NP based cmRNA delivery.

Conclusion

The poly(amidoamine)s-based NPs proved successful for delivery of therapeutic cmRNAs (i.e. Il1ra, Pdgfß) resulting in anti-inflammatory and pro-regenerative effects in tendon cells and tissue in vitro and in vivo, potentially paving the way for future therapeutic approaches.

Transforming nanosafety to SSbD: adopting emerging concepts and integrating novel tools into established workflows

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Abstract

Nanosafety assessment has experienced an intense era of research during the past two decades driven by a vivid interest of regulators, industry, and society. Toxicological assays based on in vitro cellular models have undergone an evolution from experimentation using nanoparticulate systems on singular epithelial cell models to employing advanced complex models more realistically mimicking the respective body barriers for analyzing their capacity to alter the immune state of exposed individuals. We have thus arrived at a state where underlying mechanisms are being elucidated, effects on vulnerable groups addressed, material mixtures tested, realistic doses used, and sophisticated realistic models applied. Moreover, data access, quality assurance, metadata availability, and reproducibility have become a significant demand, driven by the FAIRification process. The Bio-Nano Interactions Group at PLUS contributed in the area of respiratory human health, with expertise in allergy and nanosafety, by studying the interaction of allergens and nanomaterials at molecular and cellular levels. Impact on the epithelial integrity has been recognized as having high potential of compromising the general health state of humans, responsible for increase in allergy, autoimmunity and other chronic conditions. Major advancements in the use of relevant cell models, exposure conditions, and doses for respiratory health assessment for the understanding of bio-nano interactions at the molecular level, and the issue of mimicking diseased state or integration of other pre-existing conditions will be discussed. We studied adverse outcomes pathways resulting in immune activation and modulation. Studying protein corona formation, a genuine nanomaterial-specific molecular initiating event, we pursued data enrichment from in vitro experimentation by use of in silico modeling. Computational protein corona prediction was tested and evaluated for its potential to complement the experimental workflow. Combined (meta)data was uploaded to the NanoCommons Knowledge Base ading data FAIRness. Such integrated workflows promote early-stage decision-making, thus, safe-and-sustainability-by-design in nanomedical/-biotechnological innovation.

NextGenMicrofluidics: low-cost, high-throughput manufacturing approaches for the development of microfluidics-based molecular diagnostics devices

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Introduction

The COVID-19 pandemic has highlighted the importance of population-scale screening to identify infected and often asymptomatic individuals, making the need for low-cost and reliable tests that can be widely-implemented even more pressing.

Methods

To address this need, and within the context of the H2020 NextGenMicrofluidics project, we have focused on the development of a microfluidic-based Lab-on-a-Chip (LoC), for the multiplexed detection of SARS-CoV-2 as well as Influenza A (both H1N1 and H3N2), combining a roll-to-roll (R2R) fabricated sensor foil with an injection-molded cartridge. Detection of viral genetic material relies on the Linear-after-the-Amplification (LATE) PCR protocol, while their detection is achieved through hybridization with a virus- and strain- specific microarray of probes, spotted onto an appropriately-functionalized polymer foil. The latter also serves as a waveguiding element, where a sensitive TIRF (total internal reflection fluorescence) readout is realised. Integration of the probe-spotted foil with a disposable microfluidic cartridge, consisting of several reservoirs for reagents as well as a capillary chamber for viral RNA amplification by means of convective PCR (cPCR), permits further reductions in the LoC footprint to be attained. Finally, liquids are moved within the cartridge by integrated electrochemical micropump, making PCB-based fluidic actuation obsolete.

Results

Herein, the sensitive and selective detection of viral genetic material in real patient samples with the use of the novel LoC is demonstrated, while the challenges faced upon integrating the individual and highly-heterogeneous components of the molecular diagnostics assay are also discussed.

Conclusion

The proposed microfluidic-based LoC addresses the current global demand for sustainable and efficient processes in the diagnostics field as it enables high-throughput, cost-effective manufacturing, while the high degree of process parallelisation accomplished renders it suitable for the test quantities needed for mass screening and viral strain discrimination.

Design and characterization of a novel multi-storey DNA nano-structure as a doxorubicin delivery system

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Introduction

The clinical application of doxorubicin (DOX) has been limited in treating various types of cancers due to its different side effects. Anti-cancer drugs could be delivered more precisely, increasing therapeutic efficacy while reducing off-target effects. Herein, we describe a novel DOX-loaded multi-storey DNA nano-structure with AS1411 aptamer as a targeting agent to target nucleolin positive cell lines.

Methods

The formation of the DNA nano-structure and DOX loading in the complex were investigated using a gel retardation test and fluorometric analysis. The release patterns of DOX from the produced formulation were investigated at pH 5.5 and 7.4. In 4T1, MCF-7 (target cells), and CHO cells (non-target), cell viability tests were performed to evaluate the cell cytotoxicity ability of the DOX-loaded multi-storey DNA nano-structure. Finally, the DOX-loaded multi-storey DNA nano-structure was tested in vivo to determine if it could stop tumor growth and increase the survival rate.

Results

The DNA structure with a size of approximately 80 nm was successfully constructed. In a pH-dependent manner, the medication was released from the complex (higher release in citrate buffer compared to phosphate saline buffer). DOX loaded DNA nano-structure can damage nucleolin positive cells while not affecting nucleolin negative cells, according to MTT assay findings. Internalization of the formulation was effective in target cells (4T1 and MCF7) but not in non-target cells (CHO). Furthermore, DOX-loaded DNA nano-structures can slow tumor growth, improve survival rates, and accumulate considerably more drugs in the tumor site compared to free DOX.

Conclusion

Finally, DOX-loaded multi-storey DNA nano-structure can be used as a novel targeted anti-cancer treatment which can encapsulate a considerable amount of DOX and simultaneously target the cancer cells with AS1411 aptamer. As a result, additional research and studies can be applied to evaluate its application in clinics.

Cluster decorated functional DNA origami based biosensor: Towards a safe nano-innovations

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Abstract

The emergence of nanotechnology in the medicine field indicates the high expectations towards new nanotechnology-enabled health products1. The DeDNAed projects intendes to develop a cutting-edge bioanalytical biosensor platform with advanced sensitivity and versatility by utilizing Surface Enhance Raman Spectroscopy (SERS) as an ultrafast optical analysis method. The platform will be based on the assembly and integration of sensing elements (transducer and bioreceptor) by DNA origami2. The DNA origami will serve as a "nano-breadboard" in order to precisely control the position of these elements and thus the sensor architecture at the nanometer scale for enhabling highly sensitive SERS measurements.

Within the development and innovation process, clarity about the safety surrounding new technologies is one of the most important conditions for acceptance of the technology. Eliminating hazards at the design or planning stage is often easier and cheaper to achieve than making changes later when the hazards become real risks. Thus, throughout the DeDNAed project, we will consider Safe-by desing (SbD) approach that refers to identifying the risks and uncertainties concerning humans and the environment at an early phase of the innovation process so as to minimize uncertainties, potential hazard(s) and/or exposure. The SbD approach addresses the safety of the material/product and associated processes through the whole life cycle: from the Research and Development (R&D) phase to production, use, recycling and disposal3.

In the present work we present first approaches on the SbD implementation within an early stage nanoenabled biosensor multicomponent device that will develop new nanoscale components. Some sustainability considerations will be presented as first impressions for a more sustainable development of innovations.

Next Generation of Microfluidics for a safe and sustainable diagnostics devices

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Abstract

Microfluidics devices

Biological assays have been shifting towards miniaturization increasing lab work efficiency and enabling high-throughput. Microfluidics have shown intrinsic ability to manipulate very small volumes of fluids in a variety of integrated ways including sample processing, accurate control of fluids and delivery of results with a fast time [1]. The translation of lab scale devices to Industry (and clinical studies) requires a large number of integrated microfluidic devices, being relevant for the high-volume manufacturing methods for upscaling of such microfluidic devices. Roll-to-roll (R2R) imprinting enables parallel and high-throughput generation of micro or even nanostructures in various designs due to a production performed on flexible polymer foils and the possibility of post-processing steps such as bio-functionalization, chip lamination and others[2]. The Next Generation Microfluidics Open Innovation Test Bed (OITB) aims to offer customers a single-entry point service catalog to a wide range of existing cutting-edge microfluidic technologies to accelerate the demonstration of scientific breakthroughs towards a working prototype and beyond into mass manufacturing. In the present work we present a preliminary assessment on Safety and Sustainability aspects related to next generation microfluidic devices for diagnostics applications.

Roll-to-roll manufacturing process, a safe and sustainable process for massive device production

Five demo cases are being used for the Safety and Sustainability assessment, ranging from biosensor development through molecular diagnostics and smart-phone-supported home diagnostic to pharmaceutical tests and sensors for monitoring bioprocesses. All of them will optimize their biochemical and molecular assays for the selected antigen detection prior to their upscaling process. For upscaling, the R2R manufacturing process is being used.

References

[1] Lab Chip, 2018,18, 1552-1559 DOI https://doi.org/10.1039/C8LC00269J
[2] Lab Chip, 2020,20, 4106-4117 https://doi.org/10.1039/D0LC00751J

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Micro and Nano fabrication technologies for skin contact materials

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Abstract

Nano fabrication technologies and nano technologies at least are subject of research in several fields but mainly invisible, still. The development and commercialization of nano-inside products next to powders, inks and microelectronics are still waiting for its break through and wide acceptance. However, this paper will describe the research work with implemented and integrated nano patterns and new functionality in fields of nano patterned surfaces for flexible substrates for skin contact devices and wearables.

Within a joint project between Fraunhofer ENAS and the Karlsruhe Nano and Micro Facility at Karlsruhe Institute of Technology, the micro- and nano-structuring of biocompatible materials is investigated. Doing so and in order to adapt natural adhesive structures such as Gecko feet, Parylene is patterned into micropillars using hot-embossing. Intended applications for these structures are medical wearables that can measure vital signals or other flexible electronics that can be attached to the skin or other surfaces without any chemical adhesive, which could irritate the skin or leave residues on the surface.

Focus Session: Non-Invasive Health Monitoring and Diagnostics

Breath analysis with chemoresistive sensors

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Introduction

Portable and inexpensive gas sensors are essential for the next generation of non-invasive medical diagnostics. Therein, analyte selectivity in complex breath mixtures remains the major challenge. Filters are an effective and versatile, though often unrecognized, route to overcome selectivity issues by exploiting additional properties of target analytes (e.g., molecular size and surface affinity) besides reactivity with the sensing material.

Methods

The sensor and filters are prepared by flame spray pyrolysis. Sensing films were obtained by depositing Pt-doped SnO_2 or Si-doped WO_3 nanoparticles directly by thermophoresis onto interdigitated Pt electrodes. The filters consisted of Al_2O_3-based or TenaxTA particles assembled to packed beds. End-tidal breath was extracted in a monitored and reproducible fashion with a tailor-made and modular sampler. Proton-transfer-reaction mass spectrometry is utilized to validate the sensor performance. Volunteers were recruited at the University Hospital Zürich after receiving ethical approval.

Results

Breath sensors were developed for the selective quantification of acetone, isoprene and methanol. These showed high agreement ($R2 > 0.8$) to proven mass spectrometry and robustness to other confounders (e.g. ethanol released from sanitizers). When monitoring humans under physical activity, such sensors recognized in real-time the onset of muscle activity and enhancements of the fatty acid metabolism. The methanol sensor correctly indicated situations of intoxication.

Conclusion

Tailor-made breath sensors provide new tools for medical diagnostics and monitoring. Due to their non-invasivness, these face high user tolerance, even in a healthy population. Such sensors have been readily incorporated into handheld devices communicating results wirelessly to smarphones.

miRNA Detection System based on self-assembled nanoscale DNA Origami arrays

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Introduction

MicroRNAs (miRNAs) are short, non-coding endogenous RNAs (18-25 bases) that are responsible to regulate gene expression. Expression levels of miRNA are dysregulated in various cancer types, making miRNAs ideal tumor biomarkers for diagnostics and prognosis. However, specific and sensitive detection of miRNAs and absolute quantification of multiple miRNAs are still remaining as challenge. DNA origami method allows the generation of nanoscale structures with precisely defined geometries and decoration of biomolecules at nanoscale resolution and therefore can be used as a nanoarray platform for multiplex detection of miRNAs. A recently developed super-resolution microscopy technique, DNA-PAINT is providing high detection sensitivity, specificity and absolute quantification with imaging resolution lower than 10 nm. Here, we developed a DNA origami nanoarray system allowing distance-dependent detection of miRNAs using DNA-PAINT.

Methods

The experimental workflow is as following: 1) DNA origami structure design using caDNAno software. 2) Self-assembly and characterization of structures by gel electrophoresis and transmission electron microscopy. 3) Preparation of miRNAs (ordered synthetically or isolated from breast cancer cells (BT-474, MCF-7, MDA-MB-231)) 4) Super-resolution microscopy imaging of single DNA origami structures with pre-designed nanoarray patterns for multiplex capturing of miRNAs. 5) Image analysis using online available Picasso software package.

Results

We initially tested 4 miRNAs that are differentially expressed in breast cancer cells using our system. We detected all miRNAs either separately or in combination based on the relevant distance to the boundary markers. The detection was highly sensitive (10-450 fM) and sequence-specific (discrimination of 1-base mismatch targets). Moreover, 1D polymerization of DNA origami structures further increased the multiplexing capacity (4x4-plex).

Conclusion

Overall, we developed an ultrasensitive and amplificaton-free, super-resolution fluorescence imaging based miRNA detection method using DNA origami nanoarray system for the detection of breast-cancer associated miRNAs which potentially provides a sensitive and accurate alternative of current multiplexed diagnostic technologies.

Multiplexed, digital urine analysis for point-of-care

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Introduction

Clinical triage in low resource settings typically relies on fever and blood pressure measurements as well as questionnaires. The use of non-invasive body fluid testing can greatly improve the clinical decision making. Nowadays, basic urinalysis is done with paper dipsticks with color indicators, which are prone to misinterpretation.

Methods

The solution developed by CSEM is based on digital electrochemical sensors. A point of care cartridge (fig.1, including reader) with printed sensors allows the accurate quantification of urine analytes at levels that are not detectable with urine dip sticks, thereby providing relevant data for improved medical decision making. So far, glucose, sodium and pH can be measured with this device, and a further panel of 3-6 sensors (K^+, albumin, creatinine, urea, uric acid) is envisioned to complete the cartridge. The digital data allows remote assistance and smart processing for data interpretation.
Assays were developed and applied on low-cost screen-printed sensors integrated in a fluidic chip cartridge equipped with storage pouches containing the necessary solutions for the reference electrode and the calibration solutions for the sensors. Electrochemical measurements were run in parallel.

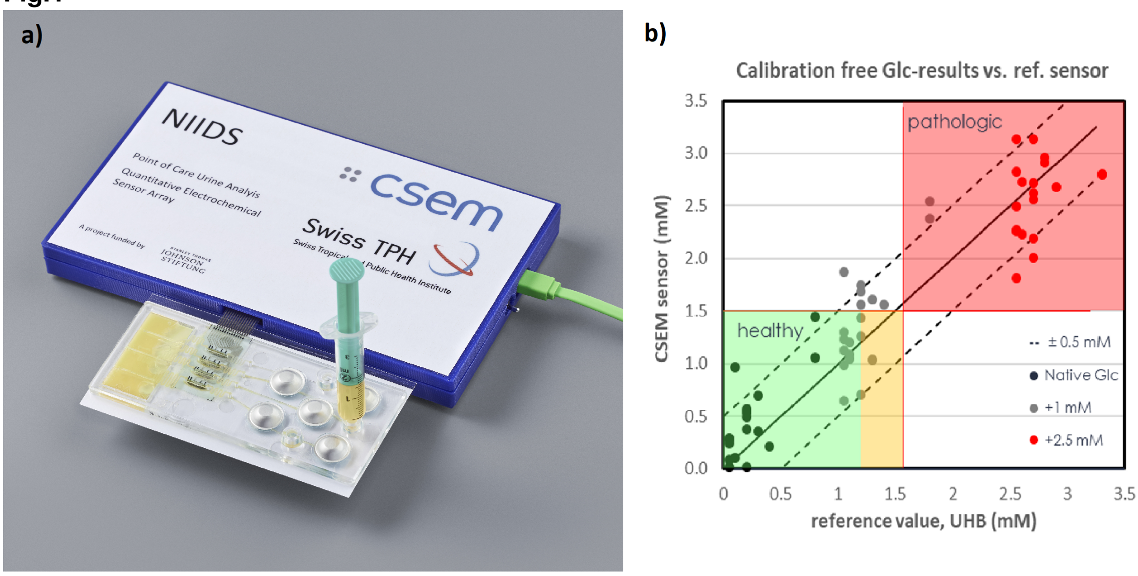
Results

The use of an additive for our pH sensor allows a completely calibration free system (compared factory calibration vs. calibration within cartridge). Low bias voltage measurement and protective coatings reduced the interferences for the glucose sensor and ion-selective polymer membranes and resulted in sensitive and accurate sodium measurements, with good correlation (PCC=0.983). Validation measurements were carried out with 20 urine samples from healthy donors and showed good correlation with conventional laboratory analysis results (glucose PCC=0.935 & pH PCC=0.793).

Conclusion

The feasibility of calibration free, digital measurements with low-cost sensors was shown for urine. Ultimately, the technology allows the direct integration of sensors into disposables, for example, urine collection beakers or other commonly used medical devices.

Fig.1



Investigation of everyday influencing factors on the variability of exhaled breath profiles in healthy subjects

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Abstract

The human breath is an accurate but complex readout of many physiological processes in the organism that can be monitored via volatile organic compounds (VOCs) in the exhaled air. However, there are many confounding variables that limit the transfer and application of breath analysis to become a clinical procedure. This work aims to establish a systematic procedure for sampling and characterization of various everyday influences of healthy subjects using proton transfer reaction-mass spectrometry (PTR-MS). In order to limit the influencing factors on the breath profile, a standard analysis procedure for sampling and evaluation of the exhaled breath samples was developed. Moreover, the correlations between the selected experimental conditions and the resulting VOC profiles were investigated using statistical test methods. In addition to the relevant influence of methodological experimental parameters, interesting insights into the effect of everyday factors on the exhalat gas were also obtained and discussed. Furthermore, subject and condition-specific differences were found in the exhaled air of male and female subjects. With a more robust, standardized and reproducible breath sampling protocol, breath analysis is a promising non-invasive tool towards a system-wide understanding and personalized diagnosis and treatment of a wide range of diseases.

Cochlear health as a predictor of CI outcome

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Introduction

Cochlear implant (CI) users show high variation in terms of speech intelligibility. Evidence from the literature (Schvartz-Leyzac and Pfingst, 2018) suggests cochlear health as one potential factor behind the CI user's variability in performance. To better understand the relationship between cochlear health and speech intelligibility, this study investigated the role of speech band importance function as well as the demographic data.

Methods

Measurements of speech reception thresholds (SRTs) and eCAP recordings were made in both ears of 13 bilaterally implanted subjects. Cochlear health was estimated locally for each stimulating electrode. The IPG effect on slope (IPGEslope), i.e., the change in the slope of the amplitude growth function as a result of increasing the interphase gap (IPG) from 2.1 µs to 30 µs was used as the measure of cochlear health (Ramekers et al., 2014). To compare this local measure with monotic SRTs, the relative importance of each frequency band for speech intelligibility in noise was also taken into account by applying a weighting function (ANSI, 1997) to the IPGEslope. Correlation analysis was applied to investigate the relationship between IPGEslope, speech intelligibility and demographic data.

Results

A weak but significant correlation ($R2 = 0.24$, $p < 0.05$) was observed between IPGEslope and SRT which was increased ($R2 = 0.32$, $p < 0.01$) after applying the speech band importance weighting function. A larger, negative and significant correlation was also found between IPGEslope and age at implantation ($R2 = 0.51$, $p < 0.001$) as well as a weak and negative correlation between IPGEslope and hearing aid experience ($R2 = 0.17$, $p < 0.05$).

Conclusion

This study indicated cochlear health as one of the factors describing the variation in CI outcome. It highlighted the role of the employed weighting function inspired by the speech band importance function in correlating cochlear health to speech intelligibility.

Camera-based Pain Assessment during Surgical Interventions

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Introduction

Pain assessment in clinical settings is a challenging task for clinic staff and patients. An automatic and contactless pain estimation system via facial expression is a decisive advantage. We introduce a mimic descriptor based, contactless pain recognition in a realistic scenario. Therefore, we conducted a surgical feasibility study in cooperation with the Leipzig Heart Center of the Leipzig University. We developed a simple classification procedure for binary pain estimation and evaluated its performance on the UNBC-McMaster Shoulder Pain Expression Archive Database. Afterwards, we applied this classifier to our real OP setup.

Methods

In this publication we utilized OpenFace 2.0 to automatically determine the intensity of the Action Units (AUs) belonging to the Facial Action Coding System based on video data from the studies. For classification of the AU data, we created a simple logistic regression algorithm and a leave-one-out cross-validation procedure. We first evaluated this algorithm using the UNBC-McMaster data and then applied the optimized implementation on our experimental OP data.

Results

We reached a f-score/accuracy of 47.79%/80.94% for the UNBC-McMaster data. Compared to other common publications, these results are promising and it can be deduced that pain classification based on camera recordings is possible in principle. For our experimental OP data, the f-score/accuracy is 20.02%/73.14%. Given the fact that we recorded the study data under surgical conditions (illumination and camera perspective changes etc.) the results are adequate and a promising step towards pain recognition in real-life clinical and nursing settings.

Conclusion

We introduced a camera-based pain classification approach for experimental OP data, validated on common laboratory data. For both datasets, we showed feasibility with varying degrees of success. Further research will be directed towards the development of a method to automatically estimate pain during surgical interventions.

Home Monitoring of the Carotid Arteries Using a Mobile Auscultation Device with App - An Overview of the Needs and Concerns of Potential Users

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Introduction

Cerebrovascular diseases like atherosclerosis pose a great threat to health and wellbeing of people worldwide. To enable early diagnosis and treatment of a gradual progressing occlusion of the carotid arteries, we propose the BODYTUNE system. Consisting of a custom-built auscultation device and a mobile application, it aims at enabling the monitoring of the blood flow within the carotid arteries on a regular basis at home.

Methods

In this work, we present the results from a survey with 65 participants of the system's target group to investigate aspects like technical affinity and experience with comparable systems. These results potentially influence how the BODYTUNE system should be designed to be user-centered, match the users' needs and address their concerns.

Results

Participants generally expressed a positive stance towards digital medical systems for a home-monitoring approach, as well as acceptance and openness towards the BODYTUNE system. They also expressed confidence when it comes to the usage of these systems and bring a decent amount of experience in handling them. Not all participants have experience with using mobile apps as part of their 'medical routine', though. Additionally, various concerns e.g. related to the measurement process or privacy issues were mentioned.

Conclusion

While it is important to note that these results are only based on a small number of participants, they provide a first overview of the potential target groups. When designing the system, it is important to consider the diverse set of experiences and abilities (especially the technology affinity) by using an adjusted design that supports where needed without disrupting. It is also crucial to consider the mentioned concerns and develop a design that reassures and "accompanies" during usage.

Design of Wearable ECG Electrode based on Conductive Textile

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Abstract

Cardiovascular disorders are difficult to predict and often lethal to people. The current ECG technology, which uses Ag/Ag-Cl electrodes, is cumbersome and can be performed in hospitals. This study attempted to overcome the problem by substituting traditional gel electrodes and developing a textile-based wearable ECG monitoring device. The copper conductive fabric was used as electrodes, and the 12-lead ECG was reduced to three-electrode systems. The electrodes were placed on the right arm, left arm, and right leg to capture readings while resting. When testing ECG, it was discovered that the copper fabric produced identical signals to the commercial electrodes. The data is collected with an Arduino, an AD8232 module, and viewed on a laptop.

Focus Session:
Novel Developments in Additive Manufacturing

Graded fiber scaffolds for musculoskeletal tissue engineering via melt electrospinning

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Introduction

In the musculoskeletal system, damages to bone/tendon junctions, related to aging or metabolic diseases, are associated with a wide range of pathologies. Melt electrospinning (MES) has been increasingly used for the production of graded polymeric fiber scaffolds to address the reconstruction of interfaces between different tissue structures. The main advantage of this method is the controlled deposition of the polymer fibers. It can be used to manufacture scaffolds with a three-dimensional, reproducible fiber structure. In the presented study, melt electrospun fiber mats are evaluated for their suitability as graded fiber scaffolds.

Methods

Electrospun fiber scaffolds were manufactured from a polycaprolactone (PCL, MW=45kDa) melt. To achieve different fiber diameters pumping pressures between 50 and 150 kPa were used, while the reservoir temperature was kept at 75°C. The influence of the melting process on the chemical properties of the fiber scaffolds was investigated using DSC and FTIR. For mechanical testing, uniaxial tensile tests for 5% and 10% path elonguation were carried out for all three parametric sets.

Results

It was possible to produce fiber scaffolds with fiber diameters of 25, 50 and 100 µm by variying the pumping pressure. Compared to native PCL (Tg=33,6°C), fiber scaffolds showed a lower glas transition temperature (25µm Tg=29°C, 50µm Tg=26,05°C, 100 µm Tg=22,4°C). PCL showed the absoption bands of a linear aliphatic polyester. In all investigated fiber diameters the amorphous carbonyl bands at 1722 cm^1 were increased 20% compared to the unprocessed PCL. Uniaxial tensile tests showed increased forces from 34 to 76 N at 5% and 10% elonguation with increasing fiber diameter.

Conclusion

The results presented here show that MES can successfully be used to produce three dimensional fiber mats with a wide range of chemical and mechanical properties. The process widens the scope of manufacturing methods for graded fiber scaffolds for bone/tendon replacement.

A Six Degree of Freedom Extrusion Bioprinter

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Introduction

The research on 3D Bioprinting has increased steadily over the last decades, aiming to address the high demand for organ donations. Extrusion-based Bioprinting (EBB) is the most common bioprinting technique, combining a simple and affordable printing process with high versatility and the ability to produce large-scale 3D constructs. Several EBB have been published. The functionality of these systems is often limited by few Degrees of Freedom (DoF) and unprecise flow-rate control due to pneumatically actuated extrusion. To address these challenges, we developed a 6-DoF EBB with mechanically actuated extrusion.

Methods

The EBB is based on a 6-DoF pharmaceutical robot. For the extrusion, a custom printhead extruder is built from three identical mechanically actuated syringe pump modules (SPMs), thus enabling the extrusion of three materials simultaneously. Each SPM consists of a linear drive stepper motor, the corresponding motor controller, and a holding mechanism for a 20 mL syringe. The holding mechanism allows to remove and re-insert the syringe easily, e.g. for loading of printing material. To control the Bioprinter, a custom software is implemented within the Robot Operating System framework. This software calculates the robot trajectory based on a Cartesian printing path, given in a custom Gcode dialect, and controls the robot motion and the extrusion.

Results

The EBB offers 6 DoF and therefore advanced dexterity. The mechanical actuation of the SPMs allows for precise flow-rate control, since the extrusion does not depend on the viscosity of the fluid.

Conclusion

The presented setup offers advanced dexterity, thus enabling printing on non-planar surfaces and working cooperatively with a second EBB. The printhead can extrude a wide variety of bioinks and is not influenced by a change in fluid viscosity. As next steps, the setup will be tested extensively with various bioinks, in order to gain knowledge for further optimization.

3D printed patient-specific thorax phantom with realistic CT imaging properties of different bony regions using filament printer technology

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Introduction

Medical imaging phantoms are widely used for validation and verification of surgical guidance and diagnostic imaging. To fabricate realistic imaging phantoms, replication of the entire tissue morphology and the associated Hounsfield Units (HU) of the CT image is required. 3D printing is a promising technology to fabricate medical imaging phantoms, but most available phantoms only mimic the average HU of human organs or bones. In this study, the aim was to develop a thorax phantom with realistic bone-equivalent HU, including some bone heterogeneity, that was 3D-printable with one single material.

Methods

The considered bone regions, i.e spongy and cortical parts of the ribs, vertebral bodies, dorsal vertebral column, and some surrounding soft tissue, were segmented from a patient's CT image. Cylinders with different in-fill densities ranging from 10% to 100% were 3D-printed from StoneFil concrete filament (Formfutura). A CT-image of the cylinders was made, and appropriate in-fill densities were chosen to fit the HU of each of the above-mentioned bony regions. The thorax-phantom was printed using the determined parameter and a CT-scan of the phantom was compared to the patient's scan. In addition, a reproducibility study was performed by printing 12 replicates of selected cylinders.

Results

A HU-range of -482 to 968 was achieved in the printed cylinders, which includes the realistic densities for the chosen regions. The cylinder samples also revealed a good geometric and radiodensity reproducibility. Regarding the thorax phantom, an excellent match of HU to the original patient's CT was achieved.

Conclusion

The proposed 3D-printed thorax phantom could match the HU of different bony regions and has the potential to be efficiently used for validation of imaging- and radiation-based procedures in precision medicine. Considering the reached HU range, a full thorax imaging phantom including different soft tissue would also be possible.

Effect of enzymatic degradation and hydrolysis on 3D-printed resin-based composite material for temporary dental crowns and bridges

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Abstract

Additive manufacturing of dental prostheses e.g. composite materials is continuously finding broader application in dentistry. In the oral environment, the materials are subjected to hydrolysis and accelerated hydrolysis by enzymes. With the aim to compare an additively manufactured composite with a self-curing and a CAD/CAM material of the same composition, the effect of enzymatic degradation and hydrolysis on the materials were investigated. The experimental composites consisted of 50 wt. % inorganic filler and 50 wt. % monomer matrix (BisEMA, BisGMA, TEGDMA). The influence of hydrolysis via a buffer system was investigated in comparison to enzymatic degradation by cholesterol esterase over 22 days. The detection of degradation products over time was conducted by HPLC-DAD analysis. Degradation products and monomers calibrated were: TEGDMA, BisGMA, BisEMA, MA, TEGMA, Bis-HPPP and E-bis-PA. Surface roughness of polished specimens was measured by AFM and hardness with a Vickers micro hardness tester. After enzymatic degradation and hydrolysis, BisGMA was detected in the eluates of the additively manufactured composites. The samples fabricated by CAD/CAM behaved similar during hydrolysis, where additionally MA was detected. After enzymatic degradation, furthermore TEGMA and BisEMA were detected qualitatively. In contrast, the self-curing material exhibited traces of MA, TEGMA, TEGDMA and BisGMA after enzymatic degradation. Hereof detectable upon hydrolysis were MA, TEGMA and BisGMA. Surface roughness was comparable for all manufactured samples whereas the hardness was lowest of the 3D printed material. Enzymatic degradation and hydrolysis had no effect on surface roughness and hardness. The additively manufactured composite appeared to have low susceptibility to enzymatic degradation and hydrolysis. Due to the manufacturing process, the polishability and initial hardness are poorer.

Combining Metamaterials and Metasurfaces with Two-Photon-Polymerization

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Introduction

Metamaterials have been artificially engineered to prompt novel properties due to their porous building blocks or lattices. Contrarily, metasurfaces are the metamaterials 2D equivalent. A combination of metasurfaces and metamaterials, metastructures, and their promising advantages and future application stand unexplored, whereby a possible application in the biomedical field is promising. Aim of this study is to evaluate the manufacturability of a combination from metamaterials and metasurfaces for enhanced osteointegration.

Methods

Microtopography was added to a lattice cell via a combination of 3D CAD modelling and 2D topographical mapping. Six different microsurface structures, consisting of protrusions and cavities with feature size down to 70 µm in diameter and 14 µm in height, were added to lattices of cylindrical and block building units, producing a total of eight different models with sizes of 3x3x3 mm, placed on a base structure with the dimensions of 10x10 mm. The digitally fabricated micro-textured lattices have been manufactured using the two-photon polymerization (2PP) NanoOne (UpNano GmbH, Vienna, Austria) with upbrix (2-photon resin, UpNano), to confirm the feasibility of merging metasurfaces and metamaterials. Dimensional evaluation was performed using scanning electron microscopy (Zeiss EVO MA10, Oberkochen, Germany).

Results

All the structures could be printed without major problems. The volume of the eight models amounts to 131 mm3, with a printing time of 9 hours and 45 minutes. Protrusions of 70µm diameter and 80µm height have been printed as 70.14 +- 1.32 µm diameter (n=10) and 77.43 +- 1.38 µm height (n=10). A 90° overhang could be printed with a deviation of 3.31 +- 0.36 ° (n=5).

Conclusion

In this study, metastructure design and manufacturing has been established. Thus paving the way for possible applications in the biomedical field. In bone implants for example lattices (Loh QL. Tissue Eng. Part B Rev., 2013) as well as microtopography (Gui N. Biomater. Sci., 2018) have been found to have positive effects, while combination of both have not yet been examined, although a synergistic effect can be expected.

Characterization of Using Infused PLA for 3D Printed Radiation Shielding

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Introduction

3D printing has been integrated in various applications in biomedical and medical imaging. A prominent new field is that of radiation protection and shielding, where the introduction of infused filaments makes it possible to manufacture customized 3D printed shielding. In this study we examine the use of a Polylactic Acid (PLA) infused with tungsten to shield a Positron Emission Tomography / Computer Tomography (PET/CT) scanner. The goal is to reduce the effects of the radiation emitted from outside the field-of-view (FOV) on the PET image and to protect the PET electronics against the X-rays from the CT.

Methods

The shielding properties were examined using the radioactive sources Ba-133, Na-22, and Cs-137, as well as two X-ray sources with energy ranging from 20 to 125 kV.

Results

For X-rays below 40 kV, less than 1 cm of the tungsten infused shielding was sufficient to block more than 95% of the X-ray beam intensity. However, only around 30% of the 511-keV rays from Na-22 was attenuated.

Conclusion

Our results support the application of tungsten infused PLA materials to shield the PET electronics. However, further studies are required to determine if shielding the PET crystals with tungsten infused PLA can improve image quality by reducing the contribution of scattered rays from outside the FOV. Additionally, our results show new possibilities for the use of infused filament in the field of X-ray imaging. For example, where lead coverings or skirts are excessively bulky or rigid, it could be employed to optimize shielding for radiation-sensitive organs.

Focus Session: Novel Developments in Biomaterials and Medical Implants

Streaming potential analysis and cell viability testing of polyelectrolyte implant coatings with chitosan of different degrees of acetylation

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Introduction

In situ tissue engineering requires functionalization of implant surfaces, to release pharmaceuticals or to achieve better biocompatibility and long-term tissue integration. Here, the surface chemistry plays a major role. [1]

Methods

Modified electrospun polycaprolactone (PCL)-fiber mats were coated with polyelectrolyte layers using suspensions of chitosan/tripolyphosphate nanoparticles (CS/TPP-NP) [2]. Therefore, the degree of acetylation (DA) of the chitosan was varied (10 % / 42 %) and different polyanions were used, such as polystyrene sulfonate, alginate and carboxymethyl cellulose. Streaming potential analysis were performed in order to investigate the zeta potential of the coated fiber mats [3]. The viability of human mesenchymal stromal cells, isolated from bone marrow, was studied with a viability cell proliferation assay (WST8) and the morphology was analyzed by staining the cytoskeleton with phalloidin and the nucleus with DAPI after 3 d and 7 d.

Results

Analysis of the streaming potential measurements showed different courses of zeta potential, depending on the DA of the used chitosan, and therefore different interpenetration of the polyelectrolyte layers into the coatings could be observed. For example, using carboxymethylcellulose (CMC) with chitosan with a DA of 10 % showed no interpenetration and low cell viability, in comparison to using chitosan with a DA of 42 %, which showed interpenetration and led to higher cell viability.

Conclusion

The effect of polyanion layer and interpenetration of polyelectrolytes and the surface composition on cell viability can be severe.

References

[1] Boudou T et. al. Multiple Functionalities of Polyelectrolyte Multilayer Films: New Biomedical Applications. Adv Mater. 2010;22(4):441-467.
[2] de Cassan D et. al. Attachment of nanoparticulate drug-release systems on poly(ε-caprolactone) nanofibers via a graftpolymer as interlayer. Colloids Surf B. 2018;163:309-320.
[3] Sandri G et. al. Chitosan/glycosaminoglycan scaffolds for skin reparation. Carbohydr Polym. 2019;220:219-227.

Hydrogel Modified Silica Gel Fibers as an Exudate Absorbing Component in Monitoring Wound Regeneration

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Introduction

Inorganic silica gel fiber fleeces (SGF) are CE-certified as a resorbable wound patch for regeneration of chronic wounds (diabetic ulcers and 2nd degree burns). Here, the authors present a hydrogel modification of SGF that not only provides a softer tissue interface, but also offers the possibility of harvesting wound exudate via in-vivo absorption as a diagnostic tool for monitoring wound regeneration.

Methods

Viscous spin sols were synthesized via sol gel processes starting from liquid precursor tetraethoxysilane and spun to filaments with a dry spinning technique applying pressure of 20 bar on the viscous spin sol. The resulting µ-fibers (adjustable diameter: 30 - 120 µm) were fabricated to a non-woven fiber fleece. In a next step, hydrogel was grafted on SGF starting from the precursor N,N-Dimethylacrylamide (DMAA). Polymerization of Poly(dimethylmetacrylamides) (pDMAA) was induced by a Xenon Excimer light source (172 nm) at atmospheric pressure. The resulting hybrid material was evaluated regarding its cytotoxicity (WST-1 activity) according to DIN ISO 10993-5 using human fibroblast cell line HFF-1. Absorption processes were performed with dye solutions as a model solution for wound exudates.

Results

After polymerization process, SGF surface was fully covered with pDMAA throughout the whole fiber fleece. This hydrogel modification resulted into a water absorption capacity from up to 600 w%, whereby the dimension of the modified fiber fleece remains constant. The absorption capacitiy of dyes was quantified using a photometer. Extracts of modified SGF showed no cytotoxic effects towards the mitochondrial activity of HFF-1.

Conclusion

Due to its dimensional form stability under physiological conditions, hydrogel modified SGF are a promising hybrid material in wound regeneration supporting companion diagnostics. In perspective, this absorbent and cytocompatible material can be used as a component in digital wound monitoring.

Acknowledgements

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Nanoengineered amorphous calcium phosphate coated barium titanate facilitates rapid mineralization of cyclically loaded hydrogel scaffolds

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Introduction

Cell-laden alginate hydrogel scaffolds are sought after materials owing to their potential to create bone organoid models, excellent biocompatibility and tunability for 3D bioprinting. However, extracellular matrix mineralization is in vitro a diffusion limited process, thus, these hydrogels show slow mineralization.

Methods

We prepared amorphous calcium phosphate coated barium titanate nanoparticles (BT@ACP) for incorporation into cell-laden graphene oxide (GO) hydrogels. The amorphous phase was confirmed by vibrational spectroscopy and the coating by electron microscopy. Bioinks based on graphene oxide (GO) alginate/gelatin were formulated with various concentrations of BT@ACP and bare BT nanoparticles. The bioprintability of the nanocomposite inks was characterized by rheology. Then, the nanoparticle's influence on the 3D printed scaffold's mechanical properties and structural fidelity were investigated. Additionally, cell viability and shape were studied after 1 and 3 weeks of static cell-laden scaffold culture. Finally, the scaffold mineralization was monitored by time-lapsed micro-CT imaging during six weeks of 3D culture in dynamic compression.

Results

We demonstrated that unstable amorphous calcium phosphate, which usually transforms into crystalline hydroxyapatite, was stabilized when coated on barium titanate nanoparticles via surface hydroxylation. The incorporation of the nanoparticles improved the shear-thinning properties of GO hydrogels and cell elongation during osteogenic culture. Time-lapsed microstructural imaging showed that after six weeks of regular cyclic loading, these rapid mineralizing hydrogel scaffolds had ca. 1.5-fold higher scaffold mineral density maturation rate than scaffolds containing bare barium titanate or just GO.

Conclusion

Extrapolating mineralization rates in BT@ACP scaffolds, mineral density of murine woven bone was within reach by additional 11 weeks of culture in the dynamic compression bioreactors as compared to over 17 weeks in the control samples. Improving the mineralization rate of hydrogels by nanoengineered BT@ACP may prove advantageous for bone tissue engineering applications or the development of bone organoids.

Vascular structures from blood proteins

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Introduction

Scaffolds made from blood proteins are a promising approach for patient-specific cardiovascular implants. The native blood protein concentration has to be increased for improved processability by electrospinning. In this study, we investigated different methods to improve solution properties. Blood protein solutions were processed via electrospinning, cross-linked and further characterized.

Methods

Plasma separated from porcine blood was processed to different protein concentrations by filtration and rotary evaporator. The protein concentration was determined by a BCA Protein Assay Kit. Protein solutions were electrospun to tubular scaffolds with 4 mm inner diameter using a custom-made electrospinning device. Crosslinking of the samples was carried out via EDC. Tubular scaffolds were characterized with regard to fiber morphology and diameter.

Results

Preliminary results show that both methods can be used to increase plasma protein concentration. With the use of rotary evaporatorion, a fifteenfold increase in concentration was observed, whereas filtration resulted in a fourfold increase. Tubular scaffolds were successfully electrospun and crosslinked via EDC with protein solutions from both processes. The mean fiber diameter increased with increasing protein concentration.

Conclusion

The experimental results show that blood proteins can be successfully processed to tubular scaffolds. Our process offers the possibility to produce patient-specific vascular prostheses from autologous blood. The fiber diameter and thus die extracellular matrix can be tailored by varying the protein concentration.

Acknowledgements

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Mechanical Behavior of Human Articular Cartilage and Hydrogels for Cartilage Repair

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Introduction

In this study, we aim to understand the complex mechanical behavior of human hyaline cartilage and of substitute materials for implantation, as this is crucial for tissue engineering applications and cartilage regeneration approaches. We also develop an experimental testing protocol for reliable material parameter identifications to perform numerical simulations.

Methods

For mechanical characterization a Discovery HR-3 rheometer from TA instruments was used. We tested human hyaline cartilage as well as two hydrogels, ChondroFillerliquid and ADA-GEL. ChondroFillerliquid is a collagen type I based material, which is already in clinical use. ADA-GEL is a hydrogel made from ADA (alginate di-aldehyde, oxidized alginate) and gelatin. We subject the materials to a series of tests from which we generated a combined testing protocol containing multi modal loading conditions, including cycling loading and stress relaxation to obtain parameters for numerical simulations. Furthermore, we investigated the microstructure by multiphoton microscopy imaging.

Results

The main mechanical characteristics of the materials include nonlinearity, tension-compression asymmetry, recoverable conditioning behavior, and stress relaxation. Using multiphoton microscopy imaging, we also revealed that ChondroFillerliquid is composed of fibrous and non-fibrous structures, whereas cartilage is mainly fibrous and ADA-GEL is purely non-fibrous. The cyclic tests showed that the hysteresis decreases significantly between the first and second cycle and only slightly in the following cycles. Cartilage shows the slowest stress relaxation behavior and ChondroFillerliquid the fastest.

Conclusion

Our study revealed that the materials exhibit a distinct material behavior, which is in accordance with their individual microstructures. These insights may provide a guideline for effective material design in the future and can allow for the reliable calibration of numerical simulations.

Focus Session:
Patient-Specific Bioelectric Field Modeling and Simulation in Brain Research

Individualized EEG/MEG targeting and optimized multi-channel transcranial electric stimulation in focal epilepsy

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Introduction

In recent years, the use of combined EEG/MEG (EMEG) source analysis has gained considerable attention in the diagnosis of focal epilepsy due to the complementarity of both modalities. An accurate reconstruction of the epileptogenic zone by means of EMEG source analysis enables also new therapeutic approaches such as individually targeted and optimized multi-channel transcranial direct current stimulation (mc-tDCS) for inhibiting the epileptogenic zone.

Methods

New techniques of forward and inverse modeling in EMEG source analysis will be presented. Standard dipole scanning will be compared to beamforming for the inverse problem. In a retrospective study with two patients suffering from focal epilepsy due to focal cortical dysplasia type IIb and seizure freedom following lesionectomy or radiofrequency-guided thermocoagulation (RFTC) we used the distance of the localization of interictal epileptic spikes to the resection cavity resp. RFTC lesion as reference for good localization. For forward modelling, we investigate the difference between skull-conductivity calibrated six-compartment and standard three-compartment head modelling.
For targeted and optimized mc-tDCS, distributed constrained maximum intensity (D-CMI) will be introduced.

Results

We found that beamformer localization can be sensitive to the choice of the regularization parameter, which has to be individually optimized. Estimation of the covariance matrix with averaged spike data yielded more robust results across the modalities. EMEG source analysis can have advantages when compared to single modality EEG or MEG. For appropriate regularization parameter choices, the beamformer localized better than the standard dipole scan.
Analysis of mc-tDCS montages and resulting electric fields show D-CMI to reach high target directionality with reduced side effects and skin sensations and potentially improved sham conditioning. In a double-blind sham-controlled N-of-1 trial, EMEG targeting and D-CMI optimized mc-tDCS significantly reduced epileptic activity.

Conclusion

EMEG source analysis and D-CMI optimized mc-tDCS can contribute to the diagnosis and therapy of focal epilepsy.

CutFEM forward modeling for EEG-Sourceanalysis

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Introduction

A central step in source-analysis using Electroencephalography (EEG) lies in accurately solving its forward problem, i.e. determining the scalp potential induced by a neural source. Doing so requires an accurate depiction of the volume conduction effects in the human head, represented by a partial differential equation (PDE). Among the options to solve said PDE is the finite element method (FEM) which requires a volumetric discretization, a mesh, of the head domain. When creating the mesh one usually chooses between either hexahedral or tetrahedral elements. Due to their cubic structure, hexahedral meshes are unable to accurately represent the folded and curvy structure of the head while their tetrahedral counterparts, while being more geometrically accurate, are difficult to set up in situations where the head compartments (scalp, skull, gray/white matter,...) are not entirely contained in one another.

Methods

The above mentioned issues can be avoided by introducing a category of unfitted finite element approaches where the mesh is disentangled from the geometry which is represented through level set functions. The purpose of this paper is to introduce one such approach, CutFEM. Following a description of the method, we will employ it in controlled spherical scenarios as well as a realistic head model where CutFEM is used for a reconstruction of somatosensory evoked potentials.

Results

CutFEM outperforms an existing unfitted FE method with regard to memory consumption and speed and a geometry adapted hexahedral model with regard to accuracy while being able to mesh arbitrarily touching compartments.

Conclusion

CutFEM strikes a balance between numerical accuracy, computational efficiency and ability to model complex geometries that was previously not possible in FEM-based EEG forward modeling.

Sensitivity of EEG forward and inverse solutions to conductivity uncertainties

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Introduction

The variance of head tissue conductivities between patients leads to considerable uncertainty with regard to the results of electroencephalography (EEG) source analysis. In this study, we elaborate upon previous studies by determining the sensitivity of EEG source analysis to tissue conductivity variations with an unprecedented spatial resolution in a highly-realistic state-of-the-art head model.

Methods

EEG forward solutions of dipole sources regularly distributed in the brain compartment were simulated in a detailed six-compartment tetrahedral head model with standard literature tissue conductivities using the finite element method (FEM) multipole approach. Subsequently, a generalized polynomial chaos approach (gPC) was employed to rapidly calculate EEG leadfields for varying tissue conductivities. EEG source analysis of the simulated dipole sources was performed using goal function scans (GFS) based on the EEG leadfields for varying conductivities. Based on the results of 100,000 variations of tissue conductivities, empirical distributions of the source reconstructions were obtained and analyzed.

Results

Our results confirm previous findings that variations of skin and skull conductivities in general have the strongest influence on EEG source localizations. However, our results also show how the influence of variations of the different tissue conductivities depends on the characteristics of the source, such as source orientation and depth or thickness of the covering skull.

Conclusion

Our results provide important guidance to estimate the uncertainty related to the reconstruction of sources in different brain regions. Furthermore, they allow to understand the specific benefit of individual conductivity estimation for a certain source analysis scenario.

Estimating Target Orientations: A Comparison of Beamformer Algorithms and their Performances in Estimating Orientations of Neural Sources

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Introduction

The efficacy of transcranial electric stimulation (TES) to modulate neuronal activity depends critically on the spatial orientation of the targeted neuronal population. Therefore, correct estimation of the target orientation is of utmost importance. Different beamforming algorithms provide orientation estimates, however, a systematic analysis of their performance is still lacking.

Methods

For fixed brain locations, data from sources with randomized orientations is simulated and noise is added (Gaussian or realistic). The orientation is then estimated (1) with EEG and (2) with a combined EEG-MEG approach, in which the tangential component is extracted from the MEG data and the radial component from EEG data. Three different beamformer algorithms are evaluated: Unit-gain (UG), unit-noise-gain (UNG), array-gain (AG). Reliability is tested using bootstrapping.
In an additional real data example, the orientations of the visual network areas V5 and the Frontal Eye Field (FEF) are reconstructed with this method.

Results

Differences between the beamformers' abilities to estimate the correct orientation are shown: especially the UNG is outperformed by the UG and the AG beamformers.
Performance furthermore depends on the ratio of radial and tangential components of the orientation, on regularization parameters and on noise levels. In the real data example, the test-retest-reliability of two measurements was best in the combined estimation approach using UG for both, FEF and V5.

Conclusion

Choosing the correct beamformer algorithm and combined MEG-EEG data allow a stable reconstruction of source orientation. This study is a first step towards establishing best practice for source orientation estimation.

Structural and Functional connectivity of Deep Brain Stimulation in the Nucleus Accumbens for Treatment-Resistant Depression

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Introduction

Deep Brain Stimulation (DBS) is a therapeutic approach for Treatment-Resistant Depression (TRD), a severe form of Major Depressive Disorder. The prolonged benefit of DBS may rest upon the patient-specific connectivity of the Volume of Activated Tissue (VAT) to other network nodes.

Methods

In this longitudinal study we studied the connectivity of DBS in the nucleus accumbens area of three TRD patients implanted at Inselspital, Bern, Switzerland. Lead localization and generation of VATs was performed with the Lead-DBS toolbox in Matlab. Patient-specific VATs were estimated using the stimulation parameters from the clinical assessments. The structural connectivity was described through probabilistic tractography in MRtrix3. A whole-brain tractogram was generated and the filtering algorithm SIFT2 was applied to provide a quantitative estimation of connectivity. The streamlines inside the VATs were selected and assigned to a cortical area according to their endpoint.
Functional connectivity was estimated by combining the patient-specific VATs and a normative connectome generated with data from the Human Connectome Project. We obtained a functional connectivity fingerprint for each VAT and coupled it with the clinical outcome to derive a patient-specific optimal connectivity R-map.

Results

We observed a consistent structural connection to Brodmann area 25, a known DBS target for TRD. VATs were structurally connected to the insula when good outcomes were present. The functional connectivity analysis resulted in patient-specific maps describing brain areas significantly correlated to symptom's improvements, notably the prefrontal cortex. These preliminary results require confirmation in a larger cohort and over longer time periods.

Conclusion

Our connectivity results are in accordance with the findings of previous studies, in which DBS leads were implanted in other targets. This is in line with the notion that beneficial DBS engages a network rather than a structure. Furthermore, it suggests that the insular-nucleus accumbens connection may mediate symptom's improvement in TRD.

The Localized Subtraction Source Model For EEG and MEG forward modeling

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Introduction

One of the basic problems in EEG and MEG source analysis is simulating the sensor measurements that a given neural activity would generate, i.e., the so-called EEG and MEG forward problem.
The neural activity is typically modeled as a linear combination of mathematical point dipoles. When using a finite element method (FEM) for the forward problem this leads to difficulties, as it is not clear how the singularity of a point dipole can be properly incorporated. Various FEM source models have been proposed, and among these the so-called subtraction source model. The subtraction approach is not only well founded in theory, but also produces accurate results in practice. The major downside of the subtraction source model is that it is computationally prohibitively expensive in practical applications. To overcome this we developed a new source model, called the localized subtraction source model.

Methods

The localized subtraction source model is designed in such a way that it preserves the mathematical foundation of the subtraction source model, while also leading to sparse right hand sides in the FEM formulation, making it efficiently computable. In my presentation, I will present this source model. Furthermore, I will compare it to other state-of-the-art source models with regard to accuracy and computational effort.

Results

In multi-layer sphere models, where quasi-analytical solutions for mathematical point dipoles exist, the localized subtraction source model is shown to be as accurate, and in most cases even more accurate, than the other investigated source models, while being largely more efficient than the subtraction source model, and comparable in effort to a Venant source model.

Conclusion

The localized subtraction source model is a theoretically sound method that rivals, and in many cases even surpasses, other state-of-the-art source models in terms of efficiency and accuracy.

Focus Session: Photoplethysmography for the Unobtrusive and Continuous Monitoring of Vital Signs

Proof-of-Concept Study for Reflectance Pulse Oximetry Using Optical-Fibre-Based Sensors

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Introduction

Optical fibres enable to design of new textile-based sensors for an unobtrusive, continuous, and long-term acquisition of photoplethysmography (PPG) signals. However, no research has been done about the accuracy of measuring blood oxygen saturation (SpO2) and the feasibility of PPG based blood pressure measurement.

Methods

This proof-of-concept study examined these aspects for a woven sensing patch applied on the forehead in five healthy participants in a controlled desaturation study.

Results

The SpO2 estimation revealed an amplitude of the root-mean-squared error of 3.6%, and sufficient high signal quality for blood pressure estimation was achieved for 40% of all data.

Conclusion

These results indicate that textile-based sensors can reach the required PPG signal quality to simultaneously estimate multiple vital signs, including blood pressure.

Improving Photoplethysmography-Based Multiclass Cardiac Arrhythmia Detection via Pulse Wave Analysis

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Introduction

Photoplethysmography (PPG) is an interesting candidate for less obtrusive long-term cardiovascular monitoring. While many studies have shown the ability to differentiate atrial fibrillation (AF) from normal sinus rhythm (SR) based on PPG, other cardiac arrhythmias (CA) are less studied, and can induce errors in common AF detectors. To address this, we investigate the potential of novel features extracted by pulse wave analysis (PWA) for the PPG-based detection of both AF and non-AF CAs.

Methods

PPG signals were acquired from the wrist simultaneously with 12-lead ECG (used for gold-standard annotation of CAs) from 42 patients referred for catheter ablation at the Lausanne University Hospital. PPG segments of 30 s were automatically classified as either SR, AF or non-AF based on spectral and temporal features extracted from raw PPG time series and from inter-pulse interval series. In addition, novel PWA features extracted by detecting specific points in the PPG waveform and its derivatives provided insights into the morphology of individual pulses. Their discriminative power was evaluated based on the Relief algorithm for feature selection. Finally, we compared performance metrics for CA classification with and without PWA features.

Results

The classification accuracy using ridge regression was significantly increased by 2.8%, from 73.5% to 76.3% ($p = 0.009$), when using PWA features on top of temporal and spectral features. Likewise, the sensitivity in detecting AF increased by 3.4%, from 77.3% to 80.7% ($p = 0.09$). The most discriminative PWA features were the acceleration magnitude of the pulse upstroke and the timing of the dicrotic notch.

Conclusion

PWA features showed some potential for the detection and classification of AF and non-AF CAs. Although further work and extensive data is required to classify each type of CA individually, these results show the potential for improving our understanding of the peripheral hemodynamic signature of CAs.

Limitations of Calibration-free PPG-based Blood Pressure Estimation

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Introduction

Hypertension is a serious condition that greatly increases the risk of developing cardiovascular diseases. A regular and continuous blood pressure (BP) monitoring allows early detection and prevents eventual complications. In the effort of developing non-invasive, continuous and cuffless BP monitoring devices, photoplethysmography (PPG) has recently gained more interest. Such a simple and low-cost optical technology detects blood volumetric variations, which may be related to cardiovascular parameters. Each individual has however unique cardiovascular dynamics and PPG waveforms. A calibration process typically helps PPG-based BP monitoring approaches to cope with such inter-subject variability and achieve clinical acceptable accuracy. However, such a process complexifies the measurement procedure in real-world applications.

Methods

The present work investigates to which extend a calibration-free PPG-based model could achieve acceptable performance for BP estimation. The challenge is not only to remove the calibration step but also to limit pre-processing of input data. We use PPG signals with associated invasive BP readings from 3208 non-cardiac surgery patients. The proposed model combines the feature learning task with the regression task in a single architecture. It exploits convolutional and recurrent layers, such as long short-term memory, to extract representative information from 10-second PPG windows and estimates systolic (SBP) and diastolic BP (DBP) accordingly. Due to inter-subject variability of the PPG waveform, integrating demographic information to the extracted features, such as age, weight, height and gender, might help to guide the learning process.

Results

The model achieved errors of -0.24±15.62 mmHg for SBP and -0.53±9.55 mmHg for DBP. The demographics did not help to further improve the performance.

Conclusion

Compared to a similar approach with calibration, the proposed model seems limited to fully compensate the inter-subject variability. However, the results are promising, especially with low cohort-wise biases. Altogether, they reveal the complexity of the task and the limitation of calibration-free PPG-based BP monitoring technology.

Blood Pressure Estimation via the OptiBP Smartphone Application - Performances Across Different Body Mass Index

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Introduction

The association between obesity and hypertension has been demonstrated and both are considered public health priorities. Cuff-based Blood Pressure (BP) measurement may be biased by cuffsize and upperarm shape and represents a challenge affecting accuracy.
The OptiBP™ smartphone application is a cuffless approach that estimates BP using the optical signal collected through the patient's fingertip applied on the smartphone's camera. Access to the measure could be facilitated while decreasing the challenges related to the cuff-based technique.

Methods

We assessed the accuracy of OptiBP across different Body Mass Index (BMI) categories via a dedicated analysis of a prospectively collected dataset. The study protocol followed the ISO 81060-2:2018 standard for "Non-invasive sphygmomanometers" adapted for a cuffless device. Differences in simultaneously taken systolic (SBP) and diastolic BP (DBP) between OptiBP and the gold-standard dual-head stethoscope measure were calculated by subtracting the latter by the smartphone values. Data are presented as mean±SD, and data analysis was carried out according to both criteria 1 and 2 as required in the ANSI/ AAMI/ISO 81060-2:2013 standard. Patients were defined as obese (BMI > 30 kg/m2), overweight (BMI>= 25 kg/m2) and normal.

Results

The acceptance rate of OptiBP was of 82% and 414 recordings could be obtained from 95 patients. OptiBP estimations fulfilled Criterion 1 and 2 in each subgroup for systolic BP and diastolic BP. The accuracy of these estimations are strengthened by absolute error proportions in accordance with the recommendations of the European Society of Hypertension and clinically relevant margin of error.

Conclusion

Altogether, these results illustrate the accuracy of OptiBP estimation regardless of the patient's BMI. This is a further step toward reliable, comfortable and inclusive medical care for population diversity. Further research is in progress to improve the algorithm and validate it across other population diversities and pathologies.

A phantom for noninvasive fetal pulsoximetry with a high-precision positioning system for the optical sensor

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Introduction

The method of noninvasive transabdominal fetal pulse oximetry is a promising approach for continuous monitoring of the fetal health during the pre- and perinatal stages of pregnancy. Its noninvasive character reduces the risk of infections for the mother and the fetus, in comparison to other existing methods.

Methods

An important aspect in the development of this new approach is a test environment that enables the testing and refining of the involved hardware and software components. Therefor a simplified physical-like phantom of a pregnant woman was developed. The developed artificial vascular system consists of two independent fluid cycles representing the maternal and fetal vessel system.

Results

The arterial pulse waves are reproduced by a pre-pressure and an artificial vascular system. Each pulse wave can be emulated by a digitally controlled magnetic proportional valve, an adjustable viscoelastic element, and an adjustable fluidic resistance. This physical-like phantom is embedded into a photo sensor positioning system for semi-automated attenuation mapping of the artificial tissue on a sub-millimeter scale while also ensuring high levels of reproducibility. All electronic components are integrated into a wireless communication network based on the MQTT protocol to control and monitor the artificial vascular system and the positioning system. In this wireless network a Raspberry Pi 4 board with Raspbian OS serves as MQTT broker, while several nodeMCUs in their usage as MQTT clients represent the interfaces between the electronics and the network infrastructure. Using the NodeRed software, the Raspberry Pi also provides a web interface, which can be utilized to control the sensor position, adjust the emulated pulse curve and manage the data acquisition wirelessly via a web browser.

Conclusion

First measurements did not consider different optical attenuation characteristics of the different blood gas levels. Further steps will be experiments with artificial blood substitutes mimicking different oxygenation levels of maternal and fetal blood.

Focus Session: Signal-Based Risk Prediction in Cardiovascular Diseases (Joint Session GMDS-DGBMT)

Variable Projection Networks for Arrhythmia Detection

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Introduction

Over the last decade, deep learning (DL) has exhibited a huge advancement in many fields including biomedical engineering and healthcare informatics, although they continue to raise several concerns. First, due to the large number of nonlinear model parameters, DL approaches can be considered as black-box methods, where the parameters have no or little physical meaning. Second, training these DL models requires vast amounts of labeled data, which is problematic to collect in medical applications due to the involvement of clinical experts, the measurement costs, and the usually low prevalence of abnormal cases.

Methods

In order to surpass the limitations of pure data-driven DL approaches, the so-called model-driven machine learning methods have been recently introduced. This concept is an emerging trend in signal processing, which combines the advantages of model-based methods and DL techniques. In this talk, we propose VPNet, a novel model-driven neural network architecture based on variable projection (VP) that is adapted to the problem of arrhythmia detection. As a case study, we consider the classification of normal and ventricular ectopic beats in real ECG recordings of the PhysioNet MIT-BIH Arrhythmia Database.

Results

We show that applying VP operators to neural networks results in learnable features, interpretable parameters, and compact network structures. In fact, VPNet can achieve a heartbeat classification accuracy of ~98%, that is better than its fully connected and convolutional counterparts while using a smaller number of parameters.

Conclusion

Model-driven neural network solutions can have a great impact in biomedical engineering and healthcare informatics, where medical data classification alone is usually not enough, as physiological interpretation and explainability of the results are also important.

Risk prediction of premature autonomic ageing based on non-invasive cardiovascular measurements - A project outline

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Introduction

The premature ageing of the autonomic nervous system is expressed in symptoms like elevated blood pressure and cardiovascular dysregulation. It is strongly associated with cardio- and cerebrovascular diseases (CVDs) and neurodegeneration in the later life of patients.

Methods

We aim at developing a system to predict the extent of this premature ageing.
As a basis for the prediction, raw time series related to electrocardiograms and continuous non-invasive blood pressure recordings will be analysed. Moreover, well-established and manually derived scalar features relating to the heart rate variability, blood pressure and pulse wave dynamics will be used.

Results

We have already evaluated classical machine learning approaches like Gaussian process and support vector regressions that make use of manually defined features for this task. In the upcoming stage of the project, we will combine these features with those that are automatically defined and extracted from the described time series with the help of deep recurrent and convolutional neural networks. This combination will lead to a rich and interpretable latent feature space that will serve as the basis for an age predictor.
In the light of our experiences with deep learning-based anomaly detection, we anticipate that the predictor can be modified into a risk estimator for premature autonomic ageing. By training the predictor on a healthy population the system will learn to correctly predict the age of healthy participants. However, it will predict inaccurate ages for patients showing premature autonomic ageing and cardiovascular measurements that deviate from the ones of their healthy peers. Thus, during inference, the difference between the prediction and the biological age can serve as a risk score.

Conclusion

The proposed framework will lead to a comprehensive indicator of autonomic cardiovascular function and consequently enable precise, preventive, and patient-centred management of CVDs.

Towards Explaining Decisions of a Deep Learning Model for AF Detection in 12-lead ECGs

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Introduction

Currently, an increasing number of deep neural networks (DNNs) for biosignal classification are developed, often outperforming conventional methods based on handcrafted features. Understanding the reasoning of DNNs is a challenge, making their application difficult in clinical settings. In previous work, we applied a pre-trained DNN by Ribeiro et al. for 12-lead ECG classification to our local clinical data and reproduced the reported performance. In this work, we evaluate the feasibility of the attribution method "Integrated Gradients" (IG) for explaining the DNN's classifications by means of a qualitative visual inspection and a quantitative analysis based on complexity.

Methods

We apply the Ribeiro model to a subset of the China Physiological Signal Challenge 2018 dataset. The model assigns probabilities for six ECG abnormalities, but we limit our analysis to atrial fibrillation (AF). We change the activation of the last layer to linear and apply IG to 200 AF and 200 sinus rhythm (SR) signals (10s duration) by using iNNvestigate. It assigns a positive or negative relevance value to each ECG sample. Subsequently, we calculate the sample entropy (SampEn, m=2, r=0.2std, N=4096) of these relevances w.r.t. lead and label and aggregate results as boxplots.

Results

Analyzing the relevances of model probabilities for AF classification with SampEn showed similar ranges of [0.03,0.80] and [0.06,0.82] for AF and SR patients, respectively. 11 out of 12 leads showed lower median values for AF patients, with the highest difference being 0.15 (lead V5). Regarding visual inspection, we observed a clustering of relevances in the area of QRS complexes. During measurement noise (e.g. inadequate skin-electrode contact) clusters with high absolute values and interchanging signs agglomerate.

Conclusion

We observed a tendency of IG relevances showing a higher complexity in SR than AF patients during AF detection, suggesting a higher uncertainty of the DNN when tending towards low probabilities.

Predicting NT-proBNP from ECGs using deep learning — about the generalizability and calibration when using multiple data sources

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Introduction

The cardiac peptide hormone brain natriuretic peptide (N-terminal pro hormone: NT-proBNP) is released physiologically in the left ventricle and in the atria during myocyte stretch. It is an established biomarker for the diagnosis and monitoring of heart failure. As alterations in the heart affect its electrophysiology, we expect that even minimal changes in the electrocardiogram (ECG) may correlate with elevated NT-proBNP concentrations.

Methods

Well-characterized population-based cohort data was used to develop and test a predictive model of NT-proBNP from raw 12-lead ECGs. Data from the Hamburg City Health Study (HCHS) was used to train a 1D-Residual-Network in a 5-fold internal validation scheme. Various ECG sources of the Study of Health in Pomerania (SHiP) were used to test generalizability, including measurements from spiroergometry, sleep and orthostatic testing. Probands without follow-up data, a history of heart disease or cancer were excluded. The predicted NT-proBNP compared in Bland-Altman analysis was further used in logistic regression to discriminate subjects who developed heart failure over the 15 years of follow-up. Calibration and discriminative power were examined in analysis of the receiver operating curve.

Results

The neural network was trained on 10s-ECGs of 8,256 participants (median age 62 years, 49.6% men) and corresponding NT-proBNP concentrations (mean$\pm$sd 144$\pm$385 pg/ml). Good performance in predicting NT-proBNP values was observed in HCHS data (R-squared 0.26 [95%-CI 0.24-0.28], mean absolute error 83 [95%-CI 82-84]). Within the 2,395 resting state ECGs of the younger SHIP-cohort (SHIP-Start0: median age 46 years, 45.7% men, NT-proBNP: 71$\pm$80 pg/ml), we observed a shift of predicted NT-proBNP that requires calibration.

Conclusion

We investigated the relationship between digital ECG information and NT-proBNP as a basis for the subsequent development of a screening instrument for the general population. For the application in the general population and the portability of models trained on specific data sources, calibration is required and generalizability is limited.

Focus Session: Vestibular Implants for the Artificial Restoration of Balance: Modelling, Recent Developments, and Steps Towards a Clinical Application

Simulation of evoked compound action potentials for the investigation of neural stimulation in a 3D model of the human vestibular system

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Introduction

Our inner ear consists of the cochlea, which is responsible for hearing, and the vestibular system, which contributes substantially to our sense of balance and spatial orientation. Several studies have shown that vestibular implants can partially restore the function of the vestibular system. To analyze the effects of stimulation parameters and electrode positions, computer models are considered valuable tools. Evoked compound action potentials (eCAPs) are a quantitative measure to estimate the neural stimulation. A methodology to simulate and investigate eCAPs in a 3D human vestibular system is presented.

Methods

A semi-automatic modular workflow was applied to realize electrical computer models based on segmented high-resolution µCT scans of human vestibular systems. Spherical electrodes with diameter of 300 µm were placed in the center of each ampulla and considered as active electrodes or recording electrodes. For each nerve branch, the nerve fiber orientation was evaluated separately for considering the anisotropic conductivity of the neural tissues. Simulations were performed in quasi-static condition by applying a unit current to the active electrode and the extracellular potential distribution is then scaled according to the time dependent stimulus waveform. The transmembrane current flowing through each node of Ranvier was obtained and used to compute the eCAPs response at the recording electrode. By applying different stimulus amplitudes, the amplitude growth function (AGF) is obtained.

Results

The obtained eCAPs waveforms show a comparable shape with respect to experimental recordings in literature. Moreover, the AGFs obtained by considering inter-canal electrodes are comparable with studies on living patients.

Conclusion

Simulated results of eCAPs and AGFs, based on a 3D human inner ear model, are in good agreement with experimental findings. Our approach will improve electrodes placement and yield additional information about stimulation effects. In future work, patient specific anatomy and recorded eCAPs will be compared with the 3D computer model.

The VertiGO!-trial: towards a safe and efficient multichannel cochleo-vestibular implant

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Introduction

Bilateral vestibular loss is an as-of-yet untreatable and often underestimated clinical condition affecting more than 500.000 people in Europe. Since 2012, the Geneva-Maastricht group performs research on the cochleovestibular implant (CVI) to aid these people. By directly stimulating the vestibular nerves, the vestibular implant (VI) aims to restore vestibular function. Recent studies already showed feasibility of the prototype, with compensatory eye, body, and neck movements after short, acute stimulation. Optimal electrode placement during surgery is crucial to ensure good clinical results. The effects of long-term chronic stimulation with a CVI are as-of-yet not investigated. The VertiGO!-trial is a new and extensive clinical trial which aims to investigate the safety and efficiency of long-term chronic stimulation by the CVI, while for the first time also stimulating the CI and VI together.

Methods

A total of eight patients suffering from bilateral vestibular function loss will be included in a randomized single-blind cross-over controlled clinical trial and will receive a unilateral CVI. Fluoroscopy and semi-CT are used to ensure optimal electrode placement during implantation, with multiple follow-up scans to assess position over time. Throughout various stimulation weeks, patients undergo extensive auditory and vestibular testing to assess and optimise the function of the CVI. The efficiency of prolonged VI stimulation will be evaluated by collecting both fundamental, functional, and subjective outcome measures.

Results

Since October 2021, five out of eight patients have received a CVI, of which three are already fitted. Using perioperative imaging techniques, electrode positioning improved in all five patients. A more in-depth overview of the VertiGO!-trial in general and the used imaging techniques to improve electrode positioning will be presented.

Conclusion

The VertiGO!-trial is a new and ongoing extensive randomized cross-over clinical trial, aiming to evaluate the safety and efficiency of long-term, chronic vestibular and cochlear co-stimulation by the CVI prototype.

Vestibular implants: from the concept to the clinical application

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Introduction

Vestibular implants are implantable devices that attempt to partially restore vestibular function using electrical currents to patients with severe bilateral vestibulopathy of peripheral origin (BV). This disorder results in many disabling symptoms, including imbalance, oscillopsia, reduced mobility, and increased risk of falling. Unfortunately, the prognosis is poor and currently available treatment options have very low efficacy.

Methods

There have been substantial research efforts towards the development of vestibular implants. Our group, the Geneva-Maastricht team, developed an original concept based on a modified cochlear implant. This device, developed in close collaboration with MED-EL (Innsbruck, Austria), provides 1 to 3 extra-cochlear electrodes which are implanted in the vicinity of vestibular afferents in addition to the “standard” cochlear implant array. Specific stimulation paradigms as well as a novel, combined processor allowing specific activation of cochlear and vestibular electrodes according to stimuli captured with incorporated microphones and motion sensors have also been developed.

Results

We started implantations in humans in 2007 and, to date, 18 patients with severe BV were implanted with these prototype devices without surgical or medical complications. Humans have demonstrated surprising adaptation capabilities to the artificial vestibular signal. Successful restoration of the different vestibular reflexes has been demonstrated using standard clinical tests (rotatory chair, video-head impulse test, and cervical myogenic vestibular evoked potentials). Controlled postural responses could also be obtained with our prototype vestibular implant device. Finally, visual abilities in dynamic settings were restored with the vestibular implant. The latter is a major step forward, providing the first ever demonstration of useful rehabilitation of this patient population.

