3D MR image analysis of the developing human fetal brain from in utero clinical studies

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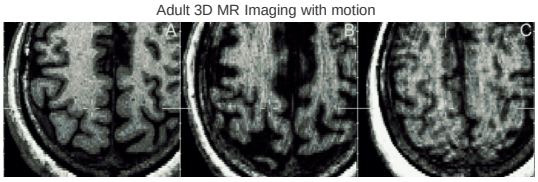
Fetal Brain Imaging: Mapping Normal Development and detecting early abnormality

- Standard Clinical Tool: Ultrasound imaging
  - Noninvasive, relatively low cost, fast
  - Reveals main tissue boundaries
  - But: Cannot easily delineate soft tissue characteristics
- Fetal MR imaging
  - Recently emerged as a safe tool to image the developing fetus
  - Patients referred after Ultrasound scan picks up abnormality
  - MRI Provides high resolution and tissue contrast
  - Detects fine scale structure, subtle tissue abnormalities
    eg grey/white matter, lesions

Fetal MRI vs Adult MRI

- Adults (generally) can be told to remain still during an MRI study
- Fetuses move and (generally) respond less well to requests than adults
  - Smaller fetuses have more space and move more
- Typical 3D adult structural MRI scans take 2-12min
  - Motion artifacts occur if head motion during study
- To acquire full 3D MR image during motion without significant artifact:
  - whole study would have to take fraction of a second

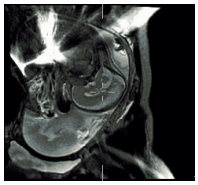
Adult 3D MR Imaging with motion



Approaches to Clinical Fetal Imaging

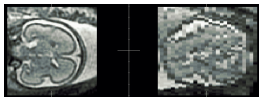
- Faster 3D MR Imaging techniques available:
  - Eg 3D EPI
  - But: These do not provide clinically optimal tissue contrast AND still not fast enough
- Motion correction for 3D imaging:
  - Acquisition (navigator echoes) and retrospective K-space correction techniques
  - Generally assume rigid object surrounded by air
  - Fetus: rigid head surrounded by deforming tissues
- Solution: Current Clinical Fetal Imaging -> 2D multi slice
  - Each slice takes < 0.5 sec

Example Clinical Images

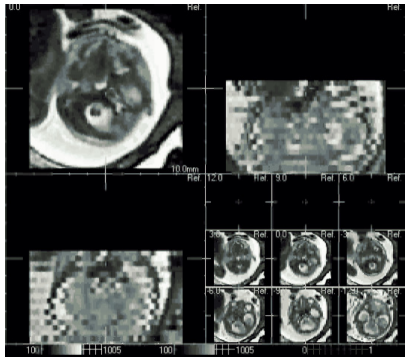


- T2W Multi Slice
  - Single shot fast spin echo (SSFSE; 2D)
  - T2 weighted (½ sec/frame)
  - TR = 6000 ms, TE = 90 ms
  - Approximately 0.5x0.5x3 mm^3 voxel dimension
  - 15~30 slices in each stack
- Anisotropic resolution with thick slices
- Fetal motion during study:
  - Fetal motion commonly occurs between slices,
  - Set of 2D slices not consistent geometrically in 3D,
  - Missing portions of the underlying anatomy in a given stack.
- Intensity distortion between scans:
  - Inhomogeneous sensitivity of the coilsover FOV
  - Fluid/Air boundaries in Maternal Anatomy:
    - Distortion because:Susceptibility and Motion

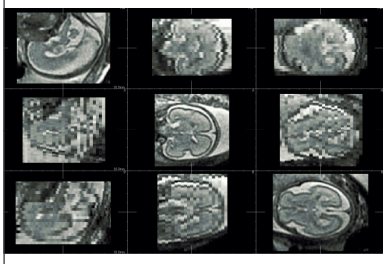
coronal slice slice stack



Fetal Motion in Multi Slice SSFSE



Aim



Single
High resolution
volume

- We would like to Compound several acquisitions,
- We need to Correct fetal motion,
- and Correct relative intensity distortions.

