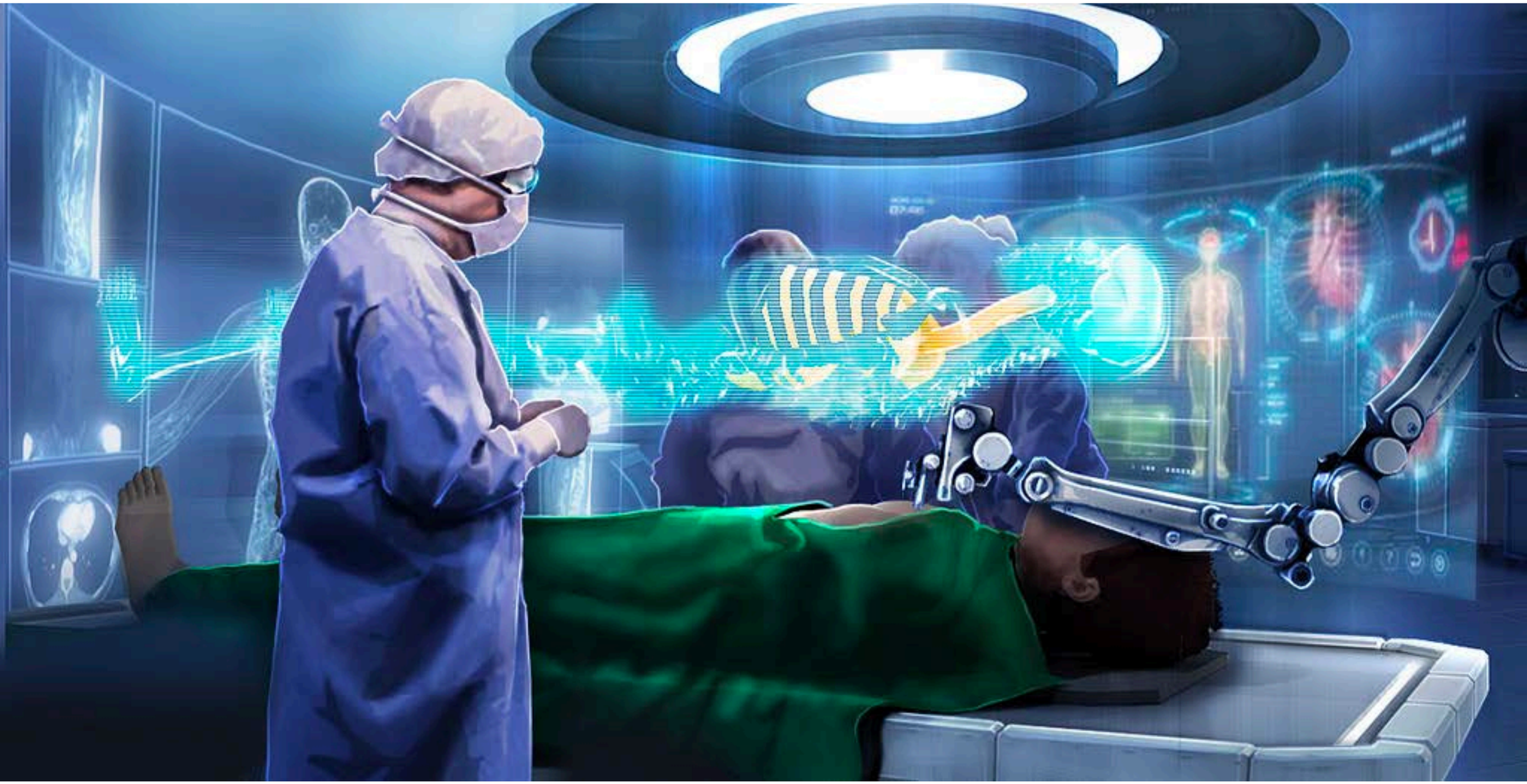
Validating Simulation Pipelines With Potential Recordings

A PhD thesis defense for:
Jess Tate

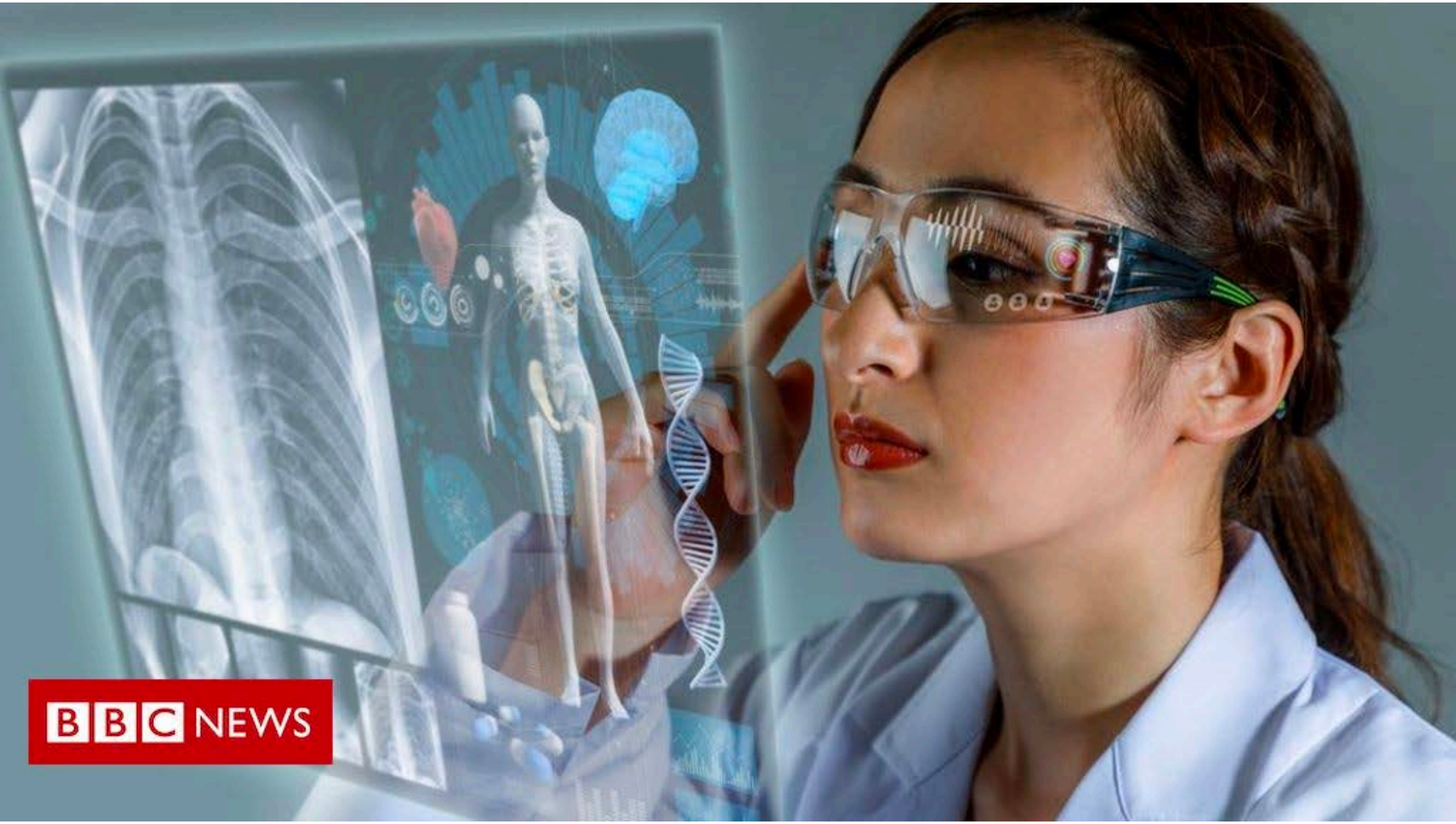
Advisor: Rob MacLeod

Pre-surgical Planning



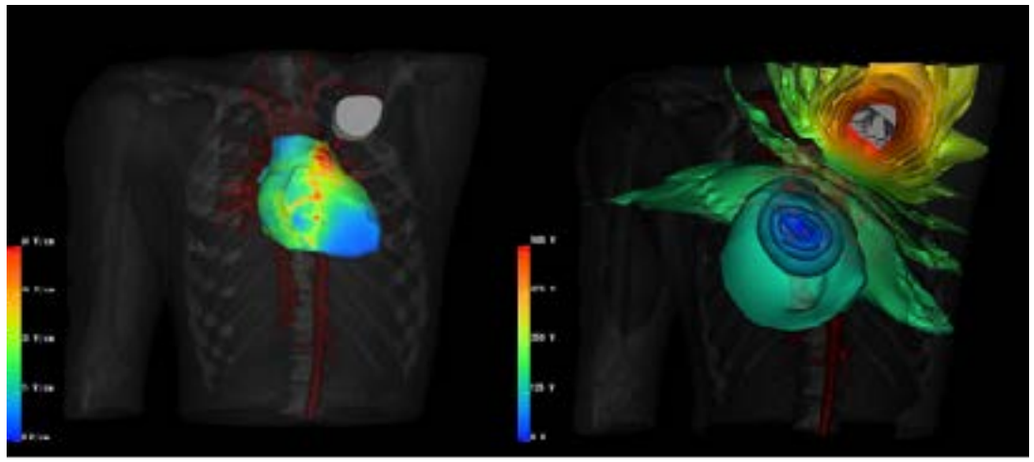
https://brightside.me/wonder-curiosities/10-futuristic-medical-innovations-that-will-redefine-our-lives-407760/

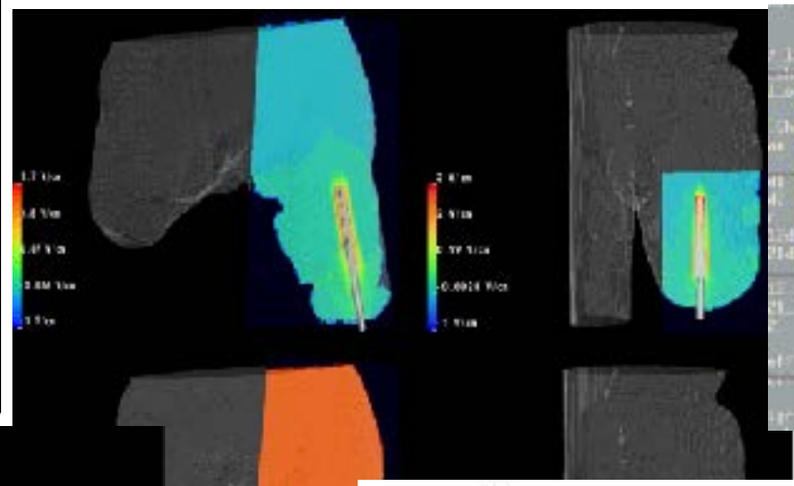
Predictive Medicine

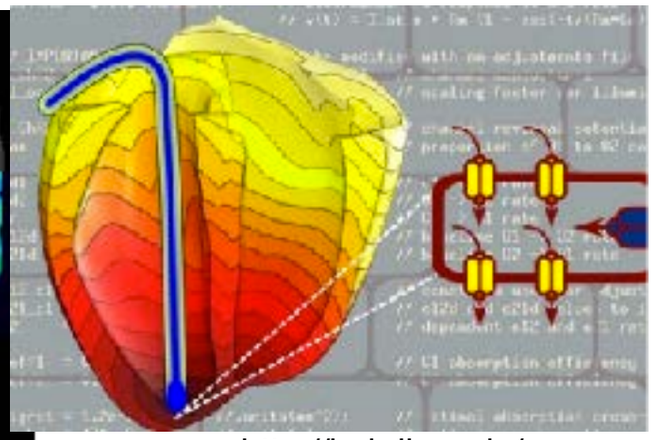


https://lifeboat.com/blog/2018/04/the-nanobots-and-ninja-polymers-transforming-medicine

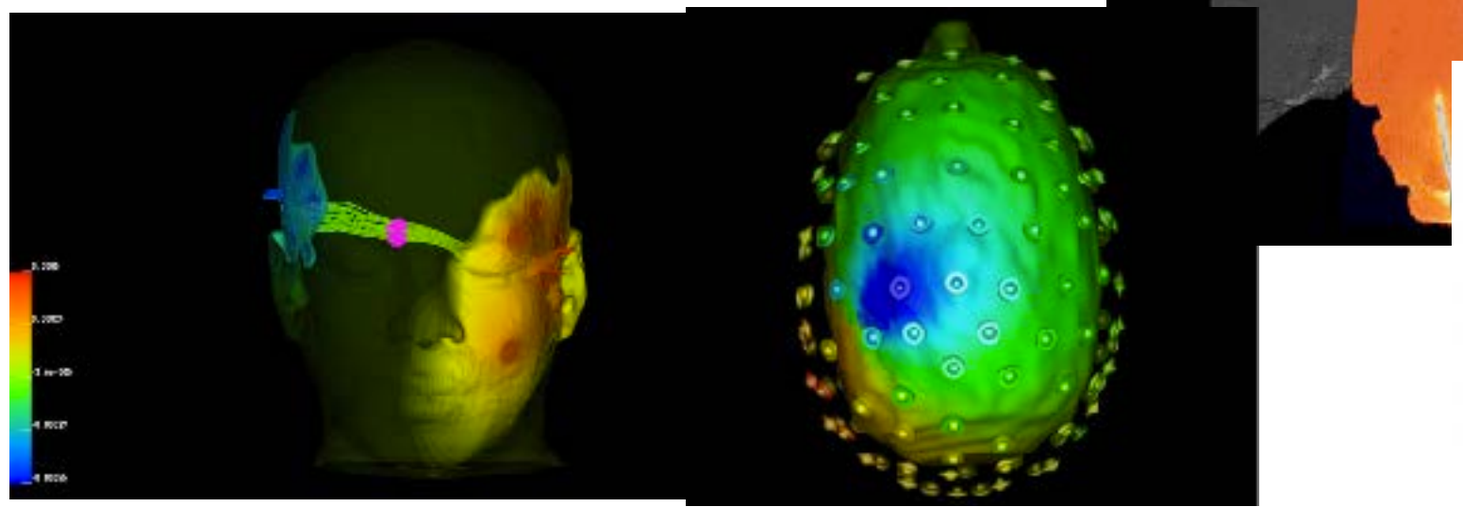
Biomedical Computational Modeling

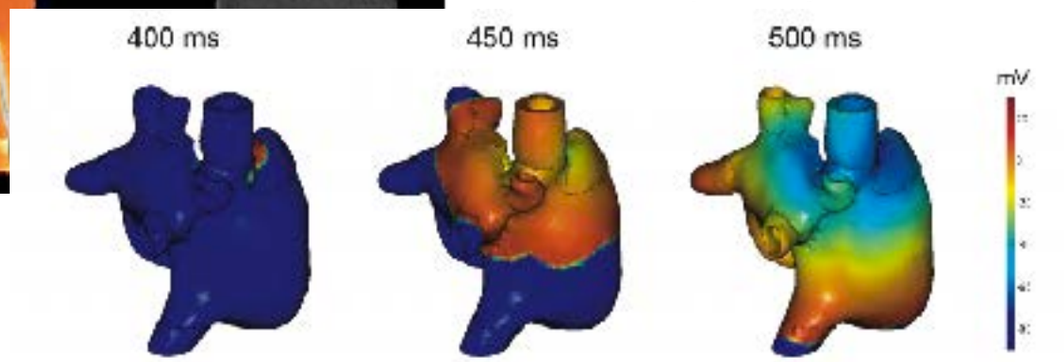




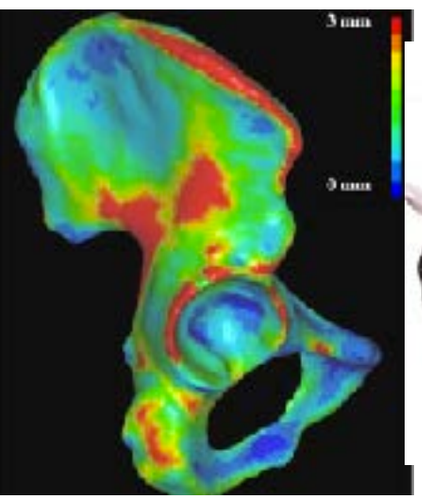


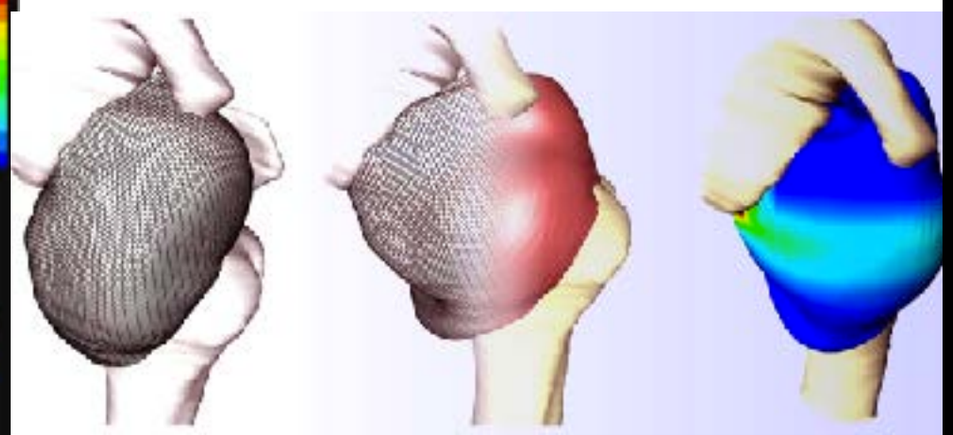
http://hub.jhu.edu/



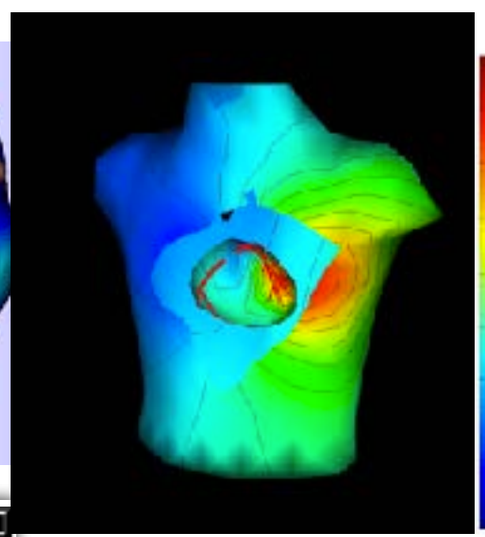


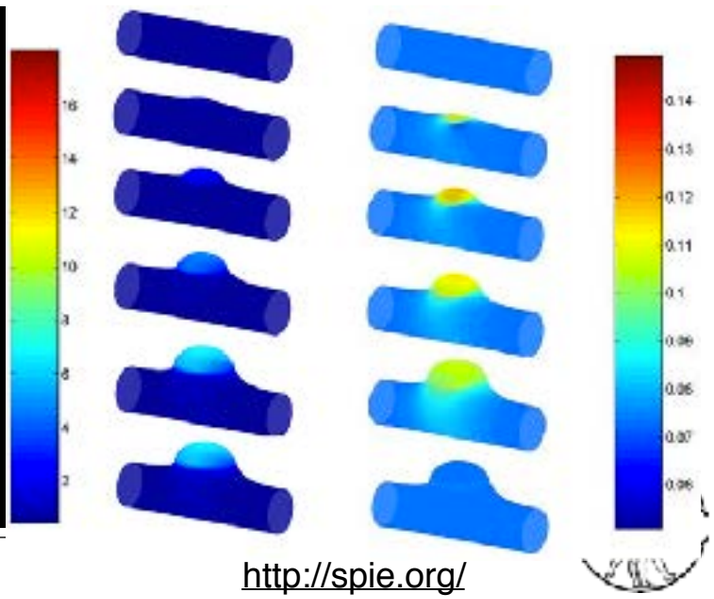
https://www.engineering.unsw.edu.au/





http://sci.utah.edu





http://spie.org/

Virtual Physiological Human

VPH Institute
Building the Virtual Physiological Human

http://www.vph-institute.org/

CIBC

Why aren’t computational models used more?

Validation

Virtual EP Lab

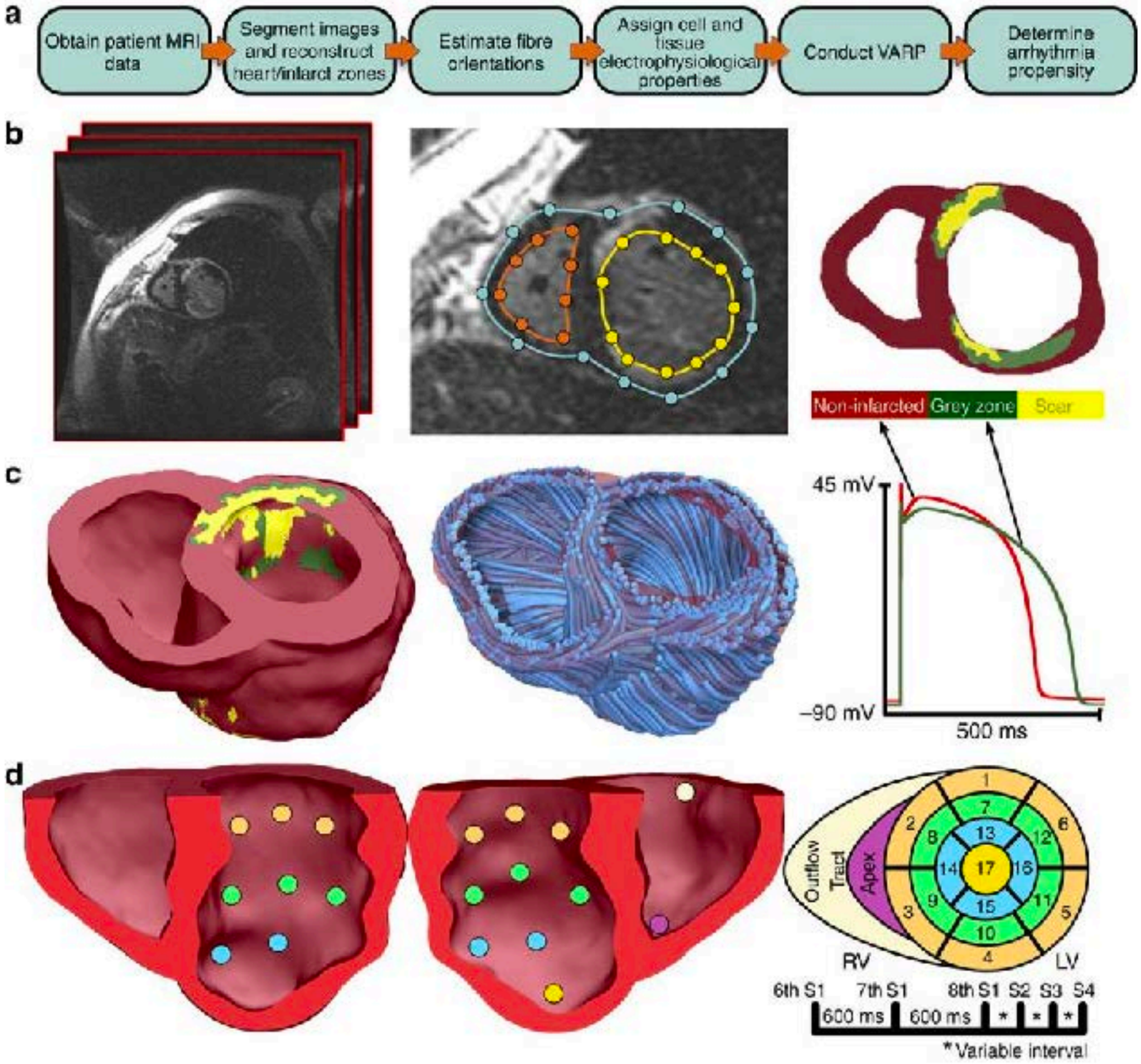
nature biomedical engineering

ARTICLES

https://doi.org/10.1038/s41551-018-0282-2

Personalized virtual-heart technology for guiding the ablation of infarct-related ventricular tachycardia

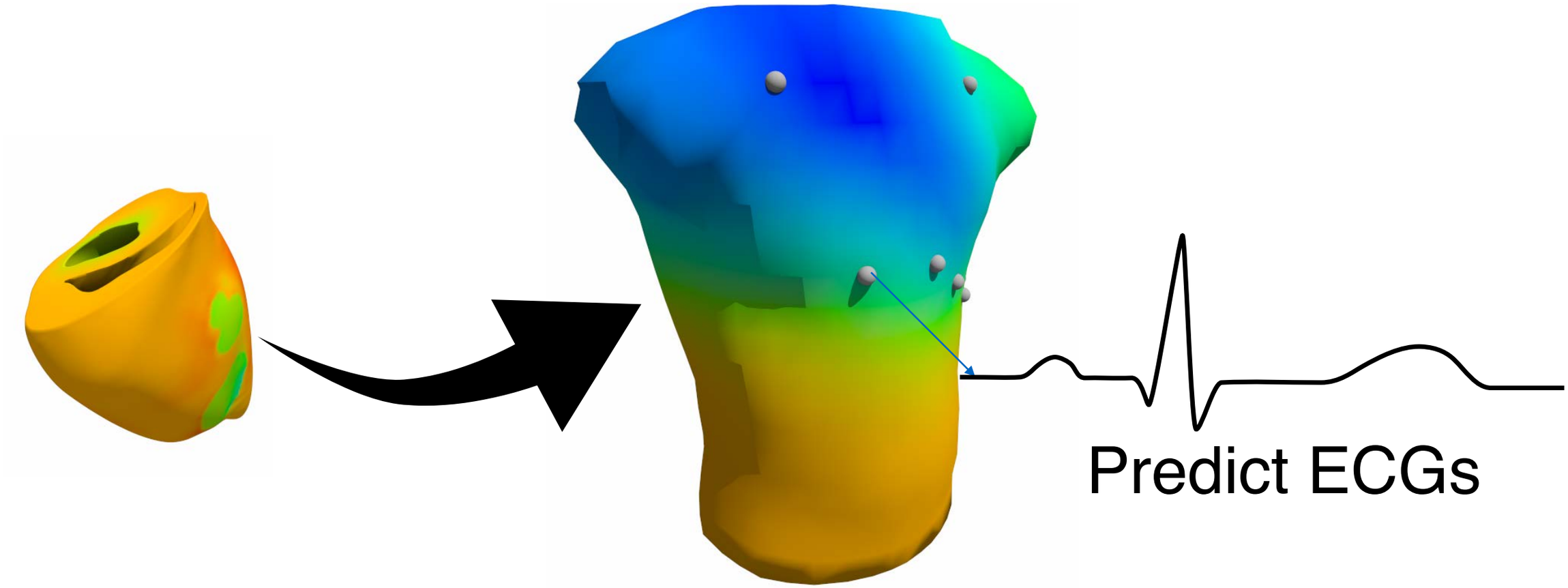
Adityo Prakosa[1,7], Hermenegild J. Arevalo[1,2,7], Dongdong Deng[1,7], Patrick M. Boyle[1], Plamen P. Nikolov[1], Hiroshi Ashikaga[3], Joshua J. E. Blauer[4], Elyar Ghafoori[4], Carolyn J. Park[1], Robert C. Blake III[1], Frederick T. Han[5], Rob S. MacLeod[4], Henry R. Halperin[3], David J. Callans[6], Ravi Ranjan[4], Jonathan Chrispin[3], Saman Nazarian[6] and Natalia A. Trayanova[1,3]*



Hermenegild, et al. *Nature Communications,* volume **7**, Article number: 11437 (2016)

Incomplete

ECG Forward Simulation



Heart Potentials

Torso Potentials

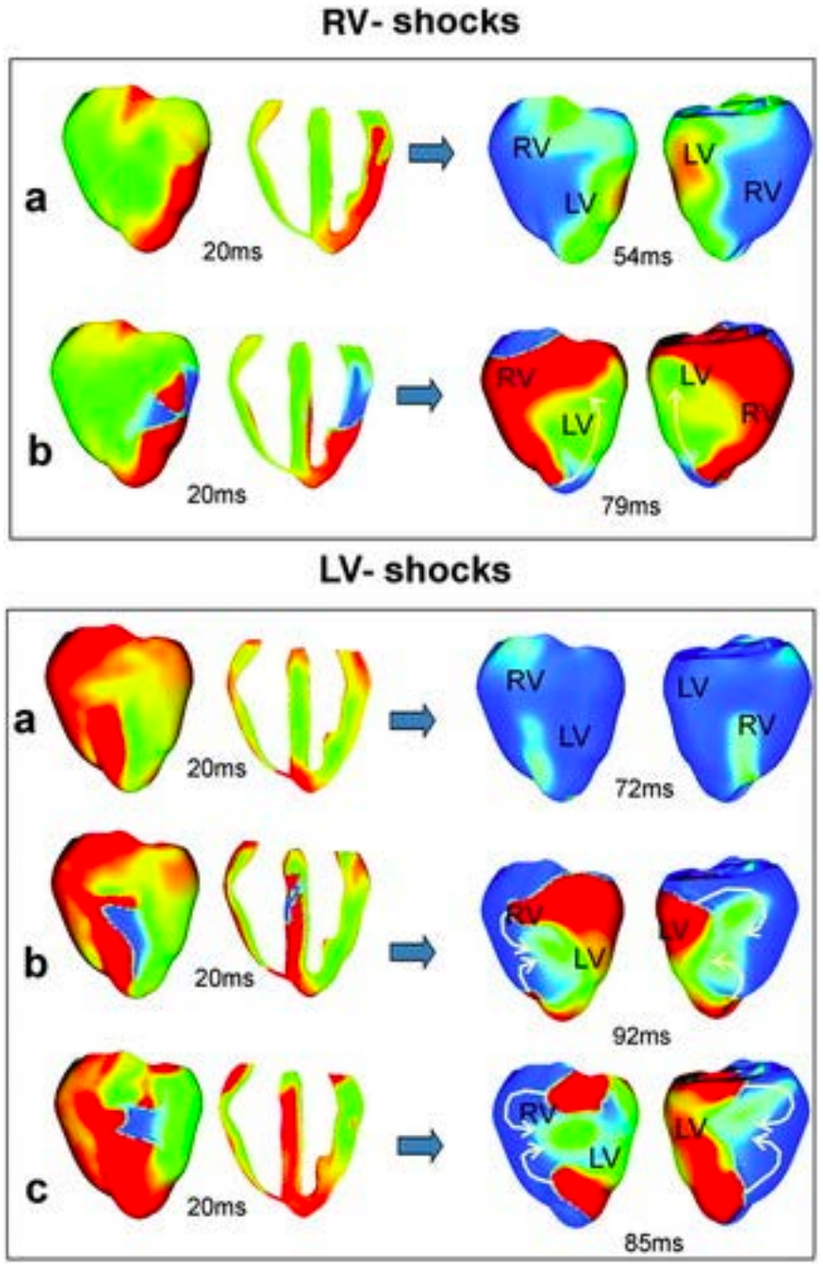
Defibrillation

http://www.defibrillatorinformation.com/

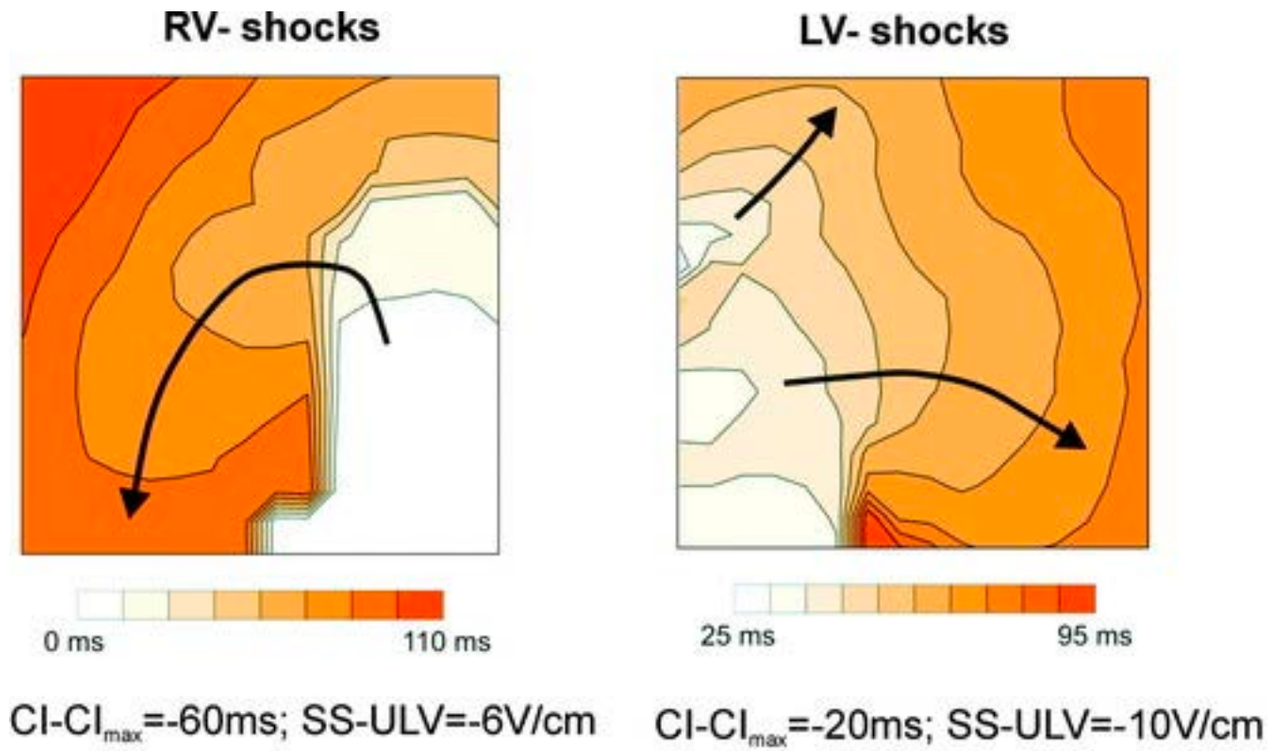
Mechanisms are not well know

Simulation has been key understanding

Defibrillation



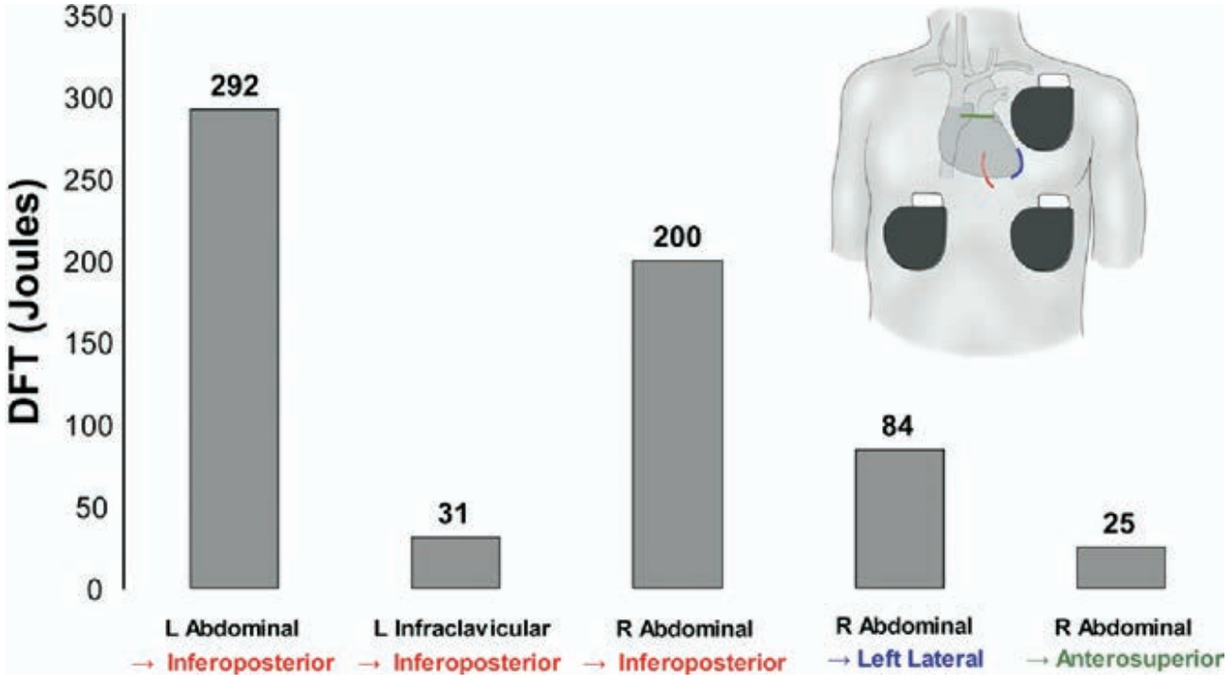
Rodriguez, etal., Circ Res. 2005 Jul 22; 97(2): 168–175.



