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Assessment of brain growth in early childhood using non-rigid registration

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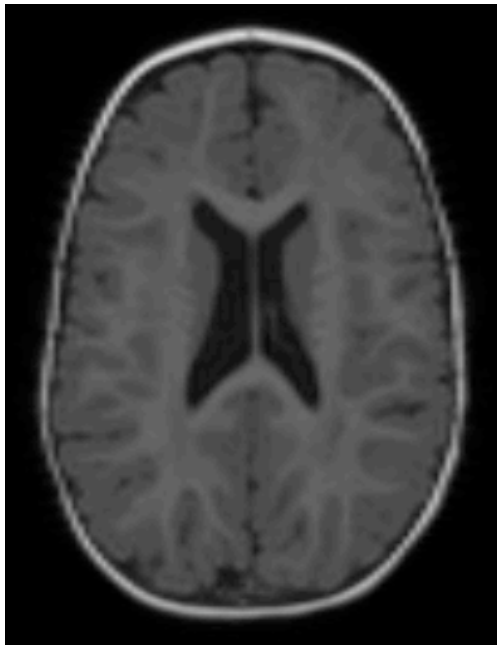
Quantification of brain development

- Most longitudinal studies of brain growth have focused on older children and adolescents.
- However, the majority of brain growth occurs before age 2, much occurring in-utero prior to birth at 40 weeks GA.
- Previous work:
  - Tissue growth models for ages 4 to 20: Giedd, Nat Neurosci. 1999
  - development tracking of particular structures in a group of six children (3 - 15 years): Thompson, Nature 2000.
  - Cortical thickness measurements (5 - 11 years): Sowell et al, J. Neurosci. 2004.
- Other studies have used cross-sectional designs, in which inter-subject variability can add an additional confound (Gilmore, J Neurosci, 2007).

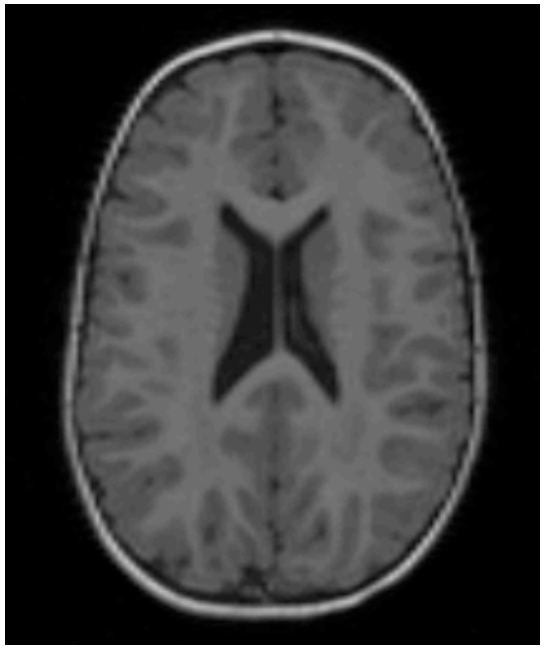
Quantification of brain development

- Quantification of brain development during early childhood
  - Calculation of growth maps
  - Groupwise registration and segmentation
- Quantification of neonatal brain development
  - Segmentation of neonatal MRI
  - Cortical reconstruction of neonatal MRI
  - Cortical registration of longitudinal neonatal MRI
  - Analysis of neonatal diffusion tensor MRI
- Fetal MR imaging
  - Image acquisition and reconstruction

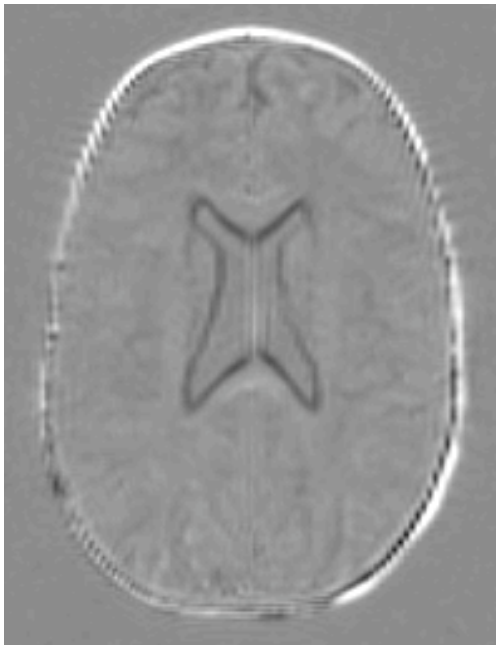
Brain development during early childhood



1 year old

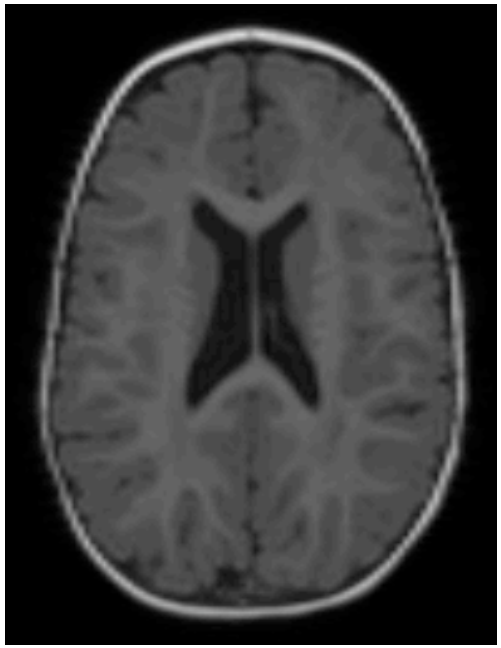


2 year old after
affine registration

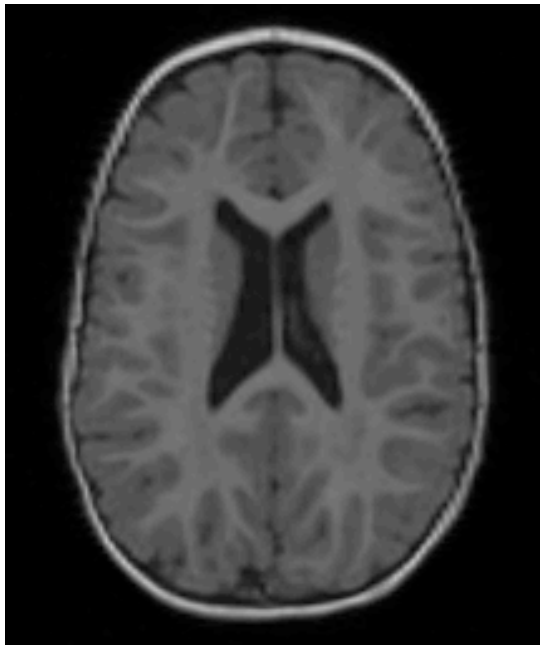


Subtraction after
affine registration

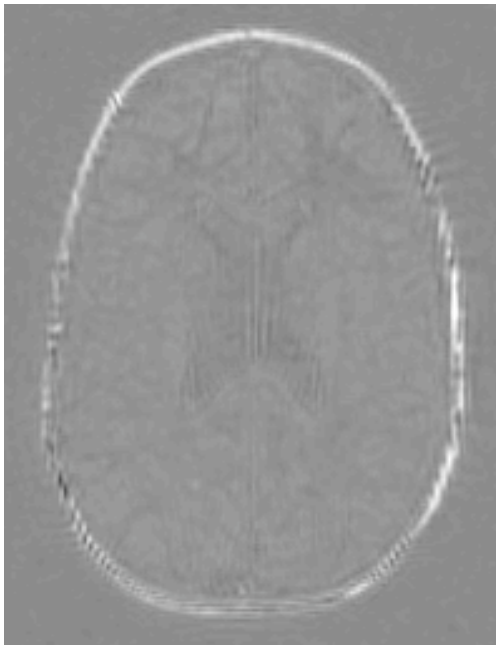
Brain development during early childhood



1 year old

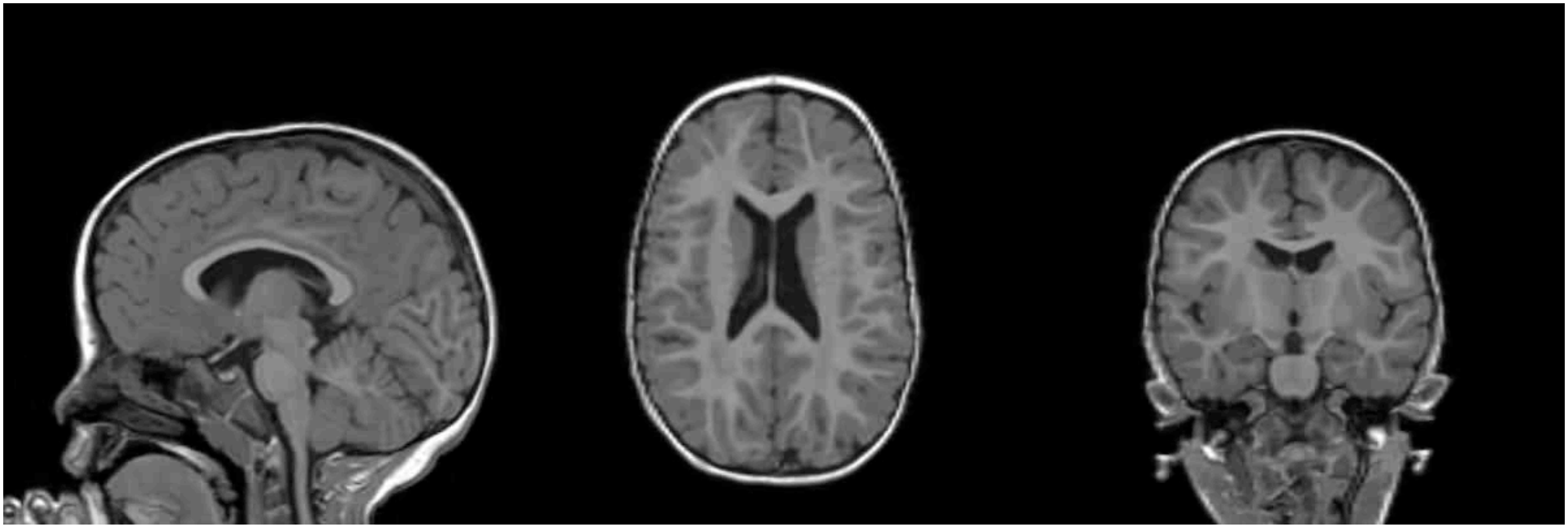


2 year old after
non-rigid registration



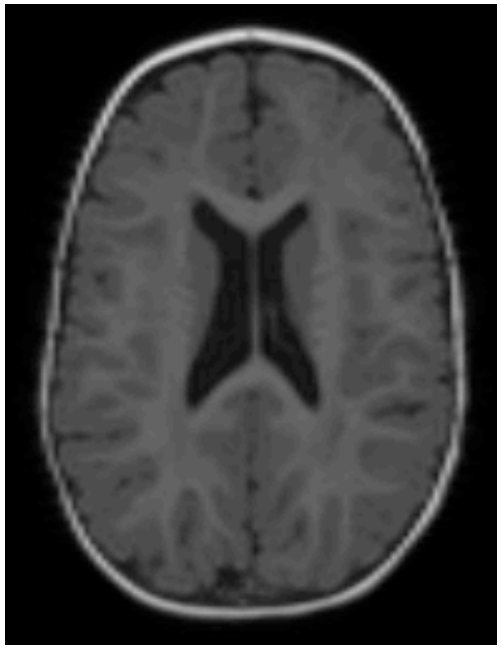
Subtraction after
non-rigid registration

Serial registration for growth quantification

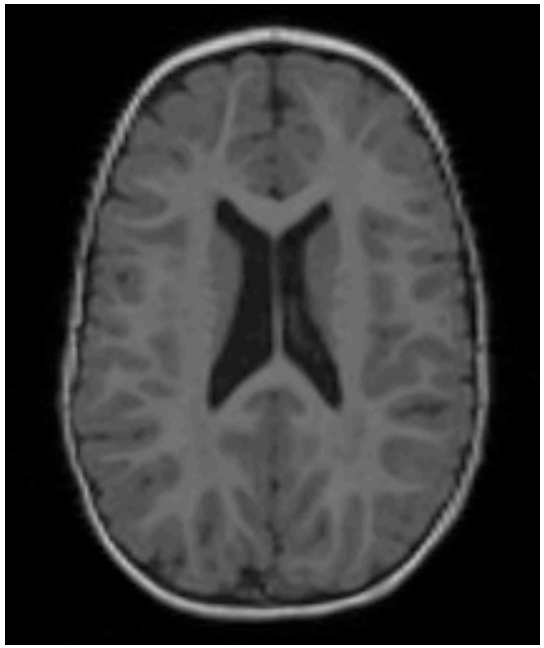


Growth in a single subject between 1 year and 2 years

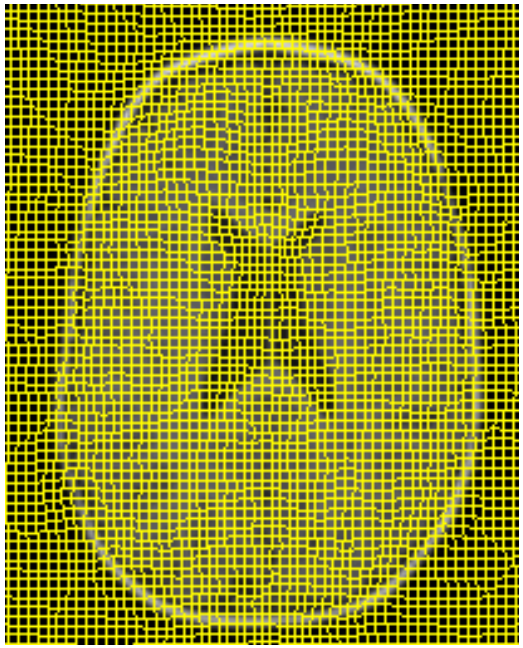
Brain development during early childhood