Reconstruction Based Slice Alignment

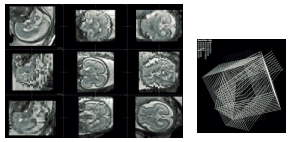
Francois Rousseau, PhD
Postdoc 2003-2005

F. Rousseau, O. A. Glenn, **B. Iordanova**, **C. E. Rodriguez-Carranza**, D. Vigneron, J. A. Barkovich, and **C. Studholme**, "A novel approach to high resolution fetal brain MR imaging," in Medical Image Computing and Computer-Assisted Intervention, LNCS, vol. 3749, pp. 548-555, October 2005.

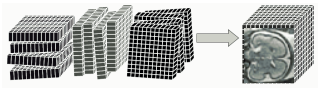
F. Rousseau, O. A. Glenn, **B. Iordanova**, **C. E. Rodriguez-Carranza**, D. B. Vigneron, A. J. Barkovich, and **C. Studholme**, "Registration-based approach for reconstruction of high-resolution in utero MR brain images," Acad. Radiol., vol. 13, no. 9, pp. 1072-1081, September 2006.

Reconstruction Based Slice Motion Correction

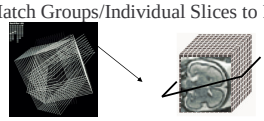
1. Initial Global Rigid Stack Alignment
   - Ignoring individual slice motion



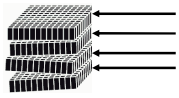
2. Form a single Image Volume on Regular rectangular lattice
   - Using an reconstruction method (Scattered Data Interpolation)



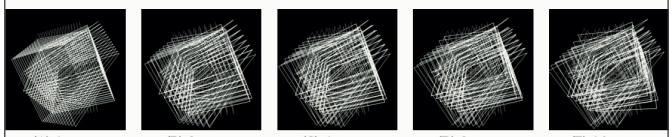
3. Match Groups/Individual Slices to Reconstructed Volume



Hierarchical Slice Registration: Multi-resolution Accounting for Spatio-Temporal Order of Acquisition



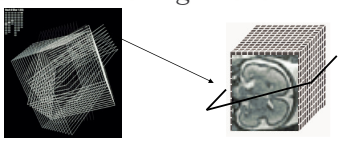
Spatially: Odd slices in stack acquired
Then even slices are acquired



(A) 1 group (B) 2 groups (C) 4 groups (D) 8 groups (E) 16 groups

- A Stack Level Registration
- B Interleave Level Registration
- C-E interleaves further divided into two, until individual slice based alignment

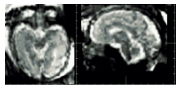
Slice to Volume Alignment



- Maximize Similarity Measure between 3D volume and slice:
  - Normalized Mutual Information of image intensities
    h(A), h(B) : marginal entropies, h(A,B) : joint entropy

$$NMI(A,B) = \frac{h(A)+h(B)}{h(A,B)}$$

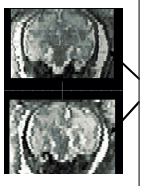
- 'Multi-modality' criteria that allows differences in structure and contrast



Reconstructed Volume
Before slice alignment

- 3D Rigid Transformations:
  Full 3D fetal head motion allowed between slices

Volume Reconstruction

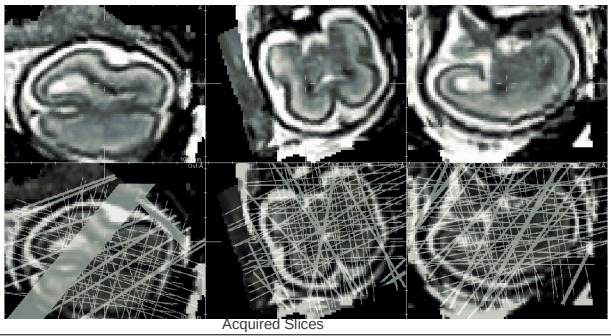


- 3D Reconstruction from Scattered Data:
  - Local neighborhood approach : Anisotropic Gaussian Kernel (orientated with the slices).
- Relative Intensity Correction between slices
  - Remove Slowly varying (spatial) differences in image contrast
- Algorithm :
  - One image stack is chosen as a reference,
  - Assume: Multiplicative distortion, varying smoothly over the image
  - Correction of a stack to reference is estimated from low pass filtered images :

$$\beta_i(x) = a_i * \frac{\mathcal{G}(IR(x))}{\mathcal{G}(I^i_{LR}(x))} \quad with \quad a_i = \frac{\sum_x I^i_{LR}(x)}{\sum_x I^i_{LR}(x)\frac{\mathcal{G}(IR(x))}{\mathcal{G}(I^i_{LR}(x))}}$$