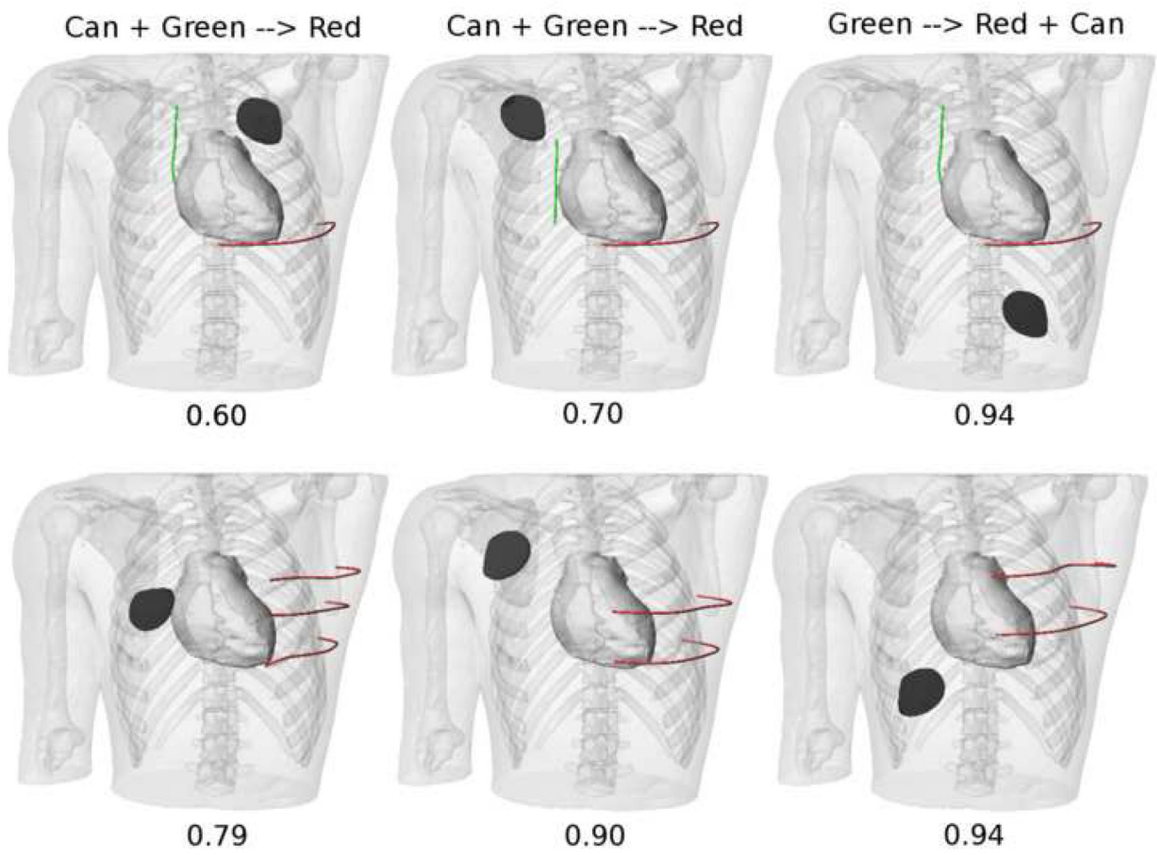
Rodriguez, etal., Circ Res. 2005 Jul 22; 97(2): 168–175.

Simulation with experiments

Defibrillation



Jolley, et al. Heart Rhythm 2008;5:565–572



Jolley, et al. Heart Rhythm. 2010 May ; 7(5): 692–698

Still a Lack of Validation

Validation

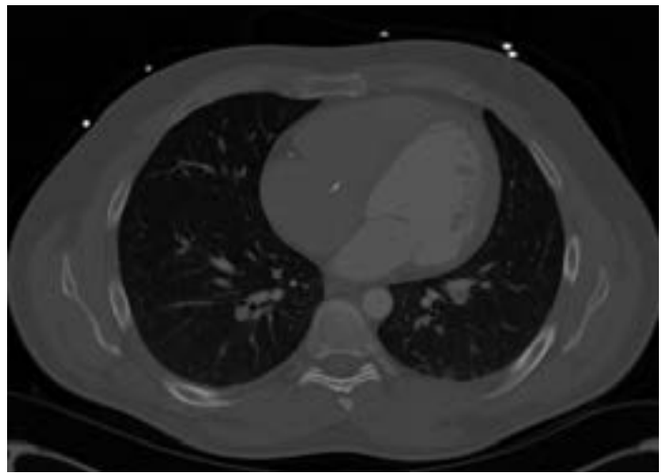
Why is Validation Missing?

https://www.timeslifestyle.net/20180318/where-is-your-heart-located/

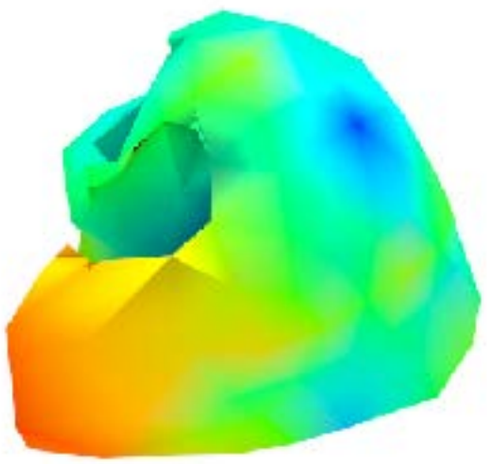
http://www.defibrillatorinformation.com/

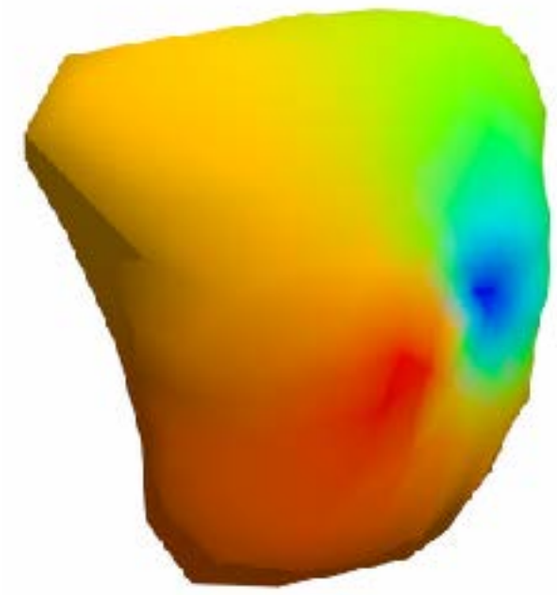
Challenges of Validation

Bear, etal., Circ A & E.2015;8:677-684.



Source → System Parameters → Response

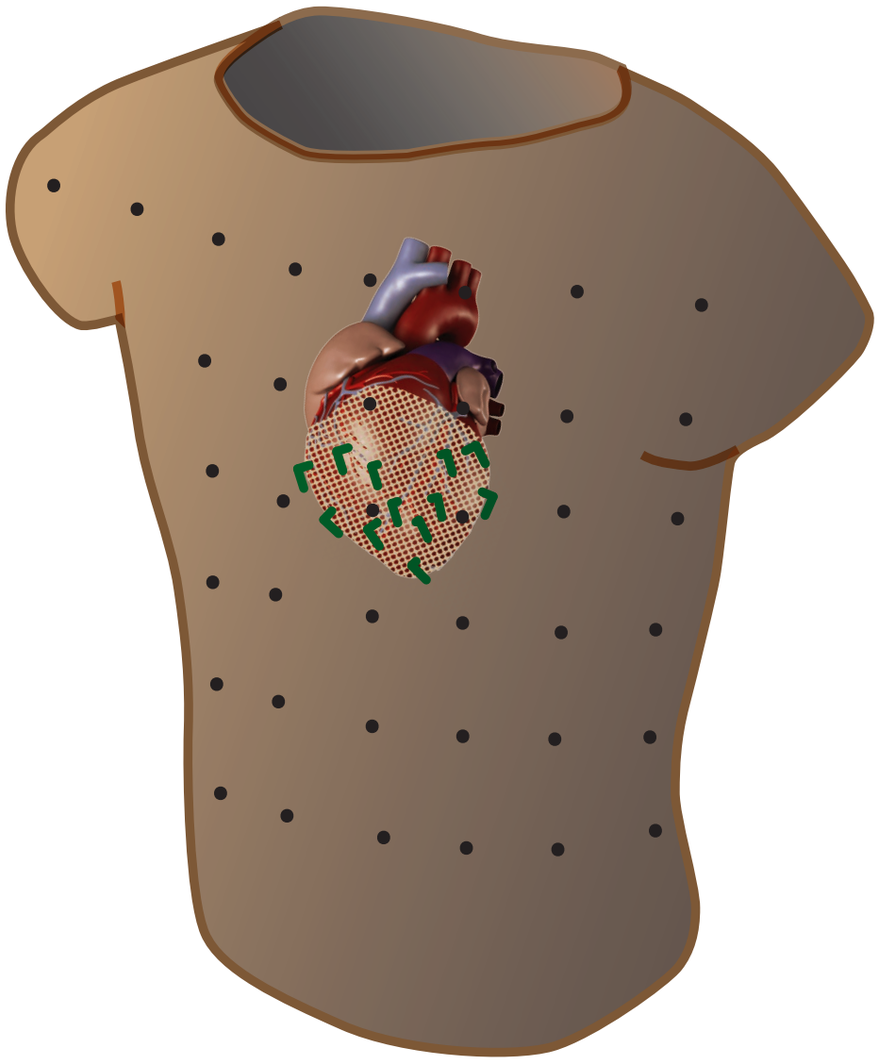




What Makes Validation Hard

https://www.army.mil/article/202490/
advancements_in_technology_change_the_way_health_care_is_delivered_at_the_tamc_cath_lab