1 year old

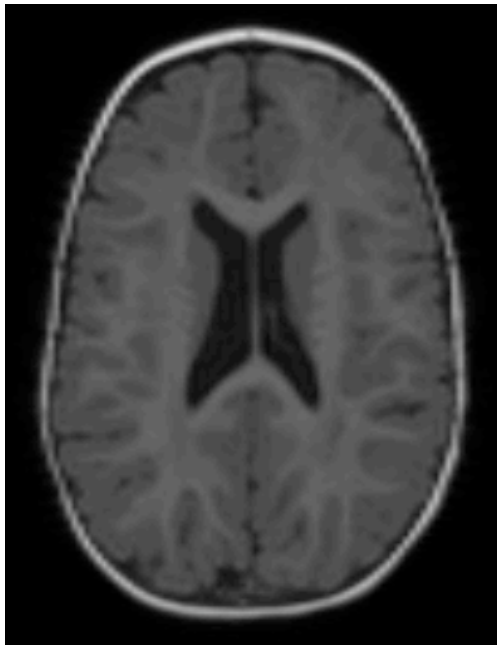


2 year old after
non-rigid registration

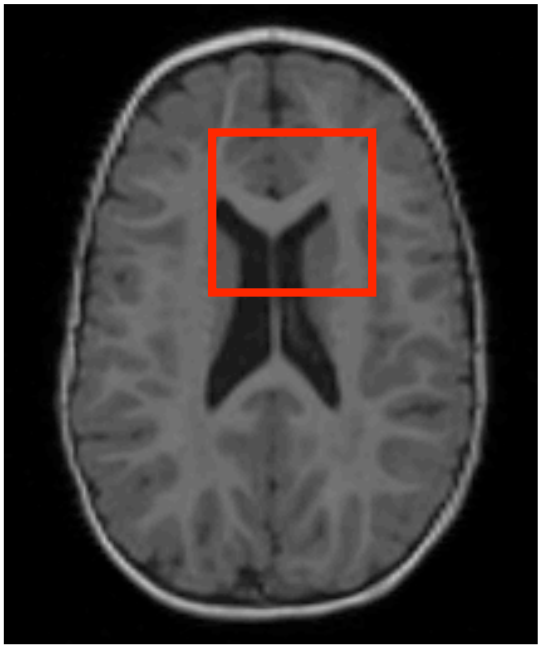


Deformation field after
non-rigid registration

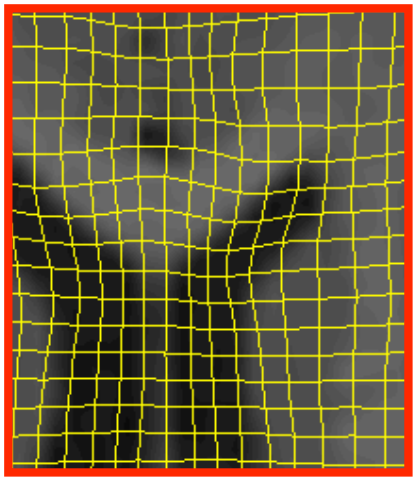
Brain development during early childhood



1 year old



2 year old after
non-rigid registration



Non-rigid registration

- Non-rigid registration is based on a combination of global and local transformations:

$$\mathbf{T}(\mathbf{x}) = \mathbf{T}_{global}(\mathbf{x}) + \mathbf{T}_{local}(\mathbf{x}) = \mathbf{M}\mathbf{x} + \mathbf{d} + \mathbf{T}_{local}(\mathbf{x})$$

- Local transformation is represented by a free-form deformation (FFD) based on B-splines:

$$\mathbf{T}_{local}(x, y, z) = \sum_{l=0}^{3} \sum_{m=0}^{3} \sum_{n=0}^{3} B_l(r) B_m(s) B_n(t) \mathbf{\Phi}_{i+l, j+m, k+n}$$

  controlled by a mesh of control points.
- Control point locations are found by maximizing mutual information as a similarity measure.

Quantification of growth using non-rigid registration

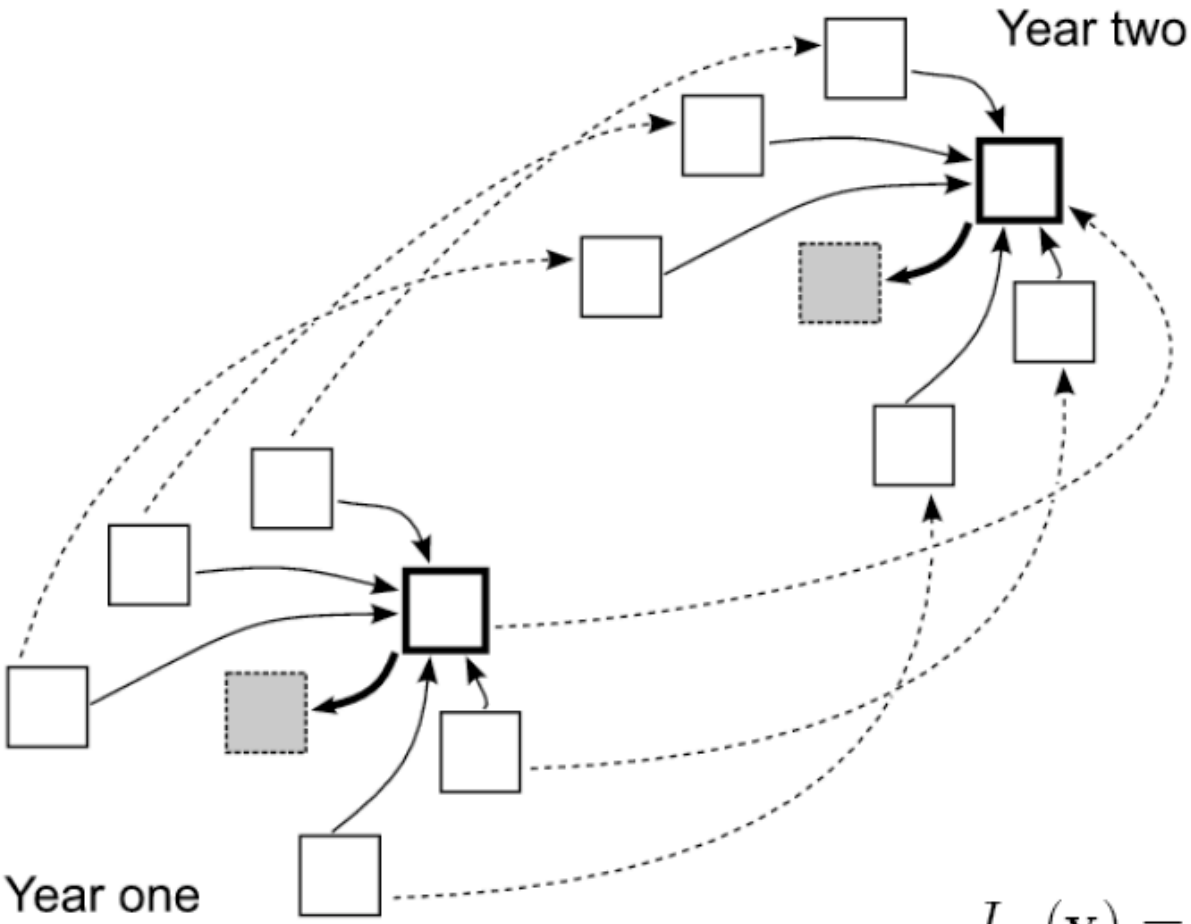
- To characterise growth in individual subjects, we carried out intra-subject registrations using the baseline and follow-up scans.

$$D\mathbf{T} = \begin{pmatrix} \frac{\partial T_x}{\partial x} & \frac{\partial T_x}{\partial y} & \frac{\partial T_x}{\partial z} \\ \frac{\partial T_y}{\partial x} & \frac{\partial T_y}{\partial y} & \frac{\partial T_y}{\partial z} \\ \frac{\partial T_z}{\partial x} & \frac{\partial T_z}{\partial y} & \frac{\partial T_z}{\partial z} \end{pmatrix} \qquad \begin{aligned} J(\mathbf{x}) &= \det(D\mathbf{T}(\mathbf{x})) \\ &= \det(D\mathbf{T}_{global}(\mathbf{x}) + D\mathbf{T}_{local}(\mathbf{x})) \end{aligned}$$

- The growth factor for the tissue class can be estimated as

$$\frac{|\mathbf{T}(\Omega)|}{|\Omega|} \approx \frac{\sum_{\mathbf{v}\in V} p(\mathbf{v}) J(\mathbf{v})}{\sum_{\mathbf{v}\in V} p(\mathbf{v})}$$

Calculation of population-specific growth maps

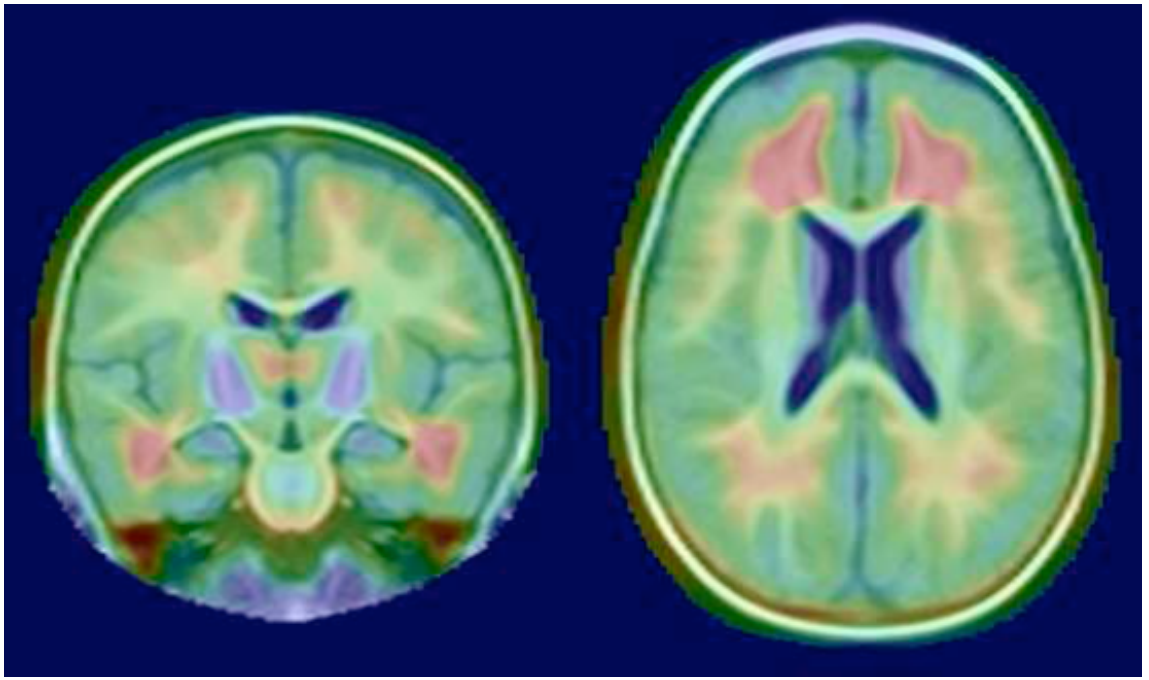


$$J_{av}(\mathbf{v}) = \left(\prod_{i=1}^{n} J_i(\mathbf{v}) \right)^{\frac{1}{n}}$$

Results: Growth maps

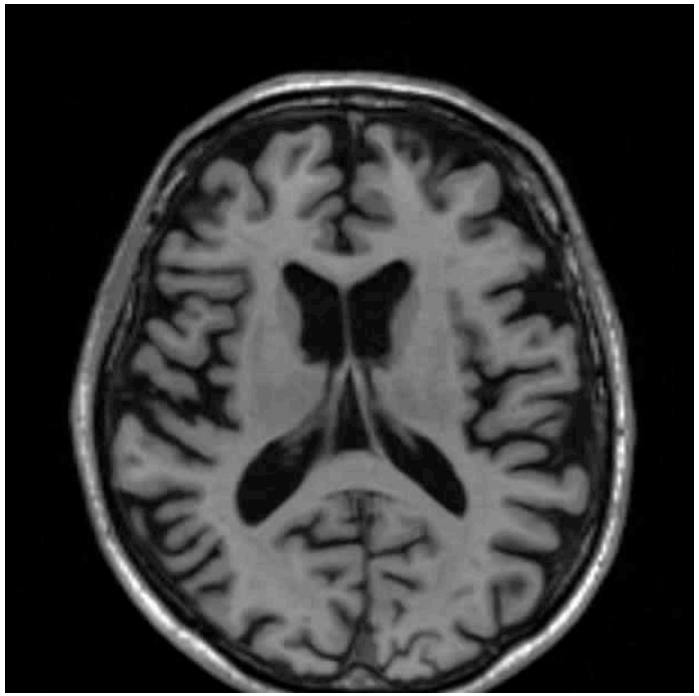
- 25 preterm born children (9 female, 16 male)
  - mean GA at birth 27.7 weeks (SD 2.2
  - mean corrected age at scan 1: 54.0 weeks (SD 5.8)
  - mean corrected age at scan 2: 106.4 weeks (SD 4.4)
- T1 weighted MR volumes with 1 × 1 × 1.6mm resolution
- Non-uniformity was corrected using N3
- Brain masks were extracted using BET
- Images are segmented using a modified EM algorithm (Murgasova et al., MICCAI 2006).
- Other segmentation methods (e.g. Prastawa et al., Weisenfeld et al.) can be used instead

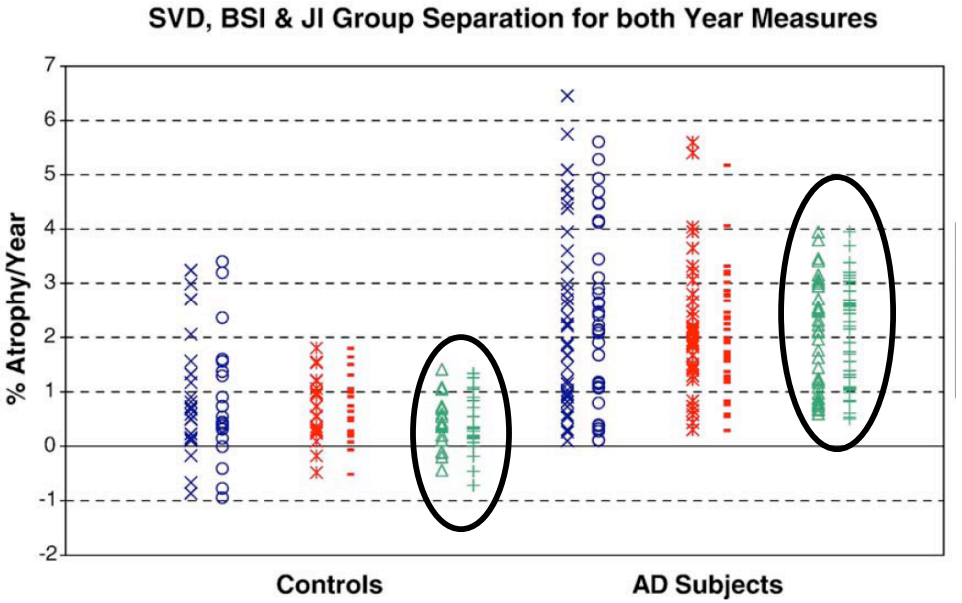
Results: Growth maps between 1 year and 2 years