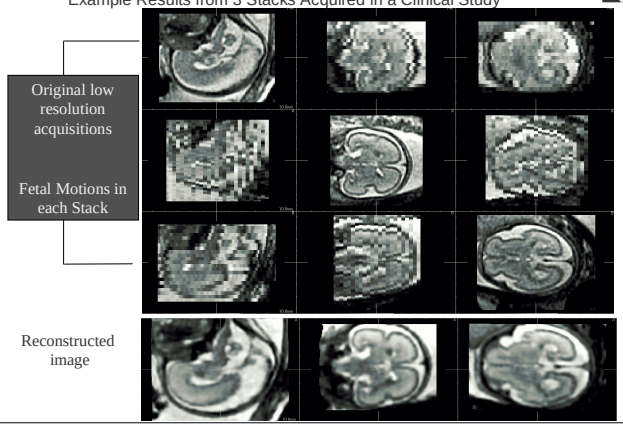
$$I^i_{LR}(x) = \beta_i(x) I^i_{LR}(x)$$

Reconstruction from Randomly Sampled Anatomy



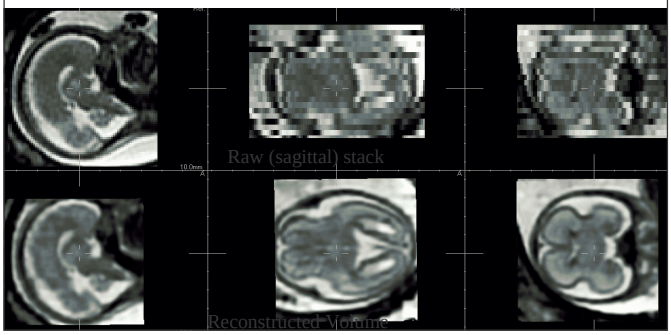
Acquired Slices

Example Results from 3 Stacks Acquired in a Clinical Study

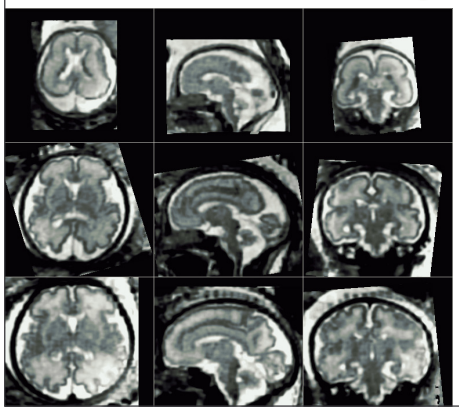


Example Younger Fetus with significant motion

- **Smooth cortex -> few registration features**
- **Large Step Motion during part of study**



Results on clinical data (tracking development)

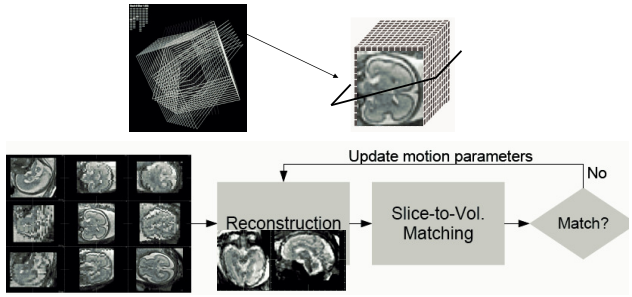


Intersection Based Slice Alignment

Kio Kim PhD

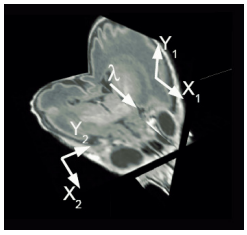
K. Kim, **M. F. Hansen**, **P. A. Habas**, F. Rousseau, O. A. Glenn, A. J. Barkovich, and **C. Studholme**, "Intersection-based registration of slice stacks to form 3D images of the human fetal brain," in Proc. 5th IEEE International Symposium on Biomedical Imaging: From Nano to Macro, pp. 1167-1170, May 2008.