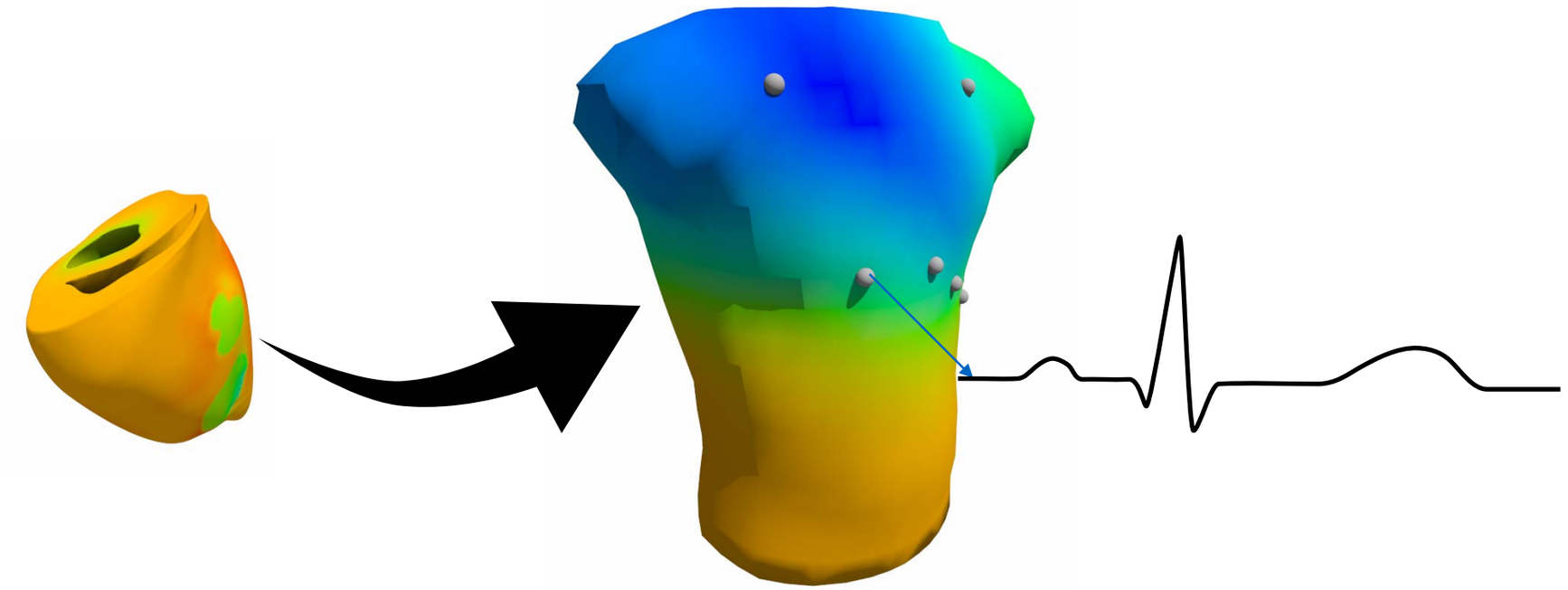
Access



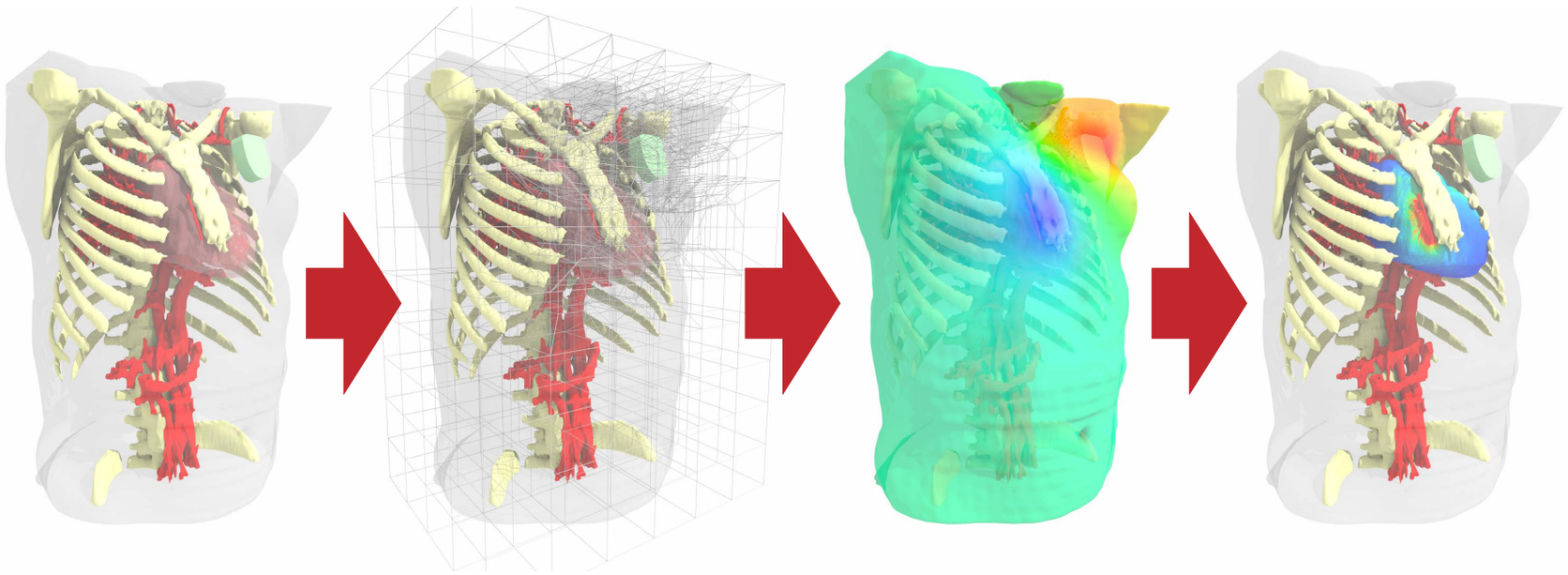
Experimental Complexity

Goal: Validate Two Pipelines

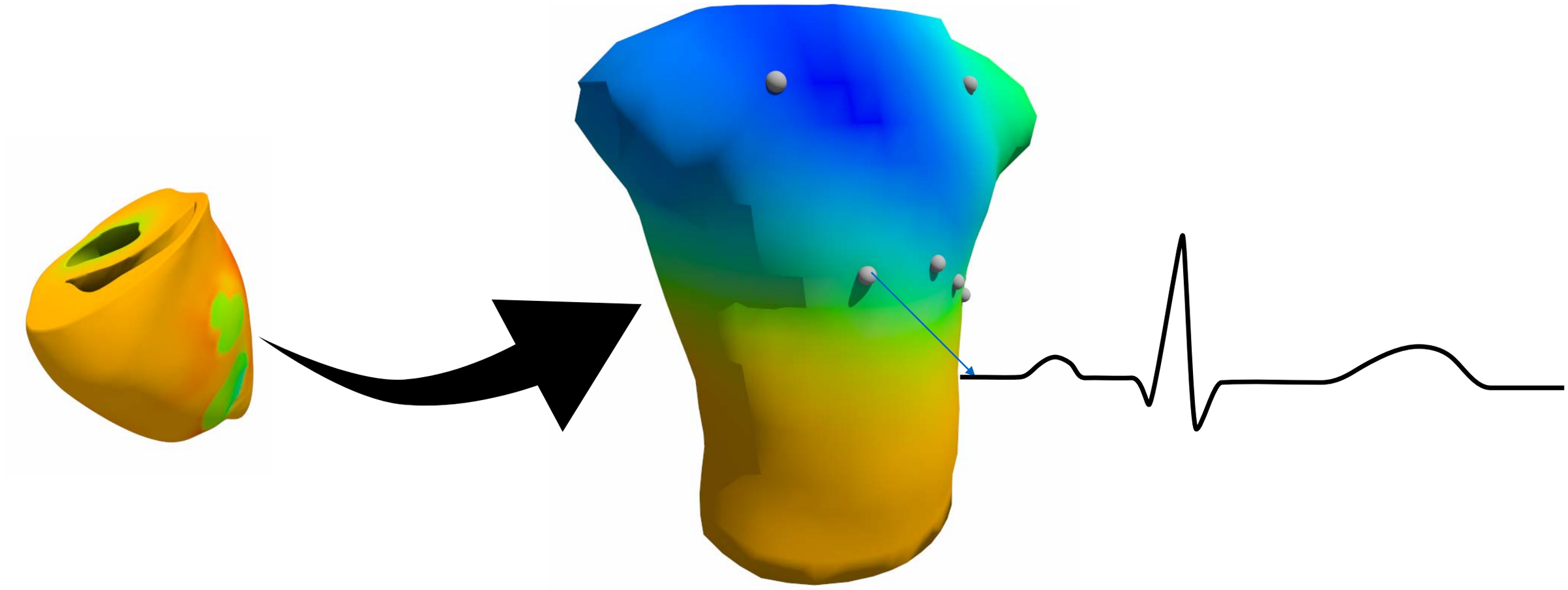
ECG Forward Simulation



Defibrillation Simulation

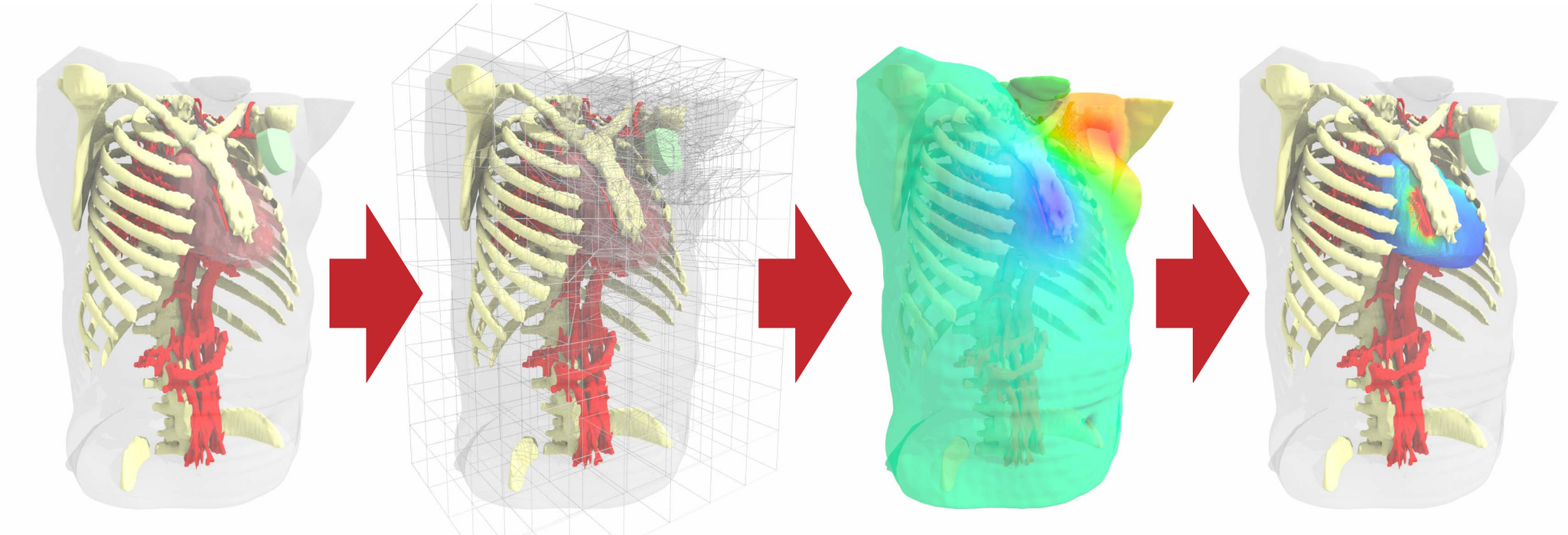


Specific Aims



1. Evaluate the effect of missing sources sampling on the ECG forward simulation

Specific Aims

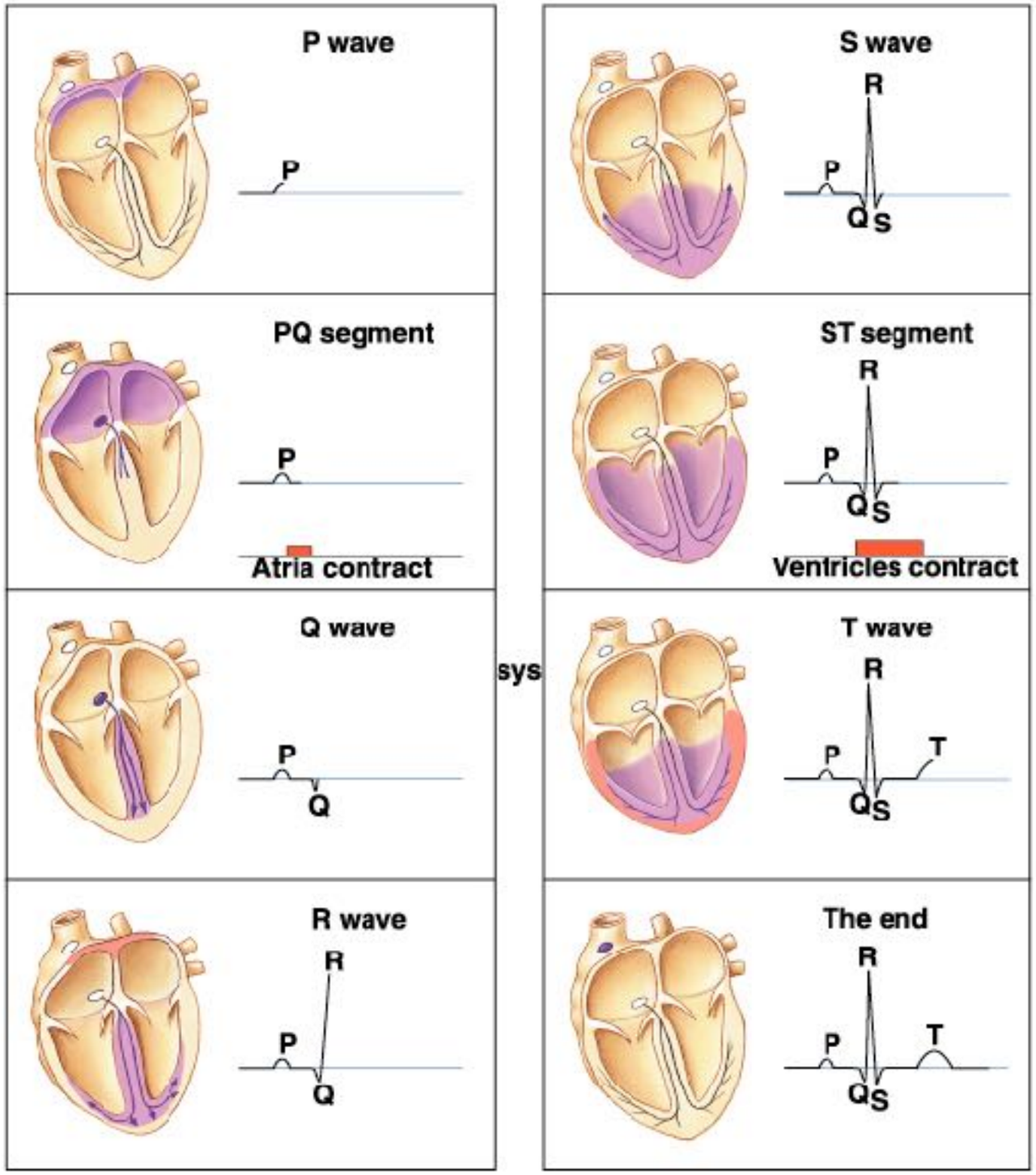


2. Record potentials in a torso-tank preparation to validate the simulation pipeline

3. Record body-surface potentials on patients to validate the simulation pipeline

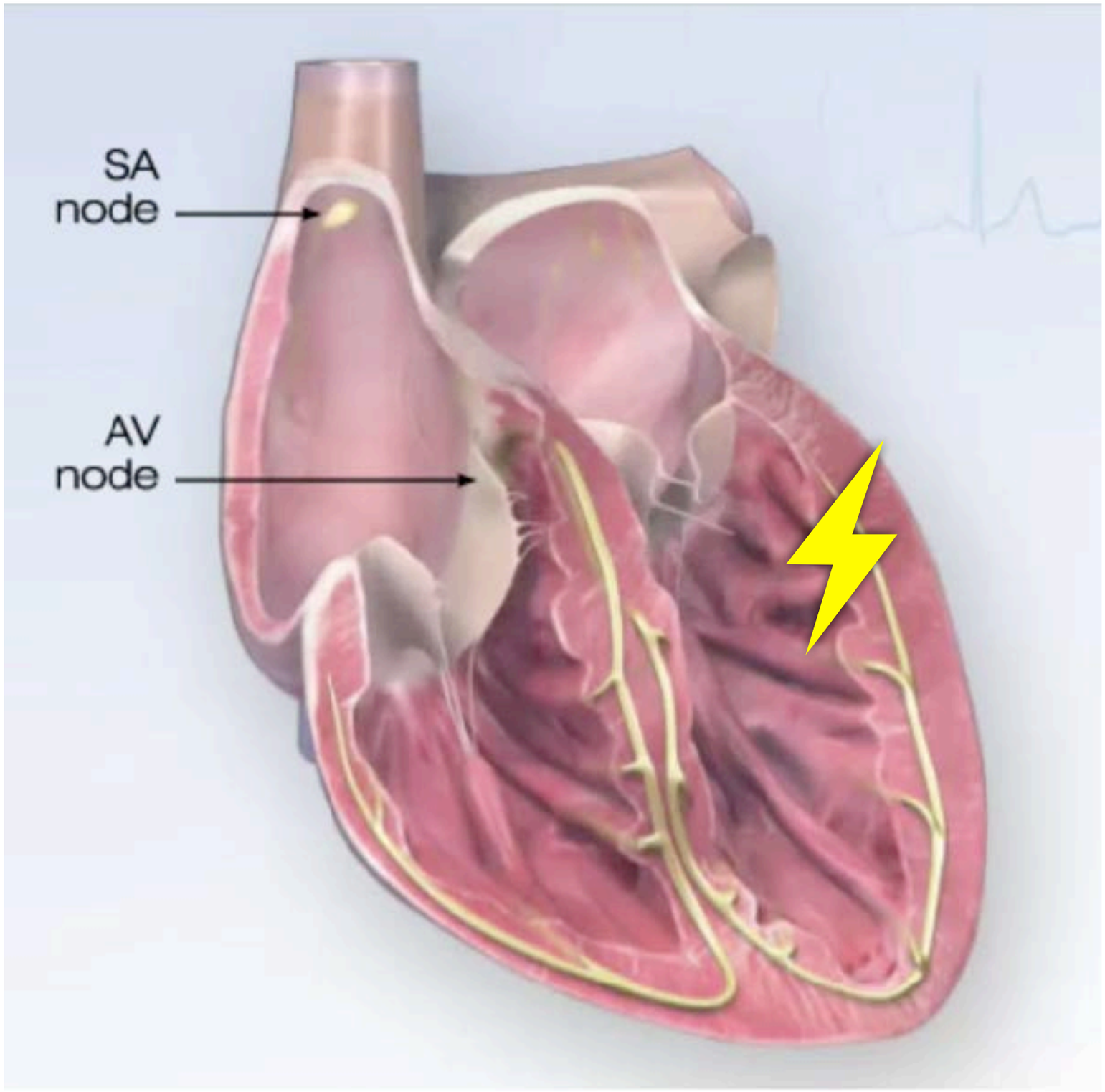
Tools for Clinicians

Cardiac Activity

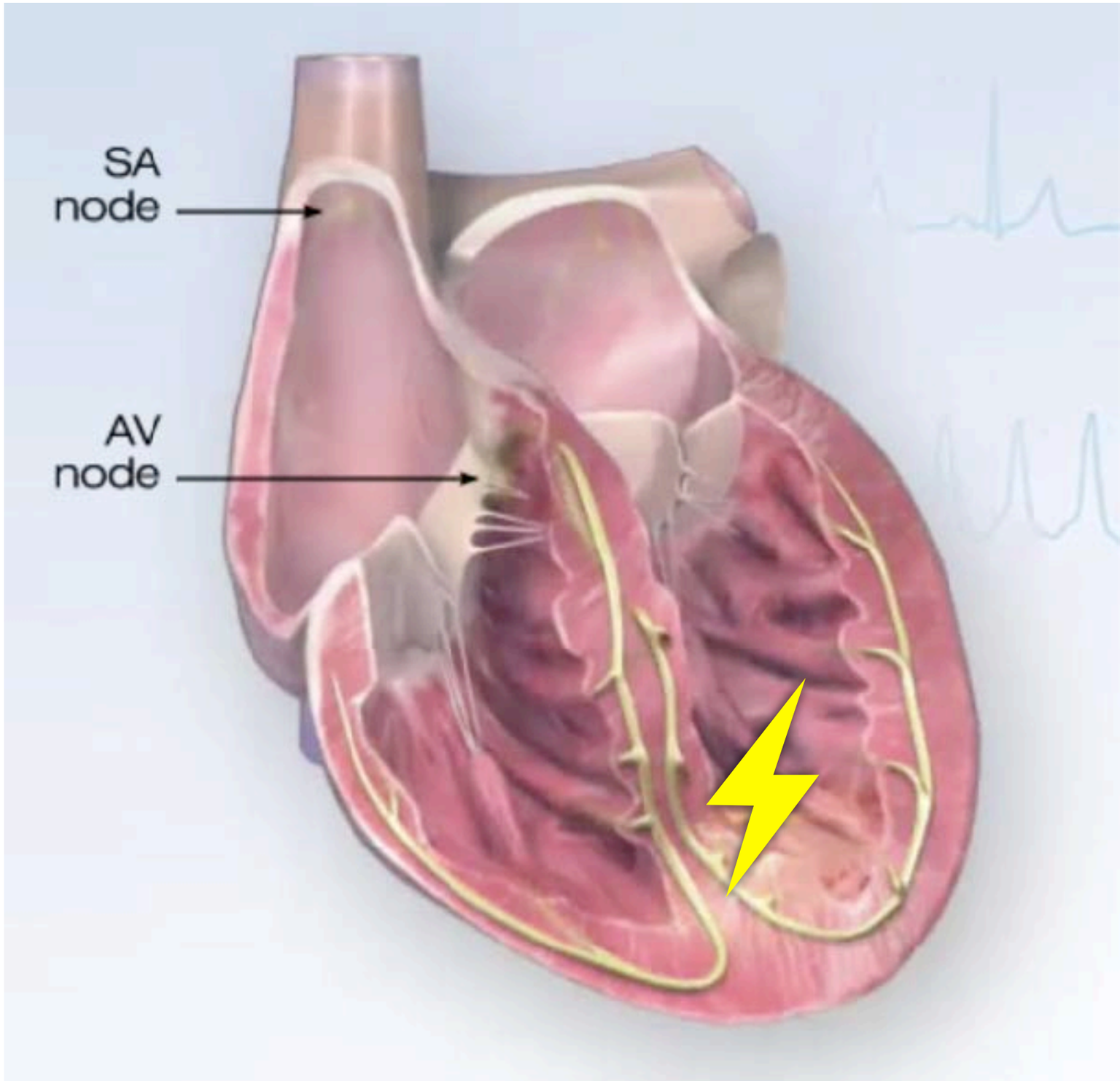


sys

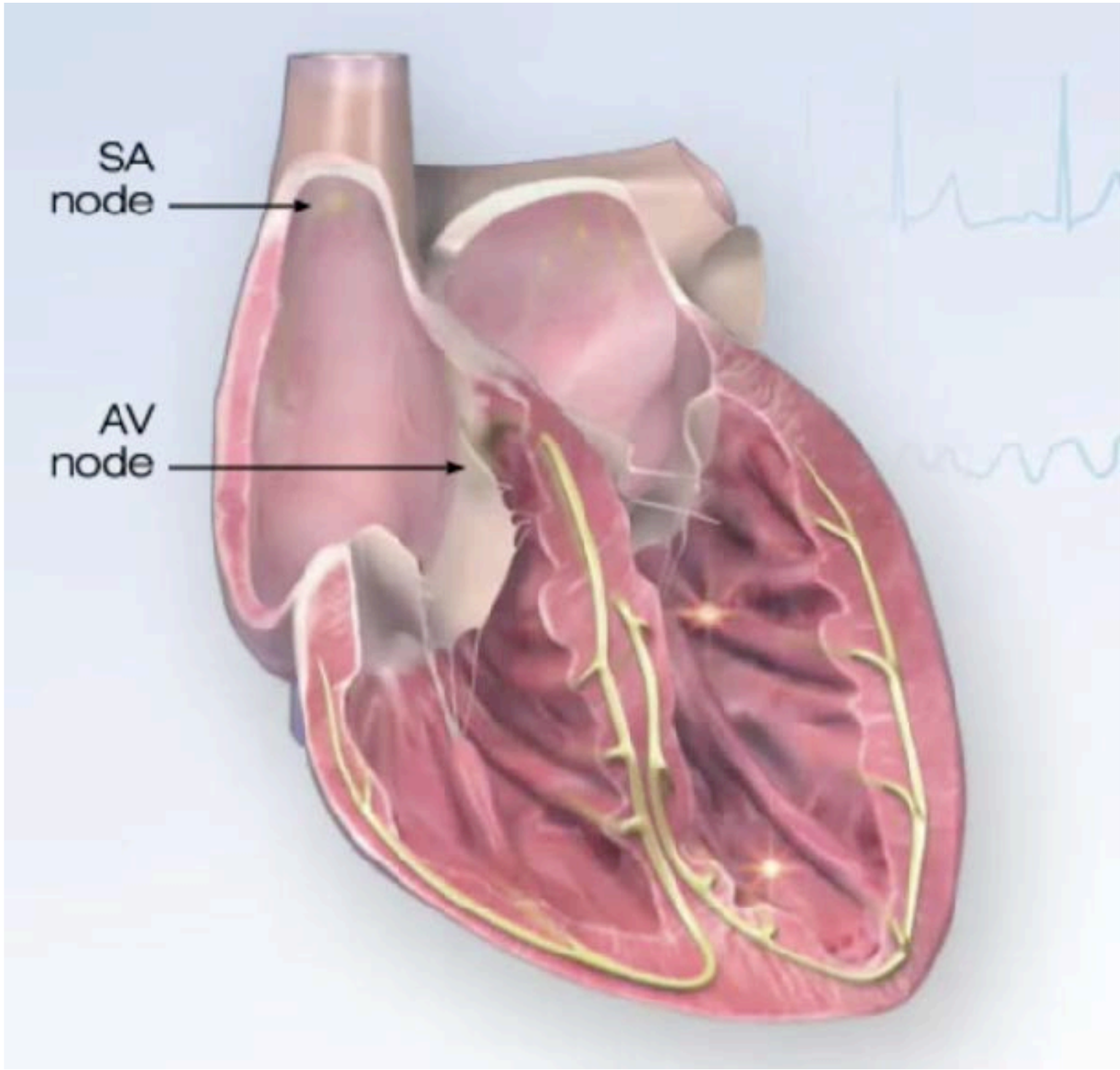
Cardiac Activity



Ventricular Tachycardia



Ventricular Fibrillation

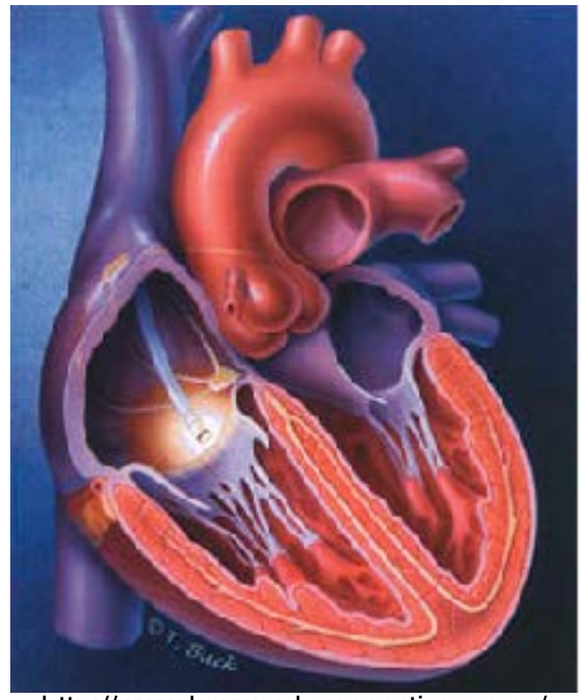


Arrhythmia Treatments

Anti-Arrhythmic Drugs

http://mvpresource.com

Ablation Procedures

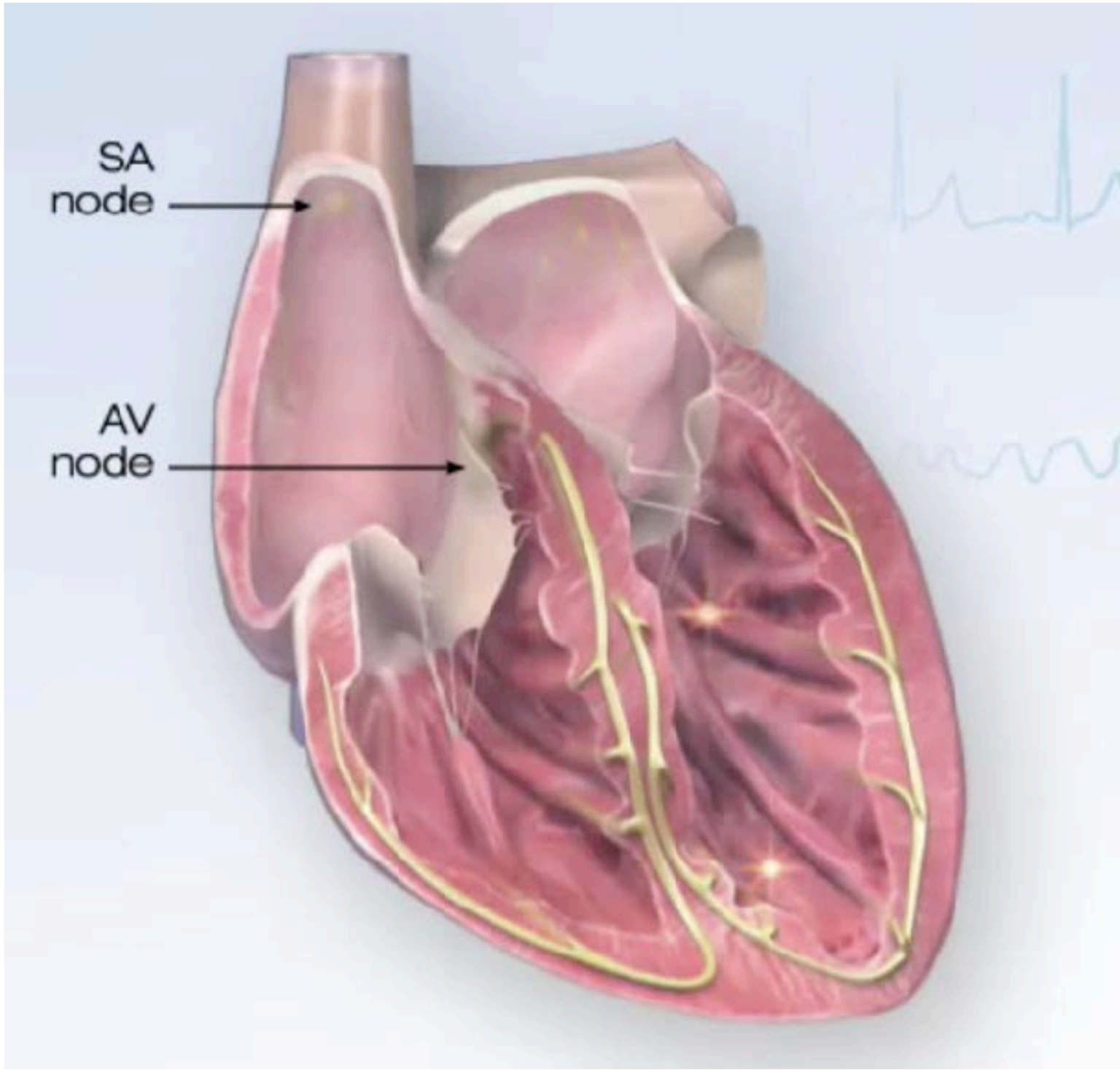


http://www.keyword-suggestions.com/

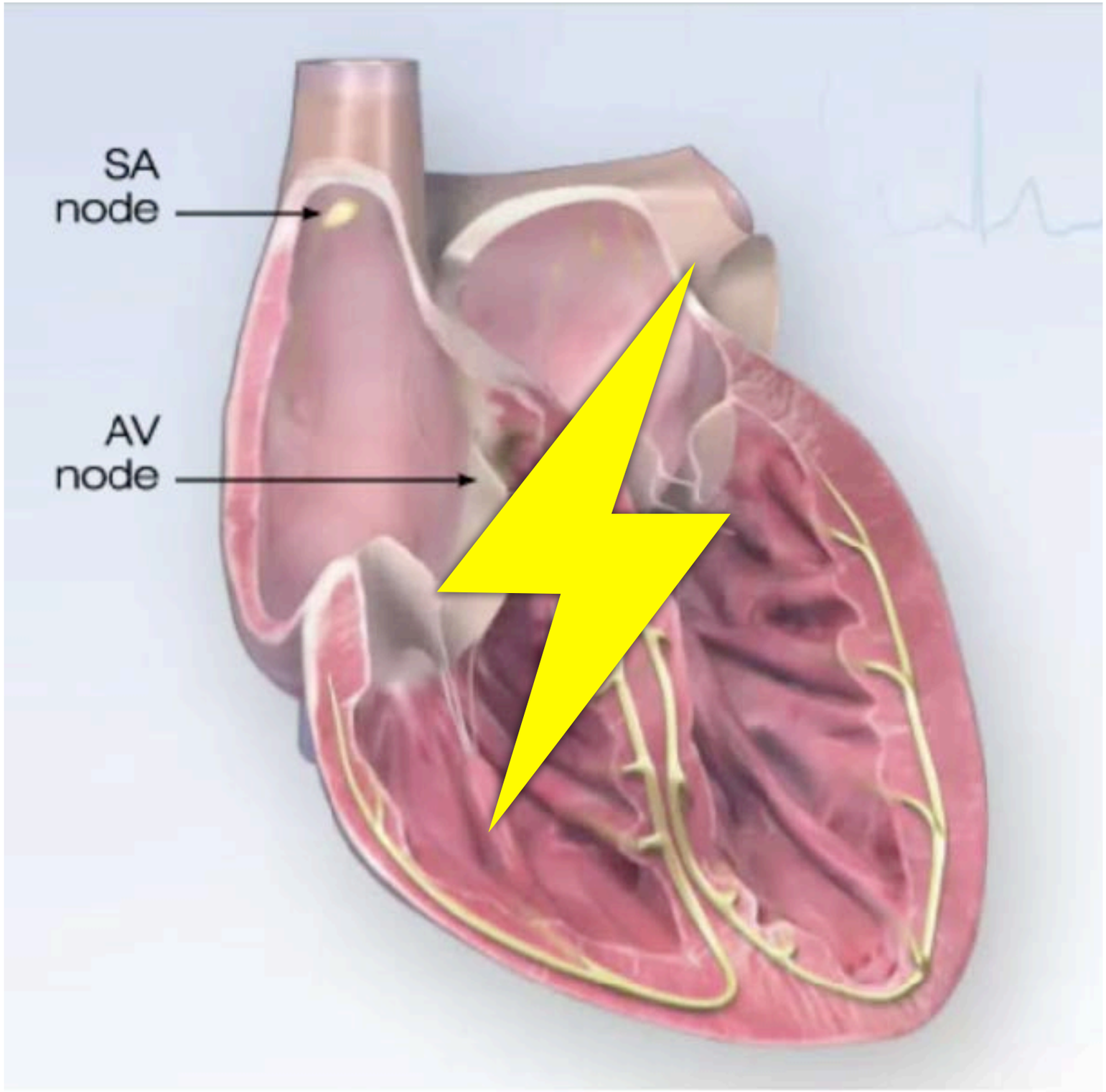
Defibrillation

http://www.defibrillatorinformation.com/

Ventricular Fibrillation



Cardiac Activity



Defibrillation

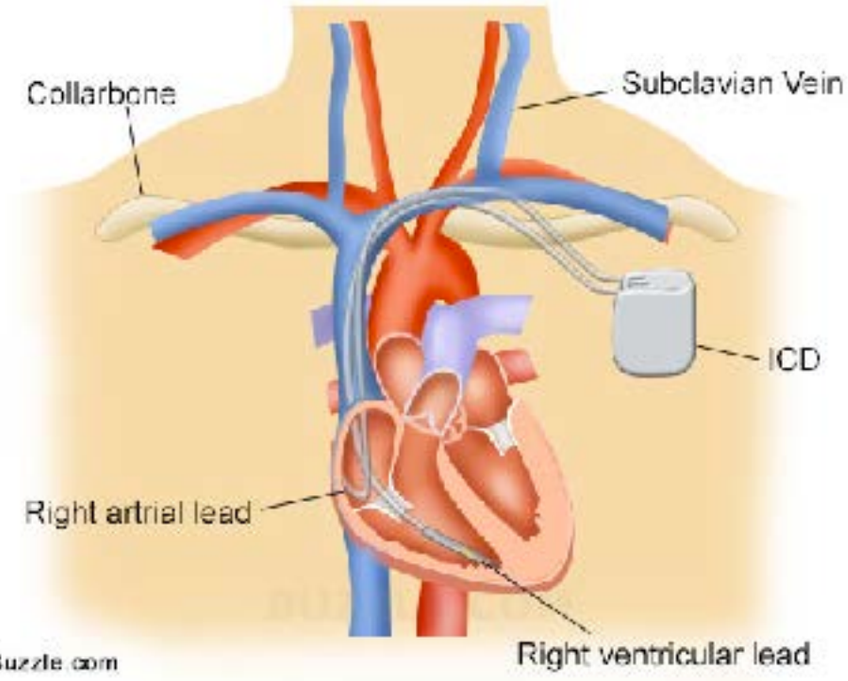
Automatic External Defibrillator- AED

http://www.wtamu.edu/

Wearable Cardioverter Defibrillator- WCD

http://www.fda.gov/

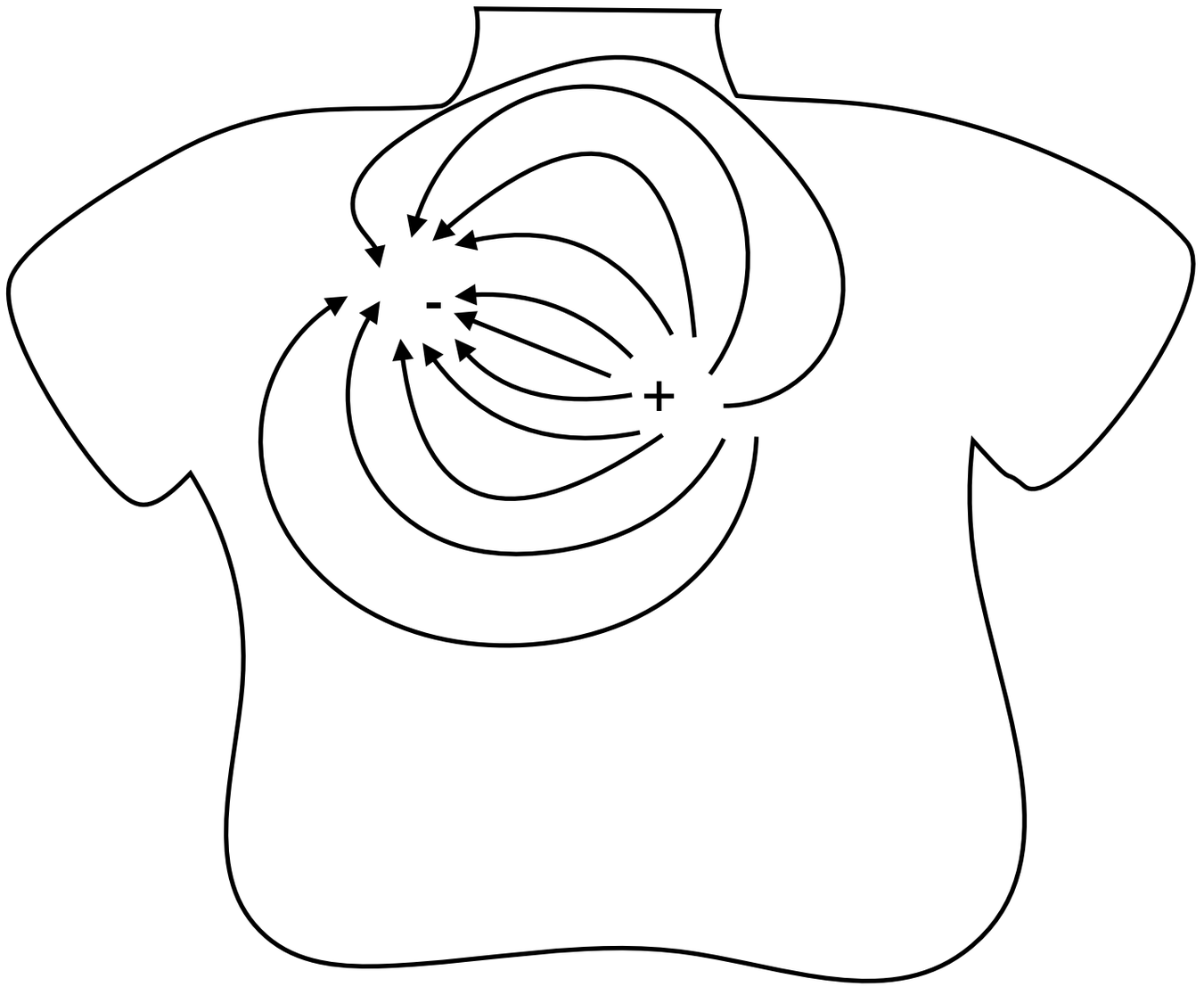
Implantable Cardioverter Defibrillator- ICD



http://www.buzzle.com/

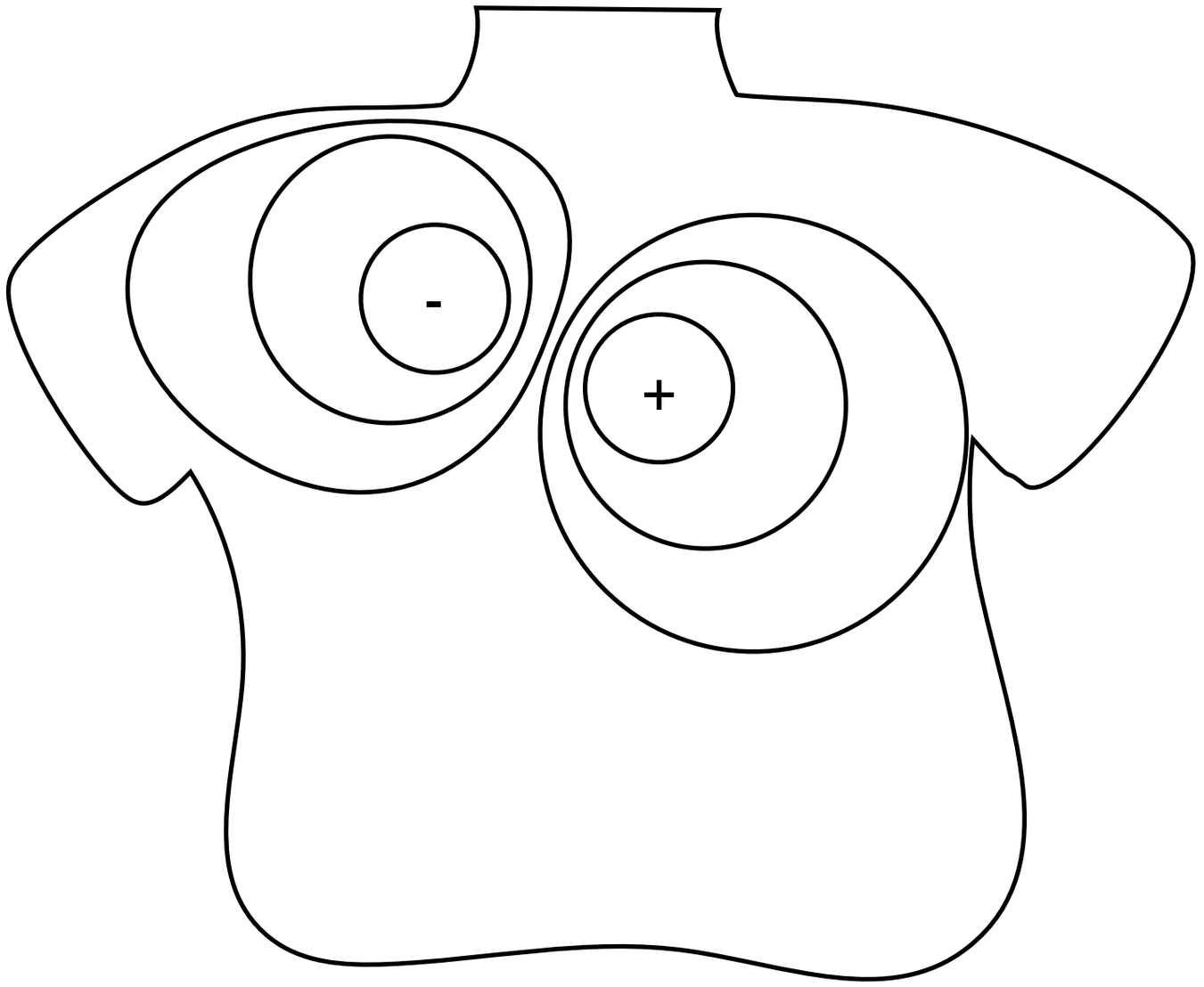
Defibrillation Threshold (DFT): Lowest Energy Needed for Effective Defibrillation

Bioelectric Fields



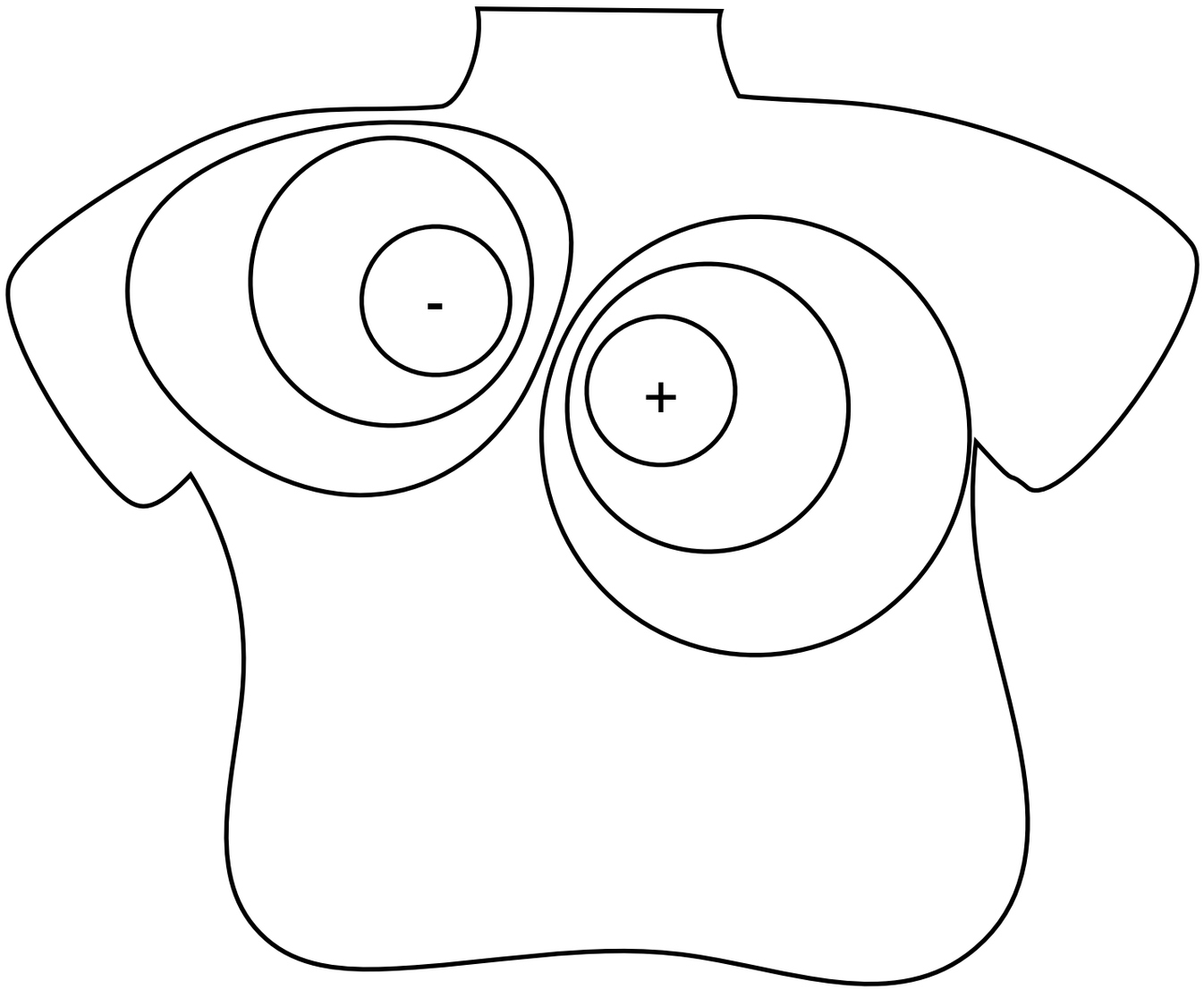
Stem from currents generated within the torso