Conclusion

First results in humans are very encouraging. We hope that the increasing interest in this field and the substantial research efforts allocated will lead to a successful clinical application in the near future.

Translating Head Movements into electrical VestibuloCochlear Implant Stimulation

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Introduction

recent implantations with a VestibuloCochlear Implant (VCI) by the Maastricht-Geneva group, and the development of the wearable Audio Motion Processor (AMP) by MED-EL make it possible to deliver movement related electrical stimulation to the vestibular system in order to restore balance in patients with bilateral vestibulopathy. The AMP is capable of encoding head movement real time in electrical stimulation with a patient freely moving around. In order to be able to restore balance, the electrical stimulation should represent the head movement in a way that is correctly processed by the brain. This makes the encoding an essential part of the development of the clinically available VCI. This study aims on optimizing the movement encoding in a patient specific manner, resulting in a clinically applicable fitting procedure.

Methods

The optimal basic characteristics of the vestibular stimulation will be studied in eight newly implanted patients, as well as the patient specific encoding of movement related output modulations. Output modulating will be optimized by testing multiple stimulations paradigms. Multiple objective and subjective outcome measures, e.g. eye tracking and perception, will be used to evaluate different stimulation paradigms.

Results

the acute vestibular response to electrical stimulation with different characteristics is tested in the first three implanted patients, resulting in eye responses and perception with varying characteristics amongst patients and stimulation parameters. In addition, the effect of multiple encoding paradigms is explored, giving first insights for optimizing fitting strategies for prolonged stimulation testing.

Conclusion

as part of the current trial, the vestibular response to electrical stimulation by a VCI is investigated, aiming on developing an effective patient specific fitting routine. The first results as shown here give valuable input for the following experiments with prolonged stimulation.

Challenges in the development of the Audio-Motion Processor

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Introduction

Cochleo-vestibular implants aim to offer a treatment option for patients who suffer from bilateral vestibulopathy with severe sensorineural hearing loss. Combined implants have been implanted at the Geneva University Hospitals and at the Maastricht University Medical Centre. Until now, these implants are used daily by patients with both severe hearing loss and bilateral vestibular loss but only for hearing restoration. To address this limitation, we have developed a portable Audio-Motion Processor (AMP) that is capable of providing appropriate stimulation to both inner ear structures.

Methods

The AMP consists of an off-the-shelf audio processor, a novel motion processor, and a transmitting coil. As for a clinical cochlear implant system, sound from the environment is recorded with microphones and transformed into cochlear stimulation commands by the audio processor. In addition, head movements are recorded with a 6-axis inertial measurement unit and transformed into vestibular stimulation commands by the novel motion processor. Both the cochlear- and vestibular stimulation commands are then merged within the system and transmitted via an inductive link to the cochleo-vestibular implant. A set of experiments was conducted to assess sensor fixations, system latency, and stimulation strategies for the device. A clinical study to evaluate speech perception performance was conducted to investigate the effect of auditory stimulation gaps, as required for merging cochlear and vestibular stimulation.

Results

Our results showed that this causes no significant deterioration in speech perception and that the technical requirements regarding latency and sensor fixation of an audio-motion processor have been met.

Conclusion

The presented work provides insights into the main challenges of developing a combined audio motion processor for cochleo-vestibular stimulation, and solutions that have been implemented to overcome these challenges. We demonstrate that the concept of an audio-motion processor is technically feasible, making the developed device a viable tool for future research studies.

Simulation of vestibular afferent stimulation considering realistic inner ear and head anatomy

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Introduction

Vestibular implants offer a treatment option for patients suffering from vestibular disorders. In addition to experimental studies, computer simulations are used to obtain a better understanding of electrical stimulation outcomes, contributing to improved implant designs and stimulation protocols. Finite element simulation results were previously presented considering realistic human inner ear anatomy encapsulated in spheres with homogeneous electrical properties to model surrounding tissues, where the reference potential was homogeneously applied at the outer boundary of the model. This simplified consideration of the surrounding anatomy and the reference electrode might have a substantial effect on the stimulation outcome. To investigate potential effects of these simplifications, an existing inner ear model is extended by considering publicly available anatomical data of surrounding structures in the simulations.

Methods

A realistic anatomical model of a human head was acquired (MIDA Head & Neck Model, IT'IS Foundation), enabling the consideration of a realistic reference electrode at the implant housing on the cranial surface together with realistic surrounding structures close to the inner ear. To further improve the level of anatomical detail, segmented data of the mastoid cells and the middle ear from the OpenEar library was taken into account. Neural activation of monopolar stimulation scenarios with electrodes in the ampullae of the semicircular canals were simulated and compared with corresponding results of the simplified model.

Results

Compared to the simulation results of the model with simplified surrounding anatomy, considerably lower stimulation amplitudes were required for activation of the nerve branches of the inner ear when considering the extended model.

Conclusion

The simulations showed that surrounding anatomical structures can have a considerable influence on the overall stimulation outcome. Additional evaluations are planned using the extended model to derive anatomical factors and effects of varying reference electrode positions, which could potentially influence the stimulation outcome of a vestibular implant.

Track:
Additive Manufacturing and Bioprinting

Fabrication of Silver Nanowire Based Conductive Silver Ink

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Introduction

Conductive inks are used extensively in electronic devices like sensors, batteries, photovoltaic devices, antennae, and organic light-emitting diodes. These inks are typically made from silver. Wearable technology is another industry that requires inks to be flexible. These devices need low-temperature cured silver pastes.

Methods

Low-temperature pastes typically make use of silver nanoparticles. These pastes have some problems with sintering and substrate adhesion. In this thesis, to overcome these problems, silver nanowires are used to formulate pastes. Conductivity, bonding strength, flexibility, transparency, and compliance of the silver nanowire pastes were determined. The promising performance was obtained from silver nanowire pastes due to the one-dimensional nature of the nanowires in terms of adhesion to the fabric surface.

Results

Silver nanowires have a big area to adhere to, network form of them is more conductive and transparent than the network form of silver nanoparticles.

Conclusion

The aim of this study is the fabrication of low-temperature silver paste by synthesis long silver nanowires.

Acoustic Droplet 3D Bioprinting of Cell-Laden Structures

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Introduction

Bioprinting technology has gradually made tremendous progress in the fabrication of complex hydrogel-based cell-containing constructs, especially for advanced 3D in vitro models. Most state-of-the-art bioprinters typically use a nozzle to print droplets or extrude material. Nozzles are a critical component. For high resolution printing the nozzle size should be as small as possible. However, the smaller the nozzle size the more often clogging occurs. In addition, printing-related shear stresses increase with the decrease of the nozzle size. Critical shear stresses can damage the printed cells.

Methods

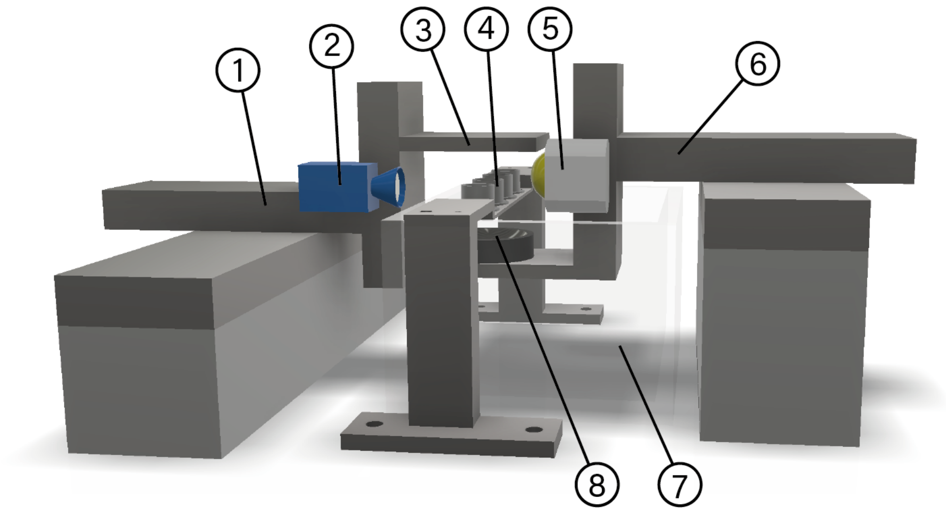
Acoustic droplet ejection, as presented here, does not require a nozzle at all. Consequently, nozzle-induced wall shear stresses are eliminated. The printing technique has so far been associated mainly with single-cell printing. A customized printer based on the acoustic droplet ejection principle has been developed to enable macroscopic 3D bioprinting. The structure of the acoustic bioprinter includes six separately controllable and movable axes. Three orthogonally arranged axes each are combined as a set, one of which is for the movement of the build platform and the other for the movement of an ultrasonic transducer. The transducer, centered under an open-pool bioink reservoir, is aligned in height so that the focal point of the ultrasonic signal is focused to the air-liquid interface. This arrangement allows the emitted ultrasonic signal to eject single droplets of bioink towards a building platform above the reservoir. Two camera systems help determine and control the optimal printing parameters.

Results

We showed that the cells embedded in the hydrogel structures show high viability after printing without negative long-term effects. In addition, complex 3D structures were realized by the described technique.

Conclusion

In summary, acoustic bioprinting has proven to be a cell-gentle technique and enables precise spatial placement of cell-laden hydrogel droplets at high printing resolution.



1. Axes system 1 (Building platform)
2. Side view camera
3. Building platform
4. 4x bioink reservoirs
5. Flash illumination
6. Axes system 2 (Ultrasound transducer)
7. Water bath
8. Focused ultrasound transducer

Fig.: Schematic representation of the acoustic droplet ejection (ADE) 3D bioprinting setup.

3D printed microfluidic modules: passive mixers and cells encapsulation in alginate

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Introduction

Microfluidics is an increasingly growing technology that finds applications in cell biology, biochemistry but not only. In recent years, 3D printing was demonstrated to be an alternative to traditional manufacturing methods allowing faster, cheaper and more complex structures. Our goal is to develop 3D printed solutions for microfluidic suitable for applications in life science. Therefore, microfluidic droplet generator and mixing modules were designed and printed. The system was used to encapsulate breast cancer cell in alginate droplets and assess drug induced cytotoxicity at increasing concentrations.

Methods

All the parts were printed using Form3 SLA printer and ClearV4 resin. Mixing efficiency was simulated using FEM at increasing Reynolds numbers. The biocompatibility of the resin was tested by assessing contact cytotoxicity on MCF-7 cells after 30min incubation. Cells were encapsulated in 1wt.% alginate using external gelation with Ca-acetate. The alginate beads were treated for 48 h with the cytostaticum doxorubicin at different concentrations. The liquid was controlled with an Elveflow OB1.

Results

Highway and Diamond mixers were specifically created for 3D printing. FEM analysis demonstrated that the mixing performance are >80% for both already at 10 Reynolds. The droplet module allowed cells encapsulation in 300-800µm alginate droplets depending on the W/O pressure ratio. The encapsulation process and the short contact with the cured resin did not affect the cell viability as shown by the cytotoxicity test. The encapsulated cells in contact with doxorubicin led to a concentration dependent decrease in viability detected with WST-8 and with Calcein-AM staining.

Conclusion

3D printing makes possible to easily fabricate low-cost microfluidic modules with novel designs for liquid mixing and droplet generation. In addition, the biocompatibility of the printed material and its transparency make it an attractive alternative to state-of-the-art fabrication methods for life-science applications such as cells encapsulation and drug screening but not only.

Evaluation of Flexible 3D-Printing Materials in Cardiovascular Research

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Introduction

Additive manufacturing allows printing of patient-specific models for cardiovascular applications. For the selection of flexible 3D-printing materials, knowledge of material characteristics and behaviour are necessary. Therefore, the aim of this study was to evaluate and compare the biological, chemical and physical parameters of six commonly used acrylate- and silicone-based 3D-printing materials.

Methods

An analysis of the native surfaces was performed after the production of the samples for each material. The basic mechanical behaviour was evaluated by uniaxial tensile tests, the shore A duration and compliance analysis. The effect of the solvents water, glycerin and ethanol was analyzed for an incubation period of seven days. The impact of different sterilization protocols (steam, plasma, ethylene oxide) was determined by tensile testing and SEM analysis. Cytotoxicity was evaluated by a WST1-proliferation assay with human endothelial cells.

Results

Tensile strength showed significant differences between the materials (e.g., 0.60 compared to 6.61 N/mm^2; $p<0.0001$). Even materials with similar shore A duration had a significant different elongation at break (91.4 compared to 362.2 %; $p<0.0001$). Water and glycerin were tolerated well according to relative solvent absorption. However, the relative absorption of ethanol varied in between a wide range of 5.6 and 104.6 % among the materials. Steam sterilization had negative effects on the tensile strength of one acrylate-based material (0.60 compared to 0.52 N/mm^2; $p<0.0001$), while plasma sterilization destroyed one silicone-based material (6.61 compared to 1.25 N/mm^2; $p<0.0001$). Additionally, the surface of these sterilized samples changed in SEM analysis. WST1 assay showed low cytotoxicity for silicone-based compared to acrylate-based materials.

Conclusion

This study builds a catalogue with the biological, chemical and physical parameters for different flexible 3D-printing materials. It enables a streamlined selection process for individual cardiovascular applications.

Digital Light Processing of Round Window Niche Implant Prototypes for Implantation Studies

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Introduction

A new approach that offers the potential for local drug delivery to the inner ear is a 3D printed, patient individualized, drug-loaded implant that precisely fits into the round window niche (RWN). Anatomically correct digital light processing (DLP) 3D printed implant prototypes are beneficial for the rehearsal of implantation techniques. The aim is to define desired mechanical material properties for future RWN implants.

Methods

Patient-individualized RWN implant prototypes (RWN-IPs, ~3x2x1 mm) were DLP 3D printed (VIDA device, Envisiontec GmbH, Gladbeck, Germany) using commercially available E-Shell 500 and E-Shell 600 materials (Envisiontec GmbH, Gladbeck, Germany) and a self-established PEGDA700 composition. Different 3D printing layer heights ranging from 25 µm to 100 µm were utilized. The photopolymers are suitable for 3D printing of RWN-IPs that feature different mechanical characteristics. Firstly tensile tests were investigated. Secondly the implantation feasibility and fitting accuracy in human cadaver RWN were evaluated.

Results

E-Shell 500 has relatively high stretchability (εm ~ 60%), while E-Shell 600 and PEGDA700 are brittle and PEGDA700 has low strength. E-Shell 500 performs by far the best at handling and insertion because of high stretchability and softness. Minimal 3D printing layer height is 100 µm. E-Shell 600 has adequate strength but is hard to handle because of rigid material behavior. Minimal 3D printing layer height is 50 µm. PEGDA700 enables highest 3D printing accuracy (layer height of 25 µm) but lacks mechanical behavior for adequate insertion of implant prototypes in RWN.

Conclusion

The implantation tests revealed a need for soft/stretchable/flexible materials for ease in handling of the RWN-IPs, which speeds up the insertion into the RWN. Future studies must investigate whether the implant material's softness and flexibility may be relevant for preventing the likelihood of traumatizing sensitive structures such as the RWM during insertion. In addition, the implant-tissue-interface should be investigated to define needs for 3D printing layer height.

Dependencies and limits in cold extrusion silicone rubber 3D-printing

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Introduction

Additive manufacturing with liquid materials like hydrogels, waxes or rubbers offers significant innovation opportunities in medical technology. However, depositing liquid materials to form an object is challenging, as various factors like viscosity, nozzle size, speed, and temperature all influence printing accuracy.

Methods

In this study, a custom 3D-printer, featuring a filament extruder and a fluid extruder, was used. The printed materials were three different high-viscosity, single-component, condensation-crosslinking liquid silicone rubbers, and a polylactic acid (PLA) filament. The influence of silicone viscosity, nozzle diameter and extrusion speed on printing accuracy was assessed by depositing silicone with various speeds and nozzles. A speed-dependent extrusion compensation was proposed and implemented in firmware. This was validated by weighing printed objects. These objects contained various unstable features like thin walls, slender towers, bridges, and overhangs. Finally, the limits of printable geometric features were investigated by assessing deformations using an optical profilometer. These results were compared to the same objects printed with the PLA filament.

Results

Increasing material viscosity (range: 400 - 1100 Pas) or extrusion speed (range: 0 - 10 mm^3;/s), or decreasing nozzle diameter (range: 0.51 - 0.33 mm) all increased errors in extruded volume. Since these errors were large (range: -10% to -80%) a speed-dependent volume loss compensation was implemented. This was validated by printing objects with weight errors less than 5%. Unstable geometric features on these silicone rubber objects showed larger deformations than on PLA-printed objects. In silicone objects, various dimensional errors showed correlation coefficients over 0.9 with material viscosity.

Conclusion

It was concluded that cold-extrusion silicone rubber printing has similar design constraints to thermoplastic filament printing, but unstable features are less accurate. Since silicone rubbers are frequently used in medical technology, the resulting design guidelines may help projects where 3D-printing a silicone medical device is included.

Topology-optimized patient-specific osteosynthesis plates - Methodology to semi-automatically design additive-manufactured osteosynthesis plates for the fixation of mandibular fractures

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Introduction

Patient-specific osteosynthesis plates can be used to reduce complications related to bone fracture treatment, such as infection, malocclusion and fatigue fractures of plates and screws. However, the implant design process is tedious. We propose a semi-automatic workflow to design patient-specific titanium osteosynthesis plates for mandibular angle fractures computationally.

Methods

In this process, the plate stiffness is maximized while the mass is reduced. Two plate designs with different numbers of screw holes (implant #1 with four holes, implant #2 with eight holes) were generated with identical topology optimization settings and compared in a finite element model simulating various biomechanical masticatory loads.

Results

Differences in von Mises stresses in the implants and screws were observed. The load case of clenching the jaw on the opposite side of the fracture showed the highest stress distribution in implant #1 and higher peak stresses in implant #2. Stress concentrations were observed in sharp corners of the implant and could be reduced using local stress-based topology optimization.

Conclusion

We conclude that the design process is an effective method to generate patient-specific implants.

Elastic properties of mix-materials fabricated by two additive manufacturing methods

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Introduction

The range of materials available for 3d-printing has grown rapidly in the last few years. However, for very specific requirements of the printed parts, such as elasticity, color or surface properties, a suitable material is not always available. In these cases a significant advantage would be to mix the desired material from just a few basic materials, thus expanding the current range of possibilities. This study aims on simulating and predicting elastic properties of such mix-materials.

Methods

Primary materials available for bottom-up stereolithography (SLA) printer (Photon-Mono, Anycubic, China) and a polyjet printer (Objet500, Stratasys, USA) were mixed and the elastic properties of the resulting materials were experimentally determined by mechanical tests. Analytical (Matlab, MathWorks, USA) and FEM (ANSYS-Mechanical, ANSYS, USA) simulations were established to predict mix-material properties from their basic components and these compared to the experimental results. Two different mixing methods were evaluated during the fabrication: whereas in the SLA-printer two photopolymers were thoroughly mixed before the printing process, during the polyjet printing, spheric or cubic inclusions of one material were printed inside the matrix of the other material.

Results

The tensile and bending tests showed that the elastic properties of fully cured mix-materials, stirred together before the printing process, can be approximately predicted with a linear interpolation of the base materials. For the polymers used in this study, the uniaxial Young's modulus ranged from 1.6GPa to 2.2GPa. In polyjetted matrix-inclusion composites the printing process and the interfaces between the phases play a major role, so that the overall structure has a lower Young's modulus than a linear interpolation would suggest. With primary materials ranging from 1.6GPa to 2.5GPa, the Young's modulus of the mix-materials go down to 1.3GPa.

Conclusion

In conclusion, the possibility to predict material parameters of multimaterials allows to fabricate structures with precisely defined mechanical characteristics and gradients.

Recent Developments on Engineered Materials for Orthopaedics

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Abstract

The future of several medical devices will turn on the use of regenerative engineered biomaterials which mimic natural body functions. The challenge is therefore to create functional and good quality neo-tissues. Due to regulatory constraints, new biomaterials cannot be used by the industry ; new designs and engineered materials represent a viable solution, at least for the next years.
It is well known that periosteum plays an important role in bone regeneration. This is particularly true for long bone defects. In the current work, we present recent advances in the construction of 3D printed scaffolds and electrospun membranes mimicking the bone structure and periosteum.
Since present biomaterials and concepts would not be able to stabilize cases with important bone loss, the design of implants aims to create synergies with surgical procedures. The combination of intramodular nails or stabilisation plates might be necessary to stabilise the bone failure.
The manufacturing processes include 3D printing of functionalised biomaterials and a gradient of mechanical properties through the lattice variation. The composition of materials versus compression strains and resorbability rates have been studied. Bacteriostatic functions have been incorporated in the spongious scaffold to make it compatible with surgical procedures.
Research has been done mimicking the periosteum membrane towards multi-shell electrospun membranes containing liposomes and growths factors. As a result of tuning surface energy, porosity and liposomes concentration, a suitable combination of properties has been identified.
After validating mechanical versus resorbability kinetics as well as drug release rate from the membranes and in vitro functionalities of the principles, long bone defects induced on sheep and treated with prototypes have led to promising results.
All materials are certified and commercially available. All processes are standard and all designs meet clinical needs and are adapted to surgical procedures. All of which lead to industrial and societal perspectives.

Additive manufacturing of novel scaffold-based phenotypic platforms for tissue engineering

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Introduction

Two-Photon Polymerization (2PP) represents one of the most flexible and high-resolution Additive manufacturing (AM) processes, as it enables the full three-dimensional fabrication of complex structures with sub-micron resolution. One of its most important applications today is the manufacturing of 3D scaffolds in the field of tissue engineering.
In this talk, we will present our results from the H2020 projects MESO-BRAIN and PLATFORMA, focusing on the fabrication of novel scaffold-based high-content phenotypic platforms to create purpose-built, 3D modular human tissues from which electro-physiological status of the cells can be monitored. These platforms can be applied for screening cosmetics, pollutants and new therapeutics.

Methods

The various 3D scaffolds were fabricated from biocompatible photosensitive materials by two-photon polymerization using a BioScaffolder+ system from Laser nanoFab GmbH. Complementary technologies such as photo- and stereolithography were used to fabricate additional components to complete the functionalities required for each application.

Results

Within the scope of our work, platforms for different tissue types such as skin, muscle and brain have been successfully designed and fabricated using the mentioned AM techniques. In cell culture studies, the application of these platforms for the construction of modular human tissue was validated. The functionality of the designed platforms was confirmed by electrophysiological measurements and calcium imaging.

Conclusion

AM techniques such as 2PP are a powerful tool for the fabrication of three-dimensional scaffolds for tissue engineering. By building phenotypic scaffold-based platforms, the construction of various tissue types such as skin, muscle, bone, cornea and brain is possible. This will allow the screening of cosmetics, pollutants and new therapeutics to be performed in vitro in the future, replacing animal testing. The use of scaffold-based culture systems is also of great importance for in vitro disease modeling. For example, the modeling of neurological diseases using NSCs could be made possible in this way.

3D printed highly flexible phantom for realistic dynamic flow measurements

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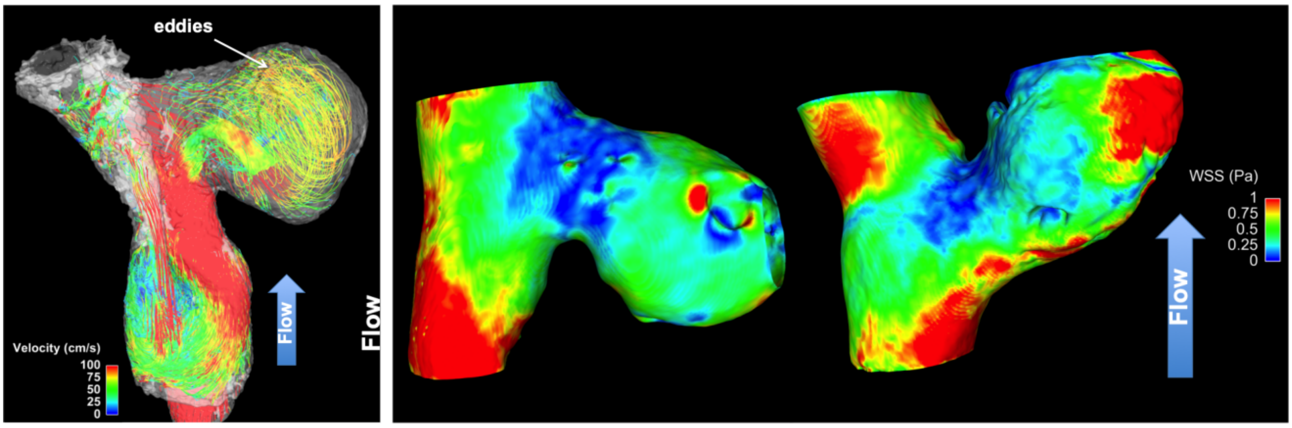
Introduction

4D phase contrast MRI is a versatile tool for measuring hemodynamic flow within complex vessel geometries such as the aortic arch or aneurysms. The use of realistic vessel phantoms in combination with pulsatile flow has great potential to study the complicated fluid dynamics and the mechanisms leading to pathological changes under controlled conditions. In this abstract, we demonstrate the use of this technique in a 3D printed vessel phantom under pulsatile flow.
Materials and

Methods

The fabrication of the vascular phantoms was performed in several steps. First, the desired vessel structure is extracted from acquired 3D data. The generated STL file was 3D-printed as a solid model using polyvinyl alcohol filament. Afterwards the phantom was coated with a small layer of xylitol and finally casted with two layers of silicone. The PVA model and xylitol coating was immersed in water and finally prepared for flow experiments.
All experiments were conducted in a 7T small animal MRI system running a custom self-gated radial 4D phase contrast cine MRI sequence using a balanced 4-point flow-encoding scheme.
A threshold-based segmentation of the magnitude data and the velocity obtained from the phase differences of the flow-encoded acquisitions were used to calculated the wall shear stress from the spatial velocity derivatives at the vessel wall.

Results



Flow was measured in vascular phantoms using continuous flow and displayed in as streamlines through the vessel, indicating the direction and magnitude of the velocities (Fig. left). Near the bottleneck of the phantom, an increase of the flow velocity is observable. In the bulge, strong eddy currents are prominent.
WSS values were determined from the time-dependent velocity fields (Fig. right). The image displays mean WSS maps averaged over the pumping cycle. The results show distinct differences in the WSS distribution depending on the orientation of the connections.

Design of configurable prefab master models for patient-specific treatment with CPC-based bone replacement structures

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Introduction

Bone replacement structures offer the potential to build up missing bone areas in order to enable subsequent prosthetic restoration. However, additive manufacturing of CPC structures is limited in technical and economic terms due to the material behavior. The aim of the presented approach is to separate the functionalization and shaping. Thus, prefabricated CPC-prefabs, which show different density phases (porosity) as functionalization, are to be manufactured additively. Subsequently, the patient-specific shaping will be carried out by milling (CAD/CAM).

Methods

Several CPC-prefabs are developed, which differ in the mapping of the transition geometry from porous to dense phase as well as in the overall size. Therefore, categorized CT datasets of mandibular scans are analyzed and the cross-sectional contour of the bone at each tooth position is determined. Mathematical regression is used to determine a parametrically described average contour, which is used to design the prefab models. The parametric description allows the geometry to be controlled as desired depending on the prefab variants to be mapped. Furthermore, the overall dimensions of the bone of the respective category and the mathematically described curve of the mandibular arch are taken into account in the modeling.

Results

First prefab demonstrators have been additively manufactured and subjected to initial milling tests. The feasibility in principle of the intended process has thus been demonstrated. Concrete conclusions on the exact number of prefab variants required have yet to be drawn, as this is the subject of the current research work.

Conclusion

The separation in terms of time and manufacturing technology enables time and cost savings, as the additively manufactured prefabs are already available at the time of application, thus eliminating the multi-day process of curing. At the same time, the accuracy increases due to the shaping by milling as well as the robustness and repeatability of the process.

A multiaxial FLM process adapted for the manufacture of orthoses

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Introduction

Individually fitted orthoses are usually manufactured using a thermoforming process, with all manufacturers adopting their own approaches. This results in products that are not comparable or reproducible. The aims of the project 3raceIT are to establish the basis for a systematic, reproducible and automated fitting with scoliosis braces. For the manufacture of these braces, an adapted multiaxial Fused Layer Manufacturing (FLM) process is being developed with the goal of overcoming typical drawbacks of the FLM process and allowing for a completely digital health care process. This novel FLM process is also applicable for other kinds of orthoses, like leg or arm braces.

Methods

Parts manufactured with FLM typically suffer from anisotropy along the z-axis, resulting in poor mechanical properties. To compensate for this problem resulting from the layer structure, a conventional FLM architecture is extended to include rotational axes that allow material to be deposited along all load directions. The toolpaths are being generated by algorithms specifically developed for the manufacture of functionally designed braces.

Results

Mechanical tests of multiaxially manufactured test specimens show that functional and safe orthoses can be manufactured with the new method. Materials can be processed which normally cause major problems when processed using FLM.The approach solves the problems of the layer structure and allows full freedom of design. Other characteristics of the braces, such as the impairment of the body climate, can thus be improved by design.

Conclusion

Adding additive manufacturing as the final step to the digital health care process can ensure complete product reproducibility. This opens the door for long-term optimization of the braces and the whole process. Using FLM as additive manufacturing technology can ensure a cost-effective and sustainable product life cycle. The accessibility of this technology also allows on-site manufacture in the medical supply store by orthotists.

Track:
Biomaterials and Biocompatibility

Temperature-induced modulation of the electrophysiological behavior of A549 lung cancer cells

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Introduction

Cancer cells typically exhibit an altered ion channel expression and membrane potential, which plays a vital role in various cellular processes such as proliferation or apoptosis. Hence, therapeutic strategies that modulate ion channel activity or shift the membrane potential prove to be promising for cancer therapy. Since temperature significantly affects ion channel function and thus the membrane potential of cells, deviations from normal body temperature might provide a key factor in terms electrophysiological processes, potentially interfering cell proliferation and thus tumor progression. In this pilot study, we focused on a first insight on the temperature-induced modulation of A549 cells at hypo- and hyperthermal conditions.

Methods

Whole-cell currents of 14 cells under hypo-, normo- and hyperthermal conditions were measured and related to investigate the temperature-dependent electrophysiological behavior. Experiments were conducted with an automated patch clamp device, equipped with an integrated heating element. Cells were measured in whole cell configuration applying a voltage-step protocol ranging from -60 to +60 mV.

Results

Both, hypothermia and hyperthermia led to changes in the measured current and thus the reversal potential of the cells. At hyperthermia the reversal potential tends to more hyperpolarized values. Conversely at hypothermal conditions we observed mainly a lower current response and depolarization of the membrane potential.

Conclusion

Temperature changes below and above normal body temperature can affect the behavior of channels and thus the whole-cell currents and membrane potential of cells. We here could show that hypo- and hyperthermia influences the registered current response and reversal potential of A549 cells. Despite a rather small sample size and expectable cell variations, a trend regarding the temperature-dependent modulation is nevertheless evident, providing a first and important insight on how temperature might affect the cells electrophysiological behavior.

Chronic in vivo test of anti-inflammatory cochlear implants

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Introduction

Sensorineural hearing loss affects millions of people worldwide. If the auditory nerve is intact, the cochlear implant (CI) is a possible treatment. After CI implantation connective tissue growth around the electrode array. This leads to increased electrode impedances and poorer signal transduction. In this study, anti-inflammatory substances (diclofenac and immunophilin inhibitor MM284) released from polymeric CI coatings and surface patterning were investigated for their efficacy to reduce connective tissue growth.

Methods

Cochlear implants with 4 contacts were implanted in guinea pigs for 4 weeks. Animals were divided into 6 groups (control (no coating), Poly-L-lactid acid (PLLA), PLLA with diclofenac, PLLA with MM284, surface patterning and surface patterning with PLLA and diclofenac). Hearing thresholds were determined on day 0, after which the CI was implanted. Impedances were measured daily for 14 days and on days 21 and 28. On day 28, another hearing threshold determination was performed, the cochleae were harvested for histological processing.

Results

All animals survived the 4 weeks without major complications or connector loss. On day 0, impedances were initially high (7 to 10 kOhms), but then decreased on day 1. Subsequently, a continuous increase was observed at all 4 contacts in all groups. The groups treated with diclofenac and immunophilin inhibitor MM284 showed a slower impedance increase in the first 7 days compared to the control group. At day 28, impedances were nearly similar in all groups (10 to 14 kOhms). In the groups with surface patterning, contact 4 (located at the cochleostomy) had the lowest impedances in contrast to the other groups where it had the highest.

Conclusion

The results indicate that diclofenac and immunophilin inhibitor MM284 reduce connective tissue growth in the first days after CI implantation. However, based on the impedances a long-term effect was not observed.

Acknowledgements

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Ultrasound-based powering and communication for implantable medical devices

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Introduction

Ultrasound has a high potential for communication and power transfer with implantable medical devices (iMDs). In particular, ultrasound suffers less losses in tissue when compared to established methods such as inductive loading. Furthermore, when considering implant safety and data security aspects, the need for acoustic coupling between the body and an external transmitter / sensor represents a further advantage.

Methods

For active communication tasks with iMD intrinsically requiring high bandwidth, we developed a single element cMUT transducer optimized in a FEM model. Different encapsulation approaches were numerically investigated with respect to their impact on the transducer oscillation behaviour. For powering of an iMD, we developed an external module allowing generation of customized transmit sequences (up to DC = 100%; Vpp = 200V), a 1 MHz 2in1 transducer with distinct elements for powering and communication and energy harvesting and communication module (HCM) for iMDs.

Results

We demonstrated a cMUT bandwidth of 100% in our experiments and confirmed our numerical study on the encapsulation optimization with a signal drop of only 10-20% was realized after silicone encapsulation. Using our customized electronics, a power transfer of 0,1-1 mW with only 15 V transmit voltage was realized using different receive transducers. Finally, we were able to demonstrate load modulation as an approach for passive ultrasound communication with our HCM, which was used for driving and read-out of a LED/PD sensor. In our experiments, the PD current could be encoded in the amplitude with up to 10% modulation.

Conclusion

We developed an ultrasound approach for communication and powering of iMDs based on different cMUT and PZT transducers as well as customized electronics. Our FEM model allows optimization of cMUT encapsulation schemes. The proof of concept was established by powering an optical sensor and encoding the sensor readout in an acoustic signal.

Cytocompatibility of a novel biofilm repellent coating of commensal microflora for biomaterials

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Introduction

Biomaterial-associated infections by bacterial biofilms stimulate uncontrolled secretion of inflammatory cytokines, which result in tissue damage and peri-implant bone loss. With the limited ability of antibiotics to eradicate biofilms, it is necessary to develop alternative therapeutic strategies. As a novel antibiofilm therapeutic, heat-mediated adsorption of commensal microflora on biomaterials antagonized the initial bacterial adhesion and subsequent biofilm formation. A detailed characterization with mammalian cell culture assays and animal models is needed to use this effect in clinical patient care. The present study is aimed to investigate the interaction of commensal microflora-coated biomaterials with mammalian cells.

Methods

A multilayered coating of commensal microflora was established on biomaterial through the heat mediation process. Murine fibroblasts and osteoblasts at 1×105 cells per implant were cultured directly with commensal microflora-coated and un-coated biomaterials under standard cell culture conditions. After 72 hours, type I interferon (IFN-β) expression was measured by beta serum ELISA kit (pbl assay science) in cell culture supernatants from both cell lines. Cells on biomaterial surfaces were fluorescence stained with a mixture of Calcein AM and Propidium Iodide solution (1:1000 dilutions in PBS) and imaged with a confocal laser scanning microscope (CLSM) (SP-8, Leica Microsystems, Wetzlar, Germany).

Results

Both fibroblasts and osteoblasts showed compatibility with the commensal microflora-coated implants. The level of IFN-β expression in cell culture supernatants from fibroblasts or osteoblasts cultured with coated implants was slightly but not significantly higher than with uncoated implants. This low-level difference in IFN-β expression was not indicative of inflammatory reactions.

Conclusion

Murine fibroblasts and osteoblasts were compatible with novel biofilm repellent commensal microflora-coated implants. The expression of IFN-β in cell culture supernatants was moderate, suggesting that these coatings are not inflammatory. Good compatibility of coated implants with murine cells supports implant safety and is prospective for future investigation in animal models.

Long-term stability and biocompatibility of bacterial magnetosomes from Magnetospirillum gryphiswaldense

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Introduction

Bacterial magnetosomes provide a promising biomaterial for many biomedical applications. In the model organism Magnetospirillum gryphiswaldense, they consist of a cuboctahedral magnetite core that is surrounded by a biological membrane [1]. As long-term stability represents an important quality parameter, we evaluated the colloidal stability, the integrity of the magnetosome membrane, their magnetic properties as well as potential cytotoxic effects when applied to mammalian cell lines.

Methods

Magnetosomes were isolated from M. gryphiswaldense cells using magnetic separation techniques [2]. Afterwards, the particles were resuspended in 10 mM HEPES with 1 mM EDTA, pH 7.2, and stored under a nitrogen atmosphere at 4°C. Iron concentration was determined by atomic absorption spectroscopy. Physico-chemical characterization was performed by dynamic light scattering, vibrating sample magnetometry, small-angle-X-ray scattering and transmission electron microscopy. Membrane protein content and distribution was monitored by SDS-PAGE. Cell-based studies were conducted with the hypopharynx carcinoma cell line FaDu and the lung cancer cell line HCC78. The PrestoBlue cell viability assay and the SYTOX assay were used to evaluate the biocompatibility of magnetosomes with regard to concentration and duration of treatment.

Results

Over a period of one year, aliquots of purified magnetosomes were monthly analysed. The size distribution, morphology and colloidal stability remained constant (overall particle diameter: month 1: 40.1 ± 5.7 nm; month 12: 39.6 ± 5.1 nm; zeta-potential: month 1: -35.8 ± 3.4 mV; month 12: -35.7 ± 3.7 mV). The same held true for the protein composition of the membrane. Magnetosomes exhibited a concentration-dependent effect on the viability of the investigated cell lines, which was reproducible over the investigation period.

Conclusion

Our investigations demonstrate that magnetosomes can be safely stored for at least one year as an aqueous suspension without quality deficits.

References

[1] Uebe R., Schüler D. Nat. Rev. Microbiol. 2016, 14, 621
[2] Rosenfeldt S., et al. Acta Biomater. 2021, 120, 293

The influence of PEGDA's molecular weight on its mechanical properties in the context of biomedical applications

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Introduction

Hydrogels are 3D polymeric networks, which exhibit properties such as softness, viscoelasticity and their ability to absorb large amounts of water. These characteristics make them exceptionally suitable in biomedicine as e.g. tissue scaffolds, drug delivery systems, wound dressings or contact lenses. One of these hydrogels is the biocompatible, hydrophilic and photopolymerizable poly(ethyleneglycol) diacrylate (PEGDA). It is used in different biomedical applications due to its tunable mechanical characteristics. In our study, the mechanical properties of different PEGDA hydrogel compositions with variyng molecular masses and contents of water/methanol, were investigated.

Methods

Different compositions containing 20 m%, 30 m% or 40 m% of PEGDA4K (4,000 g/mol), PEGDA10K (10,000 g/mol) or PEGDA20K (20,000 g/mol) in ultrapure water/methanol (1:2) were produced. Dumbbell-shaped samples were prepared in molds via photopolymerization in a UV chamber. Lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) was used as photoinitiator (0.5% w/w). The mechanical testing was performed using a uniaxial testing system.

Results

The obtained results showed averagely 78% higher tensile strength (σmax) values for 30 m% and 40 m% samples in comparison with 20 m% samples for all of the tested polymers. PEGDA20K 30 m% samples showed the highest σmax among all of the samples with 12.8 MPa. All of the PEGDA20K samples exhibited the highest elongation at break (εB) values (up to 958%), whereas the lowest values were found for PEGDA4K (up to 105%). The obtained stress-strain curves for most of the samples were typical for deformable, amorphous polymers with a deformation upon reaching a critical stress point.

Conclusion

The PEGDA materials showed variable mechanical characteristics according to changing molecular mass or polymer concentration. These promising results showed that it should be possible to compose scaffolds with desired mechanical stability according to the needed application.

Optimizing barium titanate nanocomposite bone scaffolds for biomineralization using time-lapsed microstructural imaging

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Introduction

Barium titanate nanocomposites with electrical stimulation potential have attracted considerable interest in bone tissue engineering for promoting osteogenesis. However, the micro-computed tomography (micro-CT) analysis of mineral formation is challenged by the barium titanate's high attenuation coefficient. Here, we present an improved image processing methodology combined with time-lapsed micro-CT imaging to facilitate the optimization of such scaffolds.

Methods

Micro-CT imaging and registration was combined with smart thresholding during image processing to detect mineralized collagenous extracellular matrix (ECM) formation in polydopamine functionalized nanocomposites containing 3-27 vol% barium titanate. This method was applied to high-resolution end-point scans of static human mesenchymal stem cell (hMSC)-laden scaffolds and time-lapsed scans obtained from dynamic cultures in compression bioreactors. Additionally, histology and Raman spectroscopy were used to validate the image analysis and identify cell-mediated mineralized ECM unambiguously.

Results

All compositions showed well-connected ECM and birefringent matured collagen after seven weeks of static hMSC cultures. The processed micro-CT scans showed overall modest differences in ECM mineralization between the groups. Nevertheless, the improved method indicated that a volume fraction of 9-21 vol% barium titanate facilitated the formation of dense mineral clusters in the pores even in the absence of mechanical stimuli, further corroborated by Raman spectroscopy. In dynamic compression bioreactors, scaffolds containing 9 vol% barium titanate were the best nanocomposite composition, resulting in a significant twofold increased maturation rate under dynamic conditions. On the other hand, barium titanate content of $\geq$15 vol% did not improve mineralization. At 27 vol%, the biomineralization of the collagenous ECM was even impeded in the nanocomposite scaffolds, as evidenced by histology stainings.

Conclusion

Our approach enables time-lapsed quantitative assessment of high X-ray absorbing nanocomposite scaffolds for biomineralization under dynamic compression. Thus, the presented approach facilitates the optimization of such mechanically responsive scaffolds considering potential future applications in load-bearing bones.

Analysis of the Flow Properties of a Transparent Two-Phase Blood Model Fluid

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Introduction

The two phases of blood have a great influence on the flow, that single phase models like water-glycerol-mixtures cannot represent. Therefore, it is necessary that the model fluid represents both phases of blood: the plasma and the cells. The objective of this work is the analysis of the flow properties of a novel two-phase blood model fluid and the comparison with blood.

Methods

Transparent alginate microspheres in a defined size were used as a model of red blood cells. A water-calcium-chloride mixture was used as a model fluid for plasma. Different flow properties and the deformation of the alginate microspheres in water-calcium-chloride were tested in microchannels with specific geometries and compared to blood flow properties.

Results

Using a developed production and sorting system, alginate microspheres of a defined size of 8 µm ±2µm could be obtained in large quantities. Compared to a water-glycerol mixture, the proposed blood model fluid enabled the visualization of the strong influence of the two phases on the flow. Because of their transparency, it was possible to visualize the flow field at several layers in the fluid. A good agreement with the flow properties of blood could be observed. The viscosity of the blood model is in the same order of magnitude as blood, the microspheres are deformable, and the blood model shows a shear thinning effect.

Conclusion

The proposed blood model fluid showed promising results. The flow properties are comparable to those of blood and a good visualization capability in experimental setups could be shown. In the long term, the model can be used for experiments on flow analysis and optimization in blood pumps or as a validation model for CFD to calculate multiphase flows.

Susceptibility artifacts evaluation for non-metallic biopsy needles in a biological-engineered 3D tumor model

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Abstract

Nowadays, needle artifacts are an essential restriction for MRI-guided interventions, as they influence the visually perceived needle size and needle destination. Standard MRI needles made of Nickel-Titanium (NiTi) alloys still produce massive artifacts in MRI due to materials' interactions with the magnetic environment. The use of non-metallic materials can reduce these artifacts.

we propose a non-metallic concept of a coaxial needle design concept with a fiber-enforced inner core and an outer polymeric hollow sheet. This work aims to evaluate the artifact performance of the proposed needles in a custom-made three dimensional (3D) tumor model with a relevant size and thickness for medical interventions under MRI guidance using a 3T field strength with a T1-weighted gradient-echo sequence

Three coaxial MR-compatible needles were inserted in the custom-made 3D tissue phantom, one standard needle from NiTi, and two proposed non-metallic needles. Artifact's width and length were measured for each needle

the non-metallic needles showed significantly lower artifacts than the standard NiTi needle inside the 3D tumor model

A time-resolved fibrosis model - in vitro assessment of antifibrotic implant coatings

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Introduction

Wound healing after implant surgery represents a spontaneous repair process that, when disturbed, can lead to a pathological situation known as fibrosis, characterized by excessive proliferation, increased extracellular matrix deposition, and scarring of the tissue. Tissue-specific cell culture models simulating (patho-)physiological cell responses are valuable research tools in the field of fibrosis, among others. In such in vitro systems, endpoint measurements are typically used to assess cell viability and/or proliferation, which are costly and only provide a singel snapshot of the sample at the end of the experiment. Therefore, we aimed to evolve the fibrotic disease in vitro model established by Stahnke et al.

Methods

In this study, we chose a time-resolved, non-invasive approach based on cell impedance measurements and bright-field microscopy that allows continuous monitoring of the cells. Such measurements can be directly conducted using the xCELLigence RTCA eSight system (Agilent). This system was used to characterize the cellular response of the fibrosarcoma cell line HT-1080 and primary fibroblasts isolated from the Tenon's capsule of human donors (hTFs) to TGF-β1, a key cytokine involved in the pathogenesis of fibrosis.

Results

The data shows that compared to hTFs the response of HT-1080 cells to TGF-β1 is less pronounced and only detectable within a narrow time frame. In contrast, the increased proliferation of hTFs is detectable even at low TGF-β1 concentrations over a time course of 24 h. In both cases, cell morphology is not affected irrespectively from cytokine concentration.

Conclusion

We conclude that if cell lines have to be used due to the lack of hTFs, further cell types need to be tested with respect to their ability to respond to TGF-β1 stimulation. If possible, primary cells should always be used for analyses, as their behaviour clearly reflects the in vivo situation more closely than that of cell lines.

Thermal annealing of injection molded VHMW PLLA

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Introduction

Thermal history drastically affects the properties of polymeric materials, such as tensile strength and degradation behavior. In this study, DSC experiments were used to elaborate an annealing protocol for injection molded very high molecular weight (VHMW) PLLA. The material obtained from injection molding process was found to be highly amorphous and not in thermodynamic equilibrium.

Methods

To adjust crystallinity of very high molecular weight (VMHW) PLLA, samples with two different molecular masses, (PLLA L210, M_w = 320.000 g/mol and PLLA L214, M_w = 700.000 g/mol), have been thermally treated using a DSC device. Initial experiments were carried out at 80 °C using different annealing times (t_a = 30 - 180 min). Following this, the elaborated times were applied to different annealing temperatures (T_a = 65 - 155 °C). The effect of the annealing on thermal material properties has been examined using coupled DSC measurements. The annealing protocol was subsequently transferred to a manual annealing of large sample geometries followed by dynamic mechanical analysis.

Results

In comparison to the unprocessed polymer granules, injection molded samples were highly amorphous, giving no distinct cold crystallization (T_c) peaks, but broad cold crystallization signals and strong enthalpy relaxation. Thermal treatment to 85 °C for 60 - 90 min was sufficient to stabilize the polymer and increase the crystallinity up to 50 % whereas annealing at this temperature did not result in any signs of thermal decomposition. Manual annealing of DMA specimens using a heating plate gave similar outcome regarding the thermal properties compared to annealing of microsamples.

Conclusion

Thermal manufacturing of PLLA semi-finished products requires dedicated thermal treatment to adjust thermal properties and to stabilize the material. Whereas PLLA L210 requires 90 min treatment at T_a = 85 °C, 60 min of annealing at T_a = 85 °C are sufficient for PLLA L214.

Characterization of Ball-milled Poly(N-isopropylacrylamide) Nanogels

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Introduction

The fabrication, characterization and application of micro- and nanogels is a highly active area of research due to the fact that micro- and nano gels provide benefits like high surface-area-to-volume ratio and easy combination within other biomaterial systems. Poly(N-isopropylacrylamide) (PNIPAM) based micro- and nanogels are some of the most commonly studied due to the unique thermo-responsive behavior of PNIPAM. However, standard emulsion polymerization methods used for PNIPAM micro- and nanogels lead to inhomogeneous crosslinking within microgels. In this work, we investigate ball milling as an alternative method for creating PNIPAM nanogels and confirm that the resulting gels maintain critical temperature sensitive properties.

Methods

Bulk PNIPAM gel was produced by polymerization of N-isopropylacrylamide with the crosslinker N,N'-Methylenebisacrylamide. The bulk gel was processed into PNIPAM nanogels via ball milling. The hydrated nanogels were characterized based on hydrodynamic diameter and zeta potential at temperatures from 25 to 37°C.

Results

The average hydrodynamic diameters of the PNIPAM nanogels decreased with increasing temperature (436.9 $\pm$ 40 nm at 25°C to 218.2 $\pm$ 6 nm at 37°C) in a manner similar to the change in size seen in bulk PNIPAM hydrogels. Additionally, the zeta potential became significantly more negative at higher temperatures (-0.60 $\pm$ 0.6 mV at 25°C to -13.7$\pm$ 0.3 nM at 37°C).

Conclusion

The investigated PNIPAM nanogels showed the expected thermo-responsive behavior. The hydrodynamic diameter and zeta potential changed as expected with temperature, showing distinct transitions of the measured properties near the LCST of bulk PNIPAM. These results demonstrated that the ball milling process did not impact the thermo-responsiveness of the PNIPAM and that ball milling is a quick and simple method for creating PNIPAM nanogels.

Fiber orientation on 3D structured collectors for electrospinning

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Introduction

Electrospinning, a standard technique for producing nonwoven fabrics, is widely used in the biomedical field. Due to local electric fields, fiber deposition is influenced by 3D surface structure of metallic collectors. On complexly shaped structures deposition may occur in an unexpected way. Investigations on well-defined structures permit a more detailed insight. Design recommendations for the microstructuring of collectors can be derived to achieve targeted control of the local fiber orientation and layer thickness.

Methods

Metallic blocks with round, slit and square holes of different size and depth were machined, and electrospun with a thin layer of polymer fibers. The fiber arrangement of the layer was investigated by optical microscopy and scanning electron microscopy.

Results

Findings showed less fiber deposition on round holes and well-bridged aligned fibers over gaps, which were less than four times wide as deep. At upper margins of round holes fibers deposited predominantly in circumferential orientation. The edge steps of shallow holes were bridged with a slope of 45 degree by straight aligned fibers.

Conclusion

Experimental findings confirmed the theoretical predictions, and hence can help to design specific collector structures to predict and achieve desired local fiber orientation as well as layer thickness. High potential is seen in manufacturing of fabrics or scaffolds for specific biomedical applications.

PLLA crystallization kinetics in dependence of molecular weight

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Abstract

Poly(L-lactide) is one of the most widely used materials in medical engineering, such as surgical sutures, bone fixation devices, and controlled drug delivery systems. PLLA exhibits complex polymorphism, which is controlled by the specific crystallization path or thermomechanical history imparted during processing. The α'-α-crystal polymorphism considerable affects the material properties, including thermal properties, hydrolytic degradation and mechanical performance. Molecular weight is also one of the key variables governing the crystallization kinetics and polymorphism of polymers. So, it is quite important to control the polymorphism for optimizing the properties and production process of polymers.
The effect of molecular weight M_w on the polymorphous crystallization and melting behavior of PLLA (L206, L210 and L214) were systemically studied by DSC. Melting and reorganization of conformationally disordered crystals (α'-phase) of PLLA are analyzed with respect to the cooling rate q_c in a range between about 4 and 50 K/min and the heating rate q_h in a range between about 5 and 200 K/min.
It was shown that the α'- to α-crystalline phase transition prior to the dominant melting depends on cooling rate q_c and M_w. Unlike very high-M_w PLLA L214, for low-M_w PLLA L206 crystallized at high q_c, the α'-form crystals only partially transformed into the α-modification, and certain amounts of α'-form crystals melted directly without α'- to α-transition during the heating process. With increasing q_c, the melting of PLLA L210 changed from phase-transition- and -melting mechanism to the common melt-recrystallization mechanism.
It was found that with increasing M_w α'-α crystal were formed at lower cooling rate. Furthermore, the reorganization of α'-crystals into stable α-crystals could be inhibited by fast heating (q_h > 150 K/min). The effects of M_w on the polymorphism were quite important to interpret the thermal behavior of PLLA as well as for controlling the physical properties of PLLA by optimizing the crystallization process.

Biological test methods for stents: cellular responses to microstructured biomaterials

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Introduction

One of the greatest challenges in the development of novel implants is to find materials that optimally interact with the tissue and support the function of the implant. Especially considering the fact that biomaterials are used in multiple applications in modern implants, a better understanding of the physiology of the tissue in contact with the material becomes more and more important. However, in most cases, immortalized cell lines instead of tissue-specific primary cells are used to study the biocompatibility of implant materials.

Methods

Within the current study, fs-laser-based manufacturing technologies were used to assess the cellular responses of an immortalized cell line (L929 mouse fibroblasts) and primary cells (porcine Tenon fibroblasts) to microstructured implant resembeling structures. Cells were seeded on material samples resembeling different stent designs and were allowed to grow for two days under standard conditions. After incubation the cell metabolism was elvaluated using cytotoxicity assays, followed by fixation and staining for fluorecense microscopy.

Results

We could observe, that the mouse fibroblast cell line showed a higher metabolic activity in general and also a higher ability to adhere to the tested material samples. The primary porcine fibroblasts however, displayed a generally lower metabolic activity and only very few cells were able to adhere to the material samples. We discuss our observations with respect to the use of cell lines for biocompatibility testing of medical devices.

Conclusion

Our results show that primary cells are more sensitive to their environment and the biomaterials which they might come into contact with. Therefore, it has to be kept in mind that cell lines do not behave like primary cells and can only provide an indication of the behaviour of primary cells. In order to strengthen findings obtained with cell lines, key control experiments using specific primary cells should always be performed.

Endothelialization of 3D-printed polymers for the development of customizable blood contacting biomedical device components

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Introduction

With 3D-printing, construction of implantable biomedical device components, with geometries individually adjustable to patient's anatomy, are within reach. However, current polymers cannot be used for long-term application, since their inevitable contact to the circulating blood results in surface depositions of pro-coagulative proteins, thrombocytes adhesion and life-threatening thrombus formation. Covering these artificial surfaces with an endothelial cell monolayer (EML) is an efficient strategy to inter alia avoid thrombus formation. Therefore, we assessed selected 3D-printable resins for facilitating endothelial cell (EC) adhesion and their resistance to physiologic flow conditions.

Methods

Disk shaped samples were printed from resins DentalClear(DC) and BiothoughMF90(BT90) using the HalotOne 3D-printer and from Med610 using the Objet350-Connex3. Eluate and contact cytotoxicity tests(ISO10993) were carried out from samples after one, two or three washing cycles in a sonicator, using WST-8 assay with human ECs. For contact-, adhesion- and viability tests, half of the samples were additionally coated with fibronectin(FN) to support EC attachment. ECs were visualized by calcein staining. In parallel-plate flow chambers, CellTracker-stained EMLs on FN-coated resins were exposed 24h to physiological flow conditions, cell detachment was quantified by fluorescence-microscopy analysis before and after flow.

Results

Eluate tests indicated that cytotoxic substances leached from all printed samples after one washing step, which could sufficiently be depleted already after second washing. When directly seeded and statically cultivated on twice washed samples no loss in EC-numbers was detected on any sample after 24h, but unaffected EC proliferation after 72h was only detected on FN-coated DC and BT90. Confluent areas with viable cells were found more consistently on all samples after FN-coating. After flow exposure no sample showed significant EC detachment.

Conclusion

3D-printed, FN-coated DC and BT90 resins were non-cytotoxic after two washing cycles and allowed the establishment of a flow-resilient EML, demonstrating their eligibility for printing individualized endothelialized blood-contacting devices.

Pre-Endothelialized Spider Silk-Reinforced Fibrin Patches for Cardio-Vascular Reconstruction

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Introduction

Patches made from synthetic polymers or glutaraldehyde-fixed xenogeneic pericardium are frequently used for cardio-vascular reconstruction. Although initially well-tolerated, foreign materials lack regenerative potential as they are prone to calcification and chronic rejection, entailing the need for redo-operations. In order to provide a fully bio- and hemo-compatible patch with sufficient mechanical strength and regenerative properties for long-term tolerance, we assessed spider silk-reinforced, condensed fibrin patches with respect to their endothelialization capacity for following surgical reconstruction.

Methods

Condensed fibrin patches were manufactured in vitro with or without enclosed spider-silk (nephila edulis). Eluate and contact cytotoxicity (ISO10993) were determined by metabolic activity-assay (WST8) using porcine endothelial cells (ECs) that comply for following testing in prospective ex vivo and in vivo pig models. After calcein-staining, EC-adhesion and viability assessment were performed using fluorescence microscopy. qRT-PCR of seeded ECs with or without deliberate TNFa stimulation was carried out to detect patch-induced activation of pro-inflammatory/pro-thrombogenic genes. For assessing the feasibility in vascular reconstruction, celltracker™-labelled endothelialized spider-silk patches were sutured on coronary arteries from hypothermically stored porcine hearts and EC retention was assessed by fluorescence microscopy before and after the procedure.

Results

ECs formed a viable and confluent monolayer on all fibrin patches, indicating no cell-detrimental effects from the condensed fibrin and the enclosed spider silk. Also, no patch-induced differences in expression levels of pro-inflammatory or pro-thrombogenic genes were found among seeded EC-monolayers, which also still responded physiologically to TNFa stimulation. Pre-endothelialized spider-silk patches could be successfully sutured on the arteries, and fluorescence microscopy analysis attested only negligible cell detachment after this procedure.

Conclusion

Spider silk-reinforced patches from condensed fibrin promoted the formation of a viable, confluent and non-inflammatory/non-thrombogenic EC-monolayer, which was retained after vascular reconstruction. These positive results justify now assessing long-term efficiency and under blood flow in ex vivo or in vivo models.

Influence of crosslinking on the drug release of PLLA/gelatin nonwovens

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Introduction

In order to mimic the ECM, the use of electrospun fibers based on synthetic and natural polymers, for mechanical stability and cell-polymer interaction is a promising approach, respectively. Both the medical grade poly-l-lactide (PLLA) and the natural gelatin are well established. However, to obtain a stabilized structured PLLA/gelatin blend, crosslinking of the gelatins is required. In this study, the influence of the post proceeded crosslinking via Glutaraldehyde (GTA) vapor and solution on the morphological, physicochemical properties of the blend and on the in vitro dexamethasone release was investigated.

Methods

PLLA/DMS and untreated PLLA/gelatine/DMS nonwovens were fabricated from polymer solution by needle electrospinning (Contipro (Dolní Dobrouč, Czech Republic) 4SPIN C4S LAB2). The model drug, DMS (20 wt%), was dissolved in TFE and added immediately prior to the electrospinning process. The air-dried PLLA/gelatine/DMS nonwovens were crosslinked by GTA using vapour and solution (25 %). All investigated samples were characterized and discussed in view of surface morphology, fiber diameter (SEM), surface hydrophilicity (contact angle) and the in vitro drug release.

Results

The addition of gelatin decreased the fiber diameter and increased the surface hydrophilicity, unaffecting by the crosslinking process. The in vitro release of DMS was decisively changed by the addition of gelatin and the subsequent crosslinking processes. For all modified samples, a very rapid initial burst release of DMS was detected. Moreover less DMS were released for both crosslinked nonwovens than for the untreated PLLA/gelatin/DMS system.

Conclusion

The results indicate that the addition and crosslinking of gelatin influenced crucially the in vitro DMS release from PLLA/gelatin blends and open a broad range of possibilities for biomedical application such as tumor therapy.

In vitro biostability of cardiac pacemaker lead insulations under static mechanical loading

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Introduction

Patients with cardiac arrhythmias are currently treated with conventional transvenous rhythm implants. Complications are frequently associated with intracardiac implanted leads primary insulated by silicone and polyurethane. However, experiences show that polyurethanes in particular are susceptible to various degradation mechanisms including hydrolysis, environmental stress cracking (ESC) and metal ion induced oxidation (MIO).

Methods

In vivo, pacemaker leads are exposed to a complex thermal, chemical, mechanical and biological loading. The current study focusses on in vitro analyses to assess the biostability of Pellethane 2363 55D and the silicone MED 4765 as cardiac pacemaker lead insulations. Degradation processes were simulated in vitro in a load-free state and under static mechanical loading by subjecting a coaxial lead design to bending radii from 3 mm to 19 mm. Physiological environmental conditions were mimicked using a physiological saline solution and a tempered oxidative solution. Surface morphological and thermal analyses were performed before and after in vitro testing by means of scanning electron microscopy (SEM) and differential scanning calorimetry.

Results

Melting temperatures of silicones of 40°C were measured, before and after in vitro testing, respectively. Pellethane insulation layers had two endothermal melting regions at 100°C and 170°C before and a third melting region at 45°C after in vitro testing. The additional melting peak may indicate a change of thermal material properties due to degradation. SEM images showed degradation phenomena similar to in vivo studies, varying in severity and depending on the bending radius.

Conclusion

Thus, the relevance of mechanical loading for in vitro replication of clinically relevant lead insulation degradation was demonstrated.

Water-supported femtosecond laser ablation of Nitinol for cardiovascular stents

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Introduction

Nitinol, an alloy of nickel and titanium, has become one of the most outstanding materials for biomedical applications. Combining distinct features such as the shape-memory effect and superelasticity with biocompatibility enables fascinating applications in cardiology, orthopedics, and orthodontics. However, the mechanical properties are coupled to thermosensitive crystal characteristics, and thus heat exposure, particularly during material processing, is critical. Here we investigate the femtosecond laser ablation of Nitinol supported by a water flow inside the processed tube.

Methods

The samples are prepared using a commercial Nitinol tube having a wall thickness of 220 µm. The laser ablation is performed by a femtosecond laser embedded into a commercial 4-axes CNC system, operating at a repetition rate of 500 kHz and a pulse duration of 300 fs and 10 ps. The CNC system is equipped with an water circuit to provide water flushing of the tube during processing. The analysis is performed using a field emission scanning electron microscope.

Results

Radial grooves are structured into a tube using different pulse energies and pulse durations. For high pulse energies, the water, which flows through the Nitinol tube, acts as a beam block and prevents the tube's backside from being annealed. When analyzing the geometrical parameter of the grooves, fluence-dependent and pulse duration-dependent deviations become apparent for high pulse energies when using water flushing. Additionally, an improvement of the cutting edges is observed.

Conclusion

Although an ultrashort pulse duration already minimizes the heat generation during ablation, laser absorption by the water inside the tubes enables processing with higher pulse energies. Furthermore, the obtained results can lead to improved control of heat transfer during laser ablation and thus may build the foundation of new fabrications techniques. This opens up new possibilities in the design and implementation of thermally sensitive biomedical devices with micrometer dimensions.

A constitutive model of the porcine cornea based on a depth- and orientation-dependant mechanical characterization

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Introduction

Understanding and characterising the biomechanics of the cornea is critical to the development of ophthalmic treatments and surgical procedures. Therefore, this study presents mechanical testing of porcine corneal stroma at various depths and orientations and its numerical characterization using the Gasser, Holzapfel, and Ogden (HGO) hyperelastic material model.

Methods

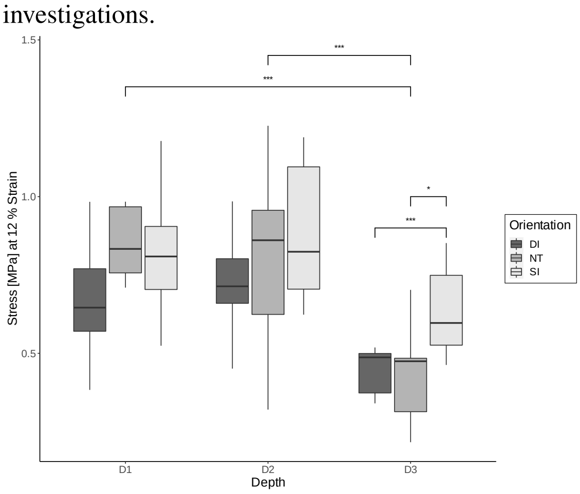
Experimental: Freshly obtained porcine corneas were cut into strips of 8 mm x 3.5 mm x 0.15 mm using a femtosecond laser in the nasal-temporal, superior -inferior and diagonal directions. The samples (n=86) were taken at 100 µm, 350 µm and 600 µm depth and tested by uniaxial extension. The average cornea thickness was 910 µm. The tissue was pre-stretched with a force of 10mN and pre-conditioned with 6 cycles of 13 % strain. The last cycle of force displacement data was recorded for analysis.
Computational: The geometry of the corneal strip and the experimental loading were replicated in ABAQUS 2021. The strips were modelled with collagen fibers running in a circular orientation. The material behaviour was described using the anisotropic model proposed by HGO. A Bayesian optimization process was used to identify the material parameters that best fit the experimental data.

Results

The results showed that the corneal mechanical properties in the anterior half of the cornea remained independent of orientation, but the material softened in the posterior layer. The numerical model fit lay well within the experimental results.

Conclusion

This work characterizes porcine stroma as transversely isotropic and proposes a numerical model with a circular orientation of collagen fibers, compatible with X-ray scattering data. The parameters obtained for the model were able to reproduce the published inflation experiments, indicating its validity and thus providing a surrogate to experimental investigations.



Surface analysis of different O2-activated polyurethane-co-silicones using XPS

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Introduction

Polycarbonateurethane co-silicone (PCU-Sil) are gaining increasing interest in biomedical application, such as drug delivery systems, coatings and combination products, due to their adjustable mechanical properties. They can be easily processed using a wide range of methods. The possible lack of biocompatibility can be solved by surface modifications, such as coupling drugs, proteins, antibodies or polymer layers, which extends the range of biomedical applications. To generate additional coupling, the first step would be the generation of functional groups on the polymer surface using surface activations, such as plasma activation. In this context, the assignment of the functional groups is important, which can be done by XPS measurements.

Methods

For this study we used foils with two kind of PCU-Sil differing in hardness. Than a cylindrical dipping block was immersed several times in the polymer solution (> 20), with drying time of 10 min in between. After activation with cold O2 plasma, we investigated the modification on the surface by XPS. After 24h we repeated the analysis.

Results

In summary, it was possible to investigate the surface modifications caused by O_2 plasma activation by X-ray photoelectron spectroscopy (XPS). Compared to the untreated sample, significantly more oxygen was covalently bound, which can be attributed to different functional groups. It was surprising that the generated groups were differently stable and also different groups were generated or rearranged over time.

Conclusion

Using the example of foils made of different PCU-Sil, the changes caused by O_2 plasma modification using XPS could be investigated. It allows for the optimisation of the plasma activation towards a more specific generation of functional groups, and it can be used to track their stability over time.

Towards 3D bioprinting of a hypoxia-gradient for generating a heterogenous cartilage scaffold

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Introduction

Heterogenous, patient-specific tailored cartilage scaffolds are needed to repair large nasal septum perforations. Recent work has shown that the phenotype of chondrocytes can be controlled by regulating their oxygen concentration. The inclusion of oxygen gradients in scaffolds offers a strategy to control chondrocytes phenotype by activating specific pathways that lead to the formation of hyaline or hypertrophic cartilage. This study aimed to investigate hypoxia-related activation of differentiation pathways in nasal chondrocytes (NCs) to further translate this knowledge into fabricating a biomimetic scaffold that mimics cartilage zonal organization.

Methods

Primary human NCs were isolated from the nasal septum cartilage of patients undergoing septoplasty. Cells were cultured either in 2D or 3D aggregates (i.e., pellets) under normoxic conditions (21%-O2), hypoxic conditions (2%-O2), or in a normoxic environment supplemented with hypoxia inducing compound (21%-O2 + 1mM DMOG). The effect of oxygen tension on chondrogenesis was determined with histological assessments of matrix deposition (by Alcian Blue, AB, or Safranin-O) and evaluated gene expression through RT-qPCR.

Results

Cells cultured in hypoxia and those conditioned with DMOG maintained their native spheroidal shape and were positive for AB stainings. Conversely, NCs cultured in normoxic conditions showed an elongated-fibroblastic morphology and limited amount of AB positive matrix. Moreover, hypoxia conditioned NCs exhibited statistically significant higher gene expression of the hypoxia marker PHD3 and chondrogenic markers COL2A1, ACAN, and SOX9, and lower expression of the hypertrophic cartilage markers MMP13, RUNX2, and ALPL. Similar results were obtained in 3D pellet cultures.

Conclusion

Hypoxia positively affected NCs chondrogenic potential and supported the generation of hyaline-like cartilage tissues. Future activities will be carried out using 3D bioprinting to generate scaffolds with a controlled topology resulting in scaffold-intrinsic oxygen gradients to guide the formation of different cartilage phenotypes.

XPS-Analysis of solvent residues in different polymeric biomaterials

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Introduction

Polymers are widely used in biomedical engineering and implant development. Therefore, solvent based processes may be performed such as solvent-casting or electrospinning. As fabrication of implants makes use of potentially hazardous or toxic solvents, they have to be extracted from the final medical device. For analyses of residual solvents different methods can be used e.g. gas chromatography. Here first results are presented for the use of X-ray photoelectron spectroscopy (XPS) to yield elemental as well as spatial information on residual solvents in polymeric materials.

Methods

PLLA as biodegradable electrospun polymer, solvent-cast TPC-ET as biostable polymer and a solvent cast PLLA-iron composite as example of a polymer metal composite were analysed via XPS. XPS-analysis was performed with photons of 1486.6 eV from an Al Ka monochromatic source (Thermo K-Alpha, Thermo Scientific, Inc., UK). Samples were etched with an Ar+ ion-beam, Cl2p- (Chloroform, for all specimen) and F1s-spectra (trifluoroethanol, for TPC-ET and ePLLA,), were obtained by high resolution scans.

Results

Survey spectra of the polymer metal composite PLLA-iron, of the TPC-ET and the electrospun PLLA showed only oxygen and carbon signals corresponding to the PLLA. After etching high resolution scans of PLLA-iron revealed the presence of iron and chlorine species.
High resolution scans of the TPC-ET film and electrospun PLLA nonwoven showed signals that indicate residual chloroform and trifluoroethanol contents.

Conclusion

It was possible to determine residual solvents in all tested polymers processed from different polymeric solutions.
As discrimination between polymer and solvent was made possible by specific elements, XPS measurements may be a suitable tool to identify even small amounts of solvent. Identification of chloroform and trifluoroethanol in the TPC-ET film came as a surprise, as it already underwent further washing steps. Therefore XPS analyses will help to optimize polymer processing in order to remove residual solvents.

Experimental Setup for Controlled Freezing/Thawing of Tissue Samples for Evaluation of Tissue Properties and Relevant Factors for Cell Death during Cryoablation

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Introduction

Cryoablation is a minimally invasive procedure, in which tumors or arrhythmogenic cardiac tissues are ablated by freezing. Several factors of the applied protocol (minimal temperatures, cooling/warming rates, holding times, freeze-thaw-cycles, etc.) influence the ablation outcome. Furthermore, intra-operative measurements like cryoimpedance and activation propagation for cardiac tissue depend on cell survival and ice formation. In this work, an experimental setup is presented that allows for investigating cryoablation scenarios by controlled freezing/thawing of multiple samples in parallel.