Slice to Volume Alignment



- Two Step Process: 3D reconstruction and slice-to-volume alignment
- No global or even local convergence guaranteed
- Final registration accuracy limited by blurring in reconstruction

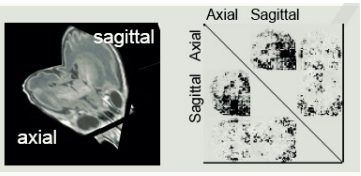
Intersection Based Slice Alignment
Consider Direct Match of Any Pair of Slices



Dissimilarity is measured directly by sum of squared difference in intensity along intersection

$$\mathcal{D}_{ij} \equiv \frac{1}{|I_i \bigcap I_j|} \int_{I_i \bigcap I_j} ||I_i(\mathbf{x}_{ij}(\lambda;\theta_i,\theta_j)) - I_j(\mathbf{x}_{ji}(\lambda;\theta_j,\theta_i))||^2 d\lambda$$

I_i: The i-th image slice
θ_i: Motion parameters of the i-th image slice
$\mathbf{x}_{ij}$: Position vector of the intersection segment in slice i against slice j



∂D w.r.t. X-displacements of an axial slice is negatively correlated to that of a sagittal slice.

Relationship between slices: Each slice Influences the location of all others

- Location of each slice influences match with all other intersecting slices

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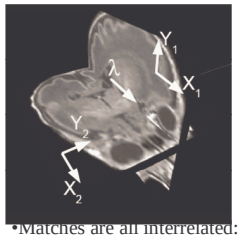

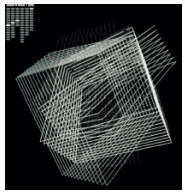

- Matches are all interrelated:
  Need to resolve relative collective alignment simultaneously

Relationship between slices: Each slice Influences the location of all others

$$\mathcal{D}_{ij} \equiv \frac{1}{|I_i \bigcap I_j|} \int_{I_i \bigcap I_j} ||I_i(\mathbf{x}_{ij}(\lambda;\theta_i,\theta_j)) - I_j(\mathbf{x}_{ji}(\lambda;\theta_j,\theta_i))||^2 d\lambda$$

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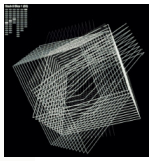
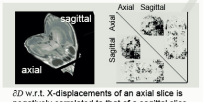


Iterative Parameter Update Used:

$$\Theta^{k+1} = \Theta^k - [2(\nabla_\Theta D)^\top \nabla_\Theta D + \alpha I]^{-1} \nabla_\Theta E$$

$$\frac{\partial D}{\partial \theta^t} = \sum_{i,j} \left(\frac{\partial \mathbf{x}_{ij}}{\partial \theta^t} \right)^\top \nabla_{\mathbf{x}_{ij}} D$$

$D(\Theta)$: Lexicographical representation of differences between all intersection profiles, given the motion parameters Θ



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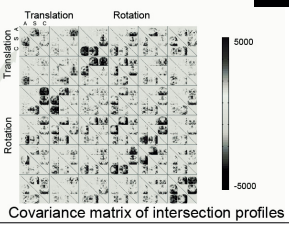
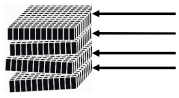
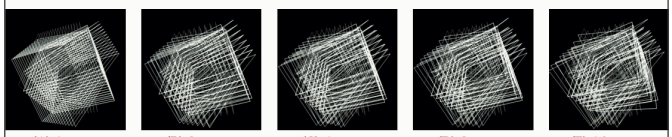


Covariance matrix of intersection profiles

Hierarchical Slice Registration: Multi-resolution Accounting for Spatio-Temporal Order of Acquisition