Bioelectric Fields



Potential Fields

Potential Fields



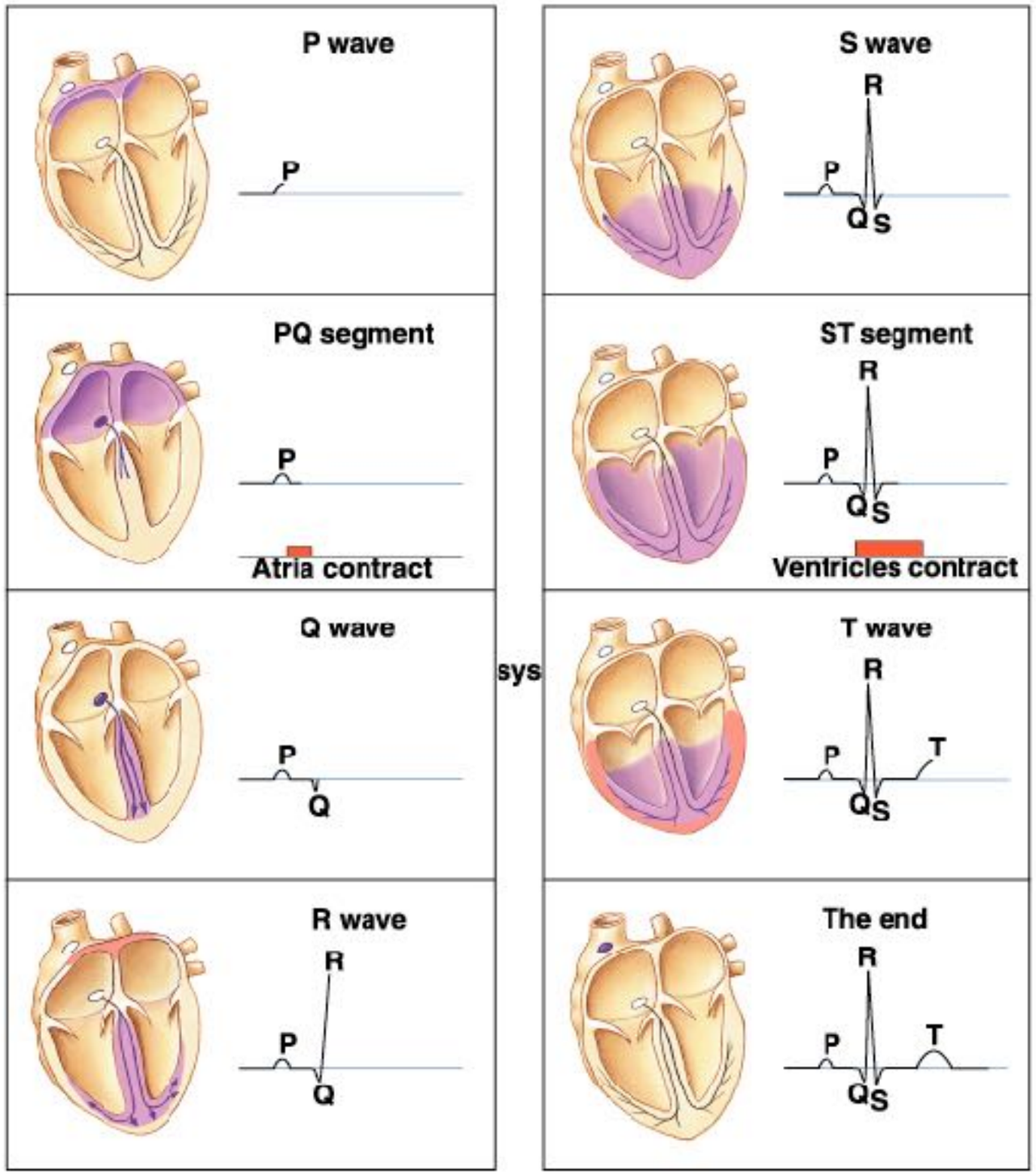
Dissipate with Distance

Superimpose

Intrinsic or Extrinsic

Heterogeneous Conduction

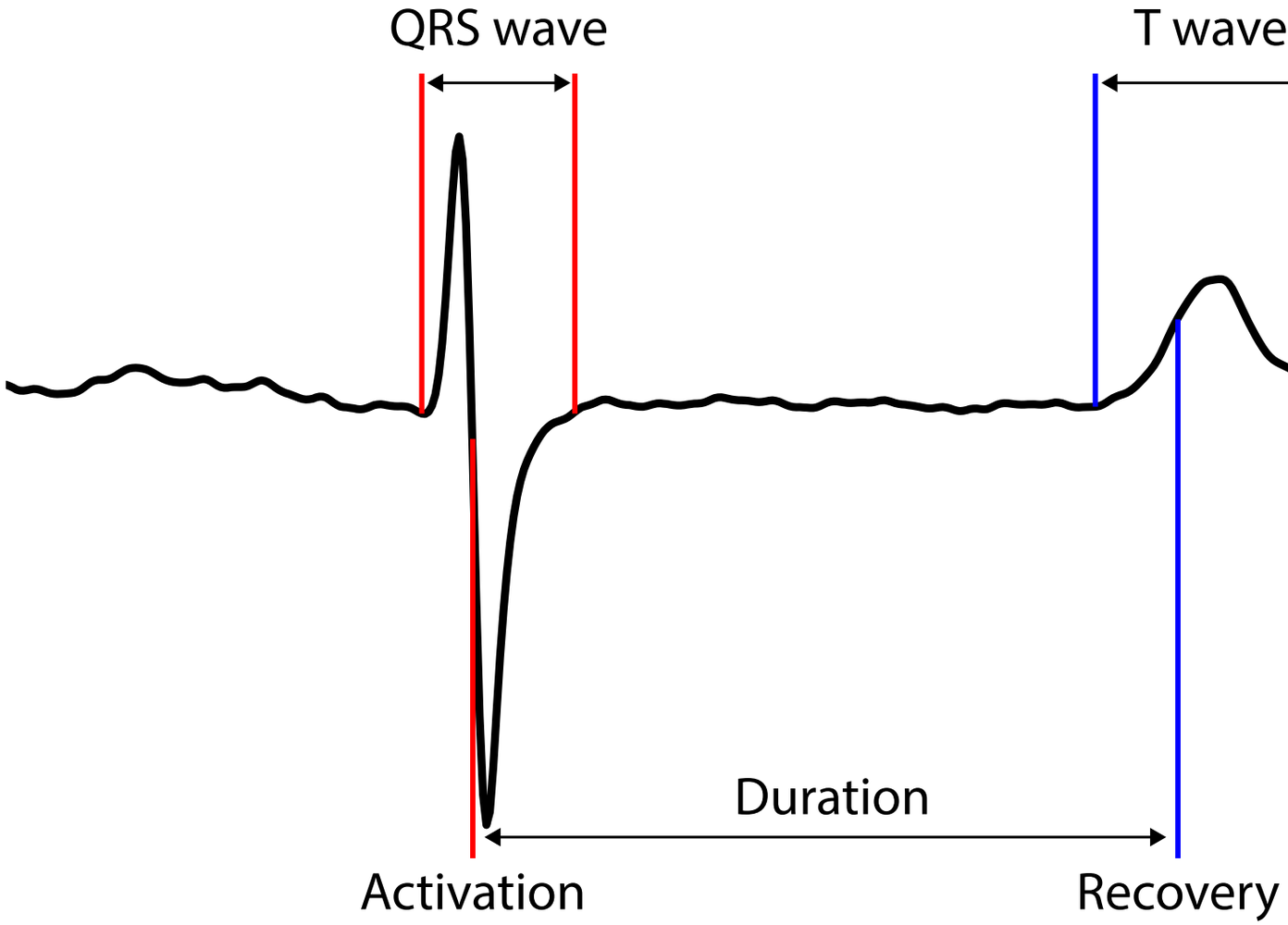
Cardiac Sources

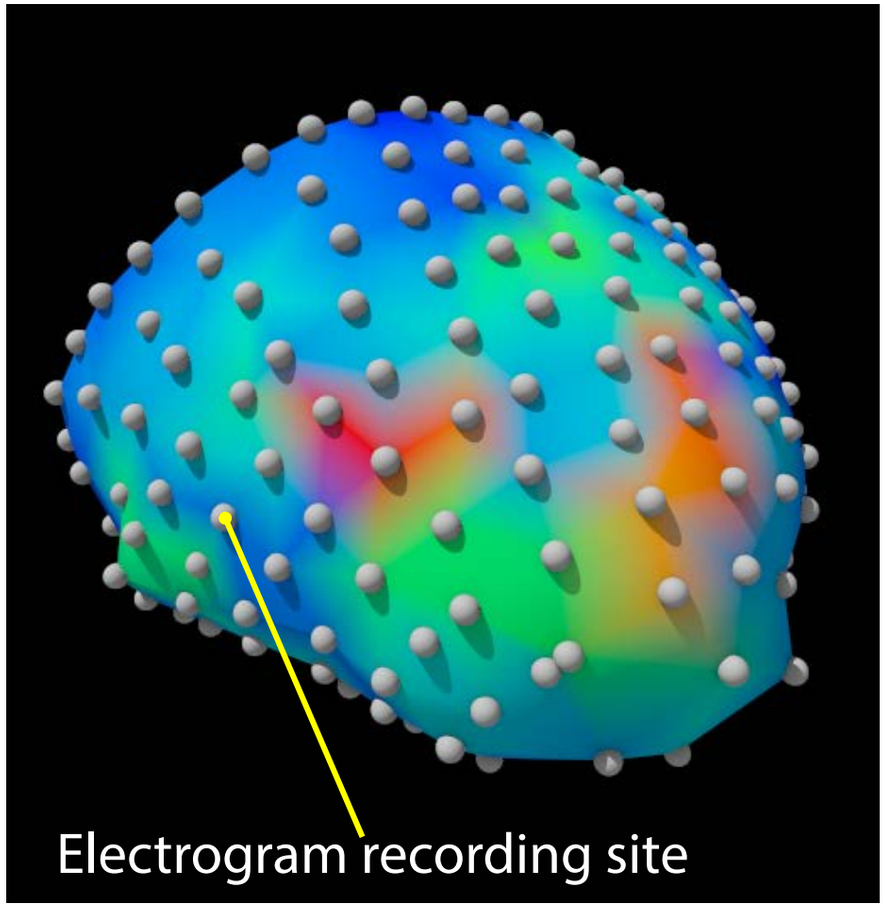


Time Varying

Spatially Varying

Electrogram



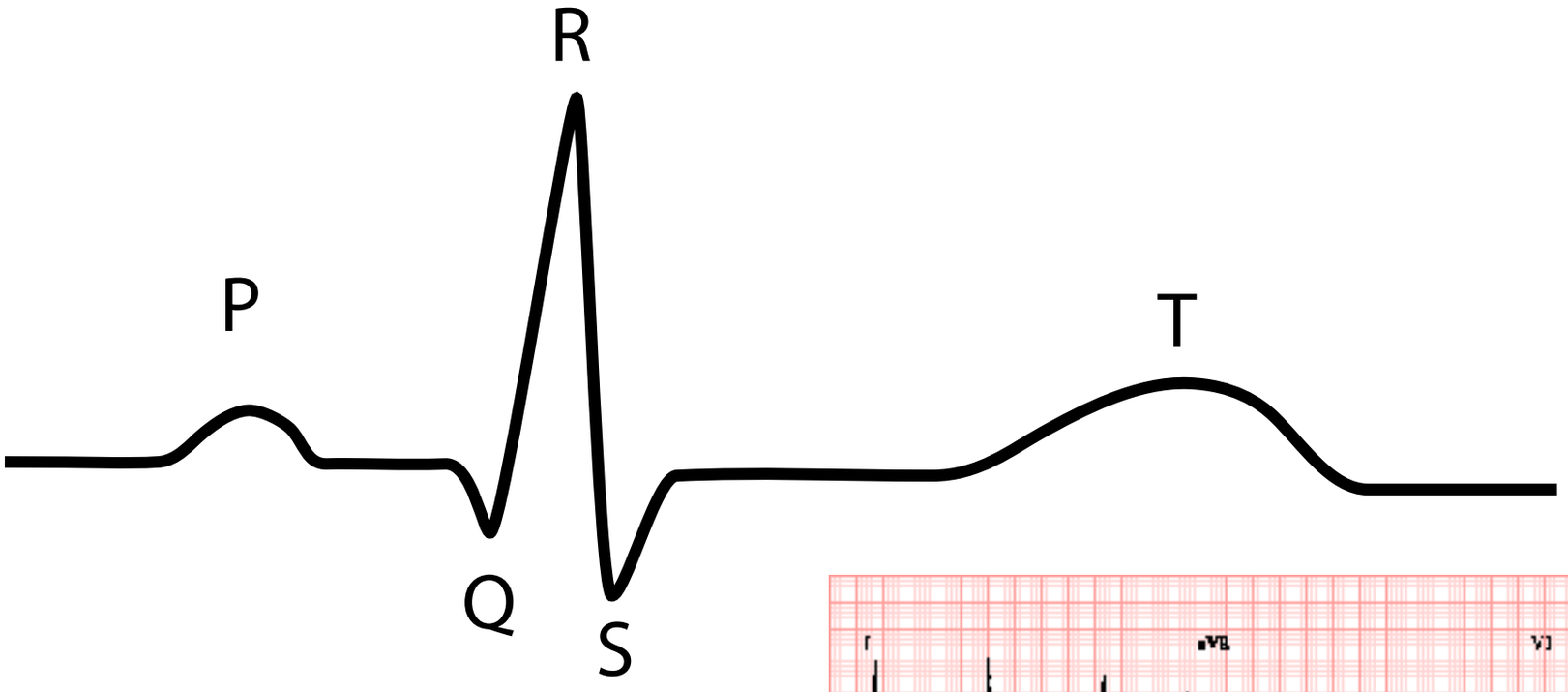


Electrogram

Acvation Map

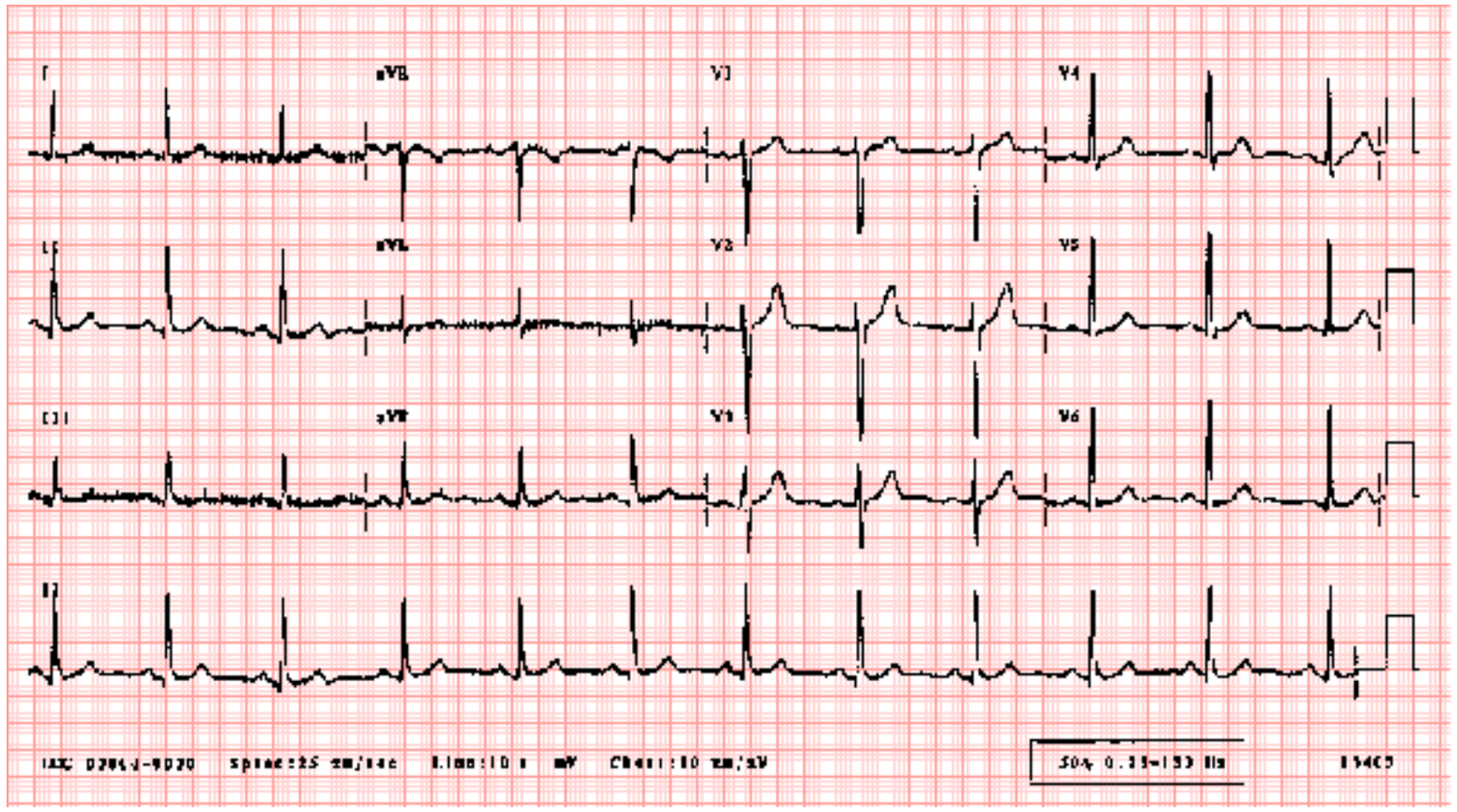
Locally Sensitive Invasive

Electrocardiogram (ECG)

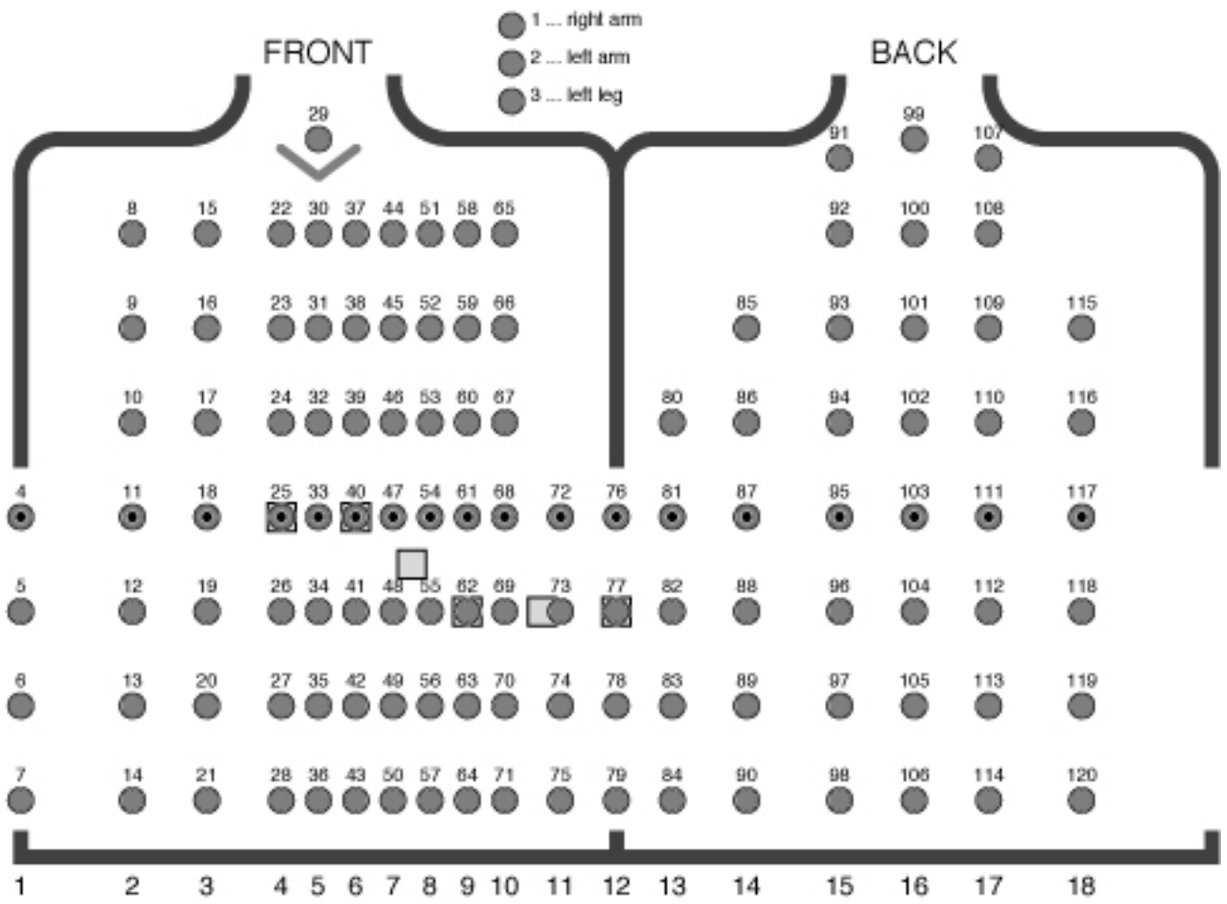


Globally Sensitive

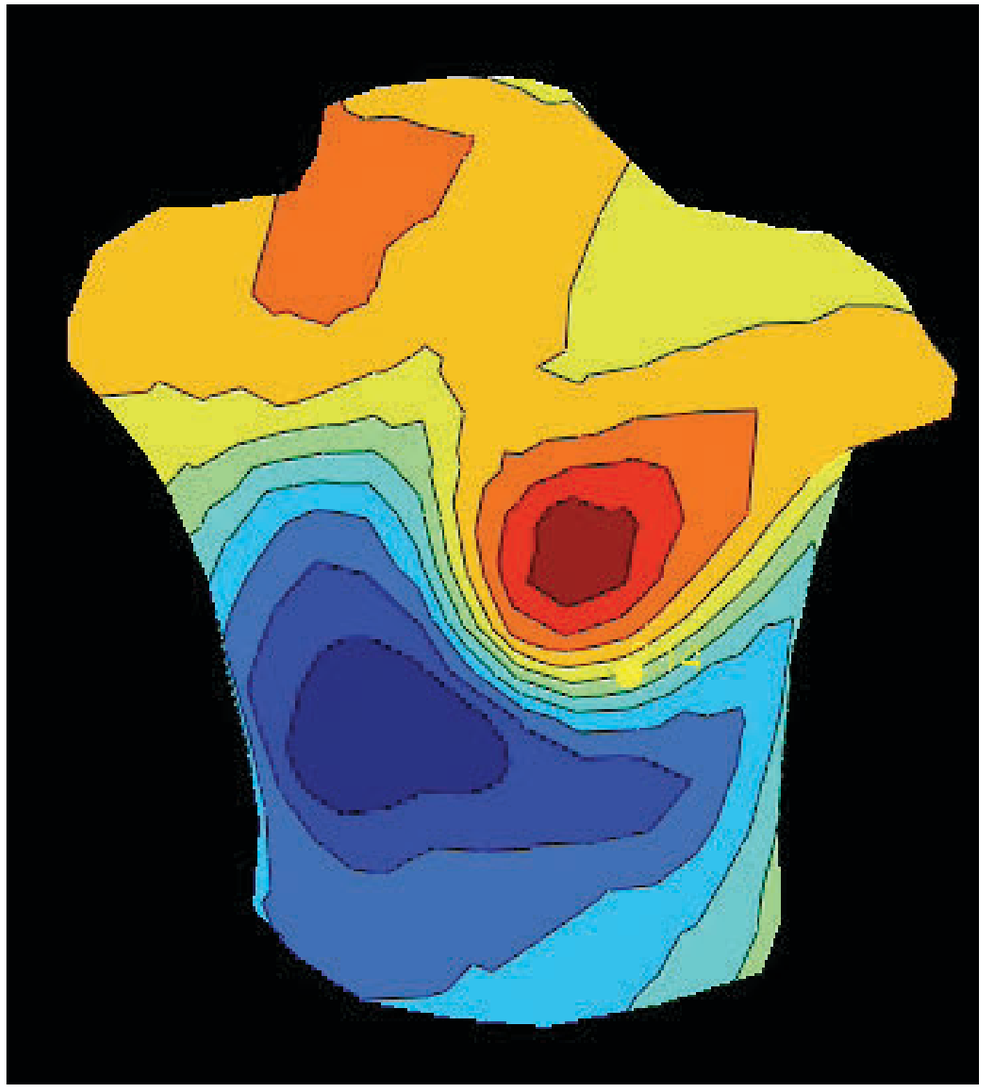
Little Spatial Information



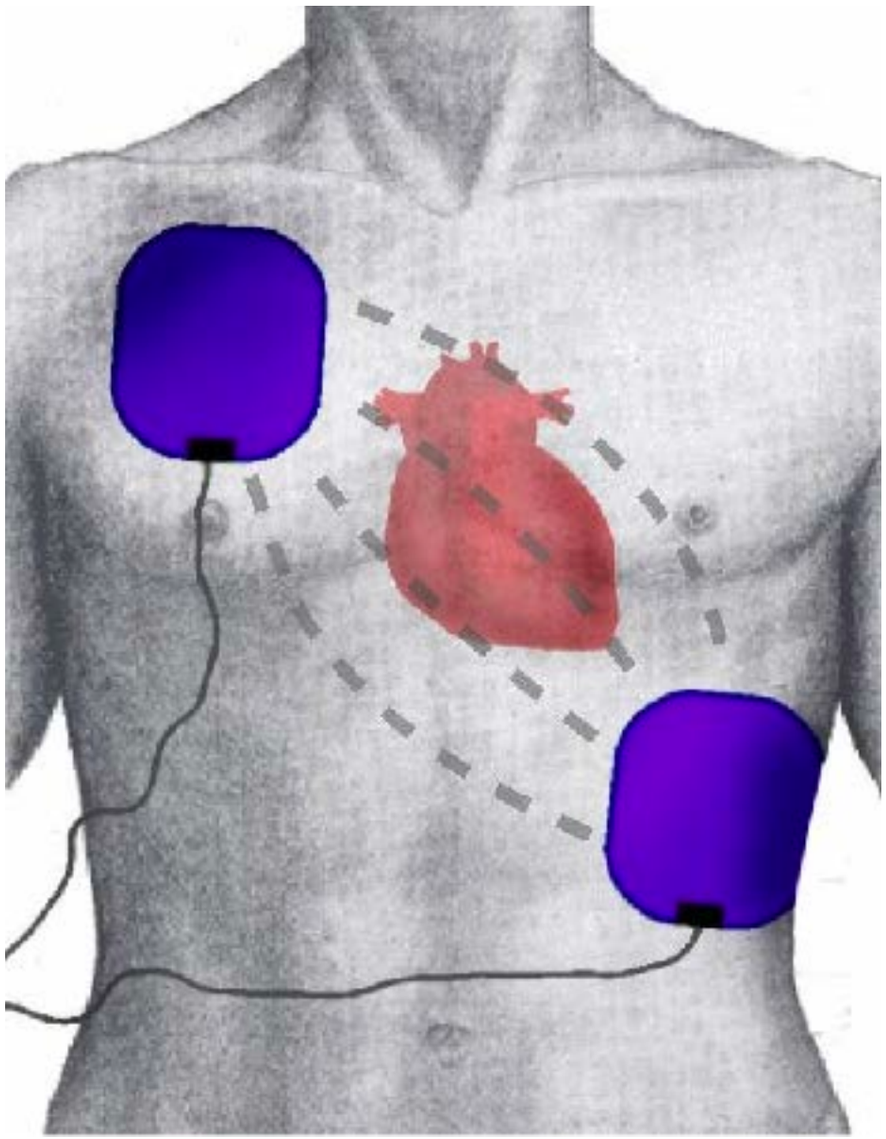
Body-Surface Potential Mapping (BSPM)



BSPM Electrode Placement

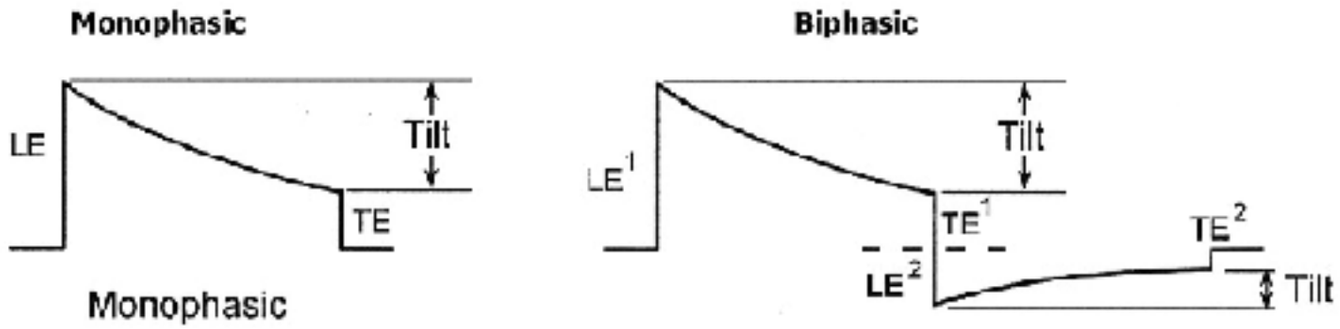


Defibrillator Source



https://en.wikipedia.org/wiki/Defibrillation

Waveform



http://www.cardiocases.com/en/pacingdefibrillation/specificities/icd-therapy/medtronic/medtronic-therapies

Mathematical Description

$$\nabla \cdot \sigma \nabla \phi = I \qquad\qquad \nabla \cdot \sigma \nabla \phi = 0$$

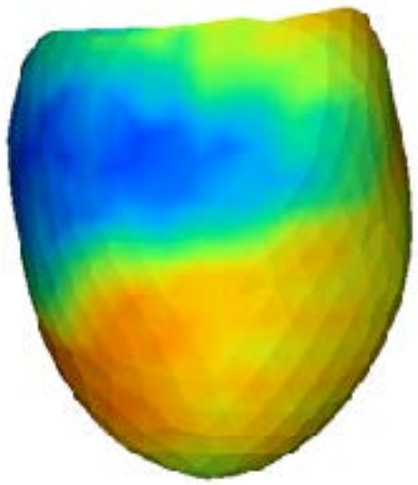
$$\phi(x_h) = \phi_h$$

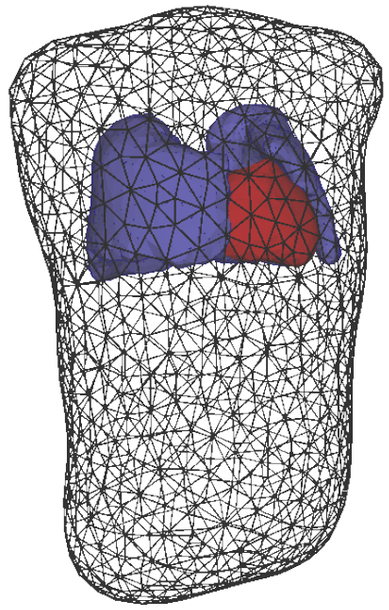
$$\frac{\partial \phi(x_t)}{\partial \hat{n}} = 0$$

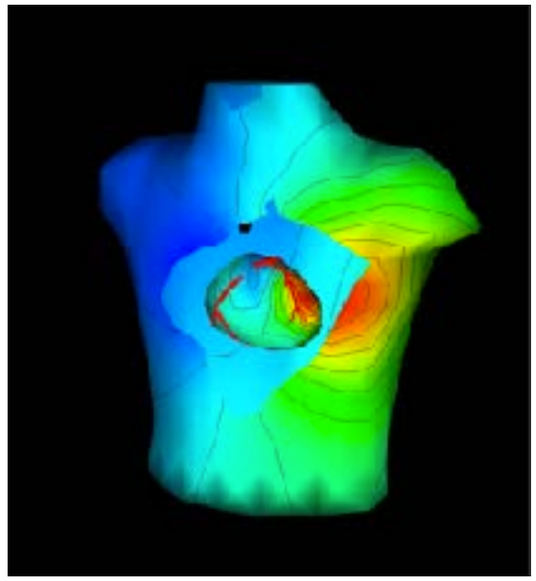
Finite Element Method (FEM)

Boundary Element Method (BEM)

Modeling Bioelectric Fields







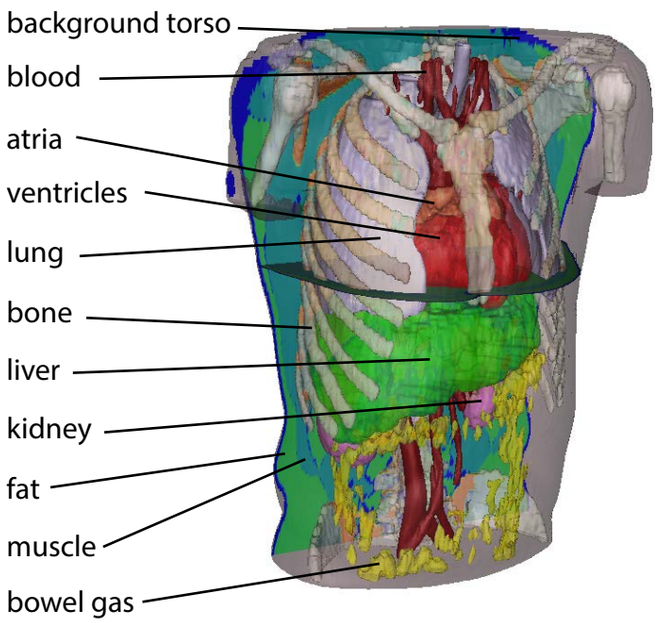
Sources

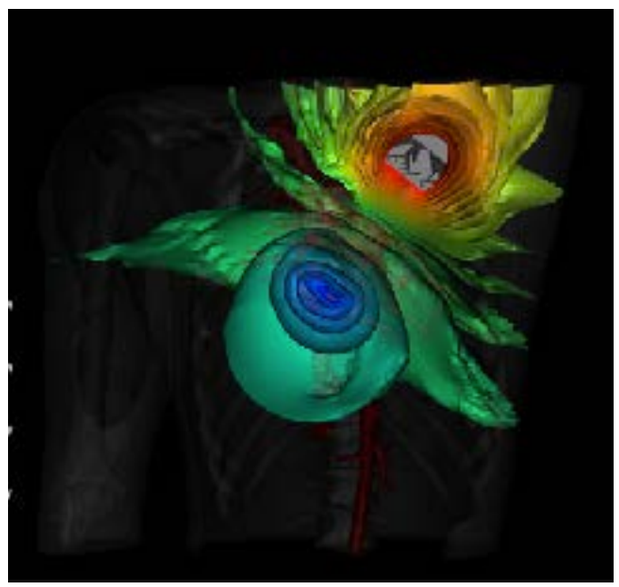
Segmentation
Meshing

Geometric Domain

FEM
BEM

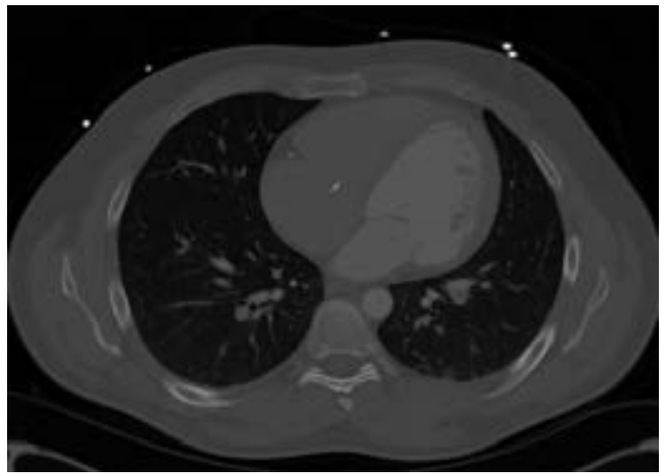
Computed Potentials



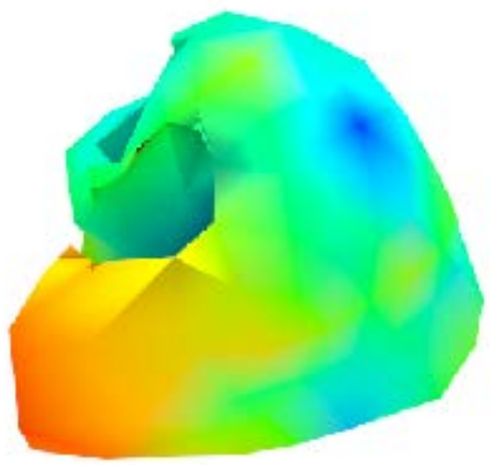


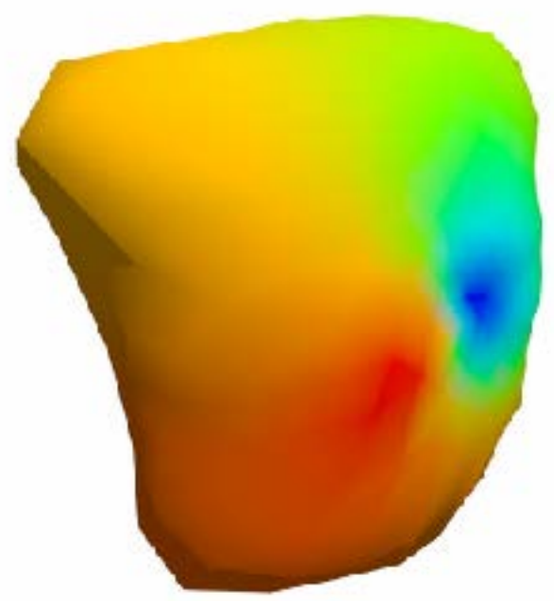
Validation

Bear, etal., Circ A & E.2015;8:677-684.



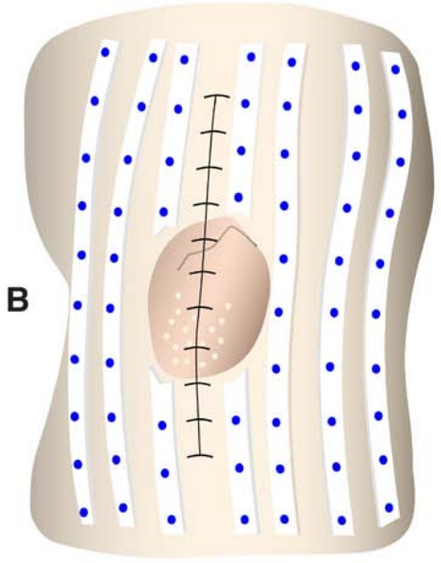
Source → System Parameters → Response



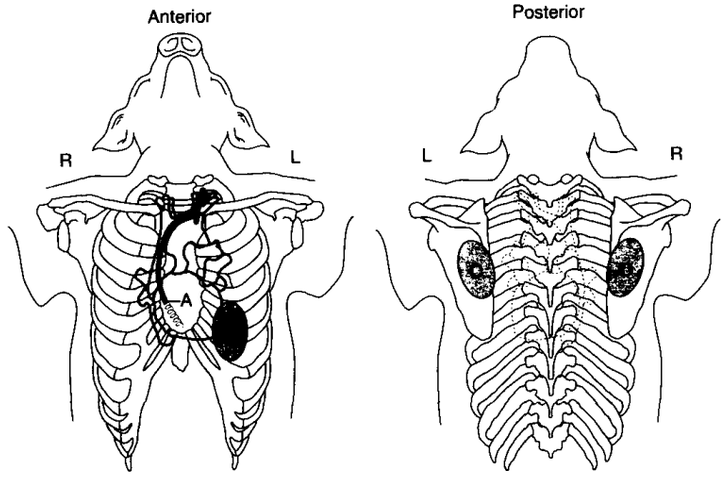


Validation Approaches

In Situ Animal

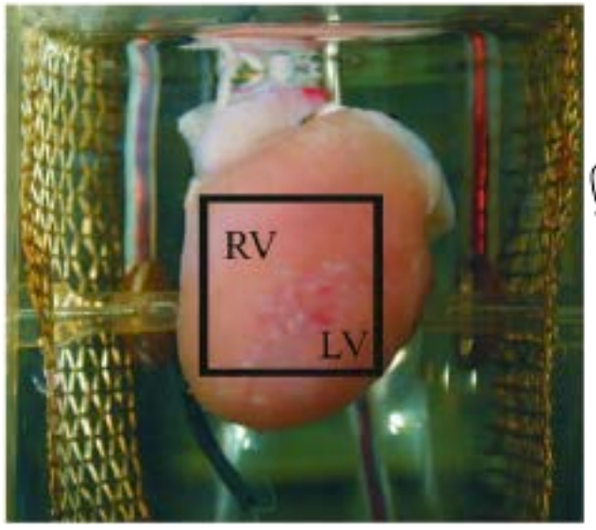


Bear, etal., Circ A & E. 2015;8:677-684.

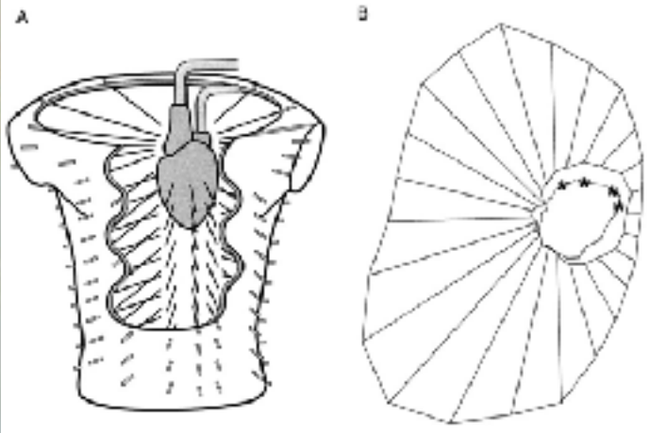


Jorgenson, *et al.*, *IEEE Trans. Biomed. Eng.*, VOL. 42, NO. 6, JUNE 1995

Torso Tank

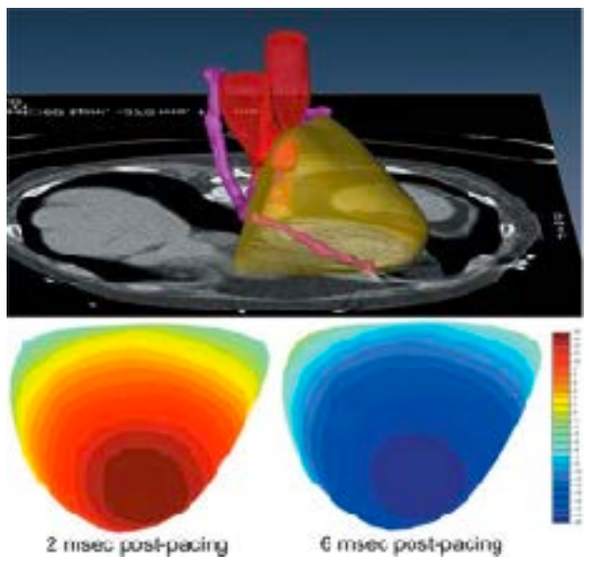


Rodriguez, etal., Circ Res. 2005 Jul 22; 97(2): 168–175.