Methods

The experimental setup consists of two Peltier elements placed on a heat sink together with a 3D printed thermal insulation container, the walls and lid of which are filled with foam material. A thin aluminum container was placed on top of the Peltier elements within the insulation container for a nearly homogeneous temperature distribution. The samples are placed inside self-made dishes consisting of laser-cut plastic walls fixed on thin glass bases to allow for low thermal resistances and subsequent analysis by microscope. The sample dishes and thermocouples are fixed by 3D printed mounts. A temperature controller with a Pt1000 thermistor attached to the aluminum container regulates defined target temperatures. The heat sink is placed in a container with ice water that is moved using a circulating pump.

Results

First experiments with the setup showed that temperatures lower than -30°C can be obtained in the samples. Results of experiments using saline, wet sponge cloths and cancer cell layers will be presented. Temperature deviations between and within samples during the same experiment were caused by different freezing onset temperatures and concentration differences caused by inhomogeneous freezing.

Conclusion

Various cryoablation scenarios can be performed using the presented experimental setup. Further investigations considering living cells are planned in the near future. Latent heat release and resulting temperature deviations between and within samples pose challenging tasks for future developments.

Bioengineering of Tubes, Rings and Panels for Guided Bone and Vascular Regeneration.

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Abstract

Scaffolds prepared by electrospinning of poly-(D,L)-lactide (PDLLA) generally have a two-dimensional (2D) geometry (non-woven mats or fleeces). In aqueous in vitro and in vivo applications these 2D mats lose their geometry by shrinking and scrolling. Three-dimensional (3D) scaffolds, such as tubes for vascular tissue engineering, tube-derived ring shaped scaffolds and sandwich panels (combination of rings and mats) offer a higher stability. Electrospinning of tubes with I.D. < 4 mm is a formidable task, since the deposited tubes adhere irreversibly, being destroyed by peeling from the mandrel.
The instrumentation consists of a high rigidity tube mandrel (diameter 3 mm x 10 cm length) rotated by constant torque motor at wobble-free 10-100 rpm with simultaneous back and forth movement. Two DC high voltage power supplies with respective positive and negative polarity provided the anodes (feed needle and copper wire lens) 14 cm above the mandrel with +20 KV. The mandrel and an auxillary plate (ca. 144 cm2) underneath formed the cathodes with -5 kV via a sliding connector. The mandrel was wrapped with a thin, siliconized cellulose sleeve, allowing for a complete tube retrieval. The electrospun scaffolds were bioactivated with adsorbates of 125I-rhBMP-2 as previously described.
Whipping instabilities were reduced by the "copper wire lens" and the novel "removable mandrel sleeves" allowed an intact retrieval of the tubes. Thus 2D fleeces (skins, 144 mm2) and 3D scaffolds (tubes and rings with an I.D. 3.5 mm) were synthesized by PDLLA electrospinning. Sandwich PDLLA ring panels can be formed from the skins and rings which are stabilized against bending stresses, buckling and shear forces. The mean PDLLA fiber diameter of the fleeces was ~93 nm and that of the tubes ~1.1µm. The fleeces and rings were bioactivated by adsorption of 125I-rhBMP-2 in amounts of 0.33-0.40 µg/g and 1.3-2.6 µg/g respectively. (Supported by DFG JE 84/15-3)

Chemical characterization of plasma polymerized allylamine coatings with addition of ammonia and oxygen by XPS

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Introduction

In addition to wet- and plasma chemical surface activation, the deposition of stable organic coatings by plasma enhanced chemical vapor deposition (PECVD) using reactive monomers, such as aminosilanes and allylamine, is often described to generate functional groups at biomaterial surfaces. PECVD can also be used to gentle modify the surface of complex structured biomaterials, such as nonwovens. Focus of this work was studying the potential of allylamine plasma coatings regarding the chemical composition, particularly the primary amino groups, for subsequent covalent coupling modifications.

Methods

To alter the chemical surface gas mixtures of amino groups containing pure allylamine, allylamine with ammonia and allylamine with oxygen were used for generating coatings on aluminum substrates by PECVD. Chemical surface composition was determined via X-ray photoelectron spectroscopy (XPS).

Results

Results reveal no higher primary amino content for plasma polymer with added ammonia. The addition of oxygen resulted in further oxidation of amino groups yielding in more signals for the N1s spectrum. The pure allylamine plasma without additional gases was the most suitable to generate a thin coating with the most free amino groups.

Conclusion

Therefore, pure allylamine appears suitable for PECVD coatings of nonwovens and to generate desired superficial amino groups for subsequent covalent crosslinking, e.g. to adjust mechanical properties.

Design and fabrication of a mechanically strain-stiffening structure for soft tissue engineering using 3D printing

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Introduction

Soft biological tissues like tendons, skin or arteries and single cells show a strain-stiffening behavior upon extension. In single cells, strain-stiffening occurs due crosslinking of actin-filaments into stress-fibers as a response to stretch. This crosslinking was the inspiration for a novel, minimalistic, 3D-structured design which is based on slats between several backbones in an elastic material: During elongation of the material, the flexible slats touch each other leading to mechanical interaction and hence to the stiffening of the material.

Methods

To study the effect of this phenomena in single strain-stiffening units, cm-sized molds were printed for PDMS molding using fused filament fabrication. By uniaxial tensile tests, adaptations in geometry and variations in total scale and their respective effect on the mechanical behavior were studied. Using stereolithography, elastic materials were 3D-printed directly as strain-stiffening units and their respective mechanical behavior was compared to the molded samples. Additionlly, three-dimensional arrangements of strain-stiffening units were used to test the combined mechanical properties. Using two-photon direct laser writing, the printability of strain-stiffening units was studied at micrometer level.

Results

The studied geometry shows a highly non-linear strain-stiffening behavior that is tuneable, rate-independent, reversible and can be incorporated into different elastic materials. Changes in geometry result in variations of the initial and final stiffness of the material and influence the point of stiffening. The strain-stiffening mechanics can be achieved not only for single units but also for complex three-dimensional arrangements like sheets or tubes.

Conclusion

Using different AM techniques, strain-stiffening units and complex strain-stiffening arrangements were fabricated and mechanically studied. By variations and adaptation of the three-dimensional structure, the mechanical properties can be tuned. Thus our strain-stiffening structures can resemble the mechanical properties of biological tissue like native blood vessels or skin and thus, promoting the integration of strain-stiffening units in future medical implants.

Stretchable electrodes for biopotential measurements in wearable patches

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Introduction

Electronic skin (e-skin) and patches with integrated electronic functionality for rapid, accurate and on site detection of pivotal biopotential signals have gained significant interest in recent years. To monitor biopotential signals from the skin, thin, flexible, stretchable and soft electrodes are highly beneficial. With such electrodes, a variety of physiological conditions, including electrocardiography (ECG) signals, can be monitored. Stretchable electrodes are used to increase the signal-to-noise ratio of the biopotentials and to reduce motion artifacts. In addition, it is easy to attach them to the human skin.

Methods

We present a cleanroom compatible fabrication process to realize a pair of ECG electrodes using the medical-grade, translucent and flexible Styrene-ethylene-butylene-styrene (SEBS) material. After fabrication with a dextrane realease layer on 4-inch wafers, we used these electrodes in ECG tests. We attached them to the chest of test persons and compared their recording performance with standard Ag/AgCl electrodes typically used for ECG recordings.

Results

The comparison of both signals recorded from the same person at the same position of the chest showed similar signal-to-noise ratios of both recordings. In addition, the measurements with the flexible SEBS electrodes were less susceptible to motion artefacts compared to the classical electrodes.

Conclusion

Skin-conformable, flexible electrodes are useful for extended ECG recordings, because of their conformablity and the tight adhesion of the soft SEBS material to the human skin. With our fabricated electrodes it was feasible to apply large strain rates as well because of the excellent adherence of the microgalvanic Au structures onto the SEBS material. In future we will expend our fabrication process to include more electrodes for different signal purposes for multifunctional e-skin applications.

Towards graded polymer implants for the tendon-bone junction

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Introduction

Polycaprolactone (PCL) is the most used material for fiber scaffolds for treatment of tendon ruptues in the rotator cuff. Yet, the hydrophobic properties of electrospun PCL inhibit cell viability and growth. To overcome these limitations pure PCL is blended with Chitosan-graft-Polycaprolactone (CS-g-PCL) to improve cell viability and ingrowth. In this study, process parameters of of the blend polymer as well as cell viability is investigated.

Methods

Electrospun fiber scaffolds were manufactured from a PCL:CS-g-PCL polymer blend solution in TFE. A collector speed of 2 m/s, a voltage of 20 kV and a flow rate of 4 ml/h for the polymer solution were chosen to fabricate the fiber scaffolds. To test the influence of the CS-g-PCL on the fiber diameter, three different PCL:CS-g-PCL ratios were tested (9/1; 18/1; 24/1) and compared with pure PCL. Afterwards their influence on the cell viability was tested. For this, the different PCL:CS-g-PCL ratios where mixed with pure PCL in 0, 5, 10, 15, 20wt.% ratios respectively. Cell proliferation of mesenchymal stem cells (MSC) on the scaffolds was investigated after 24h, 3d and 7d.

Results

The results show that the CS-g-PCL blend decreases the fiber diameter of the polymer scaffolds compared to pure PCL fibers. The fiber diameter was smallest with the 9/1 PCL:CS-gPCL ratio. As the proportion of CS-g-PCL increases, the average fiber diameter increases, but remains below the fiber diameter of pure PCL fiber scaffolds even with a 24/1 PCL:CS-g-PCL proportion. Cell viability tests show, that high concentrations of CS-g-PCL enhance the cell proliferation.

Conclusion

The study shows that the use of PCL:CS-g-PCL polymer decreases the average fiber diameter of the fabricated scaffolds. Furthermore, high concentrations of CS-g-PCL enhance cell viability. In ongoing experiments, the optimal PCL:CS-g-PCL ratio needs to be evaluated in order to combine good processability with high cell viability.

Reparative capacity of ex vivo developed 3D scaffold-free tissue regenerates for tendons - First Results

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Introduction

Tendon injuries are difficult to heal because they do not regenerate by restitution but by the formation of a fibrotic scar. This scar tissue has poorer mechanical properties and often leads to long-term pain, discomfort, and disability in range of motion. To date, there are no techniques of restoring the original native structure of fully injured or torn tendons. One of the most promising methods is the tissue engineering procedure. In this paper, first results for the production of 3D scaffold-free tendon regenerates (3D-SFTG) are presented.

Methods

Equine fibrocytes were used for the development of the 3D-SFTG. These were taken from the equine lumbar region as a biopsy specimen using a skin punch (∅=3mm), isolated and propagated in monolayer cultures. Tendon regenerates were prepared using cells from passage 3, after which the monolayer cells were transferred to three-dimensional state. During cultivation, the 3D-SFTG were stretched on an elastic support and mechanically stimulated. The cultivation time was 8-12 weeks. For the evaluation of the produced 3D-SFTG, they were examined biomechanically, histologically and biochemically.

Results

The favored equine fibrocytes are suitable as a cell type for the production of tendon regenerates because they both differentiate into tendocyte-like cells in vitro and form three-dimensional tendon equivalents ex vivo. Continuously applied mechanical stimulation provides the newly synthesized ECM molecules of the tissue regenerate with a force vector along which they can align in the direction of stretch, allowing the structure and morphology of tendogenic tissue to form. Initial biomechanical experiments showed that 3D-SFTG (n=3, L=65mm, ∅=2mm) had a mean maximum tensile force of (0.27+/-0.05)N at a mean strain of (31+/-6)%.

Conclusion

The first results of the generated 3D-SFTG show a promising perspective in further application as in vitro model as well as in in vivo treatment. In particular, the mechanical stimulation will be optimized in further work.

Establishment of an in vitro foreign body reaction model for medical device testing

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Introduction

The foreign body reaction (FBR) can lead to serious impairment of implants and is a major cause for medical device (MD) failure [1]. Since the FBR is currently not part of biocompatibility testing according to ISO 10993, it is of interest to establish a protocol for prediction of potential FBR induction.

Methods

About 2*105 primary rat alveolar macrophages were seeded onto different MD-related materials in a 24-well plate. At indicated time points, supernatants were collected for determination of membrane damage (lactate dehydrogenase release) and cytokine/chemokine production by an enzyme-linked immunosorbent assay (ELISA). After 72 h of incubation, cells were analyzed by immunofluorescence of alpha-tubulin and confocal microscopy.

Results

Latex as natural rubber, often used as a positive control in biocompatibility testing, induced significant membrane damage, but no marked CINC-1 release, an immune response marker. In line with its use as implant material, medical grade high density polyethylene (HDPE) was shown to mediate neither cytotoxicity nor CINC-1 release. In contrast, non-medical grade high density polyethylene (UHMWPE) mediated significant, time-dependent CINC-1 release from macrophages, however, without inducing membrane damage. Notably, also formation of foreign body giant cells (FBGC) by UHMWPE could be visualized by confocal microscopy.

Conclusions

The results indicate that UHMWPE exhibited a pro-inflammatory potential with induction of FBR in the absence of marked cytotoxicity. Based on cytotoxicity testing only, UHMWPE would, therefore, have passed ISO 10993-5 biocompatibility testing, irrespective of mediating FBR. The present approach for FBR detection, thus, might represent an important add-on for ISO 10993 biocompatibility testing of implant materials to better ensure safety.

References

[1] Zhang, D. et al. Advanced Functional Materials. Vol 31. No 6. 2021.

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Track:
Biosignal Analysis and Control

Non-invasive early detection of abdominal aortic aneurysms based on in-vivo photoplethysmography data: Comparison of different machine learning techniques

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Introduction

Digitalisation and the generation of large amounts of data from examinations and medical interventions are making an ever-increasing amount of data available, of which only a fraction has been used to date to generate new insights using Artificial intelligence. Aortic aneurysms are problematic and underdiagnosed: existing diagnostic techniques are not suitable for effective screening at the family physician level. In a previous study (Hackstein et al.2021), the authors achieved promising, but still expandable results using machine learning techniques on non-invasive in-vivo PPG-data at thumbs and toes of 55 patients.

Methods

We use a variant of these methods on this in-vivo data set and compare the results with other classification approaches and one via a bidirectional recurrent neural network (BRNN) for abdominal aortic aneurysms (AAA) from recent literature. Moreover, a classification approach of Hackstein et al. (2021) is applied on an in-silico PPG-data set and on smaller subsets of it. The BRNN is trained on in-silico data and applied to our in-vivo data set.

Results

The variant of the earlier approach increases the classification accuracy by 4% to 64%. On the in-silico PPG-data set, accuracies of more than 86% are achieved, as better as younger the virtual patients and as bigger the aneurysms are, even on much smaller subsets of the data. For the application of the BRNN, the sensitivity was lower than 50%.

Conclusion

It is possible to increase the accuracies of Hackstein et al. by traditional classification methods. The results for the BRNN do not support - as expected- the assumption that it is suitable for the detection of AAA on in-vivo data if it is trained on in-silico data. On in-silico data, traditional methods produce as good results as the BRNN and have the advantage that they need less training data and are comprehensible.

Comparison of EOG and VOG obtained eye movements during Head Impulse Testing

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Introduction

Video Head Impulse Testing (HIT) is frequently used test to assess vestibular function. During HIT, eye movement responses are recorded with video-oculography (VOG). However, the use of VOG has some significant limitations, such as low sampling frequency of camera (up to 250 Hz), substantial artefacts due to the goggle slippage, pupil detection problems (e.g. blinking, droopy eyelids, etc.). Electro-oculography (EOG) is another eye-tracking technique based not on pupil tracking, but on the measurement of the corneo-retinal potential induced by the eye. The aim of study is two-fold: 1) to check whether EOG is reliable to be an alternative to VOG for capturing eye movement responses during HIT; 2) to check vestibule-ocular reflex gain asymmetry with both VOG and EOG.

Methods

HIT was carried out in 19 healthy subjects without a prior history of vestibular symptoms. Horizontal eye movements were recorded simultaneously with EOG and VOG. For each subject, eye movement traces were included in the analysis if they were accepted by the VOG system. Then, the selected eye movement responses of both techniques were compared using a linear regression model and t-testing. The model's slope (k) and the intercept (b) were chosen as eye velocity traces similarity indicators, where the k=1 and b=0 would indicate a perfect match.

Results

EOG and VOG obtained eye movement traces correlated strongly with each other during head impulse testing ($k_L=0.98\pm0.07$ 95% CI, $p=0.63$; $k_R=0.94\pm0.10$ 95% CI, $p=0.13$; $R^2>70\%$). EOG did not show any significant VOR gain asymmetry (2% to the right, $p=0.53$) in contrast to VOG (5% to the right, $p<0.001$).

Conclusion

EOG might potentially be applicable as an alternative to VOG for collecting eye movement responses during HIT.

On the use of singular value decomposition for QRS detection and ECG denoising

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Introduction

QRS detection is a pre-processing step to detect the heartbeat for subsequent rhythm classification. ECG waveforms may differ due to intrinsic variability or due to artifacts or noise, often leading to QRS detection difficulties. A high QRS detection performance is an important part of an ECG analysis algorithm that must work even for highly noisy signals. We report on singular value decomposition (SVD) based QRS detection and ECG denoising.

Methods

Suppose there are a large number of appropriately sampled ECG segments from different subjects containing P-waves, QRS-complexes, and T-waves. Then segments of equal length, aligned with respect to their R-peaks, are written in the columns of matrix X. Applying SVD yields $X=USV^T$, where U contains the left singular vectors u_k, note u_1 belongs to the largest singular value s_1, etc. Superposition of the first n uk, weighted with the associated s_k, yields a signal that is correlated with an ECG segment to be analyzed for QRS-complex location. To remove the noise from an ECG segment, u_k, k=1,...,p, are used to calculate coefficients for subsequent rank-p noise-reduced representation of this ECG segment.

Results

ECG of 40 subjects, each sampled at 100 Hz, were segmented in 40x10 sets of 95 data points each. Segments from 20 subjects were used to calculate the SVD and the rest were used for R-peak localisation and denoising for various signal-to-noise ratios. For original signals temporal R-peak localisation accuracy is 0.4 ± 2.8 ms. For Gaussian white noise contaminated signals accuracy decreased, e.g., S/N=0dB: -0.1 ± 4.4 ms, p=1, for maximum detection we get 37.3 ± 93.4 ms. The quality of R-peak localisation and noise-reduction depended on analysis window, singular values and left singular vectors selection.

Conclusion

The presented approach uses low-rank approximation of matricificated signals. It has been successfully applied for QRS detection and denoising of ECG.

A validation study for a consumer-grade auditory-visual stimulation device

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Introduction

Self-care and improving one's well-being has been growing rapidly in recent years for manifold reasons (e.g. higher workload, corona pandemic). Consumer-grade non-invasive stimulation devices are therefore on the rise to counteract the occurrence of mood disorders and burn-out symptoms. Here, we aim at investigating the impact of dynamically varying auditory-visual stimulation patterns on neural entrainment patterns and resonance phenomena.

Methods

Twenty-two healthy volunteers (11 female, 25.4±5.1 years, one dropout, seven in control group) participated in the study. EEG data (64 channel; equidistant layout) were acquired pre- and during stimulation for each volunteer. Visual and auditory stimuli were presented via a headset (ATUM, NeuroBright; https://www.neurobright.co.uk/). Presentation patterns (frequency, intensity, spatial distribution) varied within a presentation session but were kept constant across all volunteers. Stimulus intensity was adjusted to individual comfort levels. Individual alpha peak frequencies (iAPF) were calculated via the power spectral density with 50% overlapping 10s epochs from pre-stimulation segments. For both, the study and the control group, a time-frequency representation was calculated for the pre- and during-stimulation segments. From this, power values were determined for different frequency-bands (iAPF, stimulation frequencies and second harmonics of the latter). Statistical analyses focused on contrasting the power values between pre- and during stimulation.

Results

Mean iAPF values were 10.25±0.99Hz for the study and 10.63±1.21Hz for the control group respectively. Both, power values at the stimulation frequencies and their second harmonics differed significantly between pre- and during stimulation (p_{stim}=0.001; p_{harm}=0.001) in the study group. No such difference was found for the control group (p_{stim}=0.352; p_{harm}=0.237). Further, neither the study nor the control group showed significant iAPF power differences (p_{study}=0.035; $p_{control}$=0.352; alpha*=0.008).

Conclusion

Our results suggest that lightweight, portable auditory-visual presentation devices represent an effective tool for generating entrainment and resonance effects at home. Further analyses will focus on the investigation of individual differences driving such modulatory effects.

Onset Detection of Pulse-Shaped Bioelectrical Signals Using Linear State Space Models

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Introduction

Bioelectrical signals are often pulse-shaped with superimposed interference signals. In such signals, the precise identification of pulse onsets, peaks, amplitudes, and duration is not trivial, and often essential in diagnostics. A common example of this is the identification of QRS, P, and T wave characteristics in electrocardiogram signals. In this work, we present a versatile analysis method of rather low computational complexity to robustly identify such features in real-world signals.

Methods

We fit a Two Straight Line Model (TSLM) to the observed signal in a least squared error manner. For the optimization, we use discrete-time Autonomous Linear State Space Models (ALSSMs), leading to a highly efficiently computed recursive least squares problem. Finally, we apply a likelihood measure (or cost ratio) to identify the location of the desired event(s). To target specific events, this method provides a small number of intuitive tuning parameters.

Results

To demonstrate the concept and facilitate access to the method, we provide examples from the field of cardiology: we give a method for robust P wave onset identification and to find the centers of indistinct T waves. In addition, all example source code is provided in an open source software library.

Conclusion

We present a versatile and powerful method for detecting features in pulse-shaped signals. The method is of rather low computational complexity, which makes it attractive for a wide field of applications, including for battery-driven devices such as implants. The method has already proven to be of practical use in many applications.

Simultaneous measurement of DC-EEG and transcutaneous pCO2

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Introduction

DC potential shifts are the shifts observed in the EEG baseline which can last from seconds to minutes. The significance of these low-frequency components in healthy as well as pathological states of human physiology is getting more and more attention not only in scientific research but also in clinical applications.

Methods

In this paper, we present our novel multimodal measurement setup for simultaneously investigating DC potential shifts in EEG (DC-EEG) and the changes in noninvasive transcutaneous pCO2 measurements.

Results

We present preliminary results of our measurements during hyperventilation and apnea, which are two commonly used activation methods for changes in pCO2.

Conclusion

Using our multimodal measurement setup, we are able to simultaneously monitor changes in the DC-EEG and transcutaneous pCO2.

An algorithm based on continuous wavelet transform (CWT) to detect physiological bioimpedance signals for a new approach to intraoperative pelvic neuromonitoring

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Introduction

Low anterior resections are frequently associated with complications such as urinary and fecal incontinence as well as sexual disorders, the typical risk factors include surgery-related damage of pelvic autonomic nerves. A new approach to intraoperative pelvic neuromonitoring based on impedance measurement on the innervated organs has been investigated to enable the surgeon to spare pelvic autonomic nerves. The objective of this work is to develop an algorithm to distinguish physiological bioimpedance signals from artifacts to automate and facilitate signal interpretation.

Methods

Twenty-one patients included in a clinical trial (DRKS00017437) underwent nerve-sparing robotic surgery for rectal cancer using intraoperative pelvic neuromonitoring. Smooth muscle contraction of the urinary bladder and/ or the rectum in response to direct stimulation of innervating nerves correlate with a change in tissue impedance compared with the pre-contraction state, allowing the nerves to be identified and preserved. 122 stimulation induced impedance signals on the bladder and 45 signals on the rectum assessed in the study were used to develop the algorithm. The impedance signal is pre-processed including IIR and moving average filtering for noise reduction, signal characteristics are calculated using LabVIEW.

Results

The algorithm uses a feature vector including signal characteristics from time representation, such as the percental amplitude of the impedance change and the onset latency of the signal. In addition, a time-frequency analysis is performed by discretized continuous wavelet transformation (CWT) of the first derivative of the impedance signal using the Ricker wavelet. Physiological impedance changes can be distinguished from artifacts by detecting peaks in the CWT scalogram resulting from determination of the scaling and translation parameters of the signal sweeps.

Conclusion

Differentiation between physiological impedance changes and artifacts can be accomplished by calculating signal characteristics in the time and time-frequency representations, which facilitates signal interpretation for intraoperative pelvic neuromonitoring.

Initial investigations to determine higher-value cardiovascular parameters with a mobile IMU-based ballistocardiography system

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Introduction

Ballistocardiography (BCG) is a long-established method of measuring the movement of the human body triggered by the mechanical activity of the heart. In addition to simple parameters such as heart rate, complex anatomical conclusions such as valve activity can be drawn. Although the BCG has many advantages, it is rarely used in clinical practice. In the following, we show the possibilities of the BCG in a proof-of-concept study.

Methods

A mobile device is applied, in which two Inertial Measurement Unit (IMU) boards (ICM20948, 9DoF) for deriving the BCG and a photoplethysmography (PPG) module for reference are used. Each sensor's data is parallel acquired (fs=100Hz) and recorded on SD-card.

The BCG is derived from two positions (carotid artery and sternum, elastic-strap-fixed) and the PPG is acquired from the earlobe (clip-fixed). To evaluate the system's potential, the following initial signal processing steps (window based, length=30s, shift=0s) are used: low-pass filtering (Butterworth, 3rd-order, fc =0.45Hz) to distinguish the respiratory activity, band-pass filtering (Butterworth, 4th-order, fc =[0.7Hz..3Hz]) with subsequent calculation of the energy signal and its envelope and a peak detection for the derivation of the cardiac activity.

Results

After initial tests (six subjects, supine and lateral position, total data 120min), the individual BCG complexes could be derived. On average, it is possible to derive the heart rate with a deviation of about 1 BPM compared to a reference system.

Conclusion

As can be seen from the results, the BCG is suitable as a basic tool set for use in cardiology with simultaneous ease of use and low costs. In next steps, further investigations are planned to make statistically significant statements about the accuracy/quality of the system and, to expand the signal processing to be able to derive higher-value parameters (e.g., stroke volume, valve activity, cardiac ejection forces, pulse wave velocities, cardiac diseases).

Semi-Automated sleep classification

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Introduction

The rise of wearable electroencephalography (EEG) for sleep monitoring has led to an explosion of recordings that cannot be processed with the established manual scoring approach. Automated sleep scoring with deep learning has the potential to overcome this limitation. We investigated whether a human-in-the-loop approach could improve state-of-the-art automated scoring algorithms.

Methods

To evaluate the approach, we used 98 nights from 24 subjects wearing an MHSL-SleepBand [1] within a larger trial [2] at home. As baseline, 4 experts scored the nights according to standard AASM criteria [3]. Scoring was then automated using a deep learning architecture based on SeqSleepNet [4] and DeepSleepNet [5]. We constructed a scoring confidence estimate based on the sleep stage probability distribution predicted by the model. Epochs scored REM sleep and N2 stages displaying equivocal probabilities were defined as low confidence and re-presented to a fifth expert, blinded to the initial scorings. We compared the agreement on low confidence epochs between baseline, automated, and human re-scoring.

Results

The model predicted 5.5% low confidence epochs. The agreement between baseline and human re-scoring (51%) on these epochs was lower than between baseline and automated scoring (64.1%). Therefore, semi-supervised scoring did not improve the automated scoring.

Conclusion

With current scoring standards and sleep stage granulation, both, human and machine scorers, display similar uncertainty to score ambiguous epochs. Automated scoring is already highly performant, and the effort of conducting semi-automated scoring is only justified in rare cases.

Acknowledgements

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References

[1] ML Ferster, et al., IEEE Sensors Lett.3,5(2019):6000904
[2] C Lustenberger, et al., Commun Med.2(2022):30
[3] RB Berry, et al. J Clin Sleep Med.8,5(2012):597-619
[4] H Phan, et al., IEEE Trans Neural Syst Rehabil Eng.27,3(2019):400-10
[5] A Supratak, et al., IEEE Trans Neural Syst Rehabil Eng.25,11(2017):1998-2008

LA-TT-EALR / PromCERA: Comparison of preoperatively performed electrically evoked auditory potentials at the brainstem and cortical level during local anesthesia

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Introduction

In the past years, some groups established methods to use promontory stimulation and subjective responses as a tool for preoperative stimulation of the cochlea before cochlear implant (CI) surgery by a temporary trans-tympanic needle placed on the middle ear. Our research group tested CI candidates when the presence of the auditory nerve could not be confirmed by other pre-operative tests and analyzed objective results of electrical auditory brainstem response recorded with trans-tympanic promontory stimulation in local anesthesia (LA-TT-EABR) with a "golf-club" electrode placed on the round window niche (Polterauer et al. 2018).
However, EABR recording suffers from an electrical artifact from the stimulation and focuses on the excitability of the solely auditory nerve. We hypothesize that late evoked potential response (EALR) can be used for the assessment of the auditory pathway up to the cortical area with less electrical artifact interference.

Methods

The trans-tympanic electrically evoked auditory late response in local anesthesia (LA-TT-EALR) was added to our protocol right after the LA-TT-EABR in a unique recording session. In this study, we investigated the feasibility of LA-TT-EALR using MED-EL hardware and software. These two pre-operative trans-tympanic measurements, LA-TT-EABR and LA-TT-EALR, were compared.

Results

In a total n=18 tested subjects, it could be possible to record LA-TT-EABR in 10 and LA-TT-EALR in 13. In contrast to the fact that acoustically evoked auditory late responses are often hard to detect, and an electrical artifact heavily affects LA-TT-EABR, we did not experience these problems on LA-TT-EALR recordings. The matching between two measurement was present in 67% of the cases.

Conclusion

LA-TT-EALR may be a complement to the existing state-of-the-art LA-TT-EABR for pre-operative assessment before cochlear implantation offering information about auditory pathways in the auditory brainstem and cortex with a small increase of recording time. The equivalency of these two methods is encouraging.

Apnea detection from photoplethysmography signal using dicrotic notch

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Introduction

A comprehensive analysis of the photoplethysmography signal (PPG) provides information about the activity of the cardiovascular, respiration, or nervous system. Recent studies proposed methods of evaluation of respiratory rate and apnea from PPG in time domain using amplitude or baseline modulation, or the area under the curve. Because of the cardiovascular system and the respiratory system are connected, a change in the shape of the dicrotic notch is affected by respiration. The aim of our work is to extend the available methods for apnea detection from PPG by considering the dicrotic notch, and to test the proposed methods on experimental data.

Methods

We applied four methods to detect apnea from PPG. We adopted the Area under the PPG parameter and the Pulse wave amplitude parameter from literature, and we proposed the Dicrotic notch area parameter as well as a combination of Area under the PPG and Dicrotic notch area. We tested the methods on PPG records experimentally obtained from 10 volunteers, where each volunteer simulated three apneic pauses. For all the proposed methods, we determined the delay between the onset of an apneic episode and its detection. We also evaluated the sensitivity and specificity of the apnea detection.

Results

The average delay in detecting an apneic pause from the PPG using the Dicrotic notch area was 6.1 s. Combining the Area under the PPG parameter with the Dicrotic notch area parameter increased the specificity of apnea detection from 73.8% to 80.0%, although the sensitivity decreased from 91.1% to 85.6%.

Conclusion

This paper proposed a new method of apnea detection from PPG combining a previously documented parameter Area under the PPG with a newly proposed parameter Dicrotic notch area, and showed their potential for automatic apnea detection.

Detection of Muscle Fatiguing Dynamic Contractions Using Dispersion and Bubble Entropy of Surface Electromyography Signals

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Introduction

Detection and prediction of muscle fatigue is crucial to prevent exercise induced damage of skeletal muscles. Surface electromyography (sEMG) is a non-invasive measurement of the ensemble myoelectric activity that is widely used for muscle fatigue assessment. The complexity of sEMG signals arises due to the nonlinear response of the physiological system and can be captured using entropy measures. In this work, an attempt has been made to differentiate the muscle fatiguing contractions using two novel entropy measures, namely dispersion entropy (DspEn) and bubble entropy (BubEn) extracted from sEMG signals.

Methods

For this purpose, sEMG signals are recorded from the biceps brachii muscle of 58 young healthy volunteers under dynamic contraction protocol. The participants are instructed to perform biceps curl using 6 kg dumbbell load until they attain fatigue. The acquired signals are further pre-processed and the two entropy features namely, DspEn and BubEn are extracted from the first and last curls of the contractions, which corresponds to the nonfatigue and fatigue segments. Paired t-test is performed to analyze the mean difference between the nonfatigue and fatigue conditions.

Results

The results show that these features are able to differentiate the nonfatigue and fatigue conditions. Both DspEn and BubEn are observed to decrease in the fatigue state ($p < 0.001$). The mean percentage differences between the nonfatigue and fatigue conditions are 7.68 % and 34.10% for DspEn and BubEn, respectively.

Conclusion

The decreasing trend of the entropy features indicate the reduction of signal complexity in response to the increased synchronization of motor units during fatiguing contractions. It appears that these entropy measures could help in the detection of manifestation of muscle fatigue, and thus find use in the domain of sports medicine and rehabilitative designs.

Tiffeneau-Testing by means of a Smart-Shirt

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Abstract

Tiffeneau manoeuvres are an important method in pulmonary function testing of the human lungs and can help to diagnose respiratory obstructions. Data from a motion capture system and a spirometer was used to evaluate Tiffeneau indexes derived via a Smart-Shirt that incorporates three circumference measurements of the upper body. The mean error was 4.5% regarding the Tiffeneau indexes gained by the spirometer, indicating that clinical diagnosis of obstruction is potentially possible using a Smart-Shirt.

Full-field electroretinography examinations of the human eye with the eye diagnostic device PEP-2000 - First results

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Introduction

Full-field-electroretinography (full-field-ERG) forms the diagnostic basis for numerous pathologies of the eye. For this reason, fast and accurate diagnostics in the field of ophthalmology are essential. Two examination techniques, full-field-ERG and pupillometry were combined in a diagnostic device developed by ICM e.V. to reduce the examination process for both examiners and patients. In this abstract, the device is examined for the quality of the full-field-ERG measurements.

Methods

A feasibility study with 12 healthy subjects (3 females, 9 males, mean age: 36.33±11.94 years) was conducted to evaluate the full-field-ERG-function of the device (two measurements: light-adapted and dark-adapted, flash strength 3cds/m^2) according to ISCEV standards. To evaluate the results, mean values of the analysis parameters (amplitudes and peak times of the a- and b-wave) were calculated from all measurement data and compared with the results of other studies described in the literature.

Results

The evaluation of the results showed that the peak times for both light- and dark-adapted measurements were within the range of researched literature values (photopic a- and b-wave: 14-20ms, scotopic a-wave: 20-26ms, scotopic b-wave: 40-60ms). However, the amplitudes were markedly lower in both measurements compared to the averaged literature values (light-adapted about 5.5-fold and dark-adapted about 8.5-fold) and are clearly outside the range of values researched. The main reason for this difference is the use of cup electrodes, which were placed on the skin of the lower eyelid.

Conclusion

On the basis of these investigations, it can be concluded that the eye diagnostic device PEP-2000 for full-field-ERG provides plausible analysis parameters which are comparable with the literature. The determined analysis parameters should provide the basis for further investigations in the form of device-internal guideline values. To improve the quality of the measurement further studies with wire electrodes will be performed. Furthermore, the application in the veterinary field will be tested.

Contributions beyond spectral alterations to sEMG fatigue detectors

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Introduction

Neuromuscular fatigue may show in surface electromyographic recordings (sEMG) by a shift in spectral features. As of now, it is unclear whether other parameters may influence reported fatigue-detection methods as well.

Methods

Artificial test signals were constructed matching the spectrum of real sEMGs with evolving fatigue from one-minute long segments of eight subjects' forearms. Frequency based method mean frequency (MNF), spectral moments ratio (SMR5), wavelet-based WIRM as well as non-linear fatigue indicators sample entropy (SampEn), fuzzy approximate entropy (fApEn) and recurrence quantification analysis percent determinism (RQA%DET) were included in a comparison. Pearson correlation of fatigued signals from sEMG and corresponding artificial segments and their quadratic error were used to quantify deviations. Furthermore, separability of fatiguing and non-fatigued situations was evaluated for sEMG signals and corresponding artificial segments.

Results

Most frequency-based methods exhibited high correlations and low squared errors implying that there is hardly any difference between fatigue detection in sEMG and corresponding artificial segments. Non-linear entropy methods diverged from this observation: SampEn yielded reduced correlation and elevated squared error accompanied with poorer separability of fatiguing and non-fatigued situations. However, fApEn results were close to frequency-based methods.

Conclusion

Although some non-linear fatigue detection methods seem to incorporate non-linear fatigue features in addition to spectral changes, these have limited influence to the overall fatigue detection performance. Our investigation suggests that fatigue detection methods based on spectral properties are of maximal relevance.

Resynchronizing arrhythmic optogenetic murine hearts using multi-site structured lighting and multi-lead ECG monitoring

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Abstract

The chaotic electrical behavior of the heart during arrhythmias has, up to know, been intensively investigated with ECG measurements and optical mapping. In the case of optical mapping at the expense of using chemicals which change the electrophysiology of the cardiac tissue. At the same time, while continuously monitoring the heart with ECG electrodes, it is not possible to assess the obtained data during electrical shocks, such as in defibrillation events, due to the saturation of the input amplifiers.

Some years ago genetically modified murine hearts expressing channelrhodopsin-2 were developed, opening the path for studying the heart with optical methods. Since the optogenetic cardiac tissue can be excited with light, no electrical artifacts in the ECG are aroused during photostimulation. Taking advantage of this fact, the authors have designed an experimental setup for the acquisition of ECG data from several electrodes simultaneously, providing spatio-temporal information about the current state of the heart even during photodefibrillation attempts. Furthermore, considering that targeted photostimulation of delimited regions of cardiac tissue is possible, a multi-site lighting system based on micro-LEDs was designed and is presented in this work.

Using this novel experimental setup, different types of arrhythmias were induced and the termination success rates were analyzed while different lighting patterns were applied. Post-processing of the obtained Multi-Lead ECG data, suggests that there is relationship between the dominant arrhythmia frequencies, their change during photostimulation and the outcome of the defibrillation attempt.

Optimal EEG Segmentation for Microsleep Detection Based on Machine Learning

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Introduction

Paroxysmal brain state changes, such as microsleep events in drivers, are presumably subcortically induced and accompanied by cortical processes. This raises questions of how stable and persistent are the cortical processes that can be observed with EEG in real time. For this purpose, recordings of four night-driving simulation studies including 79 subjects are used to analyze how large the time window and how the temporal offset of the EEG segment must be to achieve maximum classification rate.

Methods

From each EEG segment, power spectral densities were estimated using the modified periodogram method and averaged in narrow spectral bands. They were then processed using gradient boosting machines in order to map them to one of two brain state types: microsleep or sustained attention.

Results

Segment length and offset were found to have moderate and dramatic effects on recognition rate, respectively. With optimal settings, the grand mean of classification accuracy and its standard error were at 92.6 ± 0.1 % across all subjects.

Conclusion

It turned out that the segment offset is a significant parameter that crucially influences the recognition accuracy. In publications of other author groups, we could not find information about the choice of this parameter. The results can be interpreted as indicating a minimal recovery effect due to microsleep. This has also been demonstrated by other authors, but in oculographic parameters, not in EEG. It supports the hypothesis that MSEs are spontaneous events that do not manifest cortically several seconds in advance. This is of importance for forensic questions.

Pupillometry for pain tracking of induced heat stimuli

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Introduction

This study includes the development and testing of a microcontroller based pain tracker to identify and quantify pain by different pain-specific biosignals with a focus on pupillometry. Therefore, a pain tracker was designed enabling the measurement of pupil dilation, skin conductance and heart rate.

Methods

The pupillometry uses an IR-Camera with 30fps mounted to a glasses frame to reduce movement artifacts. To calculate the pupil dilation, several image processing techniques including thresholding, dilatation, erosion and edge detection are performed to determine the pupil size in pixel. The pain stimulation is applied using a peltier ATS thermode on the inside of the subject forearm. Each subject received 8 stimuli with a duration of 5 seconds each and a temperature of 49°C, with an inter-stimuli-time of 30 seconds. Simultaneously, a 64-channel EEG is recorded according to the 10-10 system with linked earlobes as reference. EEG data is then processed using a 1Hz highpass and a 40Hz lowpass filter to reduce artifacts. Further processing is done using the MATLAB based toolbox “eeglab”. ECG and skin conductance are recorded with 200Hz. Measured data of all systems is synchronized using a trigger signal.

Results

Results show a percentage change of the pupil width of about 13% at 6 seconds after the stimulus onset. For skin conductance, a percent increase of 20% is seen 11 seconds after the stimulus onset. The heartrate exhibits a maximum percentage increase of the baseline of 20% at approximately 10 seconds after the stimulus.

Conclusion

The results indicate that the developed methodology performs the function of a pain tracker. Further, the methodology needs to be tested and validated using a new study design and different types of pain applications as well as the intensity of the stimuli to determine to what extent the pain tracker can provide information regarding the pain intensity.

Track:
Devices and Systems for Surgical Interventions

Steerable Flexible Laparoscope to Facilitate Camera Guidance During Minimally Invasive Procedures

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Introduction

In conventional laparoscopy, the field of view of the surgeon is limited. Angled laparoscopes enable the observation of surrounding structures, however, to change the viewing perspective on a specific object, permanent repositioning and rotation of the shaft is required. In this paper, a demonstrator of a steerable flexible laparoscope is presented, enabling the user to intuitively adjust the perspective onto an object by means of a single control element. Further, the assessment of the steerable flexible laparoscope comprising control, handling, and orientation in the situs in comparison to a conventional rigid device is described.

Methods

The laparoscope consists of a distal flexible section, a rigid shaft, and an actuation unit, which is used to manually control the tip with the camera attached. The flexible section enables the laparoscope to adopt to an S-shaped curve, thus allowing an adjustment of the viewing perspective. The flexible section and the actuation unit are additively manufactured and wire cables are used to transmit forces. A survey with 10 unexperienced individuals was performed, comparing a conventional laparoscope and the presented device in different tasks in a boxtrainer setup. The tasks resembled common surgical tasks and were carried out with both, the conventional and the presented laparoscope.

Results

The steerable flexible laparoscope provides a viewing angle of $\pm$ 50° at 50 mm working distance. In first tests, the presented device showed advantages regarding intuitiveness of the control, easier handling, and improved depth perception.

Conclusion

The steerable flexible laparoscope shows great potential to improve multiple aspects of laparoscopy, however, further evaluation with professionals needs to be carried out to verify benefits for clinical use. Future work will focus on the manufacturing process and the enclosure of the flexible section to achieve a cost-efficient and robust disposable device.

A method to analyze the motion profile of hydraulically actuated automated electrode insertion using video-based data analysis.

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Introduction

During the insertion of a cochlear implant electrode array (EA) into the inner ear, a slow and continuous movement is ideal to reduce insertion forces and thus intracochlear trauma. Therefore, we recently introduced the Cochlea Hydrodrive (CHD) as a simple way for automated and ultra-slow EA insertion. The hydraulic piston of the CHD actuator is achieved by repurposing a commercial disposable syringe, which is driven by an infusion pump. The aim of this ongoing study is to investigate the resulting motion profiles of the plunger of different commercial syringes to select those providing the most constant and smooth forward movement.

Methods

A test setup was developed with an optical marker fixed to the syringe plunger. The marker was captured by camera allowing video recording of the motion from hydraulic actuation. A Matlab algorithm evaluated the displacement-time- and velocity-time-profiles of the motions. So far, we identified eleven types of different syringes from four manufacturers, of which five have already been tested.

Results

The proposed method was proven suitable to investigate the characteristics of hydraulic actuation. Motion profiles derived from the video images were used to analyze the smoothness and constancy of the velocity over the whole traveling distance. Furthermore, the movement profile analysis provides a conversion factor to convert the flow rate of the pump (ml/h) to a forward velocity value (mm/s) for specific syringes.

Conclusion

Through the presented methodology, it will be possible to select the best commercially-available syringe(s) to be used as a hydraulic cylinder in the CHD. Furthermore, it will provide evidence about the smoothness and the reliability of a hydraulically actuated automated electrode insertion as another important step toward clinical use of the device.

The Insertion Speed at Different Filling States Show an Influence on the Insertion Forces of Cochlear Catheters in Human Cadaveric Ears

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Introduction

To prevent endocochlear insertion trauma, the intraoperative use of pharmaceutical agents administered directly into the cochlear using catheters becomes increasingly the focus of research. However, which insertion forces act on the cochlear at different insertion speeds or filling states of the cochlear catheter has not yet been investigated.

Methods

In this study, cochlear catheters (MED-EL) were automatically inserted into a cadaveric human cochlear while insertion forces were recorded. The catheters were inserted at different insertion speeds (0.5, 1.0, and 2.0 mm/s), in unfilled or filled state.

Results

Data show that the mean insertion force of filled catheters is significantly increased at 1.0 mm/s when compared to 0.5 mm/s (1.0 mm/s=0.006 $\pm$ 0.00015 N vs. 0.5 mm/s=0.0070 $\pm$ 0.0005 N). Furthermore, it was found that there is no significant difference between insertion forces of unfilled and filled cochlear catheters.

Conclusion

The data show that the insertion speed significantly affects the mean insertion forces of filled cochlear catheter and the speed of 1.0 mm/s causes the lowest insertion forces. Concluded, an unfilled catheter should be inserted into the cochlear at an average insertion speed of 1 mm/s to minimize insertion forces and associated insertion trauma.

3D endoscopy: Towards fast and easy registration for navigated ENT surgery

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Introduction

Optical and electro-magnetic systems for surgical navigation have been an essential part in the daily routine for more than 20 years. However, such systems still have some drawbacks (line-of-sight, interference), making the navigational process cumbersome, e.g., functional endoscopic sinus surgery (FESS). This is especially true for the initial registration step for pre-operative data, which could take up to 15 minutes depending on the surgeon's experience or the lighting conditions in the operating room. This work describes a real-time approach utilizing 3D endoscopy, which facilitates and fastens the registration process significantly.

Methods

We use a 3D endoscope (XION Medical, Germany) and a navigation software (Localite, Germany) using a NDI infrared tracking system. All devices are calibrated and equipped with retro-reflecting markers. The 3D endoscope is stereo-calibrated to reconstruct 3D information. An interactive user interface guides the surgeon through a coarse-to-fine registration process. First, three prominent facial landmarks (left/right temple, nasal bridge) are registered using a tactile probe. Second, the facial surface is 3D reconstructed by the endoscope generating a dense point cloud which is fine-registered to pre-operative data using an iterative-closest-point algorithm.

Results

We evaluated the method using ground truth data of an ENT phantom (Phacon, Germany). The registration was completed in less than two minutes. The accuracy of the 3D surface is in the sub-millimeter range and fulfills the requirements for surgical navigation. The point cloud is computed in real-time (60fps) using a modern GPU and is interoperable using a Gstreamer-based network transmission pipeline.

Conclusion

The method is evaluated on ENT phantoms. The complex and error-prone registration process is improved in two ways. First, the registration time is reduced significantly. Second, using a 3D endoscope to generate point clouds allows an easier, faster, and more accurate registration of pre-operative data instead of manual probing markers at the patient's head.

Hologram accuracy evaluation of HoloLens 2 for thermal imaging in medical applications

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Introduction

Surgical navigation-assisted interventions, providing augmented previously acquired image data to support the physician, are routinely used. The way of providing the images enriched by annotations impacts the usability and user experience. Commonly used monitor-based visualization approaches have to deal with hand-eye coordination due to the displacement between the situs and the visualization device. Visualization techniques like extended reality (XR) promise improvements because the desired information can be shown where most suitable. The accuracy of such systems is essential for usability in clinical interventions but lacks research.

Methods

A system was developed consisting of a thermal camera (PI450, Optris GmbH, Germany) and a depth camera system (D415, Intel Inc., USA) which comprises a visual and a depth camera. A HoloLens 2 (Microsoft Corp., USA) was used to superimpose the thermal image on the real-world object. The inter camera and the camera system to HoloLens registration are described. The accuracy of the system was evaluated.

Results

5 probands annotated the locations of 9 marker points on a calibration pattern of the real object and the projection in the XR headset. The mean and max residual projection errors were 2.8 and 6.2 mm, respectively.

Conclusion

An XR system to superimpose thermal images was shown. The mean projection error of 2.8 mm is sufficient for further exploration of medical applications, but the camera to Hololens registration process as well as long-term drift needs to be analyzed in detail in the future.

360° Laparoscopic Imaging System to Facilitate Camera Control and Orientation in Minimally Invasive Surgery

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Introduction

A crucial limitation during laparoscopic procedures is the limited field of view and the associated need for permanent active repositioning of the laparoscope. The surgeon's view of the situs, and thus his or her performance, heavily depends on the skills of the camera assistant. The surgeon lacks control over his own field of view, and there is high potential for reducing mental load and workflow issues. In this paper, a research setup for a 360° laparoscopic imaging system for minimally invasive surgery is presented and assessed. The work aims at investigating an immersive imaging modality, giving back the surgeon the independent control over the viewing direction.

Methods

The system consists of a 360° laparoscope, a handheld controller, and a head mounted display, through which the surgeon can inspect the situs. The spherical video of the 360° laparoscope is live streamed to the head mounted display. The usability of the system is assessed in a user test covering different tasks and different use case scenarios in a box trainer setup with both, the 360° laparoscopic imaging system and a conventional laparoscope.

Results

In the user test, the system showed advantages over a conventional laparoscope regarding orientation in the situs, intuitiveness of operation, and faster task completion. For three of four tasks, the participants stated to choose the 360° laparoscopic imaging system if they had to redo a similar task.

Conclusion

The presented 360° laparoscopic imaging system forms a research setup allowing investigations regarding the implementation in surgical workflows, intuitiveness of use, the orientation of the surgeon in the situs, and possible potential and challenges of an immersive imaging modality for laparoscopy.

Analysing attention convolutional neural network for surgical tool localisation: a feasibility study

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Introduction

Image-based surgical tool localisation and detection play an important role in developing intelligent systems for operating theatres of the future. In literature, proposed approaches require large amounts of data that are fully annotated with tool positions in the image. In this paper, a deep learning framework, trained on binary tool presence, was evaluated for surgical tool localisation in laparoscopic images.

Methods

An SE-ResNet50 network (ResNet50 with squeeze-and-excitation (SE) attention modules) was trained on the Cholec80 dataset to perform tool classification. Cholec80-Boxes dataset was generated by annotating five videos of the Cholec80 with corresponding bounding boxes of surgical tools. After the training phase, the gradient class activation maps (Grad-CAMs) were extracted, from the trained model, for every tool-class in the image. Binary masks were then created by normalising and thresholding the extracted Grad-CAMs. Finally, bounding boxes for each surgical tool were generated from the binary masks.

Results

The Dice coefficient and precision were used to evaluate the localisation capability of the SE-ResNet50 network. Experimental results showed better performance of the attention-CNN compared to the base CNN model with mean tool localisation precision of 72.4% and 28.3%, respectively.

Conclusion

The achieved results show the potential of using attention modules to improve tool localisation in laparoscopic images. However, the method requires ongoing improvement. This improvement may either target the network architecture or the following visualisation and processing step. An ablation study is required to figure out the best location of the attention modules inside the network.

Thoracic pedicle screw anchorage using the modified slide vs. conventional technique for screw placement

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Introduction

Thoracic pedicle screw placement remains challenging and confers a significant risk of screw misplacement. Vialle et al. proposed a pedicle screw insertion technique named "slide technique" to increase safety and accuracy of thoracic pedicle screw placement. This involves decortication of the posterior cortex of the transverse process as a slide to the pedicle insertion point. The purpose of the study was to compare thoracic pedicle screw anchorage after screw placement with the modified slide (MS) technique and the conventional technique.

Methods

Fifteen human thoracic vertebrae were used for this study. For pairwise comparisons, one randomly selected pedicle of each vertebra was instrumented using the MS technique, while the contralateral pedicle was instrumented using the conventional technique for screw placement. Each pedicle screw was subjected to cyclic cranio-caudal loading with an initial load ranging from -50 N to +50 N and with stepwise increasing compressive loads (5 N every 100 cycles) until screw loosening. After screw loosening, pullout testing was performed.

Results

Thoracic pedicle screws inserted using the MS technique resisted a significantly lower number of load cycles until loosening than screws inserted using the conventional technique (7987.9 $\pm$ 1871.9 vs. 9927.0 $\pm$ 2352.5, $p<0.01$). These numbers of load cycles correspond to load magnitudes at loosening of 442.3 $\pm$ 94.0 N vs. 545.7 $\pm$ 177.4 N, respectively ($p<0.01$). Maximum pullout force of loosened screws did not significantly differ between the two insertion techniques (511.3 $\pm$ 205.4 N vs. 544.7 $\pm$ 177.4 N, $p=0.52$).

Conclusion

Our data indicate that screw anchorage of thoracic pedicle screws placed with the MS technique is lower than that of screws placed with the conventional technique. However, the load magnitude at loosening is still higher than that reported for cement augmented lumbar pedicle screws. Therefore, the MS technique might be useful to facilitate correct thoracic pedicle screw placement.

Concept for a retractor with force indicator for reduction of tissue trauma in abdominal surgery

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Introduction

Retractors are used in surgery for the displacement of tissue and organs and to keep the surgical area open. The retraction can lead to a tissue compression that can cause irritation on nerves, perfusion deficits, hematoma or late sequelae like wound healing disorders, pain and numbness. The retraction force and thus the load on the tissue can not be measured with retraction systems today. We present a new concept for a retractor with an integrated spring element and an indicator to visualize retraction force and allow an adjustment of the organ compression.

Methods

The new retractor was designed considering organ compression limits, requirements on sterility and easy manufacturing. Two retractors were built up as a prototype by 3D printing and tested in a distinguished test setup. The first test of the retractors was performed on a force measurement test bench using a fixed retractor, and in a second test, a liver specimen in a bowl. Tests were repeated for both retractor variants.

Results

The tests showed how different spring characteristics could be realized with the new retractor design. Depending on the spring characteristics, the compression could be limited to a certain level and flexibility that can compensate for unwanted patient motion. An indicator is integrated into the design showing the applied load on the retraction system.

Conclusion

The presented concept can help to increase patient safety and reduce tissue trauma and late sequelae. The indicator is an easy way to visualize applied forces and allow the adaption of the setup to the surgeon's needs.

Haptically enhanced VR surgical training system

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Introduction

This paper proposes a cost-effective VR surgical training system which computes haptic feedback forces when a VR surgical tool interacts with virtual tissues.

Methods

A 3DoF reverse linear Delta mechanism is used to render computed force feedback data which are then received by the fingertip of the operator. Additionally, the moving plate allows rendering of surface properties and lateral forces occurring due to a tumor with different stiffness parameters below the skin surface. Controllers are designed and implemented to regulate the haptic feedback device's end-effector position and applied force. The virtual surgical instruments are controlled by a 7DoF serial link manipulator which captures the operator's movement by the utilization of various sensors.

Results

The controllers to regulate forces as well as the positions are evaluated with the proposed haptic feedback device. The mean RMSE of the force and mean error of the angular displacement are 0.0707 N and 1.95°, respectively.

Conclusion

The presented system can provide multisensory feedback including visual, auditory and haptic feedback interactively depending on the operator's input in the presented VR surgical training system.

Initial engagement and axial force model for self-tapping bone screws

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Abstract

Bone screws are used in many orthopaedic procedures to secure implants or fix fractures to facilitate healing. Surgeons generally tighten screws by hand, however over- or under-tightening can negatively impact the fixation through thread stripping or loosening over time, respectively. Previous work has proposed an automated model-based smart-screwdriver to regulate insertion torque. One notable factor that has been neglected was the initial engagement of the screw in the hole, and the axial forces applied to the screw; these factors are addressed in this paper.

During insertion of the screw, more area of the front side of the thread (towards the hole) is in contact than the back side. Due to the reaction forces from this contact after deforming the hole walls to cut the thread, this leads to a net force pushing the screw out of the hole. This force is counteracted by the shear strength of the hole material around the screw. By carefully considering the geometry involved, we developed quantitative equations to estimate the net force and shear stress as a function of insertion distance. To verify this approach, screws were inserted into 3 different strength polyurethane blocks with a 20 N axial force.

The plot of the net force equation showed a linear ramp up until the screw was fully engaged, then was constant, while the shear stress continually curved downwards. Applying an axial force around the midpoint of the force ramp would minimise the maximum absolute net force and should minimise thread damage; the states of the holes from the experimental insertion are consistent with this.

Two main equations were derived. One can be used to recommend insertion axial forces, while the other can predict thread stripping from exceeding shear strength. These can be used in the future to improve other existing models for parameter identification.

Track:
Digital Health, TeleHealth, Wearables

Monitoring of Vital and Gait Parameters by an intelligent Sensor Network using AI Methods

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Introduction

The measurement and compilation of vital human data is of particular importance, as it opens up the possibility of supporting a person in their area of life and being able to provide information as to whether diseases are developing or, for example, the gait changes too much so that an early fall could be avoided. In these investigations, the focus is on diabetes mellitus patients with reduced mobility of the lower limbs. The age of the patients was between 40 and 75 years.

Methods

In this paper, a new type of sensor systems is presented, which measure the step size, foot pressure and foot temperature at different points on the foot print in a smart insole. Additionally, a new concept of the measuring method is applied: data acquisition by gamification The sensor system measures the temperature as well as the contact pressure of the ball of the foot and heel at six points on the sole of the shoe. Furthermore, the step width and step height are analyzed by an IMU system. In addition, the blood oxygen content and the heart rate was recorded via smart watch. An app system with three special games was developed to playfully analyze the function of balance and strength development in order to obtain comparable values of the practicing clients. The patients were given feedback to evaluate how their gait confidence and stress levels developed during the exercises.

Results

The investigations have been carried out with more than 20 clients all over Germany. The evaluation shows that the patients are using the tool 2 times a week and the acceptance measurement of using the tools lies by 80%. Balance and strength in the lower extremities improved in more than 78% of all patients. The increase in the score and thus the successful game percentage has been statistically proven.

Conclusion

It could be proven that in patients with disorders of strength and sensitivity in the lower extremities, with the help of intelligent shoe soles in combination with playful exercises, both a high level of acceptance of the regular exercises through playful exercises and a significant improvement in the symptoms was achieved.

How medical devices can meet hospital IT security requirements: A Catalogue of measures for IT risk management in hospitals

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Introduction

Increasing digitalization in hospitals increases the importance of IT security, especially for medical devices. Implementing systematic IT risk management to manage typical threats (e.g. hacking, unauthorized system access) is crucial for hospitals. In practice, implementing such IT risk management is not trivial because existing standards (e.g. ISO/IEC 80001) do not describe concrete implementation measures. The aim of the study was to develop and verify a catalogue of measures to implement risk management for medical devices.

Methods

A Delphi study with 22 experts was conducted to identify measures with which hospitals can implement a risk management process for medical devices. We performed a case study in an Austrian hospital to verify the practicability of these measures.

Results

We identified 49 measures to implement IT risk management. The case study showed the practicability of these measures. One of these measures describes the need to share IT security-related information between engineers or developers of medical devices and hospital IT risk managers. Based on this information, a hospital can then decide whether a medical device meets internal safety requirements and can be purchased. For example, for this decision, the hospital needs information on how a medical device is protected against malware (e.g., hardening of the operating system, whitelisting procedures) and how applicable laws are observed when processing the data (e.g. encrypted data transmission of personal data).

Conclusion

As existing standards (e.g. ISO/IEC 80001) do not describe concrete implementation measures, we developed and verified such a catalogue and showed its practicability in a case study. Hospitals have specific IT security requirements that need to be considered by biomedical engineers and developers early. Engineers and developers need to be aware of these requirements to take them into account during development and to prevent delays in their purchase.

The Design of an Avatar in a Multiplayer Serious Game

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Introduction

Avatars are often used to represent people in the virtual world. In the process, they can also have numerous psychological influences on the users.Therefore, this paper discusses a multiplayer application in virtual reality and how a appealing avatar could be designed in it.

Methods

To evaluate the influence of avatars on users, an existing serious game was extended by a server connection and various avatar representations (Ready Player Me, Reallusion, own abstract design). In a small study with six persons the application was tested competitively in teams of two. The users filled out the "Avatar Embodiment. A Standardized Questionnaire" by T.Peck and answered some additional questions.

Results

While an increase in motivation was observed in all participants, the choice of the preferred avatar was not uniform. The Reallusion avatars achieved the best questionnaire results. The overall embodiment for Reallusion was a score of 4.19. In contrast, the Ready Player Me models had a score of 3.81 and the abstract avatar only a score of 3.61. Despite this result, people preferred the abstract avatar when asked which one they would choose.

Conclusion

Thus, this showed that an appealing avatar for everyone could not simply be determined, but personal preferences and experience must be taken into account. Therefore, a character editor could be added to the application. Instead of selecting an existing avatar, this would make it possible to personalize the avatar according to the respective preferences of the players.

Towards multi-channel electroencephalography "in the wild": exploring a new wearable 8-channel system based on cooperative sensor technology

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Introduction

Multi-channel electroencephalography (EEG) is a landmark tool to monitor brain function and disorders. Similar to recent advances in wearable cardiovascular sensors, the access to long-term EEG recordings performed throughout daily life could bring game-changing new insights to clinicians and neuroscientists. However, the development of compact, sensitive, motion-robust, multi-channel EEG systems poses important technical challenges.
In this work, we developed a proof-of-concept wearable 8-channel EEG system based on cooperative sensor technology, which enabled connecting all 8 sensors with only 2 wires. The system was tested in healthy volunteers, using both wet and dry electrodes.

Methods

The 8-channel system was developed at CSEM and attached onto a textile head cap, with the 8 sensors arranged approximately in a ring around the head, intercepting positions Fp1/2 frontally and O1/2 occipitally. The system was tested in four healthy participants undergoing an eyes-open/eyes-closed paradigm, for alpha wave modulation. Some trials of the paradigm also included intentional head and body motion added to the task, to evaluate the impact of motion on signal quality. The tests were repeated with wet gel (cup-type) electrodes and with dry electrodes (pin-type for more posterior regions with hair, flat-type for more anterior regions without).

Results

The EEG recordings displayed typical features such as alpha waves (more prominent in occipital channels) and eye-blink perturbations (frontal channels). Clear alpha modulation between eyes-open and eyes-closed conditions could be detected in 3 of the 4 participants. Head and body motion introduced important artifacts, although not completely preventing the detection of alpha modulation. Overall, the wet electrodes offered the best performance in terms of signal quality, alpha wave sensitivity and robustness against motion. Nonetheless, the dry electrodes still achieved a very favorable, almost comparable performance.

Conclusion

Cooperative sensor-based EEG can detect meaningful brain activity, and offers a promising path towards high-quality wearable multi-channel EEG.

A concept and technical requirements for the Temi platform supporting care and nursing

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Introduction

With a growing number of people in need of care and the shortage of skilled workers, caregivers express the desire for improved support to reduce physical strain and psychological stress. One task for burden relieve is documentation of nursing actions and treatment processes, as this can be done in parallel with the action. Hence tools capturing information in real time could improve information sharing. Also, contactless assessment of patients' vital signs and emotions is desirable. Thus, the idea is to enhance an existing mobile platform, which can follow the nurse, includes a voice-controlled assistant, and be able for wireless (e.g., via Bluetooth) assessment of vital data from patients in its direct vicinity.

Methods

Using the Temi telepresence robot as an open technical platform, we provide and discus requirements for this platform to potentially aid and relief to medical staff within caring and elderly homes, with respect to voice-control, Bluetooth-based vital data collection, interfaces to a digital patient manager and automated emotion recognition.

Results

On-board voice control is possible with Temi, but safety regulations suggest that a local server with a dedicated vocabulary should be used. Bluetooth assessment of wireless vital sign devices works with open protocols. Emotion recognition is possible. Bidirectional connection to a web based EPR can be achieved using a local WiFi connection.

Conclusion

The presented concept and the rating of the associated technologies leads to the conclusion that - if adequately implemented and installed - the caregivers could potentially receive noticeable relief from them. Nevertheless, as next steps, the examined technologies and ideas must be completely implemented, thoroughly fused with each other, and evaluated to provide a real support system for clinical care and assisted documentation

Towards the Development of a Medical App for the Detection of Diabetic Foot Syndrome and Pressure Ulcers. Design thinking in medical app development

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Introduction

Diabetic foot syndrome is a secondary disease of diabetes mellitus that can lead to amputations, reduced mobility and in some cases death if treatment is delayed. The objective of this study was to collect user requirements for the development of a shoe insole accompanied by a medical app for continuous pressure measurement, applying a user-centered Design Thinking process.

Methods

We conducted a systematic competitor analysis and performed 10 context-interviews with both health care professionals (HCPs) (n=7) and patients with diabetic foot syndrome (n=3) at the University Hospital Graz (Austria) and a medical supply store. Structured interview guides, tailored to user groups were used for qualitative interviews. Questionnaires on the acceptance of eHealth applications were designed for quantitative analysis (n=14 patients, n=7 HCPs).

Results

The competitor analysis identified 12 in-shoe-systems for plantar pressure measurement for patients with diabetes. No current system on the EU market meets the requirements of the users interviewed in this study. Quantitative evaluation showed that 95% of future users would support the use of a medical app to monitor plantar pressure in patients with diabetic foot syndrome. Based on the identified user requirements, a first user interface was developed iteratively. Usability tests of the prototype resulted in a score of 71.7 on the System Usability Scale.

Conclusion

The medical app will be further developed and tested in clinical studies. Future research efforts include the role of gait analysis and temperature measurement in diabetic foot syndrome.

Towards Development of a Mobile App for Continuous and Unobtrusive Monitoring of Fetal Movements using a Design Thinking Approach

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Introduction

Fetal movements are an essential indicator of fetal well-being. Currently, no appropriate medical device is available for recording fetal movements throughout the day. This study uses a Design Thinking approach to gather user requirements for a mobile app accompanying a newly developed unobtrusive mobile sensor solution based on PyzoFlex® pressure sensors.

Methods

We conducted a structured literature review, systematic competitor analysis, and 14 consented qualitative interviews with potential future end-users (pregnant women, new mothers) and experts (gynaecologists, midwives). Interview participants and eight additional potential future end-users completed a quantitative questionnaire to evaluate the current mHealth utilisation and determine market potential and general acceptance of the new sensor technology. We developed an app demonstrator based on our findings and assessed its overall user acceptance by performing summative Thinking-Aloud usability tests with two technicians and three potential end-users.

Results

A query-based PubMed search retrieved 96 papers, including 24 for further research. Six relevant (medical) devices and nine experimental setups for continuous fetal home monitoring were identified. Two are intended explicitly for continuous fetal movement monitoring, but none of them is a cost-effective, unobtrusive, uncomplicated method for fetal movement home monitoring. Based on competitor devices and qualitative interviews, we defined software requirements and iteratively developed an app demonstrator while simultaneously collecting feedback during the interviews. The app scored 94.5 (=excellent) out of 100 on the System Usability Scale (SUS). Overall acceptance of the proposed solution was high among potential future end-users and experts. The quantitative evaluation showed that 85% of potential end-users believe the application would give them more safety, and 83% of experts believe it could reduce complications in high-risk pregnancies.

Conclusion

The app is still early in development and does not use actual sensor data yet. Quantitative evaluation indicates a potential future need, especially in high-risk pregnancies. Presumably, further iterations are necessary for market readiness.

Evaluation of spatio-temporal electrocutaneous warning signals

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Introduction

Acoustic or visual warning signals for workers in hazardous situations might fail under loud and/or low- visibility work situations. A warning system that uses electrocutaneous stimulation can overcome this problem.

Methods

The aim of this pilot study was to find spatio-temporal stimulation patterns for appropriate electrical warning. Eight electrode pairs were attached to the upper right arm of 16 participants. The stimulation was conducted with bi-phasic rectangular pulses of 150 µs and an amplitude of up to 25 mA. Pulse intervals that generate a single pulse, pulsating, vibrating, and continuous perception as well as varying spatial patterns (e.g. alternating between electrode pairs or circumferentially around the arm) were investigated and evaluated with regard to alertness, discomfort, and urgency.

Results

The pilot study revealed that a stimulation signal that generates a vibrating perception and is applied as a circumferential signal around the arm showed the highest values of alertness and is therefore considered a potential warning pattern for future studies with larger study groups.

Conclusion

We conclude that the use of a circumferential stimulation pattern that causes a vibrating sensation or an alternating vibrating/single pulses sensation might be used as a warning signal pattern. The resulting recommendations should be confirmed in a larger group of participants and under working conditions, e.g., using a vibrating machine during electrocutaneous stimulation.

Development of a pain journal for chronic pain management and remote monitoring

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Introduction

Chronic pain is a global health problem, having a tremendous effect on the quality-of-life (QoL) of patients. Monitoring the outcome of a specific therapy and the condition of the patient is of utter importance for effective pain management.

Methods

A smartphone application was developed for comprehensive pain management in chronic pain patients. It allows patients to enter and keep track of their health related QoL, pain, and medication intake in an easy, fast, and regular daily routine. The app was built based on standardized questionnaires and the needs of pain specialists and patients assessed via a brief survey in a small target group.

Results

The survey showed an unmet need for applications in clinical practice, which enable comprehensive monitoring of QoL, pain, therapeutic progress, and thus allow for patient engagement and overall improved pain management. Beneficially, patients can share their reported outcome measures gathered via the app with their pain specialist via PDF exports for remote monitoring. The smartphone app has been realized and is currently evaluated in beta tests.

Conclusion

The easy, comprehensible, and routine assessment of the patient's condition, combined with a future integration into an online therapy management system, may further advance pain management in chronic pain patients.

Using a single inertial sensor to control exergames for children with cerebral palsy

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Introduction

Children with cerebral palsy (CCP) benefit from intensive arm training. Exergames that can be played at home offer the possibility to increase the frequency of therapy but require reliable and accurate real-time motion tracking via easy-to-use sensors in unsupervised settings and magnetically disturbed environments.

Methods

We propose an inertial-sensor-based method with a single sensor on the wrist for real-time tracking of the inclination of the forearm during exercise motions that were selected for home rehabilitation of CCP. The control parameter of the game was validated with an optical marker-based ground truth system.

Results

First experiments with a therapist performing training movements in a healthy and simulated spastic manner show that the forearm inclination well captures the motion dynamics. The accuracy of the inertial-sensor-based measurement is validated with respect to the reference systemin three healthy subjects. Orientation offsets between the inertial sensor and the forearm marker set in the range of 2° - 6° and dynamic measurement errors about 3.1° were obtained.

Conclusion

This work demonstrates that the proposed method is suitable for real-time control of exergames in home therapy of CCP. The validation with an optical reference system has shown that the forearm inclination is a suitable parameter for feedback and therapeutic progress monitoring.

Management by Digital Responsibility in Health Organizations - An Approach for Implementing the Digital Responsibility Goals within Organizations

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Introduction

The trustworthiness of digital products, services, and processes is not just a question of technology, but one in which human behaviour and procedures within and between organizations are equally important. For the digital health vertical, patients' possibilities regarding digital access, education and integration can still be improved to enhance trust. Oftentimes, critical decisions about the future of digital developments are made without a clear framework. Trustworthy, ethically sensitive, and sustainable guidelines that focus on the benefits for people are missing.

Methods

The Digital Responsibility Goals (DRGs) aim to define this framework and work towards a truly human-centered digital transformation. Leading organizations and companies are committed to the United Nations' 17 Sustainable Development Goals (SDGs). Following the same logic, addressing the digital dimension, 7 DRGs aim to guide decision makers, companies, and other stakeholders, such as researchers and users, to develop trustworthy digital products and services.

Results

This paper describes the Digital Responsibility Goals, their purpose, and their exemplary relevance for the health sector. In addition, the document makes a first proposal for implementing digital responsibility through a management system based on the Digital Responsibility Goals, aiming to enable patient participation and enhance trust.

Conclusion

Each of the seven DRGs represents an urgent need for action in the digital space. Comprehensible, innovative, and applicable measures are needed and most of all, need to be implemented and actively pursued within and be activated by an organization. The DRGs offer an opportunity to promote greater responsibility in the digital space across sectors. Responsible behavior and responsible leadership all along the data life cycle is at the core of establishing trust. By adhering to the framework of the DRGs, and implementing it with a dedicated management system, building trust will no longer be a random by-product, but a pro-active and targeted achievement.