Spatially: Odd slices in stack acquired
Then even slices are acquired



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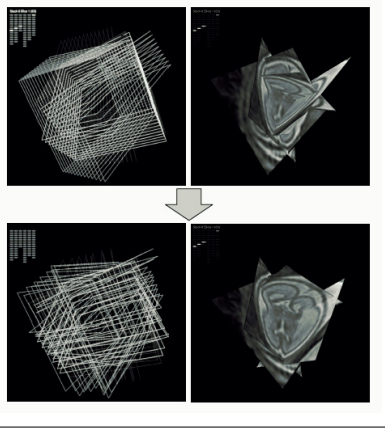
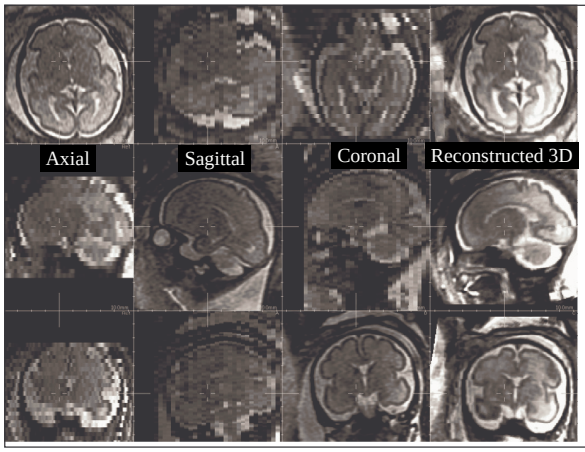
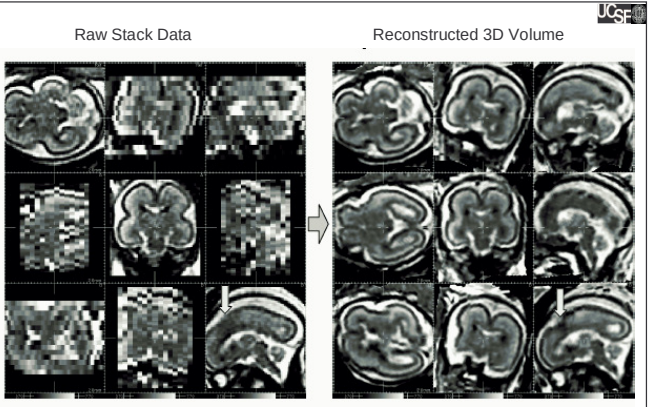
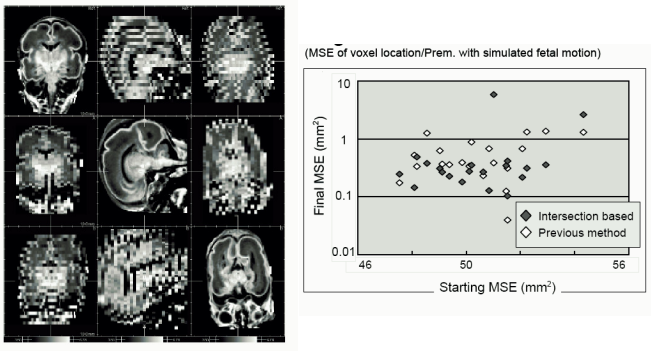


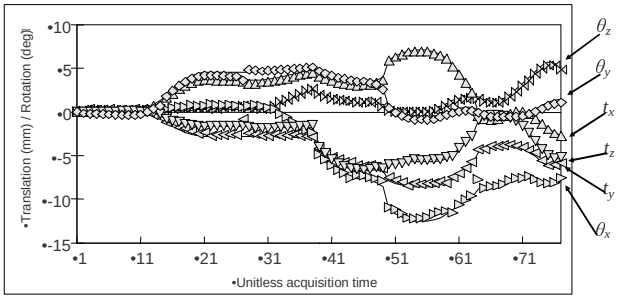




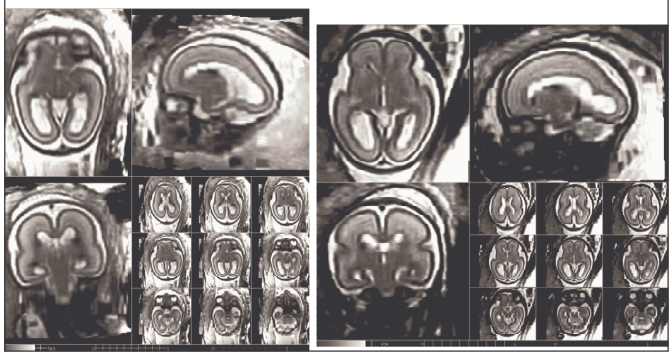
Accuracy Estimation Using Simulated Motion Corrupted 3D Premature Neonatal MRI