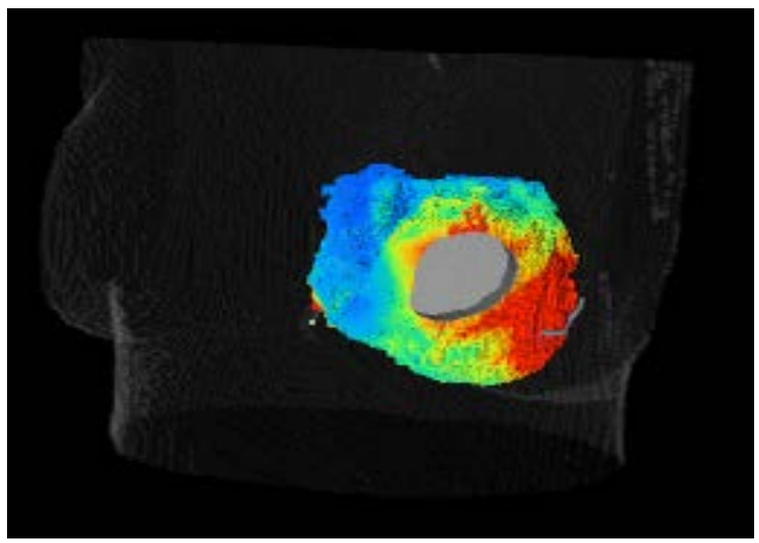


Oster, *etal.*, *Circulation*, Volume 96, Issue 3, 1997

Clinical

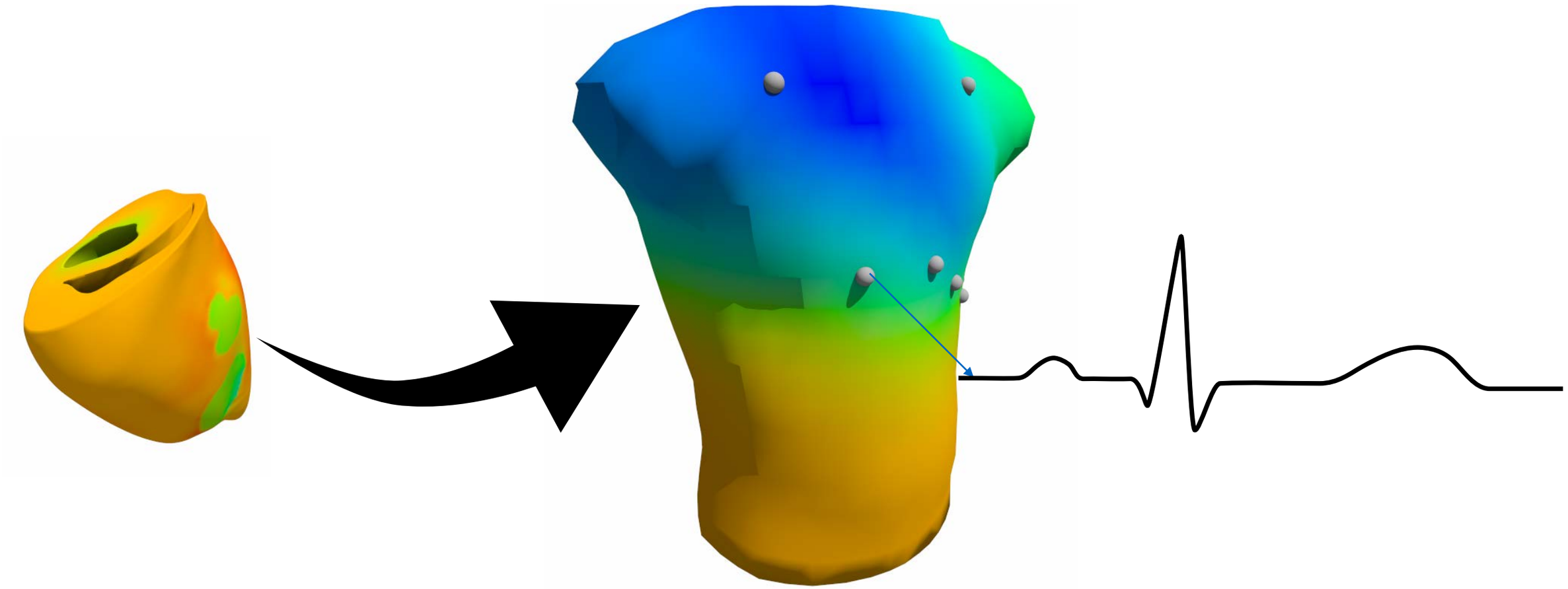


Sapp, etal,. *Circ. A & E.*, 2012; 5(5):1001–1009



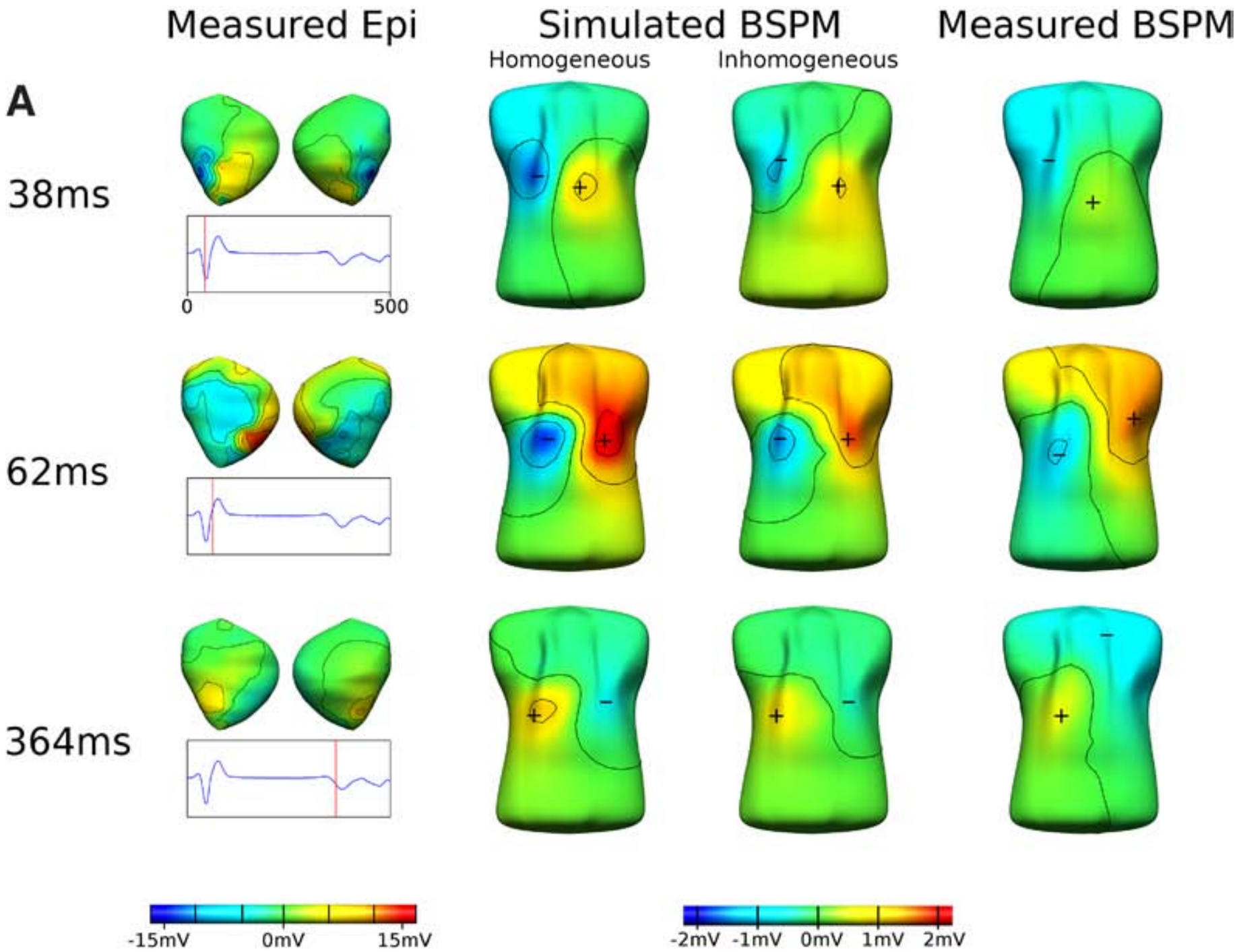
Jolley, et al. Heart Rhythm J 2008;5(4):565--572

Specific Aim



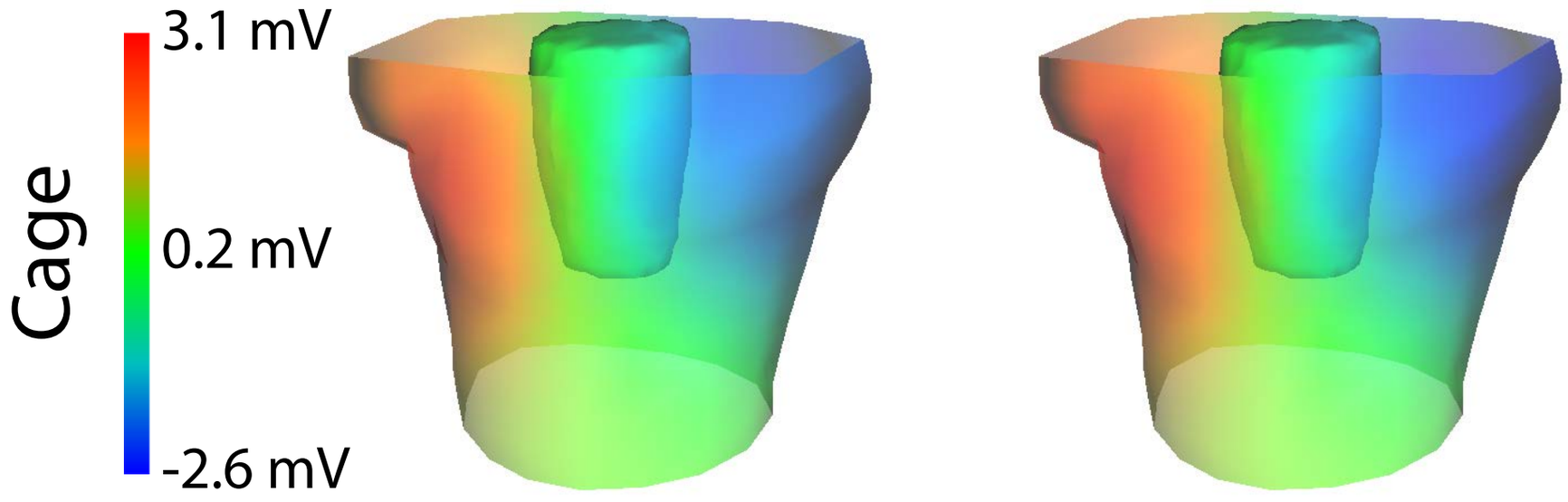
1. Evaluate the effect of missing source sampling on the ECG forward simulation

Error in Forward Simulation



Bear, etal., CircArrhythmElectrophysiol.2015;8:677-684.

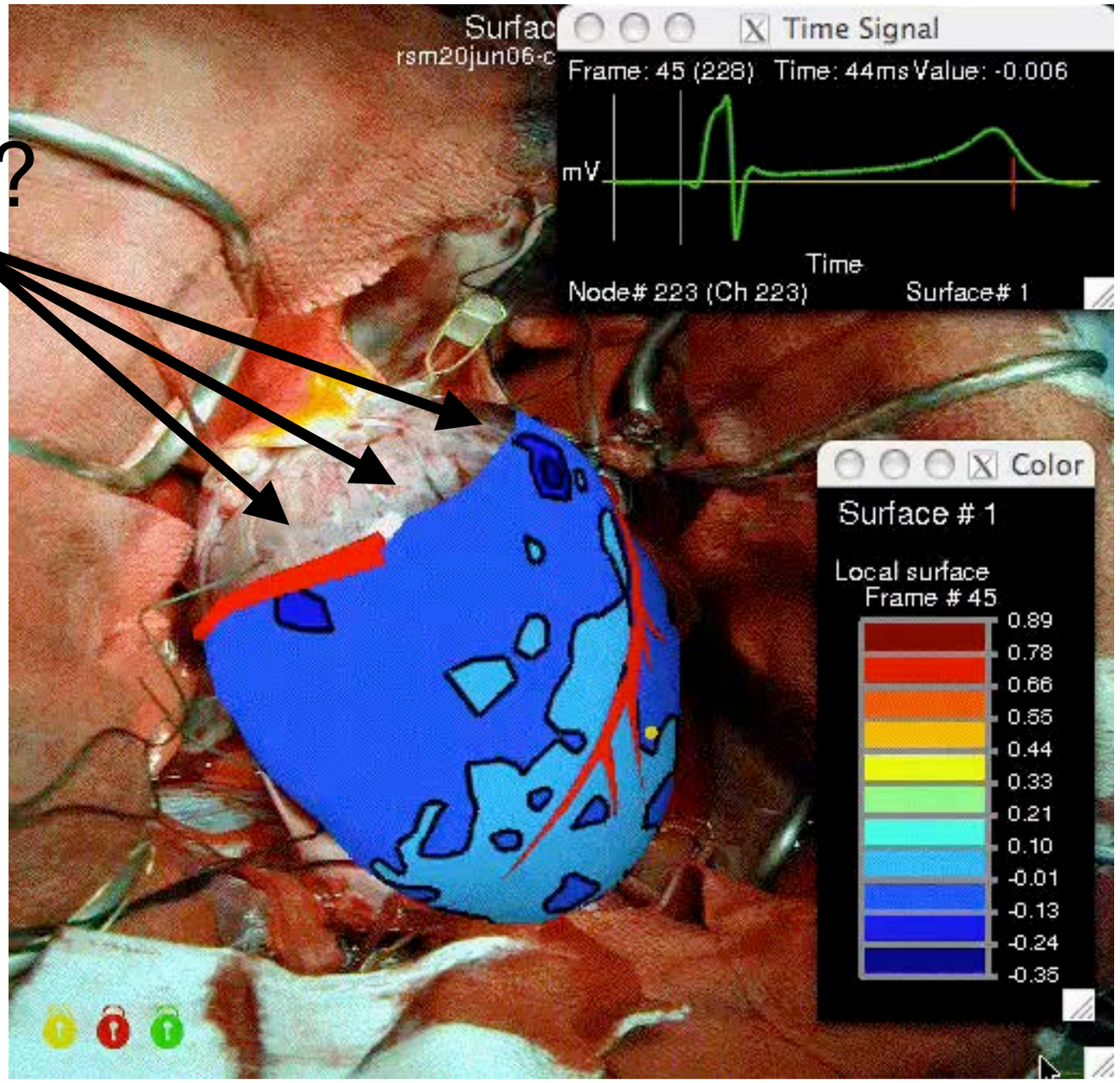
Error in Forward Simulation



Source Recording

Missing Sources?

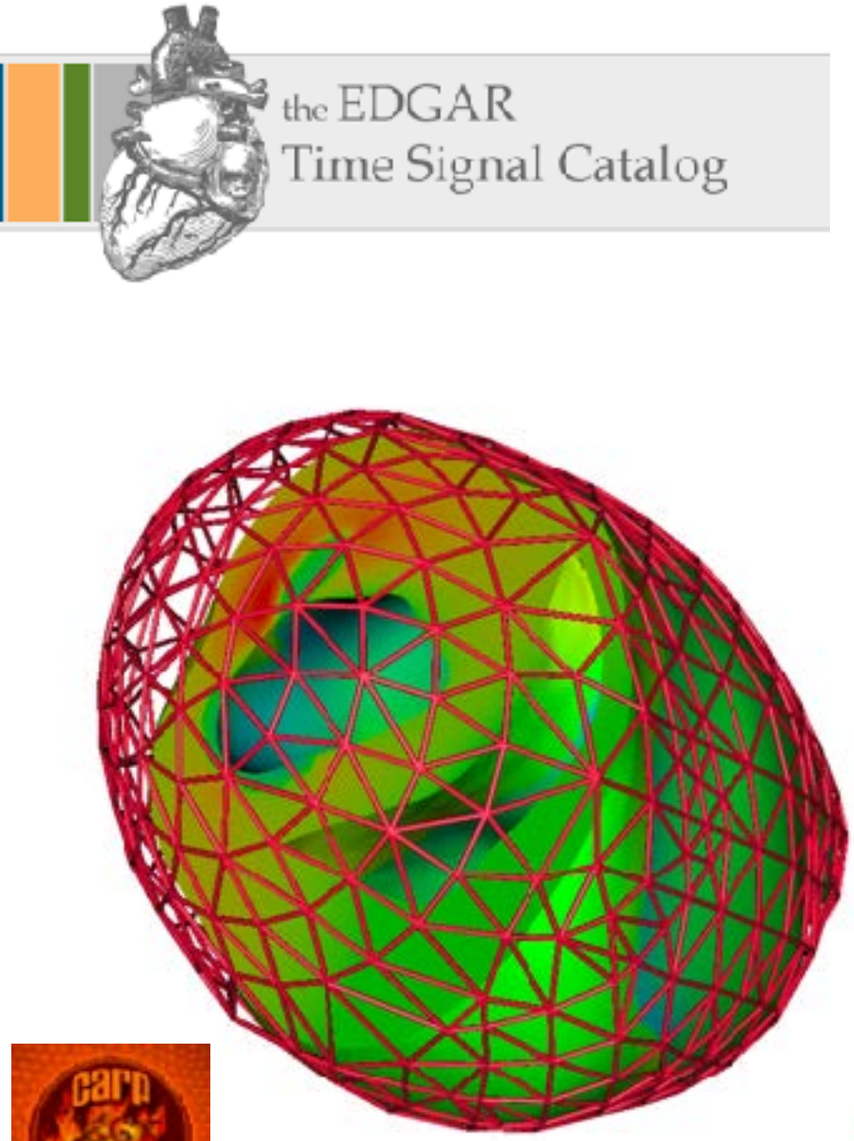
Bear, etal., Circ A & E.2015;8:677-684.



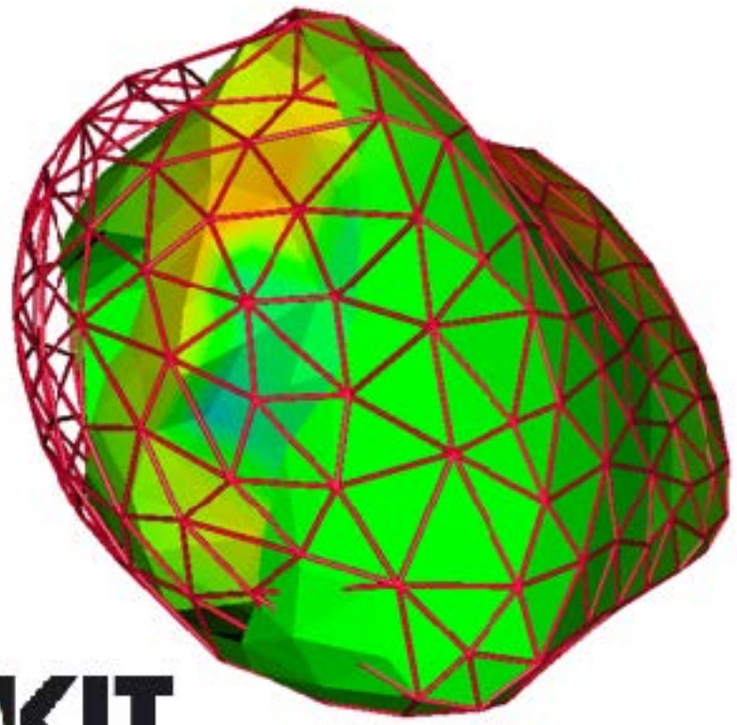
Epicardial Sock (Ventricle Only)

Test sampling strategies of the atrial region to reduce error in forward simulation