Smartphone based Monitoring of Pediatric Craniofacial Deformities

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Introduction

Craniofacial deformities such as positional skull deformities are widespread in infants. The early detection of these deformities is crucial for the effective treatment and the associated minimization or prevention of visual and pathological abnormalities. This paper presents a solution for the early detection of craniofacial deformities using easy available materials in both the domestic and clinical environments.

Methods

For this purpose, suitable web technologies as well as webserver systems are used in the context of app and server development.

Results

Users can use the app to take a bird's eye view of the child's head and use a 50ct coin as scale to then automatically obtain calculated clinical parameters which they can compare with clinical standard values to rule in or out a skull deformity.

Conclusion

The concept represents a way to compensate for the lack of specialists in craniofacial surgery as well as knowledge gaps and to digitize care concepts in the healthcare system.

Experience with Remote Programming for Cochlear MED-EL Implants in Italy during the Covid-19 Pandemic

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Introduction

Cochlear implant (CI) fitting is typically performed with the CI user and the audiologist/clinical engineer being present in the same location. There are, however, situations that require programming to be conducted remotely with the use of networked tools, a procedure known as Remote Programming. Remote Programming allows the fitting and measurement procedures to be performed as in a face-to-face CI fitting session, but with the additional flexibility that the audiologist and the CI user can be at different locations. The advent of the COVID-19 pandemic, with its attendant need for social distancing, has accelerated importance of telemedicine during this time.

Methods

The experience with Remote Programming was collected using an anonymized online survey. Data was collected to cover situations of initial activation of the CI system as well as regular follow-up programming sessions performed by participating audiologist/ clinicians and CI users.

Results

There was a high level of satisfaction among the CI users and the clinicians. There were only a few delays and interruptions, and the Remote Programming sessions could be performed in each case successfully without any safety incidences. Remote Programming is effective evidenced by the number of recommendations for others by the CI users and the clinicians.

Conclusion

Remote follow-up programming is a safe, feasible, and effective way of programming the CI user's devices. Most of the study participants were satisfied with Remote Programming and its results. In the end, our study confirms that Remote Programming is a beneficial tool for CI users and demonstrates that it was an effective instrument during the Covid-19 pandemic.

A Comparative Overview of Digital Health Applications between Belgium and Germany

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Introduction

The increasing use of mobile digital technologies in our daily life is also affecting the healthcare sector. Digital health applications have the potential to improve disease monitoring and management, avoid hospitalizations, and more. A main task for the health care system is to create a framework that facilitates the identification of safe and effective apps for health care professionals and patients to generate the most health benefit as well as guide payer coverage decisions. Currently some European countries have already developed a national framework for market access approval, nevertheless only Belgium and Germany have additionally created a reimbursement system.

Methods

The aim of this investigation is to compare the two different approaches of Belgium and Germany, based on the framework itself, the access requirements, and the experience so far.

Results

The overall approach seems to be similar, but scrutinizing the details, there are several significant differences. The evaluation procedure in Belgium consists of a 3 level validation pyramid while in Germany there is a normal procedure as well as a DiGA-Fast-Track. Only applications in stage 3 are reimbursable in Belgium whereas in Germany applications from provisional and permanent listing are reimbursable.

Conclusion

The comparative overview shows that the two forerunners, Belgium and Germany, use similar but not identical approaches, with partly relevant differences such as the evaluation procedure, the formulation of the target group. The current situation (status 11.04.22) shows that the focus of the app indications differs between both countries. Furthermore, not a single app is listed in Belgium and Germany at the same time. From our perspective it should be a goal for manufacturers of CE marked medical devices to achieve reimbursement in as many member states as possible.

Virtual Memory Training with Innovative Haptical Features

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Introduction

Dementia is a chronic disease of the brain that results in the gradual deterioration of all memory processes. Worldwide, approximately 46.8 million people are currently affected. Studies show that the symptoms of dementia can be reduced and slowed down by memory training.

Methods

For this reason, a virtual reality (VR) application was designed that uses individualization and personal memoirs in an attempt to preserve the memory of those affected. To extend this approach, haptics were now integrated into the existing program to provide additional stimulation to the brain. The VR application uses the game "Pairs" as a basis, whereby personal pictures and music pieces are used, which can be perceived visually and auditorily by the users. In addition, the "Tactsuit" from "bHaptics" has now been integrated into this application. In addition to the previously mentioned impressions, each pair of cards was assigned an exact haptic pattern, which can be perceived by the user via the haptic vest. This should help to better perceive and distinguish the content and furthermore possibly increase motivation.

Results

Through the integration, different processes are now possible. For example, the haptics can be based on self-determined patterns or synchronized with the already integrated music. This enables different possibilities to support dementia patients in a playful way.

Conclusion

The application was successfully extended to include haptic feedback. A study is necessary to test if the effectiveness of the VR memory training and the effect of haptics on the users. The different haptic effects should be tested against each other to see how they affect the memory process and motivation.

Behavioural Approach Task - Virtual Reality vs. Reality

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Introduction

People suffering from arachnophobia have reduced quality of life in many aspects. In this project, we designed a virtual reality (VR) application to perform a Behavioural Approach Task (BAT) for arachnophobia. The application is used to assess the level of avoidance experienced by the individual. Studies with these types of BAT usually require a lot of overhead: for example, the spider used during the task must be fully grown and be kept appropriately. Furthermore, the behaviour of the spider cannot be controlled.

Methods

In order to solve some of these issues, we designed a VR application for two different types of BAT: A BAT where people walk towards a spider and one, where they pull the spider towards themselves with a crank. These were created using the Unity game engine. To ensure that the application performs as well as the real BAT, we have worked closely with experts in clinical psychology. Together we have designed the various processes needed to transfer the BAT into VR as accurately as possible.

Results

We have developed a VR demonstrator containing these two types of BAT, as well as a tutorial scene, in which the test persons learn the controls of the VR Application.

Conclusion

A study is necessary to test if the effectiveness of the VR-BAT is comparable to that of the regular BAT. In order to test this, a study is currently in preparation, where patients perform both types of BAT - in VR and in a normal setting. During this time physiological signals are recorded in an attempt to determine the fear felt by the patients to be able to optimize the design of the exposure therapy.

Wearable foot pressure sensors to predict the risk of falls: Which data are worth collecting for the forward inclination of the upper body?

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Introduction

Falls have a high socioeconomic impact in the elderly population. A detection of the forward tilt using foot pressure sensors could lead to early prediction of falls, such as those associated with freezing of gait episodes in patients with Parkinson's disease. Objective measures could overcome subjectivity and assist medical doctors in diagnosis.

Methods

In this work, we explored whether shoulder-mounted motion sensors, such as accelerometers and gyroscopes could potentially be omitted to predict the risk of falls. A wearable foot pressure sensor (ActiSense System, IEE S.A., Luxembourg) consisting of a shoe insole was used to measure the pressure distribution on both feet. To mimic an unstable posture, healthy subjects performed movement tasks, such as bending the upper body to each side while standing on a spot. The correlation between the two sensor setups was analysed to investigate whether the forward tilt measured by the shoulder sensors could be detected early by the foot pressure sensors. Sensor data were recorded at a frequency of 200 Hz and analysed offline with custom-written software in MATLAB (R2021b, MathWorks Inc., USA). Supervised machine learning algorithms were used to predict the forward tilts.

Results

Preliminary results from four healthy subjects show a strong correlation between the averaged sensor data from the foot pressure and shoulder sensors. An overall accuracy of 83% was achieved using a random forest model to predict the forward tilts.

Conclusion

The results of this work indicates that the foot pressure sensors are suitable for detecting the forward tilt of the upper body. Future work will focus on validating the method by including data from patients at high risk for falls, such as those with Parkinson's disease. Finally, this could lead to an intelligent detection system that supports home monitoring for a personalised fall risk assessment in elderly people and patients.

Track:
Education and Training

Realization of a practical course on treatment planning in radiation therapy using the software matRad

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Introduction

Treatment planning represents an integral part of radiation therapy. Nowadays, it relies on software-based treatment planning systems (TPS). Teaching practical treatment planning is hindered by the high costs of commercial TPS. To address this problem a course was developed at the Westsächsische Hochschule Zwickau (WHZ) based on the free, open source software matRad.

Methods

matRad is a TPS written in the programming language MATLAB® and is specifically developed for the purpose of teaching and research. At the WHZ it is used for a practical course on treatment planning for undergraduate students of biomedical engineering. The course consists of three-hour units, in which the participants work through different phantom and clinical cases (e. g. prostate and head and neck cancer) on their own or in small groups. It takes place in a computer room with up to 15 students.

Results

In the course the students get acquainted with the typical workflow of treatment planning for (intensity-modulated) photon therapy. They get an impression of the significance of the choice of different treatment parameters like the number and angle of the treatment beams. Also, they gain first insights into the optimization of dose distributions dealing with dose objectives and constraints. Finally, the critical evaluation of the proposed treatment plans using the computed dose distributions, dose-volume-histograms, etc. is trained. In an advanced section of the course, variables generated by the TPS such as the dose cube are further processed by the students by means of MATLAB.

Conclusion

Practical aspects of radiation treatment planning can only be imparted using a TPS. matRad is ideally suited to do this in a classroom setting. The software is easy to use so that the students can concentrate on the task of treatment planning. The developed course is able to illustrate each step of the planning procedure.

World first 1:1 transparent 3D printed various inner ear anatomies for cochlear implant (CI) electrode insertion training

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Introduction

The main aim of creating 3D printed transparent models of different inner ear anatomies is for training young ear nose throat (ENT) surgeons with the insertion of the CI electrode variants in various cochlear anatomies.

Methods

3D Slicer software was used for segmenting on clinical computed tomography (CT) scans of the patients with different malformed inner ear conditions to create hollow structures of the inner ear. The segmented 3D models in .stl file were sent to 3D print by Formlabs Form 3B machine with a standard clear material from Formlabs, and the 3D models were polished to maximise the clarity of the models using NOVUS 2 fine scratch remover. The models were tested by inserting CI electrodes inside the fluid-filled cochlea, and videos were captured to verify the success of complete electrode insertion.

Results

The transparent 3D printed inner ear shell has thickness of 1mm. overall with fluid-filled and lubricated electrodes, it replicated a realistic CI electrode insertion scenario. All models were able to be fully inserted to its maximum insertable volume. The visibility of the models was clear enough to identify the electrode contacts in the video.

Conclusion

The transparent 3D printed models of the various actual inner ear anatomies are possible to be fabricated from normal available clinical CT scans of the patients for electrode insertion training purposes. These replicated inner ear models allow the surgeons to train themselves on difficult or rare cases prior to the surgery. Further tests on the insertion forces of different electrode variants shall be followed to observe the changes with these models of various inner ear anatomies.

Using Social Network Analysis to monitor Social and Learning Processes in Online Courses

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Introduction

Many universities offer online or blended learning programs. In online settings, it is crucial that the teacher can monitor the social and learning processes of the group. Social network analysis can support this and is a key component of learning analytics. Indicators of social network analysis could be used to analyze social and learning processes online. For example, it could be helpful to analyze students' network positions (centrality measures) for social interactions. However, it is unclear which network indicators can give the teacher valid information on social and learning processes. Our research tries to find such accurate and valuable indicators for teachers.

Methods

First, we manually coded 3,546 students' postings from online discussions and calculated 13 indicators from social network analysis based on the interaction data from students in the online learning environment (Moodle). We then conducted a path analysis to identify which indicators are valuable network proxies to identify social engagement.

Results

Our findings showed that the size (path coefficient = -.56**) and constraint (path coefficient = -.51**) of the individual egocentric students' networks are useful indicators to measure social interactions in online learning environments. In addition, our findings revealed trends that network density and hierarchical positions could serve as valuable indicators. To put it in a nutshell, our findings reveal that the number of students in online courses (size), as well as the communication between them (density), and the positions single students hold (hierarchical positions/constraint) are indicators to measure social interactions in online settings.

Conclusion

We were able to identify indicators that allow teachers to monitor the social and learning processes. We will now investigate how these indicators develop in ongoing courses and compare the development of social processes in various courses. Our vision is a teacher dashboard that visualizes the state of social and learning processes.

Getting Published: What You Need To Succeed

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Introduction

“Publish or perish”? Institutional pressure still exists in order to succeed in academic career. However, we also have an obligation to publish our results to make our data available to the wider scientific community and more increasingly to the general public. Successful publication brings attention to researchers and sponsoring institutions. To be successful in publication there are simple concepts that should be followed.

Methods

This presentation highlights the important preparatory steps for creating a publishable manuscript. A brief overview of structuring a manuscript using the IMRaD format (Introduction, Materials and Methods, Results, and Discussion) and tips and tricks for getting your paper published. A brief overview of the submission and review process of a manuscript for publishing in a biomedical journal will be provided.

Results

The publication process starts long before the write-up of a manuscript. Write clearly. Get expert help. A researcher must take a step back from their research, because although the concept is clear to them it is not to the reader. Please the reader by pleasing the eye. Journal choice affects your chances of success.

Conclusion

Plan effectively. Use the resources that are available to you. Choose your journal wisely.

Virtual Reality Surgical Simulation in training of physicians and engineers

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Introduction

The basis of medical device technologies' success story is the fruitful collaboration of biomedical engineers and healthcare professionals. Complementary education and training of young academics in both fields represents an important factor in continuing this success story. Surgical simulation has been an interesting addition to educational options in both worlds. However, clinical educators have so far mostly driven use of such systems whereas surgical simulation in education of engineers is still less common.

Methods

We applied virtual reality surgical simulation as well as dissection of 3D printed physical anatomy models extensively in educational courses focusing either on novice to intermediate surgeons, or on clinical engineers. Feedback was collected from both course participants and expert instructors in the form of questionnaires and personal feedback.

Results

Surgical simulation has demonstrated a measurable and significant positive effect on the development of skills in novice surgeons. Two hours of added virtual reality training in novice otorhinolaryngology residents yielded a 52% increase in cadaveric mastoidectomy dissection performance assessed by blinded expert raters. Cognitive load imposed in simulated surgery was demonstrated to be significantly lower when compared to cadaveric dissection, which could allow adaptive curricula based on individual cognitive load. Learners' as well as experts' feedback on the use of surgical simulators was positive in both surgeons and engineers groups, however engineers anecdotally reported more tangible effects on their everyday work.

Conclusion

Digitalization in the educational sector has been an important trend over many years, but recent events have boosted online teaching, digital training systems and distributed learning. Surgical simulation systems have demonstrated an impressive ability to improve education and training of novice surgeons. We need to utilize these potentials more and more by integration into the training curricula of physicians and engineers. More research is needed on the benefit of use in training engineers.

Internship Digital Medicine - Biomedical Sensors for Medical Computer Scientists

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Introduction

The Internship Digital Medicine - Biomedical Sensors taught how to measure and process signals with circuit technology and programming. For that course the students should have basic understanding in computer science, medicine and electrical engineering.

Methods

The internship switched to new adapted course concept with the move of the course from the Faculty of Science and Technology to the new founded Faculty of Life Sciences at the University of Siegen. In the previous faculty, the internship only taught to medical computer scientists with a high background in computer science. Now, the internship is primary designed for students from our minor Digital Medical Technology (DMT) of the curriculum Digital Biomedical and Health Sciences (DBHS) at the new faculty. It is an advanced internship course of the fifth semester. Because the students from DMT haven't that much focus on computer science like the pure medical computer scientists, the course switched from straight microcontroller programming to the Arduino based Physical-Computing-Plattform. The learning success was surveyed by a questionnaire (4 pages) and a final report (5 pages text).

Results

The adaptation of the course was a success. All participants passed the course and achieved good to very good results. By reducing the amount of theoretical computer science knowledge and expanding it with the relatively simple programming language of the Arduino, even non-computer scientists were able to handle the tasks well.

Conclusion

All in all, this course model can be used in the future to teach the basics of circuits and biomedical signal processing to non-technical computer scientists.

Augmented Reality Application for Simulation of Mamma Palpation

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Introduction

The teaching of medicine is in a state of flux. New technologies enable students to learn faster and more efficiently than ever before. Especially the possibilities that augmented reality brings with it can be applied very well in this field.

Methods

The possibility to project additional information directly into the user's field of vision allows him to perceive additional knowledge without being distracted from the actual work. In this paper, a possibility of training Mamma Palpation is presented, which teaches students the course of action and the detection of possible tumors through virtual points.
For the analysis of the requirements, guideline-based expert interviews were conducted with three doctors. They either had experience with augmented reality applications in the medical field or were specialists in gynecology. In this way, the experts' statements were structured and assigned to different subject areas, such as teaching in medicine or augmented reality applications.

Results

The expert interviews revealed the following requirements, among others:
The full breast palpation application should be realistic, interactive, and provide different types of feedback (visual, haptic, etc.). In addition, the application should be able to correctly represent the human anatomy with a lot of details. Other requirements were the ability to palpate the breast tissue, as well as one as well as the lymph nodes, the function to color and an option to locate a virtual tumor.

Conclusion

In summary, it can be said that the most important requirements defined with the help of the expert interviews could basically be met in the implementation of an AR application for breast palpation. The basic function of the application is already given and further requirements can be increasingly improved. For example, by integrating haptic gloves or visualizing the examination procedures instead of explanatory texts.

Suitability Testing of the LucidGloves Prototype 4 for Extended Reality Medical Teaching

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Introduction

Augmented reality (XR) is increasingly finding its way into medicine. Haptic gloves are one way to enhance the realism. They are supposed to simulate realistic interactions with the virtual environment and thus give the user the feeling of actually being able to touch virtual objects. Due to their low availability and high manufacturing as well as licensing costs, they are hardly used in medicine. For this reason, Lucas VRTech has developed LucidGloves, which are intended to be a low-cost substitute for high-end haptic gloves.

Methods

The goal of this thesis is to replicate prototype version 4 of the LucidGloves and extensively test its capabilities and capabilities in a VR environment. In doing so, the research question of whether Prototype #4 is suitable for use in current XR-based medical teaching will be answered. To answer this research question, a qualitative study was conducted based on expert interviews with four physicians. The interviewees independently tested the LucidGlove Prototype 4, designed for the left hand, in an existing VR environment and evaluated a standardized questionnaire.

Results

The results of the expert interviews show that the haptic feedback of the LucidGloves is still far from real impressions, so that the use in a medical context is not possible at the current time under the current conditions and circumstances. However, the gesture recognition and the general idea at least go in the right direction.

Conclusion

Prototype 4 of the LucidGloves is therefore of limited suitability for initial use in medical teaching. The XR-learning programs used should not be designed to teach sensitive skills, but only elementary processes in diagnosis and therapy, and should offer added value from teaching the haptics of virtual models.

Digital Learning Objects Suitable to Deliver Teaching Content in the Field of Regulatory Affairs for Medical Devices

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Introduction

For engineering students heading for the medical device industry knowledge in engineering subjects such as mathematics, physics, mechanical and electrical engineering should be complemented by the basic concepts of regulatory affairs for medical devices (RA for MDs). The former do not change over time and are the same all over the world, the latter do not only differ between regions but are additionally changing over time. Furthermore, the question for the one and only correct concept is not easily answered: "It depends..." on the problem, the alternatives, the rationale etc. The development of digital learning objects (DLOs) needs time and money and thus strives for long lasting results with high pedagogic quality. And the result should be broadly accepted by the students. These characteristics and requirements build the frame for this work.

Methods

An interdisciplinary team representing, among others, medical engineering and pedagogics as well as lecturers and students used a three-step-process: subtopics of RA for MDs suitable for teaching within digital learning objects considering the above mentioned characteristics are identified and the learning objectives phrased (first step). Different kinds of DLOs are identified and listed (second step) and rated by their suitability to deliver content of RA for MDs and criteria to describe the effort to produce and update them (third step). This process is followed by a rating of popularity by the students.

Results

This procedure leads to a list with types of DLOs that are suitable to deliver teaching content in the field of RA for MDs with a first preliminary estimation of their acceptance by students: DLOs for playback are preferably shorter than a typical 90 minutes-lecture and interactive DLOs are very popular.

Conclusion

The list builds the foundation for the future work with a broader study asking medical engineering students about their preferences in relation to DLOs for the teaching of content of RA for MDs.

How can life science students, especially biomedical engineering students, benefit from the extra-curricular offerings and systems already established in other scientific fields?

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Abstract

The landscape of extracurricular activities, e.g. the hosting of Summer Schools, is broad and deeply rooted in many areas of education. This is also evident on the various international platforms such as https://www.summerschoolsineurope.eu/ . It is also shown that there is still a need to catch up in the area of medical technology, as the offerings in German-speaking countries and throughout Europe are very limited.
What are the established systems and motivators in other fields of education? The study of Pinto and Ramalheira (2017) clearly shows that in the field of economics, extracurricular activities can be decisive for the selection of an applicant and this can also influence the decision-makers already in the pre-selection process. The study of Abuelenain, Farooq and Sarr (2021) also shows that extracurricular as well as co-curricular activities can have positive effects on universities and students. It was showed at the example of the course "Natural Sciences", provided at Abu Dhabi University, a reduced failure rate of the students in the course after the students participated in an extracurricular program. Thus, the study even recommends increasing the number of summer programs offered at the university.
This study investigates the motivators of students who have participated in established summer schools of the UAS Technikum Wien for the field of Life Science Engineering. On the one hand, the motivation of the students to participate in summer schools, such as venue, format of the summer school (online, workshop series, project-based), and on the other hand, a possible correlation between academic success and the willingness to participate in extracurricular activities will be investigated. Is it only the students with good to very good academic success who participate more in extracurricular activities or are other factors motivating the students?

MedTech-mR - Creating a Virtual Enviroment for Medical Training and Room Planning

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Introduction

MedTech-mR (Medizintechnik in Mixed Reality) focuses on providing suitable and customized solutions in the medical engineering field using state-of-the-art mixed reality technologies. It introduces various solutions for medical education, training, planning and may highlight potentials for further applications.
Introducing a realistic immersive experience in a critical healthcare environment can be of great importance. Exemplarily, a fully equipped ICU, conformant to applicable standards and introducing simulations of medical and administrative processes, is of great interest. Rare conditions could be trained without interfering with ongoing medical processes.

Methods

To build a virtual ICU, which meets the standards, users are put into the design focus. The gathered information and requirements are then used as the basis for the room design. Unity Engine is chosen as a development platform.
The created prototype allows the interaction with the surrounding room's environment and objects. Additionally, a voice communication functionality can be provided to give the healthcare professionals the opportunity to communicate even in a decentralized training scenario.
In order to evaluate the developed solutions, training activities with key users from different countries and from different backgrounds are performed.

Results

The prototype facilitates the training of medical professionals over distance and acts as a digital twin for training in an ICU environment. Under the pandemic situation, decentralized training activities, also over long distances, have shown positive outputs and fostered the detection of further potential applications. The evaluation of the user experience to this immersive environment will expand insight to the potential of such digital solutions in healthcare.

Conclusion

This project shows the great potential of implementing cutting-edge mixed reality technologies in teaching and learning in the healthcare environment. Integrating this technology in practice, allows for more customized, cost-effective, and immersive training experience, and helps decision-makers to plan for effective facility design and optimize resource planning

Current topics in Life Science Engineering lectures

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Introduction

At FH Technikum Wien, the bachelor study programs Biomedical Engineering and Human Factors and Sports Engineering contain a broad, but focused set of specialisation fields, within the area of Life Science Engineering. The students chose their field of interest in lower semesters. However, to broaden their scope of knowledge and to increase international competencies a new teaching format has been created.

Methods

The novel lecture "Current Topics in Life Science Engineering" has been introduced into the third year. This course gives the chance to deepen the knowledge and closely interact with experts during presence classes. The course starts with common presentations of ongoing research topics for four weeks. Students are randomly distributed into groups and prepare two abstracts from different fields of interest. The abstracts shall describe an idea, or solution and must be presented using a two-minute video at a later stage. The groups will be assigned to the topic of one of the two abstracts. During the preparation time, the students will have the opportunity to schedule a check-up meeting with one of the experts. After video submission, they will get graded by two groups, the respective expert, and students which will act as a peer review group.

Results

This novel lecture will be introduced in winter semester 2022, and the expected results are internationalisation of teaching in LSE through the invited experts and strengthening the collaboration between students from different fields. Winning videos will be made publicly available.

Conclusion

The setup of this course includes several challenges. The international lecturers must be timed accordingly, the topics should slightly interact with each other, but should not necessarily build upon each other. Moreover, the topics covered by the course, shall show a clear link to each of the specialisation topics, but still be specific enough to include a degree of novelty.

Experiences of intercultural teaching activities in the field of eHealth

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Abstract

The funded research Project HealthCONNECT implements measure to promote the term eHealth in teaching and means to ease the exchange of lecturers and students to perceive different views of this topic. This report introduces the activities that have been implemented, stresses challenges that were observed and derives suggestions how to establish a co-operation between different institutes of higher education. This includes the mutual participation and inclusion of lecturers in teaching and evaluation activities; spanning from assessing students' projects till chairing master examinations. The co-operative organization and hosting of eHealth Summer Schools is another mean to share knowledge in the domain of eHealth with students and colleagues abroad. Such activities require a stable co-operation between the involved institutions that only can be build upon a trustworthy relationship between the lecturers as they are paving the way.

Hybrid polymer vessel phantoms for feasibility studies and clinical training of MRI-guided interventions

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Introduction

Catheter-based interventions are usually performed using X-ray fluoroscopy, involving ionizing radiation, nephrotoxic contrast agents, and yield poor soft tissue contrast. MRI-guided interventions could overcome these drawbacks and further benefit from arbitrary slice orientation. Development of novel MRI-guided medical procedures including medical devices, catheters and workflows state the need of extensive testing. Goal of this study is to show the manufacturing and evaluation process of polymer based vessel phantoms for performance of minimally invasive procedures using MRI-visualization techniques

Methods

First, we generated a 3D computer model of a human arterial vessel system by segmentation of medical patient data. Based on this 3D model, PHACON GmbH (Leipzig, Germany) produced vessel shaped corrodible cores via plaster additive manufacturing, using a DESIGNmate Cx printer. After a first material assessment of haptic (friction) and visibility properties (Ultrasound, X-ray imaging and MR imaging), the full featured silicone vessel model is produced using a described layer-based silicone molding process. Finally, the model is mounted inside an acrylic glass housing using specially designed connective elements.

Results

This work shows the manufacturing process of a patient data based vascular phantom for performance of novel interventions, prototype stage medical device testing and clinical training. The complete manufacturing process for one model took up to five working days, including model preparation steps and manufacturing process.

Conclusion

Our developed hybrid molding process allows combination of patient specific 3D printing approaches with the advantages of flexible materials (freedom of material). Additionally, it enables the production of models with almost unlimited building space. These characteristics allow the manufacturing of polymer vessel phantoms for simulation of a high variety of MRI-guided interventions.

Development of Internationalized Teaching and Training Modules for Healthcare Professionals

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Introduction

PrepaCare(XR) is an ongoing research project focusing on healthcare training for medical professionals and is funded by Erasmus+. It involves five institutions from Austria, Finland, Italy and Portugal. The aim of the project is to identify gaps in education and training of medical professionals and support training by a multi-fidelity-level solution containing various concepts.

Methods

The project seeks to develop and strengthen the digital competences of current and future healthcare professionals. This is realized by a collection of current knowledge creation in Learning, Teaching and Training (LTT) supported by a questionnaire, a facilitator handbook including different approaches of online simulation-based learning and best-practice examples, design guidelines for LTT information transfer and an e-learning course for selected use cases. The first practical example was the emergency scenario of a complex airway management. Based on detailed workflow and decision diagrams, a multi-fidelity-level solution was developed. This included a theoretical part using different didactic concepts and self-checking methods, an interactive video-based solution with feedback, and a learning platform-based Virtual Reality room for workflow training. To evaluate the developed solutions, LTT activities with key users from different countries are planned.

Results

Current results of PrepaCare(XR) are the questionnaire on medical simulation and the e-learning course containing the first practical use case as multi-fidelity-level solution. First evaluations by the creators of the medical workflow descriptions revealed good applicability on regular training activities in the hospital environment.

Conclusion

The project gives an overview about the current situation of simulation used in healthcare, potentials for improvement and an attractive variety of approaches for diverse training on different levels. Advantages are a flexible design of the learning environment, various training components specific to the subject area, unlimited repetition possibilities and, above all, a conservation of the financial resources of the users or their institutions.

Importance of interdisciplinary training for successful development of innovative biomedical implants

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Abstract

The development of novel and innovative biomaterials and biomedical devices like medical implants is a sophisticated task that requires expertise ranging from physicians over engineers and natural scientists to regulatory officers for clinical translation to be most efficient. This short communication should highlight the specific requirements and perspectives of the different disciplines and conclude on the importance of interdisciplinary training for early-stage researchers.
For this purpose, experts for clinical practice, material development, biological testing and medical device approval with profound experience in interdisciplinary research summarized and discussed current literature and knowledge.
Multiple interactions right from the start of the design phase until the medical device approval could clearly be identified. As not all relevant study programs already include interdisciplinary training, implementing structured interdisciplinary doctoral programs is advised to accelerate innovative biomedical implant development.

3D Printed Preterm Neonatal Pleural Drainage Training Model

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Introduction

Medical imaging-based 3D printed models offer an anatomically and haptically realistic platform for skill training in critical conditions. One such condition associated with high morbidity is neonatal pneumothorax occurring in 4-7% neonates. It is treated by chest tube insertion and drainage. For this procedure commercially available models have been in use that do not correctly represent the anatomy and haptics of a preterm neonate. We hypothesized that image-based lifelike 3D printed neonatal chest models offer an efficient platform for simulation training.

Methods

Neonatal chest CTs were rendered and segmented using Materialise USL software and designed for printing using Connex3 Objet500 polyjet printer. The model consisted of different skin, muscle, skeletal layers, lungs and heart, in digital material mixed of three bases (VeroPure, TangoPlus, VeroClear) mimicking the biomechanical properties of the respective tissues. Replaceable double windows were designed on the skin with a snap fit. Pressure sensors were included in the model. The model was tested for feasibility in pleural drainage by students and will be tested by pediatric healthcare providers in the next step.

Results

The polyjet printer replicated the designed structures (thoracic cage, muscles, lungs, bronchus and heart) accurately. The biomechanical properties of the skin (10.89 MPa) and lungs (6.00 MPa) closely resembled the human tissues and was denser using the polyjet printer. The replaceable windows made the model cost-effective, however, repeated puncture necessitated change of windows due to lower tear resistance of the material. The pressure detector gave a positive feedback in case of lung puncture.

Conclusion

This realistic replica of an extremely preterm infant's chest offers increased patient safety and quality treatment.
Supplementary trainings with heterogeneous groups and higher sample size are necessary to optimize and analyze simulation-based skill retention.

Acknowledgements

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Making change tangible. Enhancement of a Virtual Reality Stoma Training with Haptic Feedback

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Introduction

Patients with colon cancer often must undergo stoma surgery. In many cases, this means a big change in the patient's life. While some patients have time to prepare for this change, for others, the change comes suddenly. Patients must take care of their stoma on a daily basis, e.g. to clean or renew it. The necessary steps in this area are usually taught through demonstration. However, patients and their relatives are often unsure and are afraid of trating the stoma incorrectly.

Methods

In order to prepare patients and their relatives for dealing with a stoma, we have already developed and evaluated a VR application. Within the scope of a feasibility study, surveys were conducted which showed that most of the test persons wanted haptic feedback as well as working with their own hands instead of the controllers.

Results

To meet these requirements, the application was combined with the Manus Prime X Haptic VR Gloves of Manus Meta. These offer very good hand tracking, which should significantly improve the immersion and the embodiment in addition to the already existing full-body tracking. Furthermore, the gloves allow haptic feedback in the fingertips to simulate touching virtual objects.

Conclusion

The application was successfully extended to include hand tracking and haptic feedback. This improved application will be tested with stoma users in the near future. The focus will be on the realism of the VR training as well as on the benefits of the hand tracking as well as the haptic feedback.

Track:
Health Care (and Hospital) Engineering

Assessment of accuracy and glycemic control of FGM and CGM and impact on mental well-being

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Introduction

Diabetes mellitus (DM) describes a group of endocrine disorders that lead to a chronically elevated blood glucose level. DM is classified into four types. These are type 1 diabetes (DMI), type 2 diabetes (DMII), gestational diabetes (GDM), and other specific types of diabetes. They have in common that they can cause short- and long-term complications. Therefore, it is necessary to achieve a good glycaemic control to reduce possible complications and improve quality of life.

Methods

Technical devices for flash glucose monitoring (FGM) or continuous glucose monitoring (CGM) measure the interstitial glucose and help to prevent hypoglycemic and hyperglycemic events. FGM systems display the glucose concentration when the user specifically calls up the information. In contrast to CGM systems, the FGM does not continuously send and evaluate recipients' data.

Results

A study using the diabetes treatment satisfaction questionnaire (DTSQ) with the Freestyle Libre FGM system in pediatric and young adults with type 1 diabetes was carried out. 36 points were able be achieved as a total of all questions in the DTSQ, with a high number of points indicating a high level of satisfaction. The results show an increasing score for DTSQ from 14.4 ± 6.0 at baseline to 31.7 ± 1.9 after 12 weeks. This applies to patients with an insulin pump and patients with multiple-dose injections, while a greater change in treatment satisfaction was observed in patients with multiple-dose injections.

Conclusion

HbA1c is an important indicator for glycemic control. All studies considered showed significant improvements with CGMs. A positive effect is a significant decrease in hospital admissions for acute diabetes complications, especially severe hypoglycemia. By continuously sending glucose levels to smart devices, a reduction in fear of hypoglycemia, as well as improved peace of mind, was reported.

Cold plasma as a fast acting alternative disinfection method

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Introduction

The use of cold plasma, i.e. ionized gas, for disinfection has already been described in several publications. In contrast to conventional disinfection methods, the advantage of this technology is that it is easy to use and can be carried out quickly. In this paper, the germ-reducing effectiveness of a portable cold plasma device from the company Logfive (logfive GmbH, Germany) was investigated.

Methods

In order to test the effectiveness of the portable cold plasma disinfection device, carriers for sample plates were manufactured using the 3D printing process. Contaminated test samples with samples of different bacterial concentrations (1x102 CFU/ml - 1x108 CFU/ml) were placed on these carriers. Cold plasma disinfection was then carried out and the residual contamination on the test samples was determined by contact plate tests. Test samples that were not disinfected with the procedure were used as controls.

Results

In our first test runs, it was possible to establish the effectiveness of the process in principle. By selecting larger dilution steps, it was possible to determine a concentration range at which the efficacy of the process could be well assumed. In the experimental setup we chose, the germ reduction of the method could be determined between log 2.9 and log 3.6. Through further optimization of the process and the consecutive execution of several disinfection cycles in a row, the efficitiveness of the process could even be increased to log 4.7.

Conclusion

Our experiments showed a great potential for disinfection with the cold plasma technologie. It was possible to decrease the germ load on our test samples up to log 4,7. Nevertheless there are many unanswered questions regarding the reliability and performance of the technology. A next step is the adjustment of the plasma concentration in the device and therefore a optimized germ reduction in a reduced time span.

Dry-fog disinfection as a method for processing vehicles for passenger transport

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Introduction

Due to the corona pandemic, the demand for efficient and fast-acting disinfection measures is high. Some publications have already dealt with the possibility of dry-fog disinfection for entire rooms. In this work, the disinfecting potential, a dry fogging technology (Apollon Biotech GmbH, Germany), was investigated for the possibility of disinfection of vehicles for passenger transport. This could represent a new approach for processing emergency vehicles or local passenger transport quickly and cost-efficiently.

Methods

A public bus was used as a model for a passenger transport vehicle (Ferienfahrschule Hense GbR, Germany). This vehicle was probed at predetermined points before and after dry fog disinfection with swab and contact plate samples. In addition, contaminated sample tiles (Staphylococcus aureus ATCC 6538; 5x104 CFU) were placed at some locations in order to be able to record a standardized germ reduction. In order to determine the decontamination effect of the air in the vehicle, active airborne germ measurements were also carried out.

Results

In the airborne germ measurement we could show a reduction of approx. 68% of the microbiological air contamination. Screening of the total contamination of the service bus at several selected sites showed an average load of approximately 348 CFU per test site. After disinfection, the average bacterial count was reduced to approx. 18 CFU per test site. The disinfecting effect could also be shown with the standardized test tiles. Here, an effectiveness level of between log 0.8 and 3.7 was obtained at the various test sites.

Conclusion

The tests confirmed the basic applicability of the process for vehicles. However, further tests are necessary to determine whether the disinfection performance of the process is sufficient for use in vehicles in the medical sector. In addition, it must be examined whether the measure could be potentially harmful to medical or technical equipment.

Ankle Rehabilitation Robotic Systems for domestic use - a systematic review

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Introduction

Robotic assistance in rehabilitation procedures has gained increasing popularity for both scientists and patients. However, aside from the practicality and safety issues, the ability to motivate patients to pursue rehabilitation therapy is a hindrance and is still limiting the domestic usage of Ankle Rehabilitation Robotic Systems (ARRS). Most of the available ARRS are either applicable under clinical setups, or are dull to operate. New advancements have led to the fusion of virtual realities (VR) and augmented realities (AR) with ARRS. This paper presents a classification of contemporary ARRS based on their usability and practicality along with required modifications to make them befitting for domestic use.

Methods

A systemic literature search is applied for these systems on Web of Science and PubMed databases and the search is confined to the last twelve years' research from 2011 to 2022, older than twelve-year studies were excluded from the study.

Results

Overall, 219 ARRS were detected, among which 62 were shortlisted to be used in domestic use. Additionally, considering the size and requirement to apply the rehabilitation therapy at home, 14 robotic systems met the criteria. Ultimately, 4 of the surveyed systems used any of AR, VR, gamification, or visual feedback therapy.

Conclusion

In conclusion, although ARRS have evolved greatly over the past decade in terms of feasibility and function, there are still various obstacles to overcome so that they could become an integrated part of our everyday life. One solution is merging the rehabilitation systems with one of the aforementioned gamification types which better enables ARRS to be fitted into domestic use. Additionally, due to the availability, and excitement that arises from playing games, better results are yet expected to be achieved from the home-based therapies.

Experimental setup for the ultrasonic fractionation of flowing whole blood in a capillary

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Introduction

If an ultrasound driving pulse is chosen such, that its frequency is greater than the resonance frequency of one cell type and less than the resonance frequency of another cell type, the cells are separated in different nodes and antinodes of a standing sound field. The purpose of this study was to build an experimental setup for the ultrasonic fractionation of whole blood in flow conditions.
Blood fractionation is the separation of whole blood into its separate components, commonly used for analysis and transfusions.

Methods

The experimental setup comprised a container with single-element ultrasound transducers customisable in elevation and azimuth, focussed on a capillary through which blood was flowing. The acoustic focus coincided with the optical focus of a microscopic system to which a high-speed camera was attached. Ultrasound transducers were used with centre frequencies between 1 MHz and 20 MHz and with pressure amplitudes less than 1 MPa. The duty cycle was greater than 10% in all experiments. The field of view was $0.2\times 0.2\ \mathrm{mm}^2$.

Results

The optical resolution and camera speed allowed for visibility of red and white blood cells during flow conditions.
Throughout the experiments, the points of accumulation did not change with acoustic amplitude, confirming they were nodes and antinodes of the ultrasound field.
Irrespective of sonication pressure amplitude, white blood cells were observed to move in distal direction with respect to the transducer, whilst red blood cells were observed to move in proximal direction. The results during sonication are in stark contrast with measurements of movement without sonication.

Conclusion

Preliminary results show that red and white blood cells could be forced to move in opposite directions. The acoustic frequencies and pressures used were representative for those used in clinical diagnosis.
We have shown that ultrasonic whole blood fractionation is feasible using ultrasound.

Development of a compact sterilization and shredding machine for infectious or toxic wastes (MACS 800)

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Introduction

The amount of toxic waste generated in hospitals and medical facilities is steadily increasing. This increased volume is caused by a constantly growing population, the improvement of medical care and the increase in life expectancy. The introduction of uniform standards in the medical fields will keep this volume at a high level. It is true that centralized disposal or operator solutions for the removal of waste are largely available in highly developed industrialized countries. However, in developing and emerging countries, this is not the case and always involves a great deal of logistical effort.

Methods

For this reason, a compact sterilization and shredding machine has been developed. This is characterized by the following features: integrated 2- or 4-shaft shredder, maximum capacity of 400 liters of waste per cycle as well as an integrated steam generator and vacuum pump. The infectious or toxic waste are converted into non-hazardous household waste with cutting and sterilization through saturated steam. For the use of the steam sterilization the sterilization and shredding machine must be designed for extreme environmental conditions (temperatures of 134°C+4K and pressures from 480 to 3500mbar). Special blade geometries made of Hardox for the shredding system are used for cutting the waste.

Results

The developed sterilization and shredding machine was able to process contaminated materials also liquids (according to AVV-Waste-Code 180101, 180201, 180102, 180103 and 180202) - loose as well as in sealed disposal container (C-boxes). The steam sterilization used is in accordance with the approved procedure of the Robert-Koch-Institute (without chemical substances). The shredding system could appropriately cut abrasive material such as glass, plastics, metals or rubber.

Conclusion

The aim of the present project was to develop a compact machine capable of processing infectious or toxic wastes (including liquids) - loose as well as in sealed C-boxes without chemical substances.

Introducing a deflectable video camera system for endoscopy based on shape memory alloys (SMAs)

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Introduction

Endoscopy has revolutionized minimally invasive diagnostic and therapy of abdominal diseases 60 years ago. Since then, the basic mechanical design of endoscopes has improved only slightly, which means they are still operated by bowden cables. This simple but outdated operation principle has many drawbacks, as it is not possible to integrate these tools into cybermedical systems or to use smart assistance functions.

Methods

To overcome these drawbacks, we are developing endoscopic tools based on shape memory alloy (SMA) actuators. This smart material is deformable in cold state and goes back into its initial shape when it is heated above a certain temperature. For first proof of concept-studies we developed a rigid endoscopic tool. The user interface was designed based on the results of user studies at the university hospitals in Dresden and Rostock.

Results

Our first prototype is equipped with four SMA actuator wires, a custom designed Nitinol joint and a camera in the instruments tip. To change the cameras viewing direction we developed an intuitive, joystick-based user interface. Using a force-based control algorithm, the user input is transferred into a precise and smooth movement of the instrument. The maximum bending angle is $\pm$ 90° in two axes with a frequency of 0.25 Hz. For smaller actuation angels the movement becomes much faster. At 70°, we reach 1 Hz of actuation frequency in all directions.

Conclusion

We successfully developed a rigid endoscopic tool with movable tip actuated by SMA actuators. The implemented control algorithm and user-interface allow the integration of smart assistance functions into endoscopic instruments in the future. This is to be the starting point to close the gap between present endoscopic tools and computer assisted medical systems.

Determination of Infusion Filter Efficiency applying Dynamic Light Scattering

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Introduction

Filter membranes (pore size 0.2 µm) are frequently used to realize a sterile filtration for the clean preparation of solutions for infusion. A method was tested to define the efficiency of the filtration membrane analysing the filtrated suspension containing spherical standard particles applying Dynamic Light Scattering (DLS).

Methods

The hydrodynamic diameters h_D and the concentrations of the spherical standard particles were determined with a DLS system (Litesizer 500, AntonPaar Ostfildern-Scharnhausen, Germany). In order to generate a calibration curve, suspensions were diluted containing spherical standard particles (microparticles GmbH, Berlin, Germany) with specified sizes of D_1=150±2 nm and D_2=239±7 nm. Nine different concentrations between 0.01mg/l and 100mg/l were analysed with the DLS system for each particle size.
The particle suspensions containing the nano particles with the sizes mentioned above were lead through an infusion filter system and analysed with the DLS measurement system.

Results

The measured h_D, directly determined by the system, was up to 16.7% (for particle size D_1) and 13.8% (for particle size D_2) higher than the specified particle diameter for concentrations between 0.5 mg/l and 50 mg/l. The standard deviation of the measured hydrodynamic diameter is below 2% in this range.
The evaluation of the absolute intensities versus the specified particle concentrations showed that the relation of these values is proportional in this concentration range.
The particle concentrations of the filtrated suspensions could be calculated applying the calibration curves on the measured values of the absolute intensities. An amount of 92% of the particles were retained for the size D_1 and almost 99% of the larger particles (D_2).

Conclusion

The DLS method is well suited for the detection of spherical nanoparticles in the range of 150 and 250 nm. The method is a promising approach to characterize the pore size of infusion filters and their retention characteristics.

Network Load Evaluation of IEEE 11073 SDC Interconnected Medical Device Systems

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Introduction

The IEEE 11073 SDC family of standards was adopted in 2018 [1] [2]. This family of standards provides a safe, reliable and manufacturer-independent solution for networking different medical devices. The first SDC-enabled devices are currently approaching market launch. This paper examines how many network resources a potential value-added system using SDC would consume. The data collected is examined in terms of network bandwidth used, round trip time, packet loss and packet volume.

Methods

Based on a modified version of SDCLib/J a test setup was developed. The system is modular and consists of Java programs for consumer and provider. These are executed on a server hardware and are connected via the loopback adapter to reduce external influences. The scenarios are based on real application scenarios from the field of intensive care medicine such as vital monitoring. The frequency of transmission was gradually increased during the experiment in order to identify load limits.

Results

The analysis of the thus acquired measurements shows a linear, predictable growth in network utilization for almost all combinations of active metrics and value update rates. In the case of very high metric update rates, a stagnation of network utilization can be observed.

Conclusion

The test system used had no problems with a package transmission rate of 20 ms to 1 s. Almost all messages sent were also received by the consumer. The provider received an accept message. With a higher packet transmission rate, i.e., a clock frequency of 10 ms, the data transmission plateau was reached at 14 active metrics. After analyzing the different components we assume, that the limiting factor is the implementation of the library, accordingly, we will adapt the tests performed and run them with other implementations of the IEEE11073 SDC standard.

Track:
Image-Guided Diagnostic and Interventions

From Self-supervised Learning to Transfer Learning with Musculoskeletal Radiographs

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Abstract

Ewing sarcomas are malignant tumour entities typically found in children and adolescents. Early detection iscrucial for therapy and prognosis. Due to the low incidencethe general experience as well as according data is limited.Novel support tools for diagnosis, such as deep learning mod-els for image interpretation, are required. While acquiring suf-ficient data is a common obstacle in medicine, several tech-niques to tackle small data sets have emerged. The generalnecessity of large data sets in addition to a rare disease leadto the question whether transfer learning can solve the issueof limited data and subsequently support tasks such as dis-tinguishing Ewing sarcoma from its main differential diagno-sis (acute osteomyelitis) in paediatric radiographs. 42,608 un-structured radiographs from our musculoskeletal tumour cen-tre were retrieved from the PACS. The images were clus-tered with a DeepCluster, a self-supervised algorithm. 1000clusters were used for the upstream task (pretraining). Fol-lowing, the pretrained classification network was applied forthe downstream task of differentiating Ewing sarcoma andacute osteomyelitis. An untrained network achieved an accu-racy of 81.5%/54.2%, while an ImageNet-pretrained networkresulted in 89.6%/70.8% for validation and testing, respectively. Our transfer learning approach surpassed the best resultby 4.4%/17.3% percentage points. Transfer learning demon-strated to be a powerful technique to support image interpreta-tion tasks. Even for small data sets, the impact can be signifi-cant. However, transfer learning is not a final solution to smalldata sets. To achieve clinically relevant results, a structuredand systematic data acquisition is of paramount importance.

Detection and Segmentation of Heterogeneous Bone Tumours in Limited Radiographs

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Introduction

Bone tumours are a rare and often highly malignant entity. Early clinical diagnosis is the most important step, but the difficulty of detecting and assessing bone malignancies is in its radiological peculiarity and limited experience of non-experts. Since X-ray imaging is the first imaging method of bone tumour diagnostics, the purpose of this study is to develop an artificial intelligence (AI) model to detect and segment the tumorous tissue in a radiograph. We investigated which methods are necessary to cope with limited and heterogeneous data.

Methods

We collected 531 anonymised radiographs from our musculoskeletal tumour centre. In order to adapt to the complexity of recognizing the malignant tissue and cope with limited data, transfer learning, data augmentation as well as several architectures, some of which were initially designed for medical images, were implemented. Furthermore, dataset size was varied by adding another bone tumour entity. We applied a data split of 72%, 18%, 10% for training, validation and testing, respectively. To provide statistical significance and robustness, we applied a cross-validation and image stratification with respect to tumour pixels present.

Results

We achieved an accuracy of 99.72% and an intersection over union of 87.43% for hold-out test data by applying several methods to tackle limited data. Transfer learning and additional data brought the greatest performance increase.

Conclusion

In conclusion, our model was able to detect and segment tumorous tissue in radiographs with good performance, although it was trained on a very limited amount of data. Transfer Learning and data augmentation proved to significantly mitigate the issue of limited data samples. However, to accomplish clinical significance, more data has to be acquired in the future. Through minor adjustments, the model could be adapted to other musculoskeletal tumour entities and become a general support tool for orthopaedic surgeons and radiologists.

Toward image-guided positioning of an automated insertion tool for cochlear implant electrodes

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Introduction

Automated electrode insertion in cochlear implantation surgery is gaining more importance as it promises smoother insertions with lower forces - i.e. less trauma. Furthermore, the insertion angle or trajectory is gaining more attention as another parameter that impacts the insertion forces and the likelihood of hearing preservation. In order to merge both technological concepts we investigated how one could combine the recently presented cochlea hydro-drive (CHD) for automated insertion with accurate image-guided positioning using our moldable surgical targeting system.

Methods

First, design requirements were defined by analyzing the conventional mastoidectomy posterior tympanotomy approach (MPTA), including the handling of the electrode lead and the maintaining of an unobstructed view and access to the round window niche. Second, various design concepts were developed and assessed by experienced CI surgeons. Finally, the most promising concept was prototyped and tested using temporal bone phantoms (Phacon, Leipzig, Germany) for an initial proof-of-concept.

Results

While keeping the main concept, the moldable surgical targeting system was successfully adapted to the specific requirements resulting from image-guided positioning of the insertion tool. The decisive factor was the great freedom of design inherent in the concept that allowed extensive reshaping of the separate parts. This ensured sufficient space for an unobstructed view to the situs and for clamping and unclamping the electrode while the implant housing was already in place. The complete workflow was performed at least twice, including imaging, trajectory planning, template fabrication and automated insertion of the electrode into the artificial cochlear model using the CHD.

Conclusion

We demonstrate automated electrode insertion along an individually planned trajectory using a customized surgical template that enables image-guided positioning of the insertion tool. The high degree of freedom when designing separate parts allows adaption of the surgical targeting system to the most diverse requirements of multiple different applications.

A new method for OCT Imaging of the Eustachian tube

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Introduction

Eustachian tube dysfunction (ETD) can be connected to various clinical disorders such as acute and chronic otitis media. In addition, it can lead to hearing difficulties or even cholesteatoma in the long term. Unfortunately, the Eustachian tube (ET) diagnosis remains difficult except for obvious cases such as cleft palate or nasopharyngeal tumors. For treatment decision of ETD, a reliable diagnosis of the reason for this dysfunction is of interest. Imaging methods like CT or MRI do not show enough details today. Endoscopy is challenging but can show at least superficial structures at the pharyngeal orifice. To look into the deeper tissue layers vascular imaging methods like Intra Vascular Ultrasound (IVUS) and vascular Optical Coherence Tomography (OCT) were evaluated already. But these procedures are not made and certified for this application and come with risks for the patient.

Methods

We propose the use of an additional closed end guide catheter that can be advanced into the ET. A modified OCT catheter with a shortened tip can be placed inside the guide catheter without touching the patient's tissue. We evaluated this approach on a sheep cadaver head acquiring OCT and IVUS scans and with OCT only in a human cadaver head.

Results

In the sheep head the guide catheter placement was easy. The diameter and length of the ET could be evaluated with OCT and IVUS and a simulated swelling was detectable in a decreased ET diameter. In the human cadaver head the guide catheter could not be advanced fully because of the wax-like tissue properties of the Formalin fixated ET tissue. Only the proximal 18mm of the ET could be scanned with OCT. Nevertheless, the lumen of this section could be depicted.

Conclusion

The experiments showed promising results, the clinical value of this method has to be further investigated.

Continous Hyperspectral 3D-Imaging for Image-Guided Surgery

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Introduction

Digitization creates new possibilities to support the surgeon in complex surgical processes: three-dimensional reconstruction of the situs and spectral imaging, which can be used to differentiate optical tissue properties that are normally invisible to the human eye. The additional information can support the decision-making process and facilitates the surgical procedure using appropriate intraoperative real-time visualizations.

Methods

Two hyperspectral snapshot mosaic cameras with sensor resolution of 2048x1080 pixels, equipped with a 75mm/F2.8 optic, covering 430nm to 630nm with 16 spectral bands and 670nm to 975nm with 25 spectral bands, are used as a stereo-imaging setup. A developed modular acquisition and processing pipeline uses model-based as well as data-based algorithms allowing continuous intraoperative image analysis of the hyperspectral stereo images. The processing pipeline covers demosaicking for increasing the spatial resolution, the reconstruction of tissue reflectance and absorption with calculation of different physiological parameters and vital signs as well as tissue differentiation, the 3D stereo reconstruction for depth analysis and the visualization of all gained parameters.

Results

The system could be successfully tested intraoperatively and its modularity and visualization allow specific system setup and parameter selection for various surgical tasks. The different opportunities in continuous (1Hz) stereo-spectral analysis allow the visualization of patient-specific tissue behaviors, which is normally not visible to the human eye. The depth analysis enables accuracies in the sub-mm range for patient specific measurements. The visualization calculates an RGB representation augmented with selected additional tissue information using a color representation for e.g., SpO2, perfusion, water content, hemoglobin content and tissue differentiation.

Conclusion

This stereo-setup of two hyperspectral snapshot cameras allows real-time analysis of different optical tissue properties for image-guided surgery. Distinct tissue parameters can be visualized as well as specific structures can be measured. Thus, surgical processes could be accelerated and revision procedures reduced for an improved patient outcome.

Assessment of cortical hemodynamic response after functional stimulation by Intraoperative Optical Imaging and Fourier-based signal processing

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Introduction

Intraoperative Optical Imaging (IOI) is a marker free and non-invasive imaging technique that can be used during neurosurgical interventions for the visualization of specific functional brain areas and their spatial extent. Here, we are presenting a novel analysis and visualization approach for the imaging data that is based on a specific stimulation paradigm, the pixel wise evaluation of the temporal reflectance signal, and the subsequent evaluation of amplitude as well as phase information within frequency domain. This should allow a more detailed characterization of the hemodynamic response after functional stimulation and therefore lead to a gain of knowledge about cortical hemodynamic processes.

Methods

Datasets of 22 patients that underwent surgical resection of brain tumors were retrospectively evaluated with the new analysis approach. Different stimulation types were applied in the patients - sensory (electrical, median nerve, 15 patients), visual (flash light goggles, 3 patients), tactile (surgical brush, 3 patients), and speech stimulation (awake surgery, 3 patients), resulting in a total of 24 analyzed datasets.

Results

The results are showing that the new analysis method reveals significant differences in the hemodynamic nature of activations for the different stimulation types. On the primary sensory cortex, tactile stimulation evoked cerebral blood volume increases whereas electrical median nerve stimulation led in all patients to blood volume decreases (~180° respectively 30 seconds phase shift compared to tactile stimulation). The evaluation of speech activations revealed that two types of hemodynamic responses within the activated areas in one patient can be observed. Both are characterized by the different signal phases and spatially closely located to each other.

Conclusion

Summarizing the results, the new evaluation and visualization approach reveals promising new insights into the nature of the underlying physiological processes of activated functional areas. This might enable a further optimized surgical treatment of brain pathologies in the future.

Network Architecture Influence on Facial Emotion Recognition

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Introduction

Artificial Intelligence has been blending into daily life by means of many useful applications from voice command to facial recognition. One therapeutic application to be supported by AI solutions is treatment of people with Autism Spectrum Disorder. A closed loop feedback system is planned in conjunction with a novel reward system that will encourage the user to express emotions and be rewarded for it in a virtual environment.

Methods

In this work five popular neural network architectures of VGG16, ResNet50, GoogleNet, ShuffleNet and EfficientNetb0 are studied and compared, with the aim of finding a relation between accuracy and developed features based on the network architecture, for the application in Facial Emotion Recognition (FER). Three datasets were used, the OULU-CASIA for training and validation, alongside FACES and JAFFE for robustness analysis. The images were first pre-processed to eliminate background noise. The performance of the model was based on the true positive predictions with Grad-CAM prediction visualizations to visualize the focus of the networks in making decisions for classification.

Results

Results showed that architectures of high parameter space i.e., VGG16 performed best in terms of model accuracy, this contrasted with the visualizations data that suggested otherwise. The visualizations data revelead that lowest accuracy, the ResNet50, performed best in terms of informative feature area focus. This was attributed to the different layer combinations as well as parameters used for feature extraction.

Conclusion

The findings revealed that network architecture design had more influence on the region of impact than on classification results. The shallow depth networks with high parameter space performed better than deep networks with low parameter space for FER application. Testing on a closed loop system is planned with a general user interface already established, with further tests and analyses to be carried out in real time.

Challenging requirements and optical depth estimation techniques in laparoscopy

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Introduction

Minimally invasive surgery has many advantages and cannot be missed nowadays. It leads to faster recovery and less surgical trauma. In laparoscopic surgery years of training are required to optimize patient outcomes. To visually support the surgeon during stomach surgery a 3D reconstruction of the whole organ shall be created prior and during the procedure. Results might be beneficial for various applications such as before-and-after documentation, navigation support and autonomous robotic surgery.

Methods

The technical implementation of 3D-reconstruction requires depth estimation which is challenged due to the environmental conditions and surgical constraints that exist in the human body during minimally invasive surgery. This paper focuses on the requirements of 3D-reconstruction in laparoscopy, reveals the current research challenges and proposes an evaluation framework for optical depth estimation techniques. Scores considering the requirements were established and assigned to each technique.

Results

Eight techniques were included in the evaluation.The methods Deformable Shape-from-Motion, Stereoscopy, Shape-from-Motion, Simultaneous Localization and Mapping, Light Field Technology and Structured Light were shown to partially fulfill the requirements for laparoscopic 3D-reconstruction. Shape-from-Shading and Time-of-Flight need extensive modifications to be applicable.

Conclusion

In conclusion, it can be stated that currently no method exists to realize a real time high-resolution 3D-reconstruction of inner organs during endoscopy.

Track:
Imaging Technologies and Image Analysis

Monitoring the gelation of gellan gum with torsion rheometry and brightness-mode ultrasound

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Introduction

Gellan gum is a hydrogel with applications in ultrasonic imaging, novel drug delivery, and tissue regeneration. As hydrogels are dynamic entities, their viscoelastic properties and therefore their acoustic properties change over time, which is of interest to monitor. To determine the speed of sound from brightness-mode images, rather large quantities of hydrogel are needed. We investigated torsion rheometry as a means to determine acoustic properties.

Methods

We derived a theoretical time-variant perceived speed of sound of gelating isotropic hydrogel undergoing periodic shear displacement from the Maxwell representation of a Zener model. According to theory, the perceived speed must converge to the true speed of sound at time infinity.
Perceived speeds of sound were computed from experimental torsion rheometry measurements of gelating gellan gum mixed with spermidine trihydrochloride crosslinker. For comparison, brightness-mode ultrasonic images were recorded of the same material in a cuboid well inside a tissue-mimicking phantom, and the speed of sound was measured from the travel times between well interfaces. The rheometry experiments were limited to one hour.

Results

The speed of sound measured from the brightness-mode images appeared to drop from $1542\pm$ 211 m/s at 240 s to $1481\pm$ 176 m/s after 3600 s.
The perceived speed of sound computed from the rheometry data had risen to 1379 m/s after 3600 s.
The latter curve could be simulated using the theoretical model derived.
The rheometry data converged to a speed of sound within a standard devitation of the speed of sound measured from the brightness-mode images. Given the minute quantity of hydrogel needed for rheometry experiments, this outcome shows great promise for determining acoustic parameters of gelating biomaterials that do not exist in bulk, including tissue samples.

Conclusion

We have shown that dynamic acoustic properties of gelating gellan gum can be simulated and experimentally determined using torsion rheometry.

Micro-computed tomography and brightness-mode ultrasound show air entrapments inside tablets

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Introduction

Purposeful slow disintegration of pharmaceutical tablets has been of interest for consistency checks in industry and for controlled drug release in vivo. Subjecting tablets to low-amplitude ultrasound has been known to increase the swelling rate and to accelerate the disintegration process. This has been attributed to the internal damage caused by pulsating microscopic air entrapments under sonication. In this study, we investigated the existence of such pockets by subjecting tablets to micro-computed tomography and brightness-mode ultrasound.

Methods

Analgesia tablets inside a acrylonitrile butadiene styrene scaffold were positioned on a rotating plate and subjected to micro-computed tomography using a MicroXCT-400 device (Carl Zeiss AG, Oberkochen, Germany) with an X-ray source operating at a 10-W power and an 80-kV peak voltage. Sonic tablet disintegration was performed on tablets from the same production batch, using the HFL38x 13-6-MHz linear probe of a SonoSite® M-Turbo® sonography device (FUJIFILM Sonosite, Inc., Bothell, WA, USA) operating in musculoskeletal pulse brightness mode.

Results

The tablets were measured to have an ultrasonic swelling rate of $162 \pm 16\ \mu m\ s^{-1}$. The micro-computed tomography images showed air pockets of up to 9 μm in diameter, some of which were visibly connected to each other. The brightness-mode images showed scattering activity inside the tablets. The low standard deviations in swelling rate confirmed earlier findings. Furthermore, this finding justifies the use of different tablets from the same batch in this investigation. We associate the scattering activity to cavitation-related behaviour. Empirical relations between solid-encapsulated gas scatterer size suggests the relatively large microcavities observed in this tablet are the strongest scatterers.

Conclusion

Microscopic air entrapments exist inside the tablets studied. We may assume that these entrapments are causing the pulsations that have been detected with brightness-mode ultrasound.

Feature-based Differentiation of Malignant Melanomas, Lesions and Healthy Skin in Multiphoton Tomography Skin Images

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Introduction

Malignant melanoma is a very aggressive tumour with the ability to metastasize at an early stage. Therefore, early detection is of great importance. Multiphoton tomography is a new non-invasive examination method in the clinical diagnosis of skin alterations that can be used for such early diagnosis.
In this paper, a method for automated evaluation of multiphoton images of the skin is presented.

Methods

The following features at the cellular and subcellular level were extracted to differentiate between malignant melanomas, lesions, and healthy skin: cell symmetry, cell distance, cell density, cell and nucleus contrast, nucleus cell ratio, and homogeneity of cytoplasm. The extracted features formed the basis for the subsequent classification. Two feature sets were used. The first feature set included all the above-mentioned features, while the second feature set included the significantly different features between the three classes resulting from a multivariate analysis of variance. The classification was performed by a Support Vector Machine, the k-Nearest Neighbour algorithm, and Ensemble Learning.

Results

The best classification results were obtained with the Support Vector Machine using the first feature set with an accuracy of 52 % and 79.6 % for malignant melanoma and healthy skin, respectively.

Conclusion

Despite the small number of subjects investigated our results indicate that the proposed automatic method can differentiate malignant melanoma, lesions, and healthy skin. For future clinical application, an extended study with more multiphoton images is needed.

Evaluation of methods for 3D imaging and analysis of vascularization in biopreparations

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Introduction

Within the field of bio-implants one hot topic deals with the in-vitro production of 3D tissues from cell cultures. A major challenge is the imitation of complex and functional tissue structures, such as vascularization.Specifically, the vascular system with its surrounding tissue is of great importance for cultivation of bio-preparations, as it provides nutrients and oxygen to the cells. With an adequate blue-print from high-resolution 3D radiographs, the vascularization could be manufactured additively.

Methods

To provide such blue-prints, the vascular structure of small tissues samples (partially treated with contrast medium) were recorded using high-resolution CT and MRI imaging modalities and optimal measurement parameters were selected for the acquisition of very small vessels. From all acquired data, interactive and semi automated segmentation of the vessel system were performed.

Results

Duration of the interactive segmentation ranges between 1 to 12 hours, The runtime of the (semi) automatic method was between 5 and 20 minutes, not counting manual adjustment of the parameters. Correlation between manual and automatic segmentation yield Hausdorff distances of 0.024 (CT) and 0.74 (MRI) and Dice coefficients of 0.7 (CT) and 0.39 (MRI).

Conclusion

Both imaging methods are appropriate for high-resolution vessel detection and segmen- tation, nevertheless, MRI with no contrast agent seems prefer- able if the imaging time can be reduced.

BigBrain-MR: Development and in-vivo validation of a multimodal digital phantom for Magnetic Resonance Imaging methods at 100 µm

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Introduction

The growing availability of powerful magnetic resonance imaging (MRI) systems that allow sub-millimeter resolution imaging has created a need for new simulation platforms to help develop high-resolution imaging methods. Here, we present BigBrain-MR: a new simulation framework for mapping real MR properties (obtained from in-vivo data) to the fine structural scale of BigBrain, a publicly available histological brain dataset collected with optical methods at 100µm. To validate this digital phantom, we compared its behavior with respect to in-vivo data in two relevant applications: (i) super-resolution imaging (SR) and (ii) parallel imaging reconstruction (PI).

Methods

BigBrain-MR: Multimodal in-vivo 7T MRI data were acquired from a healthy adult at 0.6mm isotropic resolution; the sequences included a broad range of MR properties such as T1, R2*, and magnetic susceptibility. The in-vivo data were mapped to BigBrain space at 100µm using a framework which includes non-linear registration, region-specific contrast mapping, and a partial volume model for the region borders.
SR-validation: We investigated an approach to reduce slice thickness (3x), acquiring multiple images with systematic position shifts along the slice axis. The estimation was implemented as an inverse problem with wavelet regularization.
PI-validation: We investigated PI methods for accelerated MRI relying on different undersampling schemes (e.g. CAIPI, Poisson disk) and using wavelet-regularized SENSE.

Results

The framework successfully yielded a multimodal phantom with realistic MR properties, at a fine resolution comparable to the original BigBrain (100µm).
SR-validation: The dependence of image sharpness and noise on the regularization weighting was comparable in both BigBrain-MR and in-vivo.
PI-validation: BigBrain-MR and the in-vivo data showed similar dependences on acceleration factor, sampling scheme, and regularization weighting.

Conclusion

Real-data validation indicates that this novel multimodal digital phantom constitutes a valid and useful simulation tool for ultra-high resolution methods development. This platform will be made publicly available to the community.

Algorithm for papilla depth measurement in light field fundus images for glaucoma diagnosis

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Introduction

In glaucoma diseases, morphological changes at the optic disc occur in the form of increased deepening in the disease's early stages. Light field fundus cameras offer the opportunity to capture 3D images of the papilla with only one shot. We present an automatic processing line for this novel imaging system to determine the optic cup depth, which is a diagnostically relevant parameter.

Methods

Processing of light field data was performed using a mathematical model with radial basis functions for noise reduction. The positions of the optic disc and the optic cup were defined by analyzing rising and falling edges. Based on those contours, maximum cup depth was determined as the distance between the deepest point and the mean height of the optic cup boundary.

A first validation was performed in a study with 14 healthy participants (6 female, 8 male, aged 29.3 ± 7.5 years). To analyze reproducibility, 15 images of one eye of each volunteer were taken with the light field fundus camera (FF450 from Carl Zeiss Meditec AG with light field imager R12 from Raytrix GmbH) and analyzed with the developed processing line. As reference data we used optical coherence tomography (Spectralis-OCT with Glaucoma Module Premium Edition from Heidelberg Engineering GmbH) and measured the vertical distance between the Bruch membrane opening point and the deepest point in the cross-sectional images with the associated software.

Results

Seven subjects showed a quantifiable optic cup and were included in the evaluation. The determined maximum optic cup depth of the novel imaging system agreed well to reference data. There was a median difference of -0,07 mm and a correlation coefficient of 0,85 ($p<0{,}05$).

Conclusion

The data from the light field fundus camera are suitable for the determination of optic cup depth. The created processing line offers a first possibility to evaluate the data.

Volume registration of in vivo confocal microscopy datasets of the human cornea - a comparison of two novel approaches

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Introduction

In vivo corneal confocal microscopy (CCM) with a computer-controlled focus drive can be used for volume reconstructions of the corneal tissue. So far, all volumetric approaches remain limited to 3D reconstructions from single CCM focus stacks. This contribution presents two approaches for laterally expanded volume reconstruction from CCM image sequences where the focus oscillates along a triangular wave function.

Methods

Both proposed methods initially require an exhaustive, pairwise, correlation-based 2D image registration to eliminate motion artifacts in the recorded CCM images. The continuous, motion-corrected image sequence is separated into stacks, each representing a single rising or falling part of the oscillation. The first method implements a correlation-based 3D registration. The separate image stacks are transformed into (motion-corrected) volume images and then registered pairwise. The second method infers information on the relative image depth from the exhaustive 2D registration process. The underlying assumption is that overlapping image pairs from the same tissue depth yield higher correlation values than image pairs recorded at differing tissue depths.

Results

The proposed methods were each applied to 40 oscillating focus datasets of the corneal epithelium of 11 healthy individuals, each dataset containing approx. 10 full focus oscillations. The 3D registration results of the first approach prove to be very robust, but the 3D correlation computations are extremely time-consuming (116.3±15.0 minutes per dataset; MATLAB implementation on Intel Core i7-6700 CPU). The second approach is much faster (6.1±4.7 minutes per dataset), but less reliable. A threshold is therefore required to exclude incorrect depth inference results, which necessarily excludes a substantial portion of correct results as well.

Conclusion

Laterally expanded volume reconstruction from CCM image sequences with oscillating focus is feasible but time-consuming. The 3D correlation-based approach may be used in research settings to examine the diagnostic potential of such registered volumes with cellular to sub-cellular resolution.

Measurement of contact prestrain in OCT-based pipette aspiration

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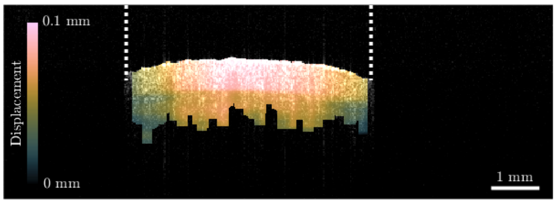
Introduction

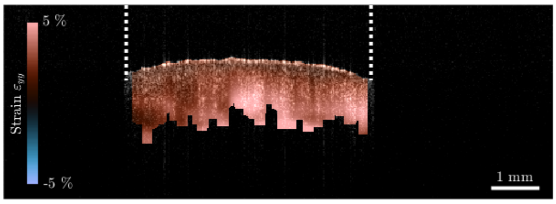
The pipette aspiration technique is well established to measure the material properties of cells, skin, and soft tissue. The benefit of this technique is that the load is transferred by air pressure which sucks the tissue into a small pipe. This eliminates the need for a complicated loading device. The method was extended by our group in a dynamic alternating pressure load to measure the viscoelastic properties of porcine vocal folds. In this approach the movement of the tissue is measured by an optical coherence tomograph.

Methods

The transfer of an alternating load requires contact between the tissue and the pipette, which causes a prestrain. This leads to a hardening of the material enclosed by the pipette and consequently to a measurement error that is difficult to control. This prestrain can be measured, using an optical flow algorithm that estimates the displacement between the non-contacted tissue and the loaded tissue.



Magnitude of the displacement



Strain ε_{yy} in compression direction

Results

The figure shows the displacement and the strain in a silicone specimen due to the contact with the pipette, whereby the edge of the pipette is indicated as dashed white line. The displacement with respect to the edge of the pipette in the sample is maximum at the surface in the center and largest strain is seen in the center of the specimen.

Conclusion

This work showed that the prestrain in the tissue can be measured and included in the analysis of the data. The quantification of the enhancement will be evaluated in the further work.