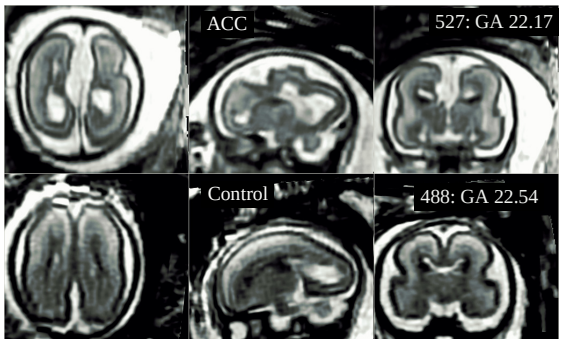
Recovery of Simulated Fetal Trajectory



Ventriculomegaly



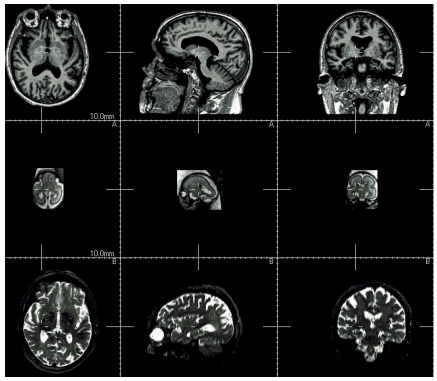
Agenesis of the Corpus Callosum



Segmentation of Developing and Transient Tissue Types in Fetal MRI.
Piotr Habas, PhD

P. A. Habas, **K. Kim**, F. Rousseau, O. A. Glenn, A. J. Barkovich, and **C. Studholme**, "Atlas-based segmentation of the germinal matrix from in utero clinical MRI of the fetal brain," in Medical Image Computing and Computer-Assisted Intervention, LNCS, vol. 5241, part I, pp. 351-358, September 2008.

T2W Fetal MRI

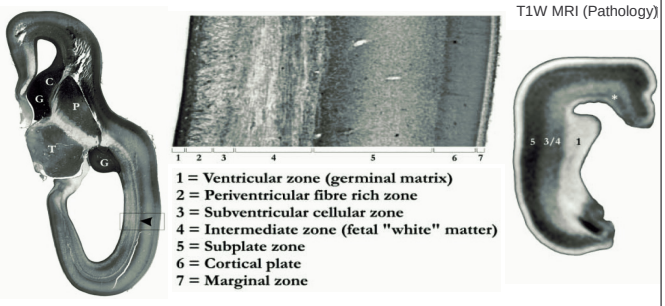


T1W Adult

T2W Fetus
Approx 22W GA

T2W Adult

Laminar organization of the fetal brain



[Kostovic et al, Cerebral Cortex, 2002, 536-544]

Phases in fetal brain development

- 19-26 GA
  - Layers well delineated in all cortical regions.
- 27-30 GA: developmental peak
  - Subplate zone/white matter border becomes less distinct.
- 30+ GA
  - germinal matrix and the subplate zone gradually disappear
- 31-36 GA: subplate dissolution
  - disappears from primary cortical areas
  - very thin around the cortical sulci.

Fetal MRI

Premature Neonate MRI

-> Transient laminar pattern transforms into mature-like structure of the cerebral wall
(cortex, white matter, corona radiata, centrum semi-ovale).