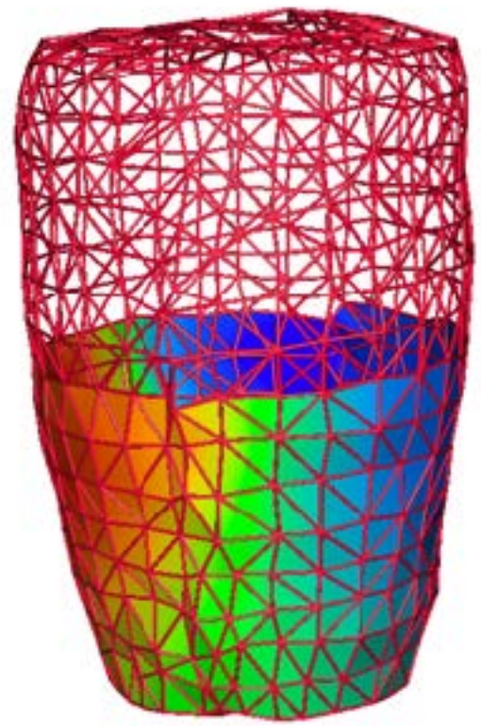
Cardiac Sources



CARP

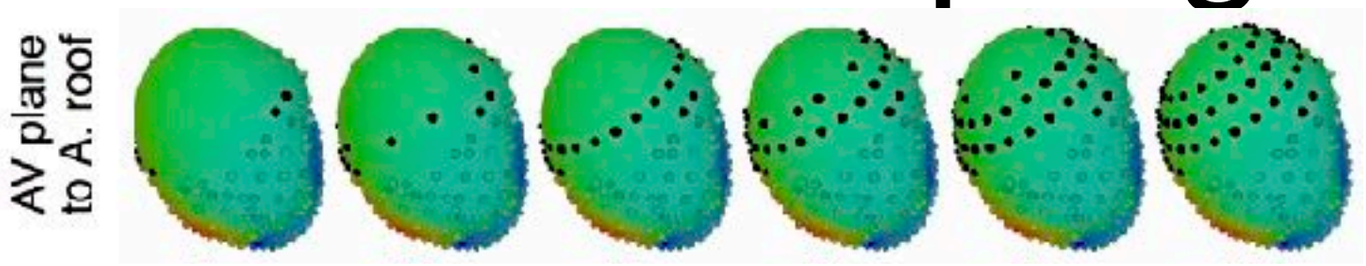


KIT



CAGE

Varied Sampling

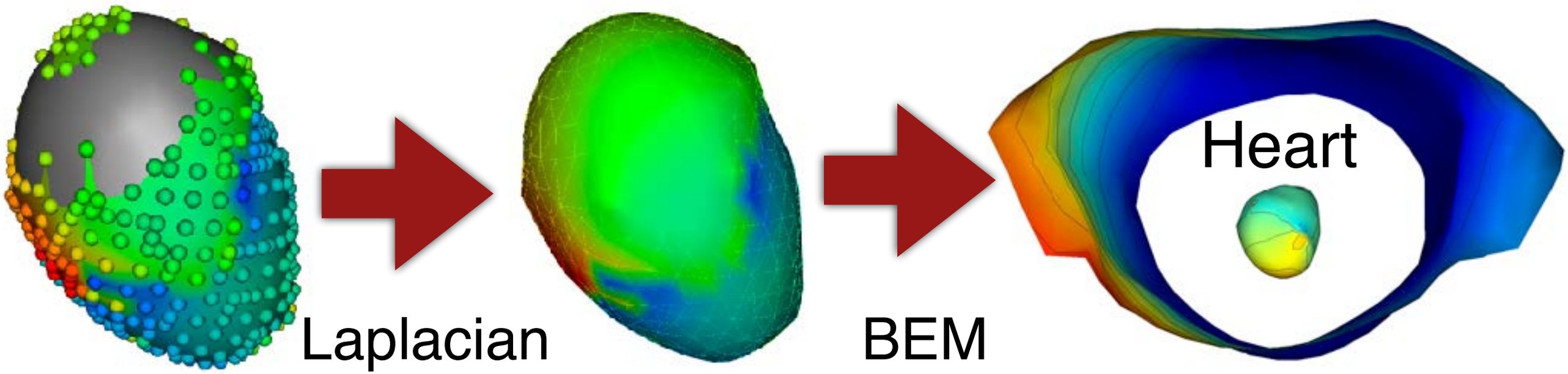


ECG Forward Simulation

Sampled Sources

Interpolated Sources

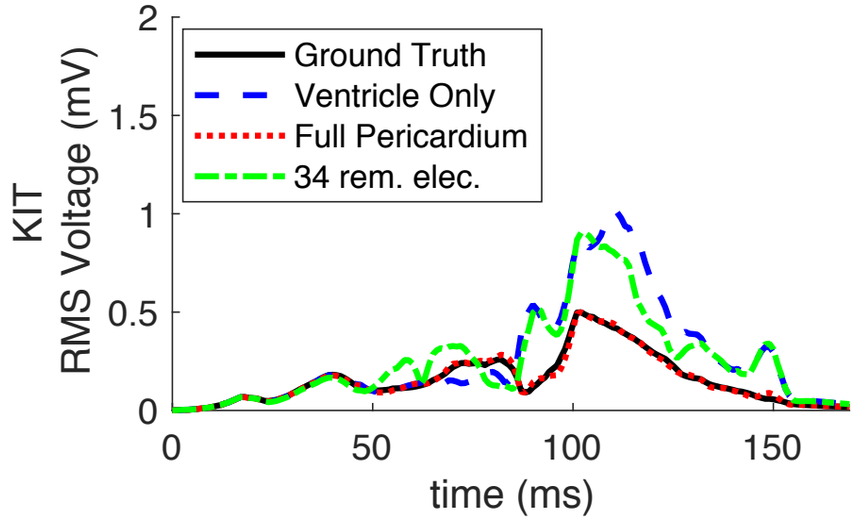
Torso

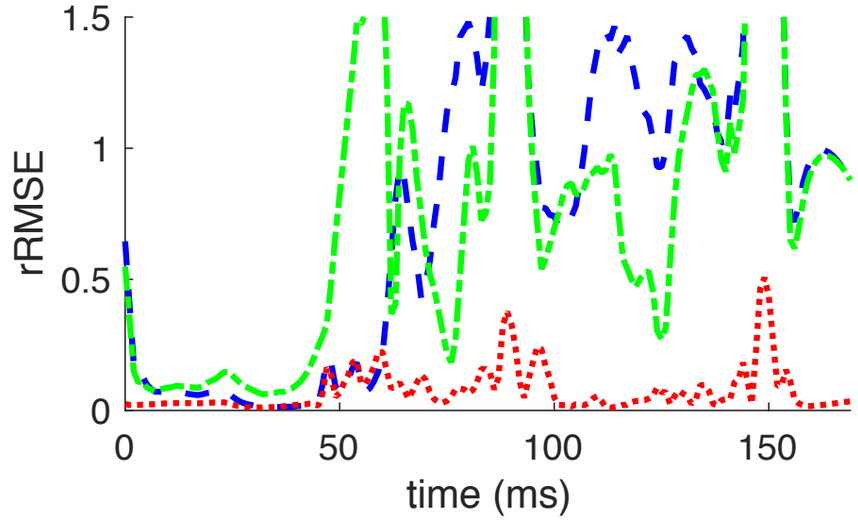


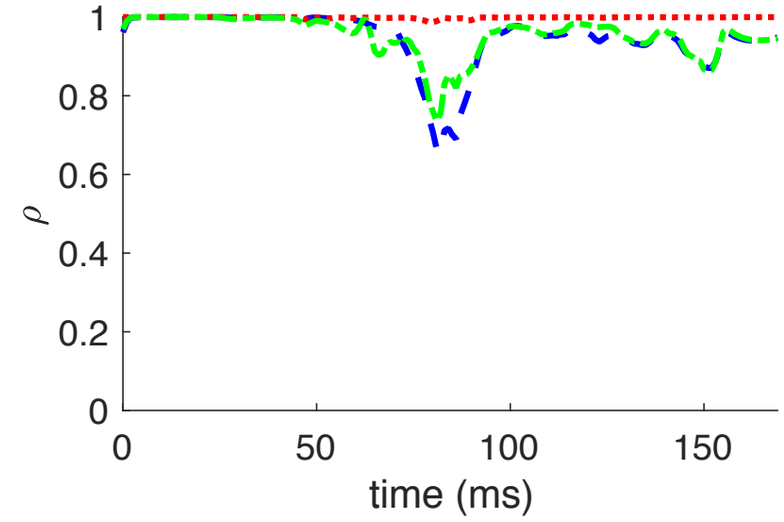
Laplacian Interpolation

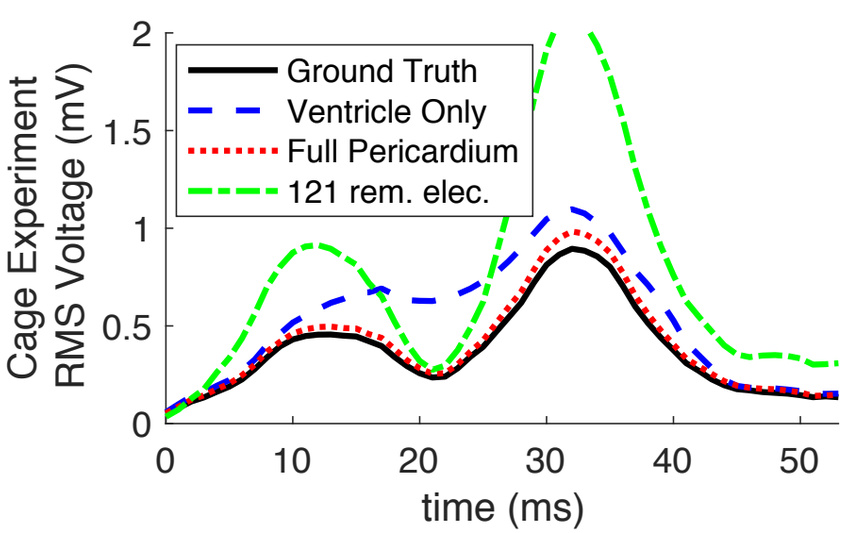
BEM Simulation

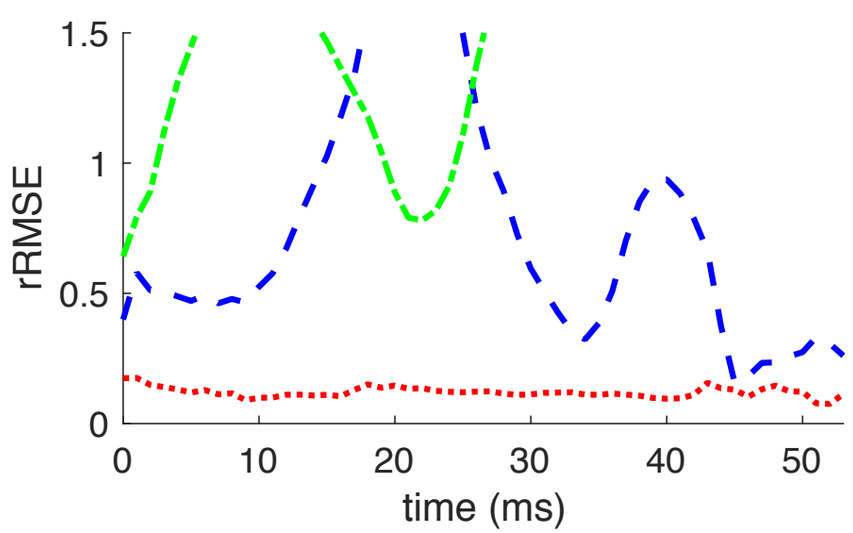
Effect of No Atrial Sampling

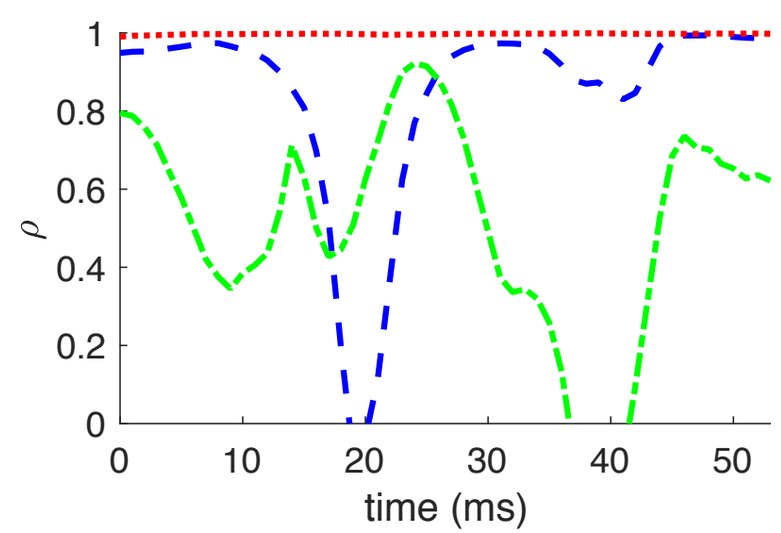




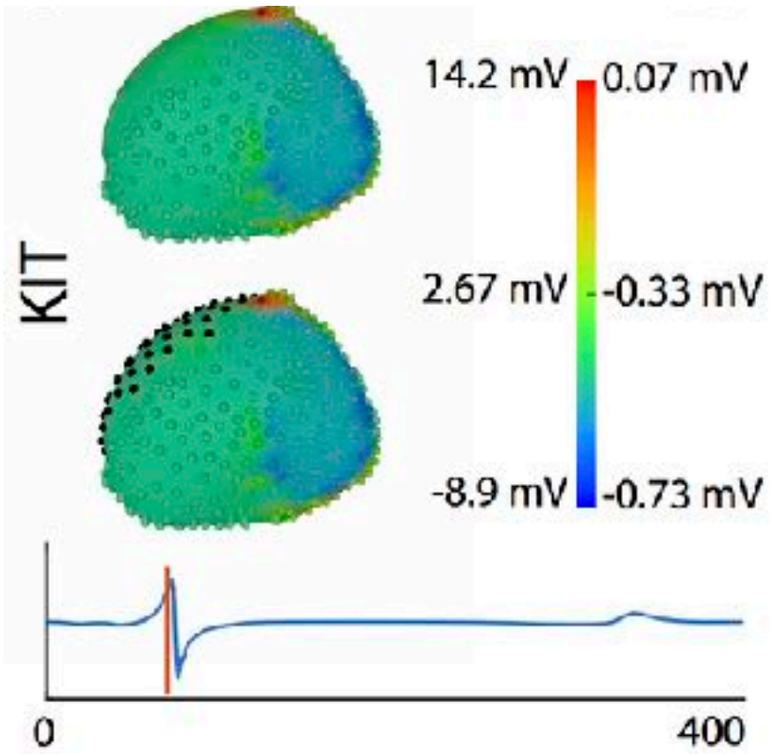


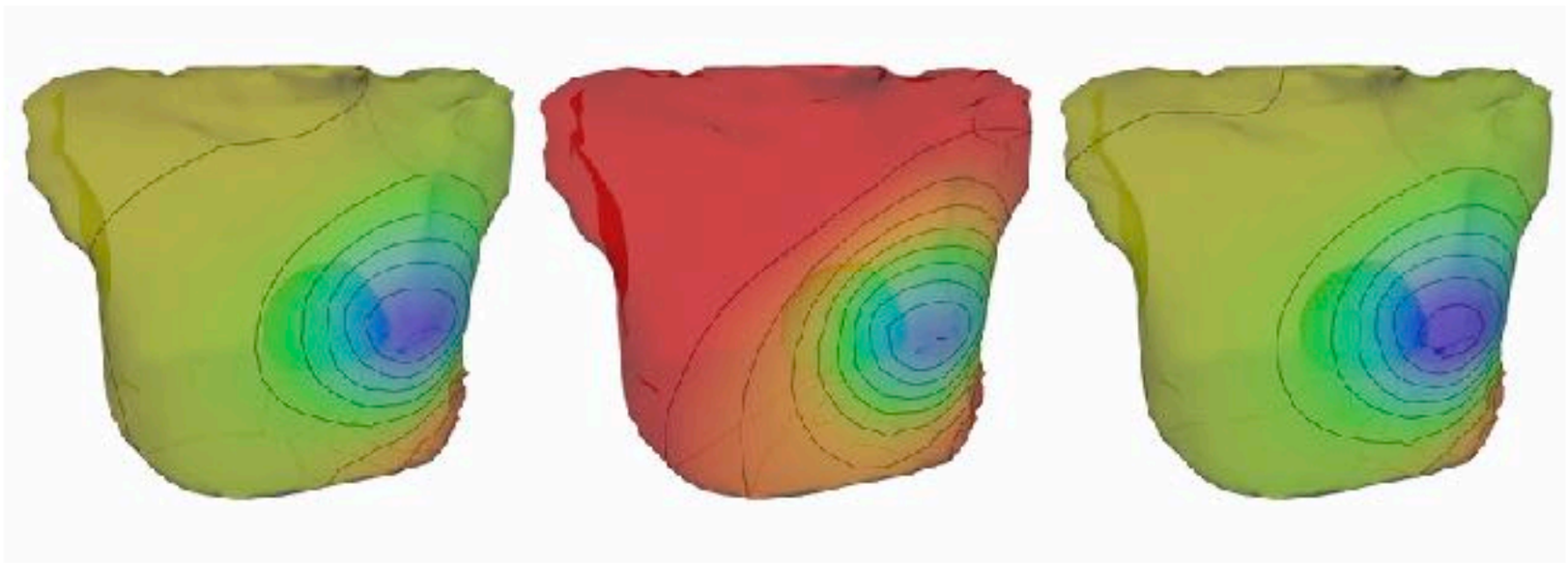




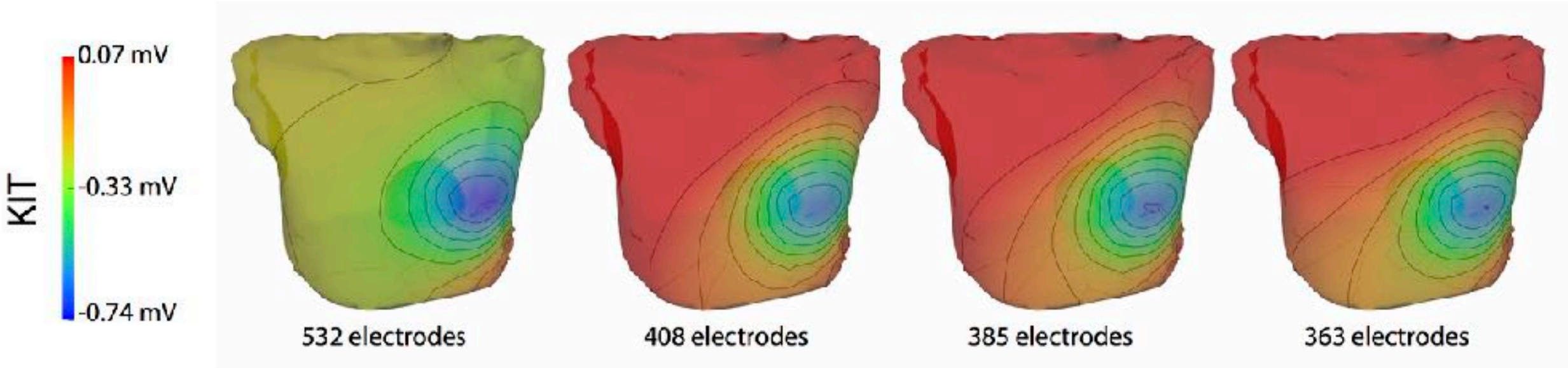


Effect of Missing Ventricle Sampling



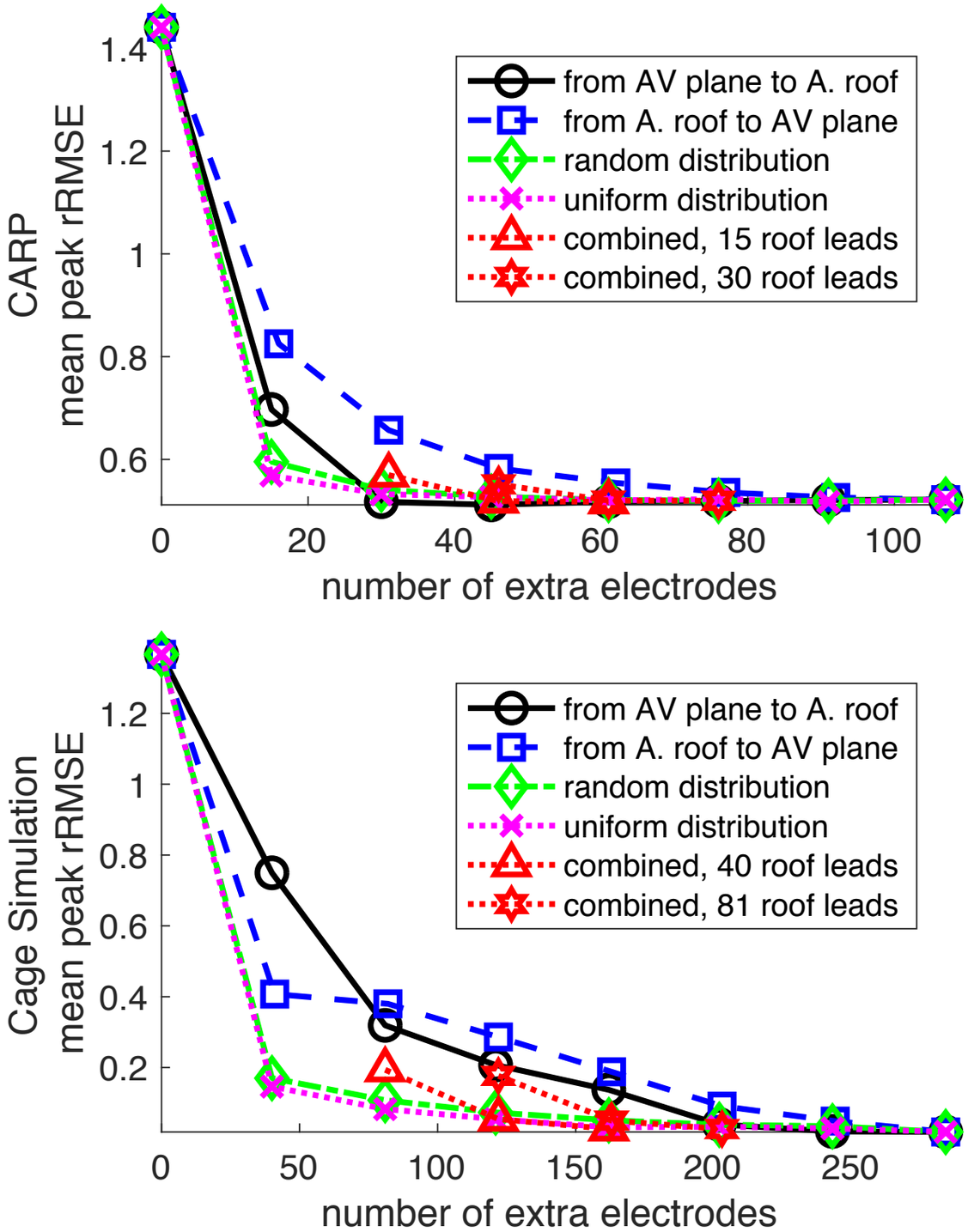


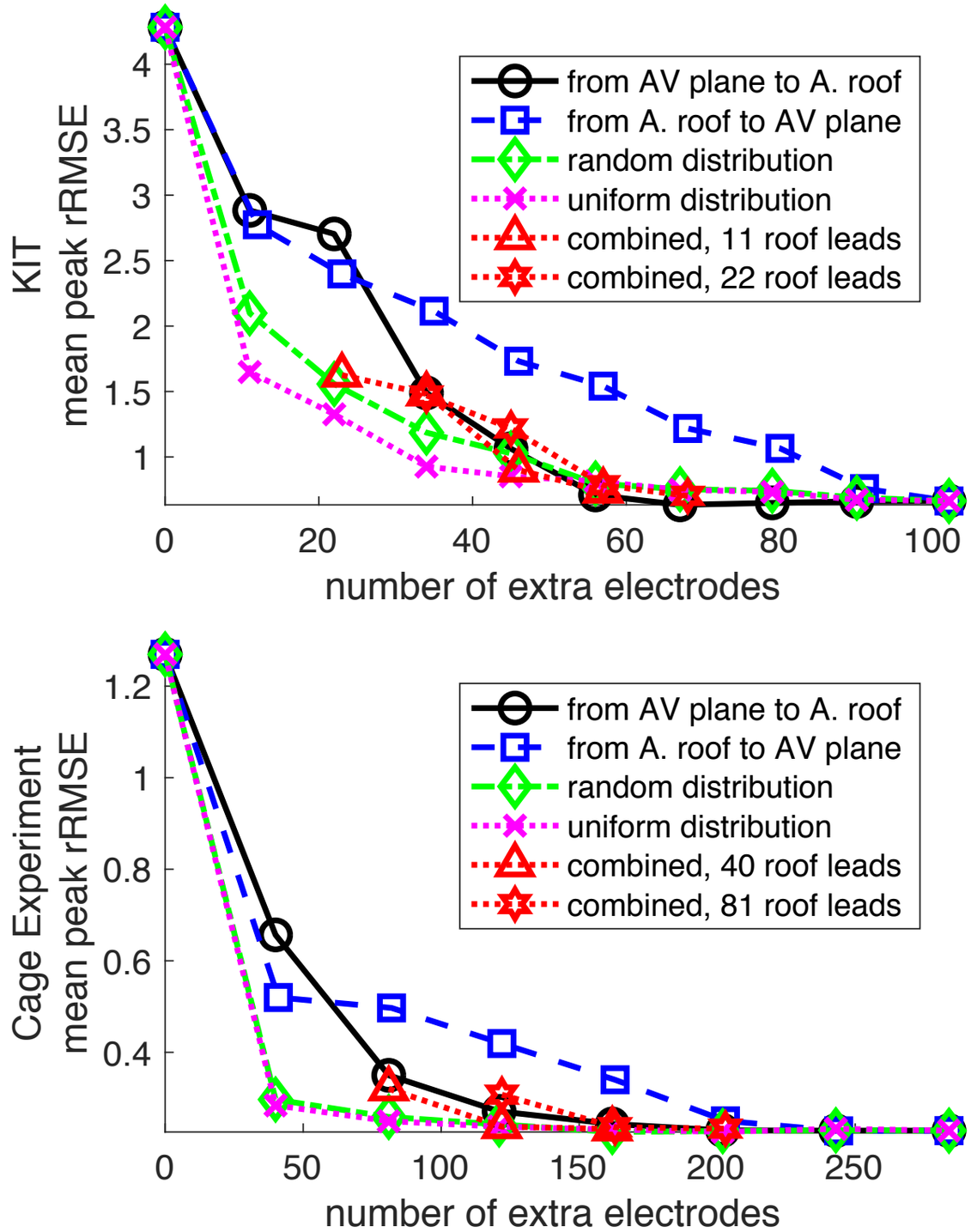
Ground Truth Ventricle Only Full Sampling



Ground Truth Reduced Ventricle Sampling

Progressive Sampling



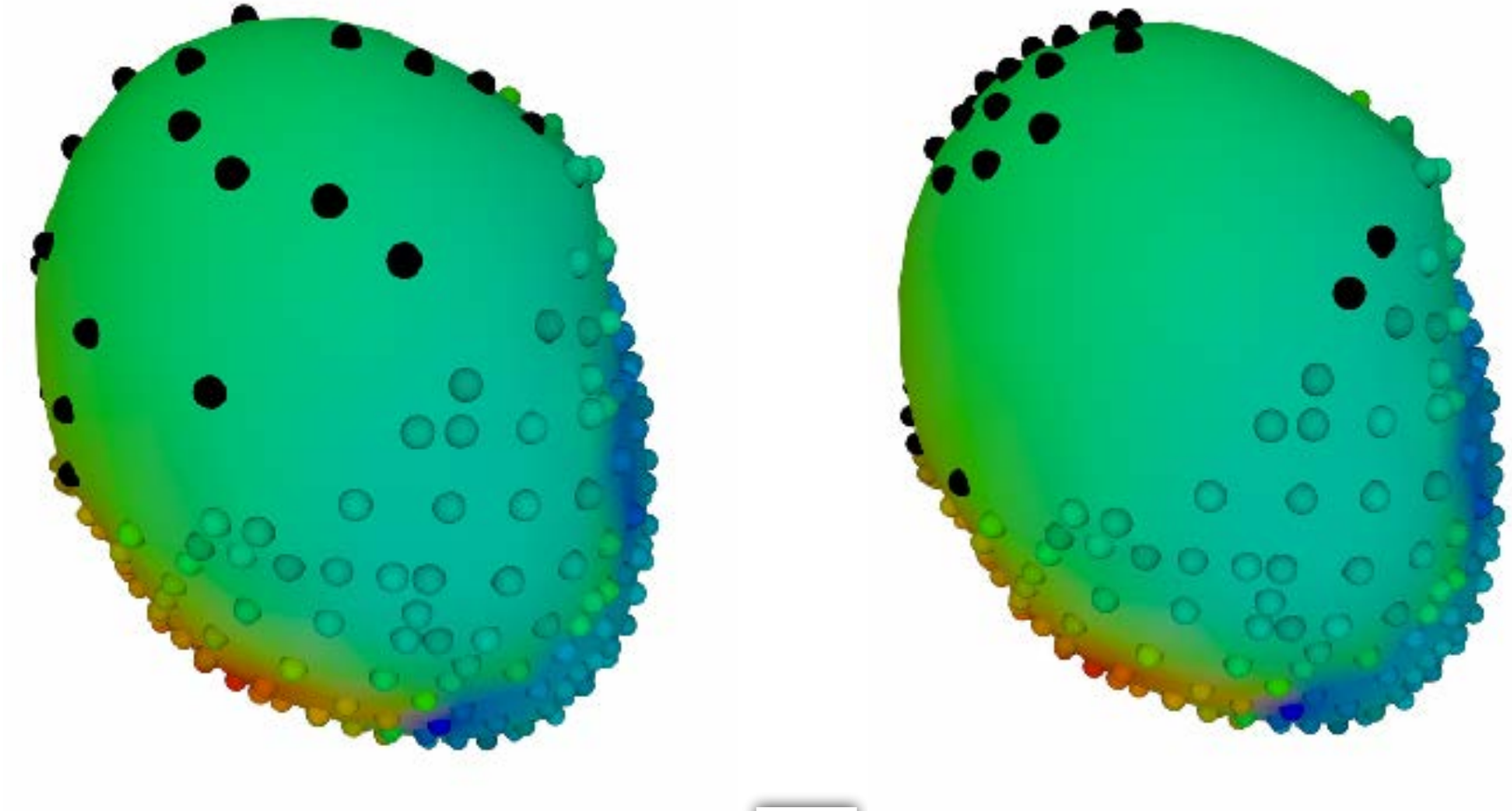


Possible Sampling

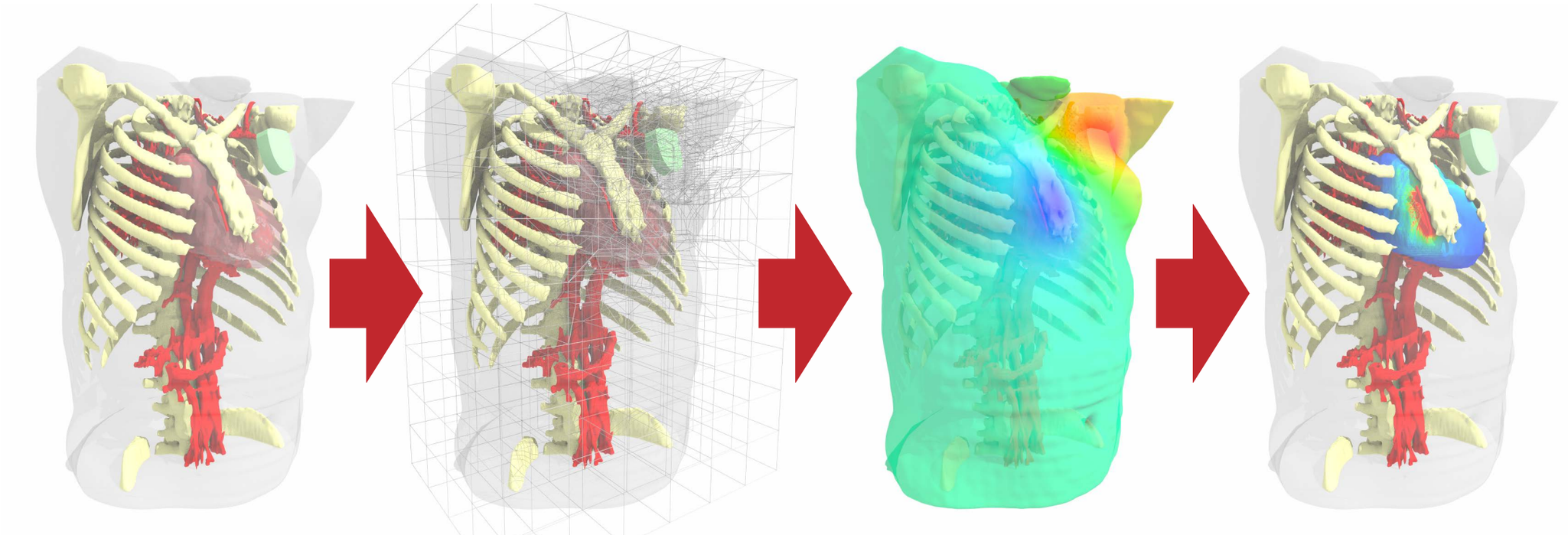
More electrodes are better

Sparse placement can reduce error

Missing ventricular sampling increases error further



Specific Aims

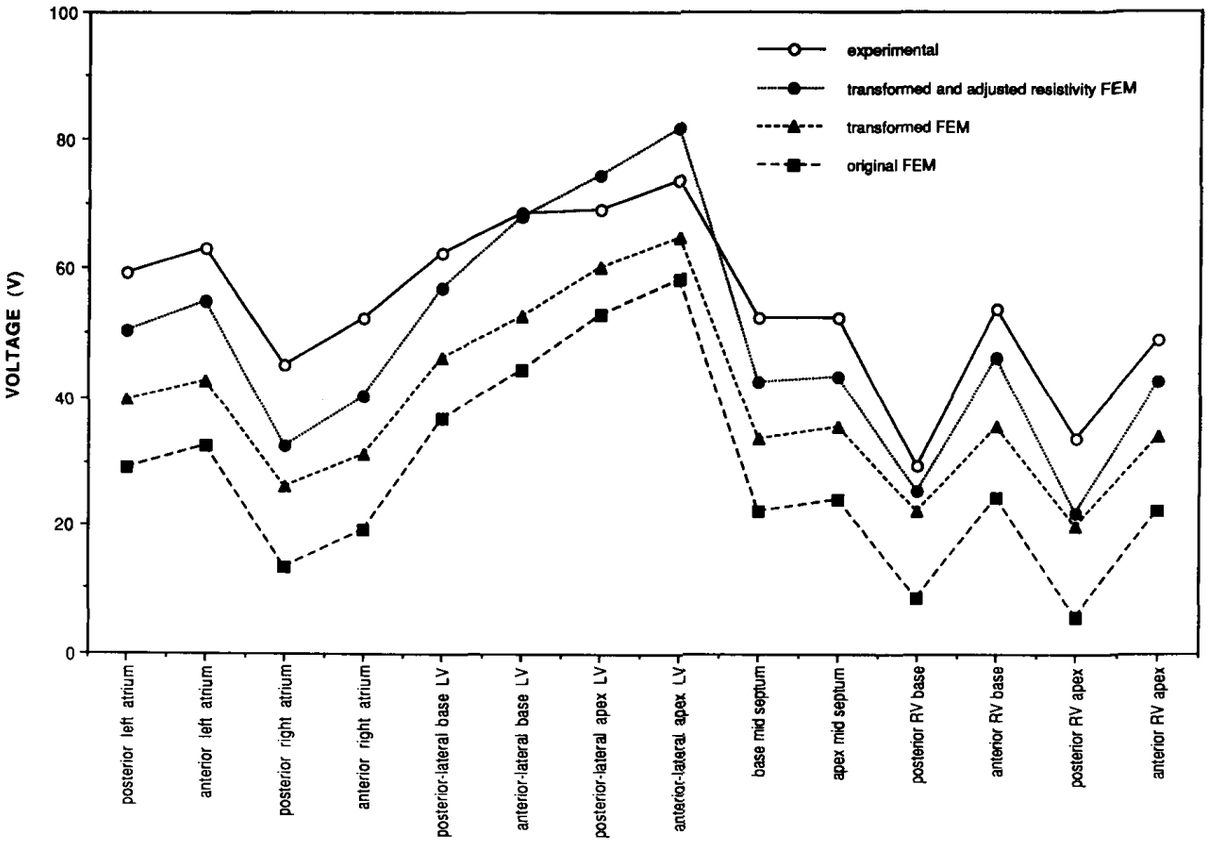


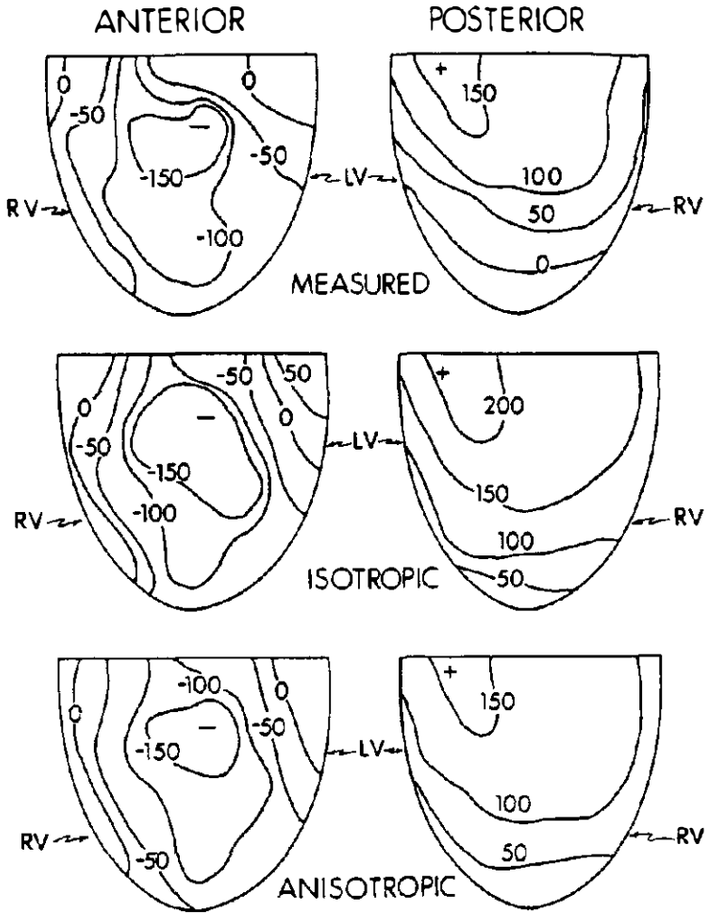
2. Record potentials in a torso-tank preparation to validate the simulation pipeline

3. Measure body-surface potentials in patients to validate the simulation pipeline

Defibrillation Simulation

Jorgenson, *et al.*, *IEEE Trans. Biomed. Eng.*, VOL. 42, NO. 6, JUNE 1995





Claydon, *etal.*, IEEE EMBS 10Th Ann. Int. Conference 1988

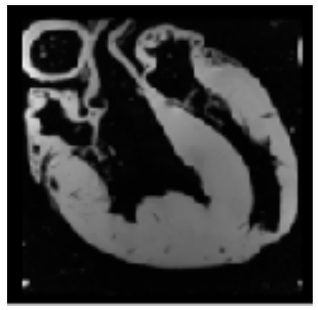
Sparse or Local Recordings
No Validation in Patients

Measure high spatial resolution volumetric potentials within a torso-tank to validate the defibrillation simulation

Measure body-surface potentials during ICD testing for validation purposes

Simulation Pipeline

MRI Scan



Seg3D

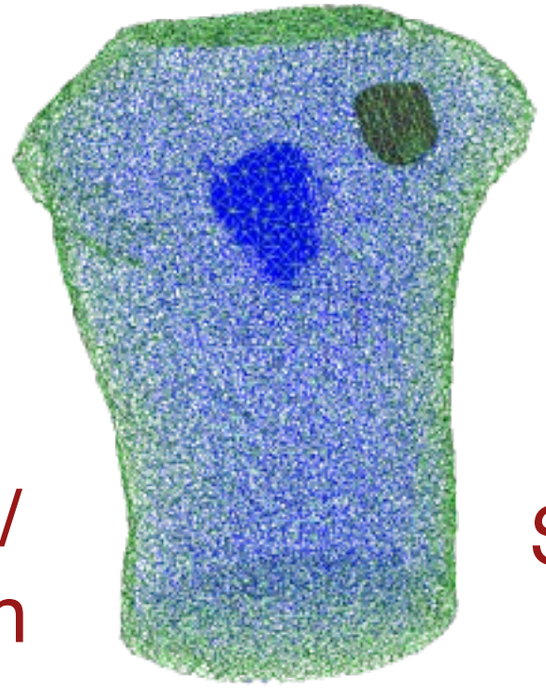
Segment

BioMesh3D

Make Heart Surface

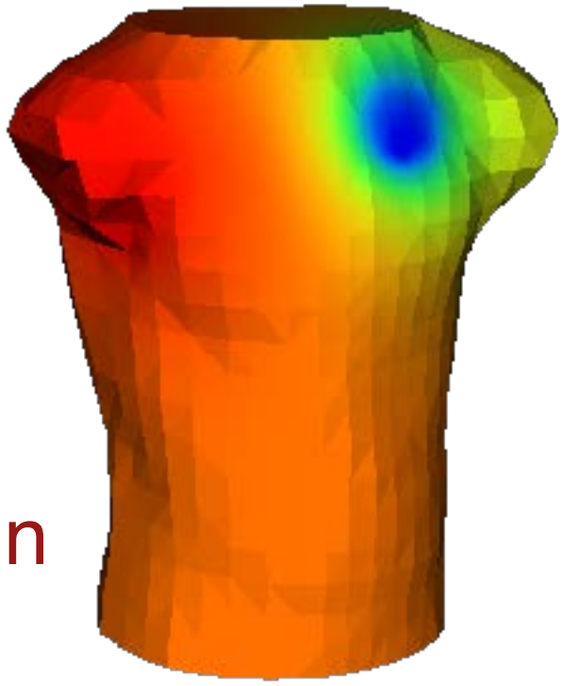
Register Surfaces

Tetgen/ SCIRun



Make Mesh

SCIRun FEM

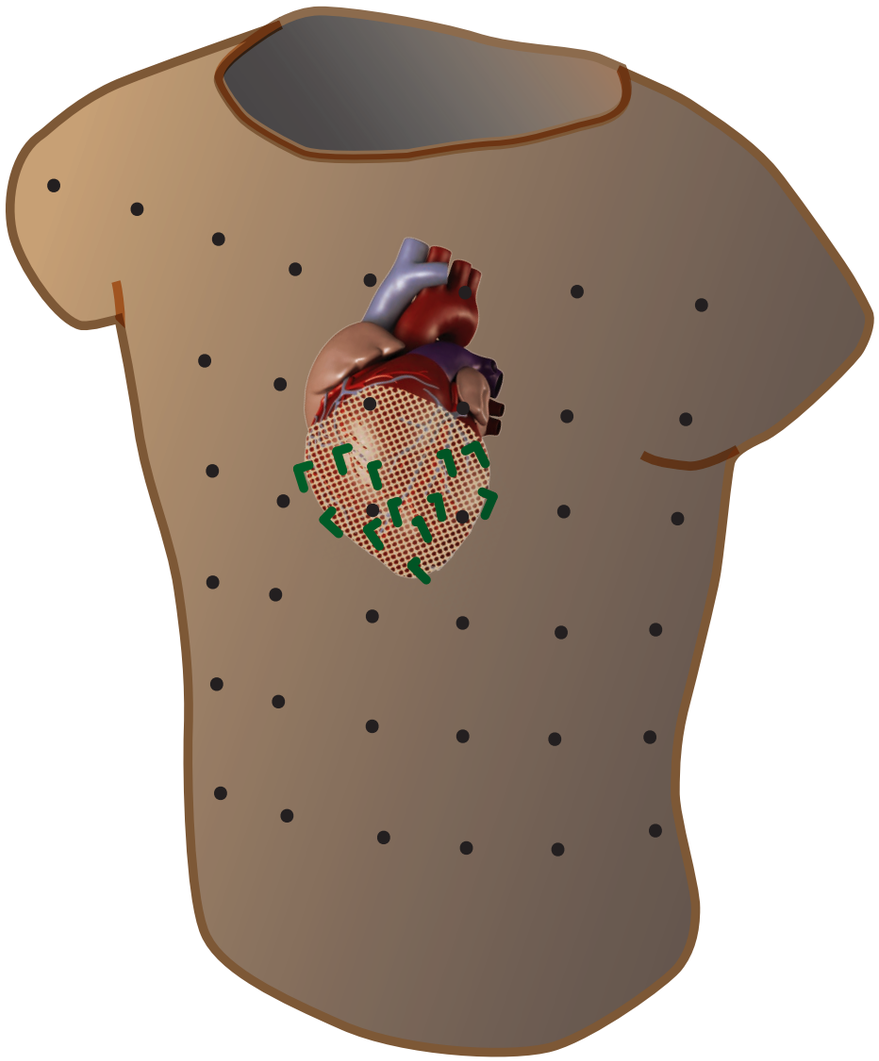


Calculate Potentials

Two Validation Environments

https://www.army.mil/article/202490/
advancements_in_technology_change_the_way_health_care_is_delivered_at_the_tamc_cath_lab

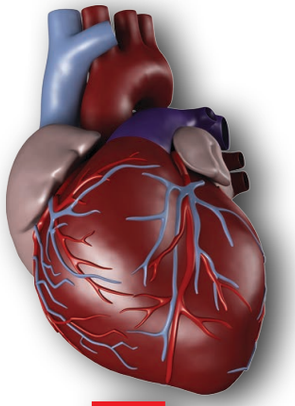
Access



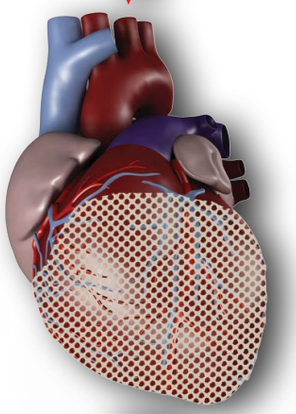
Experimental Complexity

Tank Experiment

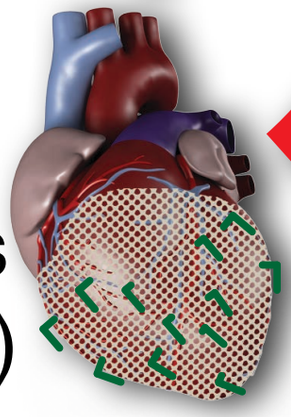
Excised Heart



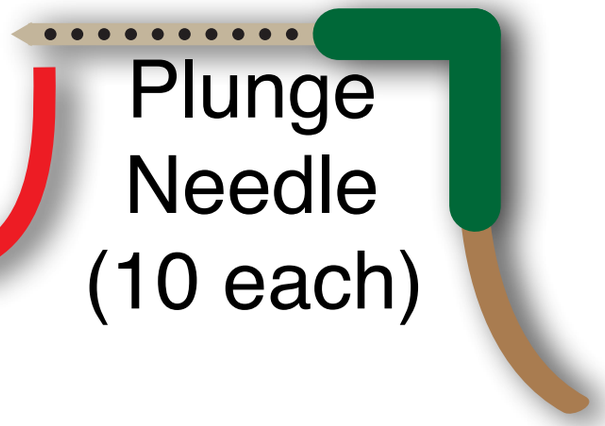
Apply Cardiac Sock (247)



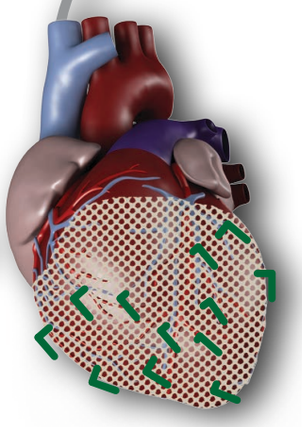
Insert Plunge Needles (20 x 10)



Plunge Needle (10 each)

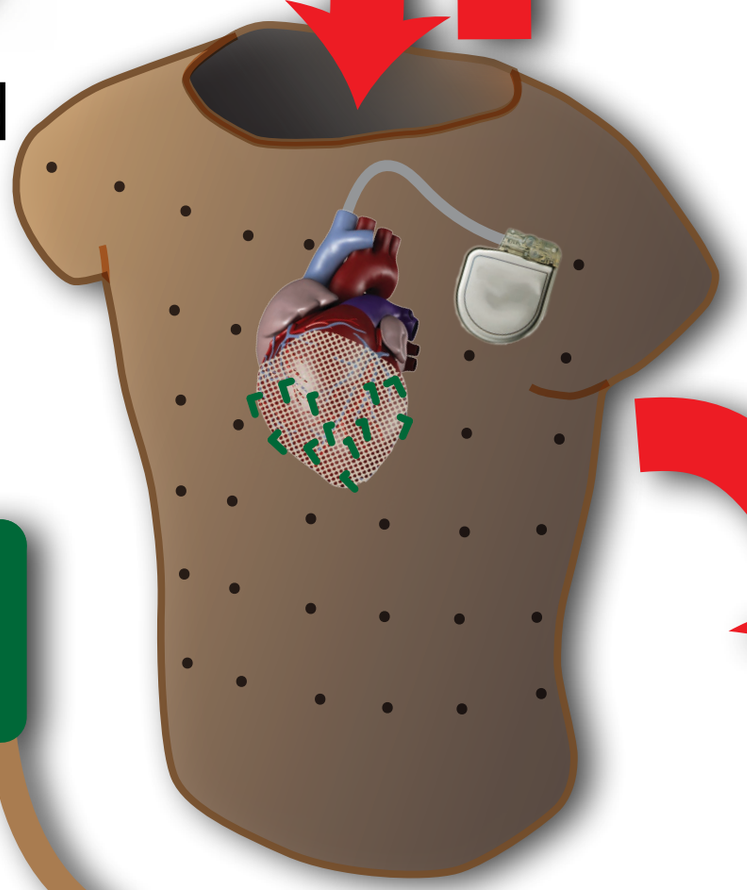


Insert ICD coil



Attenuated ICD Generator

Suspend in Tank (192)