Impact of Annotation Noise on Histopathology Nucleus Segmentation

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Introduction

Deep learning is often used for automated diagnosis support in biomedical image processing scenarios.
Annotated datasets are essential for the supervised training of deep neural networks. The problem of consistent and noise-free annotation remains for experts such as pathologists. The variability within an annotator (intra) and the variability between annotators (inter) are current challenges.
In clinical practice or biology, instance segmentation is a common task, but a comprehensive and quantitative study regarding the impact of noisy annotations lacks.

Methods

In this paper, we present a concept to categorize various types of annotation noise (oversized, undersized, contour, merged, split, jitter, holes, approximation, forgotten). Methods for simulating intra-annotator variability and inter-annotator variability are shown. In addition, the concept includes an evaluation part to investigate the impact of annotation noise on deep learning pipelines.

Results

We use the multi-organ histology image dataset MoNuSeg to discuss the influence of annotator variability.
a) Intra: The corruptions of "approximation", "jitter", and "holes" lead to no performance degradation, but "forget", "contour", "undersized", and "oversized" show strong performance reduction .
b) Inter: Excluding a single outlier (no corruption/approximation), all other combinations of corruptions yield a strong decreasing DNN performance.

Conclusion

We categorized different forms of annotator variability in instance segmentation for the first time and proposed a concept to investigate its impact on DL pipelines. Minor annotation noise of a single annotator (intra) leads to no quantifiable performance drop. Nevertheless, the corruptions of forgetting instances, undersized/oversized instances, and missing filling of instances should be avoided to achieve high-quality DNNs. We demonstrated that different annotation styles (inter) are a major issue w.r.t. DNN performance. The agreement of annotation policies is necessary in division labor cases.

Explaining and Evaluating Deep Tissue Classification by Visualizing Activations of Most Relevant Intermediate Layers

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Introduction

Deep Learning-based tissue classification may support pathologists in analyzing digitized whole slide images (WSIs). However, in such critical tasks, only approaches that can be validated by medical experts in advance to deployment, are suitable.

Methods

We present an approach that contributes to making automated tissue classification more transparent. We step beyond broadly used visualizations for last layers of a convolutional neural network by identifying most relevant intermediate layers applying Gradient-weighted Class Activation Mapping.

Results

A visual evaluation by a pathologist shows that these layers assign relevance, where important morphological structures are present in case of correct class decisions. We introduce a tool that can be easily used by medical experts for such validation purposes for any convolutional neural network and any layer.

Conclusion

Visual explanations for intermediate layers provide insights into a deep neural network's decision for histopathological tissue classification. In future research also the context of the input data must be considered.

Magnetic Resonance Current Density Imaging in Ex-Vivo Pig Hearts

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Introduction

Defibrillators use electric shocks to terminate life-threatening tachyarrhythmias of the heart. For the fundamental understanding and further optimization of defibrillation, the electrical current density in the myocardium is of particular importance.
Here, we describe the use Magnetic Resonance Current Density Imaging (CDI), focusing on the implementation of the CDI setup and a novel reconstruction method. We demonstrate the feasibility of the approach in an ex-vivo pig heart.

Methods

An explanted pig heart was submerged in Tyrode solution. ±5V were applied on two 7x6cm2 electrodes located at opposing sides of the heart, leading to a current of 0.23A.
MRI measurements were performed on a Skyra 3T scanner (Siemens Erlangen).
The current density was estimated from phase difference images reconstructed using BART (Uecker et al., 2021) using an iterative algorithm that inverts a forward model which predicts the phase from the current (Yazdanian et al., 2020).
From theoretical analysis and validation experiments, we expect our method to produce the projected current density (Park et al., 2007). Diffusion weighted images were acquired for reconstruction of fiber orientation.

Results

Quantitative analysis reveals that most current flows around the heart.
For cross-sections perpendicular to the main current direction, up to 23% of the current was inside heart tissue.
Magnitude image and streamline plot of the reconstructed current density are shown in Fig. 1, along with estimated fiber orientation.

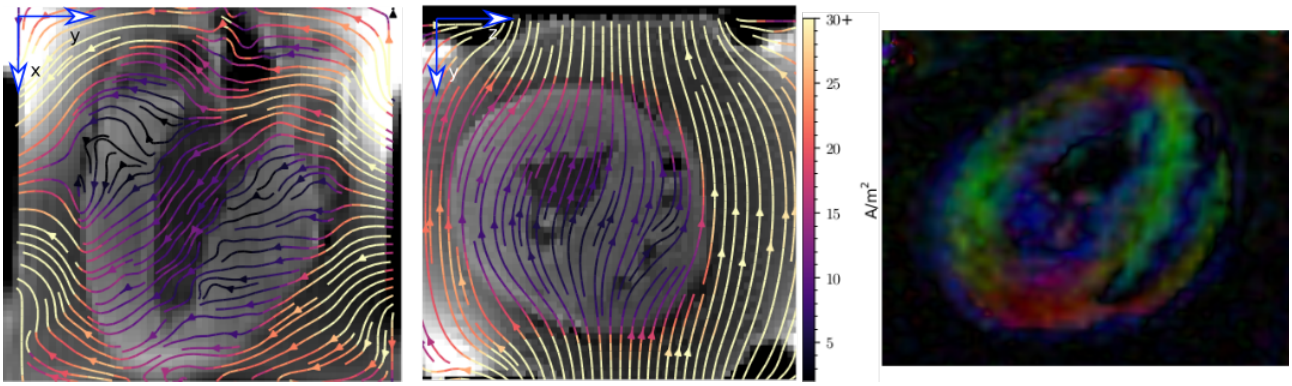

Figure 1

Preferred current paths in the heart are clearly visible from the figure. The Tyrode-filled ventricles apparently form a path of lower resistance. The reconstructed fiber orientation displays similarities to the current density patterns.

Conclusion

A new current density imaging setup was implemented and tested. Initial application to an ex-vivo pig heart shows promising results.

Prediction of Fluorescent Ki67 Staining in 3D Tumor Spheroids

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Introduction

3D cell culture models are important tools for the development and testing of new therapeutics. In combination with immunoassays and 3D confocal microscopy, crucial information like morphological or metabolic changes can be examined during drug testing.

However, a common limitation of immunostainings is the number of dyes that can be imaged simultaneously, as overlaps in the spectral profiles of the different dyes may result in cross talk.

Methods

We therefore present a 3D deep learning method, able to predict fluorescent stainings of specific antigens on the basis of a nuclei staining. For this, an adapted 3D ResUnet model is used. The training data is generated by imaging 3D spheroids stained for nuclei and the marker to be predicted. To evaluate our model, a correlation analysis is performed on a voxel and object scale level.

Results

Using the proliferation marker Ki67, we showed that the presented model was able to predict the Ki67 staining with a strong correlation to the real signal. Additional analysis showed, that the model was not relying on signal cross talk.

Conclusion

This approach, based on staining of the cell nuclei and subsequent prediction of the target antigen, could reduce the number of parallel antigen stains to a minimum and incompatible staining panels could be circumvented in the future.

Post-acquisition Framerate Improvement for Multi-channel Fluorescence Cardiac Microscopy

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Introduction

Optical fluorescence microscopy is a powerful tool for imaging the development of organs within animal models. The heart is particularly challenging to observe as the fast contractions of small size require particularly high frame rates. The weakness of the fluorescence signal requires sensitive cameras, which have a limited frame rate that is often insufficient to capture the fastest motions of the heart. Furthermore, post-acquisition synchronization of multi-color fluorescence sequences is only possible for high frame rate sequences with strong mutual information, which prevents usage for uncorrelated signals.
Here we propose a method to virtually increase the frame rate of image series of the beating heart, that can be implemented with low frame rate cameras by switching illumination in patterns and acquiring images over multiple heartbeats and multiple wavelength channels.

Methods

We use a light-sheet microscope with a custom-built illumination controller synchronized with the camera. We propose an illumination protocol that alternates between low-intensity bright-field signals and high-intensity laser signals. We combine the acquired images in a post-processing step that sorts the sequences using the bright-field signal as a common reference. We carried out simulation experiments on a multi-channel synthetic phantom of a beating heart.

Results

Our experiments show that the frame rate can be virtually increased with a performance that depends on the number of reference images and the noise level at which they can be acquired.

Conclusion

Our proposed solution both solves the problem of insufficient frame rate by virtually increasing it, as well as the temporal registration of uncorrelated multi-channel image sequences. The observed performance increase is sufficient to observe motions at speeds typically encountered in cardiac imaging. We foresee that this method can be implemented in a wide variety of existing multi-channel imaging problems of repeating phenomena observed under controlled lighting.

Differentiation of COVID-19 Conditions using Mediastinum Shape in Chest X-ray Images

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Introduction

Coronavirus Disease-2019 (COVID-19) is an infectious viral disease that is affecting the world with high morbidity and mortality. Chest X-ray (CXR) is considered a screening and triage tool for the detection of COVID-19 manifestations. These radiological manifestations are reported to cause shape variations in both mediastinum and lungs. In this work, an attempt has been made to analyze the shape variations in mediastinum for differentiation of normal and COVID-19 conditions in chest X-ray images.

Methods

For this study, the images are obtained from the COVID-19 Radiography Database, a publicly available database. Segmentation of mediastinum from the raw images is performed using Reaction Diffusion Level Set (RDLS) method. Fifteen shape-based features are extracted from the delineated mediastinum masks and are statistically analyzed. Further, the features are fed to two classifiers, namely, multi-layer perceptron and support vector machine for differentiation of normal and COVID-19 images.

Results

Results show that the employed RDLS segmentation method is able to delineate mediastinum from the raw CXR images. Eight shape features, namely, area, perimeter, convex area, major and minor axis length, equivalent diameter, maximum and minimum feret diameter are found to be statistically significant ($p < 0.01$) between COVID-19 and normal conditions. The mean values of these features are found to be distinctly higher for COVID-19 images as compared to normal images. Maximum Area Under the Curve (AUC) of 78.9% and F-score of 73.7% are achieved by the SVM and MLP classifiers, respectively.

Conclusion

The proposed approach using mediastinum shape analysis is found to better characterize and differentiate COVID-19 and normal subjects in CXR images. The extracted shape features are observed to provide significant discrimination between COVID-19 and normal images. Hence, it appears that mediastinum could be used as a region of interest for computerized detection and mass screening of the disease.

Robust Colon Tissue Cartography with Semi-Supervision

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Introduction

Deep Learning based approaches have been successfully applied in computational histology. While large amounts of data are often available and easy to gather, the lack of experienced experts for data annotation often bottlenecks successful model training in this context. Therefore, learning approaches that enable robust model training even with a small amount of annotated data are desirable. Semi-supervised learning has shown promising results in other image-based domains to improve predictive algorithms with few labeled data incorporating large amounts of unlabeled data.

Methods

In this work we compare the semi-supervised algorithm FixMatch with a strong supervised EfficientNetB0 baseline challenging the task of tissue classification for colon cancer histology in a realistic few label data regime. We further explore their generalization capabilities on a multiscanner database.

Results

Overall, we are able to yield a strong performance with relatively few annotated samples across both semi- and supervised model training. For instance, the SSL (supervised) model trained on 1,000 samples per class yields a test accuracy of 91.37% (89.89%) closing in on the fully supervised baseline trained on a total of 400,000 labeled patches which yields a test accuracy of 93.76%. In terms of model robustness w.r.t distribution shifts in the unlabeled data, we find the semi-supervised model to be prone to overfit on the unlabeled data distribution. Further, we confirm that semi-supervision can lead to increased model robustness w.r.t. to domain shifts across different scanners in our specific application.

Conclusion

In conclusion, we were able to successfully employ SSL algorithms in the field of histopathology. Performance improvements provided by the unlabeled data were limited and simple supervised models were able to compete in terms of performance and domain robustness with tailored augmentations. Further research is needed to leverage knowledge more effectively from unsupervised data in the described setting.

Dependencies in Glenoid Bone Mineral Density of Normal and Pathological Shoulders

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Introduction

Glenoid bone quality can be of critical importance for several shoulder pathologies and treatments. Our objective was here to evaluate the associations between glenoid bone mineral density (BMD) and sex, age, weight, and height, of normal and pathological subjects with primary osteoarthritis (OA).

Methods

We considered 91 (64 males, 27 females; age range, 50-83 years) computed tomography (CT) scans of the shoulder without any sign of pathology (normal) and 43 (12 males, 31 females; age range, 51-86 years) computed tomography (CT) scans of the pathologic shoulders. We automatically quantified BMD in six VOIs: cortical (CO), subchondral cortical plate (SC), subchondral trabecular (ST), and three adjacent layers of trabecular bone (T1, T2, and T3) as CT numbers in Hounsfield units (HU). To evaluate the dependency of BMD on age, sex, weight, and height, we developed a Bayesian model that considered BMD (cortical and trabecular) to be a Gaussian distribution. Sex, pathology (normal and pathological), age, weight, and height were the predictors. We also counted for the possible effects of sex, age, and pathology on weight and height in this model. Hamiltonian Monte Carlo (HMC) was used to build the posterior BMD distribution, and the effect of each predictor was first assessed separately and then assessed together by extracting samples from the posterior distribution.

Results

BMD was higher in males than females, for both cortical and trabecular VOIs, and normal and pathological shoulders. Pathological shoulders had a higher BMD than normal ones, especially in the trabecular bone. There was a negative correlation between BMD and age for all subjects. Compared to age, the effect of weight and height on BMD was negligible.

Conclusion

The present Bayesian analysis of potential dependencies of the glenoid BMD with patient characteristics could be helpful to improve the treatment of some shoulder pathologies.

Radial compliance of porcine coronary arteries ex vivo under pulsatile flow - perspectives for stent biomechanics

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Introduction

Knowledge of the elastic properties of arterial vessels is of huge importance to understand physiological and pathophysiological phenomena of blood flow. Here, the focus is on physiological data in order to match the biomechanics of vascular implants properly to the target vasculature. The aim of the current study was to upgrade an existing test setup for determination of the radial compliance of porcine coronary arteries ex vivo using a pulsatile pump to gain pulsatile flow conditions during intravascular optical coherence tomography (IV-OCT) measurements.

Methods

A porcine heart was prepared ex vivo obtaining an access to the left circumflex artery. Pulsatile flow was generated by a pulsatile pump inducing normotensive (about 120/80 mmHg) as well as hypertensive pressure ranges (about 160/100 mmHg) at different pulse rates ranging from 60 bpm to 140 bpm. Reference measurements under steady flow were performed using a centrifugal pump. The radial compliance was derived from diameter measurements via IV-OCT using a Dragonfly OPTIS Imaging Catheter (Abbott Medical) in combination with the ILUMIEN OPTIS PCI Optimization system (St. Jude Medical).

Results

The calculated radial compliance for the normotensive as well as hypertensive pressure range was largest during steady flow conditions (8.74 %/100 mmHg and 6.94 %/100 mmHg, respectively) and reduced at pulsatile flow from 4.01 %/100 mmHg to 4.65 %/100 mmHg and 3.11 %/100 mmHg to 3.84 %/100 mmHg, respectively. Average radial compliance decreased with increasing pulse rate. However, differences were not statistically significant.

Conclusion

Radial compliance under pulsatile flow conditions was significantly lower than measured at steady flow and further reduced with increasing pulse rate. This was found at normotensive as well as hypertensive pressure range. These effects can be attributed to the viscoelastic properties of the arterial wall, showing a stiffer behavior with higher loading velocity. The examined compliance data are useful to adapt the mechanical properties of vascular prostheses.

Assessing regional pulmonary perfusion using dual-energy computed tomography - A comparison with fluorescence labelled microspheres

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Introduction

Distribution of pulmonary perfusion (PPF) may be an important clinical marker to estimate ventilation-perfusion matching and thus differentiate ventilation and diffusion originated hypoxemia. Dual-energy computed tomography (DECT) allows the determination of pulmonary perfused blood volume, a surrogate of PPF, in three-dimensions with high spatial resolution without injection of radioactive tracers. To evaluate the clinical eligibility of DECT based PPF determination it is compared to fluorescence labelled microspheres (FLM) during different conditions of ventilation and perfusion in pigs during one lung ventilation (OLV) and right-sided thoracotomy.

Methods

This is a sub-analysis of data from three pigs. DECT was acquired on a SOMATOM Definition Edge scanner (120kVp, 384mAs, 1mm^3; isotropic voxel) following injection of iodine contrast agent (60ml with 4ml/s). For FLM based PPF determination, colour-coded microspheres (five colours, 15µm diameter) were injected at every measurement. Fluorescence measurement was performed post-mortem after inflating, drying, foaming and cutting the en-bloc extracted lungs into 12mm isotropic voxels. Changes in PPF were induced by switching from two-lung ventilation to left-sided one-lung ventilation (OLV) with four concentrations of inhalative nitric oxide (iNO=0,5,10,20ppm). Relative mean and lung mass normalized PPF were compared for three regions of interest (ROI): right lung, left-caudal and left-cranial lung. Shunt fraction was derived using standard formulae.

Results

Overall linear regression analysis yielded a slope=1.33 and respective coefficient of determination R^2=0.81, P<0.001. The slope of the regression analysis was highest in cranial left ROI (1.67, R^2=0.87) and lowest in the right lung ROI (1.16, R^2=0.89). Concordance of changes was 69.4% with slope=1.08. For OLV measurements there was no association between both methods, but only DECT measurements were in line with effects of different iNO concentrations on shunt fraction.

Conclusion

DECT compared to FLM based PPF determination showed good agreement with reduced scatter and higher sensitivity making it eligible for clinical use.

Neural Network Classification of Surgical Tools in Gynaecological Videos

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Introduction

Surgical tool detection is a key component in the development of context-aware systems (CAS) that will improve pa-tient safety and outcome. Laparoscopic videos represent a rich source of data. Thus, surgical tool detection in laparo-scopic videos has been extensively studied. Convolutional neural network (CNN) approaches have become dominant in the surgical tool recognition task. Previous research tackled this task mainly in cholecystectomy procedures due to availability of a relatively large and labelled set (Cholec80 dataset). However, the complexity of the procedure type has an impact on the robustness of the deep learning approaches. Therefore, the classification capability of CNNs on data of more complex procedures was investigated. In this work, the performance of a CNN base model was evaluated on performing surgical tool classification in laparoscopic gynaecology procedures.

Methods

In this work, laparoscopic videos of fourteen gynaecological procedures were recorded at the Schwarzwald-Baar clinic. The videos were labelled for surgical tool presence at 1 Hz. The surgical tools observed were grouped into main classes according to functionality. The DenseNet-121 model was employed to identify surgical tools in gynaecological images. The architecture of the model was modified to carry out a tool classification task. The data of 10 videos were used for training, while the remaining data were used to evaluate model performance.

Results

Experimental results imply high classification performance for some surgical tools such as grasper and bipolar with an average precision of 86% and 91%. The mean average precision over all the tools was 67%.

Conclusion

The complexity of surgical procedures affects CNN model training and classification performance. This study demonstrates classification capability of DenseNet-121 model on gynaecology data. The presence of various makes of some tools affected the model performance. Thus, more investigations are required to improve classification robustness for tools that have different fine types.

Transfer Learning in Facial Emotion Recognition: Useful or Misleading?

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Introduction

The use of machine learning in medicine holds a lot of potential in the domains of patient diagnosis, monitoring and treatment. One such application is the use of Emotion intelligence to aid in the treatment of people suffering from autism spectrum disorder (ASD). As training a robust network model requires large datasets, transfer learning is often implemented. The aim of this study is to show if using pre-trained weights, trained on different images, as an initial starting point for training a new model remains biased after training and does not generalize well to unseen data of the new trained model.

Methods

Image pre-processing was performed and the data trained on three models, the base model of VGG16 architecture and two with attention modules of SE and CBAM. The OULU-CASIA database was used for training with 10-fold cross validation for evaluating the performance of the model and the robustness was tested against two other emotion datasets of FACES and JAFFE.

Results

The results showed the training from scratch had better adherence to the regions of importance in the image.

Conclusion

This validates the hypothesis that prior knowledge, i.e. weights from pre-trained models of large datasets, may not be usable for special applications.

Attention Networks for Improving Surgical Tool Classification in Laparoscopic Videos

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Introduction

Deep learning approaches have been extensively developed to promote intelligent applications, such as surgical tool detection in surgical videos, inside the operating rooms (ORs). However, robustness and high-performance accuracy are demanding for such high-risk applications.

Methods

Attention Modules of Squeeze and Excitation (SE) and Convolutional Block Attention Module (CBAM) were employed and evaluated for improving surgical tool classification in laparoscopic videos.

Results

Experimental results explicate the advantage of both attention modules to the tool classification task. The SE and CBAM achieved mean average precision (mAP) of 88.38% and 88.40%, respectively, compared to 86.35% achieved by the base CNN model.

Conclusion

Attention modules improved the performance of the models with a range of 2%. They were also able to overcome the imbalanced data problem and helped focus the network on more informative features.

Quality assessment of clinical thorax CT images based on spectral and spatial features

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Introduction

Computed tomography (CT) image quality is affected by different parameters such as patient motion and anatomy, detector design, scatter, and others. The quality of CT images is not automatically analyzed by the scanner software in clinical routine. Introducing continuous monitoring of CT image quality would be beneficial for diagnostic purposes. In addition, it could be used to reduce the applied dose. Most of the existing image quality analysis approaches are based on dedicated phantoms. Our work proposes a method which combines the modulation transfer function (MTF), the frequency spectrum and the noise power spectrum (NPS) in a predefined regions of interest (ROI) and is applied to clinical thorax CT images.

Methods

Thorax CT images were acquired from 30 patients. Different radiologists annotated the images by different quality levels. In this initial study, two quality levels (either "low" or "high") were used. An ROI containing the major fissure of the left lung was manually selected and was used to estimate the image quality. The MTF was computed using the edge and line scan functions of the major fissure within the selected ROI. The edge was automatically detected using an active contour algorithm. In addition to the MTF, the frequency power spectrum of the ROI was estimated. The NPS was estimated from a homogenous area close to the major fissure. Based on the parameters, several features were derived to determine the image quality. A classifier was trained using these features.

Results

Using the estimated features, a classification accuracy of 89% was achieved using the validation data set.

Conclusion

Several features were defined to analyze the quality of clinical patient CT images. The classification results were in high agreement with the manual annotation performed by radiologists. Future work will include additional features and CT images to further improve and validate this approach.

COVID-19 Pneumonia Phenotypes Detection with Electrical Impedance Tomography

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Introduction

The course of the COVID-19 pneumonia is still poorly understood and has shown to evolve over time. The evolving pathophysiological characteristics is related to the progressive variation of respiratory mechanics. A large proportion of ICU-admitted severe respiratory failure cases of COVID-19 pneumonia fulfil the Berlin definition of acute respiratory distress syndrome (ARDS). Despite sharing the same etiology, COVID-19 induced ARDS is reported to have at least two different phenotypes. Different responses of patients, namely, recruitability, to a positive end-expiration pressure (PEEP) trial are found in different phenotypes. A common method to identify the COVID-19 pneumonia phenotype is through CT, but frequent CT-scans is not practical. It is suggested that bedside monitoring tools, such as electrical impedance tomography (EIT), can play an important role in detecting different COVID-19 pneumonia phenotypes.

Methods

Four severe COVID-19 pneumonia patients were included in our study. The same PEEP trial was carried out on each patient. During the PEEP trial, the patients' regional lung activities were monitored by EIT. Four patients were monitored for 2, 7, 4 and 12 days, respectively. Using the EIT functional image, we analysed lung recruitability in terms of accumulative overdistention and collapse ratio to identify the patient response to a PEEP trial.

Results

The results demonstrated that COVID-19 pneumonia patients respond differently to the same PEEP trial protocol, with which the patients' phenotypes were detected. EIT also showed the developing change of lung recruitability over time. In one patient, a possible phenotype transition was identified.

Conclusion

It is demonstrated that different patient responses to PEEP trials and showed the progressive change in patient status over time. EIT is capable of COVID-19 phenotype detection. We suggest that EIT may be a practical tool to identify phenotypes and to provide information about COVID-19 pneumonia progression, which facilitates decisions for an optimized treatment.

Patch Based Classification of Cell Painted ER and Cytoplasm using Block Intensity Gradient Pattern and Multilayer Perceptron

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Introduction

Differentiating cell organelles in microscopic images is a challenging task due to their high similarity in visual appearance. In this work, an attempt has been made to classify Endoplasmic Reticulum (ER) and cytoplasm using Block Intensity Gradient Descriptor (BIGD) and multilayer perceptron.

Methods

For this, Cell Painted public dataset from Broad Bioimage Benchmark collection are considered. In an image patch small squared regions called blocks at multiple scales are selected. Horizontal and vertical gradient feature vector is extracted from all block pairs at each scale and concatenating them to form the full image descriptor. Statistically significant features are selected based on the p value (< 0.05) and these discriminative features are fed to the multilayer perceptron for categorizing ER and cytoplasm. The performance of BIGD descriptor for accurate classification is evaluated for different patch sizes and block sizes.

Results

13x13 patch size at 4x4 block size achieved 96 % of classification accuracy. The results indicate that the classification accuracy increases with increase in image patch size for a fixed block size.

Conclusion

Experimental results demonstrate that BIGD texture feature could be useful for accurate classification of cell organelles by characterizing their dissimilarity in the cell structure due to cytological and cytotoxic effects.

Classification of Facial Expression using Convolutional Neural Network and Support Vector Machine

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Introduction

Facial expressions are a good indicator of a person's state of mind and can help to understand the feelings of others without using words. Since the human face is an important source of information, it can be considered as a non-verbal communication channel. Due to the individuality of humans, there are differences in the basic appearance and presentation, intensity and duration of an expression of an emotion. These differences complicate the recognition not only for a human being trained by everyday life, but also especially for a machine trained by general descriptions. In this work different methods to classify six basic emotions (Anger, Fear, Disgust, Happiness, Sadness and Surprise) and a neutral state are presented to demonstrate the potential of human-computer interaction.

Methods

For facial expression recognition a Convolutional Neural Network (CNN) is compared against classical feature engineering and classification based on geometric- and texture-based features. The CNN consists of four Convolutional Blocks, each with a Batch Normalization, Activation Function, Maxpooling and Dropout, two Fully Connected Layer and one Output Layer. Texture-based feature extraction composes the feature vector using the appearance (texture of the face), which can be the whole face or specific regions. Those features are classified with Support Vector Machine (SVM).

Results

Using the Extended Cohn-Kanade image database and dividing the data into training and testing sets, the CNN reached 87.7% accuracy on the testing set. An SVM classification with the Histogram of Oriented Gradients (HOG) featuretype could achieve 77.8%, while Local Binary Pattern (LBP) performed with 77.4%.

Conclusion

Classifying facial expressions is still a challenging topic. The approach using a Convolutional Neural Network produces convincing superior results in contrast to the classic approach using HOG or LBP features. Using multiple datasets should improve accuracy, which defines the next step to look at more closely.

Separating Respiration and Perfusion in EIT: Harmonic Analysis on 2D-Thorax Simulation

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Introduction

Electrical impedance tomography (EIT) has the potential for monitoring perfusion in addition to respiration on the bedside. Several separation methods were reported, e.g. Filtering, ECG-gating and PCA. However, the separation is not trivial, which is why harmonic analysis was introduced in EIT data analysis. It is based on several assumptions and therefore prove of plausibility is necessary.

Methods

In this contribution a two-dimensional thorax simulation is introduced, which includes simplified lungs and heart with changing shapes and conductivities due to volume variations and lung perfusion. Harmonic analysis was applied on the simulated data.

Results

The separation results are in good agreement with the simulation settings.

Conclusion

Further investigations will be required due to limitations of the simulation. Nevertheless, harmonic analysis delivered precise results in ideal and strictly defined conditions

Time Series Based Human Gait Analysis using Gait Events Detected from Videos

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Introduction

Gait analysis is important to detect gait disruptions, understand postural disturbances, and assess recovery and evaluation process. Different methods have been developed for this purpose including Inertial Measurement Unit (IMU) sensors, wearable devices, video-cameras interfaced with computer, placement of electrode on skin, force plates, foot switches and many others. These all require strict laboratory environment and other conditions. In this study Convolutional Neural Network (CNN) is used to detect gait events from the videos of walking recorded by normal mobile phone. Those gait events are further utilized to classify the gait into normal and abnormal walking.

Methods

The videos of walking were recorded from the volunteers in 4 different modes. Normal walking with shoes and without shoes and restricted/controlled walking with shoes and without shoes. Gait events were extracted using deep learning methods with combination of CNN and LSTM. After that stride interval time series developed from the detected gait events was used for the classification of the gait into normal and abnormal categories with the help of other machine learning approaches.

Results

Results showed the accuracy in detection of gait events like : left foot is on ground-right foot in air, left foot in air-right foot on ground or both feet on ground as over 90%. While a significant degree of separation between normal and abnormal gait by analyzing the time series developed from gait events was also obtained.

Conclusion

Combining the video based analysis with time series analysis methods by applying machine learning techniques will certainly helpful in reducing the strict laboratory requirements for gait data collection.

Automated identification of the sclera in high-resolution ocular surface images of healthy subjects

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Introduction

One typical ocular surface disease marker is eye redness, which signals the eye irritation by enlarging the blood vessels of the ocular surface. State-of-the-art evaluation and grading of ocular surface diseases are based on color photographic documentation and different grading scales, making it very time-consuming and subjective. Our aim is the automatic detection and evaluation of ocular surface diseases based on a novel ocular surface imaging technology. One prerequisite is the automatic classification of different ocular surface structures from the images.

Methods

High-resolution ocular surface images of both eyes of 17 healthy subjects were recorded using a clinical prototype and the sharpest images per eye were selected. Fixed regions of interest (ROIs) were defined on each side of the iris and further divided into 40 tiles each. The tiles were manually labeled (sclera / non-sclera) by two observers (inter-observer reliability: 96.99%). Intensity and texture based features were calculated for each matching tile. Different random forest models were trained as baseline classifiers. The models were evaluated for feature importance (full, feature-correlation-reduction, feature-importance-reduction) and group splitting criteria (random tiles out, random eyes out, random subjects out).

Results

Using a random forest classifier, all models yielded an accuracy of at least 94%. The best model using feature-correlation-reduction and a splitting by subjects achieved an accuracy of 0.97, an F1 score of 0.98, a precision of 0.99 and a recall of 0.96.

Conclusion

The baseline classifier shows promising results and allows the classification of ocular surface tissue. The approach can be used as an automated ROI identification procedure enabling the determination of image biomarkers like the eye redness or imaging quality control parameters like the eye opening. Expanding the problem to whole sclera segmentation as well as the integration of pathological ocular surface images will be part of future research.

R packages for reproducible analysis of microscopy images (tifs and czi files)

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Abstract

The analysis of microscopy images is time-consuming and prone to bias whenever manual labor is required [1]. Even though there exist methods to automatize different tasks of the image analysis by, for example, using the scripting or pipeline possibilities of ImageJ [2] or CellProfiler [3], we have experienced that qualitative or quantitative image analysis is often done manually and in a non-reproducible manner. We introduce three packages for the widely used programming environment R, whose use in the scientific community continues to grow [4].

We are using the python library czifile [5] to import czi files and the R package EBImage [6] for specific analysis methods (e.g., segmentation). All other methods have been developed by us.

We have created different R packages that work with original images (czi files) of various dimensionality acquired by common ZEISS microscopies or with tifs that can be exported from other microscopy software. The main functionalities of the three packages are: 1) readCzi [7] imports a czi file, converts it to tif, and saves the metadata. 2) cellPixels [8] detects, counts, and records the fluorescence intensities of stained nuclei, cell bodies, and membrane proteins. 3) detectCilia [9] detects primary cilia in cells but could also be used to detect and measure other stained particles within cells.

Our open-source R packages to obtain important information from microscopy images work with original czi files, ensuring fast, reproducible, and unbiased image analysis. Using R also avoids the use of point-and-click software without capturing the steps. The packages can also be used as a starting point for custom image analyses as well for further data evaluations.

References

[1] Kadouch et al. 2018.
[2] Schneider et al. 2012.
[3] McQuin et al. 2018.
[4] Schindler et al. 2022.
[5] Gohlke 2019.
[6] Pau et al. 2010.
[7-9] Budde 2022.

Track:
Magnetic Methods

MEMS Magnetic Field Source for Frequency Conversion Approaches for ME Sensors

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Introduction

Some magnetoelectric sensors require predefined external magnetic fields to satisfy optimal operation depending on their resonance frequency. While coils commonly generate this external magnetic field, a microelectromechanical systems (MEMS) resonator integrated with permanent magnets could be a possible replacement. In this proof-of-concept study, the interaction of a MEMS resonator and the ME sensor is investigated and compared with the standard approach to achieve the best possible sensor operation in terms of sensitivity.

Methods

The achievable sensor sensitivity was evaluated experimentally by generating the magnetic excitation signal by a coil or a small-sized MEMS resonator. Moreover, the possibility of using both approaches simultaneously was also analysed.

Results

The MEMS resonator operated with 20 Vpp at 1.377 kHz has achieved a sensor sensitivity of 221.21 mV/T. This sensitivity is comparable with the standard approach, where only a coil for sensor excitation is used. The enhanced sensitivity of 277 mV/T could be identified by simultaneously generating the excitation signal by a coil and the MEMS resonator in parallel.

Conclusion

In conclusion, these MEMS resonator methods can potentially increase the sensitivity of the ME sensor even further. The unequal excitation frequency of the MEMS resonator and the resonance frequency of the ME sensor currently limit the performance. Furthermore, the MEMS resonator as a coil replacement enables the complete sensor system to be scaled down. Therefore, optimizations to match both frequencies even better are under investigation.

Automatic Localization of an Ultrasound Probe with the Help of Magnetic Sensors

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Introduction

Ultrasound measurements are a widely used instrument in clinical practice. For later traceability of the images, the position (and orientation) of the ultrasound probe must be recorded during the measurement. Until now this has to be done manually by the physician. An easier and more accurate approach would be the automatic tracking of the ultrasound probe. This contribution shows a first approach for automatically localizing the ultrasonic head during measurement.

Methods

The proposed method is based on coils surrounding the patient bed and a 3D magnetic sensor placed on the ultrasound head. Besides some pre- and postprocessing steps, the proposed localization algorithm is based on trilateration followed by a least mean squares approach for refinement of the estimation.

Results

In a first proof-of-concept measurement with fixed positions and orientations of the ultrasound head a mean accuracy of 2.85 cm and 8.94° was achieved. Additionally, a measurement with a moving ultrasound head is presented to demonstrate the real-time capability of the system.

Conclusion

Finally, future steps for improving the automatic measurement are discussed, including a graphical user interface for the physician.

A CMOS-based biomedical NMR relaxometry system

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Introduction

Nuclear magnetic resonance (NMR) relaxometry is a very powerful tool for detecting the chemical composition of a substance. Combining small, low-field permanent magnets with custom-designed, miniaturized NMR-on-a-chip transceivers enables the design of portable NMR relaxometry systems for point-of-care biomedical applications.

Methods

We present an NMR system based on an NMR-on-a-chip transceiver manufactured in 0.13-µm BiCMOS. The NMR-ASIC co-integrates a low-noise amplifier, quadrature down-conversion mixers, intermediate-frequency variable gain amplifiers, a power amplifier, and a phase-locked loop. Due to its fully-differential architecture and tiny footprint of 1x1 mm^2, the transceiver can be placed directly next to the NMR coil, removing the need for conventional 50 Ω impedance matching, thereby greatly improving energy efficiency. In combination with a 0.36 T benchtop NMR magnet with a homogeneity of 20 ppm over a sample volume of 2.65 µl and a weight of 5.5 kg, the NMR-on-a-chip transceiver constitutes a portable point-of-care NMR platform.

Results

The electrical transceiver characterization revealed power consumptions of 41 mW (RX) and 221 mW (TX), a maximum peak-to-peak output current of 180 mA, a maximum receiver conversion gain of 85 dB, and an input-referred voltage noise of 725 pV/$\sqrt{\text{Hz}}$, all measured at the operating frequency of 15 MHz. The system performance in the target application was investigated by NMR relaxometry measurements, including CPMG measurements, to determine the T2 distribution and inversion recovery experiments to obtain T1 information. These experiments were performed on whole blood, as well as serum and plasma samples. The measured spin sensitivity is 7.8×1016 spins/$\sqrt{\text{Hz}}$.

Conclusion

Thanks to the excellent noise performance, small form factor, and low power consumption of the utilized custom-designed NMR-on-a-chip transceiver, the proposed portable NMR detection platform presents an important step towards NMR-based point-of-care diagnostics. The proof-of-concept relaxometry measurements on blood samples demonstrate the validity of the proposed approach for biomedical diagnostics.

A Concept for 6D Motion Sensing with Magnetoelectric Sensors

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Introduction

Active magnetic motion sensing relies on a combination of magnetic sensors and actuators to indirectly sense a time-varying change in position and orientation. Based on our previous work on a 1D setup with magnetoelectric (ME) cantilever sensors, we introduce a concept for a full 6D sensing system, which is positioned as a modular setup for human movement pattern capture with regard to neurodegenerative diseases.

Methods

We implemented an inverse dipole approach to estimate position and orientation based on ideal triaxial sensors and coils. It is comprised of distance, absolute position, and sign and orientation estimation. We then included results from previous experiments on 1D sensors and coils to simulate the prospective performance in a physical setup. The applied input noise of 0.5 nT was chosen based on a selected bandwidth of 100 Hz. As physical ME sensors have a certain form-factor, there is some spacing between their sensor elements required. Therefore, we also assumed a deviation of 1 cm for each sensor element from the virtual center of the 3D sensor.

Results

We assessed both the time and frequency domain performance of the approach in a simulated motion scenario with focus on superimposed sinusoidal translation and rotation at 1, 5 and 10 Hz. The mean spatial error was a few cm for position and approx. 10° for orientation. The higher frequency components were available, but partly superimposed by interference and noise.

Conclusion

Overall, the accuracy of the position (and esp. distance) estimation seemed appropriate for further research regarding the prospective use case as a supplemental sensor in clinical application. Regarding the error, deviation from the ideal 3D was more critically (esp. for orientation) than noise in this specific simulation. The might be resolved with improved sensors as well as more sophisticated estimation and tracking approaches.

Combining optically pumped magnetometer array layouts to obtain whole head MEG of auditory evoked activity

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Introduction

Magnetoencephalography with optically pumped magnetometers (OPM) is gaining in popularity, but whole head OPM coverage, well known from SQUID MEG, is costly and requires careful array design. To achieve more than 200 hundred recorded signals comparable to typical SQUID systems requires on the order of 70 OPMs if triple-axis sensors are used. This is a considerable investment and it is not simple to place 70 sensors around the head each having an individual electrical connection.

Methods

A cost-effective setup for evoked field measurements can be realised using a limited number of OPMs such as, e.g., 20-30 units. Then several blocks of the same stimulation are measured on the same participant and the sensor layout is changed between blocks to achieve full head coverage. This approach works best if the participant has an individualized sensor helmet based on the MRI of the head. These helmets fit tightly to the head and sensors can be moved between slots quickly and without discomfort for the participant. Sensor helmets with 70 - 90 slots were made for several participants and for each participant four blocks were measured, while the subject was passively listening to a 1 kHz-tone presentation. In between blocks, the OPM array consisting of 20 sensors was relocated to another set of slots on the helmet with some slots occupied in several layouts for control purposes.

Results

The data from each block were averaged to get the AEF. The resulting block-individual AEFs were combined into a whole-head coverage AEF dataset for each participant. From this whole-head AEF bi-lateral auditory sources were successfully localised.

Conclusion

This multiple layout approach is only valid if the evoked response is not modulated by habituation. But the present results show in agreement with literature that responses such as AEFs are stable across sequential recording sessions.

Simulation of a passive position control for ferromagnetic particles with multiple Halbach rings

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Introduction

Various types of magnetic nanoparticles have been developed for a range of medical applications and some have the potential to treat diseases.
In this paper, a new method for controlling the position of these magnetic particles by changing the magnetic field surrounding them is investigated using three Hallbach rings with the aid of a simulation.

Methods

The inner ring controls the direction, and the position of the two outer rings can keep the group of particles together.
In the simulation, the magnetic field is calculated analytically for each time step and the particles are simulated by their corresponding forces. These are the manipulable external magnetic field, the magnetic field between the particles, the Lennard-Jones potential to model attractive interactions between the particles and the drag force.

Results

In the simulation, we show how the particles are manipulated by a Levenberg-Marquard algorithm and develop a closed-loop control for the position of the grouped particles by manipulating the magnetic field inside the Hallbach rings by changing the angular position of these rings.

Conclusion

The control of particles larger than one millimetre is possible with the chosen parameters.
The main objective was to investigate whether it is possible to control micro or nano particles with a Hallbach ring array. At a distance of 1 to 3 cm, this is not possible with the currently available permanent magnets.
It has been shown that it is possible to use a non-linear Levenberg-Marquardt algorithm to minimise the error of the trajectory of all particles.

Limits of magnetic particle spectroscopy for quantification of magnetic nanoparticle in biological environment

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Introduction

Magnetic nanoparticles (MNP) can be utilized to investigate physical mechanisms in biological systems such as complex cellular barrier using in-vitro models. For MNP detection and quantification of MNP in biological environments magnetic particle spectroscopy (MPS) has been proven a sensitive and powerful tool. Here, we investigated limits of MPS quantification for the example of MNP capability to pass the blood-placenta barrier in a microfluidic cell model.

Methods

The blood-placenta barrier was established on a biochip using the cytotrophoblast cell line BeWo and human primary placental pericytes. The quantification of MNP in different media on both sides of and inside the cell barrier was carried out using a commercial MPS device (Bruker BioSpin, Ettlingen, Germany) operated at 25 kHz with a sensitivity of $5 \cdot 10^{-12}$ Am^2. We determine the uncertainty contributions of the pipetting process and of the measured sample volumes as well as the detection limit for quantification by considering the third harmonic A_3 of the MPS spectra. For quantification we used $A_{3,ref}$ of a reference sample of known iron content. The choice of the reference sample state also affected the measurement accuracy and was investigated by the ratio of fifth and third harmonic A_5/A_3 (indicator to assess the magnetic behaviour).

Results

The most accurate sample tube filling volume is found between 10 and 30 µL, and the pipetting process contributes with less than 1% to the uncertainty. The quantified MNP amount passing the barrier and the limit of MPS detection of about 5 ng were dependent on the used MNP type. Quantification results with a deviation of A_5/A_3 above 10% from the reference sample $A_{5,ref}/A_{3,ref}$ are not valid.

Conclusion

MPS is a fast and powerful tool for highly accurate quantification of MNP in small biological samples.

Track:
Medical Robotics

Robotic cochlear implantation: Micro-CT based evaluation of minimally traumatic cochlear access in an ex-vivo model

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Introduction

Robotic cochlear implantation is emerging with the aim to improve the clinical outcome for patients with sensorineural hearing loss. It is presumed that a robotic approach might consistently reduce trauma to the cochlea, one of the essential prerequisites for preservation of residual hearing. A robotic approach was investigated that aims to preserve the anatomical and functional integrity of critical intra-cochlear structures during robotic inner ear access.

Methods

The feasibility of minimally traumatic robotic cochlear access was evaluated in a human ex-vivo whole head cadaver model (n = 10 ears). Optimal target and trajectory planning was performed on clinical image data based on the results of a preliminary planning studies. An image-guided robotic system was used to perform the access to the middle ear and inner ear. Electrode arrays were inserted through the drilled tunnel under microscopic supervision via a tympanomeatal flap. During the experiments, microcomputed tomography images of the cochlea were acquired pre- and postoperatively to radiologically assess the surgical outcome.

Results

A safe trajectory to the middle ear and inner ear was successfully planned and robotically performed in 6 out of 10 cases. In 3 cases the facial recess was too narrow to plan a safe trajectory, and in one case the temporal bone was fractured. In 6 out of 6 drilled cases, no intra-cochlear structures in the round window periphery were mechanically damaged during robotic inner ear access. All subjects were successfully implanted with a cochlear implant in the scala tympani.

Conclusion

The approach presented demonstrates the feasibility of planning and robotically performing a minimally traumatic inner ear access based on conventional clinical imaging modalities and using current robotic technology.

Augmented Reality for 6-DoF Motion Recording, Preview and Execution to Enable Intuitive Surgical Robot Control

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Introduction

In robot-assisted surgeries, the surgeon focuses on the surgical tool and its pose, and not on the complete robot's shape. However, the joints of redundant robots (robots that have more degrees of freedom (DoF) than needed for the positioning of surgical tools) might move in unexpected/undesired ways. Joint motions that lead to patient or collisions are safety critical. We assume that the medical personnel in the operating room can best decide if a planned robot motions come too close to the patient or not.

Methods

We propose an augmented reality-based solution to interact with the robot during surgery planning, and intervention. The tool can be used to command a robot by drawing a trajectory in augmented reality (AR), visualizing the robot movement to check if it is safe before execution. The proposed solution allows surgeons to plan safe robot motion paths beforehand and adapt them when necessary in situ. We implemented the control architecture on a KUKA LBR iiwa robot in combination with a Magic Leap 1 AR device. The surgeon can draw trajectories using a hand-held control.

Results

As a proof-of-concept, we implemented and demonstrated the proposed solution on a 7-DoF redundant robot by commanding different trajectories. The control architecture to plan and execute motion for a surgical robot using AR is a key result of this work.

Conclusion

The AR device was successfully used to command the robot as per the user's command. The main benefit of the proposed solution is that the surgeon can check the robot motion to be safe before it is executed. In our future work, we will experimentally analyze the accuracy of the robot motion and perform a user-study to assess the usability of the proposed solution.

Robotic milling of the electrode lead channel during cochlear implantation

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Introduction

Robotic cochlear implantation has been developed to enable highly consistent insertion of the electrode array into the cochlea, such as to address the clinical needs of decreasing variations in audiological outcomes and preserving residual hearing. The robotic procedure now consists of the middle and inner ear access. We propose to extend it by the robotic preparation of the fixation for the cochlear implant housing and the electrode lead on the surface of the temporal bone. The goal is to further further standardise the procedure, to ensure protection of the electrode from trauma, and to prevent fatigue fractures caused by micro-movements.

Methods

We propose a workflow consisting of preoperative planning on cone-beam computed tomography and its robotic execution. The planning provides a low-curvature channel of sufficient depth below the temporal bone surface, with a channel shape designed to immobilize the electrode with a slight press-fit. The proposed workflow was executed on twelve ex-vivo full-head specimens and evaluated for safety and efficacy in micro-CT images. A safety margin of 1.0 mm around the planned channel was considered to surrounding anatomical structures.

Results

All twelve cases were completed with successful electrode lead fixations after cochlear insertion. The milled channels stayed within the planned safety margin, the probability of a violation was lower than 1 in 10'000 patients. All channels were milled with a width that immobilized the electrode leads, deep enough to always contain the full diameter of the electrode. We could show robotic milling on bone in a compliant headrest with average errors below 0.2 mm, and maximal errors below 0.5 mm.

Conclusion

This study verified a proposed approach for robotic preparation of the fixation for the cochlear implant housing and electrode lead as safe and effective in an ex-vivo model. This could enable unprecedented surgeries in the lateral skull base.

Work space analysis of a new instrument for Natural Orifice Transluminal Endoscopic Surgery (NOTES)

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Abstract

Minimally invasive procedures such as Natural Orifice Transluminal Endoscopic Surgery (NOTES) require powerful, small, and flexible instruments. A cable-driven instrument was developed, which is able to retract tissue to create sufficient space for an actual operation (e.g. cholecystectomy). In this paper, the work space of a developed instrument is presented. The work space is calculated using direct kinematics equations and verified by measurement using an electromagnetic (EM) tracking system.

The angular orientation of the instrument can be up to 85° with a length of the active section of 60 mm. However, a longitudinal rotation up to 17° becomes apparent. This is due to the characteristics of the steel cable used for actuation. Nevertheless, the instrument reaches the intended work space. Further measurements are necessary to evaluate the instrument's behavior under payload and whether this affects the work space.

Track:
Micro- and Nanosystems

Microstructuring defect analysis of platinum conductive tracks for polyimide-based neural implants

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Introduction

The miniaturization of medical devices continues to pose new challenges for their development. Especially in the transition from theoretical design to the production of microimplants, the limits of feasibility are quickly reached. In the field of ultra-small polyimide-based electrode arrays, which have already been successfully used several times in the past, the structuring of the metal conductor tracks is a critical process step. Particularly in the case of very long (several centimeters) structures with high integration density, even the smallest error can mean total failure of a device.

Methods

This study investigates which defects occur during the structuring of long, but very narrow conductive tracks and how they influence the further use of the devices. For this purpose, more than 3800 platinum (Pt) tracks were structured via lift-off process on silicon wafers coated with 5 µm of polyimide (PI). All samples and respectively any defects that occurred were then optically examined and evaluated.

Results

In general, four different types of structural defects could be observed. These include short circuits caused by unremoved platinum between conductive tracks, small material residues at the edges of the conductive tracks, and spots where platinum and thus a continuous electrical contact is missing. It could also be observed that entire traces have become detached from the PI.

Conclusion

While the smallest break-offs and material residues on the edges of the conductors could certainly allow further use of the device, the observed material gaps and short-circuits inevitably lead to total failure. Trace detachments are the extreme case here, as they can even short-circuit neighboring structures on the same substrate due to their length and thus render them unusable. These possible faults should be taken into account when designing the structures and arranging them on the carrier substrate.

Resistance behavior of printed PDMS-based electrode tracks under tension

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Introduction

PDMS-based neural implants are designed for achieving flexible structures that can physiologically and structurally integrate with the host environment. For diverse anatomical environments, different standard structures are available. In previous work, a 2.5D-printing process was developed for the production of PDMS-based electrodes. In the following phase, tests were performed to assess the behavior of the prototypes.

Methods

This work investigates the mechanical and electrical properties of printed electrode tracks under tension. The experiments were performed using a multipurpose bond-tester, which applied a tensile force on the samples while recording their elongation distance. The resistance of the tracks was measured at regular intervals during the elongation.

Results

Five electrodes were each tested three times, starting at 0 % and up to around 300 % elongation. Their resistances increased linearly from a mean initial value of $6.5 \pm 3.6\ \Omega$ up to 50-75 % elongation. The sample resistances reached 100 Ω around an average elongation of 68.95 ± 17.83 % in the first trial. The second and third trials required lower average elongations to reach 100 Ω resistance. Beyond the linear phase, the readings showed steep rises in resistance, reaching open load values.

Conclusion

The tests showed that smaller elongation ranges are required to stay within the resistance limits of the tracks. The electrodes conducted again after returning to their original length. However, the initial smooth transition in conductivity was disrupted, owing to micro-tears forming a elongations larger than 100%. The tears became weak and unstable points that increased in size with repeated stretching. Furthermore, the implemented elongations in this experiment were larger than would be expected in an implantation setting. With that in mind, limitations on the elongation up to 100 % would be sensible, to avoid stretching far beyond the resistance cut-off region.

Fabrication of a microelectrode array with embedded microfluidic channels for precise fluidic control during cell experiments

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Introduction

Retinitis pigmentosa (RP) is an inherited eye disease that causes the death of photoreceptor cells and hence a functional degeneration of the retina. Here, the neuronal network of the retina is disturbed by spontaneous oscillations, which have lost the functional input of the photoreceptors. For successful recording or stimulation of the retina by microelectrode arrays, these oscillations have to be controlled or suppressed. Electroporation offers a promising research approach for the suppression of pathological oscillations in neuronal retinal cells and for the possible therapeutic treatment of this functional degeneration.

Methods

Experiments for genetic transfection of cells and tissue by electroporation require a well-controlled environment as well as precise dosing of chemicals. For efficient stimulation or recording with microelectrode arrays (MEAs), good electrical contact of the tissue or the cells to the electrode surfaces is necessary. For this purpose, a microfluidic structure was integrated into the MEA. It can be used to tighten cells and tissue to the array through negative pressure or to supply chemicals necessary for the experiments, like plasmid DNA encoding genes or therapeutic sequences for electroporation.

Results

The microfluidic channels were patterned and sealed using a SUEXTM hardresist (K25, micro resist technology GmbH, Berlin) on top of the MEAs. Using two successive dry etching steps with oxygen and sulphur hexafluoride, the external inlets, the microelectrode surfaces, and the fluidic outlets were etched free. The chip was contacted by flip-chip alignment to a specially designed PCB carrier. 3D-printed connectors and tubings were used for the microfluidic contacts.

Conclusion

The specialized MEA setup can be used for experiments with retina slices, cortex slices or cell cultures to establish in vitro electroporation. It serves as a basis for the development of a therapeutic transfection by electroporation for future treatment of RP.

Electrochemical impedance spectroscopy as powerful method to optimize in situ electroporation of cultivated cells on microelectrode arrays

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Introduction

Electroporation guided gene therapy is an immune friendly alternative to viral based gene delivery. During electroporation, short electrical pulses are applied to the target cells. These pulses lead to a temporary permeabilization of the plasma membrane, which enables the cells to take up substances, e.g. plasmid DNA encoding therapeutic genes diluted in the surrounding buffer. Standard electroporation is performed in vitro on cell suspensions with special electroporator systems. In our research group we investigate whether microelectrode array (MEA)- based electroporation could also be used for in vivo gene therapy. To identify optimal electroporation parameters, we investigated MEAs by means of electrochemical impedance spectroscopy (EIS) and analyzed the obtained impendance spectra using different electrical equivalent circuits (EECs).

Methods

With in situ electroporation it is possible to transfect adherent cells in contact with adjacent cells, which is one step closer to in vivo electroporation compared to standard in vitro electroporation of a cell suspension.
Therefore, we cultured HEK293 cells on different MEAs that were fabricated on wafer scale with standard clean room processes, using various materials (Au, ITO, IrOx, TiN) and electrode shapes (circular, square, cloverleaf).

Results

In the presented study, we used EIS to analyze the cell-electrode coupling. Hereby, we compared EIS measurements with and without attached cells. The gathered EIS data were fitted to a dedicated EEC to explain the results and optimize the in situ electroporation.

Conclusion

With our in situ MEA setup we were able to optimize the electrical pulse parameters and the experimental protocols for electroporation of adherent HEK293 cells. EIS helped to develop an electrochemical model to describe the influence of electrode material and shape to the efficiency of the electroporation. In future we aim to use this method for in vivo gene delivery for therapy of pathological neuronal networks.

Improved aortic valve tissue culture in a micro-physiological system with adapted pneumatic pump chip and increased flow rate

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Introduction

Calcific aortic valve (AV) stenosis is one of the most common heart diseases worldwide. To develop new treatment options, knowledge of underlying (patho)physiological processes is essential. Conventional 2D-VIC cultures and applied animal models exhibit critical limitations. Use of additional complex 3D tissue-based ex vivo porcine AV models therefore allow original cell-matrix interaction and using a microphysiological system (MPS) possess the possibility to adjust pressure, flow rate and shear forces. Based on previous MPS experiments, this study aims to introduce an up-scaled pump-chip providing improved AV tissue culture conditions regarding viability and mRNA expression comparing static vs. dynamic culture.

Methods

Rectangular porcine AV-Segments of 15 mm^2, stitched in a TPU-ring, were placed inside a Tissue-Incubation-Chamber (TIC), connected to the respective pump-chip. The small vs. large pump-chip realized different flow rates (13.4 vs. 77.4 µl/s) and frequencies (150 vs. 30 bpm). Viability was monitored by resazurin-reduction-(RR)-assay. Micro-particle image velocimetry (PIV) was applied to assess media flow velocity and compute shear forces. After 14 days of TIC-MPS culture tissue RNA was isolated and qRT-PCR was performed. HIF1α and ACTA2 mRNA-expression was calculated in relation of dynamic vs. static culture.

Results

Compared to the small pump-chip the PIV depicted a 6.5 times higher maximum shear force in the large pump-chip. The RR-assay showed a significantly higher viability in the large dynamic setup compared to the small dynamic or static approach ($p<0.05$, $n=6$). HIF1α and ACTA2 expression in large dynamic setup was significantly lower than in the static culture ($p<0.05$; $n=4$).

Conclusion

Up scaling the TIC-MPS by applying larger pump-chips leads to an increased flow rate and AV tissue viability. Analysis of dynamically cultured porcine AV tissue reveal an advantage in preventing HIF1α and ATCA2 induction observed for static cultures. Intense characterization of mRNA expression after culture in the TIC-MPS also under procalcific conditions are envisioned.

Isolation of Spheroids using Fluidic Force Microscopy

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Introduction

The use of spheroids in organ-on-a-chip technologies is gaining importance, particularly in the area of neuroscience as they have the ability to replicate the complex neural networks seen in vivo[1]. This rise in popularity comes with an increasing demand to accurately be able to position such microtissues within experimental microstructures, such as microwells, in order to fully understand how they function.
Fluidic force microscopy (FluidFM) is an innovative technology, whereby an atomic force microscopy (AFM) cantilever contains a hollow microfluidic channel[2]. Thus, the system merges the force-sensing abilities of AFM with the aspiration and dispensing abilities of a micropipette, and can be used for single-cell manipulations, including picking and placing (P&P)[3].
FluidFM has already been used extensively for P&P of single cells[4], however the technique has not yet been employed to pick and accurately place larger microtissues and spheroids.

Methods

The commercially available FluidFM OMNIUM is used to select neuronal spheroids from a bulk solution and place them in a polydimethylsiloxane (PDMS) structure, creating a neuronal network. From here, the viability and growth of the spheroids can be assessed.

Results

A process flow is defined for P&P spheroids using the FluidFM OMNIUM. This is then used for P&P spheroids of various sizes and transfer them to a different location, demonstrating the versatility of the instrument.

Conclusion

The FluidFM device can be used to select, pick and accurately place spheroids. This is useful in a variety of applications such as lab-on-a-chip technologies where the precise placing of spheroids is required for experimental accuracy. Future work will develop a system for automated P&P of organoids, leveraging imaging recognition and automation.

References

[1] Park et al., 2021, DOI: 10.1126/sciadv.abf9153.
[2] Meister et al., 2009, DOI: 10.1021/nl901384x.
[3] Li et al., 2021, DOI: 10.1007/s12274-021-3573-y.
[4] Martinez et al., 2016, DOI: 10.1039/c5lc01466b.

Long Term Evaluation of the Barrier Properties of Polymer/Metal Oxide Hybrid Layers for Use in Medical Implants

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Introduction

Active implants require an encapsulation to withstand the harsh physiological environment of the body. One encapsulation material, which can be used, is Parylene-C, a biocompatible polymer that can be deposited at room temperature. However, the barrier against water permeation is not high enough to provide adequate protection over a longer period of time. Atomic layer deposition can be used to deposit ultra-thin, hermetic metal oxide layers that provide a sufficiently high permeability barrier. In this work, these two encapsulation strategies are combined to create a high barrier hybrid layer.

Methods

A Parylene-C/ALD/Parylene-C hybrid layer with 3 µm Parylene-C + 3x (15 nm Al_2O_3 +5 nm TiO_2) ALD + 5 µm Parylene-C was deposited on solid micro electrode arrays (MEA). The barrier properties were evaluated with a DC leakage measurement. The setup was capable of measuring currents below 1 pA. For accelerated ageing the samples were exposed to phosphate buffered saline solution (PBS) at 60 °C. The measurements were carried out over a period of one year. For comparison with a single thin layer, a 715 nm thick Parylene-C layer was deposited on the MEAs and evaluated at room temperature.

Results

The sample with 715 nm Parylene-C showed a strong increase in current after 15 h and thus a failure of the barrier property. After one year, no significant current increase was measured by the hybrid system, which indicates that the barrier properties are still sufficient.

Conclusion

Using the DC leakage-current measurement, it was shown that the Parylene-C/ALD/Parylene-C hybrid system could maintain the barrier properties over one year at elevated temperature. This period corresponds to 5 years at 37 °C. Thus, the biocompatible hybrid system shows a good potential for a strategy to protect active implants against corrosion in physiological environment.

KTeXpand - a novel microfluidic device for advanced cell based cross matching

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Introduction

Antibody-mediated rejection after kidney transplantation is a major limitation for long-term survival of donated kidneys within the recipient allograft. With the existing HLA cross-matching test only complement activating donor specific antibodies are evaluated. Other measurements are more sensitive, but cannot assert the clinical relevance of the donor specific antibodies. Thus, novel methods that address the more complex nature of cellular interactions with serum components are needed to improve Antibody-mediated rejection prediction. Recent studies suggest, that the interaction of natural killer cells of the recipient with endothelial cells of the donor is of major interest.

Methods

Endothelial cells of the donor were expanded from blood samples as blood outgrowth endothelial cells (BOEC). As corresponding counterpart within the assay the IL-2 and high affinity CD16 V158 FcγRIIIa receptor expressing FcR-NK-92 cell line was used in combination with the monocolnal antobody avelumab.

Results

Here we present a microfluidic cell culture device and a corresponding assay to test for the relevance of natural killer cell activated antibody-mediated rejection in vitro. Therefore, a protocol to co-cultivate both cell types and track natural killer cell activated killing within a fluorescence-based assay was established. To automate this approach, the prototype of a well plate sized microfluidic device was developed, that enables staining of the two cell types and repeatable and time-dependent co-cultivation of the cells with serum.

Conclusion

Using the KTeXpand microfluidic platform the automated handling and readout of an NK cell mediated killing BOEC by ADCC was shown.This automated approach enables further evaluation of the clinical relevance of the established assay paving the way to additional information on HLA cross-matching that helps to quickly estimate the probability of Antibody-mediated rejection and the clinical relevance of donor specific antibodies.

In-Situ Tracking of Collagen Fibril Mechanics and Morphology during Digestion by MMP-1 through Atomic Force Microscopy

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Introduction

Collagen fibrils (CFs) are important structural elements of most tissues in the human body. CFs are subject to constant remodeling; existing CFs are enzymatically digested by Matrix-Metallo-Proteinases (MMPs) and new ones are being assembled. So far some studies on CF digestion have been carried out on bulk material / macroscale and fewer ones at the molecular scale. Using atomic force microscopy (AFM) imaging and nanoindentation we investigate this process here at the level of individual CFs, the fundamental building blocks of many biological tissues.

Methods

CFs were extracted from mouse tail tendon (OT1, m, 12 weeks) were deposited on round glass coverslips and mounted on a temperature-controlled fluid cell in buffer at 34°C. AFM-based nanoindentation data was acquired on a Nanowizard 3 AFM (Bruker-JPK) in Quantitative Imaging mode at a resolution of 256x256 pixels and a setpoint of 1 nN in 20-30-minute intervals. Activated recombinant human MMP-1 was added to the buffer to achieve an enzyme concentration of 10nM. Overall digestion time was 3 hours. For indentation modulus, force-distance curves were analyzed with the Hertz-Sneddon method. Individual CFs were characterized using indentation modulus and height pixel values from the crest of each CF, to avoid invalid points of contact due to the curved shape of the CF.

Results

Our experiments reveal large variability in digestion characteristics of individual CFs in the same region of interest. Despite being exposed to the same concentration of MMP-1, different CFs show diverse behavior during digestion, especially with regards to the rate of height loss. The biggest difference thus far observed is between intact and overstrained fibrils. Digestion rates are shown to be inversely correlated with CF indentation modulus and swelling.

Conclusion

The uncovered relations are likely tied to the amount of CF cross-linking as well as prior damage.

Introducing micro physiological systems to evaluate new radiopharmaceuticals: A binding study with radiolabeled cetuximab

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Introduction

Radiopharmaceuticals can be used for target-specific functional diagnostics, such as PET or SPECT imaging, or radionuclide therapy of diseased tissue, depending on the incorporated radionuclide. Following initial in vitro testing, radiopharmaceutical candidates are usually further characterized in small animals. Since reduction, replacement and refinement (3R) of animal testing is a central precept in preclinical research it would be beneficial to replace some of these tests by alternative methods.

Methods

Using micro physiological system technology, various organ-on-chip models can be created with human cell systems/organoids, which are operated in a circulatory system under defined physiological conditions. Here we present first attempts to introduce micro physiological systems for evaluating radiopharmaceuticals using the radiolabeled anti-EGFR antibody cetuximab as reference compound.

Results

In a micro physiological system equipped with six 96-well plate-like microwells in a flow chamber, binding of 64Cu and 68Ga-labeled cetuximab to cells and spheroids grown from A431 (EGFR-positive) and MDA-MB435S (EGFR-negative) cells was measured and compared to conventional microplates. Specific saturation binding of radiolabeled cetuximab at increasing concentrations was analyzed using a phosphor imaging system. The affinity of radiolabeled cetuximab towards A431 spheroids measured in the micro physiological system was in the same range as that of the spheroids in conventional microplates. Within the assays in micro physiological systems, the results showed a trend towards increased affinity for A431 monolayers compared to the spheroids. The values of binding capacity for radiolabeled cetuximab on 2D and 3D A431 cell culture models were in the same order of magnitude when measured in micro physiological systems or in microplates.

Conclusion

Binding parameters of radiolabled cetuximab in micro physiological systems and Well plates are comparable to each other and differ inbetween monolayers and spheroids of A431 cells. These promising results are the basis to develop MPS modules containing advanced human spheroid/ organoid models.

Femtosecond laser manufacturing technology for microstents as innovative medical devices to treat open-angle glaucoma

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Introduction

The increasing trend of minimally invasive therapy methods for widespread diseases in the cardiovascular system, in the field of ophthalmology, ear, nose, and throat medicine, or gynecology, leads to an extensive demand for innovative microdevice manufacturing technologies. Femtosecond (fs)-laser technology offers a wide range of applications in the field of cutting, milling, and surface structuring on the micro- and nanometer scale. Ophthalmic devices for glaucoma therapy have dimensions in the submillimeter range. Irrespective of this, there are high demands on the safety and efficacy of these implants.

Methods

Within the current study, fs-laser-based manufacturing technologies for functional elements of a novel microstent for glaucoma therapy were developed, considering potential industrial scalability. Tubular microstent base bodies were manufactured, and methods for fs-laser manufacturing were developed. Morphological characterization of fs-laser machined prototypes was conducted using scanning electron and confocal laser scanning microscopy.

Results

A total of n = 24 tubular microstents were equipped with a micromechanical valve mechanism. The developed mounting mechanism allows reproducible fs-laser processing of microstents - 79% of the manufactured valve mechanisms met our previously defined quality criteria. Furthermore, we successfully developed a fs-laser-based process for manufacturing grooves as part of a fixation mechanism for a stable device positioning inside the eye. Fixation mechanism prototypes were successfully manufactured based on a monofil 10-0 surgical suture filament.

Conclusion

Within the current study, we successfully developed a mounting mechanism for quick and reproducible manufacturing of a micromechanical valve mechanism for a novel glaucoma microstent. Due to its minimal dimensions, the developed mounting mechanism provides maximum flexibility regarding the fabrication strategy and the positioning accuracy combined with the high usability necessary for the industrial fabrication of medical microdevices. The results show that fs-laser manufacturing represents a promising technology for manufacturers of medical microdevices, such as ophthalmic microstents.

Microscale Sensor Fabrication on Curved Needle Surfaces

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Introduction

Sensor-integrated needles with impedance or other electrochemical sensors have gained increased attention in research. Their potential use is widespread and covers applications such as early disease diagnostics or needle guidance for needle-based interventions. However, fabrication and sensor integration are crucial parts of realizing functionalized needles.

Methods

In this paper, a review of existing research on microscale sensor arrays on curved needle surfaces is presented. It focusses on medical needles excluding needle-type sensors.

Results

Especially, means of fabrications including flexible thin-film-based sensors or photolithography are discussed.

Conclusion

Although they provide satisfactory results, no manufacturing method is yet ready for bulk production.

Chemofluidic Circuits for Infection Diagnostics and Single Cell Analysis

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Introduction

Rapid and precise disease diagnostics is essential for successful therapy. Currently, diagnostic assays for infectous dieseases e.g. COVID-19 are based on manual labor, pipetting robots, or test cartridges. However, the throughput of these methods is not satisfactory for more complex tasks like single cell analysis to diagnose the cancer acute myeloid leucaemia (AML).
Lab-on-a-chip (LOC) technology promises to solve such diagnostic challenges, but is still hampered by the need for bulky off-chip equipment and external flow control with low integration density. To overcome these limitations, we develop a chemofluidic LOC platform with autonomous flow control by integrated polymer valves.

Methods

We developed three liquid-controlled valve types: One-way closing valves are based on hydrogels that swell upon liquid contact and block the liquid transport after a defined time. One-way opening valves use soluble polymers that open the liquid transport after a set time. Chemofluidic transistors can be repeatedly opened and closed. By combining these elements in fluidic circuits, basic fluidic operations for diagnostic assays such as fluid mixing, cell separation, nucleic acid isolation/ purification and amplification can be realized. Fluidic chips are fabricated by laser-structuring and assembling of polymer foils, a process which is suited for large-scale fabrication.

Results

Chemofluidic LOC with integrated valves were designed by computational methods, fabricated in laboratory scale, and reproducible flow control was achieved. Based on this, fluidic circuits for the quantification of proteins in blood samples, cell sorting, and nucleic acid amplification were realized. A future large-scale fabrication of test chips is envisioned.

Conclusion

Our concept of chemofluidic LOC promises to enable complex diagnostic assays on a miniaturized test chip at the point-of-care. The technology has the potential for large-scale integration which is necessary to realize single cell analysis of large cell samples, thereby revolutionizing disease diagnostics and treatment of malignant diseases such as leukemiaL.

Hydrophilic Nanofibrous Poly(ether-block-amide) for Biomedical Applications

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Introduction

Appropriate biomaterial selection is of fundamental importance for the success of medical devices and implants. Currently, the most common clinically used biomaterials are generally composed of well-characterized, biologically inert, off-the-shelf metals, ceramics, and polymers. The aim of this study is to promote the development of special polymeric implant biomaterials to address future needs in terms of biological inertness and fatigue strength combined with appropriate cell attachment. In order to address this, a biostable, known hydrophobic poly(ether-block-amides) (PEBA) was investigated together with a recent hydrophilic resin. On the one hand, biostable PEBA copolymers enable manifold applications in medical industry thanks to their large flexibility range. In additon, electrospinning is an extremely powerful tool for fabricating new nanofiber structured implants and has been used for the production of nonwoven surfaces. Nevertheless, the processing as well as the selection of a suitable device or implant site are currently challenging for nanostructured implants.

Methods

In this study we present the fiber generation of two different medical grade PEBA polymers, one hydrophobic and one hydrophilic, by direct electrospinning using a 4SPIN C4S LAB2. The initial characterization includes scanning electron microscopy, wettability, thermal analysis, tensile tests and biological studies.

Results

The influence of hydrophilicity or polymer composition on fiber morphology, contact angle, tensile strength and biocompatibility is shown. Comprehensive characterisation has shown, that the polymeric block unit is much more decisive for wettability or tensile strength than surface morphology. Furthermore, the choice of nanofibrous materials has been shown to be crucial for the biological response.

Conclusion

Two PEBA samples with different soft segments, which are responsible for hydrophilicity, and with similar hard segments, which are crucial for shore hardness, were investigated. Electrospun PEBA nanofibers have been successfully produced and initial screening showed promising results, especially for hydrophilic resin as alloplastic nanofiber structure for implants.

Track:
Modelling and Simulation

Fragmentation thresholds simulated for antibubbles with various infinitesimal elastic shells

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Introduction

Antibubbles are small gas bubbles comprising one or multiple liquid or solid cores, typically surrounded by stabilising shells. Acoustically active microscopic antibubbles have been proposed for use as theranostic agents. For clinical applications, it is relevant to know the fragmentation threshold of antibubbles and the influence of the stabilising shells thereon. The purpose of this study was to simulate fragmentation thresholds of shell-encapsulated antibubbles.

Methods

For antibubbles with an infinitesimal frictionless elastic shell of constant surface tension, we simulated ultrasound-assisted fragmentation by computing radial pulsation as a function of time using an adapted Rayleigh-Plesset equation, and converting the solutions to time-variant kinetic energy of the shell and time-variant surface energy deficit. By repetition over a range of pressure amplitudes, fragmentation thresholds were found for antibubbles of varying size, core volume, shell stiffness, and driving frequency.

Results

As backscattering increases with scatterer size, and as drug delivery would require vehicles just small enough to pass through capillaries with a relatively large payload, we chose to present typical results for antibubbles of resting diameter 6 µm with a 90% incompressible core. At a driving frequency of 13 MHz, the fragmentation threshold was found to correspond to a mechanical indices less than 0.4, irrespective of shell stiffness. This mechanical index is not considered unsafe in diagnosis.