P. Aljabar et al, NeuroImage 2007

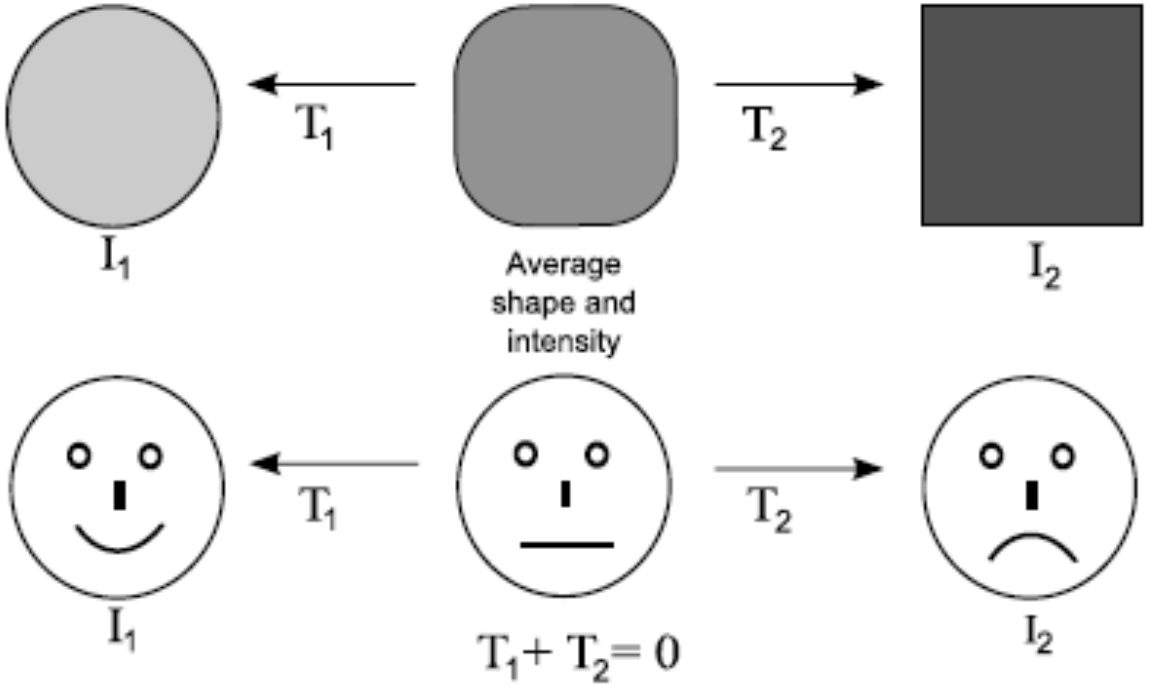
Measurement of atrophy rather than growth





R. Boyes *et al*. Cerebral atrophy measurements using Jacobian integration: Comparison with the boundary shift integral, NeuroImage, 2006

Groupwise non-rigid registration for population studies



K. Bhatia, ISBI 2004, and MICCAI 2007

Groupwise non-rigid registration for population studies

- Model deformation to each image using B-splines:

$$\mathrm{d}_i(x,y,z) = \sum_{l=0}^{3}\sum_{m=0}^{3}\sum_{n=0}^{3} B_l(u)B_m(v)B_n(w)\phi^i_{a+l,b+m,c+n}$$

- Constrain sum of deformations to be zero

$$\sum_{i=1}^{n_I} \mathrm{d}_i(\mathbf{x}) = 0 \quad \forall \mathbf{x} \in \Omega$$

- Maximise similarity subject to above constraint
  - Gradient Projection Method (Rosen)

Groupwise non-rigid registration for population studies

- Similarity measure can be either based on image intensities

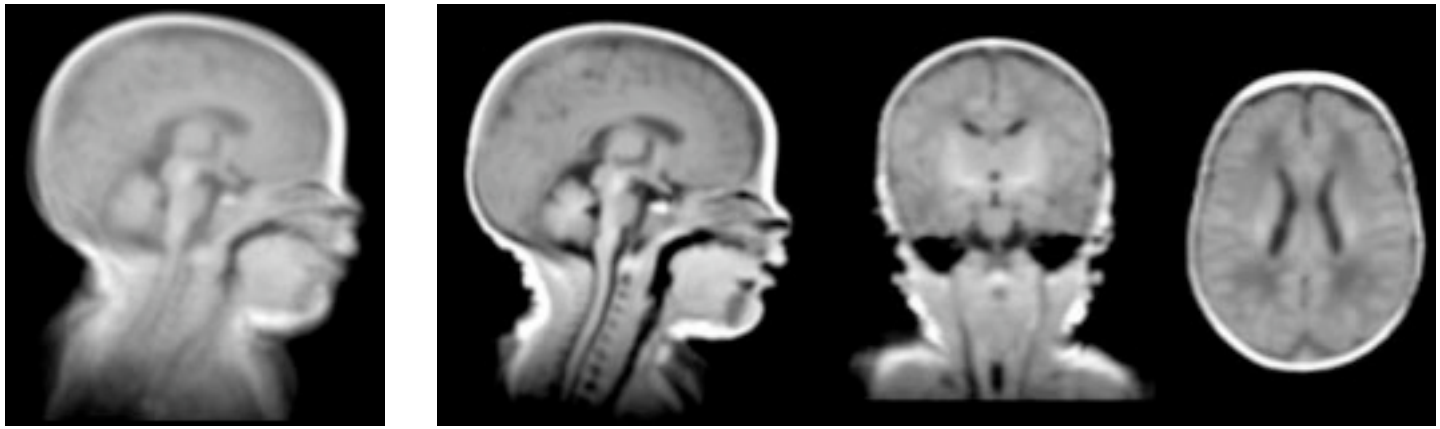
$$S_{NMI}(I_{ref}, I) = \sum_{i=1}^{n} \left(\frac{H(I_{ref}) + H(I_i)}{H(I_{ref}, I_i)} \right)$$

  or soft/hard segmentations (Lorenzen et al.)

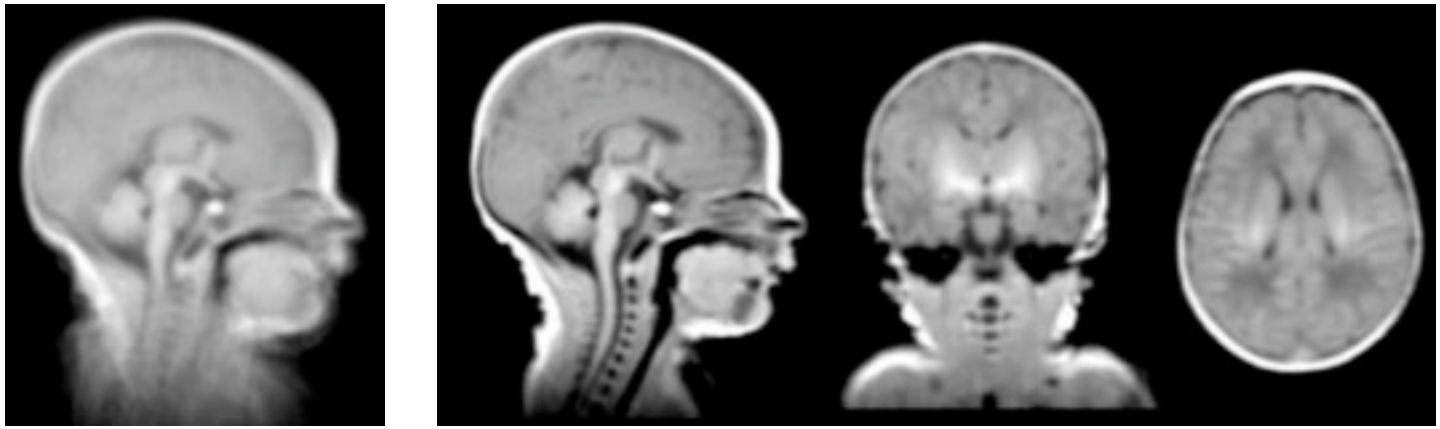
$$S = \sum_{i=1}^{n_I} \sum_{\mathbf{x} \in \Omega} \sum_{k}^{n_k} p_{i,\mathbf{x},k} \log \frac{p_{i,\mathbf{x},k}}{p_{ref,\mathbf{x},k}}$$

- Other similarity measures are possible (e.g. congealing)

Groupwise atlases at term



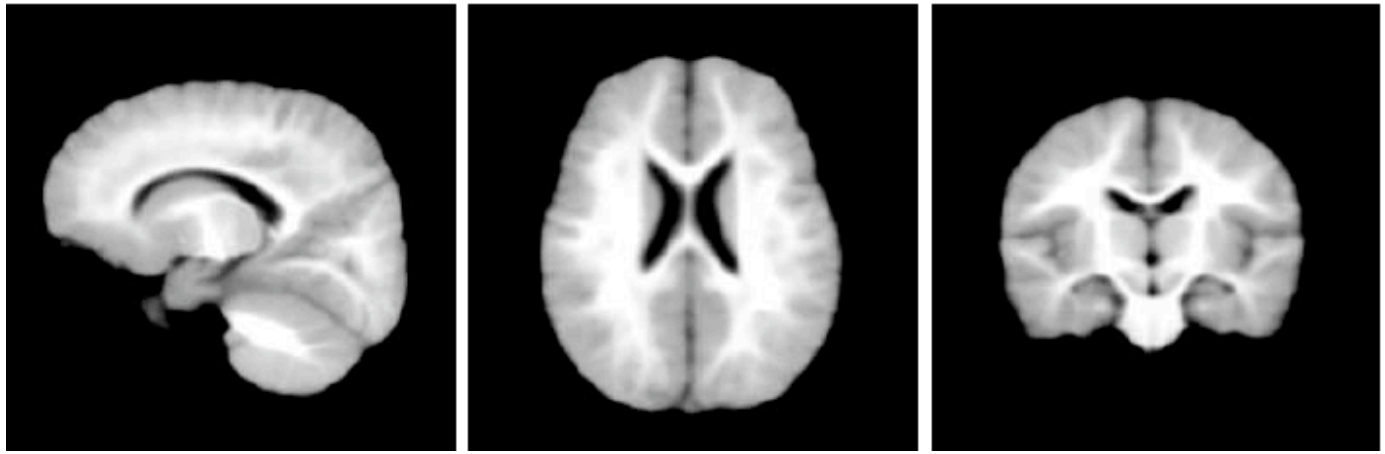
Pre-terms at term



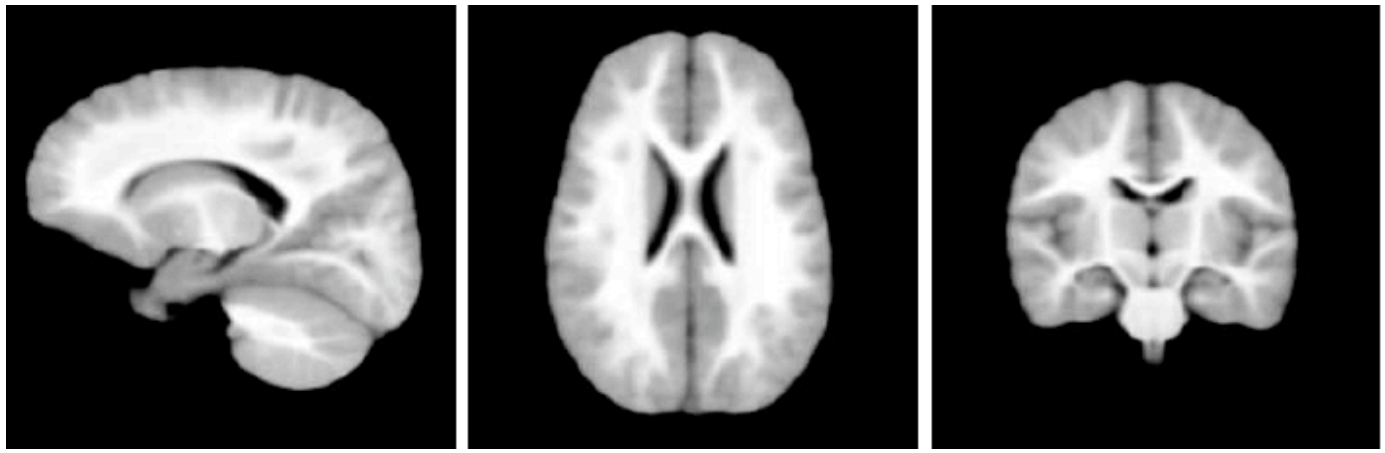
Term-born controls

Atlas using affine registration

Groupwise atlases of pre-terms



1 year



2 years

K. Bhatia, MICCAI 2007

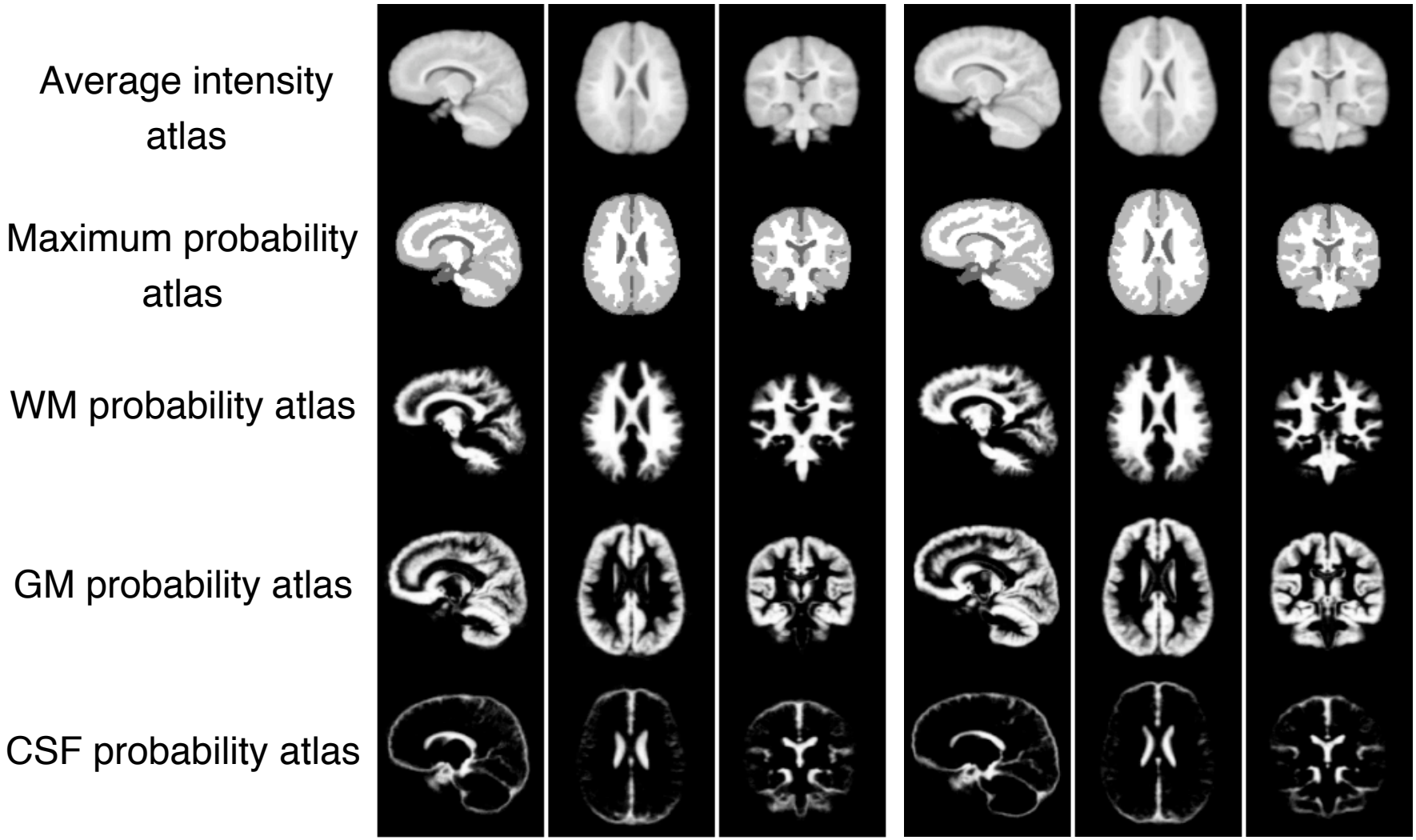
Groupwise registration and segmentation

- Assumption:
  - If subjects are well aligned, then the images are easier to segment
  - If subjects are well segmented, then the images are easier to align