->Different Analysis Approaches Required for different stages

Tissue Contrast in Fetal MRI and the need for Spatial Priors in Segmentation

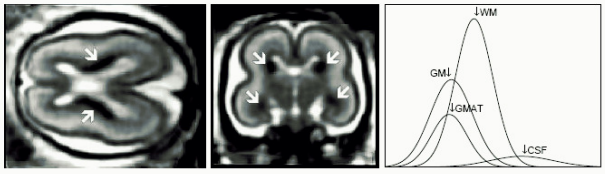
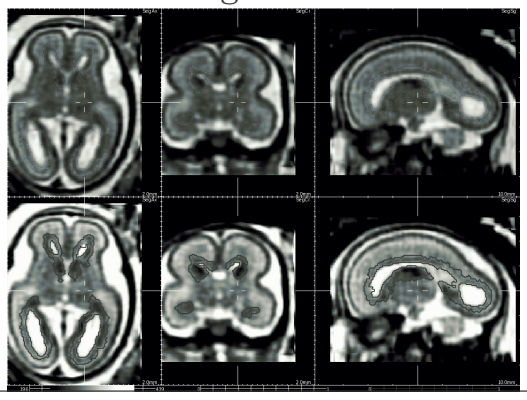
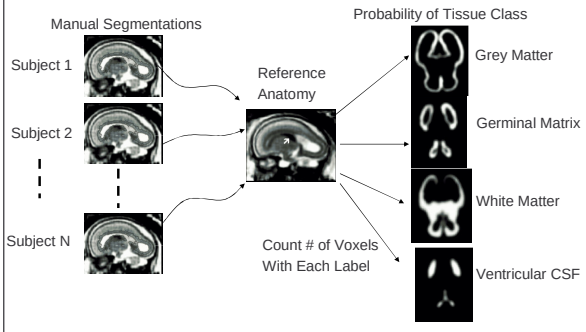


Fig. 1. Axial and coronal views of an MR T2w image with clearly visible hypointense regions of the germinal matrix. Distribution of voxel intensities for grey matter (GM), the germinal matrix (GMAT), white matter (WM), and cerebrospinal fluid (CSF).

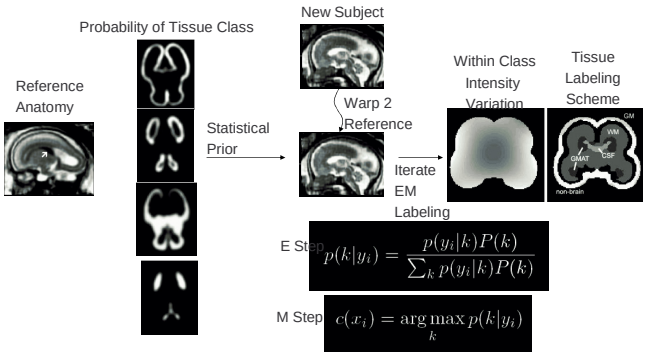
Manual Tracing of Germinal Matrix



Statistical Model of Developing Tissue Distribution



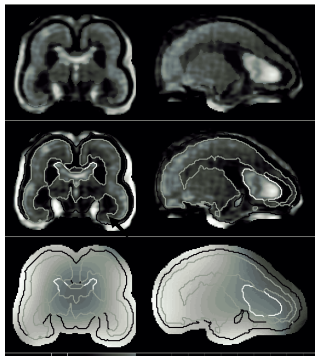
EM Segmentation of Developing and Developed Tissues

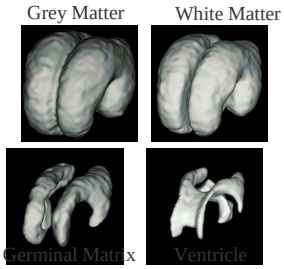


E Step $p(k|y_i) = \frac{p(y_i|k)P(k)}{\sum_k p(y_i|k)P(k)}$

M Step $c(x_i) = \arg\max_k p(k|y_i)$

Example Tissue Labeling

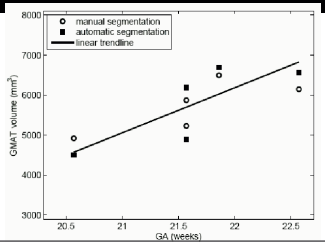




Tissue Volume Validation

Table 1. Volumes of brain tissues (in mm^3) for fetal subjects of different gestational age (GA, in weeks) obtained from automatic and manual segmentation.

Fetus	GA	automatic segmentation				man. seg.	rel. diff.
		CSF	GM	WM	GMAT	GMAT	GMAT
A	20.57	3155	13436	19287	4497	4920	8.6%
B	21.57	2831	13985	19555	4892	5229	6.4%
C	21.57	3588	18543	26549	6186	5872	5.3%
D	21.86	3223	20523	26215	6685	6495	2.9%
E	22.57	3894	18834	25339	6561	6146	6.7%



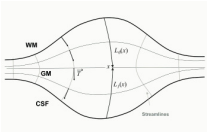
Cortical Thickness Measurements in Fetal MRI

Defining and Measuring Cortical Thickness

Problem of defining a unique measure of thickness!