Conclusion

Our simulations show that at lower driving frequencies, the shell stiffness is of major influence on antibubble fragmentation, whilst at higher driving frequencies, the shell material is hardly of influence.
At 13-MHz driving, stiff-shell-encapsulated antibubbles were simulated to fragment at acoustic amplitudes that are not considered unsafe in diagnosis. These findings imply that drug-loaded antibubbles, stabilised by rigid shells, could be forced to release their contents using diagnostic ultrasound. This research is of interest in flash-echo and ultrasound-guided drug delivery.

A Large-scale Virtual Patient Cohort to Study ECG Features of Interatrial Conduction Block

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Introduction

Interatrial conduction block refers to a disturbance in the propagation of electrical impulses in the conduction pathways between the right and the left atrium and it is a risk factor for atrial fibrillation, stroke, and premature death. Clinical diagnostic criteria comprise an increased P wave duration and biphasic P waves in lead II, III and aVF due to retrograde activation of the left atrium. Machine learning algorithms could improve the diagnosis but require a large-scale, well-controlled and balanced dataset. In silico electrocardiogram (ECG) signals, optimally obtained from a statistical shape model to cover anatomical variabilities of the atria, carry the potential to produce an extensive database meeting the requirements for successful machine learning application.

Methods

We generated the first in silico dataset including interatrial conduction block of 9,800 simulated ECG signals based on 98 atrial geometries derived from a bi-atrial statistical shape model. Automated feature analysis was performed to evaluate P wave morphology, duration and P wave terminal force in lead V1.

Results

Increased P wave duration and P wave terminal force in lead V1 was found for models with interatrial conduction block compared to healthy models. A wide variability of P wave morphology was detected for models with interatrial conduction block.

Conclusion

Contrary to previous assumptions, our results suggest that a biphasic morphology in lead III seems to be neither necessary nor sufficient for the diagnosis of interatrial conduction block. The presented dataset is ready for a classification with machine learning algorithms and can be easily extended.

Bond graph creation and automated semantic composition of SBML and CellML models

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Introduction

BioModels and PMR are two main online repositories that host thousands of biological models. However, it is challenging to automatically compose these models such that the resulting model is physically plausible (i.e. satisfies conservation of mass, charge, energy, etc.). The Bond Graph (BG) is a powerful framework for constructing physically plausible models of biology. Here, we consider the use of semantic annotations to automate the composition of BG models.

Methods

We have developed a framework that converts SBML (from BioModels) and CellML (from PMR) models into BG models. For SBML models, the reaction network was sufficient to construct a BG model whereas for CellML models, existing templates were used to construct BG models. In both cases, simulation data were used to parameterise the BG models. When composable BG modules are created, they can be automatically merged. The automated model composition was performed by identifying and linking the similarly annotated components of the annotated BG modules.

Results

We have tested our framework on multiple SBML and CellML models (such as the EGFR pathway, the MAPK cascade, and the TCA cycle) and we observed similar behaviours to the original models. Physically plausible behaviours of the composed models (for example energy consumption) were also verified.

Conclusion

Our BG conversion and semantic model composition framework provide a physically plausible environment in which we can automatically convert and compose a considerable number of existing SBML and CellML models. Currently, the reactions in SBML models must follow particular rate laws to be convertible into BGs and models must be consistently annotated. The accuracy of the BG conversion for both SBML and CellML models depends on whether the original models are consistent with energy conservation.

Evaluation of calcified mitral valve leaflet mobility and its effect on left heart hemodynamics using fluid-structure interaction simulation

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Introduction

Mitral annular calcification (MAC) is a degenerative disease that is associated with cardiovascular comorbidities. MAC leads to severe mitral stenosis and/or mitral insufficiency followed by significant hemodynamic variations within the left atrium and left ventricle. This study aims to investigate the hemodynamic changes that occur due to MAC using patient-specific Fluid-Structure Interaction (FSI) simulation.

Methods

Left atrial, mitral valve, and left ventricular models of a patient with severely calcified mitral valve were obtained from 4D-CT at mid systole and mid diastole. Patient-specific hemodynamics based on echocardiography data were generated by lumped parameter model with an atrial volume change of 25 mL and a ventricular stroke volume of 90 mL. The hemodynamics then were applied as boundary conditions for an FSI simulation in which movements of the atrial and ventricular walls were reconstructed from CT scans. Mitral pressure gradients, mitral valve area, and regurgitant volume were calculated.

Results

Calcification of the mitral valve severely restricted the movement of mitral leaflets, resulting in unfavorable hemodynamics within the left atrium and left ventricle. Impaired mitral leaflets' mobility leads to 30 mL regurgitant volume into the left atrium during systole. The mean diastolic mitral pressure gradient was 12.1 mmHg with a mitral valve area of 2.1 cm^2 at mid-diastole and 1.4 cm^2 mid-systole with a mean pressure drop for the leakage of 3.5 mmHg.

Conclusion

Mitral calcification leads to unfavorable hemodynamics as determined by FSI simulation. Patient-specific simulations are a powerful tool for studying the hemodynamics variations occurring due to mitral valve disease. In the future, it should allow the evaluation of various personalized therapeutic options.

Artificial Prostate Tissue for the Simulation of the Transurethral Resection of the Prostate

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Introduction

In-vitro models for the transurethral resection of the prostate (TUR-P) require prostate phantoms whose mechanical, thermal, and electrical properties resemble those of real tissue. This work focused on the latter.

Methods

Phantoms were fabricated with gelatin, pectin, and corn syrup solved in an aqueous solution of 0.4 wt% NaCl. The effect of each component on the phantom's electrical properties could be described in a multiple nonlinear regression model.

Results

As a result, the electrical current drawn during resection of the phantom could be predicted with an uncertainty of $\pm$ 10 %. This allows for purposive adjustment of the phantom's composition to regulate the Joule heating during resection.

Conclusion

Particularly the pectin concentration appeared to greatly affect the electrical properties as well as the mechanical stability of the artificial tissue at higher temperatures caused by Joule heating of the system. Until now, this research focused on the development of tissue that resembles porcine musculus longissimus dorsi (MLD). In the future, the phantom's composition will be adjusted based on data obtained through in-vivo resection of the prostate.

Evaluation of the influence of the nasal cavity in flow simulations of the upper airway of a sleep apnea patient

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Introduction

Computational fluid dynamics can be used to analyze the flow pattern and the anatomical predisposition of the airway collapse in patient-specific simulations of sleep apnea patients. Especially the nasal geometry is a major challenge and is often excluded.
This study investigates the influence of excluding the nasal geometry using different cutting planes in the area of the nasopharynx.

Methods

The airway simulations performed in this study are based on the airway segmentation of a sleep apnea patient obtained with a 3T MRT. Four different digital models were generated all based on the same airway geometry using different cutting planes in the area of the nasopharynx. The Reynolds averaged Navier-Stokes (RANS) equations are solved to gain the stationary CFD simulations. The resulting flow velocities and pressure distributions are compared.

Results

The velocity magnitudes were very similar in all models. Only minor deviations of the flow pattern in the oropharyngeal region can be observed. The evaluation of the maximum velocities showed that the maximum velocity of the simplified models was slightly higher than the model including the nasal cavity. The averaged pressure values of axial layers in the region of the pharynx of all four models showed large differences to each other in the area of the soft palate.

Conclusion

Since the computational cost of the flow along the nasal geometry is significantly increased, simplifying the airway model seems to be a suitable solution, since at least the mean velocities do not vary. In a previous study, the effect of replacing the nasal cavity with a simple pipe was examined and showed a good agreement of the pressure distribution. Such a good agreement could not be reproduced in this work, which might be due to the patient specific airway geometry. Moreover, this shows that the type of simplification has a great influence.

Investigation of an Acceleration Pipeline for Single Fiber Action Potential Simulation

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Introduction

Surface electromyography (sEMG) is a method to acquire the electrical potentials on the skin surface generated by the electrical activity of muscle fibers. In the past, analytical and numerical sEMG models have been developed to better understand the underlying physiology and to assess signal processing algorithms. These models are based on the action potential of a single fiber (SFAP). Analytical models can only be applied to simple geometries. Therefore, in order to accurately model a muscle, numerical models are absolutely necessary. However, these have a high computational cost making complex simulations challenging.

Methods

To make the numerical simulation applicable to muscles with a large number of muscle fibers, a pipeline that accelerates the calculation of the SFAP is studied. The pipeline is based on the principle of reciprocity. This indicates that it is possible to use the transfer behavior from a point along the fiber to the electrode for the reverse direction as well, allowing each electrode to be simulated instead of each fiber. The investigation is carried out in a simplified muscle model to enable a comparison with an analytical solution. The difference between the analytical solution and the ones obtained by numerical methods is evaluated by the mean absolute error.

Results

The results show that the numerical methods of the investigated pipeline are suitable to calculate the SFAP with a low absolute mean error against the analytical solution. The propagating signal component as well as the end-of-fiber-effect of the SFAP are clearly visible. Furthermore, the principle of reciprocity significantly reduces the calculation time.

Conclusion

Due to the small deviation from the analytical solution, the numerical methods used in the pipeline can be applied to sEMG models. In combination with the significantly reduced calculation time, this allows the simulation of highly complex geometries with a large number of muscle fibers.

A Mathematical Model of Salivary Gland Duct Cells

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Introduction

Insufficient production of saliva, or hyposalivation, could lead to severe oral consequences such as mouth infection, difficulty in swallowing and loss of teeth. The study of the salivary gland may positively impact the life quality of hyposalivation patients. At the cellular level, the salivary gland consists of acini and ducts. The acinus secretes the primary saliva, a fluid with a high NaCl concentration. The duct converts primary saliva to final saliva by extracting much of the NaCl, thus making final saliva less salty.

Methods

We develop a mathematical model for the salivary gland duct to understand the saliva modification mechanisms. Our model utilizes the realistic 3D structure of the duct reconstructed from an image stack of gland tissue. We model two duct sections: intercalated and striated duct, each with its own cell type. Immunostaining results for each type of duct cell are obtained to support modelling.

Results

Our duct model replicates the conversion from primary to final saliva, as observed in salivary gland experiments. It also demonstrates realistic biological features such as duct cell volume, cellular concentrations and membrane potentials. Immunostaining results show that intercalated duct cells express TMEM16A, aquaporin but not ENaC. Based on this, the model predicts that the intercalated duct does not absorb Na+ and Cl- like the striated duct but secretes a small amount of water.

Conclusion

We implement an anatomically accurate 3D salivary gland duct model and validate its function with experimental results. The model demonstrates that the intercalated duct is water-secretory. Lastly, we simplify the model by omitting all 3D structural details of the duct, which makes little difference to the final saliva output. This shows that saliva production is not sensitive to structural variation of the duct.

Ureteric flow with indwelling stents: The role of side hole and lumen size

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Introduction

Ureteral stents are indispensable devices in urological practice to maintain and reinstate the drainage of urine in the upper urinary tract. Most ureteral stents feature openings in the stent wall, referred to as side holes (SHs), that are designed to facilitate urine flux in and out of the stent lumen. Systematic discussions on the role of SH and stent lumen size in regulating flux and shear stress levels are yet lacking.

Methods

In this study, we first built an in-vitro platform with micro-Particle Image Velocimetry platform to measure the velocity field in the vicinity of SHs. Fluxes in and out of the SHs were quantified. Furthermore, numerical counterparts of the same geometry was realized by means of 2-D Computational Fluid Dynamic simulations to explore further the impact of the SHs and luminal sizes.

Results

Our results showed that by reducing the SH diameter from 1.1 to 0.4 mm the median wall shear stress levels of the SHs near the ureteropelvic junction and ureterovesical junction increased by over 150%, even though the flux magnitudes through these SH decreased by about 40%. The SHs were associated with low flux and low shear stress levels. Reducing the stent lumen diameter significantly impeded the fluxes in the stent lumen and those through the SHs. By means of 0-D models and scaling relations, we argued that the design of stent inlet/outlet was key in regulating the flow characteristics described above.

Conclusion

Changes in stent SH and lumen sizes have profound impacts on the flow characterstics in ureteric flow with indwelling stent. The current design of stent inlet/outlet should be further investigated.

Mathematical lung model for local gas exchange based on EIT-measurements

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Introduction

Electrical impedance tomography (EIT) is a portable, radiation-free imaging option. The EIT data contains information about the distributions of ventilation and perfusion within the lungs. Both parameters are important for an accurate description of the lungs' local condition which may change due to diseases like ARDS. We present a four compartment mathematical lung model to simulate the local gas exchange based on EIT input.

Methods

The presented mathematical model is a four compartment lung model which includes lung mechanics, gas exchange of O2 and CO2 and a body compartment to represent O2 consumption and CO2 production. The regional information about the distribution of ventilation and perfusion is extracted from EIT data as model input with a frequency-domain-filtering-based method. In order to illustrate the suitability of this approach, an ARDS patient is simulated and the results are compared to the measured patient data.

Results

The model simulates the local and global time course of the volume, the gas fraction in the alveoli and the arterial partial pressure. The results show good agreement with measurement data of the patient. The comparison to measured value of tidal volume show that simulated value matches the patient data. The modelled global values of arterial partial pressure for O2 and CO2 and etCO2 vary slightly from the measured data (O2: 1.9 mmHg, CO2: 0.6 mmHg, etCO2: 2.9 mmHg).

Conclusion

We presented a concept for a mathematical model to simulate the local gas exchange. First simulations may indicate that chosen approach is capable to satisfactorily represent the gas exchange of a patient using EIT data as input. This is a first approach to model the complex relation between ventilation and perfusion distribution in the lung and time dependent changes due to diseases like ARDS and therapeutic measures like prone position.

Comparison of the Y-90 brachytherapy and Ir-192 brachytherapy of skin tumors: a simulation study

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Introduction

Skin brachytherapy is a successful practice for treating skin cancer patients. Although a gamma source like an Iridium-192 (Ir-192) is commonly used in the skin brachytherapy, the use of a beta source like Yttrium-90 (Y-90) has also been investigated for this purpose.

Methods

In the current study, we simulated the dose distribution of a proposed Y-90 applicator and an Ir-192 Leipzig applicator in a skin phantom and compared the performance of each of the methods in treating three tumors in three hypothetical scenarios.

Results

Results of this simulation study showed that because of the sharp dose falloff of beta radiation in tissue, the Y-90 applicator may lead to better protection of the bone and/or cartilage under thin tumors. However, it may lead to excessive skin surface dose if thick skin tumors are treated.

Conclusion

To choose between the Ir-192 and Y-90 applicators, one may need to consider the thickness of the tumor and the thickness of the adipose layer between the tumor and the bone.

Biomechanical Characterization of Human Corneal Lenticules

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Introduction

Patient-specific numerical models have been proposed to improve the planning of refractive procedures such as LASIK, CLEAR, and PRK. While tomographs are used to accurately measure patient anatomy, determining patient-specific biomechanical properties is challenging. Recently, in-vivo quantification of tissue biomechanics based on Brillouin scattering is possible. However, the relationship between frequency shift and nonlinear corneal biomechanical properties remains poorly characterized. Therefore, this study proposes a technique to quantify corneal biomechanics on samples from patients undergoing CLEAR surgery. The harvested tissue, which is usually discarded, is uniaxially tested which allows us to 1) gain insight into the biomechanics of the young cornea and 2) directly evaluate Brillouin measurements in the future.

Methods

Experimental: Corneal lenticules were tested by uniaxial extension in the nasal-temporal direction or at an angle 45° to it. The tissue was pre-stretched and preconditioned. The last cycle of force displacement data was recorded for analysis. Computational: The lenticules were numerically reconstructed to build a finite-element mesh from pre-operative clinical data. These lenticules were modelled with orthogonal collagen fibers and the material was described using a HGO model. A Bayesian optimization procedure was used to identify the material parameters.

Results

Parameter identification was performed simultaneously on three patients and in two orientations. The results of the identification with four parameters showed that the model was able to reproduce the experimental data.

Conclusion

From the current data, only small differences in orientation can be noted. Further measurements are needed to confirm whether the anisotropy of the human cornea is located more in the posterior cornea than the anterior cornea. The numerical model needs to be calibrated on more patients and eventually these results need to be complemented by in vivo biomechanical measurements with Brillouin scattering to develop a predictive surgical planning tool that takes into account patient-specific corneal biomechanics.

Influence of temperature-dependent tissue parameters on monopolar coagulation model

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Introduction

The use of high-frequency (HF) generators for HF surgical treatment of biological tissue has become an indispensable part of today's surgical applications of all kinds. Generally, HF alternating electric currents between 300 kHz and 1 MHz are used to induce hemostasis by heating at the cellular level. This effect can be attributed to Joule heating, in which a current dissipated conductor converts the electrical energy into thermal energy. However, sound evidence on the reliability and effectiveness of application-specific HF generator modes is not sufficiently available. Usually, the evidence takes place empirically by means of preclinical or clinical studies. Nevertheless, a corresponding empirical data collection is time- and cost-intensive. Therefore, physiological and statistical modeling provides the opportunity to relate tissue response to the applied electrical energy to obtain a prediction of the tissue reaction.

Methods

In this contribution, we establish a monopolar coagulation finite element (FE) model of an already well-known model approach based on Pennes bioheat equation. Additionally, the vaporization of tissue water at the water boiling point is considered. Furthermore, a variation of temperature-dependent tissue parameters was performed to analyze their impact on the model output. We used the software COMSOL Multiphysics 6.0 to simulate the distribution of the applied electric field and the resulting heat distribution in biological tissue.

Results

The simulation results demonstrate that the initial electrical conductivity has the greatest influence on the temperature distribution as well as on the time until the tissue temperature reached the boiling point of water. In contrast, the tissue water content has the least impact on the model output.

Conclusion

Depending on the desired coagulation effect, HF power control as a function of electrical conductivity or its reciprocal, tissue resistance, must be added next in an improved model.

Evaluation of a nonlinear viscoelastic-plastic constitutive model in numerical simulation of thermoplastic polymers for stent application

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Introduction

Finite element analysis is a suitable tool for predicting and optimizing the mechanical behavior of polymer stents. To simulate the specific material properties of thermoplastic polymers, e.g. load type dependent, viscoelastic behavior or strain rate dependency, a suitable constitutive model is essential. The parallel rheological framework (PRF) model implemented in ABAQUS (SIMULIA, USA) was calibrated and evaluated in this study for the thermoplastic polymer poly(L-lactide) (PLLA), commonly used for polymer stents.

Methods

Tensile tests as well as recovery tests with different loading rates were performed using rectangular PLLA film specimens. In order to calibrate the constitutive model, the conducted material tests were simulated accordingly. The parameters of the model were iteratively varied to obtain good accordance of the simulation with the material tests. The equilibrium network was defined with integration of plasticity. In addition, a viscoelastic network was created. For the definition of the hyperelastic element, the Neo-Hookean model was used.

Results

Parameter fitting provided optimized values for an appropriate representation of the viscoelastic-plastic material behavior of PLLA. Loading and plastic strain region are simulated with good agreement to the experiments. Despite a slight deviation in the curve progression, the overall elastic strain is modeled accurately in the unloading curve. The viscoelastic strain portion of the experiment is not fully reached, causing the constitutive model to simulate a slightly increased plastic strain.

Conclusion

Thermoplastic polymers, such as PLLA, exhibit a strongly time-dependent material behavior. In contrast to elastic-plastic material models, this can be correctly represented with the nonlinear viscoelastic-plastic PRF model. By using tensile as well as recovery tests for calibration, the loading and unloading behavior are considered. The next step will be an investigation of other hyperelastic and viscous elements. Furthermore, a calibration software can allow faster and better adjustment of the material parameters, also for other polymers.

Hemoglobin ratio as a forgotten parameter for automatic feedback control systems in preterm neonates

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Introduction

None of the ventilator manufacturers consider the fetal-to-adult hemoglobin ratio as an input parameter for the individualization of automatic oxygenation control of a neonate. This study aimed to describe how the fetal-to-adult hemoglobin ratio changes as a function of the gestational age and weight of the newborn.

Methods

Using a mathematical model of preterm neonatal oxygenation, we simulated how a change in inspiratory oxygen fraction affected the peripheral oxygen saturation for different fetal-to-adult hemoglobin ratios. The observed difference in peripheral oxygen saturation was 7% between the simulation with the lowest and the highest fetal-to-adult hemoglobin ratio. This is higher than the common accuracy of a pulse oximeter. Therefore, we reviewed the available literature and sought a mathematical description of how the fetal-to-adult hemoglobin ratio depends on gestational age and newborn weight.

Results

We integrated available clinical data into a single 3D lookup table of hemoglobin ratio versus weight and gestational age. However, there is not enough consistent data to produce the desired smooth 3D function. At the same time, there are insufficient data to describe the evolution of the hemoglobin ratio after blood transfusion, which plays an important role in the change in the fetal and adult hemoglobin ratio.

Conclusion

We found that changes in fetal-to-adult hemoglobin ratio can notably affect the performance of a model of preterm neonatal oxygenation. Yet more clinical data need to be collected on hemoglobin ratio as a function of the gestational age and weight of preterm infants. A smooth mathematical 3D function could be constructed based on the data that would describe the development of fetal-to-adult hemoglobin ratio in preterm neonates. This would allow to refine models of preterm neonatal oxygenation and aid the development of automatic feedback control systems of neonatal oxygenation.

Can reconstructed 3D-DXA images replace quantitative CT images (QCT) as input in finite element (FE) models for femoral strength predictions?

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Introduction

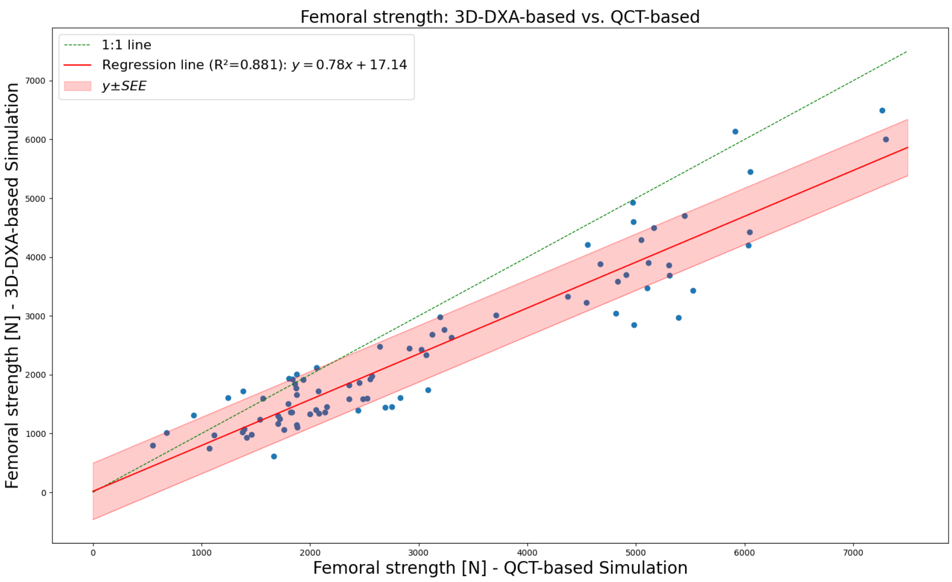
A wide screening of the population at risk of osteoporosis may help to decrease its detrimental effects. However, the current gold standard, DXA-based areal bone mineral density, is limited in its prediction capability for femoral strength and fractures. QCT-based FE models have shown to be a better predictor for strength than DXA-based measures.
The limited availability of calibrated CT images, however, poses an obstacle to a wider introduction of the technique.
3D-DXA images - 3D reconstructions based on DXA images and statistical shape modeling - may close the gap by providing similar information as calibrated CT images based on standard DXA images.

Methods

A total of 83 cadaveric proximal femurs underwent DXA and calibrated CT scanning. 3D-DXA images were built using the software 3D-SHAPER (Galgo Medical, Barcelona, Spain).
After an evaluation of the reconstruction quality, a recently developed voxel-based non-linear FE pipeline was used to compute femoral strength in the same fall configuration for both 3D-DXA and QCT inputs.

Results

Linear regression analysis showed a close relationship between the strength characteristics computed with the two images: R2=0.881. The regression line shows a slope of 0.78 and an intercept of 17.1 N. The corresponding SEE is 478.6 N (Mean: 2403 N), resulting in a CV of 19.9%.



Conclusion

This first comparison of the capability of 3D-DXA images to replace CT images as input for FE analysis shows promising results when considering the high coefficient of determination. The underestimation of strength based on 3D-DXA, can be explained by the lower mean BMD values in these images when compared to QCT. This difference may be reduced by an appropriate adaptation of the calibration procedure. The relatively large SEE, however, may be a limiting factor for the added value of the 3D-DXA based FE results in clinical applications.

A fully automated multi-fidelity approach for personalising cardiac active mechanics

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Introduction

Computational models of the heart's function have become powerful tools for improving diagnosis and therapies. However, their clinical translation is hampered by their generic nature.
This limitation must be addressed by creating personalised models that are calibrated to available clinical data; a process termed 'digital twinning'. Major challenges are the large number of model parameters and that most cannot be observed clinically. These parameters must be estimated based on clinically observable quantities which can become highly expensive. Significant improvements have recently been made in the personalisation of electrophysiology, afterload, and passive mechanics models. This study focuses on the personalisation of active mechanics models and introduces a novel fully automated approach that faces the aforementioned challenges by a two-step multi-fidelity solution.

Methods

Having a 3D model of cardiac electromechanics (EM), the first step is to represent the active mechanical behaviour by a purely phenomenological, low-fidelity model, and to personalise it at the organ scale through calibration to clinical cavity pressure data. Then, resulting nodal traces of cellular active stress, intracellular calcium concentration, and fibre stretch are extracted and processed to obtain corresponding median traces. These are utilised to personalise the desired biophysically detailed, high-fidelity model, which is done at the cellular scale using a 0D model of cardiac EM. The approach was applied to a cohort of seven models of the human left ventricle that were created from patients treated for aortic coarctation.

Results

Only between two and four expensive 3D organ-scale simulations were required and good agreement between simulated and clinical pressure-volume loops was found. Furthermore, robustness against uncertainty in the clinical data was demonstrated.

Conclusion

To conclude, the presented approach constitutes a further step towards an accurate and efficient personalisation of active mechanics models and as such it is considered suitable for the integration in digital twinning workflows.

Validation of a Fluid Structure Interaction Model for TAVR using Particle Image Velocimetry

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Introduction

Implantation of a transcatheter aortic valve replacement (TAVR) in patients with severe aortic stenosis improves pathologic blood flow through the aortic valve, but still alters hemodynamics in comparison to a healthy native aortic valve. The hemodynamic characteristics of TAVR are associated with hypo-attenuating leaflet thickening and prosthetic leaflet thrombosis, which may reduce the durability of TAVR.

Methods

For this reason we developed a numerical model to identify pro-thrombotic regions of TAVR based on the velocity field. In silico models have already been proven to be an effective tool for device optimization in other medical device applications. However, when using an in silico model, it is important to validate the model assumptions with experimental data or analytical solutions to confirm the accuracy of the model. In this study, we present an approach to validate a complex numerical Fluid Structure Interaction (FSI) model used to simulate leaflet kinematics and flow in the vicinity of a TAVR. Based on the recommendation of ISO 5840 (2021), a combined validation of the kinematic and fluid dynamic parameters was performed for this purpose. The leaflet kinematic was investigated via high-speed recordings and evaluated based on the Geometric Orifice Area (GOA). The velocity field of the TAVR was determined experimentally using Particle Image Velocimetry (PIV).

Results

The evaluation of the GOA showed a good agreement of the in silico model with the in vitro data for the systolic duration. The occurring velocities were qualitatively compared during peak systole for three planes and showed similar flow characteristics. The maximum velocity was 1.1 m/s in the in vitro and in silico model.

Conclusion

Based on the results, it can be assumed that the numerical FSI model of the TAVR can be used for thrombosis risk assessment.

Modelling of a Positive End-Expiratory Pressure Valve with a Voice-coil Actuator

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Introduction

The positiv end-expiratory pressure (PEEP) valve is one major component in devices for mechanical ventilation and is located on the expiratory branch, preventing the pressure in the lungs from dropping to ambient pressure during expiration. The goal of this work is to develop a model that captures the dynamics of PEEP valves which can be used for controller design.

Methods

As basis for the modelling of the PEEP valve a simplified dynamic model was chosen. The differential equation was derived via the force equilibrium at the valve's membrane. These forces considered are the recoil and damping of the membrane, the static and dynamic pressure and actuator generated force. As the equation of motions just describes and inner state, an output equation was introduced that calculated the flow via the membranes position and the pressure drop. In preliminary tests all parameters except the damping coefficient of the equation of motion and the flow factor in the output equation could be identified. These parameters were then estimated via a grey-box model approach and by means of an experimental test bench.

Results

The unknown flow factor could be successfully identified by measuring flow-pressure curves for fixed valve openings adjusted on the test bench. For small frequencies and flows, the estimated damping coefficient leads to a sufficient match between the model and the measurements with a fit of 76.94 %. With higher frequencies the mismatch increases leading to a fit of 40.64% in this range.

Conclusion

The derived mathematical model with fitted flow factor and a damping coefficient was capable of capturing the dynamic behaviour well for low frequencies and flows. Losses due to turbulences and frequency-depended resistances are assumed decrease the fit of the model for higher flows and frequencies, thus these effects may be included in a future model.

Image-based deep learning of finite element simulations for fast surrogate biomechanical organ deformations

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Introduction

We apply deep learning to emulate Finite Element simulations by exploiting neural networks as universal function approximators. A novel processing pipeline automates the incorporation of three-dimensional biomechanical simulation data into an image-based deep learning task where spatially resolved deformations are predicted using pixelwise regression. We show that a model trained in this way can quickly reproduce simulation results with reasonable preliminary performance.

Methods

We trained a customized U-Net (32 input features) to predict displacement models based on the input force vectors. The pipeline was applied to a basic indentation process for an idealized reference geometry (puck) and a 3D liver model from the LiTS dataset. The generated 3D simulation data is normalized and projected onto 2D images using the midpoint circle algorithm such that x, y, and z coordinates are mapped to pixel values of RGB image channels. In this way, 1500 simulations of the reference geometry and 500 simulations of the liver deformation with force-controlled, randomly initialized load distributions were performed. Simulations took about 2-5 minutes of computation time with FE models of 6000 and 10000 elements. The neural network was trained on the simulation database using pixelwise regression.

Results

We successfully trained a model on the pixelwise regression of simulation results. The model optimization reached an f1-score of 0.69 and 0.61 for the puck and the liver. The displacement images were reprojected and compared to the 3D ground truth. The trained models reached an average surface distance of 3.1 ± 1.2 and 4.2 ± 2.2, as well as 4.3 ± 0.4 and 6.4 ± 0.2 for the Hausdorff distances.

Conclusion

The model performance is still impractical for clinical decisions. Still, with mean computation times of under 250 ms, the approach's potential with a more extensive database and a more sophisticated deep learning architecture, e.g., GNN, is recognizable.

Analysis on the effect of eye globe diameters on the biomechanics of posterior ocular tissues during horizontal adduction

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Introduction

Glaucoma and myopia are characterized by structural and functional changes in the ocular components and may cause damage to the optic nerve. Increased eye globe dimensions cause higher optic nerve traction forces during eye movements. In this work, an attempt has been made to analyze the influence of pathological changes in eye globe diameters towards the mechanical responses of optic nerve head tissues during eye adductions.

Methods

For this study, a 3D baseline model geometry of posterior ocular tissues has been constructed. The eye globe diameters of the model are modified to mimic the changes in ocular globe morphology in control, glaucoma, myopia and glaucoma with myopia conditions. Adductions are simulated for the models as the rotation of the globe from 1° to 10° in steps of 1°. Maximum von Mises strain in lamina cribrosa (LC) is computed. Additionally, displacement of LC in the posterior direction is estimated for increasing adduction angles.

Results

Results show that strain developed in LC and its posterior displacement are higher in diseased eyes compared to healthy eyes. Maximum von Mises strain in LC and its posterior displacement is highest for the myopia group for all the adduction angles. The maximum percentage change observed for the myopia group with respect to the control group is 42.46% higher strain and 15.66% higher displacement.

Conclusion

In this study, finite element modelling is used to evaluate the effect of variation of eye-globe diameters in glaucoma, myopia and glaucoma with myopia on the biomechanics of the eye during horizontal adduction. It appears that eyes with higher axial length and globe anisotropy are more susceptible to optic nerve head damage. It can be concluded that pathological variation of eye globe diameters may be a risk factor for the development or progression of glaucomatous optic neuropathy.

Specific Heat Capacity Model of Saline Solutions based on the Osmotic Virial Equation verified by Differential Scanning Calorimetry Measurements

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Introduction

Cryoablation is a minimally invasive procedure, in which tumors or arrhythmogenic cardiac tissues are ablated by freezing. Temperature simulations during cryoablation scenarios are used to estimate ablation success and related measured quantities during an intervention (cryoimpedance, excitation propagation). Accurate thermal properties, in particular in the temperature range close to the freezing point, are required for simulating realistic outcomes. In this work, a heat capacity model for saline solutions based on the osmotic virial equation is described as an approximation to tissue and verified using differential scanning calorimetry (DSC) measurements.

Methods

The temperature and concentration dependent latent heat release for saline solutions was derived based on the osmotic virial equation with an additional contribution by the eutectic latent heat. Saline solutions in 4 different concentrations (1x, 3x, 5x and 10x isotonic) were prepared and heat flow measurements between -40°C and 25°C with varying cooling and warming rates were performed using a Mettler Toledo DSC 3 Differential Scanning Calorimeter. Corresponding thermal equivalent circuits consisting of the evaluated saline sample and thermally relevant components of the DSC module were derived and simulated for each experiment. Unknown thermal properties of the DSC module were estimated and fitted considering the available experimental data.

Results

The simulated heat flow profiles show a high level of similarity with the measurements for the melting peak during thawing except for the 10x isotonic concentration, in which the amplitude of the melting peak is significantly larger in the simulations compared to the measurements. The peaks of latent eutectic heat show deviations in shape and appear slightly earlier compared to the corresponding measured peak.

Conclusion

The described model enables the consideration of realistic properties of saline solutions during freezing/thawing. Extensions of the model are planned to also describe heat capacity models for tissue, enabling more accurate simulations of cryoablation scenarios.

In-silico model for the photoinduced stimulation of voltage-gated ion channels on Organic Photocapacitors

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Introduction

Therapeutic neuromodulation by means of electrical stimulation is a well-established technique to promote neuroplasticity and connectivity in neuronal tissue. Recently developed organic electrolytic photocapacitors (OEPCs) provide a fundamentally novel concept for minimally invasive neuronal stimulation at high temporal and spatial resolution. However, the effectiveness level of the stimulation device for a specific cell is not easy to determine, which can result in numerous unsuccessful in-vitro experiments. Here we provide a realistic 3D model of the OEPC coupled with a HEK293-cell to study its suitability for single cell stimulation.

Methods

The model was simulated in COMSOL6.0 with the cell defined as a flattened oblate spheroid (r=7.5 µm). An equivalent circuit represents the patch-clamp amplifier, the OEPC was modeled by a single photo-diode equivalent circuit describing photovoltaic reactions. Patch-clamp-measurements of HEK293-cells stably expressing TagRFP-Kv1.3 were carried out. The cells were clamped at a holding potential of -100mV followed by depolarization steps (400ms) from -100mV to 40mV (10mV increments). After depolarization a 5ms-light pulse was applied using a 10W-LED (660nm).

Results

The model fits the measured currents of HEK293-cells in voltage-clamp mode. Based on the simulations, an increase in the conductivity of TagRFP-Kv1.3 in response to light stimulation can be observed starting at a clamp-voltage of -60mV. At lower clamp-voltages, only the stimulation artifact can be observed. Removing the patch-clamp amplifier in the model reduces the ion-channel response.

Conclusion

We provide a realistic 3D model for the light-triggered activation of voltage-gated ion channels in a model cell, which fits experimentally acquired whole-cell patch-clamp measurements. Moreover, a clear distinction between the stimulation artifacts and ion channel responses can be made. The results show the capabilities of our OEPC-devices for stimulating voltage-gated ion channels in single cells. The provided model will serve as a basis to simulate neuronal activation in response to OEPC stimulation.

Toward personalized models of whole heart electromechanics

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Introduction

Personalized computer models of four-chamber electromechanics (EM), which are able to replicate anatomy, electrical activation, and mechanical deformation of an individual patient's heart are termed virtual-heart-technologies. Such technologies show a high potential as clinical and industrial tools in diagnostics, treatment optimization and device development. However, challenges during model generation and personalization as well as the costs for high fidelity EM simulations hamper their widespread use. In this proof-of-concept study we report on the first fully mechanistic whole-heart EM models with non-invasively personalized electrophysiology (EP) and calibrated cardiovascular mechanical function.

Methods

An anatomically accurate whole-heart model was built from cardiac magnetic resonance images. Electrophysiology during healthy sinus rhythm, including a His-Purkinje system and atrio-ventricular conduction, was personalized from non-invasive clinical data based on the 12-lead electrocardiogram (ECG). Electrical activation patterns served as input for subsequent mechanics simulations. Active and passive mechanical properties of atrial and ventricular tissue was represented by a phenomenological active stress model and a non-linear, hyperelastic, nearly incompressible, and anisotropic material, respectively. Spring-type boundary conditions were applied to mimic the effect of the pericardium and a closed-loop 0D model of the vascular system was used to provide consistent hemodynamic loading.

Results

Goodness of fit between simulated and measured ECG was used as metric to quantify the fidelity of the EP model component. Mechanics and cardiovascular hemodynamics were assessed by comparing against image-based left ventricular volume traces, and pressures against cuff measurements and values from the literature. The close agreement between data and model outputs is considered indicative of the model's physiological validity.

Conclusion

Our study presents the first fully mechanistic whole-heart EM simulations that replicate available non-invasive clinical data representative of EP, mechanics and cardiovascular function with high fidelity. Our framework can be generalized to pathological or therapeutical scenarios to be used for stratification and therapy planning.

Computational Analysis of the Release Kinetics of Natural Compounds from PEG/PVA Blended Hydrogels for Wound Healing Applications

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Introduction

The study of the release kinetics aids in the optimization of the design parameters of drug delivery systems for wound healing applications. Blended hydrogels are preferred for controlled release due to their enhanced mechanical stability and biocompatibility. The present work aims to investigate the release kinetics of natural compounds from Polyethylene Glycol/Polyvinyl Alcohol (PEG/PVA) blended hydrogels.

Methods

A one-dimensional model based on the free volume theory has been developed to simulate the fractional diffusion of the solute molecules from the blended hydrogels. The computational model has been validated using the experimental data available in the literature for both pure and blended hydrogels.

Results

The results demonstrate that the proposed framework is able to simulate the sustained release kinetics of natural compounds encapsulated within both pure and blended hydrogels. Diffusion of multiple natural compounds from pure PEG, pure PVA, and blended PEG/PVA hydrogels has been computed from the molecular characteristics. Experimental and simulated release profiles are observed to be in fair agreement with the R^2 value of more than 0.9 for all the hydrogel samples.

Conclusion

It appears that the present study will be clinically relevant as it aids in predicting the release kinetics of controlled delivery systems. This modelling approach can be further extended to develop a smart system for improving the design of the commercial drug delivery devices using blended hydrogels.

Simulation study of inflation of a high compliant balloon inside idealized non-linear tissue geometry

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Introduction

High compliant balloon(actuators) containing strain sensing elements are currently under development. This special actuator-sensor system is intended for in-vivo application in vessels such as arteries and urethra. It could potentially reveal local tissue information regarding biomechanical properties and possible inner wall shape.

Methods

This simulation study in COMSOL(v5.6) focusses on inflation behavior of a balloon being equipped with several sensing elements, whose compliance is ideally magnitudes higher than the surrounding tissue in an idealized in-vivo 2D setup. We initialize the vessel's inner wall as 5 different structures. First as a perfect circle; second, a square; third, a closed convex-concave 4-fold structure similar to surface structures found in urethrae. The fourth and fifth tissue structure are like the third structure but with its folds having higher amplitudes. Three sensing elements were initialized on the actuator surface with the first sensing element closer to the tissue boundary while the third the farthest.

Results

The inflation of the balloon inside tubular structures clearly suggests several important phenomena. The sensing elements on the balloon in the expansion within a perfect cylindrical shape undergo identical stretch throughout the input pressure range. In the other structures, the first sensing element on balloon shows a higher stretch at complete contact with the tissue wall, while the third element undergoes the least stretch within the three sensing elements.

Conclusion

It was observed and concluded from the inflation-study that balloon regions, which get into contact with tissue boundary earlier exhibit a faster rate of stretch change and a higher circumferential stretch than the balloon regions that are not getting into contact with the tissue early. The ratio of the difference between the sensing elements is positively correlated with the curvature amplitude of tissues. This study reveals that simulation studies are powerful tools to understand and evaluate biomechanics in complex situations.

Holistic Equivalent Circuit Model for Capacitive Extracellular Stimulation

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Introduction

Capacitive extracellular stimulation with wireless electrodes is a common method in implanted stimulation electrodes. The basis for investigating the transmission of stimuli from electrodes in a conductive environment are in vitro experiments using the patch clamp technique. Computational spatial models to validate patch clamp recordings require high computing power. A simplified equivalent circuit to observe mechanisms occurring at the cell-electrode interface can help in distinguishing the different physicochemical effects of signal transmission and might help in optimizing efficacy in in vivo extracellular stimulation.

Methods

Approaches such as the Stern model for characterizing the electrochemical double-layer formation and a modified two-domain model are used to describe the electrode-cell coupling. The spatial models and evaluated parameters are transferred into an equivalent circuit. A simulation of the involved control and measurement systems allows validation with in vitro patch clamp recordings.

Results

Parameters for an equivalent circuit of the electrode and the occurring electrochemical double layer are obtained from electrochemical impedance spectroscopy measurements and mathematical models. Results from a simulation of the equivalent circuit including an exemplary HEK-293 cell model could be validated in patch clamp recordings and show a junction voltage of 2.8 mV between the cell and the electrode for a stimulation voltage of 340 mV.

Conclusion

With this concept we aim to convert different complex models into a simple equivalent circuit and thus showing the correlation of mechanisms of stimulation and electrical parameters. We want to facilitate the interpretation of measured signals especially in voltage clamp measurements and distinguish different effects in extracellular stimulation for further optimization of stimulation devices.

Determining the influence of endoskeleton friction on the damping of pulsating antibubbles

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Introduction

Recent in-vivo work showed the suitability of Pickering-stabilized antibubbles in harmonic imaging and ultrasound-guided drug delivery. To date, however, theoretical considerations of antibubble core properties and their effects on antibubble dynamics have been rather sparse. The purpose of this study was to investigate the influence of skeletal friction on the damping of a pulsating antibubble and the pulsation phase of an antibubble relative to the incident sound wave.

Methods

Numerical simulations were performed to compute damping terms and pulsation phases of micron-sized antibubbles with thin elastic shells and 30% endoskeleton volume fraction.

Results

The simulations showed that the damping owing to skeleton presence dominates the damping mechanism for antibubbles of radii less than 2.5 µm, whilst it is negligible for greater radii. The pulsation phase of such small antibubbles was simulated to have a phase delay of up to $\frac{1}{6}\pi$ with respect to pulsating free gas bubbles.

Conclusion

Our findings demonstrate that the presence of an endoskeleton inside a bubble influences pulsation phase and damping of small antibubbles. Antibubbles of radii less than 3 µm are of interest for the use as ultrasound contrast agents.

A Publicly Available Statistical Shape Model for the Assessment of Craniosynostosis

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Introduction

Craniosynostosis is a condition caused by the premature fusion of skull sutures, leading to irregular growth patterns of the head. The assessment of craniofacial deformities requires patient data which is sparsely available. To overcome the lack of publicly available data, statistical shape models can be used to generate realistic, synthetic data. In this work, we built the first publicly available statistical 3D head model of craniosynostosis patients.

Methods

From a dataset of 3D surface scans of 367 patients, we employed a shape-model-creation-pipeline using data augmentation via midsagittal mirroring, initial alignment, template morphing, and statistical modeling using weighted principal components analysis. Beside the full model, we also created pathology-specific submodels and a texture model. The registration step was evaluated using landmark errors, vertex-to-nearest-neighbor errors, and surface normal deviations. The final statistical shape model was evaluated using compactness, generalization, and specificity.

Results

Using 10 components, the statistical shape model included 93% of the total variance. Generalization errors were below 3.8mm and for the first 100 components, the minimum specificity error was below 3mm. Mean vertex-to-nearest neighbor errors were below 0.01mm while landmark errors were below 6.6mm. Craniosynostosis-specific pathologies were represented in the first eigenmodes of the model. The submodels corresponded to their respective pathologies.

Conclusion

We present the first publicly available, craniosynostosis-specific statistical shape model of the human head. Typical evaluation criteria indicate a model performance close to other statistical head models of the human head. By including pathology-specific submodels and ready-to-use instances our dataset enables the assessment of craniosynostosis on a common synthetic dataset.

From the ear flap to the nerve: A complete computer model of the peripheral auditory system

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Abstract

Acoustic stimuli pass through the outer and middle ears to the Cochlea, where the mechanical signal is converted to electrical impulses, which are passed to the central nervous system via the auditory nerve. Cochlea facilitates the mechanical-electrical transduction by converting "analogue" sound waves to "digital" action potentials by decomposing the sound according to its frequency components and exciting corresponding tonotopically organized nerve terminals, thus encoding the sound pitch. The sound intensity is encoded into the firing rate of the afferent nerve fibers, as well as in a fiber class. Due to the cochlear amplifier, we can hear and distinguish a broad range of intensities, covering at least 6 orders of magnitudes, or 120 dB.

Clearly, the cochlea is a unique biological system and key part of the sensory auditory pathway, and therefore has been the subject of a great scientific interest. However, due to the complexity of the organ and experimental difficulties, the mechanism of hearing is still not fully understood.

Here we present a computer model of the outer and middle ears, the cochlear mechanics, ionic currents within the organ of Corti modulated by mechanosensitive ion channels in the inner hair cells, the ribbon synapse of the inner hair cells, and the axon of the afferent auditory nerve. The model translates into a large set of differential equations that we solve numerically in the time domain, simulating the response to arbitrary sounds. By changing selected parameters of the model, we can mimic hearing impairment of various origins.

The present model is well physiologically justified, built bottom-up using laws of physics, and based on up-to-date experimental data. Such a model is instrumental for advancing quantitative understanding of the mechanism of hearing, as well as for devising next generation hearing aids and cochlear implants.

Derivation of Mechanical Power of ventilation and the non-linear pressure-volume relationship of the lung - A model based investigation

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Introduction

During controlled ventilation mechanical power (MP) the product of mechanical energy (ME) and respiratory rate (RR) has been proposed as a means to quantify the development of ventilator induced lung injury (VILI) during intensive care therapy. The widely used equation to calculate elastic ME from respiratory mechanics and ventilatory parameters implies a linear static pressure-volume relationship (PV) of the lung to include the effect of positive-end expiratory pressure (PEEP). Here, the effects of this linearity assumption are investigated by modelling different degrees of injury using the well known sigmoidal static PV relationship of the lung. The impact of non-linearity on the error of linear elastic ME is quantified and potential clinical implications are discussed.

Methods

The sigmoidal PV model V(P)=VC/(1+e(Pc-P)r)-ERV consists of four parameters with physiological representation: expiratory reserve volume (ERV) vital capacity (VC), pressure of highest respiratory system compliance (PC) and avalanche parameter (r), quantifying the required pressure change for full recruitment. Healthy lung was modelled assuming ERV=15ml/kg body weight, VC=65ml/kg, PC=3cmH2O and r=0.33cmH2O-1. Injured lung was modelled by reduction of ERV=5ml/kg, VC=40ml/kg and r=0.17cmH2O and an increase of PC=15cmH2O. Non-linear elastic ME was derive analytically from ME(V)=∫P(V)dV=∫V(P)-1dV. Elastic ME was compared to the linear model: ME=1/2·E·VT2+PEEP·VT with E=dP(V)/dV and lung protective VT=6ml/kg.

Results

Elastic ME was overestimated by up to 0.31mJ/kg (7.9%) in PV curves representing healthy lungs and up to 1.2mJ/kg (47.8%) in PV curves representing injured lungs, especially for low PEEP values (<10cmH2O). Overestimation was highest 8 mJ/kg (250 %) at PEEP=0cmH2O and for high model parameters Pc=15cmH2O and r=0.33cmH2O-1.

Conclusion

The commonly applied linear model to derive elastic mechanical energy and hence mechanical power may overestimate true mechanical energy/power, especially for low values of PEEP in lungs requiring high pressures to initiate recruitment, yet low additional pressure for full recruitment.

Track:
Neural Engineering

Continuous error processing during a closed-loop 2D tracking task

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Introduction

The usefulness of error-related potentials for control in non-invasive Brain-Computer interface (BCI) research has been established over the last decades. To continuously correct for erroneous action of an end effector in a BCI however, these neural correlates relating only to the discrete perception of errors remain problematic. The exploration of neural correlates to continuously detected erroneous action may provide a solution to this problem. In this work, we analyzed EEG recordings of 30 sessions in 10 participants during the perception of various feedback conditions within a 2D tracking task, providing evidence that non-discrete errors can be detected during continuous tasks as well.

Methods

Following preprocessing (line noise, artifact, electrode pops/drifts removal; bad channel interpolation) and band-pass filtering to two frequency bands of interest (1-30Hz and 30-80Hz), EEG data were time-locked to and epoched within slices of [-1,3]s of the local maxima of the Euclidean error between target and feedback. Significant difference in the grand averages per condition were evaluated consulting a permutation paired t-test, FDR-corrected at a significance level of 0.05.

Results

Significant differences between correct and erroneous epochs were observed across the whole trial length for the low frequency band (1-30Hz). Additionally, modulations in the difference signals (correct-erroneous) at electrode positions FCz and Pz according to the behavior of the Euclidean error were found. In contrast, minimal significant difference can be reported between the two erroneous conditions. For the high frequency band (30-80Hz), no significant differences in the time series within any pair of conditions could be observed.

Conclusion

As hypothesized, we observed significant differences between correct and erroneous feedback conditions in the lower regarded frequency band, while minimal difference between both erroneous conditions was found, confirming that the reported results are in fact directly related to a cortical response to the erroneous feedback. Furthermore, no significant differences in the gamma band could be found.

3D-printed flexible silicone rubber ECoG electrode for neural recording

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Introduction

Miniaturized flexible sensors are getting more important for in-vivo biomedical applications e.g. electrocorticography (ECoG) for the treatment of Parkinson's disease. Using a 3D-printer for medical grade silicone rubber with a laser curing system, flexible ECoG electrodes made of silicone rubber with integrated conductive pathways and contacts were manufactured. A WST-1-Assay was used to prove biocompatibility. ECoGs were then evaluated in an acute rat model of Parkinson.

Methods

Conductive parts were printed from conductive polymer DM-SIP-2002 (Dycotec Materials™, Britain) covered in silicone rubber RTV-2 polydimethylsiloxane (Dow Corning, USA). Polymers were printed alternately, starting with silicone rubber. Silicone rubber was disposed at 3 bars, with a velocity of 300 mm/min and laser power of 11 % DC. This was changed to 2.5 bar and 600 mm/min for the second and third layer. After printing the first and third layer, the polydimethylsiloxane was tempered at 150 °C for 10 minutes, while the second layer had to be tempered at 60 - 80 °C for an additional 15 minutes due to the material properties. Then, ECoGs with three contacts were implanted onto the motor cortex of two rats under general anesthesia. Seven days after surgery, neuronal oscillatory activity was recorded in individual free moving rats in three conditions: (1) basal activity, (2) after injection of the dopamine (DA) receptor antagonist haloperidol (HALO, 5 mg/kg), and (3) with additional injection of the DA agonist apomorphine (APO, 1mg/kg).

Results

An ECoG was successfully fabricated and showed biocompatibility results with values over 70 %. The ECoGs allowed recording of neuronal oscillatory activity that was similar, although less homogenous, to those from previous studies using electrode grids with Platinum contacts.

Conclusion

It was possible to 3D-print a working and biocompatible electrode array with a maximum tolerance of 0.4 mm. First tests in an animal model showed promising results.

Powering Deep-seated Neural Implants by Ultrasound

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Introduction

Novel types of electrical neural implants aim to stimulate deep lying nerves within the body. Transmitting energy and data over a long distance through tissue poses new challenges, as established methods such as inductive coupling are only suitable for close-range energy supply. This problem can be solved by powering the implant with ultrasound. In this study capacitive micromachined ultrasonic transducers (CMUTs) and piezoelectric micromachined ultrasonic transducers (PMUTs) are used as ultrasound receivers. The encapsulation of these implants and in particular the ultrasonic transducers are of paramount importance, as this kind of implant does not only need protective coatings, but sound transmission must also be ensured.

Methods

Analysis of these encapsulation technologies and the ability to transmit ultrasound waves through encapsulations is the goal of this research.Two different coating techniques were used to achieve the thinnest and most even encapsulation possible of ultrasonic transducers withmedical grade silicone (MED-1000): spin coating and slit coating. Acoustic and mechanical properties were investigated, as well as the bonding forces. Preliminary measurements of the transmitted ultrasound energy through the coated transducers were performed in an aqueous environment (PBS) to simulate body fluids.

Results

With the investigated coating techniques, thin and even layers of 100 µm MED-1000 could be achieved with sufficient adhesion forces between 6.7 MPa and 6.9 MPa. In intial experiments, a sufficient amount of ultrasound and therefore energy was transmitted over a distance of 7 cm in body-like fluids.

Conclusion

In summary, encapsulation of ultrasonic transducers by thin layers of medical grade silicone with sufficient adhesion is possible. Furthermore, it is possible to receive ultrasonic energy through the encapsulation of the transducers, which can be converted into electrical energy to power the implant.

An in-situ perspective on brain-electrode interface investigation of chronically implanted ECoG arrays

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Introduction

It is well known that he stability of neural recordings is highly dependent on the biological responses at the material-tissue interface, whether epicortical (ECoG) or intracortical arrays are used. Studies after chronic implantation are often performed on explants by separating the neural interface from the tissue and analyzing responses at the implantation site and at the array level separately. Here, we focus on the challenge of keeping the brain-electrode interface intact to avoid potential information loss.

Methods

Three micromachined thin-film ECoGs (10 µm polyimide with 300 nm thick embedded platinum metallization and 800 nm thick iridium oxide) were studied after an implantation period of approximately 100 days. Studies in ferrets were performed in accordance with the German Animal Welfare Act. The brains were perfused before the overlaying skull was carefully removed by grinding. The electrode array was embedded in optimized LR-White resin together with the underlying brain tissue and subsequently examined by light microscopy. The influence of brain shrinkage behavior during dehydration was mimicked by using gelatin and agar-gelatin phantoms along with similar pre-embedding attempts in control slices.

Results

Optical analysis showed that the electrodes detached from the cortex due to tissue shrinkage. From a materials science perspective, the large volume embedded interface sample remained stable without cracking during resin polymerization. In addition, agar-gelatin medium was considered to be a preferable candidate for the pre-embedding step.

Conclusion

Stable tissue-electrode resin embedding of the interface requires avoiding excessive micromovement during the preparation process and controlling tissue shrinkage. The degree of encapsulation during the foreign body reaction, the specimen storage medium, and handling during preparation are other important parameters that may affect the reliability of the final sample. The implemented scenario represents a first step to gain better insight into the assessment possibilities of chronically implanted neural interfaces.

Area Selectiv Atomic Layer Deposition on Noble Metals

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Introduction

Atomic layer deposition (ALD) can be used to deposit ultra-thin, conformal, and defect-free layers. Due to the growth kinetics, lateral control of the layer-growth is nearly impossible. The area-selective atomic layer deposition aims at the lateral process control. For neural implants, the objective is to leave functional surfaces such as electrodes uncoated while the rest of the implant surface is encapsulated using ALD. Self-assembling monolayers (SAMs) can deactivate the surface, preventing the growth of layers. Plasma-enhanced ALD is used to coat temperature-sensitive materials such as those used in implant technology. However, the plasma removes the previously applied SAMs and alters the surfaces after time. Reactive ion etching (RIE) can be used, to “reset” the altered surface. By using a cluster system, in which it is possible to switch between an ALD and a RIE process, without a vacuum break, an area-selective ALD for temperature sensitive materials could be possible.

Methods

The selective growth of titanium oxide, grown by PE-ALD on platinum, gold, polyimide, and silicon substrates, which were treated with SAMs (1-octadecanethiol) before each cycle, was investigated. The surface of the substrates was minimally etched after a certain number of cycles using RIE. The growth was measured by ellipsometry and profilometry. The process parameters of the PE-ALD and RIE were varied to achieve a satisfactory selective ALD growth.

Results

So far, a delayed growth of titanium oxide on gold and platinum was observed compared to the silicon substrate. The ratio was about 5 nm on gold and 4 nm on platinum to 13 nm on silicon.

Conclusion

The experiments show a tendency towards selective growth of titanium oxide, which is applied by PE-ALD to various surfaces that have been pre-treated with SAMs and RIE. Thus, area-selective deposition without using lithographic methods should be possible.

Brain activity and event-related potential analysis in healthy and spinal cord-injured individuals

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Introduction

Spasticity has a drastic effect on people's quality of life, creating a strong need for new knowledge of its causes and any amelioration. This study proposes a methodology for better understanding the mechanism and consequences of spinal cord stimulation for neuronal repair. The brain and muscles were recorded with electroencephalography (EEG) and electromyography (EMG) to investigate the characteristics and resulting behavior of the brain and spinal cord.

Methods

A measurement system for recording EEG and EMG was built and tested. Healthy individuals, as well as spinal cord-injured, were measured during tSCS treatment, and then afterward the patellar tendon reflex (PTR) test was performed. First, 23 healthy subjects aged 20-30 years, 12 male and 11 female, were measured to obtain reference data. Then, 4 healthy individuals aged 50-70 years, 2 male and 2 female, were measured. Lastly, two SCI males were measured. The first of them had a complete cervical spinal cord injury of C6-C7 and was confined to a wheelchair. The second had a tumor growth inside the spine located at approximately T1-T4.

Results

A measurement system for research on EEG and EMG has been developed and tested with measurements of 23 healthy individuals (Age = 20-30), 4 healthy individuals (Age = 50-70), and 2 spinal cord injured individuals in this part of the study. Results show recordings, processing, and evaluation of brain potentials evoked by the patellar tendon test and tSCS. Additionally, some very interesting findings are discovered.

Conclusion

To conclude, this study has provided a database from measurements on non-injured individuals and individuals with SCI. A measurement method with a signal processing pipeline and a protocol has been developed and tested. The measurements have shown variability within the groups.

A novel reflex analysis of healthy and spinal cord-injured individuals

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Introduction

Spinal cord injury (SCI) has a drastic effect on the quality of life of those affected. There is thus a great need for new knowledge that may increase their quality of life. The goal of this research was to develop and set up a measurement system for exact measurements of times between events in a patellar reflex test and a transcutaneous spinal cord stimulation (tSCS) and compare the two in healthy and spinal cord-injured individuals.

Methods

The patellar reflex test and tSCS were tested on 21 individuals with healthy nervous systems and 2 SCI individuals to investigate their characteristics. A pipeline to analyse electromyography data from the lower extremities was designed.

Results

A measurement methodology and a pipeline for data analysis was developed and tested, giving a powerful tool for further research. Our results indicate a significant difference between the muscle response to patellar tendon impact compared to tSCS as well as a difference in the latency and duration of the muscle answer between healthy and the two SCI subjects at stake. In this one case, we detect a lower amplitude but an earlier response in the spastic leg of spinal cord injured subject 2, indicating a difference that characterizes the spasticity.

Conclusion

In this study, a processing method was created for comparing muscle signals generated by patellar strikes or electrical stimulation to the posterior nerve roots. Data from the subjects with central nervous system lesions showed characteristic differences from reference data.

An EEG-Based Framework to Continuously Detect Goal-Directed Movements and Error Processing to Enable Robotic Arm Control with Kinesthetic Feedback: Feel Your Reach

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Abstract

Establishing the basic knowledge, methodology, and technology for a framework for the continuous decoding of hand/arm movement intention was the aim of the ERC-funded project "Feel Your Reach". In this work, we review the studies, methods and findings we performed and implemented in the last 6 years, which build the basis for enabling severely paralyzed people to non-invasively control a robotic arm in real-time from electroencephalogram (EEG).
In detail, we investigated goal-directed movement detection, decoding of executed and attempted movement trajectories in sensor space and source space, grasping correlates, error processing, and kinesthetic feedback. Several of these studies have been performed in a closed-loop brain-computer interface (BCI) setup. Although we have tested some of our approaches already with the target populations, we still need to transfer the "Feel Your Reach" framework to people with cervical spinal cord injury and evaluate the decoders' performance while participants attempt to perform upper-limb movements. Furthermore, we will give an overview of ongoing activities in combining the different decoders mentioned into one single system. While on the one hand, we made major progress towards this ambitious goal, we also critically discuss current limitations and possible future directions.

Acknowledgements

We acknowledge the participation of about 320 participants, about 10 with spinal cord injury, in more than 20 studies performed during the runtime of "Feel Your Reach". Also, we acknowledge the following people, who were part of the Team: Andreea Sburlea, Reinmar Kobler, Joana Pereira, Catarina Lopes Dias, Lea Hehenberger or doing an internship in the Graz BCI Lab and contributed to the studies: Inês Almeida, Liza Kolesnichenko, and Nicola Butturini. Most of the work was part of the ERC funded project "Feel Your Reach" (681231).

Track:
Optical and Photonic Processes and Devices

Novel dynamic Pipette Aspiration approach using Optical Coherence Tomography

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Introduction

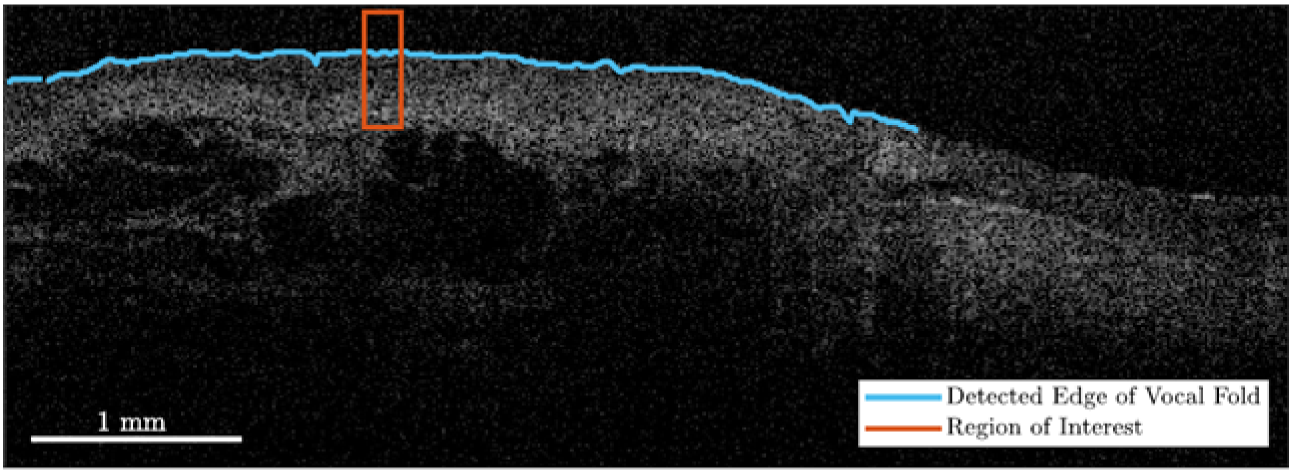
The method of pipette aspiration finds its origin in the investigation of cells and underwent a continuous development over the years. The basic principle is to determine the elastic properties of soft tissue in the near surface tissue region. Therefore, the tissue is aspirated into a thin pipette and deformation of the tissue is measured and the Youngs modulus calculated. Over the years the technique has been combined with different other methods. We have enhanced it to dynamic examination by applying an oscillating pressure. By doing so, the measurement principle can be expanded to investigate the viscoelastic behavior of the sample.

Methods

The Optical Coherence Tomography (OCT) uses an interferometer to measure the distance of reflecting elements in the sample. By scanning over the sample, an image similar to a sonography can be made, but with a much higher resolution. The presented novel technique combines pipette aspiration with the OCT. Doing so, it is possible to investigate the tissue's properties at different excitation frequencies, but also to unveil the tissues motion underneath the surface. An information which was hidden till now.

Results

A Dynamic Optical Coherence Tomography prototype pipette has been developed and first yet unpublished studies have been carried out. In order to excite the tissue, a sinusoidal pressure signal has been applied. The Figure below shows the recorded cross section, the inhomogeneous layered structure can be seen.



Conclusion

It was possible to determine the oscillation of the surface in the region of interest and further the amplitude. So, it could be shown that it is in principle possible to extract the elasticity along the surface at multiple locations.

Development of a multimodal device combination for advanced ophthalmologic diagnosis in large animals

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Introduction

The initial situation for the diagnosis of eye diseases in large animals is that different examination methods and thus different diagnostic devices are required for different clinical conditions. Especially for purchase examinations, the veterinarian usually has no objective measurement values available. Therefore a concept was developed, which combines the ophthalmologic methods pupillometry, electroretinography (ERG), as well as visual evoked potentials (VEP) in one device. In this abstract first results of the development will be presented.

Methods

For the development of a multimodal device combination of pupillometry, ERG and VEP, a prototypical experimental environment consisting of a single-board computer supported by a graphic card, an illumination unit, an 8MP camera system, and a detachable eyecup was built. The optics of the camera were equipped with an electrically adjustable focus. The illumination for image capture is optionally designed as a direct or indirect infrared source. In combination with a biosignal amplifier (f=500Hz) and time-synchronous data processing, the corresponding ERG and VEP data can be assigned to the pupil data.

Results

The experimental setup was placed in a compact 3d-printed housing and can be held and controlled with one hand. A 4.3"-display allows the veterinarian to view the eye. The homogeneous illumination of the eye was made possible with radially arranged white light- and RGB-sources (I_v=500cd) in a diffused light disk. First system tests in the laboratory showed adequate acquisition (area in pixels +/-5%) of pupil data at a rate of 30Hz. The electrical derivatives can be recorded according to the ISCEV standards. The temporal synchronization of the measured values was successfully implemented.

Conclusion

The developed eye diagnosis device is to be tested in further work through extensive studies on horses. The aim is to investigate correlations between the individual measurement results of the respective diagnostic procedures. Furthermore, funduscopy is to be integrated into the device.

Track:
Prostheses, Implants, Artificial Organs

Improving Equine Intramedullary Nail Osteosynthesis via Fracture Adjacent Polymer Reinforcement

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Introduction

Osteosynthesis of the equine femur is still a challenge for veterinary medicine. Even though intramedullary fracture fixation is possible nowadays, the varying geometry of the medullary cavity along the bone axis is a critical factor. Limited contact area between implant and bone can cause insufficient primary stability. In this study, it was investigated whether the osteosynthesis stability can be improved with a form-adaptive reinforcement for the diaphyseal part of the proximal fragment.

Methods

Eight equine femora were fitted with intramedullary nail osteosynthesis and analyzed by 4-point bending. Virtual position planning of the ex-vivo implantation using CT-data increased comparability. For five femora the proximal fragment was reinforced with a flexible polymer mixture. Longterm stability was tested via cyclic loading. Bending stiffness and its development due to cyclic loading was evaluated before and after reinforcement procedure. Finally, load-to-failure was tested in the same setup.

Results

The application of the polymer reinforcement increased the maximum torque in the load-to-failure measurement by 26%. Bending stiffness was not affected in the measured loading range by the reinforcement. Cyclic loading increased bending stiffness for a conditioned state but showed to be reversible for the most part.

Conclusion

The fracture adjacent reinforcement showed to be beneficial to the osteosynthesis stability, but further investigation is necessary for surgical application.

Visualization of platelet deposition in a flow chamber

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Introduction

The formation of thrombi is still a challenge when it comes to ventricular assist devices (VADs). This can be caused by the subsequent deposition of proteins and platelets on foreign surfaces. In VADs, the blood contacting components are mainly made of titanium alloys due to hemocompatible properties and corrosion resistance. However, surfaces where mechanical contact of the rotor and the stator occur like bearing areas of axial VADs require high wear resistance due to the greater potential of scratches.

Methods

An in vitro test bench to optically investigate the deposition of fluorescent labelled platelets on the protein layer of different surfaces is hereby presented, aiming to investigate the potential for thrombi formation of five different inorganic hard material coatings on titanium. The coating materials included Titanium Nitride (TiN), Titanium Niobium Nitride (TiNbN), Diamond-Like Carbon (Ionbond-Medthin-43 (DLCI) and Oerlikon Balimed A (DLCO)) and Wolfram Carbid Oerlikon Balimed C (WC). Uncoated titanium (Ti) was investigated as reference. Heparinized human whole blood was incubated with Mepacrine (fluorescent dye) and then pumped through a flow chamber with defined shear rate conditions over the samples. The adhered platelets were visualized via inverted fluorescence microscopy. The analyzation of the green values and the binary image of the generated fluorescent picture offers conclusions about the platelet accumulation and the percentage of the covered surface area, respectively.

Results

Statistical analysis showed a significant lower potential for platelet deposition for TiN compared to Ti and no significant differences for the rest.

Conclusion

It can be concluded that none of these coatings have a higher potential for platelet deposition than Ti and therefore point towards suitability for blood contacting components.

Criteria for Implant Fit Assessment in Total Knee Arthroplasty - A Review

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Introduction

Patient satisfaction in total knee arthroplasty is still limited and lower compared to patient satisfaction in total hip arthroplasty. While there are multiple influence factors for patient satisfaction, implant design is one aspect to consider. In clinical practice, the patient-specific assessment of implant fit is limited to a matching of the anteroposterior and mediolateral size, based on X-rays. Hence, the goal of this review was to identify other potential criteria for a patient-specific implant fit evaluation.

Methods

A literature review was performed in PubMed. Inclusion criteria were a patient-specific assessment of knee implant components, a comprehensible motivation or a statistically proven relationship with an outcome measure, and a clear method description. Implant fit was considered not only as a matching of size, shape and interface, but also to include the implant's (rotational) alignment, as proposed by Dai et al. (2014).

Results

Several studies reported a statistically significant relationship of implant fit criteria with outcome measures. Many more studies proposed fit criteria, motivated by a potential relationship with outcome measures. Most criteria assessed the bone-implant interface, second the morphology of the articulating surfaces and third the component and resulting bony alignment.

Conclusion

Obstacles for the assessment of the criteria identified is the limited availability of 3D surface models in TKA. However, with new imaging technologies this availability is likely to increase. The decision process regarding the implant in TKA could be supported by a comprehensive automated fit analysis of several designs and/or sizes. An adequate matching of the implant to the respective patient may improve patient satisfaction.

Towards Test Bench for Aspiration Catheters in Realistic Evaluation Scenarios

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Introduction

Aspiration catheters play an important role in mechanical thrombectomy in interventional neuroradiology, as they provide support for stent retrievers or are increasingly used separately for contact aspiration. To evaluate the performance of different aspiration catheters in terms of suction force, most current studies rely on manual measurement methods, these include measurements with weights or measurements with hand-held manometers. Moreover, there is currently no standardized method that records measurements digitally and with high temporal resolution. To overcome these challenges, we propose a new test bench that simulates a dedicatet aspiration scenario and takes measurements close to the aspiration catheter tip.

Methods

To meet the requirements, a simplified vascular phantom, a pressure sensor and a simplified clot model were implemented in the prototype. The technical control is realised by a microcontroller and MATLAB based scripts, which also provides a user interface on a PC. To demonstrate the applicability of the prototype, two common used aspiration catheters were measured.

Results

The obtained measurements show that the prototype is able to measure accurate vacuum curves. Therefore, it is possible to perform standardised comparisons between aspiration catheters from different manufacturers as well as different aspiration pumps and aspiration tubings and their combinations. However, there is a slight noise in the obtained data, which can be caused by the pressure sensor or the vacuum generated at the aspiration catheter tip.