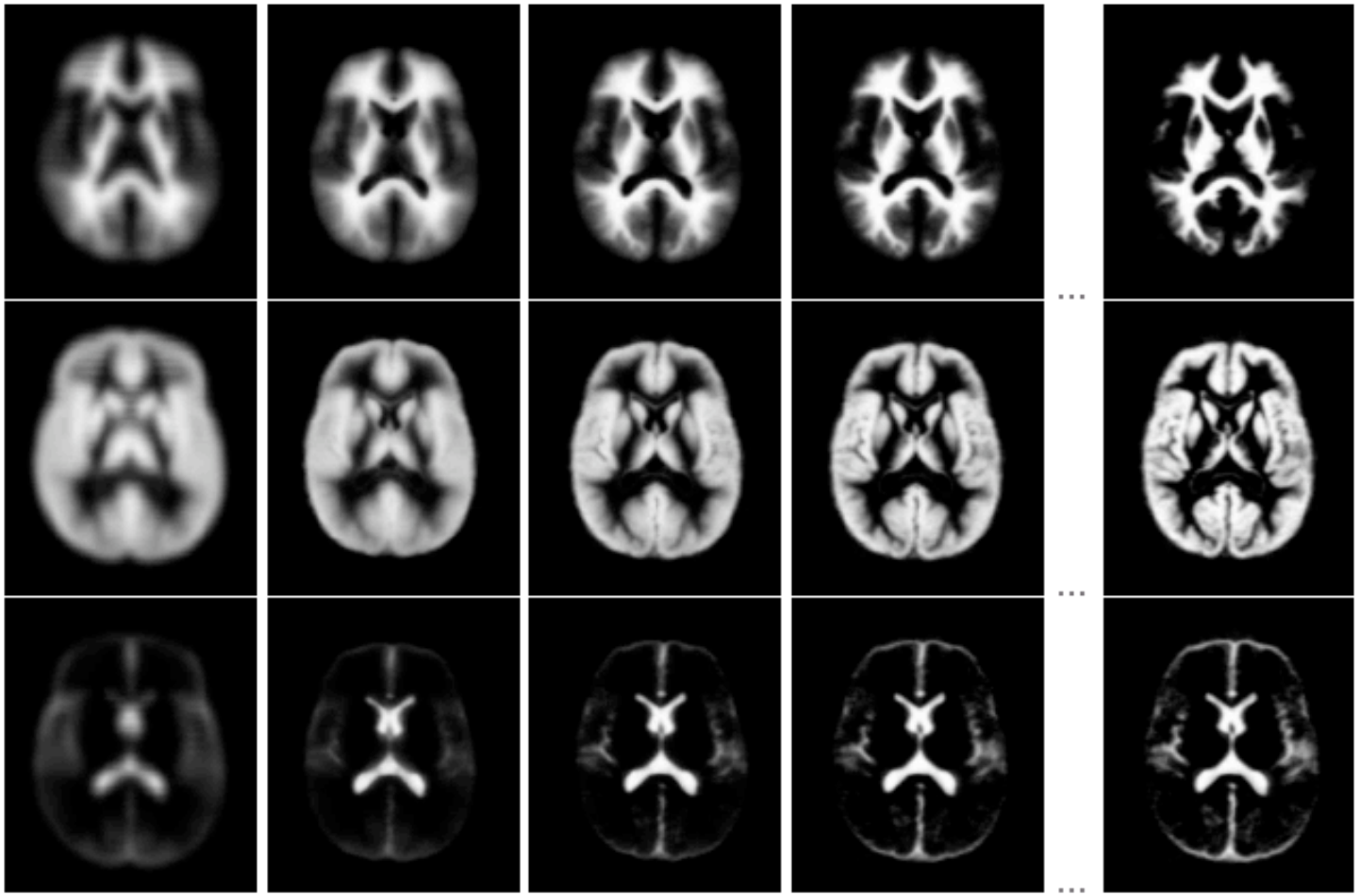
1. *Segmentation:*
   - Maximisation: calculate Gaussian parameters
   - Expectation: calculate posterior probabilities
2. *Registration:*
   - find the optimal transformation between the images using groupwise registration with KL
3. *Repeat until convergence of prior model.*

K. Bhatia, MICCAI 2007

Groupwise segmentation of 1 and 2 year old children

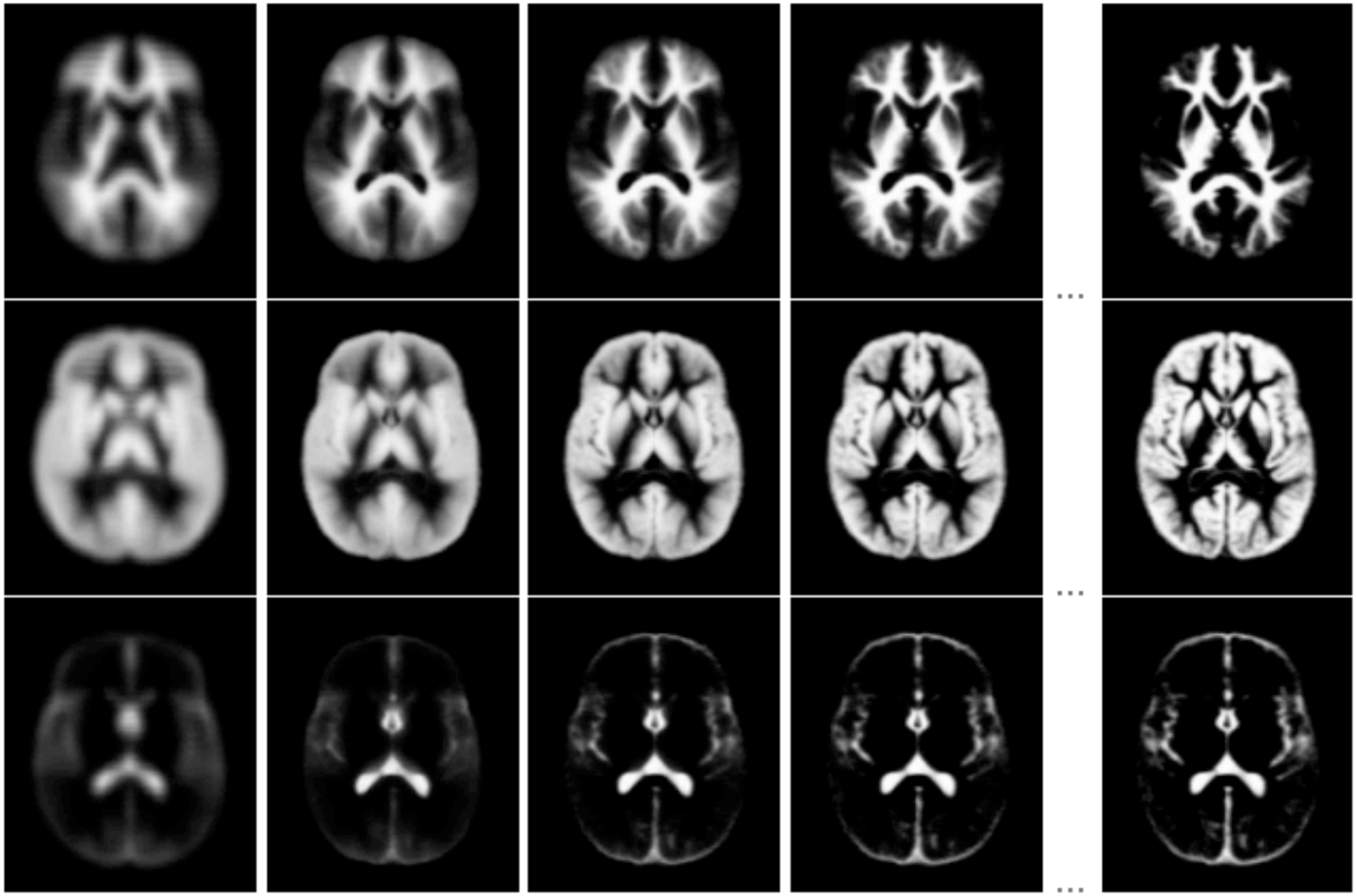


Groupwise segmentation



22 one-year old subjects K. Bhatia, MICCAI 2007

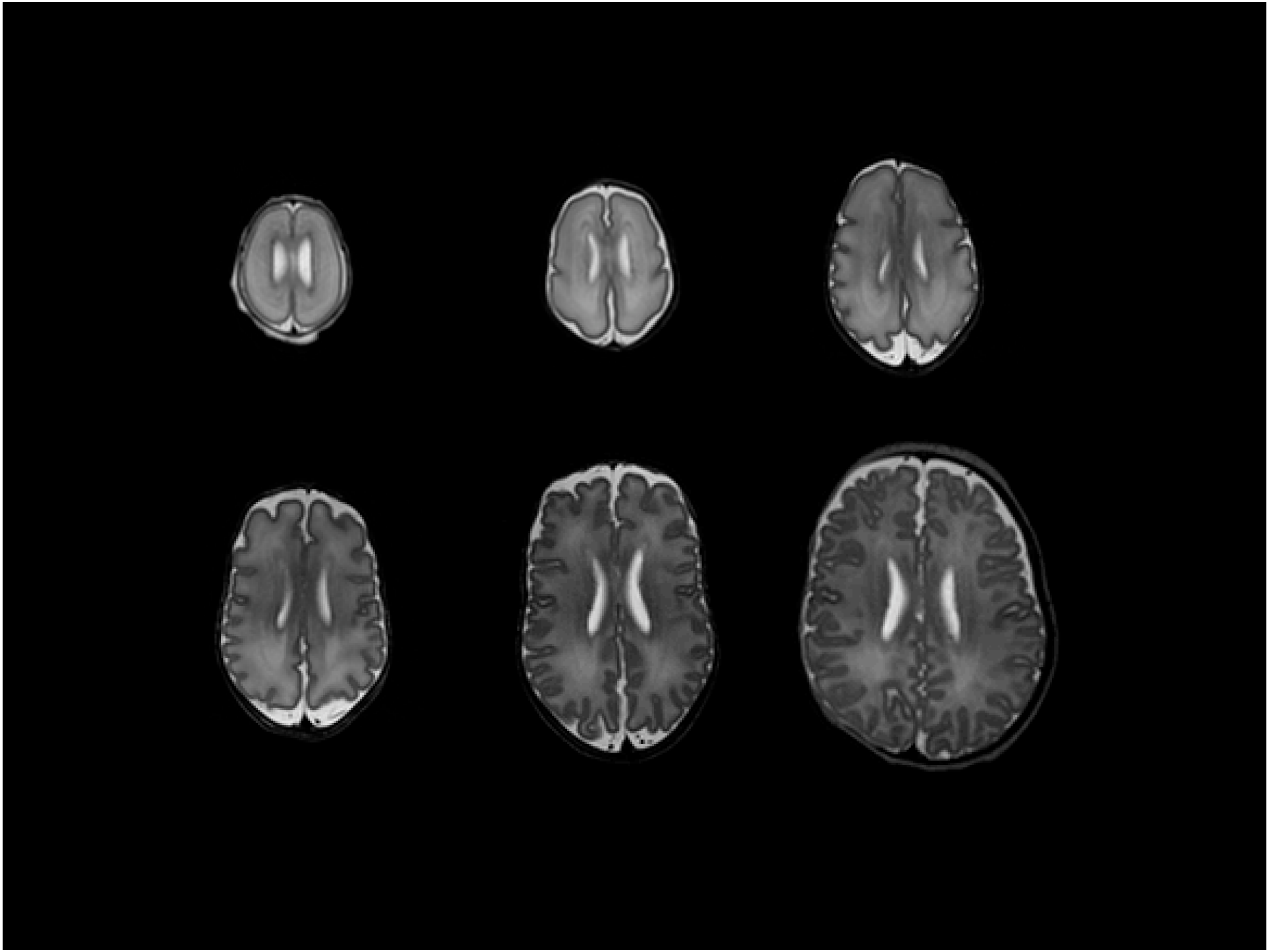
Groupwise segmentation



22 two-year old subjects K. Bhatia, MICCAI 2007

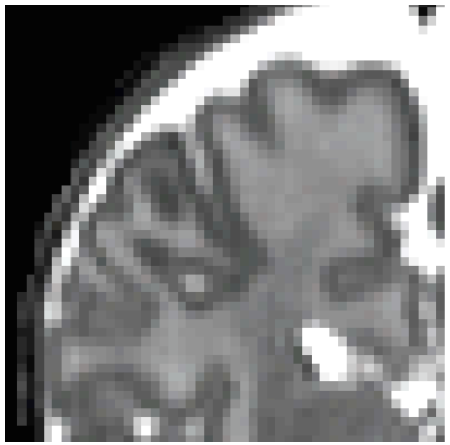
Imaging brain development using neonatal MRI

- Motivation
  - to understand differences between normal and extra-uterine brain development
  - improve neonatal care
  - to better understand brain development in-vivo
- Challenges during image acquisition:
  - neonatal brain is smaller compared to adult brain
  - neonatal brain tissues have different signal properties compared to adult brain
  - sick babies are difficult to image with MR