Scan Heart

Digitize Points for Registration

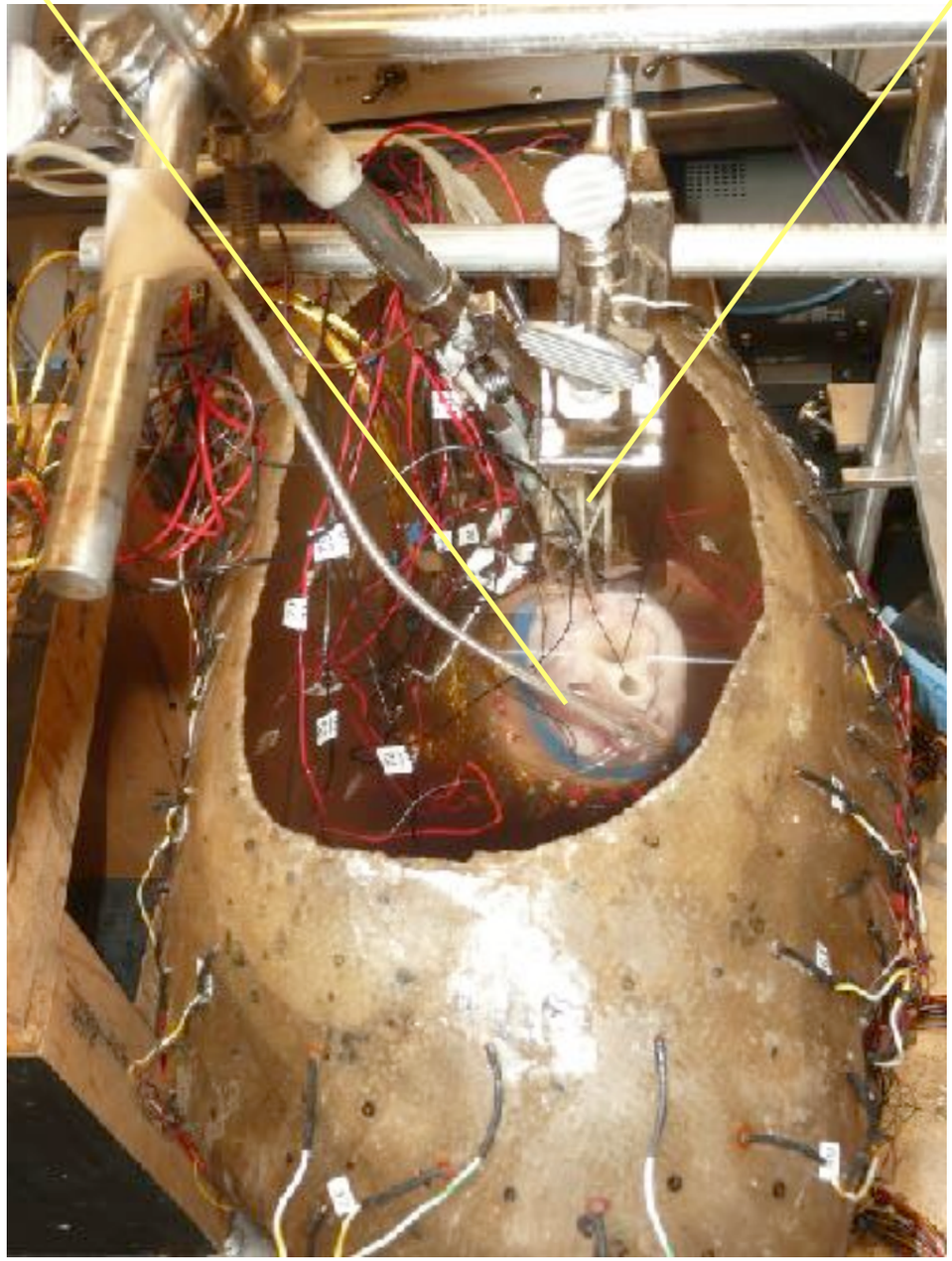
Record ICD potentials within heart and on torso tank surface

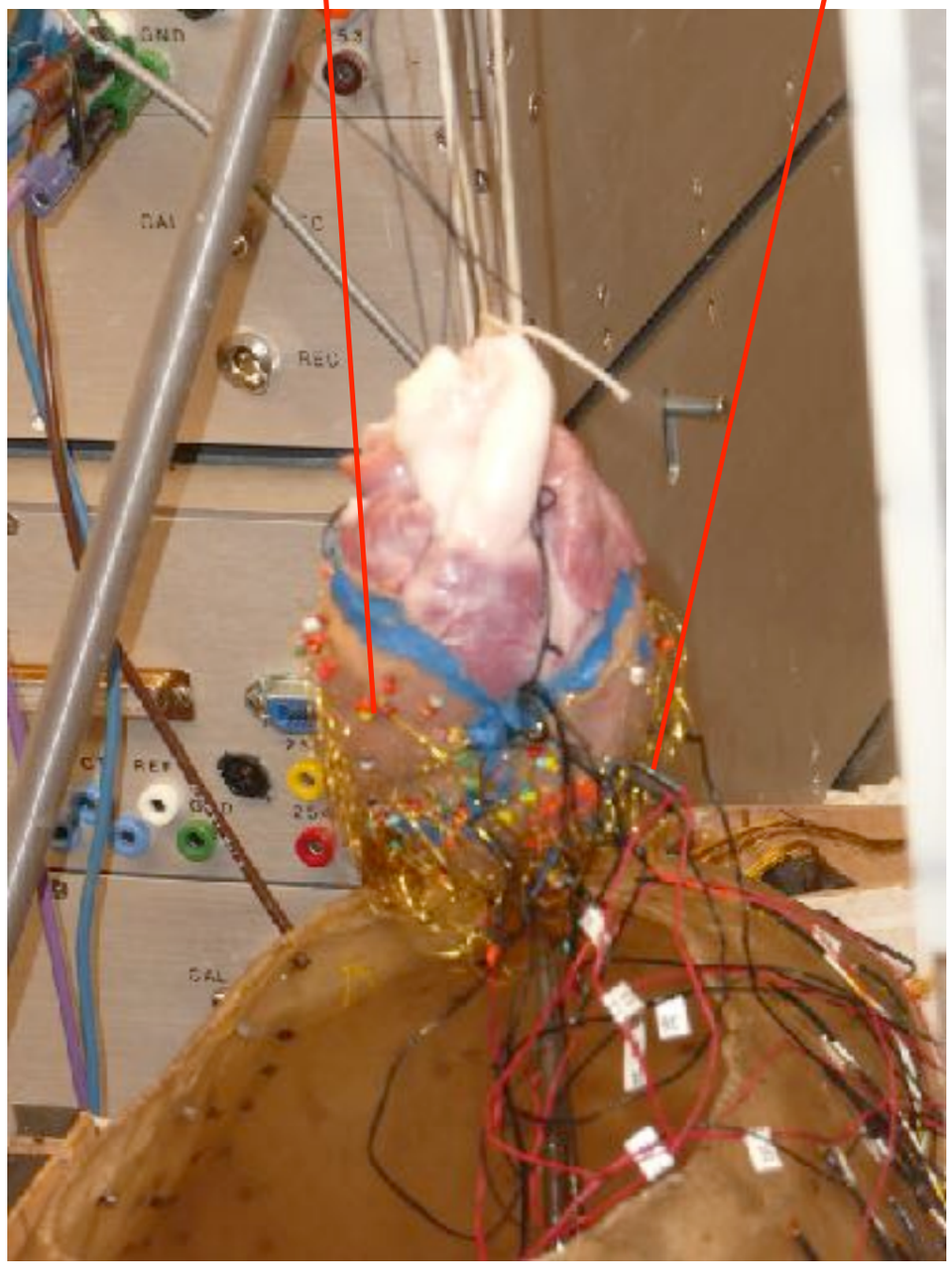
ICD coil

ICD can

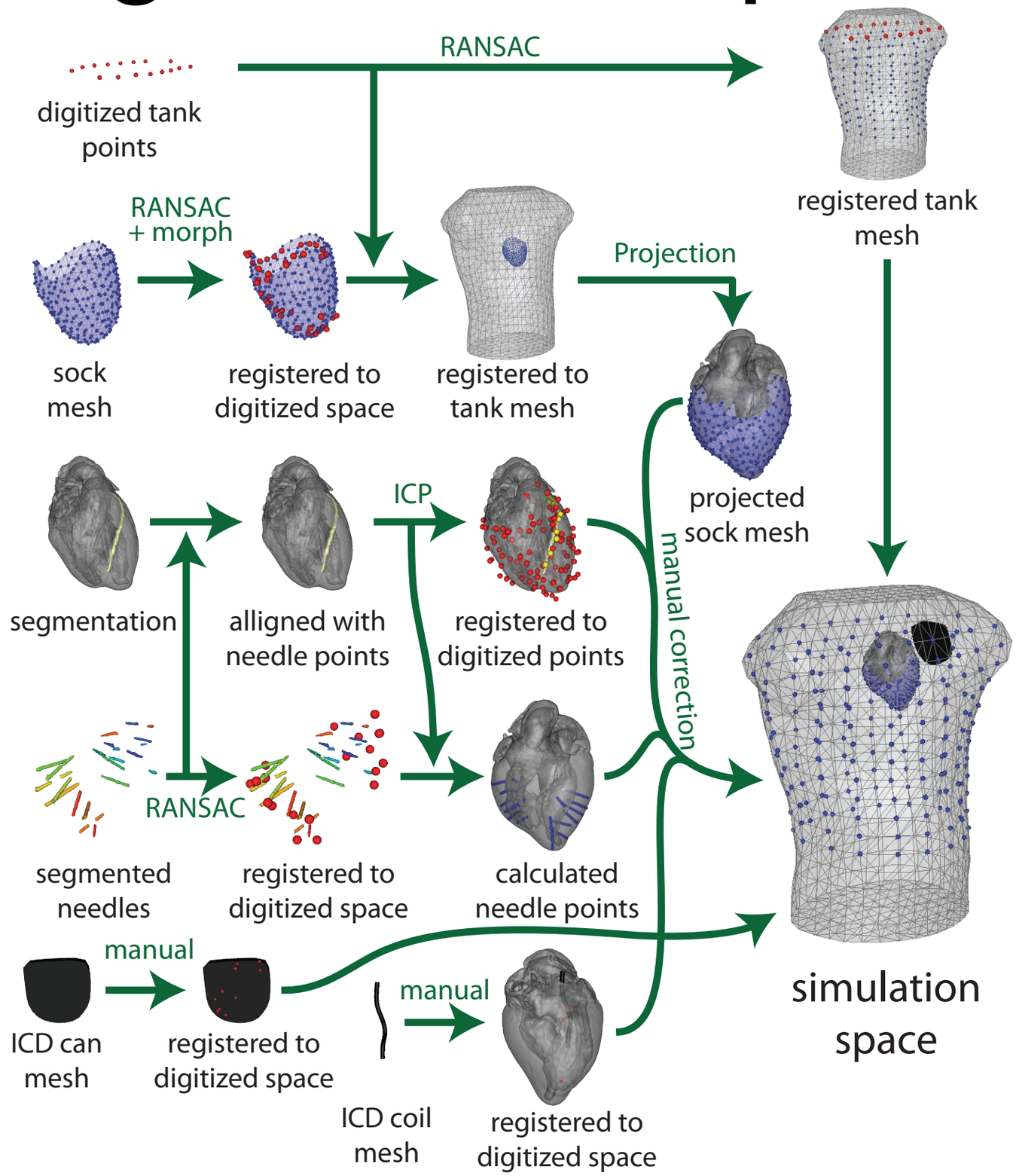
sock

needles

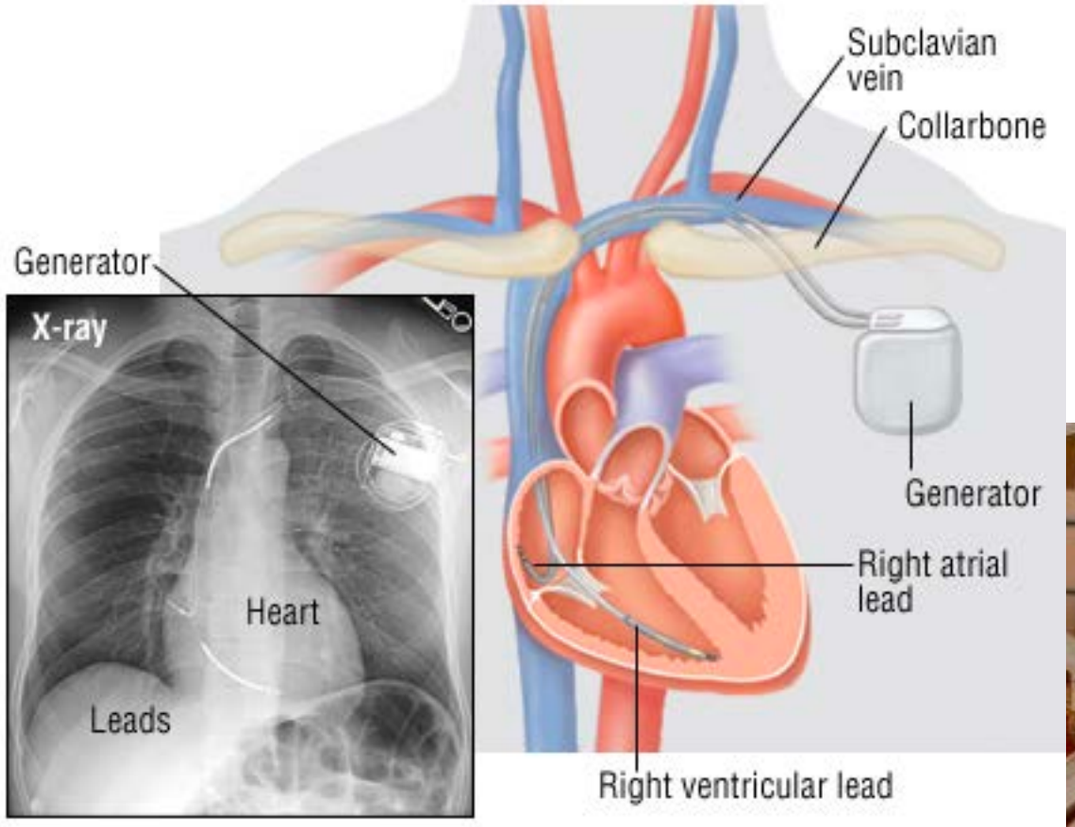




Registration Pipeline



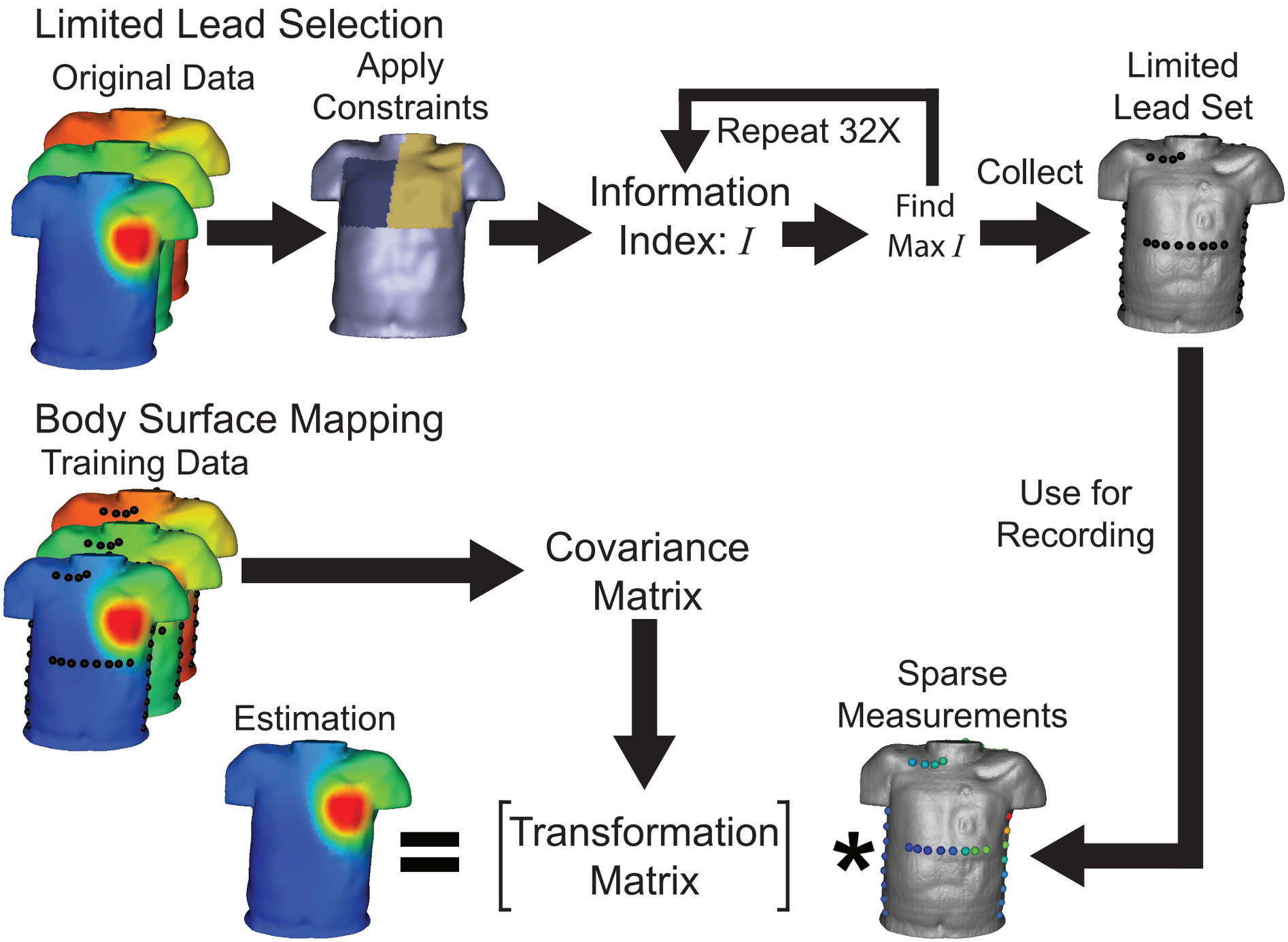
ICD Testing During Implantation



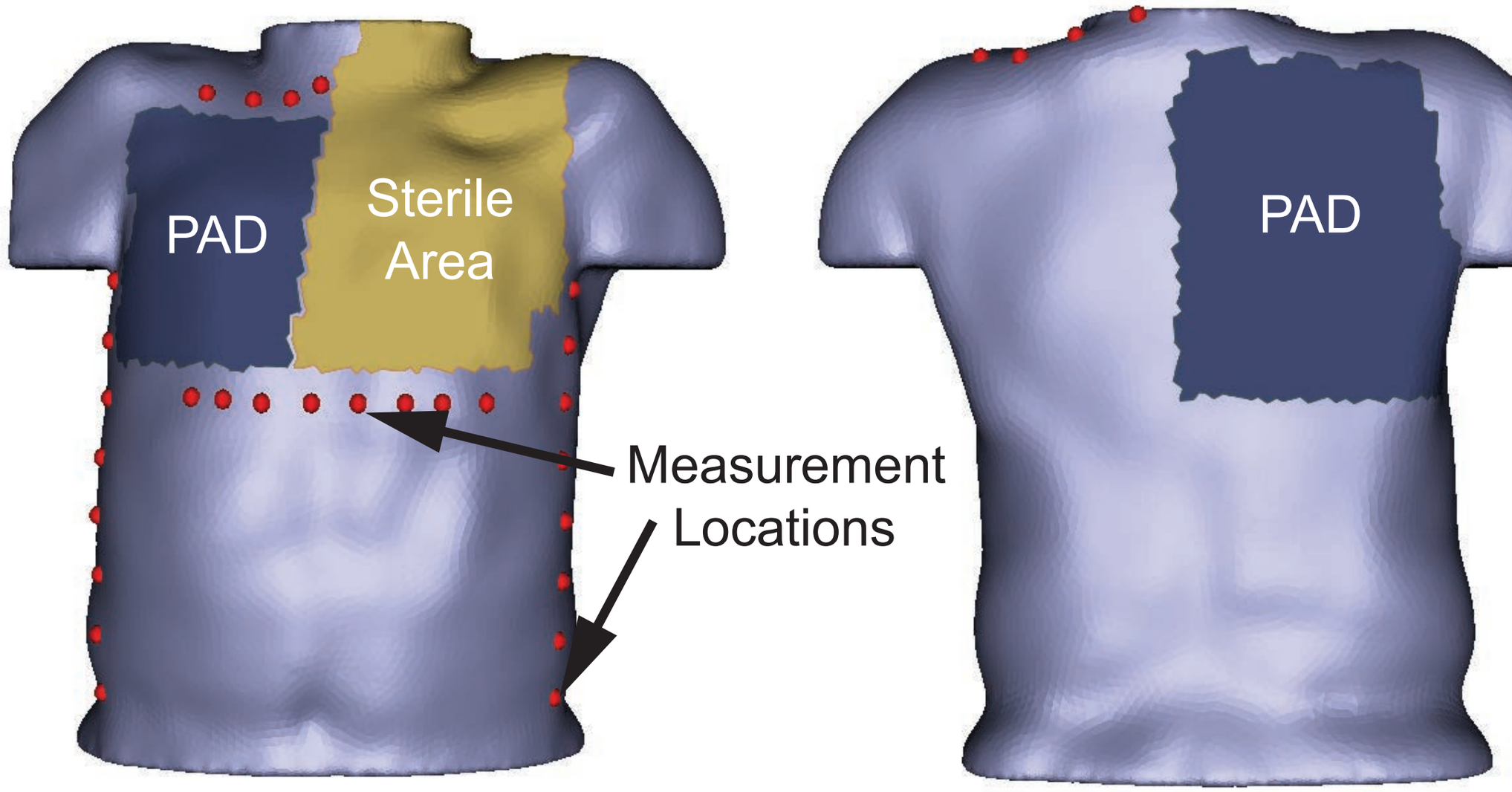
https://www.drugs.com/health-guide/implantable-cardioverter-defibrillator-icd.html

https://www.army.mil/article/202490/advancements_in_technology_change_the_way_health_care_is_delivered_at_the_tamc_cath_lab

Limited Lead Selection and Body-Surface Estimation



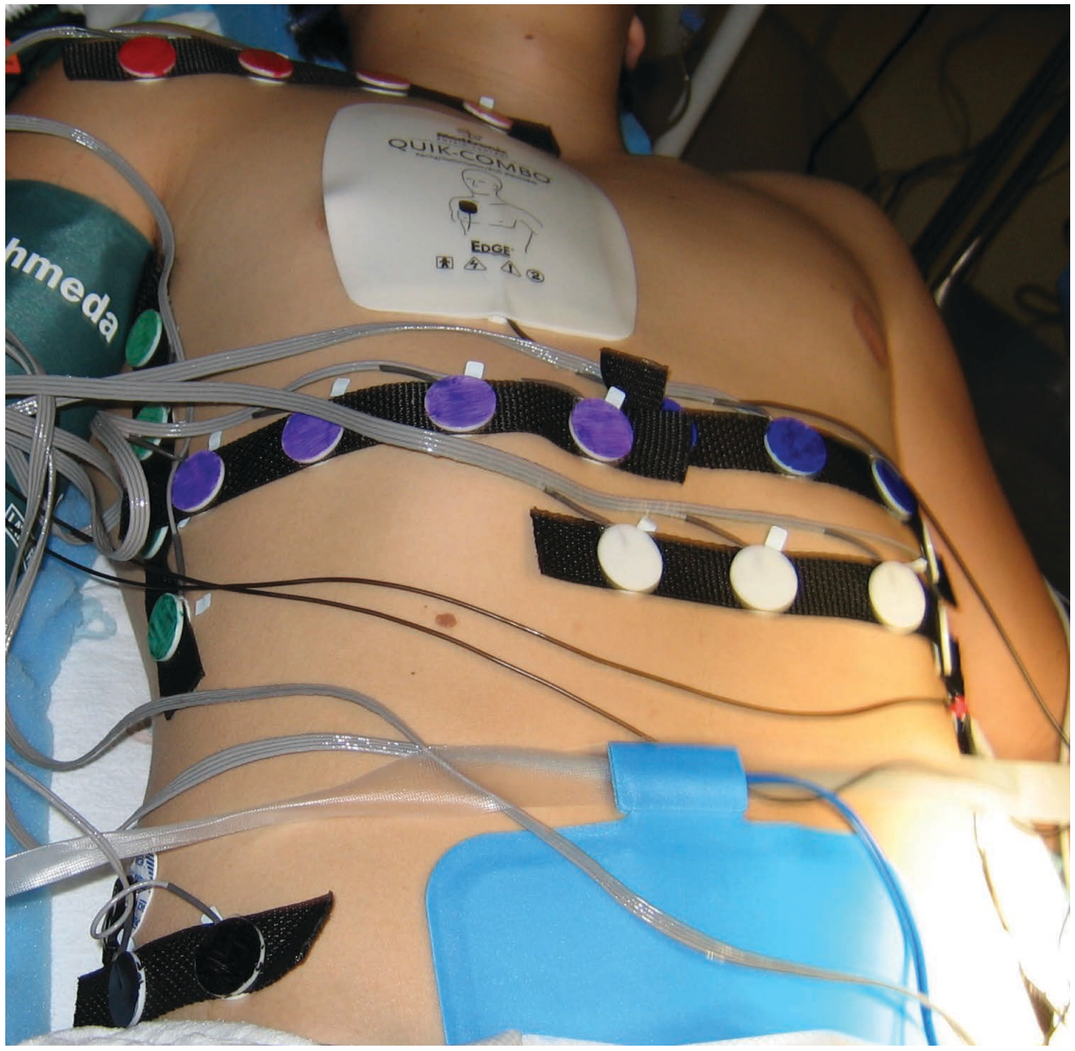
Final Leadset

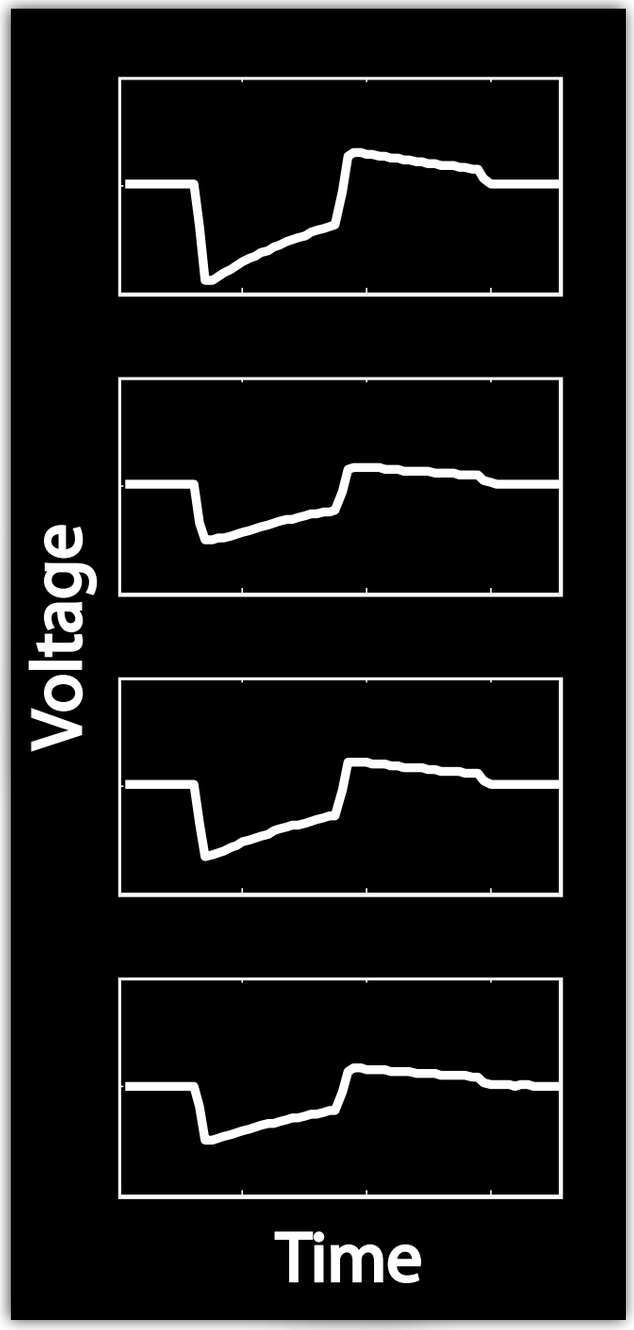


Front

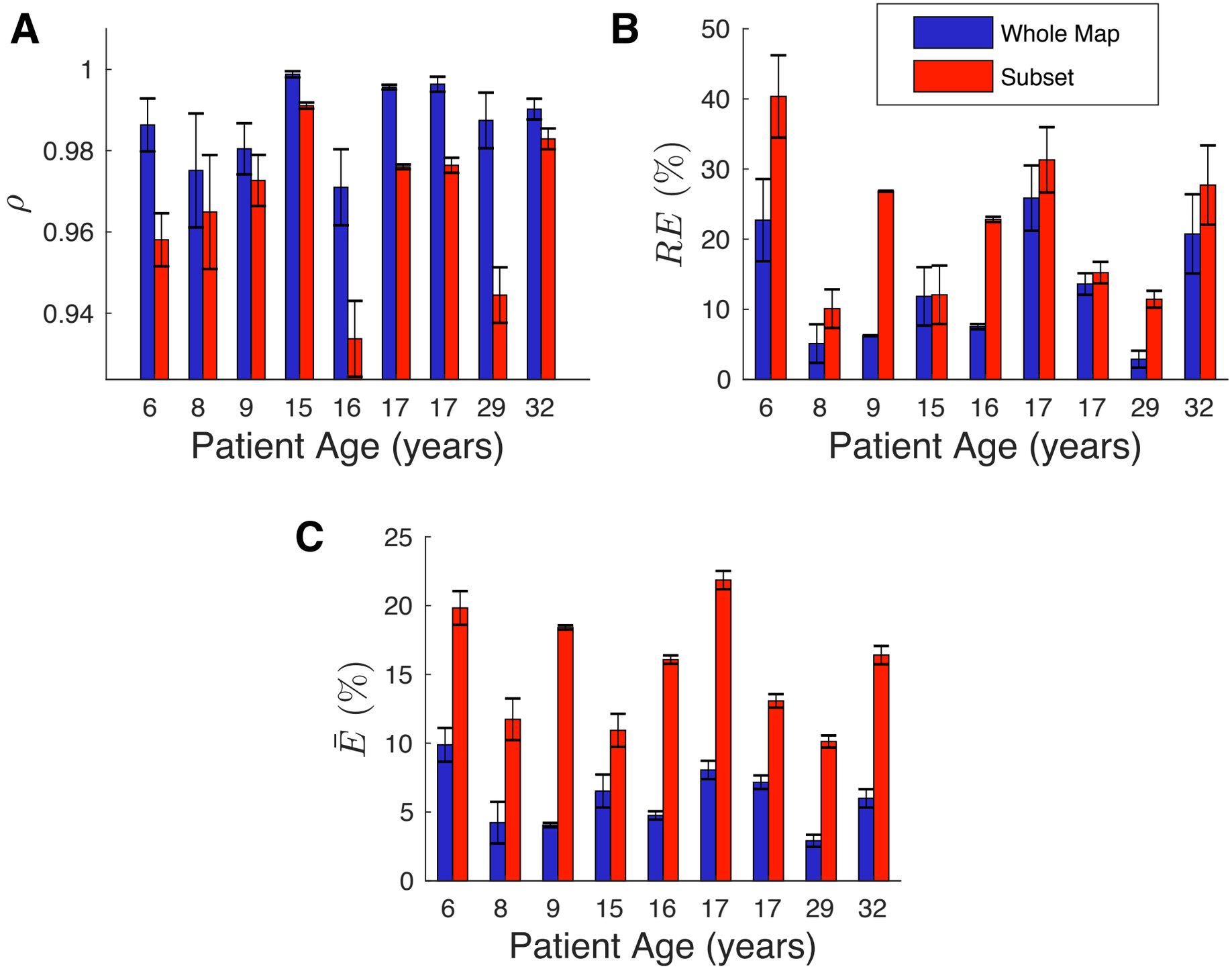
Back

Record ICD Surface Potentials During Device Implantation and Testing

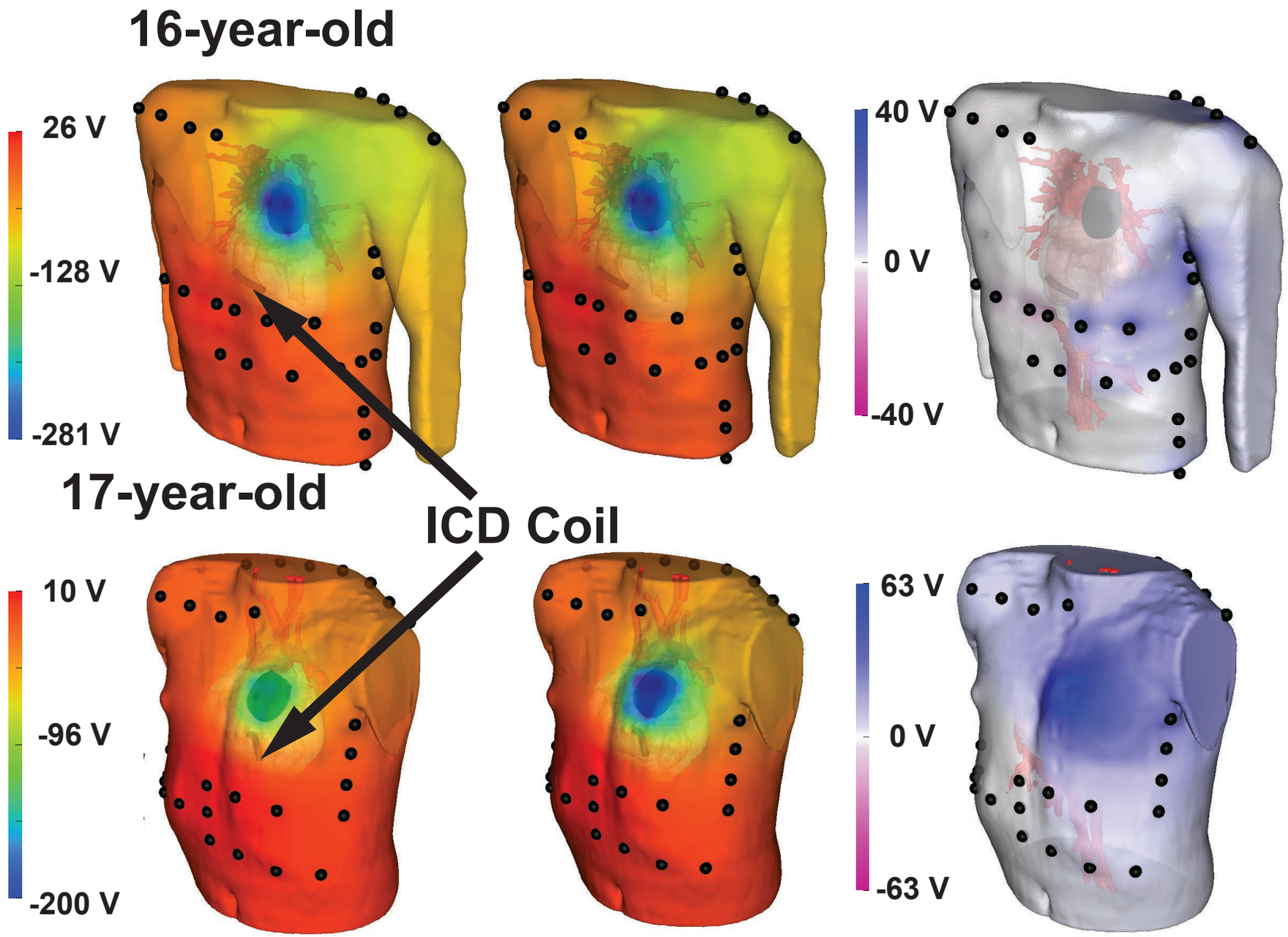




Error Metrics



Potential Field Comparison



Compare DFTs

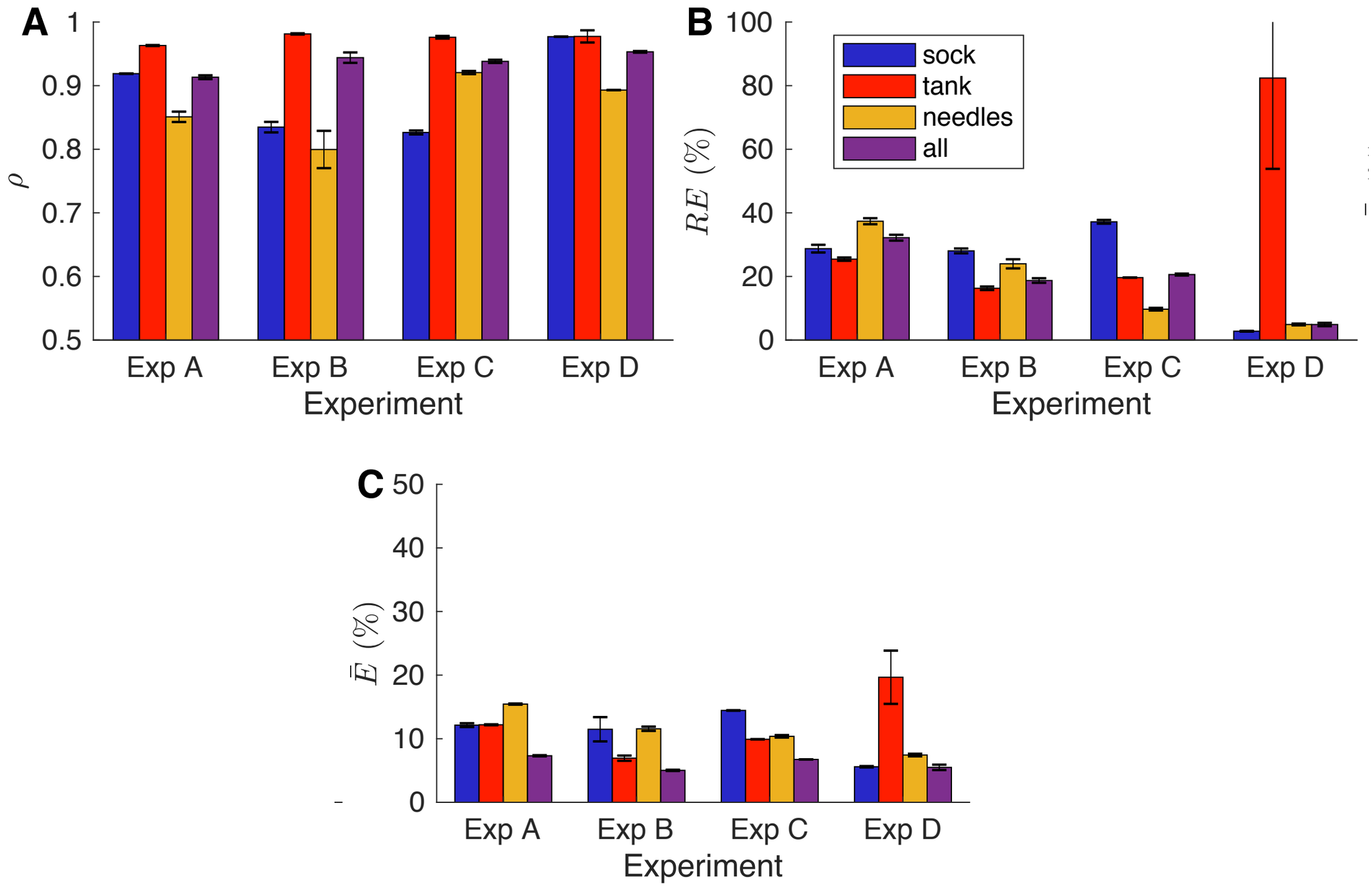
Subject age	Empirical DFT	Predicted DFT
6 years	0 – 3 J	2.7 J
8 years	10 – 15 J	8.31 J
9 years	10 – 15 J	14.5 J
15 years	3 – 5 J	5.2 J
16 years	14.6 – 20.7 J	20 J
17 years	5 – 10 J	19.9 J
17 years	20 – 25 J	26.8 J
29 years	15 – 20 J	18 J
32 years	10 – 12 J	12.9 J