Conclusion

The developed prototype overcomes the still widely used manual and semi manual and thus error prone measurement methods for the evaluation of vacuum based thrombectomy systems. The future development steps will include the integration of improved patient specific vascular phantoms and clot models.

Temporal pitch perception in CI users: Channel independence in apical cochlear regions

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Introduction

Two-electrode stimuli presented on adjacent mid-array contacts in cochlear-implant (CI) users elicit pitch percepts that are not consistent with a summation of the two temporal patterns. This indicates that low-rate temporal rate codes can be applied with considerable independence on adjacent mid-array electrodes.

Methods

At issue in the present study was whether a similar independence of temporal pitch cues can also be observed for more apical sites of stimulation, where temporal cues have been shown to be more reliable than place cues, in contrast to middle and basal sites.
In CI recipients with single-sided deafness (SSD) implanted with long lateral-wall electrode arrays, pitch percepts were assessed by matching the pitch of dual-electrode stimuli with pure tones presented to the contralateral normal-hearing ear. The results were supported with an additional pitch-ranking experiment, in a different subject population with bilateral deafness.

Results

Unmodulated pulse trains with 100, 200 and 400 pulses per second were presented on three pairs of adjacent electrodes. Pulses were separated by the minimal inter-channel delay (1.7 µs) in a short-delay configuration and by half the pulse period in a long-delay configuration. The hypothesis was that subjects would perceive a pitch corresponding to the doubled temporal pattern for the long-delay stimuli due to the summation of excitation patterns from adjacent apical electrodes, if those electrodes were to activate largely overlapping neural populations. However, we found that the mean matched acoustic pitch of the long-delay pulses was not significantly different from that of the short-delay pulses.

Conclusion

These findings suggest that also in the apical region in long-array CI recipients, temporal cues can be transmitted largely independently on adjacent electrodes.

Integration of a musculoskeletal multibody simulation of the lower extremity into a six degree of freedom joint simulator

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Introduction

Musculoskeletal multibody simulations (MBS) are an established method in biomechanical research and allow analysis of joint dynamics after total knee arthroplasty (TKA). However, experimental validation is essential for contact modelling of articulating surfaces. Complex MBS of knee joints place high demands on the experimental methods to allow its validation. Hence, our present study aimed to transfer joint dynamics generated by MBS for an active motion of the lower extremity to a six degree of freedom (DOF) joint simulator.

Methods

Kinematic data of a patient treated with a bicondylar cruciate-retaining total knee arthroplasty (P.F.C. Sigma, DePuy Synthes, Raynham, MA, USA) were acquired by an inverse kinematic analysis and used for forward dynamic analysis. To transfer the complex six DOF knee joint dynamics to the six DOF VIVO™ joint simulator (AMTI, Watertown, MA, USA), a coordinate transformation from Cartesian xyz Cardan sequence to the Grood and Suntay's system was required. Using a hybrid force/position control the flexion angle, the abduction and internal rotation moment as well as the three translational forces could be transferred to the simulator.

Results

This integration framework resulted only in minor root mean square errors for the control variables and the measured data of flexion angle (0.008°), abduction moment (0.5 Nm), internal rotation moment (0.5 Nm) and the translational forces (3.3 N, 7.3 N, 3.0 N).

Conclusion

Our data show that MBS of a knee joint treated with a TKA can be transferred to a joint simulator accounting for all six DOF. In particular, the small deviation of the controlled variables indicates that the transfer was accomplished and the data generated by the MBS were sufficiently processed before transferring. This approach will be used in future studies to validate the contact modelling in MBS.

Acknowledgements

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Development of a pulsatile test bench for the investigation of ventricular assistance devices

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Introduction

Ventricular assistance devices (VAD) operate under dynamic physiological conditions. Particularly, the dynamic pressure conditions at the inlet and outlet of the VAD determine the pump flow and its pulsatility. It was previously shown that haemolysis is significantly affected by the operating condition in terms of pump flow, pressure head and pump speed. Consequently, a pre-clinical framework with a high level of clinical realism is required to predict clinical performance and realistic boundary conditions. Here we demonstrate the pulsatile test bench (PTB) for the study of VAD haemocompatibility in a dynamic pressure environment for the pediatric sector.

Methods

Within the PTB, the VAD is mounted between two reservoirs resembling the aorta reservoir (AR) and the left ventricular reservoir (LVR). The desired pressure in the reservoirs were controlled by applying overpressure or vacuum through pneumatic proportional directional valves. The relative filling levels of the reservoirs were controlled by adjusting the backflow from AR into LVR by a slide valve. Additionally, the test fluid temperature can be controlled through the measurement.
Due to it valveless design and the thermal control, the PTB is suitable to assess pump characteristics and blood trauma under realistic pulsatile conditions.

Results

The PTB has been developed and promising preliminary tests with water and a VAD prototype were carried out: A typical pressure condition for a pediatric heart failure patient (mean pressure head: 33 mmHg, heart rate: 124 bpm). The average flow rate was 1.8 l/min with a pulsatility of 5.2 l/min. The mean percentage deviation between the specified and measured pressures was 3.4% (AR) and 5.4% (LVR).

Conclusion

Preliminary results indicate the ability of the PTB to mimic realistic physiological pressure boundary conditions of paediatric patients. In the next step, experiments with water-glycerine-mixture and blood will likely reveal the complexity of VAD prototype performance and the associated haemolysis risk.

New approach for objective measurement of a middle ear vibratory implant

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Introduction

The active middle ear implant Vibrant SOUNDBRIDGE (VSB) is widely used to treat adults and children with different types of hearing loss. An objective measurement of the implant's performance is desired by the field, especially as an intra-operative measurement during some delicate coupling cases, such as the round window placement. Recently, a new research device for transferring stimuli to the implant was developed (AcoustiAP).

Methods

The auditory brainstem response (ABR) was recorded using the AcoustiAP method in two clinical studies so far. Cebulla et al. 2022 compared the AcoustiAP to the miniTek-method, intra-operatively in 10 subjects. The study evaluated the usability, signal quality, wave V amplitude and threshold detection. Sprinzl et al. 2022 evaluated the feasibility and threshold detection of the ABR via AcoustiAP intra- and post-operatively in 14 subjects.

Results

Cebulla et al. reports about reliable connection and signal transmission without distortion using the AcoustiAP compared to the miniTek-method. The minimum detectable hearing threshold was comparable using both methods, although the median threshold obtained with the AcoustiAP was closer to the pre-operative bone conduction threshold. With increasing stimulus levels, using the AcoustiAP larger amplitudes could be evoked, however the differences were not statistically significant. The study by Sprinzl et al. revealed a median intra-op ABR threshold via AcoustiAP that was on average 3 dB (3.3 dB Cebulla et al.) higher compared to the pre-op bone conduction threshold. In addition, this study measured ABR thresholds post-operatively using the AcoustiAP.

Conclusion

The AcoustiAP provides a distortion free transmission of stimuli between an ABR machine and the Vibrant SOUNDBRIDGE. It therefore improved upon previously used methods for signal transmission to the implant. Intra- and post-operative ABR threshold measurements via AcoustiAP are feasible and provide relevant device performance data to support evaluation of coupling efficiency intra-op and for long-term monitoring.

Computational modeling insights into electrode-neuron interface and cochlear health of cochlear implant users

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Introduction

Cochlear implants (CIs) restore hearing by bypassing the degenerated hearing mechanisms and stimulating the auditory nerve fibers (ANFs) directly with electrical pulses. Functionality of the electrode-neuron interface inside the cochlea affects the hearing outcomes of the CI user and it can be assessed by measuring electrically evoked compound action potentials (eCAPs). Functionality of the interface is influenced by several neural and non-neural aspects, which creates some challenges for diagnostics and optimal treatment of the CI user. Here, a computational modeling approach was taken to gain more insight into the topic.

Methods

A computational model was designed to predict eCAPs that can be recorded as a compound response of the ANFs to the elicited electrical stimulus. The model design was kept simple by considering the distance effects between the electrodes and the ANFs only in a 2-D space and using a phenomenological model to predict the spiking activity of the ANFs. The geometrical constraints of the model were derived from posthumous and post-operative data from literature. Influences of both neural and non-neural aspects on the eCAP amplitude growth functions (AGFs) were investigated by varying both neural survival inside the cochlea as well as electrode-neuron distances and distances between stimulating and recording electrodes.

Results

Model predictions were found to agree with existing data: The model was shown to reproduce the dependency of the eCAP AGF slope on neural survival and on stimulating-recording electrode distance as observed in electrophysiological measurements with non-human mammals and CI users, respectively. In addition, increased electrode-neuron distance was shown to result in larger eCAP thresholds.

Conclusion

Our study shows how auditory models can be used to test theories of effects of neural and non-neural influences on objective measures about the electrode-neuron interface inside the cochlea. The results motivate regular eCAP measurements for longitudinal monitoring of CI user's cochlear health.

Improved Endothelialization of Left Ventricular Assist Device Impeller by Iron Oxide Nanoparticle-Loaded Endothelial Cells Enhancing Hemocompatibility

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Introduction

In fact, left ventricular assist device (LVAD) is a lifesaving therapy option for patients with severe heart failure. Nevertheless, despite high-dose anticoagulation, life-threatening thrombotic events still occur in LVAD. By establishing an anti-thrombogenic endothelial monolayer (EML) on artificial blood-contacting surfaces thrombus formation may be inhibited.

To promote flow-resistant EML-adhesion on the magnetic impeller, we exploit magnetic attraction towards endothelial cells (ECs) loaded with iron oxide nanoparticles (IONPs). In particular, EMLs, established from IONP-ECs on the disassembled impeller under static conditions, were analyzed for their anti-thrombogenic property and resilience towards LVAD flow-conditions. Following, we seeded IONP-ECs on rotating impellers to assess EML establishment inside the running LVAD.

Methods

EMLs (IONP-loaded vs. non-loaded ECs) were cultivated on impellers dismounted from LVADs (Heartware™) under static conditions. ECs adherence and viability were monitored by calcein fluorescence-staining. Expression levels of activation- and thrombogenic state markers were analyzed by qRT-PCR. Within hemocompatibility tests, a colorimetric assay was used to quantify adherent thrombocytes compared to a clinically relevant control. Flow-resistance was assessed under 1800rpm within a mock circulation loop by recirculating cell medium for 1h. EC seeding onto rotating impellers was tested in an open beaker-setup on a magnetic stirrer. Viable ECs were counted manually from images taken after calcein staining.

Results

IONP-loading did not affect EML viability. qRT-PCR revealed no signs of EC-activation regardless of IONP-loading. Compared to the positive control, EMLs with and without IONPs significantly reduced the number of adherent thrombocytes. After rotation, the number of adherent IONP-ECs was significantly higher compared to the non-loaded ECs. Additionally, EC adhesion to rotating impellers was only observed using IONP-ECs.

Conclusion

IONP-loaded ECs facilitate the establishment of non-thrombogenic EML on the LVAD impeller surface, showing improved flow-resilience under flow conditions. IONP-ECs can adhere to the rotating impeller, prospectively allowing EML establishment in already running LVADs.

Intracochlear sound pressure measurements in human cadaver temporal bones during forward and backward stimulation of the cochlea using the floating mass transducer

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Introduction

The Vibrant Soundbridge (VSB, MED-EL Medical Electronics, Austria) is the most used active middle ear implant for the treatment of sensorineural and mixed hearing loss. The floating mass transducer (FMT) can be coupled in "forward stimulation" either to the ossicular chain or stapes footplate or - in "backward stimulation" to the round window (RW) membrane. Laser Doppler vibrometry (LDV) is the standard method to determine the output in forward stimulation mode. However, LDV fails to provide correct output level results in reverse stimulation.
The objective of this experimental study was to determine the output of the FMT in reverse stimulation by combined LDV and intracochlear pressure difference measurements in temporal bones to provide reference output levels for both stimulation modes.

Methods

In fresh ASTM compliant temporal bone preparations the FMT was coupled to the short process of the incus and the equivalent output level was determined. Subsequently, the output level was determined for backward stimulation with the FMT coupled to the RW by several RW couplers. To ensure a defined coupling force at the RW membrane, a force sensor was implemented in the setup, which can be controlled by a micro-manipulator. In all configurations, stapes footplate vibration was measured by LDV and the intracochlear sound pressure difference between scala vestibuli and scala tympani was measured with pressure sensors to determine the equivalent sound pressure output level of acoustic and mechanical stimulation to the inner ear in both directions (n=10).

Results

Based on preliminary results (n=5 out of 10), the FMT generates the highest output level during forward stimulation. In reverse stimulation mode the static coupling force between the FMT and the RW membrane had a significant influence on the sound transmission into the cochlea. The results of this feasibility study still need to be extended by a comprehensive study.

Cochlear Implants as Cognition Interface to Selective Attention

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Introduction

Cochlear implants (CIs) restore hearing by bypassing the degenerated hearing mechanisms and stimulating the auditory nerve fibers (ANFs) directly with electrical pulses. The ANFs are endpoint of the efferent auditory system which enables prioritization of strongly overlapping spatiotemporal cochlear activation patterns elicited by relevant and irrelevant inputs. ANFs are sensitive for such attentional modulations, which can be recorded with the build-in recording module of CIs. The module is designed to record electrically evoked compound action potentials (eCAPs) in a clinical routine (AutoART). In a retrospective approach, AutoART recordings are analyzed with respect to attentional modulations.

Methods

AutoART data (170 runs) of 17 CI users was analyzed. Each AutoART run lasted for 25 seconds where a constant tone was presented with increasing intensity, starting from zero intensity. The participants were asked to press a button once they heard the tone (A), once it was moderately loud (B), and once to abort because of loudness (C). Subtracting single pulse responses using a running average over time yielded to continuous recordings of background activity for 25 seconds. The background activity was then separated in time intervals: 2 second time window before each button press as “high attention phases” versus the remaining intervals regarded as “low attention phases”.

Results

Time-dependent differences in background activity of AutoART recordings across low frequency bands (<30Hz) could be classified into intervals of high versus low attention phases. Frequency separated background activity was different for the 6 intervals silent, 2 seconds before threshold (A), audible, 2 seconds before second button press (B), loud, 2 seconds before abortion (C).

Conclusion

This retrospective analysis reveals the potential of extracting information on neural processes connected to selective attention from background activity recorded in state-of-the art clinical tools.

Development of an EMG-based Elbow-Exoskeleton with Twisted String Actuation

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Introduction

This paper presents an exoskeleton for upper extremity rehabilitation of stroke patients. In order to make rehabilitation widely available, the goal is an inexpensive, portable, and easy-to-use therapy for paralysis of the arm.
The exoskeleton is actuated by twisted string actuators (TSA).
To reduce the length of the TSA a motor with hollow shaft was chosen, as this allows the string to run through the motor.
The control of the exoskeleton is designed for predefined elbow flexion exercises. The start of the movement is triggered by a threshold value in the sEMG of the m. biceps brachii.

Methods

To evaluate the controller, the exoskeleton performed a flexion movement (5° to 115°) in 2 s and then an extension back to 5° in the same time after a 1 s wait. To simulate different force requirements, additional weights up to 1500 g were attached.

Results

During both, the flexion and extension movement, that angle tracking error was sufficiently small and the steady state error was zero. The angular velocity of the elbow joint showed pronounced oscillations with increasing weights.

Conclusion

The results show that TSAs can be used to actuate elbow exoskeletons. Thus lightweight, ergonomic, simple and small rehabilitation devices can now be built on this basis. The elasticity of the system must be considered in future work. sEMG must be further implemented to control more sophisticated functions of the rehabilitation device.

Development of a test rig for the diagnosis of arthritic knee joint defects in the case of lower extremity amputees in orthopaedic technology

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Introduction

If the alignment of a leg prosthesis is inadequate there will be the danger of arthritic defects occurring in the preserved knee joint. Acoustic-kinetic joint analysis in orthopaedic technology allows monitoring of the knee joint of an amputee after the alignment of a leg prosthesis and to recognize early joint defects resulting in adaptation of the alignment of the prothesis.

Methods

A test rig was developed which includes acoustic emission analysis of the knee, video-based gait analysis, ground reaction force measurement and the measurement of the holding forces of the hands. During the examination a subject must do 3 one-legged knee bends in 10 sec with the preserved leg. To support the subject two grab handles were fixed with force sensors to the frame. A series of 6 measurements were recorded with breaks of 2 min.

Results

The recorded forces of the leg show a double hump pattern during the knee bend. The rising edge of the flexion phase was not uniform. There was the effect of changes between the forces.

Conclusion

The fitness of the probands acts as an indicator for the shape of the force signals. The signals of the measurements show the necessity of the support of the hands to execute a one-legged knee bend. The knowledge of the 3 measured forces is important for the arthritic diagnosis of the knee joint.

Patient-Orientied Pain Therapy

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Introduction

The object of the presented work is a new class of implantable drug delivery systems for the treatment of chronic pain, enabling a new paradigm in pain therapy. Here, the patient will be directly and actively involved in its individual treatment, which will now allow the patient a very fast, direct response and an adaptation of the therapy to the his needs. The quality of life of particularly severely suffering pain patients will be significantly improved.

Methods

Common intrathecal drug applications are programmed by a remote control that enables the attending physician to modify the continuous pain medication according to the patient's current situation but excluded a direct change from the patient. The new approach extents the classical delivery systems to a multidimensional therapy. The combination with a pain tracking app in the super-ordinate smartphone app enables the patient to record his current pain according to his subjective perception.

Results

Providing a long lifetime of medical implants is always challenging. For that reason, a low energy consuming chip has been selected. Measurements at the body temperature of 37 °C revealed an elevated current consumption of 1.9 µA in EM2. In parallel, the patient pain communication app was programmed for Android and will be provided to patients.

Conclusion

At this early stage of research it has been demonstrated, that a predicted lifetime of 8 years of a patient-oriented system with a coin-cell battery is possible. It is long enough and does not necessitate a rechargeable battery which would arise problems related to wireless energy transfer through the body. With the new approach to a patient-orientied pain therapy the quality of life of affected people should be noticeably increased, the chronification of pain prevented or significantly reduced, and the controllability and parametrization of the therapy decisively improved .

Track:
Regulatories, HTA, Standards

A novel approach to the testing of protective filtering equipment and non-woven filter materials

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Introduction

DIN EN 149 is designed for testing particle-filtering masks for the manufacturing or construction industries. It does not reflect pandemic conditions. Testing with pathogens is hazardous and requires high safety standards. The aim of this project was therefore to develop a testing procedure replicating pandemic conditions with an appropriate, non-hazardous test fluid.

Methods

A parametric study was conducted to determine the composition of artificial human saliva (AS) with physiological properties. Mimicking the SARS-CoV-2-virus, DSPC-cholesterol-liposomes (1:1, w/w) containing sodium fluorescein were extruded in AS. Liposome size distribution was assessed using dynamic light scattering. AS viscosity, conductivity and surface tension were analysed using a drop shape analyser, conductivity meter and rotary rheometer. Fluorescence spectroscopy was used to analyse free tracer content by correlating fluorescence intensity to concentration. To later determine filter efficiencies, the variation of free tracer content was measured as a function of liposome concentration after adding TX-100 in excess.

Results

Targeted physical properties of AS were obtained by applying a combination of Na-CMC, SDS and demineralised water. Major objectives were: conductivity of 12.5 µS/cm to 2.01 mS/cm, a dynamic viscosity between 8 mPas and 12 mPas and a surface tension from 45 ± 6.51 mN/m. Liposomes showed a mean diameter of ~100 nm. Combining liposomes and AS did not result in an increase in free tracer content implying no negative effect on liposome stability through surfactants. The concentration of free tracer content showed a linear progression with increasing liposome concentration.

Conclusion

A non-hazardous virus-like-fluid was produced using modified liposomes allowing a quantitative evaluation. The test fluid and set-up enable the determination of the tracer content and the assessment of filter efficiencies and membrane-destroying effects. This will enable new concepts in protective mask testing.

This Project is supported by the Federal Ministry for Economic Affairs and Climate Action (BMWK) on the basis of a decision by the German Bundestag.

Conceptualization of a digital compass to facilitate the start of clinical evaluation

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Introduction

The novel Medical Device Regulation (MDR) is forcing many more manufacturers across Europe than ever before to quickly comply with the drastically increased requirements, particularly for clinical evaluation. Across all risk classes, the acquisition and review of data and/or literature is now mandatory throughout the product life cycle. Moreover, retrieval of data from various databases or registries is required to enable unbiased and comprehensive clinical evaluation or even monitoring, often assisted by external experts.
The complexity deters many companies from entering this task and thus both legacy and novel innovative products may get lost. Therefore, we conceptualized a digital compass that facilitates the initiation of clinical evaluation by providing first orientation to relevant clinical information and stakeholders related to the device in question.

Methods

According to lean principles, an iterative cycle was carried out to identify the needs of manufacturers and gradually improve the digital tool. A preceding workshop with MedTech companies formed the basis of composing an online questionnaire. Second, interfaces to PubMed, ClincalTrial.gov and Embase were combined to an integrated query and retrieval approach.

Results

The different query results are successfully visualized as a knowledge graph of publications, trials and conducting entities (authors, institutions, etc.) as nodes and connections (e.g. co-authorships) as edges. The ability to filter even small geographic regions, time periods or entities limits the amount of relevant documents. Activity-based profiling of actors enables a selection of potential experts for further collaboration. The use of certain metadata can solve the challenging disambiguation of author names.

Conclusion

A graph-based integration of clinical trials and publications offers a quick overview of available information and active experts considering a specified medical device. Automated query formulation or active learning seem to be promising tools to increase the precision of the digital compass.

Cost-utility Analysis of Home Mechanical Ventilation Compared to Hospital Settings in Patients with Amyotrophic Lateral Sclerosis

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Introduction

Amyotrophic lateral sclerosis is a progressive neuromuscular disease. Mechanical ventilation delays death and use at home can reduce costs and increase quality of life. The aim of the study is comparison of home mechanical ventilation with mechanical ventilation in a healthcare facility for adult patients with amyotrophic lateral sclerosis from the societal perspective in the Czech Republic.

Methods

The Markov model from a previous Czech study was used and updated with data relevant to the societal perspective, which was obtained from the literature and opinions of experts from companies dealing with home mechanical ventilation. The cost-utility analysis was carried out over a time horizon of 10 years and results were presented in incremental cost-utility ratio. Accuracy and validity were verified by probabilistic sensitivity analysis and scenario analysis.

Results

The cumulative costs of home mechanical ventilation are CZK 6,116,394 and the cumulative costs of the mechanical ventilation are CZK 8,195,848. The cumulative utilities of home mechanical ventilation are 3.55 QALY and the cumulative utilities of mechanical ventilation are 3.78 QALY. The incremental cost-utility ratio is CZK 9,094,042. Probabilistic sensitivity analysis and scenario analysis do not show significant changes.

Conclusion

Home mechanical ventilation may be considered cost-effective for patients with amyotrophic lateral sclerosis from the societal perspective.

Point-of-care production at hospitals - smart processes for tailor-made medical devices

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Introduction

There are two impactful changes in the EU medical device sector that create a field of tension between regulation and technology. While, the Medical Device Regulation defines stricter rules of the game, new technology is changing the game by enabling point-of-care (PoC) of medical devices, such as additive manufactured implants. We analyze the regulatory framework and the options for manufacturers to bring innovative and patient-specific devices into the operating room.

Methods

We highlight different technologies and processes that can enable PoC production of tailor-made medical devices co-located at hospitals, systematically evaluate the benefits and draw-backs of the different options, and present our choice for patient-specific PoC production of drilling templates for cochlear implant surgeries. Based on all applicable regulatory requirements, including the requirements of a quality management system (QMS), we list the possible options and evaluate them according to costs, required changes in hospital QMS processes, role of legal manufacturer, notified body involvement, ownership, and responsibilities.

Results

Options for PoC production are:

1. Using an automated medical device production system that can interact with other medical devices, e.g. for customization, and which can be considered to be a medical device.
2. Providing tools and equipment to force the hospital into the role of the legal manufacturer, i.e. selling the technology not as a medical device.
3. Co-locate the manufacturing at the hospital under the QMS of the company.

Conclusion

With the integration of smart and fast PoC production processes at the hospital, tailor-made medical devices will enable better patient treatment, it will change the game.

IEEE 11073 SDC for Pandemics like COVID-19: Example Implementation of an Isolation Room

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Introduction

Treating patients in an intensive care unit (ICU) isolation room is challenging for the caregivers and the patients. While this is known for years, the COVID-19 pandemic has highlighted this as if under a burning glass. The risk of infection for the caregivers is very high and the time spent for changing clothing is enormous. Thus, every treatment that can be performed from the anteroom of the isolation room at the same quality level is a potential building block for solving the challenges. Additionally, a reliable and distributed alerting and comprehensive documentation would greatly assist caregivers.

Methods

We show an example implementation of a manufacturer-independent interconnected COVID-19 ICU isolation room based on the ISO/IEEE 11073 Service-oriented Device Connectivity (SDC) standards by means of a demonstrator with four different manufacturers.

Results

The demonstrator shows the safe, reliable, and secure interoperability. Information from the medical devices in the isolation room (ventilator, patient monitoring, infusion/syringe pump) is displayed at the point-of-care cockpit in the anteroom; device parameters can be adjusted from the cockpit without entering the isolation room; alarms are distributed to mobile devices and a central dashboard; and documentation is supported. Certificate-based encryption, authentication, and authorization are key features of the SDC communication.

Conclusion

In the presented demonstrator, device connectivity and external control capabilities were impressively shown in a critical clinical area. However, for future visions like a “silent”/”quiet” ICU, there is still work to do in the field of standardization and implementation. Additional (medical grade) value adding systems will be developed in the future. IEEE 11073 SDC has shown its role as a key enabling technology. Combining this with mobile networks based on cellular technology like 5G offers a high potential for setting up clinical units quickly in crisis situations, e.g., pandemics, wars, or natural disasters.

Design study of dynamic mechanical test bench specimen grips

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Introduction

The characterization of mechanical properties for materials used in biomedical applications is essential for performance evaluation. In addition to quasi-static tests, dynamic tests extend the range of methods and allow predictions of failure, as well as information on durability. Appropriate specimen grips according to the test sample geometry are crucial for a reliable examination of mechanical testing and therefore valid experimental data. In particular, the investigation of polymers is challenging, as properties show major differences depending on temperature and applied loading rate. This could result in slipping or tearing of samples in the specimen grip area.

Methods

Numerical simulations of reference grips, as well as alternative designs, were performed evaluating possible optimizations to avoid plastic damage due to the clamping process and to provide appropriate specimen grips. Simulations were analyzed regarding stress distribution (v. Mises) in the clamped specimen and resulting deformation in the clamped area of the specimen. This analysis focused on the elements undergoing the highest compression. Prototypes were 3D-printed for preliminary testing in a dynamic-mechanical test bench.

Results

The results of the numerical simulations show a thickness reduction of 20.1 % for the original grips. A modified clamping geometry leads to a compression of 2.0 % for design D1 and 14.4 % for design D2. Preliminary tests in the dynamic-mechanical test bench showed a reasonably safe clamping and neither slipping nor tearing of the specimen.

Conclusion

Both the results of the numerical simulation and preliminary tests with 3D-printed prototypes show a distinct improvement in specimen clamping. Plastic deformation and local stress peaks were reduced while maintaining the same tightening torque.

Switzerland is now a third country to the EU: The effects on medical devices

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Introduction

26 May 2021 was a key date for the medtech industry: the new Medical Device Regulation (MDR) replaced the old Medical Device Directive (MDD). On the same day, the Swiss Federal Council broke off negotiations with the EU on the Institutional Agreement (InstA), preventing an update of the Mutual Recognition Agreement (MRA) for free bilateral trade in medical devices. On that day, the Swiss medtech sector was relegated to "third country" status, new trade barriers were put in place and the EU Commission announced that Swiss certificates would no longer be recognised in the EU.

Methods

The Swiss medtech sector has made great efforts to prepare itself for the third-country scenario and has fought at all levels to try and lower the export and import barriers. Despite some success, free exchange of goods is no longer possible as before and some patients in Switzerland, but also in the EU, may no longer have access to the best possible devices.

Results

The attractiveness of Switzerland as a medtech location has suffered greatly. What multi-national company would still choose Switzerland as its EU headquarters? And every Swiss start-up company must ask itself whether a location in the neighbouring EU area would not be better suited for market access to the EU market. Therefore, Switzerland has to re-invent itself and come up with a strategy of how to best support its academical and industrial partners - from development to manufacturing and distribution of medical devices. A possible strategy will be presented in detail.

Conclusion

There are consequences when your government decides not to take part in the EU common market. The consequences affect all of us, either as part of the medical device industry or as a potential patient.

Pulsatile flow testing of heart valve prostheses in vitro

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Introduction

For the approval-relevant testing to prove safety and effectiveness of new heart valve prostheses, a new version of the ISO-5840 was published in 2021. One of the major tests in this standard is the investigation of hydrodynamic performance by means of a pulse duplicator system. A new requirement of the ISO-5840:2021 is the validation of the pulse duplicator system, by comparing the results with a round-robin study published by the ISO Cardiac Valves Working Group in 2019.

Methods

Two pulse duplicator systems were evaluated. The results were compared between the different test benches and with the round-robin study to validate the developed test methodology.
To assess the repeatability, one measurement series was performed for the intra-institutional comparison, a second measurement series was conducted for the inter-laboratory comparison. Test parameters were selected according to the round-robin study. A mechanical prosthetic heart valve was used as test valve. The values for the effective orifice area (EOA) and the regurgitant fraction (RF) were assessed, pressure and flow waveforms were analysed.

Results

In general, the developed test methods lead to reliable results according to ISO 5840:2021 and compared to the international standard. Both pulse duplicators have achieved reliable results in terms of repeatability in the intra-institutional and inter-laboratory comparison. The test benches are therefore suitable for the hydrodynamic performance testing of heart valve prostheses according to ISO 5840:2021.
During the experiments slightly higher EOA and RF were measured by means of one pulse duplicator system although both test benches were identical. An asymmetric closing kinematic of the test valve was identified. Thus, leading to a prolonged closing time and closing volume of the valve. This in turn, led to an increased EOA.

Conclusion

Thus, it is considered to attach great importance to the leaflet kinematics when comparing or validating test benches or test methods.

Track:
Sensors and Monitoring

Impact of the fiber cutting angle on fiber optic proximity sensors in endoscopy

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Introduction

In current endoscopes, the estimation of the proximity to the surrounding tissue is based on the experience of the user. To provide precise proximity meassurement, a suitable sensor is needed. This paper presents a fiber optic proximity sensor that is inserted through the working channel of an endoscope.

Methods

The impact of the fiber cutting angle at the distal end of the optical fiber is investigated.
To record the voltage signal over the distance, the sensor was clamped in a test rig. A white matte acrylic sheet served as a reflection surface. During continuous measurement in complete darkness, the surface was moved on a linear guide towards and away from the sensor in a range of 0 mm to 30 mm.

Results

If the fiber is cut at a 3° angle to the optical axis, the measurement signal in axial direction can be increased by 126mV at the peak (measurement accuray 4.9 mV). A 45° fiber cutting angle allows radial measurement but with a weak measurement signal compared to an axial measurement. A distance between endoscope tip and intestine wall up to 15 mm can be measured.

Conclusion

In conclusion, optical fibers can be used to insert a low-cost sensor through a working channel of an endoscope. By modifying the fiber cutting angle, an increased sensor signal can be obtained in the axial direction and a measurement in radial direction is possible.

Blood Pressure Estimation based on Electrocardiograms

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Introduction

Currently used blood pressure (BP) measurement devices exhibit limitations, such as intermitted and uncomfortable measurements for cuff-based systems and an increased risk of infection and thrombosis for invasive BP sensors. In contrast to alternative methods based on photoplethysmograms which often are sensitive to movement, this paper focuses on BP estimation from electrocardiograms (ECG) enabling comfortable and continuous monitoring of BP in hospitals and during daily activities.

Methods

The proposed method is based on statistical feature extraction from ECG data. From 34 extracted features, the most relevant ones are identified by means of feature ranking followed by a recursive feature elimination algorithm. The remaining 13 features include statistical measures such as signal complexity, entropy, energy and mobility as well as skewness, kurtosis and contrast features. They serve as input to a two-output random forest regression for systolic blood pressure (SBP) and diastolic blood pressure (DBP) estimation.
This approach was validated on almost 32000 signal sections of the MIMIC III waveform database with a BP range of 60 mmHg < SBP < 190 mmHg and 50 mmHg < DBP < 120 mmHg.

Results

Results on the test set show a MAE $\pm$ SD (RMSE) of 5.92 $\pm$ 7.23 (9.35) mmHg for SBP and 3.73 $\pm$ 5.19 (6.39) mmHg for DBP scoring grade A for DBP and B for SBP according to criteria of the British Society of Hypertension. It has to be noted, that comparable studies select smaller ranges of BP values for evaluating their models, such that comparability is limited. However, the obtained Pearson correlation coefficients of $r_{SBP} = 0.91$ and $r_{DBP} = 0.92$ show, that this model predicts well on the large BP range.

Conclusion

A BP estimation method solely based on ECG was proposed, which performs well on a large BP range and enables comfortable and continuous measurement.

"Are you breathing?" - Design, build and testing of a low-cost, portable respiratory rate monitor

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Introduction

A patient's respiratory rate is one of the critical vital signs that is a determinant of patient well-being. However, it is all too often neglected or misreported by health care professionals. Additionally, many of the available methods of respiratory rate monitoring are either expensive, lack portability or can cause discomfort to the patient. This study presents the design, build and testing of a low-cost minimally-invasive respiratory rate monitor.

Methods

The developed device comprised a thermistor-based transducer to capture the breath cycle of patients based on the temperature differential created across the thermistor. The signal was conditioned using two stages of low-pass filtering to reduce the system bandwidth to 3Hz and processed such that a custom-designed peak detection algorithm could analyse the signal to identify the peaks and ultimately determine the respiratory rate. The device was subjected to three phases of testing, culminating in five test subjects participating in 131 experiments of between 30-60s to validate the performance across a range of different conditions.

Results

The analogue system was designed to operate in a temperature range of 0-40°C, demonstrating a sensitivity of 100mV/°C with a non-linearity of approximately 6%. The digital system recorded and processed the received signals with an average delay of 0.22 ± 0.07s to reporting the breath from when it happened. For a total cost at the time of development of less than €40, the integrated system demonstrated a modest average error of 5.6% across a range of different ambient temperatures, rate and depth of breathing, and orifice of breathing. This is comparable with existing commerical devices indicating that this device is a reliable method of measuring a patient's respiratory rate.

Conclusion

The presented respiratory rate monitor may be of interest for use in an emergency room or clinical setting, especially in severely resource-constrained countries.

A novel Measurement system for respiratory aerosols in venues

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Introduction

The SARS-Cov-2 pandemic has caused a great general interest for a better understanding of the spread of aerosols. Thus, the aim of this study is the development of a measurement system allowing a uniform evaluation of aerosol distribution in venues.

Methods

The Aerosol Transmission Measurement System consists of one emitter (infected person) and several absorbers (non-infected persons) that can be positioned in different spatial arrangements to each other. The system is designed to measure the transmission of tracer particles in aerosols from the emitter to the adsorbers, thus allowing the evaluation and comparison of the infection risk of different configurations. The emitter emits a 10% NaCl solution. The absorbers inhale the ambient air with the NaCl tracer particles. The vacuum pump of the absorber enables a defined inhalation volume flow. A filter is attached to the end of the inhalation tube, where the NaCl markers are separated from the ambient air and dissolved in distilled water. A roller pump ensures that the filter is constantly flushed. The solved NaCl markers cause an increase of the conductance of the water. Since the amount of aerosol emitted is known, the system allows precise determination of the amount of aerosol transferred from the emitter to the absorber. Venues with different sizes, audience arrangements and ventilation systems were measured.

Results

It was found that the presence of a ventilation system is of central importance for reducing the risk of infection. Depending on the type of ventilation and the arrangement of the audience, characteristic room airflows developed in most rooms. It has also been shown that individual aerosol exposure is highly dependent on the position of the emitter.

Conclusion

The measurement system shows promising results for the investigation of different venue properties. There are measures that can be taken to reduce overall aerosol exposure.

A novel method to isolate circulating tumor cells in vivo: A combined experimental and numerical study

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Introduction

A major unresolved challenge limiting the widespread use of circulating tumor cells (CTCs) for the diagnosis and monitoring of cancer is their unreliable detection. This problem is mainly attributed to the low sample volume (5-10ml) of commonly used ex vivo CTC isolation methods. To overcome this limitation, a novel cell probe for the in vivo isolation of CTC is proposed. It consists of a medical wire with a polymer-coated surface functionalized with a specific antibody. A combined experimental and numerical study was performed to investigate the influence of the probe‘s geometry on the number of isolated CTCs.

Methods

In a closed-loop in vitro flow system, the attachment of CTCs to the cell probes with different geometries is investigated using a dextrane solution with CTCs from cell culture. After 30 minutes the cell probes are removed and the attached CTC are fixed, dyed and counted under the microscop. To determine the screened blood volume of the cell probes, particle-based computational fluid dynamic (CFD) simulation are used.

Results

The combination of the experimental and numerical approaches provide information on the relationship between the geometry of the cell probe, the volume of blood it screens and the number of cells actually isolated. It can be shown that a cell probe geometry that disturbs the laminar flow around the probe leads to increased cell attachment. Depending on the geometry of the probe, it can screen up to 300ml of blood for CTC.

Conclusion

In particular, the geometry of the probe has a great influence on the volume of screened blood and the number of isolated cells. With an optimized geometry, this new in vivo method for isolating CTC could be a promising alternative to commonly used ex vivo methods.

In-vitro detection of lung tumor CTCs using a novel probe

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Introduction

Lung cancer is the leading cause of cancer deaths worldwide. The earlier lung cancer is detected, the better the chances of recovery. However, current diagnostic methods face a number of limitations.
The need for a new method for early detection, staging and monitoring is therefore high. Liquid biopsy focuses on the isolation and analysis of circulating tumor cells (CTCs) and free tumor cell DNA from the blood as a novel biomarker. Since CTCs are extremely rare in blood (1-10 CTCs/mL) their detection remains a technical challenge. Therefore, a novel in-vivo device was developed . It is a medical grade stainless steel wire that can be coated with different IgG-antibodies to bind the target cells to the surface of the probe. This in-vivo approach screens a large blood volume of about 400 mL. An exploratory in-vitro study is presented to determine the functionality of the probe.

Methods

To investigate the functionality of the coating, three probes with different antibody-coating and one negative control were placed in a flow system for 30 minutes to simulate the in-vivo approach. Then, the cells bound to the probe were examined under a fluorescence microscope.
The probes have been tested in the blood of 10 stage 3-4 lung cancer patients before starting therapy and 10 healthy individuals as a control group. The antibodies considered were EpCAM, Folate and Vimentin.

Results

The in-vitro study shows a correlation between tumor disease and the number of bound cells. On median, the results of the tumor patients and the control group differ significantly.

Conclusion

The probe collects CTCs in-vitro out of the blood of cancer patients. Therefore, it has the potential to make an important contribution to early diagnosis, detection of minimal residual disease and monitoring of progression and tumor therapy. A subsequent study is planned to validate the in-vivo functionality.

Electrochemical investigation of cochlear implant electrodes after chronic implantation

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Introduction

Cochlear implants (CIs) are the most widely used neural interfaces with around 1 million implanted devices worldwide. They routinely enable compensation of hearing loss in patients by direct electrical stimulation of the auditory nerve. Recently, we have demonstrated for the first time how CI electrodes can be used as chemical sensors in vivo by using appropriate electrochemical methods. We measured intracochlear oxygen dynamics in acute experiments in rats. In this work, we have now investigated the sensing capability and state of CI electrodes in vivo after six months of use for stimulation.

Methods

In a potentiostatic setup, combined amperometric/potentiometric methods were applied for chemical sensing using the CI electrodes as working/counter electrodes and an additional silver/silver chloride wire as reference electrode. Bilaterally CI-supplied rats underwent sound lateralization training for up to 6 months prior to measurements. Under anesthesia, the reference electrode was placed intramuscular or in the middle ear. Pure oxygen breathing gas was used to alter intracochlear oxygen levels. Additionally, electrochemical impedance spectroscopy measurements were performed in vivo using the electrochemical instrumentation.

Results

Intracochlear oxygen measurements with CI electrodes that had been implanted for up to six months showed similar dynamics upon breathing pure oxygen as in acute experiments. The overall increase in intracochlear oxygen during the peaks was slightly lower than in the acute experiments, which can be attributed to the sealed cochlea in contrast to the acute experiments, where perilymph had been leaking through the opening in the cochlea. Impedance magnitudes measured by electrochemical impedance spectroscopy agreed well with impedances measured with the electrophysiology setup. Subsequently, bilateral CIs were explanted for further analysis.

Conclusion

We have successfully demonstrated that CI electrodes retain chemical sensor performance even after six months of use for stimulation in vivo. Thus, advanced electrochemical measurements hold high potential for long-term investigation of implant electrode stability.

Preliminary validation system for cuffless blood pressure measurement

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Introduction

Achieving practical ambulatory blood pressure monitoring is the next step in cardiovascular health research. The development of a non-invasive, cuffless, continuous, wearable device for the measurement of blood pressure is a complex endeavour due to the high specificity of the pressure waveform at each measuring site and the need for highly accurate measurements. Proof-of-concept and validation of a prototype should be performed at an early stage for functionality assessment. Additionally, the emergence of biological computer models allows for in-silico research, which results should be verified in a practical experiment. It is unfeasible to conduct clinical trials at early development stages, due to the time and cost-consuming process.

Methods

To grant an optimal preliminary assessment of a prototype, this work aimed to develop and validate accurate in-vitro and ex-vivo arterial models, with simple construction and easily available components. The comparison between a silicone tube and a porcine artery as a mimicked radial artery was based on the stiffness parameter. Flow pressure is controlled by a centrifugal heart-like pump. Pressure values are extracted with ultrasound and a commercial piezoresistive pressure sensor is used for pressure validation.

Results

Comparison of the echo profile between vessels revealed a decrease in amplitude from the silicone tube to the porcine artery. The porcine artery showed much more realistic stiffness values (β=15.360) than the silicone tube (β=543.420), which was very stiff in comparison to the typical in-vivo radial artery stiffness (β=9.5).

Conclusion

The decrease in stiffness of 97.173 % (from the silicone tube to the porcine artery) led to an acute decrease in the derived pressure error. This work can serve as guidelines for the development of a low-budget arm phantom, as the simple setup allowed for a primary validation of a proof-of-concept ultrasound-based sensor for the measurement of blood pressure.

Automated Evaluation of the Photoplethysmogram and Pressure Signal to Determine the Blood Pressure at the Facial Artery

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Introduction

High blood pressure is a "silent killer" since it initially shows no symptoms. It is therefore essential to regularly monitor the blood pressure. We are developing a blood pressure measurement method for people that cannot use the upper arm cuff due to limb deformities or amputations. The method uses a pressure pad and photoplethysmogram (PPG) signal at the facial artery to determine the blood pressure. Previous results showed that the positioning of the sensors has a substantial influence on the measurement accuracy. Therefore, more light diodes were added to the present setup to determine the positioning of the sensors to the artery more accurately. To further improve the reproducibility of the measurement method, the analysis of the signals to determine the blood pressure was automated.

Methods

The mouthpiece now consists of six LEDs that are placed opposite to their corresponding photo detectors in the mouthpiece. During a measurement, one LED is selected at a time by a multiplexer. An automated algorithm selects the LED with the largest average PPG signal, where the measurement is then performed. The blood pressure values are determined using a sigmoid fitting (systole) and Fourier fitting (diastole). Incorrect measurements are identified based on a set of empirically determined rules.
To determine the precision of the new algorithm, measurement series were performed using a simulator that recreates the anatomy and physiology of the human cheek.

Results

In total, it was possible to determine the blood pressure with a mean error of 1.87 mmHg ($\pm$ 3.80 mmHg). The algorithm determined the wrong blood pressure value in only one out of 178 measurements.

Conclusion

The results show that the developed measurement method determines the pressure with a high precision. Now, the functionality of the method at the human cheek must be validated.

Muscle fatigue detection using near-infrared spectroscopy and electromyography

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Introduction

Muscle fatigue is often experienced by athletes and in work settings. Excessive fatigue can lead to injury and musculoskeletal disorders. Surface electromyography (EMG) is typically used to detect and ultimately prevent fatigue during isometric movement. The application of EMG to fatigue detection in dynamic movement requires, however, a secondary confirmation of fatigue based on physiological measures. Our objective was to determine if muscle oxygenation derived via near-infrared spectroscopy (NIRS) was correlated with relevant EMG indicators of neuromuscular fatigue and whether observed correlations were related to the fatigue process.

Methods

Bilateral electromyograms from three upper leg muscles and the tissue oxygenation index (TOI) of the vastus lateralis muscle were recorded in sixteen non-disabled individuals during cycle ergometry to volitional exhaustion. Six EMG activity features were extracted and the Pearson correlation coefficient between each feature and TOI was determined.

Results

The EMG root mean square, spectral standard deviation, second spectral moment, and zero-crossing rate (ZC) were strongly correlated with TOI. The time course of ZC and the correlation of this feature with TOI suggest that there could be a relation between muscle oxygenation and fatigue.

Conclusion

Future work should use the knowledge gained in this study to investigate whether NIRS can be used to verify the onset of fatigue as detected by EMG.

Development of a Venous Collapse Prevention Device for Blood Draw

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Introduction

Blood sampling typically involves puncturing a superficial vein with a needle and then creating a vacuum (e. g., with a syringe) to transfer the blood from the venous system to the collection container. In some cases, the venous walls collapse due to excessive vacuum generated. In this work, a device is presented that prevents venous collapse and can be combined with any blood collection system available on the market.

Methods

The mechanism of preventing venous collapse is based on a tubular segment interconnected between the needle and the syringe, which collapses at a lower vacuum pressure than the vein.

Results

The prototype was tested and evaluated using a test rig that simulates venous blood draw.

Conclusion

The experiments proved the functionality of the device on a vein phantom.

Wearable Wake-up System for CCHS Patients

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Introduction

Congenital Central Hypoventilation Syndrome (CCHS) leads to insufficient breathing especially during sleep. While patients can be ventilated and monitored during the night, adolescents undergo changes in their biorhythm and lifestyle and are at higher risk to inadvertently fall asleep and stop breathing during the day. In this paper, we propose a prototype mobile wake-up device worn behind both ears that constantly measures oxygen saturation and heart rate non-invasively.

Methods

If a dangerously low level of saturation is detected, it is assumed that the user fell asleep. To wake them, the device issues an acoustic and haptic alarm. The device settings are accessed via a smartphone app. To evaluate the sensor performance, a subject simultaneously wore the prototype behind his ears and a commercial finger pulse oximeter on his hand. Heart rate and blood oxygen saturation were taken for three measurements of few minutes each.

Results

Mean absolute error of oxygen saturation was less than 2~% for two data sets and 6.1~% for the third.

Conclusion

It is assumed that during this measurement, the device lost contact to the skin. The heart rate measurement showed satisfactory agreement of <~4~% mean average error. In the future, the measurement quality will be improved by calibration and more reliable attachment to the ear and a user study will be conducted in order to evaluate the prototype usability.

Intraoperative continuous perfusion monitoring of free flaps using remote photoplethysmography

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Introduction

In reconstructive surgery, flap monitoring is crucial for the early detection of perfusion problems, and there is a high need for objective, feasible, continuous, and robust perfusion assessment. Remote photoplethysmography (rPPG) is a non-contact, camera-based, non-ionizing, and non-invasive monitoring technique providing objective and reproducible information on physiological parameters in various medical applications such as tissue perfusion measurements and wound assessment. In this work, we analyze the use of rPPG for objective and reproducible intraoperative assessment of flap perfusion in patients undergoing reconstruction with free fasciocutaneous flaps (FFCF).

Methods

We captured 15 oncology patients with a high-resolution all-digital surgical microscope (ARRIscope, MSI, Munich, Germany) during the process of reperfusion of the FFCF after microvascular anastomosis to the external carotid artery. The rPPG-signal was extracted via plane-orthogonal-to-skin transformation independently for pre-defined regions within each video recording. Based on the extracted rPPG-signals, we derive the heart rate, signal-to-noise-ratio of the pulse signal, magnitude in the frequency domain, perfusion index, and correlation with the rPPG-signal of a reference skin region to detect whether the FFCF is adequately supplied with blood.

Results

For 14 patients, successful reperfusion of the implanted FFCF was quantified based on the metrics derived from rPPG-signals. For one FFCF, no characteristic parameters could be derived intraoperatively. However, this flap showed no vitality during clinical inspection postoperatively, and the necrotic flap tissue was removed after five weeks.

Conclusion

Our method allows objective and continuous intraoperative assessment of vascular anastomosis and flap perfusion. The value of the method compared to competing procedures is its widespread availability. It can be performed with standard equipment in any operating room (RGB camera, e.g., in a surgical microscope). Thus, it could detect complications intraoperatively, which would allow immediate anastomotic revision before wound closure. However, comparative clinical studies with competing methods are required before the method can be used widely.

Analysis of Dielectric Properties of Gelatin-based Tissue Phantoms

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Abstract

In this work, an electrode was developed to determine the dielectric properties of tissue phantoms using impedance measurements. For this purpose, a coaxial electrode design was selected as the most suitable electrode design. Three tissue phantoms (blood, fat, muscle) were prepared from distilled water, sodium chloride, 1,2-propanediol, agar, and gelatine, and then characterized. Measurements were performed using an impedance analyzer in a range between 1 kHz and 1 MHz. A comparison with literature values showed good correspondance of the permittivity values determined, thus proving the applicability of the electrode design. However, the conductivity values measured were different from literature values. In the future, alteration and minimization of the electrode can be done to further improve the characterization.

Novel Procedure for Determining the Finger Force in Flexion Depending on the Finger Position

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Introduction

The design and development of a novel dynamic hand orthosis that allows individual and progressive adaptation to the patient's condition require knowledge about the maximum voluntary contraction forces of the fingers (separate and combined). The following work presents a test setup and procedure that enable the determination of isometric finger contraction forces during flexion as a function of finger position and depending on various finger tasks.

Methods

The test setup places hand and fingers in certain positions (position 0: grasping of a plate; position 1-3: circular grasping of cylinders of three different diameters). The force measurement is carried out using pressure sensing: A capacitive force sensor is placed on each fingertip. To perform various finger tasks, the subjects are asked for isometric contraction of defined finger groups and single fingers against the boundary system. For proof of the concept, measurements are performed with six subjects and compared with reference values from the literature.

Results

The separated finger force of each finger can be captured during the finger tasks in varying positions. Furthermore, the total finger force of all active fingers can be determined. It is shown that the total finger force during contraction of all fingers (IMRLtask; 78.4N +/- 25.8N) is higher than during contraction of the index finger (25.8N +/- 3.4N). Furthermore, the single finger force of the index finger is higher than the index finger activity in IMRL-task. The results also show a tendency for the finger contraction force to increase with increasing flexion. Further investigations may require improvements to the method. In this proof of concept, this potential is revealed and discussed. However, the functionality of the test setup and procedure can be demonstrated.

Implementation and evaluation of algorithms to derive the heart- and breathing rate from a PPG signal of the facial artery.

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Introduction

Both the heart- and breathing rate are of crucial clinical significance as frequent monitoring may yield an early detection or prediction of cardiovascular conditions or high-risk events. In this work, various models to determine the breathing- and heart rate from a photoplethysmography signal (PPG) of the facial artery have been tested.

Methods

The PPG signal was obtained using a mouthpiece that consists of multiple light diodes, photodetectors, and a pressure pad. At the start of a measurement, the pressure pad is inflated up to 80 mmHg to ensure optimal signal quality. The light is continuously emitted from the diodes and detected by the photodetectors.
The heart rate is determined by identifying the peaks in the PPG signal, which are closely related to the heartbeat. Subsequently, the average peak-to-peak time is taken to extrapolate the number of beats per minute (bpm).
To determine the breathing frequency, the fluctuation of amplitudes and time intervals in-between peaks, that are caused by breathing, are evaluated. This is based on the premise that respiration influences the stroke volume and heart frequency, thus impacting the respective PPG signal.
The results were compared with those acquired through an electrocardiogram which served as the gold-standard reference. A dataset comprised of ten subjects with five measurements each was evaluated.

Results

The average differences from the proposed methods to the reference device is 0.68 ± 1.78 bpm and -1.6 ± 3.04 breaths per minute for heart and breathing rate, respectively.

Conclusion

The implemented methods proved to be promising and produced results with a similar accuracy like the used reference device.

Estimation of technical confounding of the tonographic effect using a pneumatic pressure modulator

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Introduction

Several studies in occulopression, repeated tonometry or ophthalmodynamometry show that the intraocular pressure (IOP) decreases during an artificial IOP increase. This phenomenon is known as the tonographic effect. In healthy eyes an IOP drop of 2-3mmHg/min was reported. However, there are studies that show a reduced decrease of the IOP drop for instance in glaucoma patients. In this work we determine the tonographic effect in healthy eyes by utilizing a novel pneumatic pressure modulator and validate the modulator technically in order to determine the technical confounding of the tonographic effect.

Methods

For both the technical validation and the in vivo application a pneumatic intraocular modulator (IOPstim) was used. Here, the IOP modulation is performed in a contact process using a silicone balloon. A force sensor was placed in front of the balloon. Pressure stability was analyzed for 2 minutes. The force values were recorded for five different target pressures (50-250mmHg, 50mmHg steps). The sequence was repeated 10 times using a new balloon in each sequence. In the subject study, the IOP of 10 healthy subjects (6m, 4f, aged 28.8$\pm$6.64yrs) was modulated and increased linearly to at least 40mmHg. At this point, the pressure inside the balloon was kept constant for 2 minutes, with IOP measurements taken every 40 seconds using a rebound tonometer (iCare).

Results

Technically, the IOP dropped by 0.35mmHg per minute at an operating point of 40mmHg IOP. In the subject study it was found that the IOP could be increased up to 42.8$\pm$3.6 mmHg in average (n=10), whereby a mean pressure drop of 2.4mmHg per minute was determined.

Conclusion

With the new pneumatically based setup, a targeted modulation in terms of level and constancy of the IOP can be realized. The technical confounding of the tonographic effect is clearly less than the physiological effect itself.

Automated human temporal-bone experiments

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Introduction

Temporal-bone (TB) experiments are useful for the investigation of middle-ear and inner-ear transfer properties, and the analysis and development of active or passive middle-ear prostheses or related devices. To acquire the mechanical middle-ear (ME) response, the Laser-Doppler vibrometry (LDV) is utilized as a preferred method. In most setups, the exact measurement point chosen on the biological structure of interest as well as the direction of the corresponding vibration measurement is not precisely defined and of unknown reproducibility. Hence, an automated setup controlling coordinates of TB and measurement direction is developed and tested.

Methods

To test the reproducibility, TBs were measured with ER7C and ER10C probe microphones employing a small industrial robot to position the TB to the ME points of interest and align it to the laser beam. The position and vibration data acquired at the same locations at different points of time were processed and compared.

Results

Measured transfer functions indicate noticeable differences at some frequency ranges. Nonetheless, the reproducibility of positioning to repeatedly measured points proved itself relatively accurate, if no manipulations in the setup are made.

Conclusion

In conclusion, the current study shows that automated LDV TB measurement system is in principle capable to adapt to the changes in setup during intermediate preparation steps. With more acquired data, the setup stability and reproducibility can be more precisely verified, and additional improvements can be made.

Remote knee endoprosthesis monitoring - alignment requirements and prototyping of the external readout unit

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Introduction

Due to inadequate postoperative monitoring of knee arthroplasty, polyethylene (PE) wear of knee endoprosthesis can progress unnoticed until symptomatic adverse effects become apparent or implant failure occurs. A currently developed measuring system, consisting of an implanted passive sensor and an extracorporeal readout unit, is intended to enable patients to regularly check their knee implants' condition at home. In this context, an appropriate product design for the readout unit is essential to meet the specific requirements of medical equipment for non-professional users.

Methods

An experimental investigation of the optimized positioning of the system's readout unit was conducted to ensure that the design enables users to take correct measurements intuitively. After identifying and specifying requirements, design solutions were systematically generated and realized as a prototype.

Results

A sleeve with Velcro and a sewn-in readout unit has been fabricated. A cutout for the patella ensures intuitive correct alignment of the measurement system. A hardware housing incorporates the electronics and is equipped with an easily accessible power-on button and indication LEDs.

Conclusion

The proposed design has easy and intuitive handling and allows a fast and safe capture of the implant condition at home. It has been designed for non-professional users with varying technical knowledge, and physical and health conditions.

On Gait Stability: Correlations between Lyapunov Exponent and Stride Time Variability

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Introduction

Lyapunov Exponent (LE) is a parameter that is often used for stochastic nonlinear dynamical systems to determine stability using time-series information. In the context of the gait, stability is defined as the ability to maintain uniform locomotion without unpredictable falls owing to perturbations either externally in the form of environmental disturbances or obstacles; or internally due to neuromuscular disorders.

Methods

In this work, we use a time-series model based on a second-order integrator for inertial measurement units placed on the foot, chest, and wrist. Stability is analyzed in a localized sense, with the Lyapunov exponent computed in the temporal region between two heel-strike points, which are determined using a peak-detection algorithm. We have attempted to show correlations between variations in the stride time and stability of the gait under normal and abnormal conditions. In the latter case, we attach a weight on foot to emulate weakness.

Results

On comparison between both cases, we observe a statistical significance of $p=0.0039$ using Wilcoxon's rank-sum test. Moreover, on observing the correlations between Lyapunov Exponent and Stride Time Variability, we notice a left-shift in the abnormal case, indicating a lower threshold for instability, with the Stride Time Variability being 0.07 as compared to 0.11 in the normal case.

Conclusion

In this article, we presented a detailed study on the relations between the Lyapunov Exponent and Stride Time Variability. By taking a higher-dimensional state-space representation of the dynamical system, we observed Lyapunov Exponent values of higher significance as far as their magnitude is concerned, and hence ease in the distinction between stability and chaotic behaviour. From these relations, we observed that a threshold can be stated w.r.t STV for gait instability, exploiting the LE-STV correlations. This hypothesis was confirmed in a comparative study between the normal and abnormal counterparts.

Microsensor-based oxygen monitoring of bioprinted breast cancer spheroids

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Introduction

Towards a personalized and more efficient biomedicine, microsensor-based metabolite monitoring of 3D microtissue spheroids provides essential real-time information on cell metabolism, e.g. during drug screening in cancer research. Bringing 3D microtissues in close contact to microsensors is highly attractive for precise monitoring, but challenging to achieve efficiently and on-demand. We combined state-of-the-art bioprinting to deposit cancer cell spheroids in a controlled manner directly onto a multiwell-format electrochemical sensor platform and showed straightforward metabolic monitoring of single spheroid metabolism from nanoliter-scale volumes.

Methods

The electrochemical sensor platform consists of a glass chip with circular spheroid microwells patterned on its surface, which can be sealed gas-tight (55 nl volume each). Oxygen sensor microelectrodes and hydrogel membranes were integrated into the pots for continuous measurement. MCF-7 breast cancer spheroids (∅ 150 µm) were cultured outside the platform and automatically placed into the sensor wells using a single spheroid deposition module, which allows precise manipulation of single spheroids, organoids or tumoroids at µm-scale and in high-throughput.

Results

Parallel amperometric measurement of the oxygen concentration in the microenvironment of the individual spheroids allowed access to cellular respiration rates. For untreated spheroids, oxygen consumption of 665 ± 173 fmol/min (n = 3) was determined, matching literature values. Exposure to drugs led to a change in cellular respiration, as measured reproducibly and in real-time.

Conclusion

We demonstrated that bioprinting techniques can be applied to precisely position 3D tumor spheroids into microelectrode wells. Off-chip spheroid generation and on-demand printing to individual electrodes enable precise and fast measurements due to the low volumes resulting in fast concentration changes. Experimental time and complexity are reduced, also because microfluidics for spheroid formation and trapping are eliminated in comparison to classical on-chip approaches. Our results pursue the much-needed effort towards the facilitation of 3D cell culture experiments while providing new opportunities for higher throughput, parallelization, and sensor integration into organ-on-chip systems.

Design considerations and applications of a biomedical test bench development kit

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Introduction

Monitoring and control of processes are major tasks of biomedical test benches. Commercially available development systems are limited with respect to high costs and information for required validation. A test bench development kit is presented which ensures high compatibility for prospective developments, adaptations and embedding of sensors and actuators.

Methods

The development kit is based on a printed circuit board built around the single-board computer Raspberry PI operating as the control unit. Supporting circuitry for power control, logics and special functions are implemented. The kit is accomplished by several types of peripheral devices, such as analog and digital sensors, voltage controlled, resistive, inductive and digital actuators, all connected via serial bus standards (I^2C, RS-485). Measurement data are stored on an internal SD card. Computing devices and peripherals (e.g. digital camera) with high-speed data are connected to the control unit via a network link (WLAN, USB or LAN). For critical hardware-timed controlling tasks, additional microprocessors can be configured as I2C nodes executing fast subroutines.

Results

Applications based on the test bench development kit are presented to demonstrate the level of automation and process control achieved. A multi-channel pH control device was designed for degradation studies in liquid sample chambers. A material testing setup was engineered to investigate mechanical properties of fragile specimens. An automated test bench for online particle measurements during simulated application of cardiovascular implants as well as a flow perfusion system to characterize the water permeability of laser-structured nonwovens were developed. All types of sensors and actuators were used including stand-alone devices with high data rates.

Conclusion

The presented test bench development system is cost-effective and provides all required information for validation and maintainance. Industrial data bus interfaces ensure high compatibility for prospective developments, adaptations and the embedding of new sensors and actuators.

Operator experience and applicability aspects of dry EEG

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Introduction

Dry electrodes for electroencephalography (EEG) enable new fields of application for monitoring brain function, including studies in ecological environments, social interaction, brain computer interfaces, and neurofeedback. Reported channel reliability, preparation time, and wearing comfort vary significantly between differing dry electrode concepts and caps. We investigate the influence of operator experience and preparation time on electrode-skin impedance, channel reliability and comfort reported in multiple studies using Multipin Ag/AgCl dry electrodes.

Methods

We investigate and compare the performance of dry Multipin EEG caps and gel-based EEG caps, comprising 64 channels each, in recordings comprising resting state EEG with open and closed eyes, eye blinks, and visual evoked potentials. Equivalent studies were carried out in six countries involving overall 116 healthy volunteers. We compare electrode-skin impedance, channel reliability, and subject comfort reports between cap types. Furthermore, we investigate the eventual impact of operator experience and preparation time on the dry electrode performance.

Results

The average impedances of the dry EEG caps are four to ten times higher than those of gel-based EEG electrodes. No considerable differences were observed between the gel-based and dry electrode EEG recordings after exclusion of bad channels. The average channel reliability of the dry electrodes is 15 to 20 % lower than for gel-based electrodes. Similarly, the average preparation time is considerably reduced, and the comfort of the dry EEG caps is slightly reduced. All findings are in line with previous publications, but exact values vary considerably between operators.

Conclusion

The considerable variability of the performance metrics across operators is suggesting a strong influence of operator training and experience. We will therefore include further studies' datasets and investigate training related specificities.

Pupillometry examinations of the human eye with the eye diagnostic device PEP-2000 - First results

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Introduction

Pupillometry forms the diagnostic basis for numerous pathologies of the eye. For this reason, fast and accurate diagnostics in the field of ophthalmology are essential. Two examination techniques, full-field-ERG and pupillometry were combined in a diagnostic device developed by ICM e.V. to reduce the examination process for both examiners and patients. In this abstract, the device is examined for the quality of the pupillometry measurements.

Methods

A feasibility study with 12 healthy subjects (3 females, 9 males, mean age: 36.33 ± 11.94 years) was conducted to evaluate the pupillometry-function of the device (two measurements: recording of the pupil diameter, observation of changes in pupil diameter over a defined time interval). To evaluate the results, mean values of the analysis parameters (maximum and minimum pupil diameter, amplitude, latency time, contraction time and peak time) were calculated from all measurement data and compared with the results of other studies described in the literature.

Results

The results showed that the minimal pupil diameter is 40% higher than the literature value (dmin=1.5mm). However, the maximum pupil diameter is within the range of the researched values (dmax=6.0-8.0mm). The results of the pupillary reaction measurements show that the values obtained (amplitude=1.46mm, contraction time=540ms and peak time=1210ms) are within the range of literature values. The latency time of 690ms is 40% too high. The reason for this could be a reduction in the pupil detection rate by maximum of 50%, caused by higher artifact occurrence and the resulting effort in the plausibility check.

Conclusion

On the basis of these investigations, it can be concluded that the eye diagnostic device PEP-2000 for pupillometry provides plausible analysis parameters which are comparable with the literature. The determined analysis parameters should provide the basis for further investigations in the form of device-internal guideline values. Futher work will focus on improving the pupil detection rate.

Surface EMG Signal based Muscle Fatigue Classification using Optimized XGBoost Algorithm

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Introduction

Fatigue is the inability of the muscle to generate the required force. Surface electromyography (sEMG) enables non-invasive measurement of myoelectrical activities during force generation and has been commonly utilized to monitor muscle fatigue conditions. The classification of fatigue conditions is nontrivial due to complex signal characteristics. Recently, ensemble learning based on extreme gradient boosting (XGBoost) is found to provide effective differentiation in complex datasets. In this study, an attempt has been made to develop an optimized XGBoost framework for the differentiation of nonfatigue and fatigue conditions from sEMG signals.

Methods

In this study, the sEMG signals are collected from the biceps brachii muscle of 45 healthy participants under isometric contraction protocol. This involves a subject performing a position control task with a six-kilogram dumbbell until fatigue. The acquired signals are preprocessed and features such as Mean absolute value (MAV), Root Mean Square (RMS), Zero Crossing (ZC), Waveform Length, Willison amplitude, Slope sign change, and Auto-regressive (AR) model coefficients are extracted. XGBoost algorithm optimized using Genetic algorithm (GA) is employed for the classification of nonfatigue and fatigue signals.

Results

Results indicate that the optimized XGBoost is able to classify nonfatigue and fatigue conditions. Features namely, RMS, MAV, ZC and AR(2,3,4) are found to characterize these states with statistical significance of $p<0.0005$. XGBoost classifer with GA optimized parameters is found to provide a maximum sensitivity of 90.1% with significant features. A decrease in sensitivity by 8% is obtained with all features.

Conclusion

The proposed methodology using XGBoost algorithm with GA optimised parameters is able to better differentiate muscle fatigue condition in subjects. The obtained results demonstrate its effectiveness in handling the time domain features which are reported to possess low computational complexity in characterizing the signals. Hence, this framework could be used for fatigue monitoring in sports and other medical conditions.

Towards Analytically Computable Quality Classes for MCG Sensor Systems

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Introduction

While metrics such as SNR (signal-to-noise ratio) and ASC (application-specific capacity) can be used to describe signal quality quantitatively, they do not allow qualitative assessment. If only the SNR of a signal is given, it is not clear for which applications it is suitable. The subjective evaluation of signals by application experts, on the other hand, can provide such a qualitative assessment, but it is not reproducible.

Methods

In this study, we investigate the relationship between these easily computable metrics such as SNR and ASC and the subjective evaluation of cardiologists using MCG signals as an example. To do this, we define four quality classes and generate a collection of noisy prototype signals. The cardiologists' assessments are then compared with the SNR and ASC of each signal.

Results

Due to the small amount of data, we only use a linear regression to predict quality classes based on common quantitative metrics. The achieved coefficients of determination are $R^2_{\mathrm{SNR}} = 0.612$ and $R^2_{\mathrm{ASC}} = 0.593$.

Conclusion

In perspective, it is therefore plausible to analytically calculate the quality class of a MCG sensor system from the system characteristics with the support of a larger cohort of cardiologists. This will allow sensor system manufacturers to optimize their systems more efficiently for specific applications, enabling faster innovation loops at lower cost. For users of sensor systems, it will simplify the selection of the most suitable system for their application.

Local field potentials of the auricular Vagus nerve - In-silico stimulation and recording

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Introduction

Measuring the activity of the parasympathetic and sympathetic nervous system (PSNS and SYNS, respectively) has always been a challenge. Until recently, usually non-invasive but unspecific heart rate variability was used, which mainly reflects activity of the cardiovagal PSNS branch only. Alternatively, invasive but specific microneurography has shown great resolution in measuring local SYNS activity in mammals. We propose the auricle, specifically the va- gally innervated regions of the Cymba Concha and the cavity of Concha, as a potential region for measuring local field potentials (LFP) which we hypothesize to reflect both the afferent PSNS and efferent SYNS autonomous activity.

Methods

Using the NEURON Simulation Environment, a simple computational model of a single auricular vagus nerve branch under human skin was developed, stimulated intracellularly and differential LFPs were monitored using two recording electrodes. To gain a better understanding of the behavior, e.g. timing and shape of individual LFPs and electrode position with respect to fiber position was varied. Furthermore, different fiber diameters ranging from 5.7μm to 16μm were implemented into the model.

Results

The differential LFPs usually show a hexaphasic form with a maximum differential amplitude of 3.05nV . Two individual peaks were always clearly visible, with a peak-to- peak time depending not only on inter-electrode-distance but also on fiber diameter. Single LFPs showed a change in shape from biphasic to triphasic depending on electrode-to-fiber distance and fiber diameters.

Conclusion

Our computational results will help in interpreting our experimental data and distinguishing ac- tual PSNS activity-related vagal peaks from SYNS activity- related interference generated by smooth muscles. In addition, the presented model will support building more complex mod- els resembling auricular vagus nerve fibers in bundles and re- alistic geometric layout.

Implementation of a platform for the localization of various sound sources in a real spatial environment

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Introduction

Respiratory diseases are common health problems not only in adults, but also in children. Diagnostic procedures with the help of medical technology for assessing respiratory impairment are only available for children starting from the age of five. Hence, research is being carried out on a solution for mobile and contactless audio-visual monitoring of toddlers at nighttime. Children often sleep with their parents or with siblings in the same room. For this reason, it is important to assign the detected sound to the correct source. The aim of this sub-project described here was the technical construction of a setup for acoustic measurements and the implementation of a sound source localization.

Methods

The measurement setup is based on a square construction with a sidelength of 2 m and a moveable loudspeaker placed on each side. The loudspeakers are controlled by Raspberry Pis. In the center a circular microphone array consisting of four omnidirectional microphones is placed. Using this construct, it is possible to simulate different combinations of sound sources in real spatial environment conditions.
The SRP-PHAT based localization algorithm is implemented in python. It was tested by moving one sound source in equidistant iterations. In addition, the performance during the use of multiple sound sources was evaluated. The output signal in both cases was white noise.

Results

The results of the measurements by simulating a variety of sound source combinations prove the functionality of the setup. A detection accuracy of 4 ° in the plane has been recorded. Furthermore, it is possible to separate different sources.

Conclusion

Initial measurements have shown that synthetic soundscapes can be generated via the measurement setup. In the next steps, the algorithm will be evaluated with real child data recorded in the clinic and in home environment. Moreover, the robustness against simulated noise will be tested.

11th Vienna International Workshop on Functional Electrical Stimulation

Electrical stimulation of patterned neural networks in vitro at high spatial resolution

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Introduction

Understanding information processing and memory formation of neural networks in the brain poses one of the greatest challenges in neuroscience. In vivo studies on the brain attempt to answer these questions by either monitoring subsets of neurons embedded in a complex network or by whole-brain imaging at low spatiotemporal resolution. The fundamentals of neural processing are difficult to study in such environments. Therefore, we are following the approach of bottom-up neuroscience, in which small engineered neural networks are studied in vitro.

Methods

Primary cortical neurons are seeded into polydimethylsiloxane (PDMS) microstructures to spatially confine the location of their soma and guide neurite growth with the goal of minimising the network complexity [1,2]. In order to study the neural information encoding and processing, the microstructures are placed on high-density microelectrode arrays (HD-MEAs), where network interaction is enabled by means of stimulation and recording from the network [3,4].