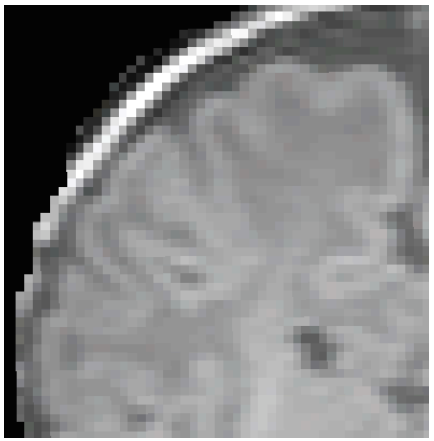


Segmentation of neonatal brain MRI: Problems

- Several approaches have been proposed (Prastawa et al., Weisenfeld et al.)
- Problems:
  - On-going process of myelination
  - Contrast between WM/GM is inverted leading to partial volume



T2-weighted



T1-weighted

EM-based tissue classification

E-step:
$$p(k|x_i) = \frac{p(x_i|k)\,prior(k)}{p(x_i)}$$

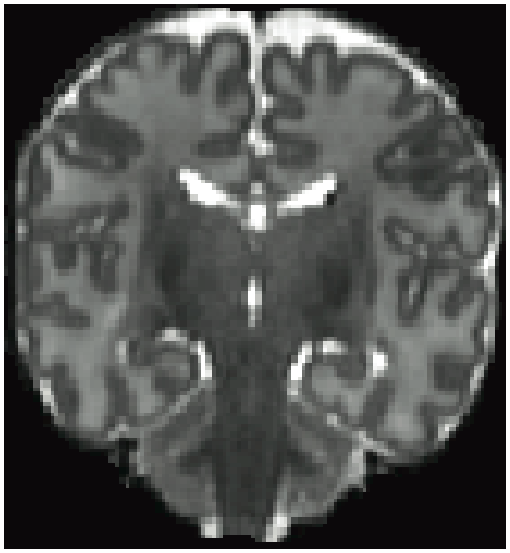
M-step:
$$\mu_k^{(m+1)} = \frac{\sum_{i=1}^{N} p^{(m)}(k|x_i)\,x_i}{\sum_{i=1}^{N} p^{(m)}(k|x_i)}$$

$$\left(\sigma_k^{(m+1)}\right)^2 = \frac{\sum_{i=1}^{N} p^{(m)}(k|x_i)(x_i-\mu_k)^2}{\sum_{i=1}^{N} p^{(m)}(k|x_i)}$$

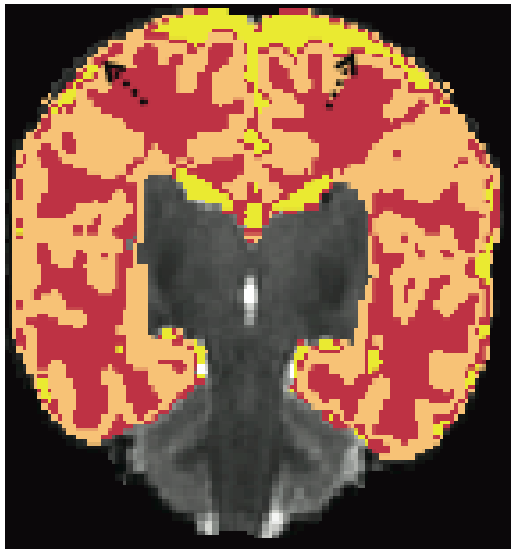
$$prior(k|x_i) = \frac{p_{atlas}(k|x_i)\cdot p_{mrf}(k|x_i)}{\sum_{j=1}^{K}\left(p_{atlas}(j|x_i)\cdot p_{mrf}(j|x_i)\right)}$$

$$p_{mrf}(k|x_i) = \frac{exp\left(-U_{mrf}(k|x_i,\boldsymbol{\Phi})\right)}{\sum_{j=1}^{K} exp\left(-U_{mrf}(j|x_i,\boldsymbol{\Phi})\right)}$$

EM-based tissue classification of neonatal MRI



Original T2 image



EM-MRF

EM-based tissue classification of neonatal MRI

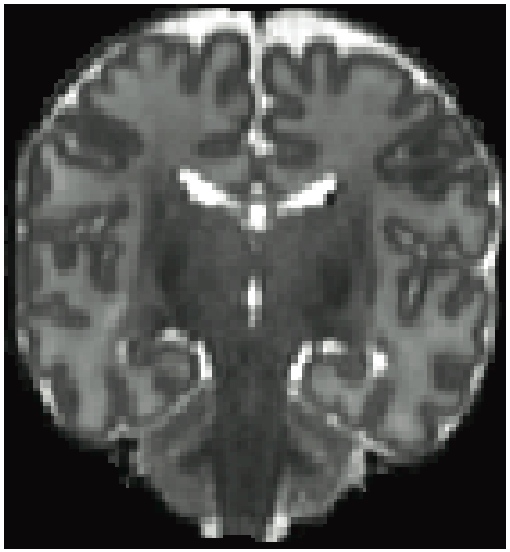
- If a voxel is classified as WM and within its neighborhood there are CSF and GM voxels simultaneously, it is likely to be a partial volume voxel.

$$p_{mrf}r^{(m+1)}\left(wm\middle|x_i\right)=\lambda p_{mrf}r^{(m)}\left(wm\middle|x_i\right),\ 0<\lambda<1$$

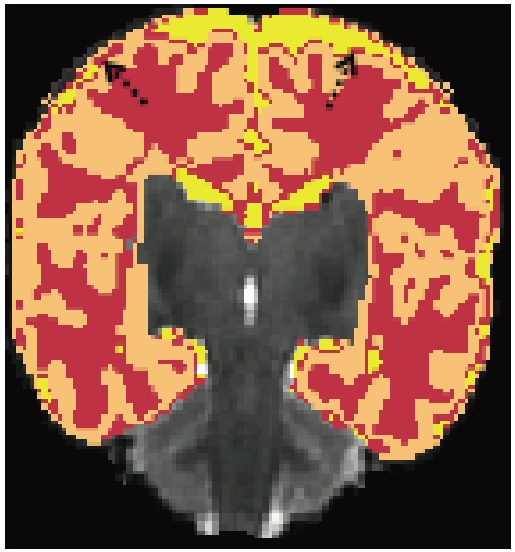
$$p_{mrf}{}^{(m+1)}\left(CSF\middle|x_i\right)=p_{mrf}{}^{(m)}\left(CSF\middle|x_i\right)\left(1+(1-\lambda)\frac{p_{mrf}r^{(m)}\left(wm\middle|x_i\right)}{p_{mrf}{}^{(m)}\left(CSF\middle|x_i\right)+p_{mrf}{}^{(m)}\left(gm\middle|x_i\right)}\right)$$

$$p_{mrf}r^{(m+1)}\left(gm\middle|x_i\right)=p_{mrf}r^{(m)}\left(gm\middle|x_i\right)\left(1+(1-\lambda)\frac{p_{mrf}r^{(m)}\left(wm\middle|x_i\right)}{p_{mrf}r^{(m)}\left(CSF\middle|x_i\right)+p_{mrf}{}^{(m)}\left(gm\middle|x_i\right)}\right)$$

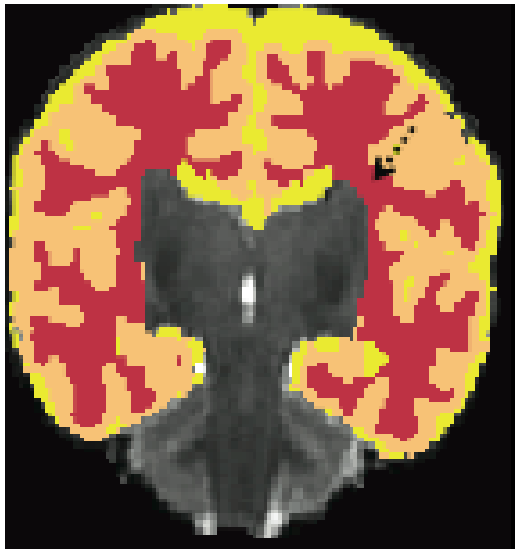
EM-based tissue classification of neonatal MRI with partial volume correction