LLS and BS Estimation can be effectively applied to defibrillator potentials

Simulation accurately predicts BSPM

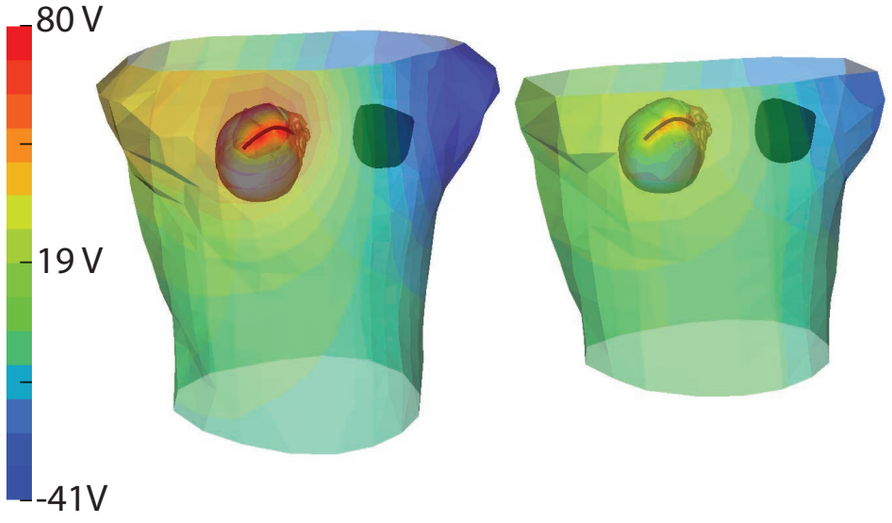
Simulation accurately predicts DFTs in most cases

Error Metrics



Potential Comparison

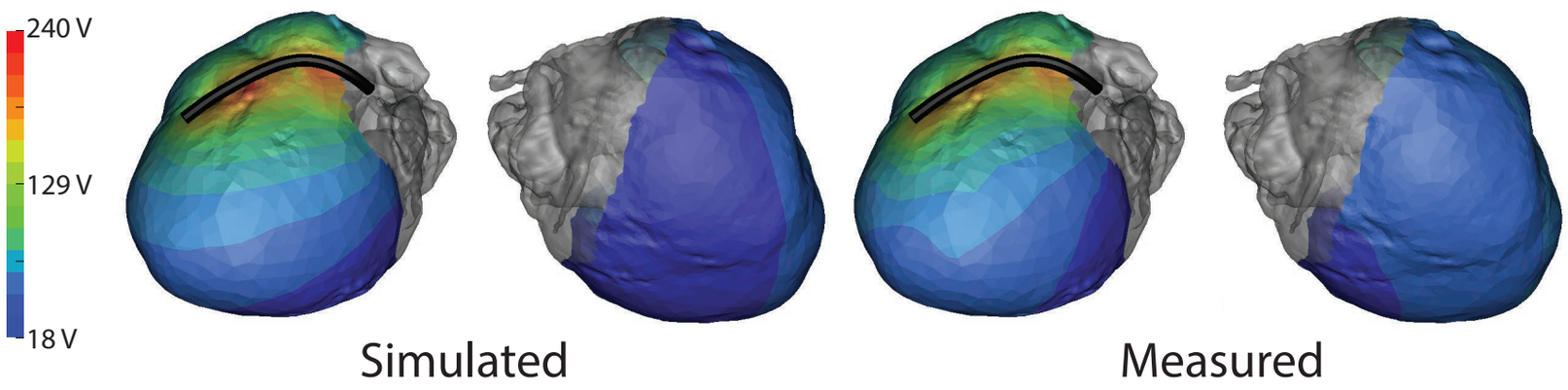
Exp D (10 J)



Simulated

Measured

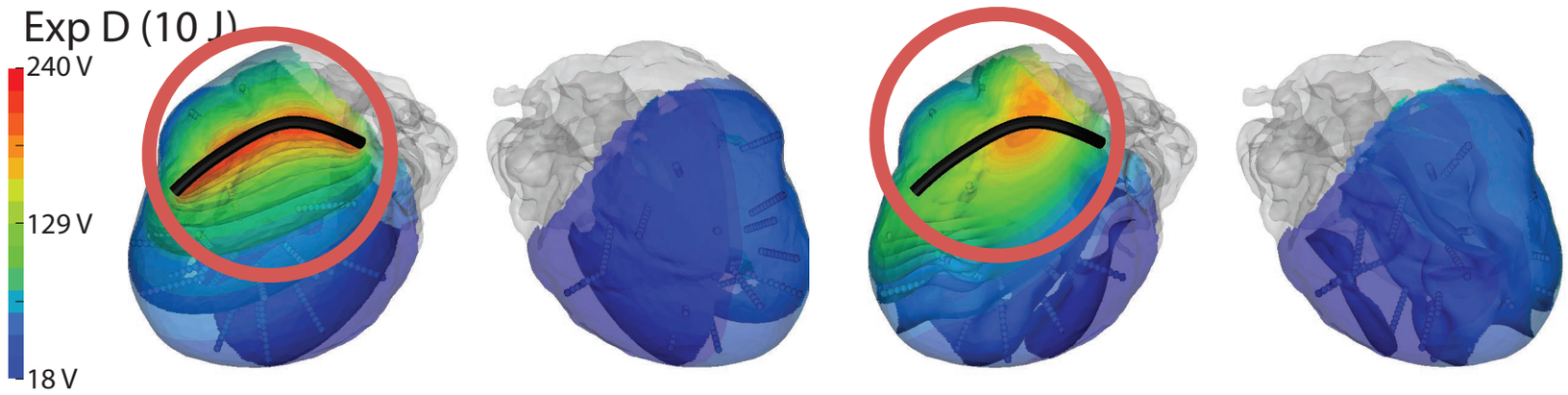
Exp D (10 J)



Simulated

Measured

Exp D (10 J)



Simulated

Measured

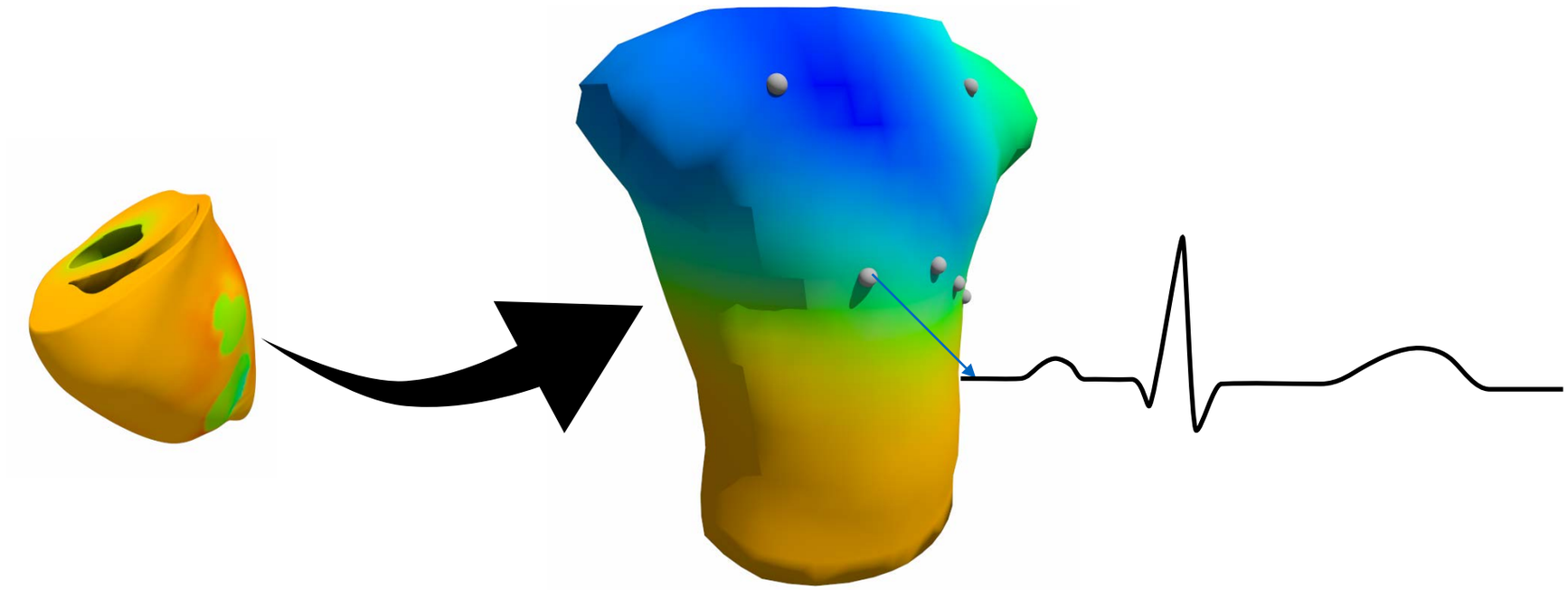
Proof of concept for measuring within myocardium for validation of simulation

Low variation over multiple shocks shows stability of the preparation

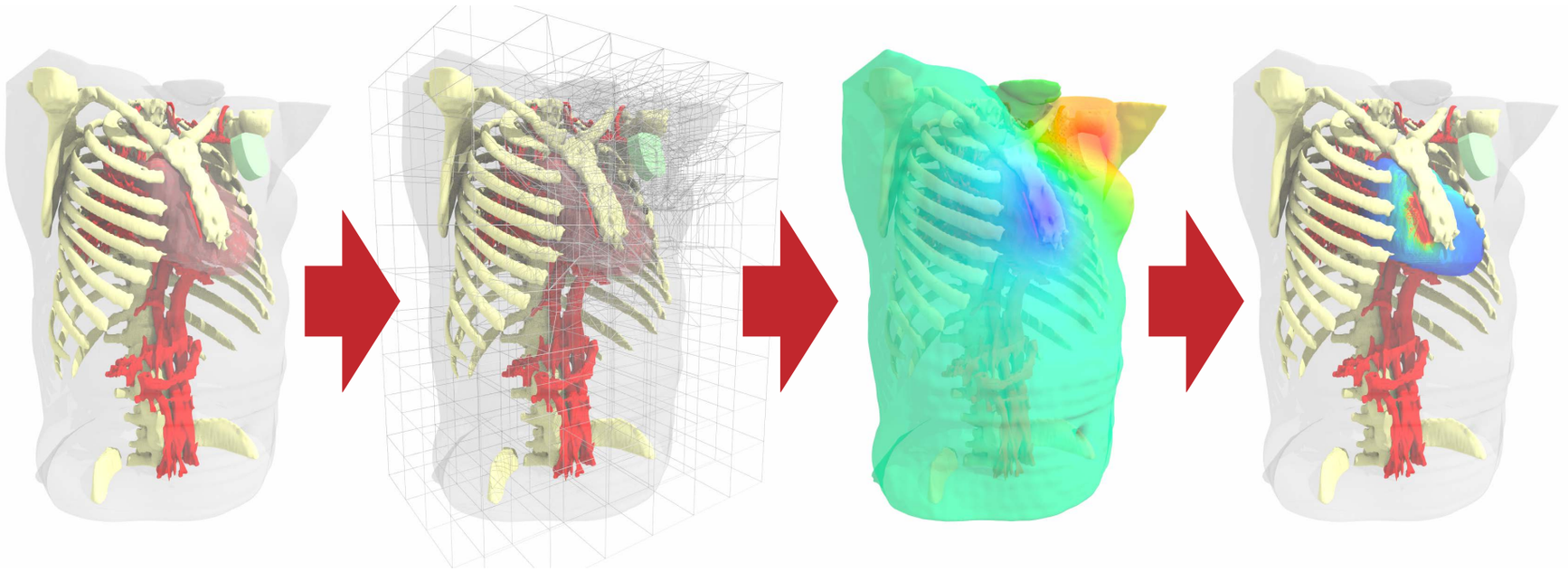
Adequate needle sampling remains a challenge

Improved Validation of Two Pipelines

ECG Forward Simulation

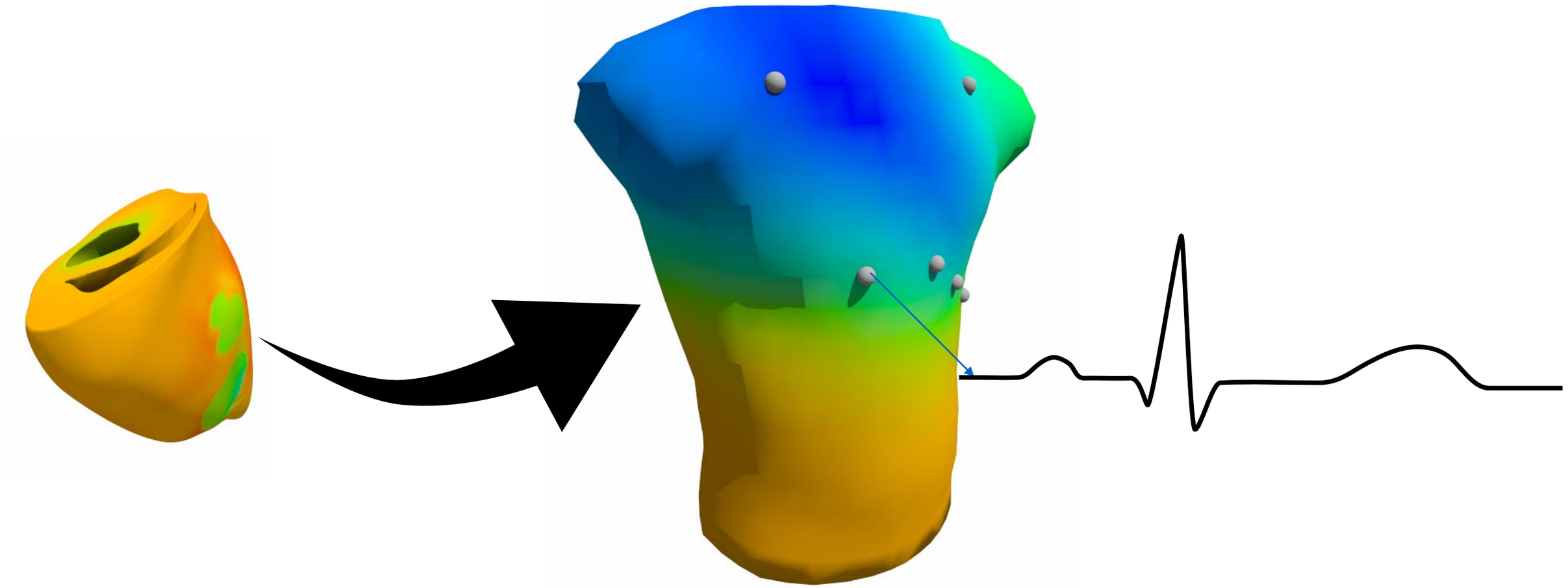


Defibrillation Simulation



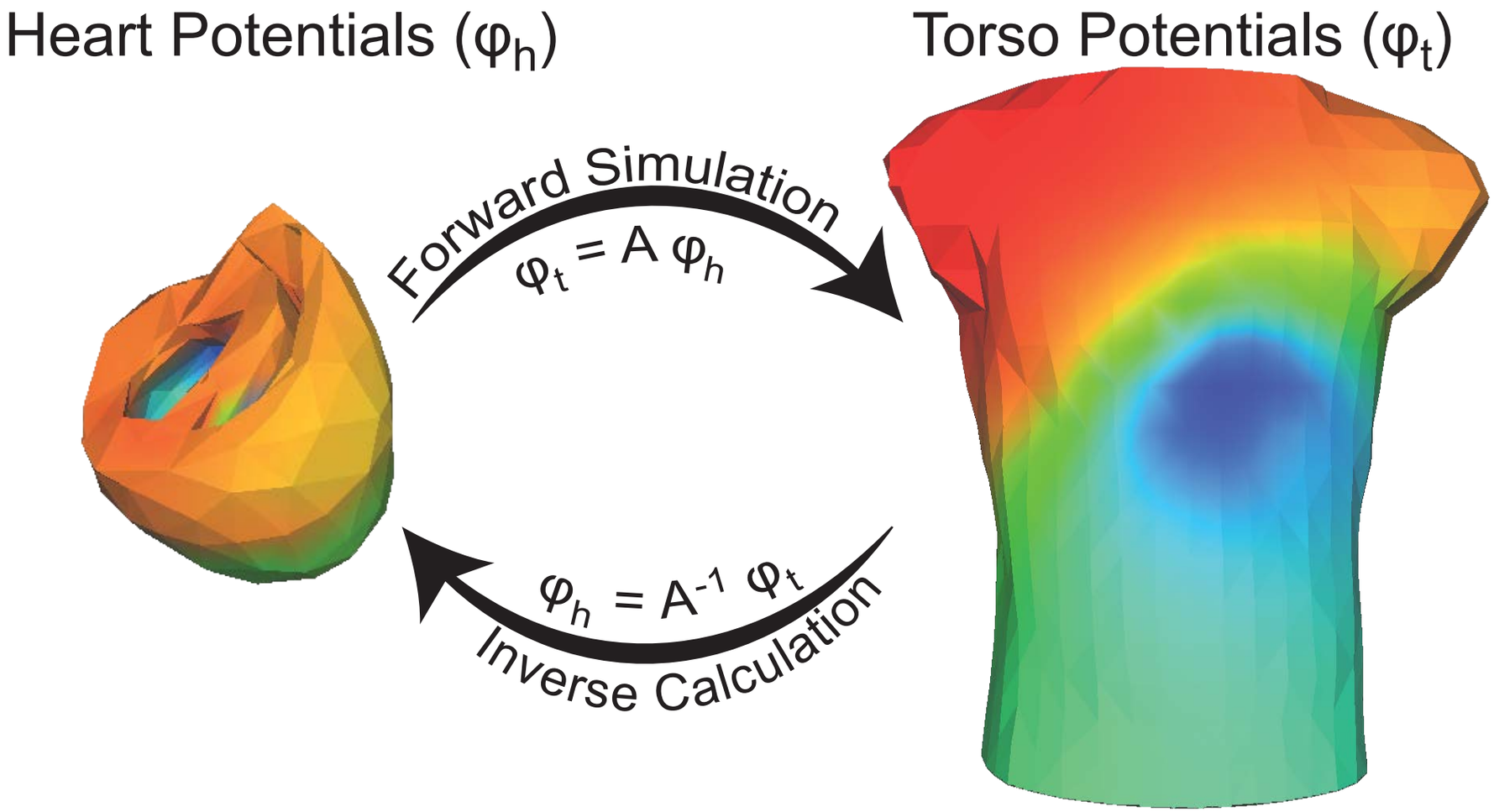
What did we learn?

ECG Forward Simulation

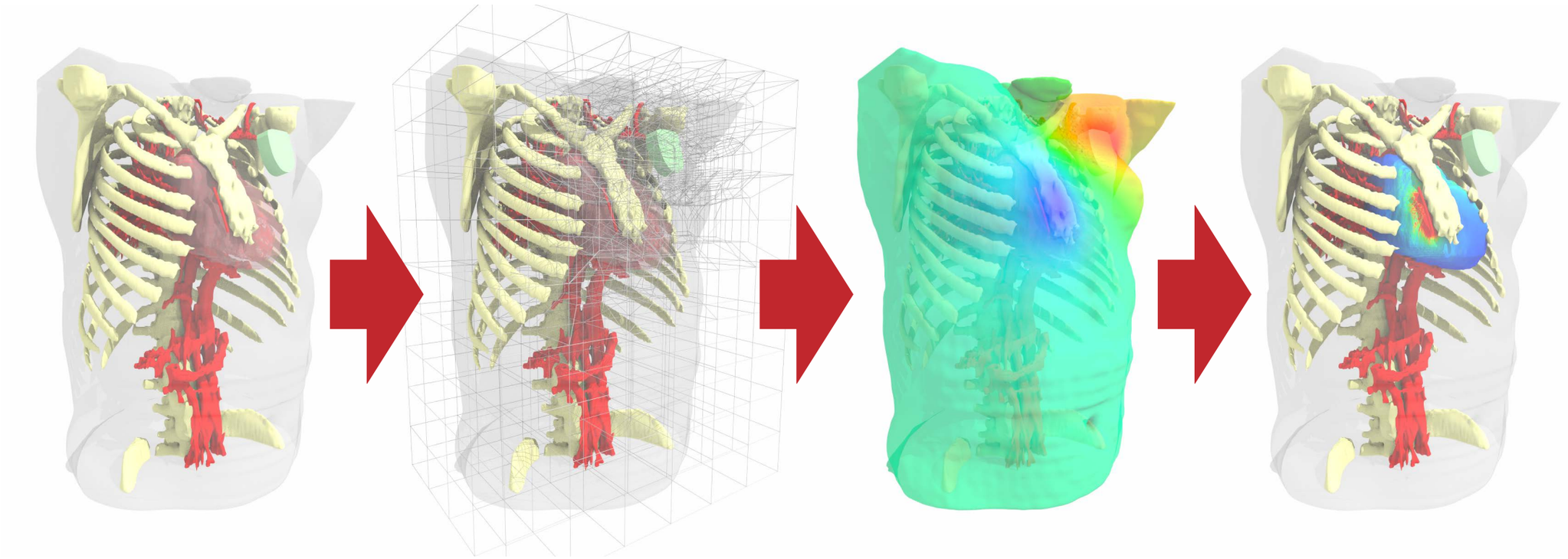


Better Source Representation
More Accurate Predictions

Improve ECGImaging



Defibrillation

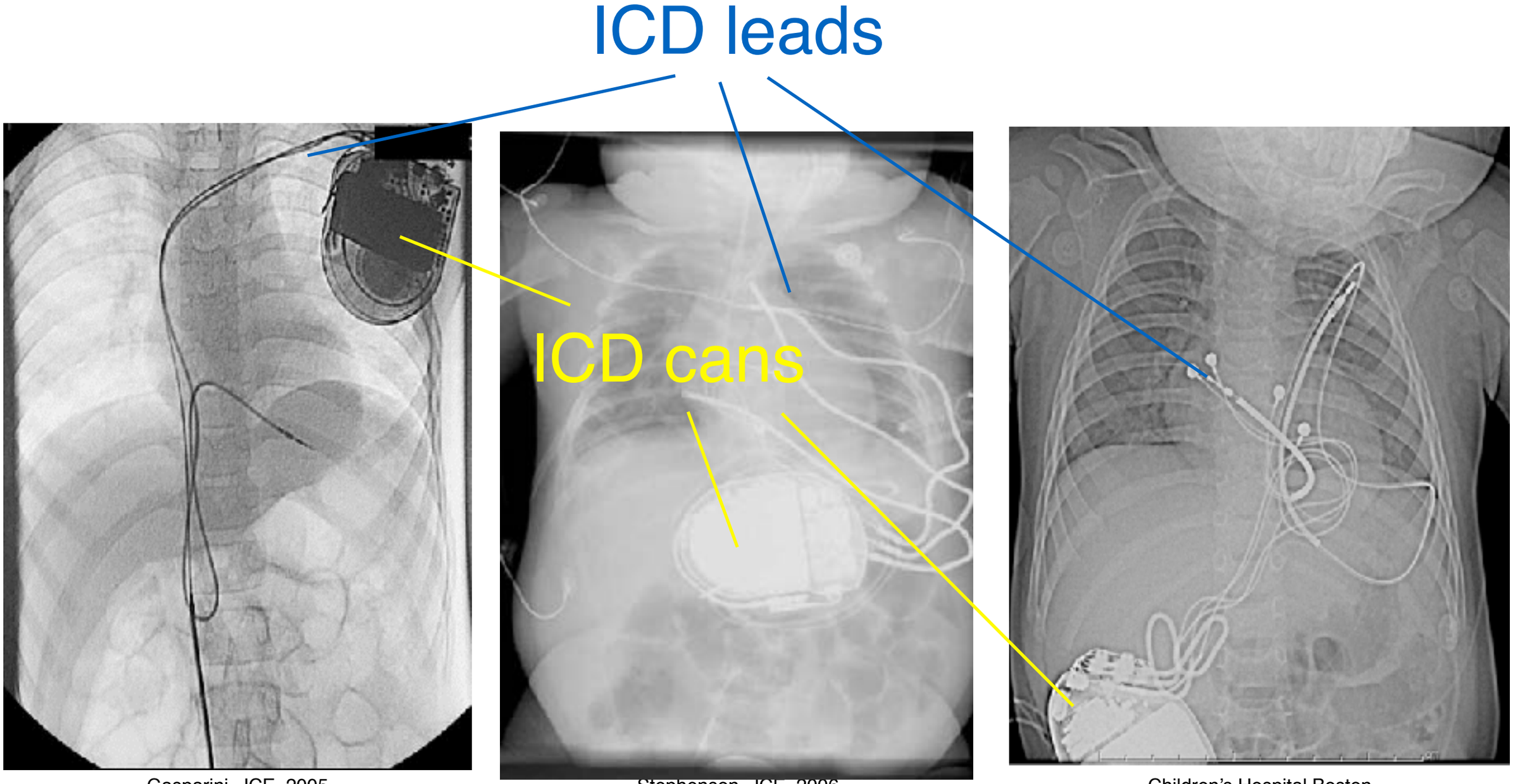


Pioneered new validation approaches

Showed accuracy: potentials and DFTs

Improved confidence in its use

Pediatric Defibrillation



Gasparini, JCE, 2005

Stephenson, JCE, 2006

Children's Hospital Boston

Guide ICD Placements in Children

Predictive Medicine

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Advisor: Rob MacLeod

Lab Members:

- Jeroen Stinstra
- Darrell Swenson
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- Kedar Aras
- Brett Burton
- Moritz Dannhauer
- Wilson Good
- Karli Gillette
- Brian Zenger
- Jake Bergquist

Committee:

- Chris Johnson
- Ed Hsu
- Frank Sachse
- Thomas Pilcher

Developer Staff:

- Ayla Khan
- Dan White
- Jonathan Bronson
- Ally Warner
- Mark Dewey

Collaborators:

- Dana Brooks
- Jaume Coll-Font
- Matt Jolley
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List of Publications

- Measuring Defibrillator Surface Potentials: The Validation of Predictive Defibrillation Computer Model Jess Tate, Jeroen Stinstra, Thomas Pilcher, Ahrash Poursaid, Matthew Jolley, Elizabeth Saarel, John Triedman, and Rob MacLeod. Computers in Biology and Medicine, Symposium on Quantitative Cardiology. In press
- Reducing Error in ECG Forward Simulations with Improved Source Sampling Jess D. Tate, Karli K. Gillette, Brett M. Burton, Wilson W. Good, Jaume Coll-Font, Dana H. Brooks, and Rob S. MacLeod. Frontiers in Physiology - Electrocardiographic Imaging research topic. In press

Second Author Journal Papers

- Finite element modeling of subcutaneous implantable defibrillator electrodes in an adult torso Matthew Jolley, Jeroen Stinstra, Jess Tate, Steve Pieper, Rob MacLeod, Larry Chu, Paul Wang, John K. Triedman. Heart Rythm 7(5):692-698, 2010
- Experimental Data and Geometric Analysis Repository—EDGAR Kedar Aras, Wilson Good, Jess Tate, Brett Burton, Dana Brooks, Jaume Coll-Font, Olaf Doessel, Walther Schulze, Danila Potyagaylo, Linwei Wang, Peter van Dam, Rob MacLeod. Journal of Electrocardiology. doi:10.1016/j.jelectrocard.2015.08.008. 2015
- PFEIFER: Preprocessing Framework for Electrograms Intermittently Fiducialized from Experimental Recordings Anton Rodenhauser, Wilson W Good, Brian Zenger, Jess Tate, Kedar Aras, Brett Burton, Rob S MacLeod. The Journal of Open Source Software 2015.
- A Framework for Image-Based Modeling of Acute Myocardial Ischemia Using Intramurally Recorded Extracellular Potentials Brett M Burton, Kedar K Aras, Wilson W Good, Jess D Tate, Brian Zenger, Rob S MacLeod. Annals of biomedical engineering 2018
- Image-Based Modeling of Acute Myocardial Ischemia Using Experimentally Derived Ischemic Zone Source Representations BM Burton, KK Aras, WW Good, JD Tate, B Zenger, RS MacLeod. Journal of Electrocardiology 2018

First Author Conference Papers

- Measuring Implantable Cardioverter Defibrillators (ICDs) during Implantation Surgery: Verification of a Simulation JD Tate, JG Stinstra, TA Pilcher, RS MacLeod. Computers in Cardiology 2009.
- Measurement of Defibrillator Surface Potentials for Simulation Verification Jess Tate, Jeroen Stinstra, Thomas Pilcher, Rob MacLeod. Computers in Cardiology 2010.
- Measuring Defibrillator Surface Potentials for Simulation Verification Jess Tate, Jeroen Stinstra, Thomas Pilcher, Ahrash Poursaid, Elizabeth Saarel, and Rob MacLeod. Conference of the IEEE EMBS 2011.
- Verification of a Defibrillation Simulation Using Internal Electric Fields in a Human Shaped Phantom Jess Tate, Thomas Pilcher, Kedar Aras, Brett Burton, Rob MacLeod. Computers in Cardiology 2014.
- Analyzing Source Sampling to Reduce Error in ECG Forward Simulations Jess Tate, Karli Gillette, Brett Burton, Wilson Good, Jaume Coll-Font, Dana Brooks, Rob MacLeod. Computers in Cardiology 2017

Second Author Conference Papers

- The Role of Volume Conductivities in Simulation of Implantable Defibrillators JG Stinstra, MA Jolley, JD Tate, DH Brooks, JK Triedman, and RS MacLeod. Computers in Cardiology 2008.
- The Effect of Non-Conformal Finite Element Boundaries on Electrical Monodomain and Bidomain SimulationsDarrell Swenson, Joshua Levine, Zhisong Fu, Jess Tate, Rob MacLeod. Computers in Cardiology 2010.
- A Toolkit for Forward/Inverse Problems in Electrocardiography within the SCIRun Problem Solving EnvironmentBrett Burton, Jess Tate, Burak Erem, Darrell Swenson, Dafang Wang, Michael Steffen, Dana Brooks, Peter van Dam, Rob Macleod. Conference of the IEEE EMBS 2011.
- New Additions to the Toolkit for Forward/Inverse Problems in Electrocardiography within the SCIRun Problem Solving Environment Jaume Coll-Font, Brett Burton, Jess Tate, Burak Erem, Darrel Swenson, Dafang Wang, Dana H Brooks, Peter van Dam, Rob S Macleod. Computing in Cardiology 2014.
- Generation of combined-modality tetrahedral meshes Karli Gillette, Jess Tate, Brianna Kindall, Peter Van Dam, Eugene Kholmovski, Rob S MacLeod. Computers in Cardiology 2015.
- Temporal dilation of animal cardiac recordings registered to human torso geometries Karli Gillette, Jess Tate, Brianna Kindall, Wilson Good, Jeff Wilkinson, Narendra Simha, Rob MacLeod. Computers in Cardiology 2016
- The consortium for electrocardiographic imaging Jaume Coll-Font, Jwala Dhamala, Danila Potyagaylo, Walther HW Schulze, Jess D Tate, Maria S Guillem, Peter Van Dam, Olaf Dossel, Dana H Brooks, Rob S Macleod. Computers in Cardiology 2016.
- Overcoming Barriers to Quantification and Comparison of Electrocardiographic Imaging Methods: A Community-Based Approach Sandesh Ghimire, Jwala Dhamala, Jaume Coll-Font, Jess D Tate, Maria S Guillem, Dana H Brooks, Rob S MacLeod, Linwei Wang. Computers in Cardiology 2017.