Results

Electrical stimulation on individual network electrodes is used to elicit network responses. Exploiting the electrode pitch of only 17.5 µm, we are able to detect the information flow in the network at a much higher spatial resolution compared to previous studies on 60-electrode glass MEAs [5].

Conclusion

The combination of microstructures with HD-MEAs enables analysis of network responses with respect to stimulus location. With these tools we aim to describe the complex input-output relationship of small neural networks. We believe that this could validate fundamental neuroscience postulates, inform the design of in silico models and one day enable performing computational tasks.

References

1. Forro, C., et al. (2018) Biosensors & Bioelectronics, 122
2. Mateus, J. C., et al. (2021) bioRxiv
3. Muller, J., et al. (2015) Lab Chip, 15(13), 2767-2780
4. Duru, et al. (2022) Frontiers in Neuroscience: 16.
5. Ihle, S. J., et al. (2021) Biosensors and Bioelectronics: 113896.

Design of a multi-sensor FES-cycling device

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Introduction

Mortality in people with spinal cord injury is three times higher than in the rest of the population. Cardiovascular diseases are some of the most relevant among the health conditions that affect them, for whom physical inactivity is one of the main risk factors. Due to lower voluntary muscle recruitment levels, therapeutic interventions that provide cardiorespiratory conditioning are limited. Among the existing alternatives is functional electrical stimulation-enabled cycling (FES-cycling). FES-cycling is a method of coordinated transcutaneous muscle stimulation capable of producing the sequenced contraction of lower limbs muscles, reproducing the activity of pedaling a stationary bicycle even in people with spinal cord injury. With the course of training and the emergence of an adaptive response, the pedals resistance can be modified, generating greater aerobic overload and better cardiovascular conditioning.

Methods

The study proposes the development and use of FES-cycling with constant monitoring of heart rates, blood pressure, body temperature, and oxygen saturation. The reduction in cycling speed and variations in biological signals throughout the exercise sessions (such as a reduction in blood oxygen levels) are indicators of early muscle fatigue.

Results

Preliminary results from people with spinal cord injury who are treated with FES-cycling and are constantly monitored suggest a relationship between fatigue (characterized by reduced cycling speed), increased heart rate and negative variations in oxygen saturation.

Conclusion

There is no clear evidence of the relatinship between fatigue and other biological variables during FES cycling sessions. More studies are needed to verify the correlation between the variables in order to predict early fatigue.

Remote electrical stimulation monitoring system: design and proofs of concept

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Introduction

Functional electrical stimulation (FES) uses the controlled application of electricity to stimulate the neuromuscular system. For spinal cord injury cases, FES can be used to stimulate various muscle groups and systems, such as the respiratory muscles, bowels and bladder, in addition to the upper and lower limbs. Misuse and incorrect setup of the equipment are risks to the safe and effective use of this therapeutic intervention, demanding continuous monitoring by health professionals. The evolution of remote monitoring technologies favors the development of electrotherapy medical devices that allow remote guidance and monitoring of the operation by end users themselves.

Methods

The proposed system consists of a portable device associated with an electronic platform that allows remote monitoring and management of its operation, with the possibility of prescribing, creating and applying different therapeutic protocols. The solution comprises a portable embedded system controlled by an interface that can be operated via Bluetooth from a mobile application connected to the internet, in addition to a web-based interface for monitoring the use and history of multiple users. The application contains friendly instructions addressing the end user on all the procedures necessary to setup the device and carry out stimulation sessions in a simple and safe way.

Results

The advantages observed in the proof of concept carried out by the therapists in the team were the simplicity, versatility and potential for managing multiple patients. However, so far, all tests have been carried out by experienced professionals, and should be extended to other groups in the next phases.

Conclusion

As this is a preliminary assessment for the development of a medical equipment, further studies are needed to validate the system.

Reducing spine curvature with functional electrical stimulation (FES): a scoliosis case study

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Introduction

Scoliosis is a change in body structure characterized by the rotation and tilting of the vertebral body. The rotation of the vertebral body is related to how convex or concave is the curve. There are several conservative treatments to prevent or reduce the resulting deformity, including the use of Neuromuscular Electrical Stimulation (NMES). A parameter established by the Scoliosis Research Society, known as the Cobb angle, indicates that curve angles greater than 50° in children can augment during adulthood, causing health problems and worst quality of life.

Methods

We used NMES to treat a 7-year-old male child with incomplete flaccid quadriplegia and S-shaped thoracolumbar scoliosis. By analyzing the forces produced by the musculature originating at the apex of the scoliosis curves, our hypothesis indicated that the convex side was hypertonic, producing traction and rotation of the vertebral body, and that the concave side was hypotonic. The stimulation protocol used consisted of a one-hour daily application of NMES (frequency of 20 Hz and pulse width of 500 µs) on the quadratus lumborum and latissimus dorsi muscles in the region of the thoracolumbar concavity. Case evolution was measured by the changes in the Cobb angle over the months.

Results

Initially, measures have shown Cobb angles of 50° in the lumbar region, and of 56° in the thoracic region. After 6 months, the angle in the lumbar region was 38°, and 55° in the thoracic region. Two years after the first assessment, it reached 30° in the lumbar region, and 56° in the thoracic region.

Conclusion

This case study reports the use of NMES in a child with thoracolumbar scoliosis at high risk of complications in adulthood. The results demonstrate that, after treatment, we observed a reduction in the Cobb angle in lumbar scoliosis and a stabilization of the progression of thoracic scoliosis.

Estimation of the time fluctuation of polysynaptic responses evoked by constant spinal cord stimulation

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Introduction

Polysynaptic activity is necessary to engage the neural circuitry that controls the motor behaviour and is crucial to the recovery after spinal cord injury (SCI) [1]. Polysynaptic responses can be elicited with spinal cord stimulation, and there are few reports on these types of responses in human electrophysiology, most of them describing them as constant to fixed stimuli. However, we have observed that the responses fluctuate in amplitude and time. Amplitude variations can be analysed with statistical methods. However, time fluctuations are more complex due to the multiple parameters involved.

Methods

This work describes a methodology to analyse the time fluctuation in the responses of each pulse. It is based on the calculation of the signal temporal centroid, representing the whole activity, weighted by its latency, in a single time value. This value is then used to model the temporal fluctuation with linear regression. The methodology was verified with an electromyography dataset from a discomplete spinal cord injured patient with spinal cord stimulation.

Results

The parameter is able to follow small changes in the responses' distribution. Examples of how the temporal centroid and linear model identify the fluctuations are presented.

Conclusion

Once fitted in a linear model, the fluctuation coefficient describes time fluctuations in the interneuron processing and, together with amplitude metrics, can characterise changes in polysynaptic responses during the application of fixed stimulation parameters.

Standardised FES-induced fatigue-testing of paralysed human quadriceps muscles during a dynamic movement task

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Introduction

Muscular fatigue remains a persistent problem during functional electrical stimulation (FES). One technique known as spatially distributed sequential stimulation (SDSS), uses multiple electrodes to stimulate distinct pools of motor-units at a lower frequency to decrease fatigue. Although literature claims clear benefits, interpretation of the results and applicability proves difficult due to heterogeneous testing strategies. Thus, we present a standardized method for fatigue testing in individuals with spinal cord injury (SCI), tailored to the requirements of a practical application (e.g. FES-Cycling).

Methods

The fatigue-development of 6 paralysed quadriceps muscles of 3 different participants with complete paraplegia was assessed via a fatigue-index during 180 dynamic contractions, comparing different SDSS electrode-configurations against conventional single-channel stimulation. For standardisation, testing was conducted at 40% of the peak-torque during a maximal evoked contraction (MEC), in previously trained individuals with SCI.

Results

Our results were unable to detect a significant difference in the fatigue-development comparing SDSS against conventional stimulation. Indifferent results regarding the potential benefits of SDSS in a practical setting are widely reported across various international research groups. We hypothesise that the positive effects of SDSS diminish with increasing stimulation amplitudes (required to elicit strong contractions), due to a loss of selectivity.

Conclusion

Assessing muscular fatigue is not a trivial task. To allow for a successful practical translation of a technique, it is crucial to perform fatigue-testing tailored to the requirements of a potential use-case. In practical applications, FES is often used to elicit forceful dynamic contraction in individuals with SCI who already conducted a dedicated FES-training program. Therefore, we recommend to assess fatigue-development at higher forces (e.g. 40% MEC) in pre-trained individuals with SCI to better reflect the practical demands of FES-applications.

Avoidance of axonal activation in epiretinal implants using short biphasic pulses

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Introduction

Retinal implants allow patients suffering from degenerative retinal diseases to regain visual percepts. Despite considerable effort in developing and improving retinal neuroprostheses in the last decades, the restored vision in patients does not achieve sufficient quality. One of the main obstacles in epiretinal implants is the concurrent activation of cells close to a stimulating electrode and cells that have their axons traversing the electrode.

Methods

In this study, we employ computational modeling to examine the effect of pulse duration on the selectivity of focal versus non-focal activation. We used morphologically- and biophysically-realistic multicompartment models of mouse RGCs. Extracellular electric stimulation was applied via disk electrodes from the epiretinal side.

Results

Our results suggest that biphasic pulses in the range of 10-20 microseconds can prevent axonal activation while still reliably activating target neurons. This was the case for idealized biphasic rectangular pulses as well as for measured waveforms generated by an CMOS-based Microelectrode array (MEA). Despite the short pulse duration charge levels to induce activity were in a range well below the limit for safe stimulation.

Conclusion

Shorter pulses increase the axonal/focal threshold ratio and therefore may be applicable to generate more focal responses during epiretinal stimulation. This may improve the clinical outcome in patients with retinal implants.

The effect of neuromuscular electrical stimulation on bowel management in people with spinal cord injury - preliminary results

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Introduction

Spinal cord injury (SCI) causes a disruption of the autonomic nervous system affecting gastrointestinal function amongst many others. More than one hour is spent for defaecation in 14% of this population (Coggrave et al., 2009) and people are limited in their participation in social life activities.

Methods

We included five participants with chronic SCI (>2 years) in the analysis of the preliminary results. They applied electrical stimulation onto their abdominal musculature for 16 weeks for 30 minutes before their regular defaecation times. At each of the five study visits, participants' bladder, bowel and sexual function have been evaluated using the Qualiveen SF, Neurogenic Bowel Dysfunction Score (NBDS) and the ISAFSCI respectively. They documented the stimulation and defaecation time in an online database. Transit time was evaluated using the Corn test.

Results

NBDS varied amongst participants without recognizable pattern in regards to the stimulation. The NBDS increased in some, which indicates a worsening of the magnitude of bowel dysfunction. This is in contrast with the remaining results of the present study. Satisfaction of bowel function increased by 2.6 points (Likert scale: 0-10) on average in all participants after starting the stimulation. Furthermore, two out of five participants could successfully decrease their bowel transit time (33.8% and 85.2%). Finally, defaecation frequency and defaecation duration could be reduced in three out of five participants. The bladder function decreased by 0.45 points on average after stimulation as measured by the Qualiveen SF, indicating an amelioration of bladder function.

Conclusion

The preliminary data described above shows that symptoms of bowel dysfunction are very individual as we observe a large variability among the population. However, satisfaction of bowel management increased while stimulation was applied so that four out of five intend to continue.

Optical Quantification of Surface Electrical Stimulation to prevent Denervation Muscle Atrophy in 15 Patients with Facial Paralysis

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Introduction

Few studies showing therapeutic potentials of electrical stimulation (ES) of the facial surface in patients with facial palsy have been published so far. Not only muscular atrophy of the facial muscles but facial disfigurement represents the main issue for patient well-being. Therefore, objective methods are required to detect ES effects on facial symmetry within patients with complete unilateral facial paralysis.

Methods

Only patients with one-sided peripheral complete facial paralysis confirmed by needle-EMG were included and underwent ES twice a day for 20 min until the event of reinnervation or for a maximum of 1 year. ES-parameters were set during the first visit and confirmed/adapted every month thereafter. At each visit, patients underwent needle-electromyography, 2D-fotographic documentation and 3D-videos. Whereas 2D-images allow Euclidean measurements of facial symmetry, 3D-images permit detection of metrical divergence within both sides of face. Using the 2D and 3D-fotographic documentation, we aim to prove that ES is able to prevent muscular atrophy in patients with facial paralysis.

Results

In total 15 patients were recruited (medium 53 years, min. 25, max. 78; 8 female, 7 male). They underwent ES for a maximum of one year without serious adverse events. All patients were able to follow the ES protocol. On a short term, we could detect positive effects of ES on the extent of asymmetry of mouth corners. Preliminary results show positive effects leading to improvement of symmetry of denervated faces.

Conclusion

A positive short-term effect of ES on facial symmetry in patients with total paralysis could be shown. The improvement of optical appearance during ES has a positive effect on patients' satisfaction and resembles a promising, easily accessible marker for facial muscles in facial paralysis patients. Improving facial symmetry by ES might also be linked to preventing facial muscle atrophy.

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Surface Electrostimulation prevents Denervated Muscle Atrophy in Facial Paralysis: Ultrasound Quantification

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Introduction

Sparse evidence of the potentialities of surface stimulation (ES) for preventing muscle atrophy in patients with acute or chronic facial palsy have been published so far. Especially studies addressing objective imaging methods for paralysis quantification are currently required. Facial muscles as principal target of ES can be directly quantified via ultrasound, a swiftly feasible imaging method. Our study represents one of the few systematic evaluations of this approach within patients with complete unilateral facial paralysis.

Methods

A well-established ultrasound protocol for the quantification of area and grey levels was used to evaluate therapeutical effects on patients with facial paralysis using ES. Only patients with complete facial paralysis confirmed by needle-electromyography were included. Individual ES parameters were set during the first visit and confirmed/adapted every month thereafter. At each visit patients additionally underwent facial needle-electromyography to rule out reinnervation as well as ultrasound imaging of 7 facial and 2 chewing muscles.

Results

In total 15 patients were recruited (medium 53 years, min. 25, max. 78; 8 female, 7 male). They underwent ES for a maximum of 1 year without serious adverse events. All patients were able to follow the ES protocol. First results in the assessment of ultrasound imaging already indicate that electrically stimulated paralytic muscles do not experience any further cross-sectional area decrease in comparison to the contralateral side. Non-stimulated muscles do not provide significant changes. Similar effects on grey levels currently remain to be assessed to draw further conclusions.

Conclusion

ES is supposed to decelerate the process of atrophy of facial muscles in patients with complete facial paralysis. Thus, the muscular cross-sectional area does not seem to aggravate during the period of electrostimulation within sonographic assessment. This demonstrates the benefit of ES regarding the facial muscle atrophy in patients with complete facial paralysis.

Evaluation of mechanic muscle reflex responses elicited by transcutaneous spinal cord stimulation

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Introduction

To ensure excitation of afferent nerve fibers during transcutaneous spinal cord stimulation (tSCS), reflex responses (RR) in peripheral leg muscles elicited by double stimuli pulses are evaluated in the corresponding surface electromyographic (sEMG) signals. Amplitudes and suppression of the RRs provide feedback on tSCS intensity and electrode position. However, using sEMG sensors involves time consuming skin preparation and electrode placing.

Methods

For increasing the usability in a clinical environment, a new evaluation approach is examined by placing accelerometers on the muscle bellies using elastic straps. The acceleration signal represents force development in the muscles through the mechanical oscillation of the muscle fibers. Therefore, the signal shows longer oscillations than the sEMG data, which causes the responses of the double stimuli to overlap. Thus, double as well as single stimulation pulses are applied to extract the acceleration responses on the first and second stimuli. EMG and acceleration of different leg muscles are recorded in two subjects to expose possible correlations in the electric and mechanic RRs.

Results

The amplitude parameters of the RRs of EMG and acceleration signals indicate good correlation. However, in some muscles the regression of the second and first stimuli differ. When a suppression of the RR occurs after the second stimuli in the sEMG signal, the acceleration signal contrarily shows an increase in amplitude. This observation might be caused by twitch summation during double pulses, leading to an increase in muscular force. The effect could potentially be eliminated with a constant factor applied to the amplitude of RRs in the acceleration signal.

Conclusion

The results indicate that EMG and acceleration amplitudes of the RRs correlate. Therefore, replacing the tSCS evaluation with acceleration signals might be applicably if global muscle-specific factors for twitch summation suppression can be found. However, this would require further investigations with a larger group of subjects.

Hybrid FES-Exoskeleton Control for Walking Gait Correction

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Abstract

Walking gait correction is fundamental to restoring body motion function for patients. Functional Electrical Stimulation (FES) is regarded as a promising method and essential to Neurotherapy, and the exoskeleton is fast becoming a key instrument in rehabilitation. Applying FES or exoskeleton alone, however, has its inherent disadvantages. Therefore, the hybrid exoskeleton combined with FES promoted in recent years overcomes the deficiency of more degree of freedom control.

In this paper, a hybrid FES-Exoskeleton for walking gait control was first proposed and evaluated. With the Force Sensing Resistors (FSR) sensor, the exoskeleton actively assists in walking. Simultaneously, it also triggers the FES of the soleus, tibialis anterior, and gastrocnemius muscles for dorsiflexion and plantar flexion. Later, three different control strategies are employed for the pulse-width controlled FES. Eventually, an ILC with a PID controller is applied in the hybrid exoskeleton, following the best foot angle trajectory.

This study discussed the combination between FES and exoskeleton application in walking gait. The present research aimed to examine the control possibility of the hybrid exoskeleton, and the second aim of this study was to investigate different control strategies for walking gait correction. These experiments confirmed that FES can be used as rehabilitation and correction tools during walking, and PID with ILC control could better follow the ankle position.

Proof of concept for EMG-triggered multichannel electrical stimulation in moderate arm paresis in early subacute stroke patients - results from a randomized controlled trial

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Introduction

Neurorehabilitation aims to optimize task performance through the recovery of control of voluntary movements (CVM). In this proof-of-concept study, the effect of EMG-triggered multichannel functional electrical stimulation (EMG-MES) on the recovery of CVM and the ability to execute arm-hand-activities in early subacute stroke patients with moderate arm paresis was compared to that of single-channel cyclic neuromuscular electrical stimulation (cNMES).

Methods

Subacute stroke patients with moderate arm paresis (Fugl-Meyer-Assessment-Arm Section (FMA-AS) score between 19 and 47) were block-randomized and underwent three weeks of conventional neurorehabilitation therapy including task-oriented arm training and additionally received 15 sessions of either cNMES or EMG-MES. Before and after treatment, the FMA-AS, Box-and-Block Test (BBT), and Stroke-Impact-Scale (SIS) were recorded. Statistics included demographic comparison, descriptive statistics of the results, the Wilcoxon signed-rank test, and the Mann-Whitney U-test for describing group differences pre-/post-intervention.

Results

All 12 participants showed significant improvement in FMA-AS and BBT. Participants who received EMG-MES had a higher mean gain in FMA-AS than patients treated with cNMES (7.17 ± 2.2 versus 6.33 ± 4.5). Non-significant improvement was demonstrated by both groups in the SIS daily activities domain. Arm-hand use and stroke recovery was better in participants treated with EMG-MES.

Conclusion

The addition of a three-week EMG-MES treatment to conventional neurorehabilitation therapy has shown to be superior to a three-week cNMES treatment of the wrist only in this preliminary randomized clinical trial. A larger trial is recommended to confirm these preliminary findings.

Concept for an active multichannel microelectrode array embedded in a flexible multilayer foil for high-density stimulation of the retina

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Introduction

Retinitis Pigmentosa is a genetic disease damaging the photoreceptors inside the retina eventually leading to complete blindness. In past projects, restoring the loss of vision with generic retinal implants was challenging with limited success. Some of the visual prosthetics showed optimistic results, however, with limited resolution and small field of view. An active microelectrode array (MEA) with a high electrode count (>1000) embedded in a flexible foil could be a major step forward to increase the resolution of future retinal implants.

Methods

Stimulating the retina with increased spatial resolution and a decent field of view requires more than 1000 electrodes. For this purpose, an active matrix addressing could be advantageous. The active matrix realized in a crossbar array is used to control and activate the microelectrodes, individually. For this purpose, each microelectrode pixel in the array needs to have at least one selection transistor.

Results

In previous projects, we fabricated microelectrode arrays (MEAs) in a multi-layer polyimide process, where contact lines were realized by standard lithography from evaporated gold. Inter-layer connections as well as stimulation electrodes were fabricated from gold microgalvanics, while the stimulation pads were functionalized with sputtered iridium oxide (SIROF). In all the former designs, the stimulation electrodes were directly contacted to the stimulation electronics or to ASIC devices in a one-to-one fashion. As a first proof-of-concept for active addressing, an array of p-type transistors was fabricated on a silicon-on-insulator (SOI) wafer. After implantation and patterning, the polyimide multi-layer flexible foil with gold interconnects was fabricated. After back-etching of the wafer, the transistors were transferred to the flexible foil.

Conclusion

An SOI transfer process of active transistor elements to a multilayer flexible foil can be used to realize an addressable active switch matrix for large electrode counts. We will use this concept in our future generations of epiretinal implants.

The effect of neuromuscular electrical stimulation on skin temperature in individuals with spinal cord injury: A prospective non-controlled intervention study

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Introduction

The research on the effect of neuromuscular electrical stimulation (NMES) protocol on skin temperature (Tsk) in individuals with spinal cord injury (SCI) is a prospective non-controlled intervention study.

Methods

47 individuals with SCI were recruited from the outpatient clinic. NMES was applied to the tibialis anterior (TA) muscles. Four assessments were performed: baseline, shortly after the end of NMES session (t0), 10 min after the end of NMES (t10) and 20 min after the end of NMES (t20). The intensity used was 1.5 mA RMS (root mean square) depending on the individuals. The variables were Tsk at forehead, dermatome C2 and L5 bilaterally. The measurement device was a non-contact infrared thermometer.

Results

Results of this study demonstrated that after NMES the stimulated dermatome (L5), showed an increase in local Tsk. In addition, the t20 shows that the Tsk did not drop to the baseline, being still significant in the analyzed group.

Conclusion

The implications for rehabilitation practice and the positive effects of NMES are fundamental to improvement of the blood microcirculation and local metabolism.

A feasibility study on the clinical use of neuromuscular electrical stimulation towards neurogenic bladder in spinal cord injured individuals

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Abstract

This research assesses the effect of tibial nerve electrical stimulation on urinary incontinence in individuals with spinal cord injury (SCI) being a prospective non-controlled intervention study. 8 individuals with SCI were recruited from the outpatient clinic. This study demonstrates results of NMES (neuromuscular electrical stimulation) applied to the tibial nerves for 12 weeks. Results:Two questionnaires were applied (Neurogenic Bladder Symptom Score-NBSS and Qualiveen-SF) and presented a tendency to improve symptoms and quality of life, however, without statistical significance. With the urodynamic data: maximum cystometric capacity increased with a mean of 285.6 ml pre, to 314.8 ml post NMES (P-Value: 0.554); compliance increased from 26.38ml/cmH2O pre NMES to 29.88ml/cmH2O post NMES (P-Value: 0.461); detrusor hyperactivity in the filling phase occurred in all patients in the pre NMES assessment; the maximum amplitude of the detrusor pressure in mean detrusor overactivity after NMES increased from 62.0 to 66.6 cmH2 (P-Value: 0.674); urinary leakage pressure during detrusor overactivity pre NMES were mean of 54.0 and 53.2 after (P-Value:1). Conclusion: The implications for rehabilitation practice and the positive effects of NMES are fundamental to improving the quality of life and reducing urinary incontinence on these individuals.

Exploring methods for targeted activation of the sympathetic nervous system without exercise

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Introduction

When using functional electrical stimulation (FES) for cycling in individuals with spinal cord injury (SCI) during FES-cycling, a rapid onset of muscular fatigue can be observed. Among other reasons, missing neural feedback from the lower extremities might be responsible for a reduced sympathetic response during stimulation. Therefore, this project explores different methods to activate the sympathetic nervous system to increase the heart rate to allow better blood circulation and oxygenation in the working muscles.

Methods

Six techniques were selected to be tested on 10 healthy participants in the context of pilot measurements. Those were the cold pressor test with both hands, a virtual reality rollercoaster ride, the hot water immersion test with two hands, the Wim Hof breathing method, the Valsalva manoeuvre and the ingestion of Capsaicin through Prik Jinda chilli peppers.

Results

The results showed a significant increase in average as well as peak heart rate during all methods performed. From baselines of around 68 bpm, the strongest increases in both parameters were found for the Valsalva manoeuvre (to 118±SD bpm peak, 91 bpm average), the Wim Hof breathing method (to 112±SD bpm peak, 86±SD bpm average) and Capsaicin ingestion (to 103±SD bpm peak, 80±SD bpm average).

Conclusion

The methods as they were performed in this project, are not all directly applicable to FES-Cycling but rather serve as exploration how efficiently which stimuli can increase the heart rate. In future research, adaptation or combination of techniques might help to increase performance during FES-Cycling.

Clinical outcomes of neuromuscular electrical stimulation applied to different neurologic levels of spinal cord injuries a pilot study

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Introduction

Electrical stimulation is a tool that has been used in various ways in the rehabilitation of spinal cord injuries. Surface electromyography is an effective method for assessing the many conditions in which the patient is. Objective of the study is to evaluate the benefits through neuromuscular electrostimulation in patients with spinal cord injury and possible neuroplasticity gain observed in electromyography.

Methods

This is a pilot study on the evolution of clinical cases of different neurological levels of spinal cord injury.

Results

It was observed that the spinal cord injured patients analyzed in this preliminary study showed possible gain in neuroplasticity.

Effect of FES controlled cycling training on cardiovascular and pulmonary systems in a spinal cord injured patient

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Introduction

The results of two spiroergometric measurements are presented that were taken from a spinal cord injured patient who participated in FES cycling training sessions for 11 months.

Methods

The two measurements were taken 4 and 11 months after starting the training program. We investigated the respiratory exchange ratio (RER) and ventilation (VE/VO2, VE'/VCO2) ratios and the cycling cadence in the two investigated training sessions.

Results

In the first assessment, the RER was below 1, which is the anaerobic training limit. Seven months later, in the second assessment, the RER value exceeded the anaerobic limit a few times and remained above it at the end of the session. The VE /VO2 and VE/VCO2 curves did not intersect during the first assessment. In the second one, the VE/VO2 and VE/VCO2 curves intersected several times and the oxygen quotient curve exceeded the carbon dioxide quotient curve. The patient achieved a low but similar cycling speed during the two assessments.

Conclusion

Through the activation of paralyzed muscles with FES cycling we are able to train the paraplegic patient in aerobic and anaerobic training zones. This is shown by the value of RER, which reached the anaerobic training limit during the second assessment and remained in the anaerobic range for longer time.

Evaluation of closed-loop vagus nerve stimulation for heart rate control in a Langendorff-perfused isolated rabbit heart with intact cardiac-vagal innervation

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Introduction

Closed-loop vagus nerve stimulation (VNS) is a potential non-pharmacological treatment for persistent tachycardia. This study aimed to develop a control strategy (CS) that allows lowering the heart rate (HR) to the desired level based on a previously developed numerical model and an ex-vivo experimental setup.

Methods

A proportional-integral controller was implemented that modulates the current amplitude of the biphasic stimulation signal between 0 and 6 mA. The CS performance was quantified by the rise time (Tr), percentage overshoot (%OS), and controller stability as the mean squared error (MSE) between the desired- and the instantaneous HR for a step response reducing the HR by 20 bpm from baseline. Optimal controller gains were identified from simulations of a virtual study population consisting of 50 virtual individuals. The CS was evaluated in one Langedorff-perfused rabbit heart with intact cardiac-vagal innervation. The experiment was approved by the local ethics committee (BMBWF 2020-0.016.858 - GZ 2020-0.016.858).

Results

Optimal controller gains identified from the simulations were 0.008 and 0.01 for the proportional- and integral gains, respectively. In the virtual population these gains resulted in Tr = 4.4 $\pm$ 5.3 s, %OS = 3.4 $\pm$ 2.6 %, and MSE = 3 $\pm$ 2.9 bpm. Likewise, these gains led to excellent controller performance in the isolated heart experiment reducing the baseline HR from 169 bpm to 149.5 bpm with Tr = 7.7 s, %OS = 0 %, and MSE = 3 bpm.

Conclusion

The first experimental outcomes were very encouraging, and further experiments are ongoing for a more thorough evaluation and possible optimization of the CS. The results from the ex-vivo setup form an important step towards closed-loop VNS for in-vivo HR control.

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A novel model of an ex-vivo innervated isolated rabbit heart for selective cardiac vagus nerve stimulation

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Introduction

Neuromodulation of the cardiac autonomic nervous system is evolving as a novel approach in the treatment of pathological cardiac conditions. The purpose of this study was to develop a novel isolated Langendorff-perfused rabbit heart preparation with intact vagal cardiac innervation.

Methods

New Zealand White (n=6, 2.8-3.3 kg, age of 3-4 months) rabbits were used. The right vagus nerve was dissected from the nodose ganglion down to the heart including cardiac branches. The innervated-heart preparation was then connected to an erythrocyte-perfused working heart system. For nerve stimulation, a bipolar set of needle electrodes was used.

Results

During the experiment, the nerve was immersed in isotonic sodium chloride in order to maintain the excitability of the nerve to the electrical stimulation. The baseline heart rate was about 170-180 beats min-1, which could be decreased by 10-15% after stimulation of the right vagus nerve. In total, the vagus nerve was stimulable for up to four hours ex-vivo.

Conclusion

Taken together, this setup enables to measure the direct effects of cardiac VNS on changes in heart rate and the consequence of VNS on left ventricular hemodynamic function. In addition, this model provides a well controllable experimental environment that allows to study electrical neuromodulation of the cardiac autonomic nervous system.

Acknowledgements

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Assessing Novel Functional Electrical Stimulation (FES) Activation Patterns with Cycling Ergometer

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Introduction

By evoking contractions in paralyzed muscles, functional electrical stimulation (FES) cycling provides health benefits of exercise to persons with spinal cord injury (SCI). However, two of the main reasons why FES cycling has not gained widespread application are rapid muscle fatigue and low output power. The aim of this work is to develop a platform and design the experimental protocol for assessing muscle fatigue and power output produced while cycling by stimulating paralyzed muscles with novel stimulation patterns in participants with SCI.

Methods

A wall-mounted ergometer equipped with force measuring pedals, encoder and stimulator was developed. DC motor drive system, designed to assist participants while maintaining constant cadence, was adapted to the system. One adult with a motor-complete SCI (ASIA B at the neurological levels C6-C7), experienced with FES cycling, participated in the experiment. Each of the two multiday sessions began with a warm-up phase followed by two 5-minute trials separated by a rest period. The trials consisted of conventional (singlets, fixed frequency) or novel stimulation patterns (doublets, stochastic randomization, interferential stimulation).

Results

The ergometer produces cycling movement at a cadence of up to 100RPM while the encoder provides the position of the crank with a precision of 6000 pulses per revolution. Each pedal, equipped with a six-component force-torque sensor, measures the applied mechanical torque values up to 90Nm. Force-angle curves were successfully recorded during both sessions consisting of trails with constant-frequency trains and variable-frequency trains. Mean power, peak power and fatigue index were calculated and compared.

Conclusion

We have developed a FES cycling ergometer and designed an experimental protocol for assessing fatigue and output power. The ergometer has proven to be important for further research of novel stimulation patterns which will lead to the increase of the efficiency of FES and consequently, its application reach.

Unilateral electrostimulation of the internal branch of the Superior Laryngeal Nerve for the treatment of spasmodic dysphonia and voice tremor

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Introduction

Spasmodic dysphonia (SD) is a chronic (long-term) voice disorder, characterized by involuntary movements of one or more muscles of the larynx. With spasmodic dysphonia, movement of the vocal cords is forced and strained resulting in a jerky, quivery, hoarse, tight, or groaning voice. Voice tremor (VT) describes a periodic fluctuation in loudness and pitch and a resulting decrease in overall voice quality. Presently the standard treatment is based on the off-label administration of Botulinum toxin. The aim of our study is to determine whether unilateral electrostimulation of the internal branch of the superior laryngeal nerve (iSLN) is effective for the treatment of SD and/or VT

Methods

So far, 13 patients completed the study, 8 suffering from SD only and 5 from both SD and VT. Stimulation was delivered by means of hooked-wire electrodes very close to the iSLN with an amplitude $\leq$3mA, a frequency of 60-80 Hz, and a pulse width of 0.2ms. Stimulation was conducted for 30 min every morning for 5 consecutive days. Voice strain, spasm number, voice tremor, voice range profile, and quality of life questionnaire were used to assess the effects of the stimulation

Results

Voice strain and Dysphonia Severity Index (p=0.011), and phonation effort (p=0.002) significantly decreased after 5-day stimulation (p=0.011). The fundamental frequency (p=0.002), the sound pressure level ranges (p=0.025), the maximal phonation time (p=0.029) significantly improved. The communicative participation item bank showed a significant subjective improvement (p=0.002)

Conclusion

The interim analysis of our study showed that the unilateral electrostimulation of the iSLN is promising as alternative to the off-label use of the Botulin toxin. Metanalysis should be considered to systematically compare the effects of the 2 treatments

Electrostimulation of intrinsic laryngeal muscles for the treatment of unilateral vocal fold paresis

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Introduction

Unilateral vocal fold paralysis (UVFP) is a rare disease causing clinically relevant voice impairment. The golden standard treatment is voice therapy, even though selective surface electrostimulation (sSES) could be an effective treatment. The lack of systematic trials on sSES to treat UVFP symptoms has prevented so far its implementation in the clinical routine.

Methods

we recruited 54 patients - 26 (51%) males, 25 (49%) females - with an average age of 53 $\pm$ 15 years. 3/54 (5.6%) were withdrawn after failing selection criteria. Stimulation was delivered bilaterally with an external stimulator by placing surface electrodes (40x28mm) in correspondence of the thyroarytenoid muscle (TA); in triangular waveform, at 1 Hz, with an amplitude $\leq$20mA. Pulse widths (PWs) of 1, 10, 25, 50, 100, 250, and 500 ms were tested. Selective stimulation was deemed successful if both VFs reached a median position at rest and/or during phonation. Unspecific responses comprised swallow/coughing reflex, and/or strap/platysma muscles twitches.

Results

Bilateral VF adduction was observed in 90.2% at rest and about 80% of the cases during phonation while applying a 100 ms PW. PWs of 50 or 250 ms with a slightly lower frequency achieved the same results. The average amplitude ranged between 6.5 and 8.5 mA. Application of a 500 ms PW increased the risks of triggering a swallow reflex before a selective VF adduction could be observed, while the use of PWs < 50ms tended to trigger an immediate unspecific response of the strap/platysma muscles.

Conclusion

Our results show that sSES can elicit the selective and simultaneous VF adduction both at rest and during phonation without unspecific response as long as both the PW and amplitude are correctly selected. PWs between 50 and 250 ms correlate with the most specific results. Electrode placement is essential to elicit a specific target muscle response.

Is needle electrostimulation a useful screening tool for a laryngeal and facial pacemaker?

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Introduction

Electrostimulation implants could provide targeted and rapid help in unilateral vocal fold palsy (UVFP) and facial palsy (FP). In contrast to surgical solutions, they could provide functional and dynamic solutions with lower surgical risk and faster recovery times. We compare the stimulation parameters collected in facial and laryngeal direct muscle stimulation to show the potential of pacemakers, but also to evaluate the required stimulation parameters.

Methods

8 patients with UVFP (duration: 4-22 years) and 11 patients with FP (duration: 0.1-16 years) were included in two prospective studies. During routine laryngeal surgeries, the thyroarytenoid and lateral cricoarytenoid muscles were directly electrostimulated. In the face, needle stimulation was not only possible during open surgery but also in awake patients inserting needle electrodes under sonographical control into the zygomaticus muscle (ZYG). The paretic muscles were stimulated with the following parameters: Amplitude 0.1-10 mA, phase duration 0.1-5 ms, frequency 1-40 Hz. Adductor movements of the stimulated paretic vocal fold or movements of the corner of the mouth in response to stimulation were recorded.

Results

Motor response could be evoked in 6/8 patients in the larynx and 11/11 in the face. There were no adverse events or painful sensations. Nonspecific activations of other muscles could be avoided by selecting the right parameters. Disease duration had no effect on muscle response. With FP, mouth angle elevation was inducible with a phase duration of 0.5-5 ms and amplitudes of 1.5-2.5 mA. In UVFP cases, stimulation with 2.5-3 mA, 1ms phase duration at a frequency of 30 Hz caused partial medialization movements of the paretic vocal fold in 4/6 patients.

Conclusion

Electrostimulation in UVFP and FP seem to have similar stimulation parameters. By direct needle stimulation, we are now able to predict the required stimulation parameters for a laryngeal and a facial pacemaker.

Is surface electrostimulation a useful screening tool for a facial pacemaker?

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Introduction

An electrostimulation implant (“facial pacemaker“) could be an alternative to surgeries and provide targeted and instant help in facial paralysis. This study aimed to show whether surface electrostimulation may be useful as a screening tool for patients where a facial pacemaker may be indicated and to predict the required stimulation parameters.

Methods

7 patients with facial paralysis (duration FP: 0.1-16 years) were included in this prospective study. Surface electrodes attached on the skin above the zygomaticus muscle and needle electrodes placed under sono-control into the muscle were used to stimulate with the following parameters: amplitude 0.1-10mA, phase duration 1-1000ms for surface electrodes and 0.1-5ms for needle electrodes. Movements of the corner of the mouth in response to stimulation was recorded.

Results

A muscle contraction was elicitable in 7/7 patients with both types of electrodes. There were no adverse events. Disease duration had no effect on muscle response. With facial paralysis, mouth angle elevation was elicitable with pulse widths (PWs) of 15-1000ms and amplitudes of 1.0-10mA for surface electrodes, and 0.5-5ms PWs and amplitudes of 1.0-3.5mA for needle electrodes. A good motor response by surface stimulation with 50-250ms PWs allowed to predict a good response with needle stimulation of 1-2ms in 7/7 patients. The amplitude for good motor response by surface stimulation allowed to predict the amplitude needed with needle stimulation in 5/7 FP patients.

Conclusion

Preliminary results show that electrical stimulation of the zygomaticus muscle via surface electrodes may be useful as a screening tool for a facial pacemaker, but also for classic nerve reinnervation surgeries. By simulating the stimulation conditions with the needle stimulation, we are able to predict the required stimulation parameters but also the good tolerance for a facial pacemaker in patients with only a motor deficit and intact sensibility of the face.

Electrical imaging of axonal stimulation in the retina

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Introduction

Stimulation of axons or its avoidance plays a central role for neuroprosthetics and neural-interfaces research. One peculiar example constitutes retinal implants. Retinal implants aim to artificially activate retinal ganglion cells (RGCs) via electrical stimulation. Such stimulation, however, often generates undesired stimulation of RGC axon bundles, which leads to distorted visual percepts. In order to establish stimulation strategies avoiding axonal stimulation it is necessary to image the evoked activity in single axons.

Methods

Using a high-density CMOS-based microelectrode array comprising 4225 electrode and 1024 stimulation electrode we electrically imaged axonal stimulation in ex vivo mouse retina. After precisely localizing the sample on the sensor array, we used a subset of the stimulation electrodes to deliver a localized stimulation to the retina. Then, we analyzed the response via stimulus triggered averages.

Results

We demonstrate signal propagation tracking via stimulus triggered average during high frequency (100 Hz) sinusoidal electrical stimulation. We applied the technique to investigate the characteristic, antidromic or orthodromic, of the elicited axonal signal.

Conclusion

Stimulus triggered average is an effective technique to study axonal action potential propagation in the retina. The technique can be applied to investigate axonal stimulation in the retina to develop optimal stimulation strategies for retinal implants.

Semi-Automatic Detection and Analysis of Rhythmic Electromyographic Activity evoked by Epidural Electrical Stimulation in Spinal Cord Injury

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Introduction

Rhythmic movement patterns in the lower limbs can be elicited by epidural electrical stimulation (EES) in individuals paralysed by spinal cord injury. Analysing the associated electromyographic (EMG) activities allows for insights on how human spinal rhythm and pattern generating circuits operate. In order to avoid potential selection bias, we developed an algorithm to semi-automatically detect and extract parameters of rhythmic EMG activity from a large dataset.

Methods

EES was applied to the lumbar spinal cord of seven individuals with chronic motor-complete spinal cord injury at levels ranging from low cervical to mid-thoracic. Stimulation frequencies from 2 to 120 Hz, and amplitudes up to 10.5 V were applied. EMG responses were acquired from quadriceps, hamstrings, adductors, tibialis anterior, and triceps surae bilaterally in the supine position. A total of 75 hours of EMG recordings containing various non-modulated and modulated responses was available for this retrospective study. Envelopes were created for each EMG channel by using the Teagan-Kaiser energy operator (TKEO) and subsequent second-degree Savitzky-Golay smoothing. 20-seconds-wide moving windows running along the envelope signals rendered autocorrelograms, which were each analysed for peaks corresponding to periodicities ranging from 0.1 to 2 Hz, i.e., frequencies matching slow to fast walking gait. Close or overlapping windows tagged as rhythmic were stitched together into a sequence of ongoing rhythmic activity. Each sequence was visually confirmed using a custom GUI.

Results

The algorithm successfully detected different patterns of rhythmic unilateral co-contractions and locomotor-like EMG activities, some unaccounted for in previous studies. Burst onset and offset points could be acquired robustly, allowing for time-normalized phase relations between burst patterns of both unilateral muscles, and bilateral, homologous muscle pairs. Furthermore, the nature of EES-evoked EMG bursts - being composed of entrained and stimulus-triggered responses - provided for successful stimulus-based and response-based causal analysis of latencies and amplitudes at a high level of temporal resolution.

Conclusion

The portrayed algorithm is capable of providing new and extended information out of an existing dataset, which is necessary to gain further insight into the ingenuities of human motor control. For instance, rhythmic activities with constant frequency but varying interlimb phase relations were found, which point out commissural communication and continuous bilateral coupling, a characteristic not yet described in previous studies. Likewise, increased latencies of stimulation-triggered responses reveal additional central synaptic delays, and hence indicate relay through more complex circuitries when rhythmic activities are present. These insights will help further comprehend the spinal motor control circuitry after paralyzing SCI, allow comparisons to animal models of central pattern generators, and form the relevant basis for computational modelling.

Selective surface electrostimulation of synkinetic zygomatic muscle with ball electrodes

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Introduction

In the present study, we assessed the possibility to selectively stimulate a synkinetically reinnervated M. zygomaticus (ZYG) without eliciting aspecific contractions of other facial muscles. Such idea could support the development of implants for patients suffering from unilateral facial paresis (UFP).

Methods

10 patients were recruited, suffering from UFP with varying degrees of ZYG synkinesis. Onset period differed from patient to patient. 1 Hz stimulation was performed a single time per patient with STMIsola (BIOPAC Systems, Inc. Germany). 2 ball electrodes were placed on the most proximal portion of the ZYG to the mouth corner and slowly moved more distal to it on the ZYG path until no selective ZYG response could be seen. The most distal selective response parameters were analyzed, delivered as triangular and rectangular pulses.

Results

Selective ZYG stimulation was achieved over a 4.5x3cm area close to the mouth corner. The most effective pulse width (PW) was 100 or 250ms with triangular and 1s with rectangular pulses. Amplitudes in the range of 3-6MA delivered best results with all the assessed PWs besides 1ms, for which a range between 7 and 10mA was needed. Few patients reached the discomfort threshold or showed aspecific facial muscle response (e.g., masseter) before a selective ZYG stimulation could be achieved.

Conclusion

Selective stimulation of synkinetically reinnervated ZYG is achievable as long as the parameters are accurately assessed, and the stimulation is delivered on the target. Although encouraging, these preliminary results should be further confirmed for the development of implants to restore facial symmetry.

The evoked compound nerve action potential is shaped by the electrical pulse-width

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Introduction

Despite its central role in medicine electrical stimulation (ES) is still limited by its selectivity. Different reports did assess effects of different waveforms, intensities, and frequency on the activation threshold of nerve fibres with different diameters. We aimed to extend this knowledge by investigating the effect of short monophasic rectangular pulses (1, 2, 5, 10, 50, 100 and 200 µs) on the recruitment order.

Methods

The sciatic nerve of rats was stimulated, and the evoked compound nerve action potential (CNAP) measured at two sites on the tibialis nerve, using epineural electrodes. Changes in delay, amplitude, and the shape of the CNAP were analyzed.

Results

The amplitude and delay of the CNAP were significantly affected by the pulse-width (PW). The delay and duration of the compound nerve action potential increased with longer PW, while the amplitude decreased.

Conclusion

Found changes are likely caused by changes in the time point of excitation of individual neuron fibres, depending on electrical field strength and exposure time. This might be of particular interest when selecting PWs for design and validation of stimulation patterns and analysis of experimental and clinical observations.

SmartStim: A Recurrent Neural Network Assisted Adaptive Functional Electrical Stimulation for Walking

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Introduction

According to the Neuro Patience report of the Neurological Alliance, 1 in 6 people in the UK have a neurological condition. Functional Electrical Stimulation is a neuro-rehabilitation method that uses electrical nerve stimulation to restore functional muscle movements that are lost due to neurological problems such as stroke and multiple sclerosis. This neuroprosthetic device is frequently used to assist walking by treating a condition called Drop Foot, a result of paralysis of the pretibial muscles. This study proposes a two channel terrain-adaptive FES device called the SmartStim which has the ability to modulate its stimulation levels according to various obstacles such as stairs and ramps.

SmartStim Model

This system employs a sensor-based module with a Recurrent Neural Network to classify these different walking scenarios. The module is built with Inertial Measurement sensors embedded in a pair of shoes, and the RNN uses data from these sensors to predict various obstacles as the user is walking. These predictions are then used by a Fuzzy Logic Controller to control and regulate the stimulation current in two channels of the SmartStim system. In the two channels of the system one channel will help treat drop foot and the other will be used to stimulate another muscle group to help access stairs and ramps by the user.

Results and Conclusion

The RNN module in this system has been trained and tested using the k-fold cross validation. The evaluation of this trained model shows that it can predict obstacles from the sensor data at 97% accuracy. Currently further testing is being performed to assess the working of the fuzzy logic controller in combination with the RNN in healthy individuals. It is expected that SmartStim system may aid the users to access various walking scenarios more efficiently.

How to train muscle for FES

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Introduction

Artificial activation of muscles has been used for several decades. Muscle is a plastic tissue that responds to the disuse caused by neural injury or pathology by large changes in mass and character including the properties that determine endurance.

There has been a recent dramatic improvement in the ability to follow changes in muscle cells in terms of the gene expression of their constituent fibres. These new techniques promise a new understanding of the precise relationship between activation and cellular response including growth and improvement in fatigue-resistance. This paper will present a review of the evidence linking patterns of activation to progressive changes in muscle, including disused and denervated or partially denervated muscle.

Results

New evidence from our laboratory shows that rather little daily stimulation is necessary to cause substantial changes in muscle character, and in terms of muscle growth, that daily exercise may be counter-productive. The traditional recommendation of exercise for one muscle group once every three days may have a sound cell biological basis in terms of the timecourse of the response to acute resistance exercise. Furthermore, experiments in rats appear to show a similar time course of response in that exercise every three days produces more muscle growth than exercise every day. As well as the timing of exercise, we will also consider the effect of loading or 'intensity' in terms of the signal for growth.

Conclusion

These new cell biological findings should influence our prescription for FES in rehabilitation, and may give opportunity to follow in very tiny biological samples the progress of training in individual participants.

Evaluation of control modalities and functional impact of a self-piloted grasp neuroprosthesis in stroke patients: preliminary results from a multi-crossover N-of-1 randomized controlled study

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Introduction

Stroke is the leading cause of acquired motor deficiencies in adults. Improving prehension abilities is challenging for individuals who have not recovered active hand opening capacities post-stroke. Functional electrical stimulation (FES) applied to finger extensor muscles to restore grasping abilities in daily life, called grasp neuroprosthesis (GNP), remains confidential in post-stroke population. Thus, we developed a GNP and control modalities adapted to the characteristics of this population and assessed its impact on functional restoration of grasping abilities.

Methods

A GNP prototype was designed with specific control modalities (voice control, foot and head movements). A software allowing configuration and monitoring, interprets user commands through input signals from sensors (IMUs and microphone) and triggers a pre-programmed external electrical stimulator. Over 5 days, the users tested and selected a preferred control modality before training with the GNP to perform unimanual and bimanual tasks in a seating position. Its functional impact was assessed in a blinded evaluation multi-crossover N-of-1 randomized controlled trial (clinicaltrials.gov: NCT04804384), followed with a QUEST questionnaire.

Results

Preliminary results from eight subjects (1 to 17 years post-stroke; Fugl-Meyer motor upper-extremity score 21 to 48/66) showed a preference for non-paretic foot triggering (7/8). All subjects selected the key-pinch task as the primary outcome and the palmar grasp task as secondary outcome. All subjects successfully completed from 83% to 100% of the tasks using the GNP (100% for 5 subjects; khi2: $p<0.001$), while none of them could complete the task without GNP activation. QUEST ranged from 29 to 35 (median of 33/40).

Conclusion

These preliminary results attest that the GNP prototype and its control modalities are well suited to the post-stroke subjects in terms of self-triggering, while allowing to restore grasping capabilities. A wearable version of this device is being developed to improve prehension at home in daily life.

Short-term effects of selective transcutaneous auricular-nerve stimulation

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Introduction

The study reported here seeks to assess a short-term effect of selective transcutaneous stimulation of auricular branch fibres of the vagus nerve (tANS) on the respiratory function of healthy female volunteers, assuming that it could be altered with the tANS.

Methods

The trials were carried out with a group of healthy female volunteers, age 22 to 25.
The devices for the tANS were custom-crafted plugs that contain four platinum stimulating cathodes (geometric surface approximately 14.58 mm^2), a hydrogel common anode (geometric surface about 400 mm^2) and a microprocessor-controlled stimulator.
The stimulating sites were indicated as left (L) and right (R) plus colour code: pole position, red (R); below pole position, yellow (Y); above bottom position, black (B); and bottom position, white (W).
The parameters of the stimuli were the following: Frequency 45.5 Hz, pulse width 200 µs, interphase delay 180 µs, pulse train duration 2.0 s and time gap between successive pulse trains 1.0 s. The intensity ic however, was pre-set until the minimum discomfort was detected.
Each 20-minute trial started with the 5-minute sham, proceeded with the 10-minute tANS and ended with the 5-minute sham.
The air-flow measuring system was developed to assess the variations in the bi-directional nasal air-flow, the changes in the rhythm and the character of the respiration. Breath length, peak-to-peak air-flow and maximum slope of air-flow were analysed within the time period of ten breaths at each of three aforementioned segments.

Results

The results show that the selective tANS had an effect on the respiratory function in all trials. The respiration became shorter, more heavy/shallow, more jerky and more frequent along with the steeper inspiration and lower peak-to-peak air flow.

Conclusion

The hypothesis that the selective tANS has a measurable effect on the respiratory function was confirmed.

Facing the challenges of neonatal brain monitoring - EU ITN INFANS project workshop

A deep learning-based algorithm for automated bedside monitoring of sleep state fluctuations in neonatal intensive care units

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Introduction

In clinical practice, fluctuations of sleep and wake states have long been used to measure brain function in early brain monitoring in neonatal intensive care units (NICU) [1, 2]. The use of convolutional neural networks (CNNs) has been shown to improve automatic classification of sleep states in neonates, even using only electroencephalography (EEG) signals [3-5]. Our study developed and validated a quiet sleep detection algorithm based on single EEG recordings.

Methods

We propose a CNN that is developed and trained on a dataset of long-term 4-electrode (a)EEG monitoring in 30 near-term neonates. The dataset was annotated visually by two experts for only QS epochs. As input, the proposed CNN receives a single-channel 1-minute non-overlapping EEG segment, which is initially resampled to 64 Hz. After 11 layers of processing, the CNN produces a vector of probabilities for AS and QS classes. An external dataset of 30 polysomnography recordings was used to validate the results.

Results

Quiet sleep detection in the training data yielded a 90% accuracy rate, and the accuracy for all bipolar derivations available from the 4-electrode recordings was similar (85-86%). The algorithm generalized well to the external dataset, showing an overall accuracy of 81% despite different signal derivations.

Conclusion

We used a large dataset and annotated the EEG signals in our training data without pre-fixed epochs. Furthermore, we incorporated annotations from multiple experts rather than consensus or single annotations as has been proven to improve classifier performance in other studies [6, 7]. The present algorithm generalizes well across derivations in the training dataset, as well as across completely different derivations, recording systems, and sleep scoring systems utilized in our independent validation datasets.

Developing disposable skin-electrode interface for Infant EEG monitoring at the neonatal intensive care unit

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Introduction

Long-term EEG monitoring at the Neonatal Intensive Care Units (NICU) is challenged by solutions for setting up and maintaining a sufficient recording quality with limited technical experience. This study evaluates different solutions for the skin-electrode interface and the development of a disposable EEG cap for newborn infants.

Methods

Several alternative materials for the skin-electrode interface were compared to the conventional gels and pastes: conductive textiles (textured and woven), conductive Velcro, sponge, super absorbent hydrogel (SAH), and thick-layer and thin-layer hydro fiber (HF). The comparisons included assessment of dehydration and recordings of signal quality (skin-interphase impedance and powerline (50hz) noise) for selected materials. The recordings were done in the lab using snap electrodes integrated into a forearm sleeve or a forehead band to mimic an EEG cap. The aim was to study long-term biosignal recording on unprepared skin.

Results

SAP and HF remained hydrated almost 75% after 6 hours and 20% after 24 hours in an incubator mimicking environment. And the sponge material was dehydrated completely before 12 hours of recording. Conductive textiles achieved poor performance in absorbing and storing conductive solutions. And conductive Velcro's had rigid coated surfaces that could irritate the infant's skin. The SAH material had a fragile structure and higher powerline amplitude RMS component after 12 hours of recording. The electrical impedance for HF was significantly lower than tensive gel impregnated sticker electrode on an unprepared forehead skin, and the impedance remained under $15\text{k}\Omega$ in 10Hz frequency for the HF for about 18 hours after the recording started.

Conclusion

The HF skin-electrode interface is an effective candidate for preparation-free long-term recording that quickly activates with saline or tap water. The concept shows many advantages, such as long-lasting, disposable material, low impedance operation, no required skin preparation, and no traces on the skin after the long-term recording.

Toward Dynamic Functional Connectivity Characterization of the Newborn Brain

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Introduction

Functional connectivity (FC) is believed to facilitate neuronal information processing and network communication. Since the brain is a dynamic system, dynamic FC is believed to be a better solution to assess the brain’s behavior rather than static FC. Recently, dynamic methods based on the hidden Markov model (HMM) attracts much attention due to their ability to capture spatiotemporal correlation among different brain regions. This study aims to assess dynamic functional networks in the neonatal brain, captured from EEG recordings by means of a hidden Markov model.

Methods

EEG signals recorded from 60 full-term healthy newborn infants using 19 electrodes were used. Three-minute EEG segments recorded in the active and quiet sleep states were selected. Data were band-pass filtered between 0.3-25 Hz and down-sampled to 100 Hz. The filtered signals were transformed into the source space. Different brain states were extracted by means of an HMM with a Gaussian model observation in the time-delay embedded space. Then the lagged coherence was used to quantify the phase-coupling at different brain states. All comparisons between sleep states were done using the permutation test (repetitions = 5000, a = 0.01).

Results

Four states were identified using HMM. States 1 and 2 have the highest and lowest power values. States 3 and 4 have the lowest coherency. The neonatal brain tends to be more active during QS. There are many significant differences in brain state transitions between AS and QS. The brain has a more complex transition between brain states in QS.

Conclusion

Our results show that HMM is able to extract different brain states in the newborn brain. This pipeline can be used to assess dynamic FC in the neonatal brain in different physiological conditions.

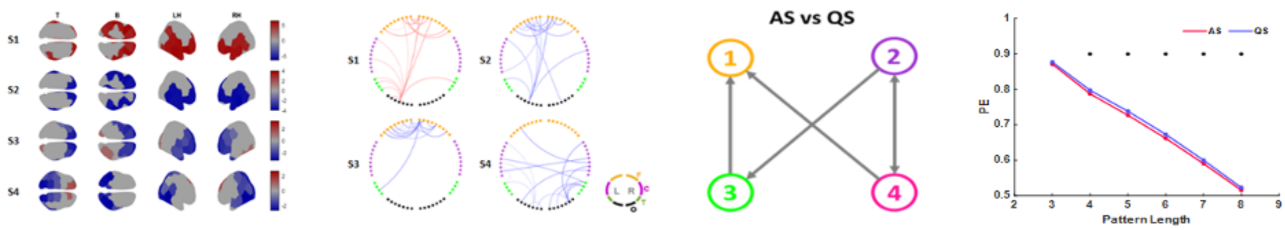

Figure 1: The power maps, connectivity patterns, significantly different brain state transitions, and permutation entropy.

Evaluation of Neonatal EEG-NIRS caps contact pressure using a force sensor matrix

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Introduction

Neuromonitoring of neonates is of crucial importance for monitoring the brain maturation and the detection of early signs of brain damage. Head caps for multimodal dry Electroencephalography (EEG) and functional near infrared spectroscopy (fNIRS) can be used comfortably during long-term monitoring.
The usability of dry electrode caps is challenged by the pressure of electrodes exerted on the neonate's head which must ensure reliable sensor-skin contact while avoiding excessive pressure. Our aim is to develop a novel, flexible EEG and fNIRS cap based on 3D anthropometry and additive manufacturing, offering better adaptivity to different head shapes and sizes, ease of application, precise sensor positioning, and homogenous adduction within the predefined range.

Methods

An experimental setup for the mechanical validation of different cap concepts has been developed using a physical head phantom. The evaluation of the caps includes evaluation of sensor position accuracy and contact pressure measurements. Positions of the electrodes with respect to fiducials are digitized using a commercial 3D camera. Next, the arc distances between the electrodes and their ideal positions are calculated.
Contact pressure between the electrodes and the head phantom was evaluated using a matrix of flexible capacitive force sensors placed beneath the electrodes' positions. The force values of each sensor were recorded as continuous digital samples and subsequently analysed.

Results

Each force sensor was calibrated separately and the calibration curve was inspected. The sensors showed a mean accuracy error of 4.23 ± 2.8 % of the full-scale range (%FSR), drift of 0.58 ± 0.84 (%FSR) over 1 hour, and hysteresis of 3.93 ± 2.03 (%FSR). The mean contact pressure exerted by dry electrodes was 1.25 ± 0.23 N.

Outlook

The placement accuracy, precision, and contact pressure will be compared between different cap prototypes and commercial caps.

The predictive role of early qualitative and quantitative (a)EEG on long-term neurodevelopmental outcome in extremely preterm infants

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Introduction

Extremely preterm (EP) infants (<28 weeks of gestation) are at high risk for long-term cognitive, intellectual, motor and behavioral difficulties. Amplitude-integrated electroencephalography (aEEG/EEG) is widely used for bedside monitoring of neonatal cerebral function and have shown potential as a predictor for later outcomes. The current study aimed to determine whether and which early qualitative and quantitative (a)EEG features are predictive for neurodevelopmental outcomes in EP newborns at pre-school age.

Methods

A total of 369 EP infants who received (a)EEG monitoring during their first postnatal 72 hours were retrospectively enrolled in this study. The qualitative analysis of aEEG evaluated the background pattern, the presence of sleep-wake cycles, and the occurrence of seizure activity. Moreover, four groups of quantitative EEG features were extracted from raw EEG signals: bursting, synchrony, spectral power, and complexity features. The combination of both qualitative and quantitative (a)EEG features was entered into a machine learning (ML) regression model to assess their predictive value for neurodevelopmental outcomes at 2 and 5 years of age. Potential confounding factors such as gestational age, morphine, maternal education, brain injury (BI) and illness severity were also included in the regression analysis.

Results

The ML regression analysis results showed that both qualitative and quantitative (a)EEG features could significantly predict cognitive ($R = 0.10$, $P < 0.01$), gross motor ($R = 0.13$, $P < 0.01$) and behavioral ($R = 0.37$, $P < 0.001$) scores at 2 years in severe BI group, and intelligence ($R = 0.14$, $P < 0.01$) scores at 5 years in mild BI group. The complexity, synchrony, and spectral power features contributed most for the outcome prediction.

Conclusion

Early (a)EEG characteristics obtained within 72 postnatal hours were able to predict long-term neurodevelopmental outcomes of EP infants and the predictive ability of quantitative EEG features was better than visual aEEG parameters.

A Spatio-Temporal Graph Convolutional Network for Neonatal Seizure Detection

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Introduction

Deep neural networks that have been proposed so far for the detection of neonatal seizures are mainly based on 1-dimensional convolutions that ignore spatial information. Here, we used a Spatio-Temporal Graph Convolutional Networks (ST-GCN) that simultaneously employs common convolutions to describe the temporal features and graph convolutions to learn the spatial patterns from graph representations of raw EEG data.

Methods

EEG recordings from 39 full-term neonates with seizures [1] were segmented into epochs of 12s with an overlap of 11s for seizure and 10s for non-seizure segments to handle the class imbalance problem.
In the network architecture, firstly, CNN is used for the automatic temporal feature extraction from each EEG channel. These features are added to the distance-based graphs as the graph signals to complete the graph representation of EEG epochs, and then are fed to graph convolutional layers to explore the spatial patterns [2]. An ablation study is also employed to investigate the importance of each layer by changes in classification performance when excluding some convolutional layers [3].

Results

The performance of the proposed ST-GCN and ablation study using the leave-one-out cross-validation method is reported in Table 1 in terms of AUC and AUC90. The mean AUC of ST-GCN model is 95.6%, which is higher than the cases with a lower number of layers.

Conclusion

We proposed an end-to-end ST-GCN for the detection of neonatal seizures which has higher or comparable performance to the state-of-the-art methods and has the advantage of exploring both spatial and temporal dependencies of EEG recordings. Moreover, the ablation study showed that each temporal and spatial convolutions play an important role so that excluding them reduces the performance. This confirms the proper selection of our proposed architecture.

Acknowledgements

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References

[1]. N. J. Stevenson, K. Tapani, L. Lauronen, and S. Vanhatalo, "A dataset of neonatal EEG recordings with seizure annotations." Scientific data, 2019.
[2]. T. N. Kipf and M. Welling, "Semi-Supervised Classification with Graph Convolutional Networks." arXiv preprint arXiv:1609.02907, 2017.
[3]. R. Girshick, J. Donahue, T. Darrell, and J. Malik, "Rich feature hierarchies for accurate object detection and semantic segmentation." Proceedings of the IEEE conference on computer vision and pattern recognition, 2014.

Table 1: AUC and AUC90 values of ST-GCN and the ablation study

	AUC (%)	**AUC (%)**
	Mean ± std	Mean ± std
CNN block2	75.0 ± 4.3	67.2 ± 3.1
CNN block3	82.4 ± 1.5	73.4 ± 1.2
CNN block4	84.2 ± 1.8	76.1 ± 2.3
GConv1	93.8 ± 2.1	84.0 ± 3.1
ST-GCN	**95.6 ± 1.1**	**89.9 ± 1.6**

AUC: Area Under the Curve

AUC90: AUC for specificity values greater than 90%.

Implementation and evaluation of a frequency based swLORETA algorithm for real time source localization in neonate brains.

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Introduction

One of the earliest tools used to measure neuronal activity in the brain is the electroencephalogram (EEG). High-density EEG systems promise to be powerful neuronal imaging modalities when coupled with detailed head anatomy and source localization algorithms.

Methods

Recently the application of high density 64 channel EEG on neonates has become possible and aids in determining the neural activation and characteristics of their early cognitive experience. It is critical to discover particular irregularities and neuropsychiatric disorders as early as possible.
In this work we aim to implement and apply a frequency based swLORETA algorithm to neonatal EEG data suitable also for real time analysis to high density EEG.

Results

For verification and validation we utilize a neonate head model for forward calculations and then use the implemented source localization method to compute the sources back from the swLORETA algorithm in the frequency domain.

Conclusion

Comparing the results shows the accuracy of the method that is than planned to be applied to recorded EEG data for source localization and connectivity analysis in upcoming studies.

Novel replaceable EEG electrode system

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Introduction

Due to the direct contact between electrode and scalp, dry EEG electrodes are exposed to increased mechanical wear compared to conventional gel-based electrodes. However, state-of-the-art commercial cap systems commonly use permanently fixated electrodes which can lead to downtime of the EEG cap during professional repair and replacement as well as reduced overall lifetime. An easily replaceable EEG electrode would furthermore improve hygiene, especially for newborn and infant applications.

Methods

We propose a novel replaceable electrode system, consisting of an electrode holder, a snap top, a contact ring fixated inside the electrode holder, and a replaceable electrode. The production process consists of 3D printing, silicone molding, resin casting, and electroless plating. The replaceable electrode system is integrated into a multichannel EEG cap system. A verification study is conducted with 30 volunteers.

Results

The operators experienced that the new electrode holder eases adjustment of the electrode to have proper contact with the scalp. During the study, defective electrodes can be replaced without a soldering process. Furthermore, all electrodes stayed in the holder and did not fall off the cap for the whole session.

Conclusion

In conclusion, the novel replaceable electrode system is suitable for EEG measurements.

Bad channel detection in EEG recordings

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Introduction

Electroencephalography (EEG) is widely used in clinical applications and basic research. Dry EEG opened the application area to new fields like self-application during gaming and neurofeedback. While recording, the signals are always affected by artefacts. Manual detection of bad channels is the gold standard in both gel-based and dry EEG but is time-consuming.

Methods

We propose a simple and robust method for automatic bad channel detection in EEG. Our method is based on the iterative calculation of standard deviations for each channel. Statistical measures of these standard deviations serve as indications for bad channel detection. We compare the new method to the results obtained from the manually identified bad channels for EEG recordings. We analysed EEG signals during resting state with eyes closed and datasets with head movement.

Results

The results showed an accuracy of 99.69 % for both gel-based and dry EEG for resting state EEG. The accuracy of our new method is 99.38 % for datasets with the head movement for both setups.

Conclusion

There was no significant difference between the manual gold standard of bad channel identification and our iterative standard deviation method. Therefore, the proposed iterative standard deviation method can be used for bad channel detection in resting state and movement EEG recordings.

Heart rate extraction from neonatal near infrared spectroscopy signals

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Introduction

Near infrared spectroscopy (NIRS) noninvasively monitors oxygenation and perfusion of the brain. The NIRS-derived intensity signals can provide useful additional functional and physiological information that is of use in daily clinical care. The most prominent physiological information in the NIRS signals are pulsatile fluctuations caused by heartbeats, allowing for the extraction of heart rate (HR).

Methods

In this study, we propose an algorithm for extracting the HR signal from neonatal NIRS (EHR). We recorded synchronously the NIRS and reference HR signals from four new-born infants (gestational age = 38 ± 2 weeks, 3 ± 2 days; 3149 ± 429 grams) admitted in neonatal intensive care units at Wilhelmina Children's Hospital, Utrecht, the Netherlands. We recorded the NIRS signals with the sampling rate of 100 Hz by using Artinis cerebral oximetry device (TOM, Artinis Medical Systems B.V., Elst, the Netherlands). We recorded the reference HR signal (RHR) by using a patient monitor, Philips MP70, with a sampling rate of 1 Hz. The algorithm has three main stages. First, the NIRS signal quality was assessed by using Signal Quality Index (SQI) algorithm. Second, the NIRS signal was segmented, and was then scaled by the SQI score. Third, the segmented signals were band-pass filtered, and their auto spectral densities were then computed in which the frequency maxima was considered as the HR.

Results

The results of comparison between RHR and EHR showed a high degree of agreement between the two HR signals: Pearson's r = 0.85, Bland Altman Ratio = 5.5%, and Bland Altman Limits of Agreement = 7.4 Beats Per Minute.

Conclusion

Deriving HR from neonatal NIRS is feasible. It is highly useful as it can eliminate the need to use extra electrode for recording HR. Eliminating extra electrodes can relieve neonates from physical stress induced by electrode placement and potentially reduces injury risks.

Reliability in automated sleep staging

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Introduction

Recent developments in brain monitoring in the neonatal intensive care unit have led to the development of automated methods for sleep staging. Since these methods are typically developed using preselected clean data segments, it is important to understand when their predictions are reliable when applied to continuous data in practice. The aim of this study is to investigate if we can automatically identify unreliable predictions of an existing sleep stage classifier.

Methods

We used a recently published automated quiet sleep (QS) detection algorithm (Ansari et al. 2020 J. Neural Eng. 17) which predicts the sleep stage when given a 30-second EEG segment. We used a labelled dataset of 30 healthy control patients which was not used in the development of the algorithm. To identify segments for which the predictions are inaccurate, we used the conformal prediction framework to find thresholds for the signal quality (assessed with an automated artefact detection algorithm), out-of-distribution (OOD) probability (from a one-class support vector machine), and predicted QS probability. Finally, we used these thresholds to automatically discard unreliable predictions and tested if this improved the reliability by comparing the remaining predicted sleep stages to sleep annotations form a clinical expert (Cohen's kappa score).

Results

Prediction uncertainty was most sensitive for identifying inaccurate predictions, while signal quality and OOD probability seemed to be less sensitive. After discarding data with high prediction uncertainty, average kappa improved from 0.907 to 0.931 by removing 4.8% of the predictions.

Conclusion

Estimating the reliability of predictions of automated sleep staging methods is an important task for the practical use of these methods. We showed that the estimation of prediction uncertainty can be a useful tool to identify inaccurate predictions in a healthy control group. Similar reliability analysis in a patient group and for other applications is part of ongoing work.

Neonatal seizure detection algorithms: The effect of channel count

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Introduction

The number of electrodes used to acquire neonatal EEG signals varies between institutions. Therefore, tools for automatic EEG analysis, such as neonatal seizure detection algorithms, need to be able to handle different electrode montages in order to find widespread use. The aim of this study was to analyse the effect of montage on neonatal seizure detector performance.

Methods

A full 18-channel montage was compared to reduced 3- and 8-channel montages using a convolutional neural network for seizure detection.

Results

Sensitivity decreased by 10 - 18 % for the reduced montages while specificity was mostly unaffected. Electrode artefacts and artefacts associated with biological rhythms caused incorrect classification of non-seizure activity in some cases, but these artefacts were filtered out in the 3-channel montage. Other types of artefacts had little effect.

Conclusion

Reduced montages result in some reduction in classifier accuracy, but the performance may still be acceptable. Recording artefacts had a limited effect on detection accuracy.

Applying a Phase Space Reconstruction Approach on the Signals Obtained by Near-infrared Spectroscopy Method to predict Future MRI scores of Pre-Term Infants

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Abstract

Pre-term Infants are a population at high risk for adverse long-term neurodevelopmental outcomes, such as cognitive- and motor disabilities. A major cause of these neurodevelopmental problems is brain injury, linked to inadequate brain perfusion during and after delivery and detected on routine ultrasound or more commonly on term equivalent MRI brain scans. Maintenance of adequate blood flow and oxygenation in the underdeveloped brain is crucial to normal brain development. A timely and guided treatment such as inotropics, sedation and fluid loading can prevent irreversible brain damage. It requires a monitoring system that can continuously assess the brain perfusion and brain development of the baby throughout the most critical first few days of life in the incubation. Furthermore, early by-proxy bedside biomarkers for future neurological outcomes such as term equivalent age MRI scans are also needed for early prognosis. Currently, MRI at TEA is considered a gold standard to assess brain injury after NICU stay. However, MRI scans are expensive and lack the time resolution needed for dynamical shifts of an infant's brain. NIRS however can be performed at the bedside, is non-invasive, and requires no ionizing radiation.. As such, this technology offers the highest potential for the required neonatal neuro-monitoring. In our study, our aim is to develop a time dynamical approach to find the connection between brain oxygenation signal (acquired right after birth) and the future MRI scores. We prove that this dynamical approach can help to predict MRI scores of gray matter from Near-infrared Spectroscopy (NIRS). The outcome is not just a discontinuous classification but can predict the continuous scores through a linear regression method known as canonical correlation analysis (CCA). Through this knowledge, we can start better and faster suitable Infant's care at NICUs before losing the time for recording and scoring MRI data.