Original T2 image

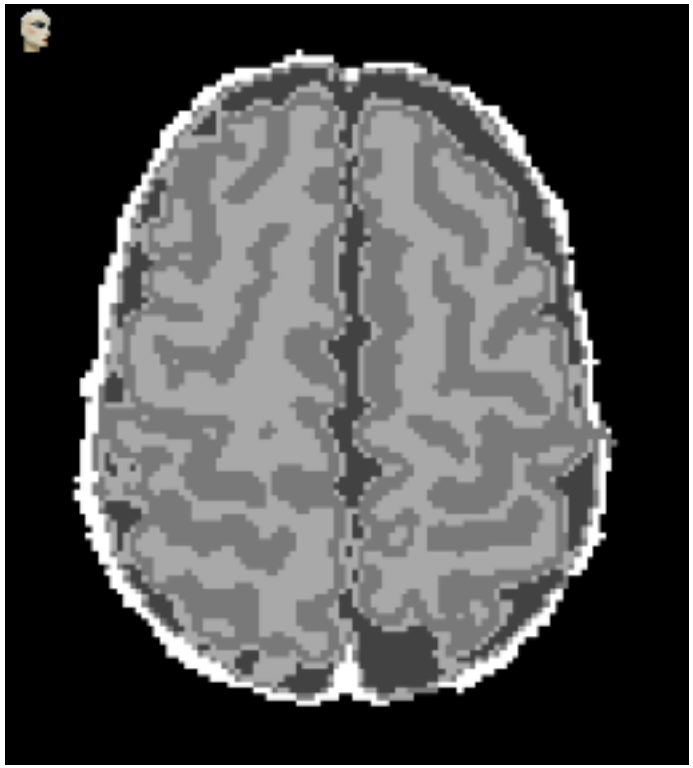


EM-MRF

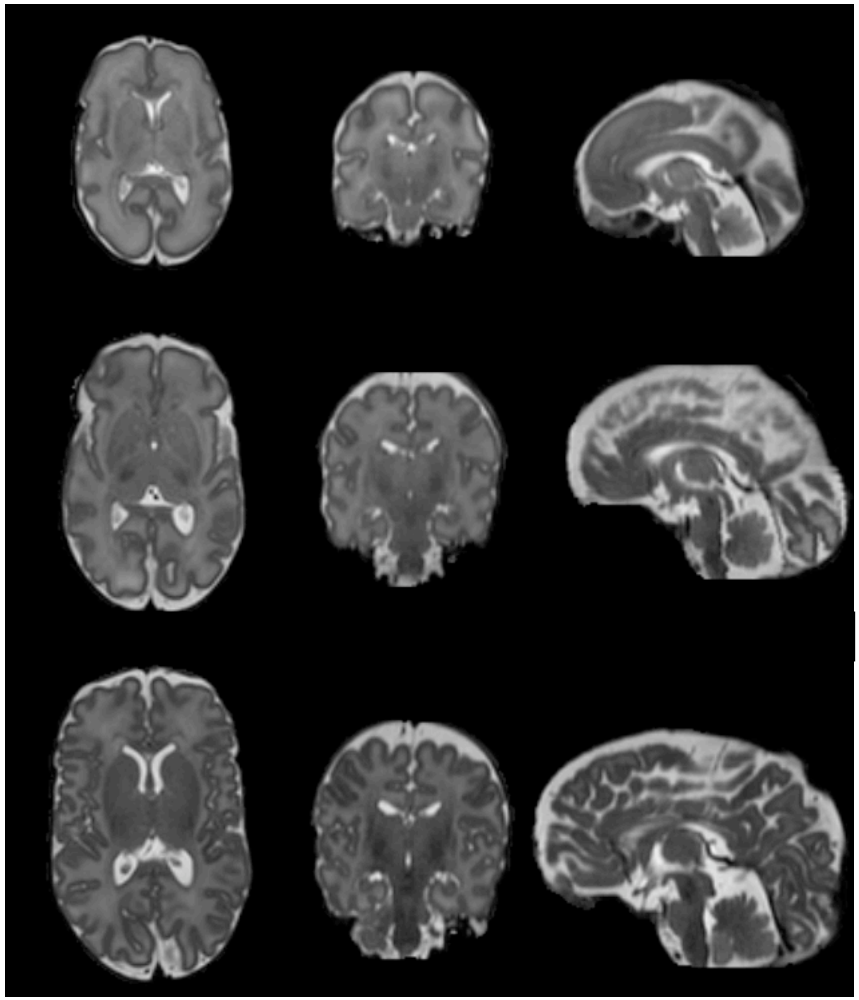


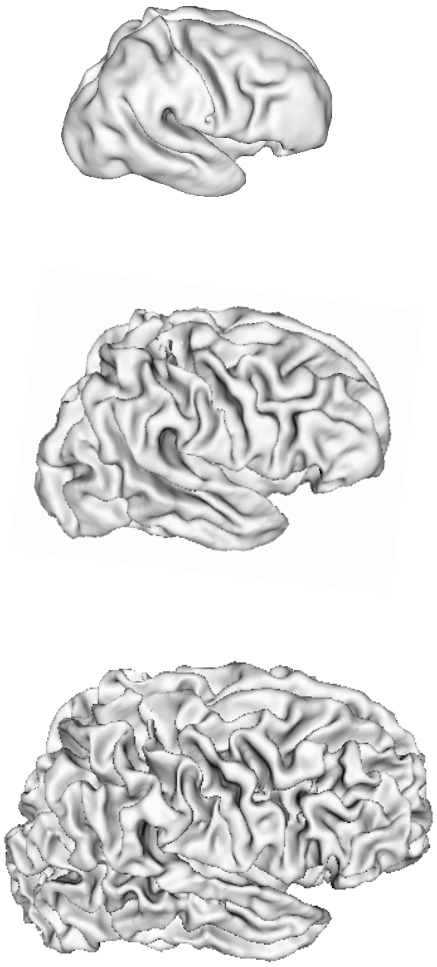
EM-MRF with
PV correction

EM-based tissue classification of neonatal MRI with partial volume correction



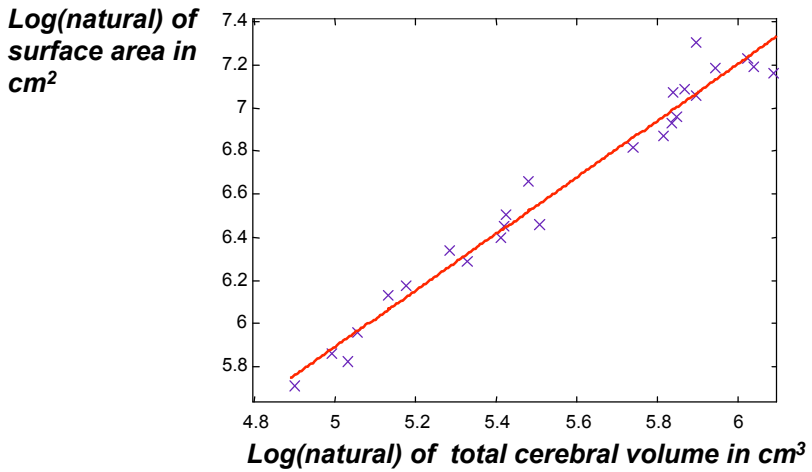
Cortical segmentation

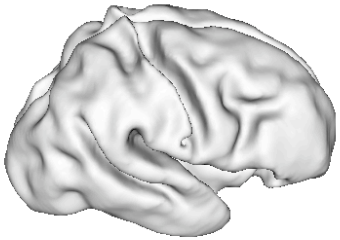


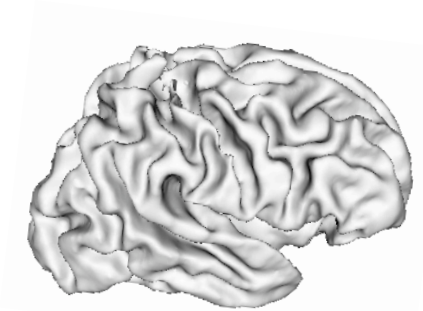


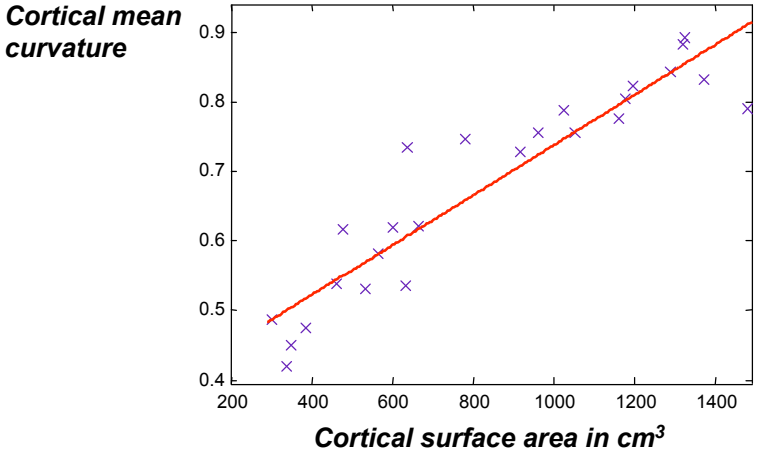
H. Xue, IPMI 2007 & NeuroImage 2007

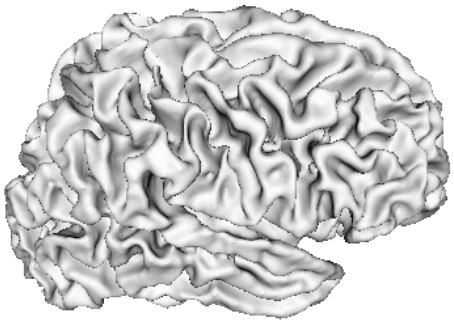
Cortical surface area and curvature





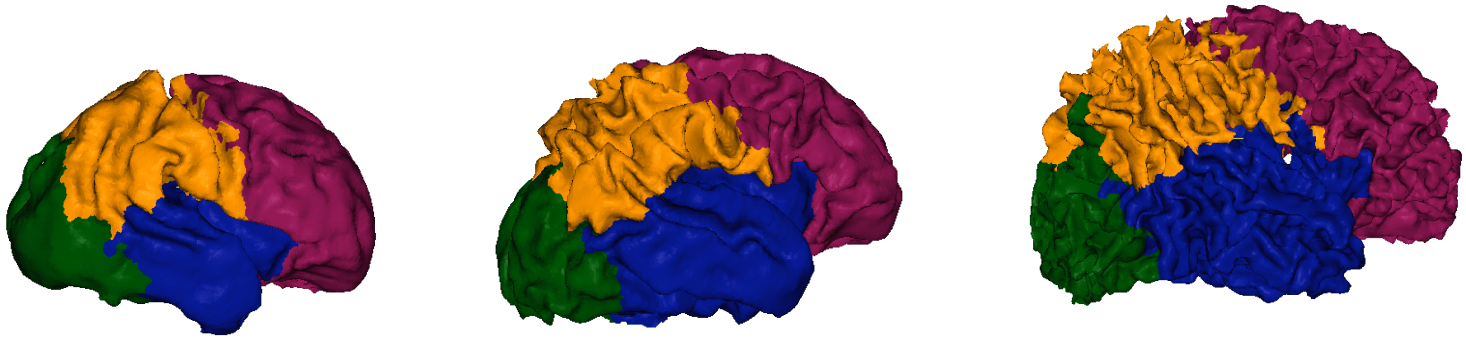


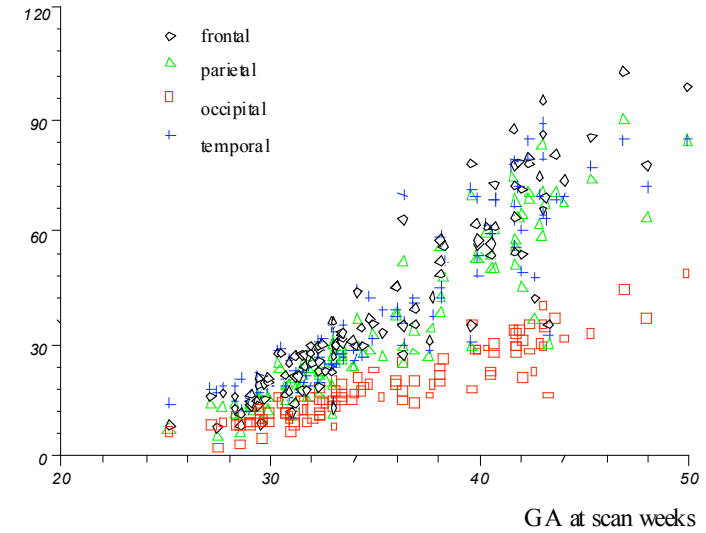




H. Xue, IPMI 2007 & NeuroImage 2007

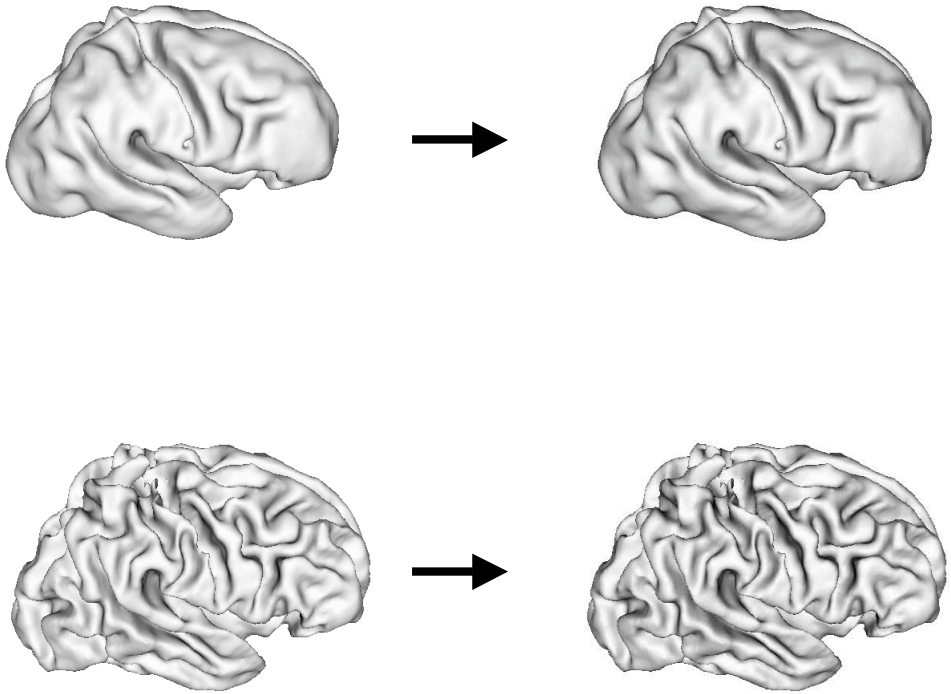
Cortical and tissue volumes





	TCV cm³	Cortical GM		WM		CSF	
		Total cm³	GM /TCV	Total cm³	WM /TCV	Total cm³	CSF /TCV
All Preterm	341.9	177.2	0.51	131.8	0.39	119.0	0.36
Term	347.0	178.2	0.53	129.2	0.36	101.0	0.27
p value	0.88	0.51	0.04	0.45	0.03	0.006	0.007