Addressed in adult image analysis

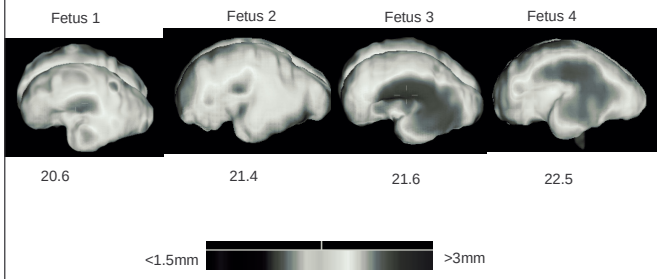
eg [S. E. Jones, B. R. Buchbinder, and I. Aharon, "Three-dimensional mapping of cortical thickness using Laplace's equation," Hum. Brain Mapp. 11(1), pp. 12–32, 2000.]



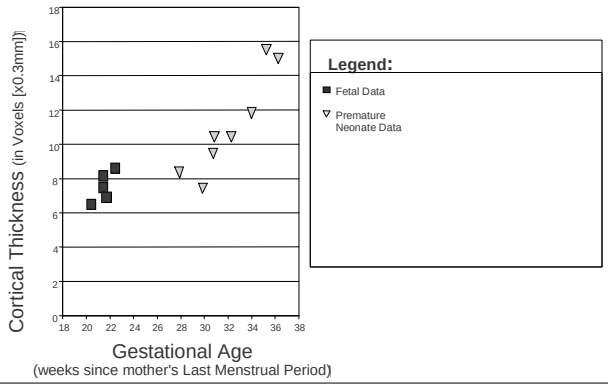
- Thickness defined as the length of a streamline through point "x" in gray matter region
- Streamline defined as trajectory tangent to the normalized gradient (T) of a harmonic scalar

$$\nabla^2 \Psi = \frac{\partial^2 \Psi}{\partial x^2} + \frac{\partial^2 \Psi}{\partial y^2} + \frac{\partial^2 \Psi}{\partial z^2} = 0$$

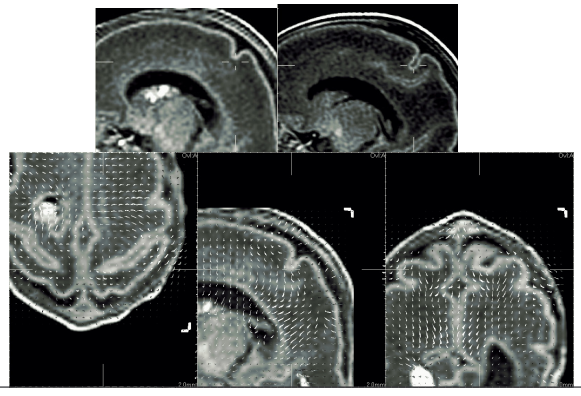
Preliminary Cortical Thickness Results

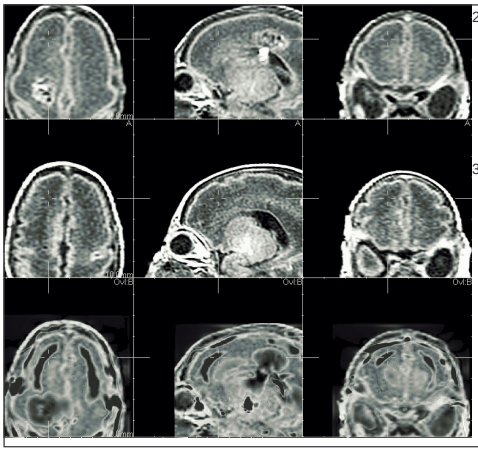


Mean Cortical Thickness vs. Gestational Age



Mapping Patterns of Brain Growth in Premature Babies





Summary

- 3D Fetal Brain Image Analysis is Possible!
- Can Correction Fetal Motion present in Clinical Studies and form a 3D volume image
- Tissue Segmentation techniques can be extended
  - To include transient and developed tissue types
- Cortical Thickness estimation from reconstructed MRI data shows promising results
  - Need to develop models of pattern vs age

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