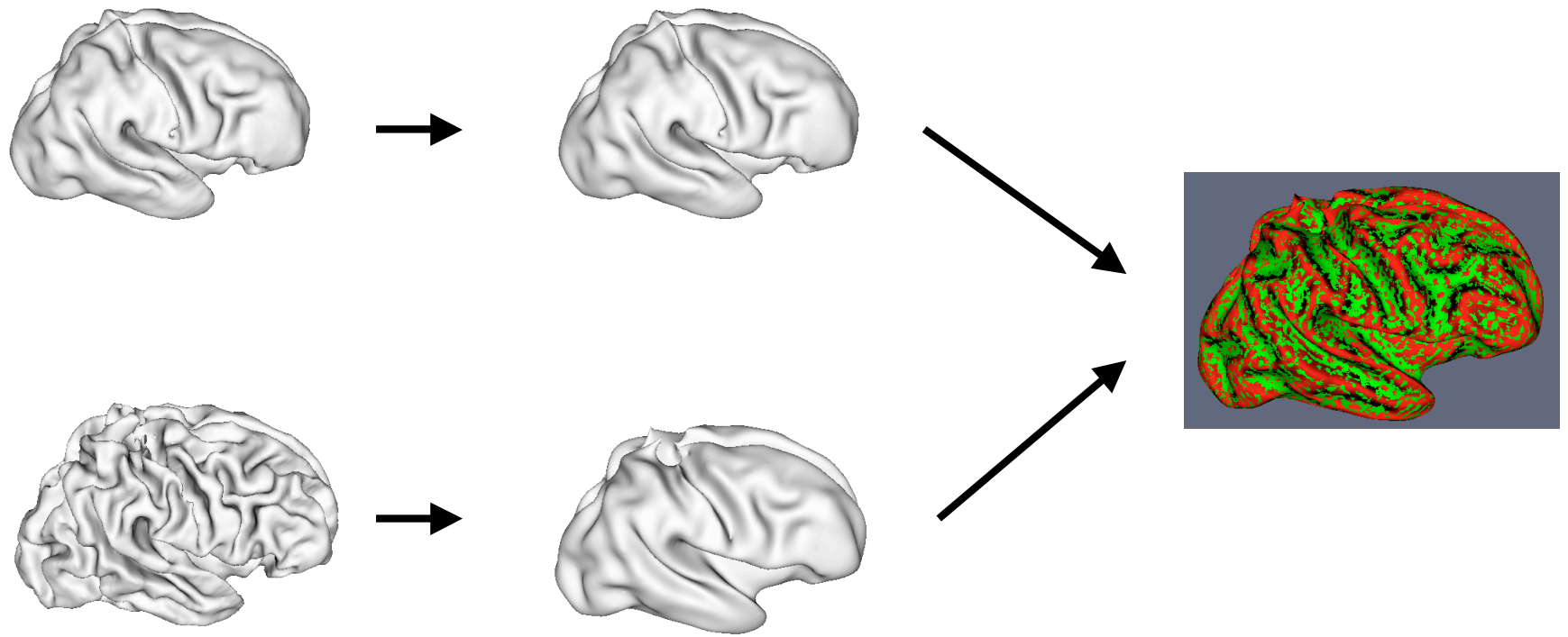
Cortical surface registration



Surface inflation

H. Xue, MICCAI 2007

Cortical surface registration

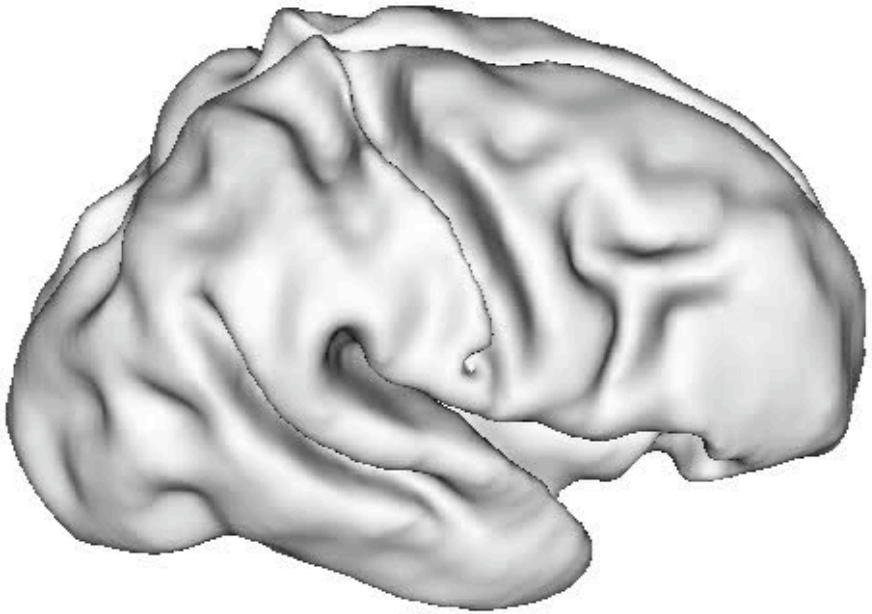


Surface inflation

Surface registration using FFDs

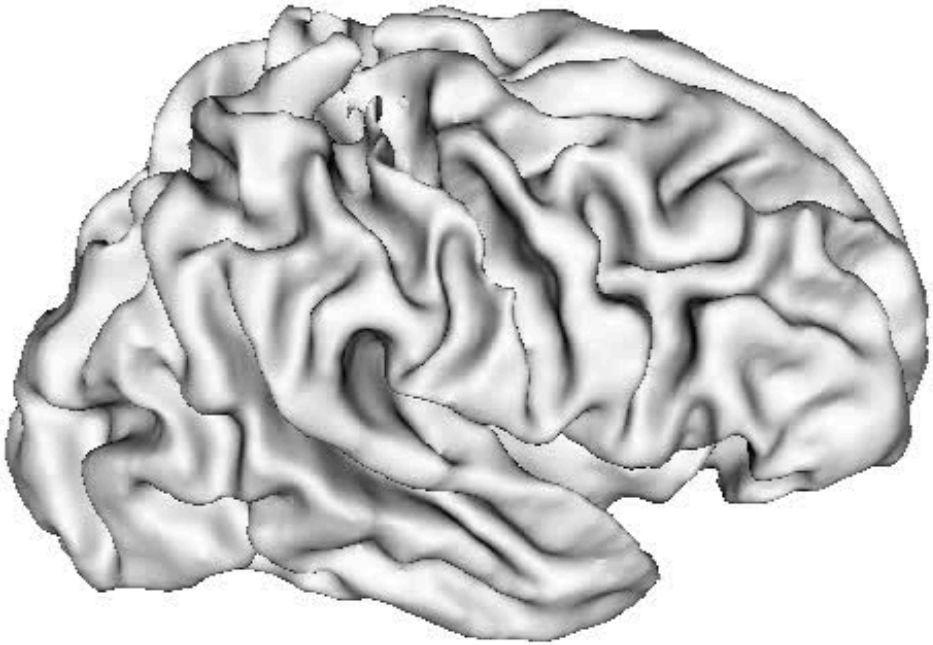
H. Xue, MICCAI 2007

Cortical registration



29 weeks to 34 weeks

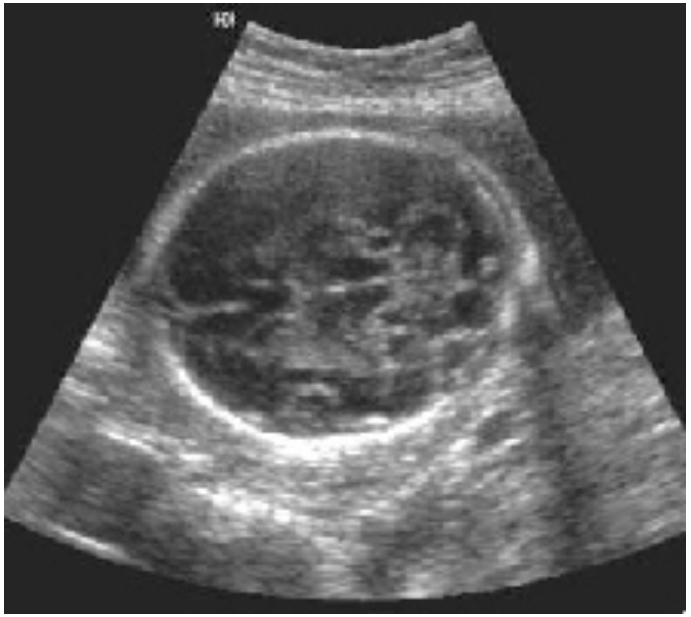
Cortical registration



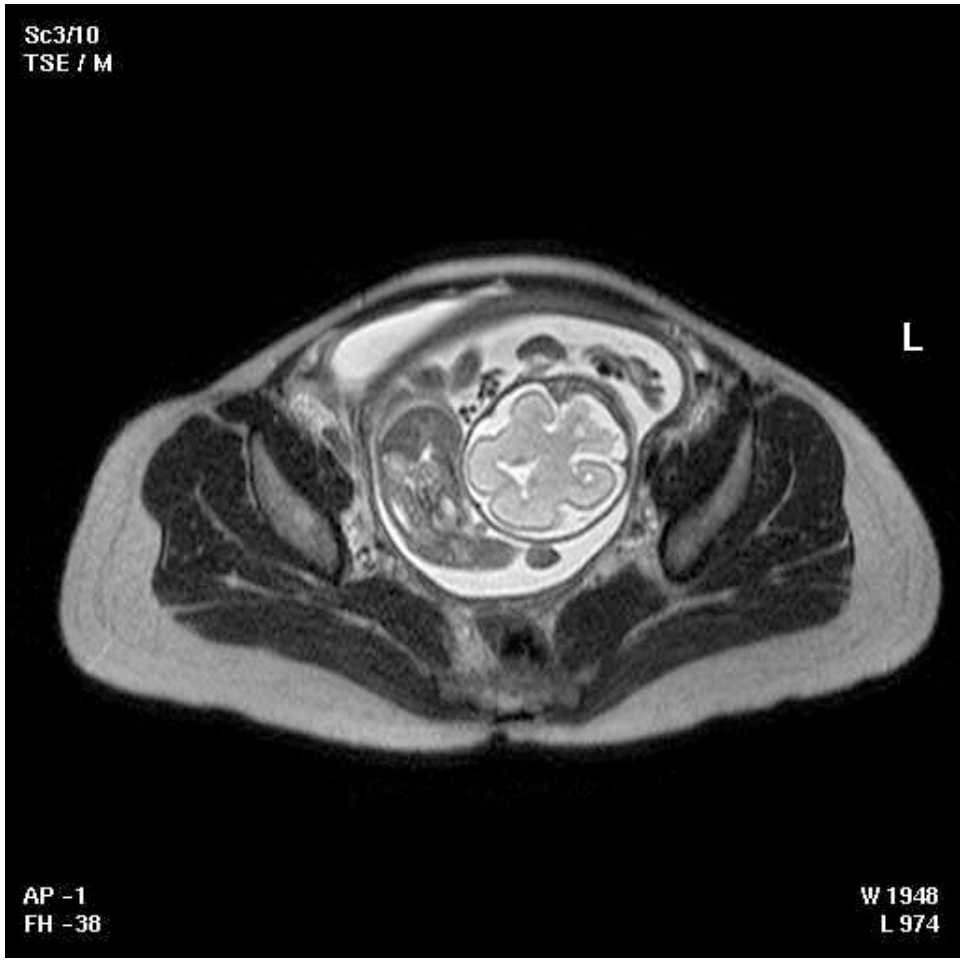
34 weeks to 40 weeks

Fetal brain imaging

Ultrasound

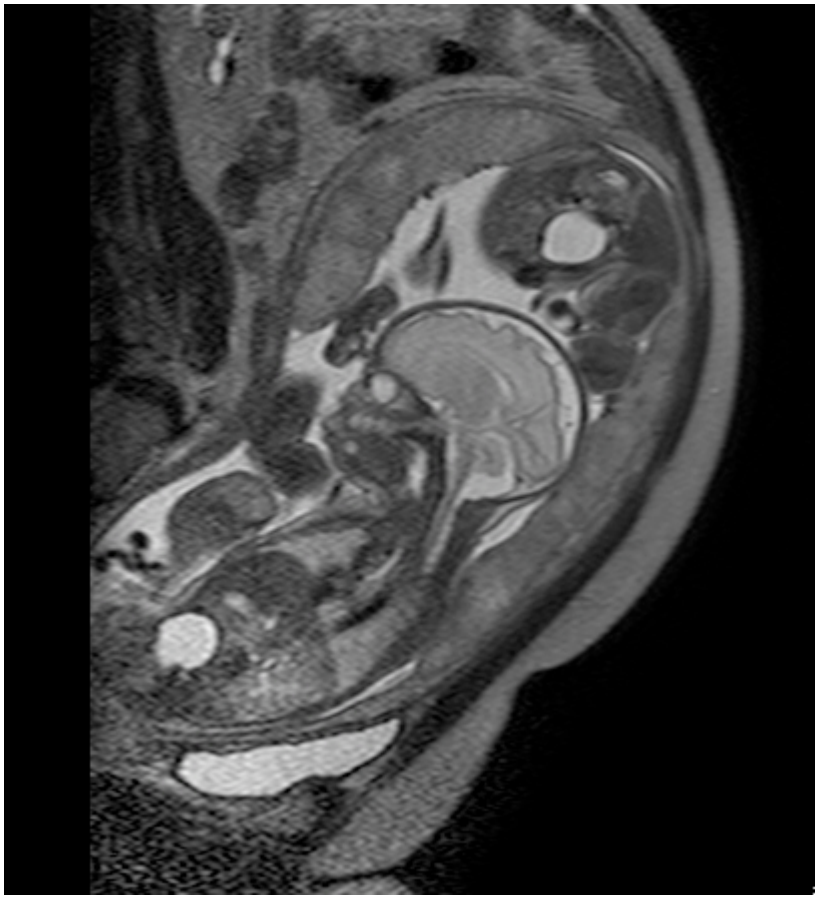


MRI T2w ssFSE

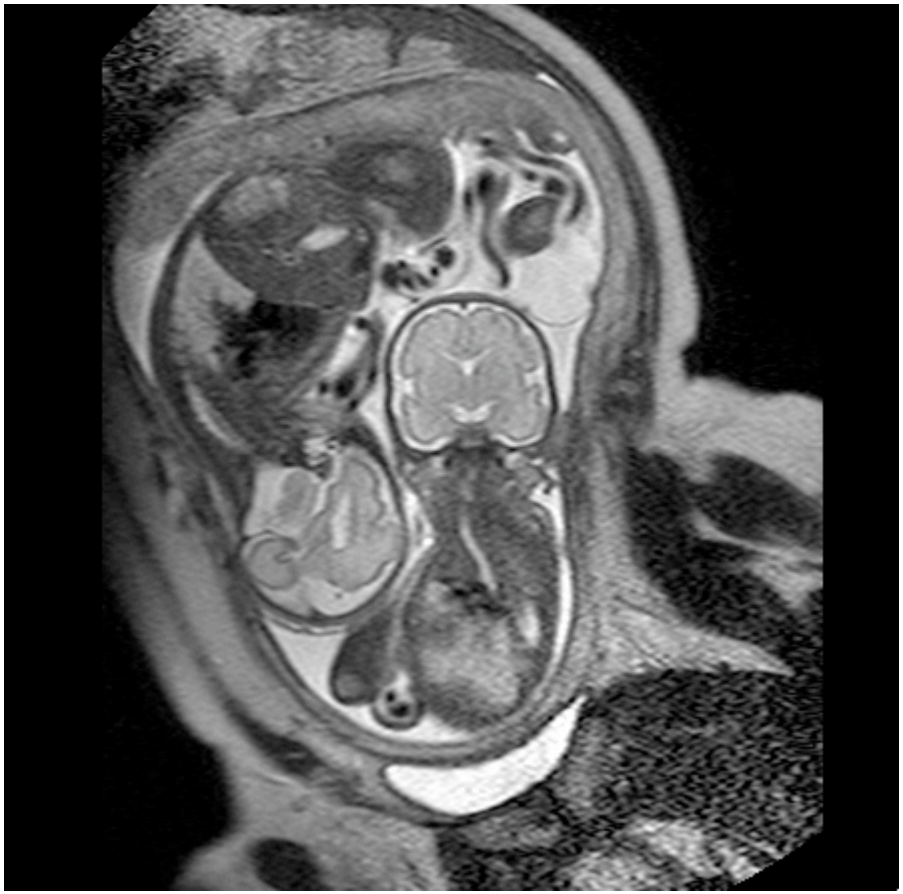


Multi-slice 2D T2 Images of the Fetus

30 Week Gestation



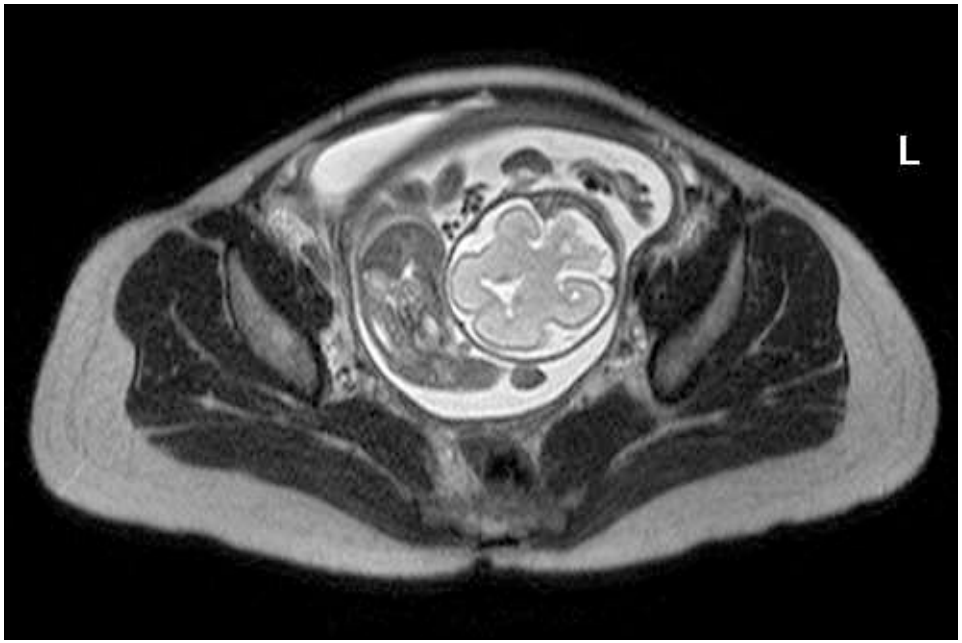
30 Week Gestation, Twin Pregnancy



Snap-shot images (<1sec/image) can freeze fetal motion

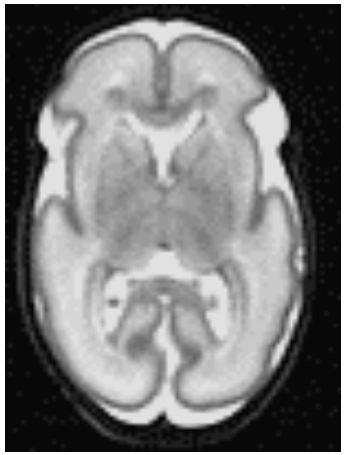
Image quality

24 week gestation
T2 FSE

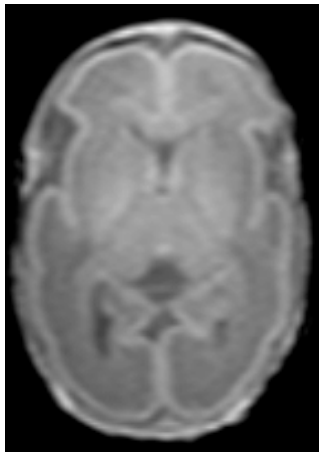


- Multi 2D T2 TSE: 512 x 512 matrix
- In-plane resolution: 0.8 mm x 0.8 mm
- Slice thickness: 4 mm
- Slice Gap: 0.4 mm

Neonate 27 weeks + 1 day

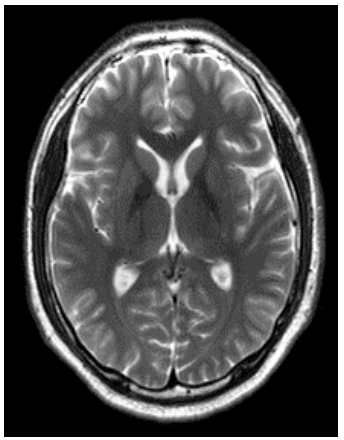


T2w FSE

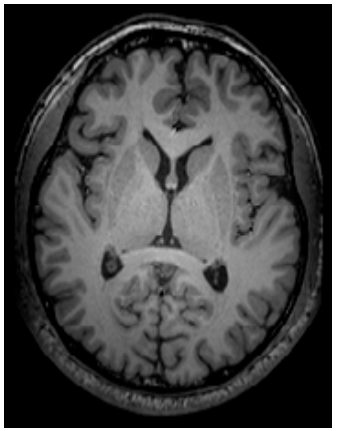


T1 3D MPRAGE

Adult



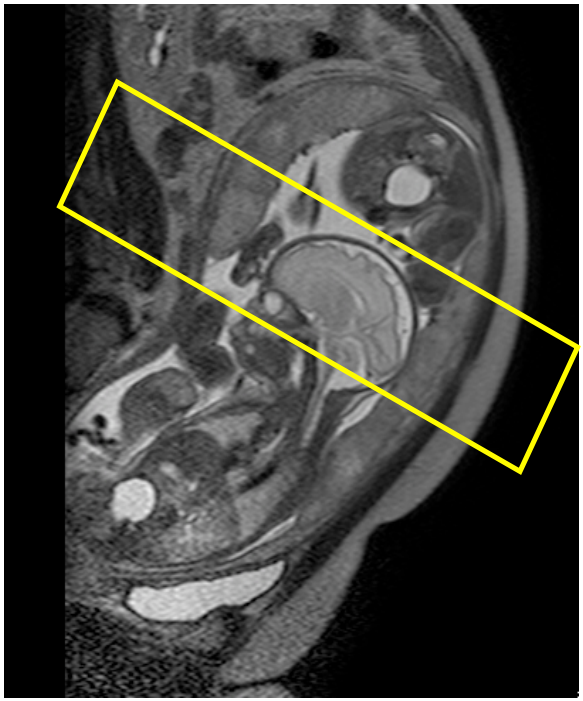
T2w FSE



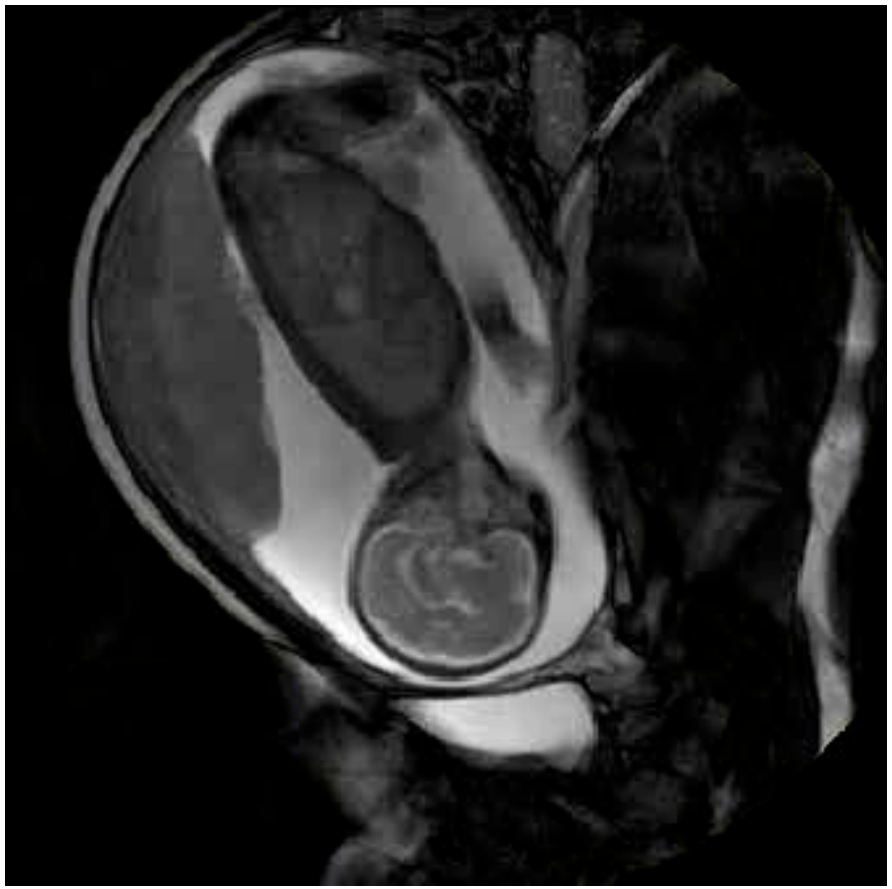
T1 3D MPRAGE

Motion damages the 3D view

Planed Scan Orientation

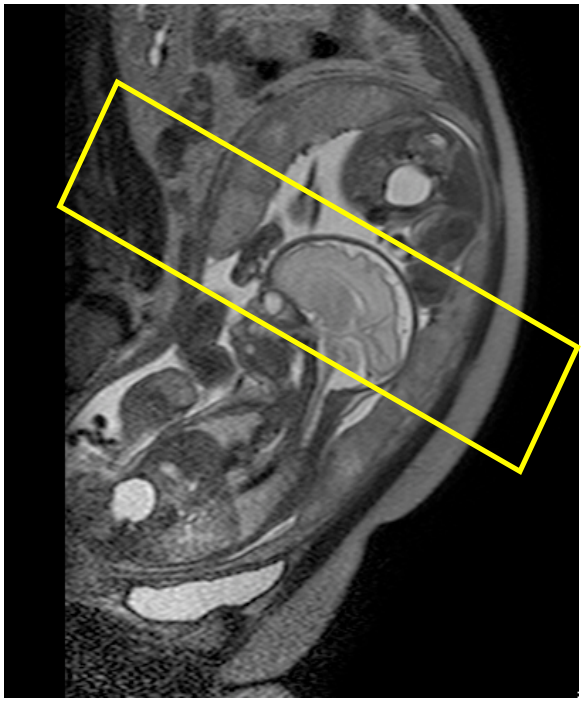


Fetus Moves

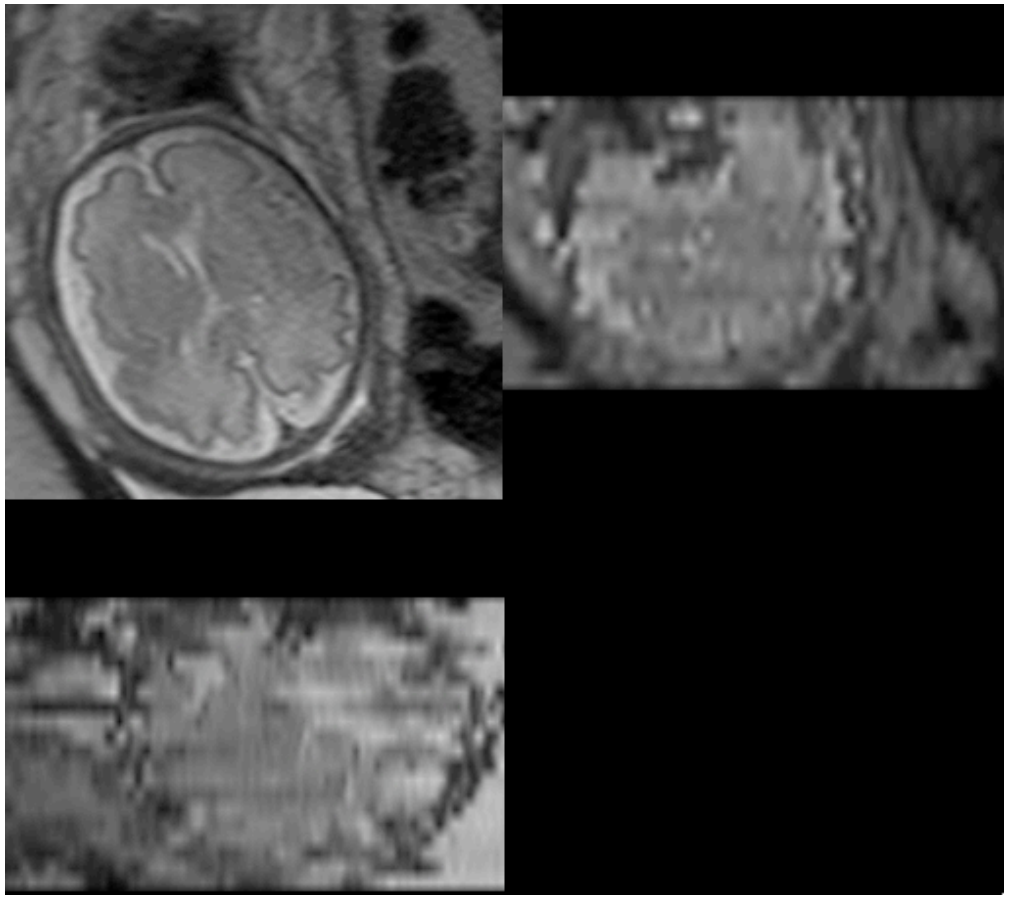


Motion damages the 3D view

Planed Scan Orientation



Fetus Moves



High in-plane resolution
other views are damaged

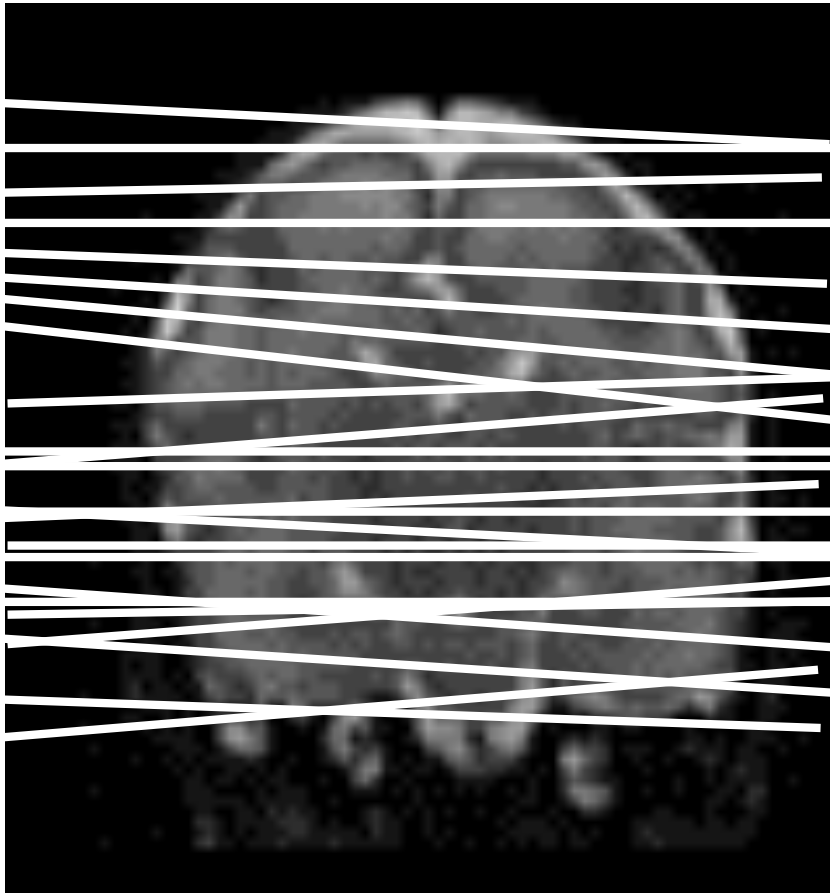
Approach

- Regard moving brain as a rigid body
- Use dynamic single shot MR scanning
- Work in image domain and exclude maternal tissue
- Repeat
  - Make fetal images self consistent by image registration
  - After imageregistration reconstruct a self consistent volume

Registration of single 2D slices to a 3D Volume

- 3D to 3D registration is well established
  - 3D data sets can offer ample information
  - Rigid body registration particularly simple (only 6 dof)
- 2D to 3D registration remains very challenging
  - Very limited information: only a single 2D slice compared to 3D/3D registration
  - Lots of local optima of the cost function
- Particular issues for fetal images
  - Very simple anatomy of fetus (less information/slice than for adult brains)
  - May have no initial guess- we do not know the fetal position

Transform to fetal brain coordinate system



Results

- 16 normal fetus were scanned at the GA from 19 to 35 weeks
  - Images acquired using a 1.5 T scanner (Philips Intera) with a T2 weighted single-shot Fast Spin Echo sequence:

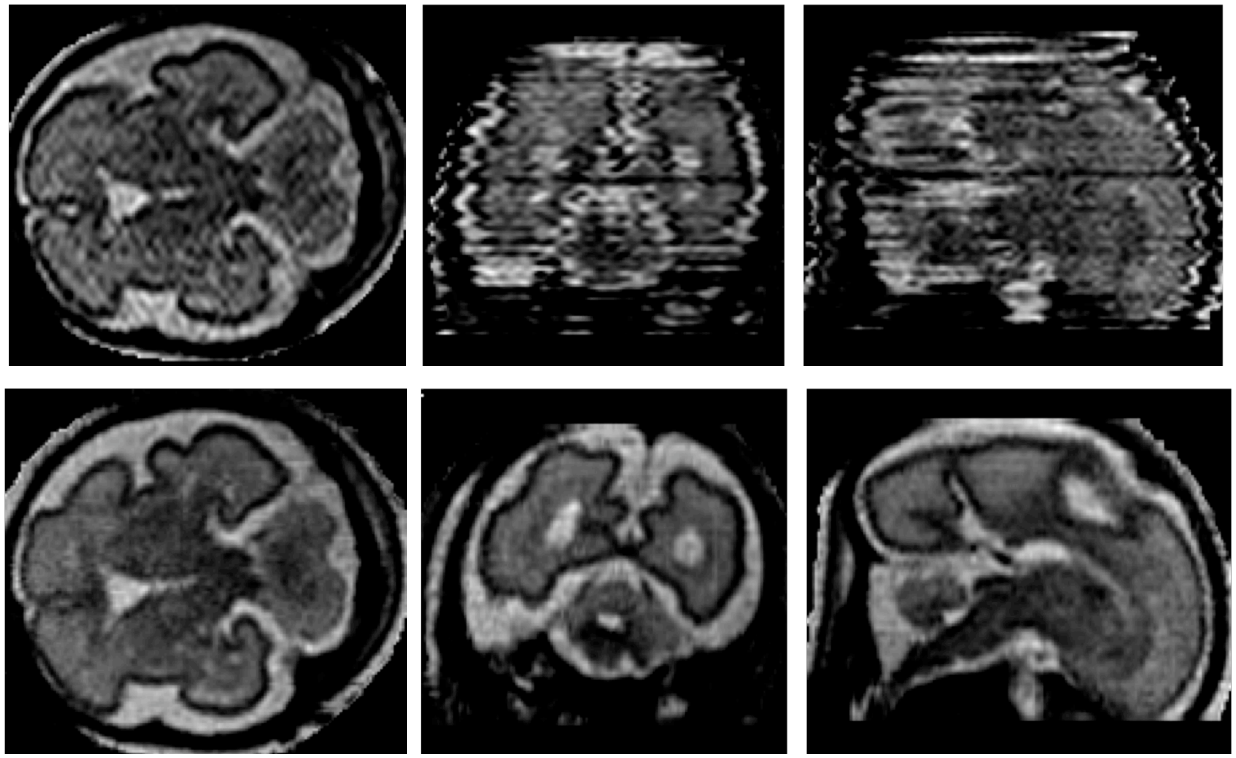
    Image matrix: 352*262, Field of View: 380 mm

    TH: 2.0-2.8 mm with minus half TH gap.

  - The mother was free breathing during scanning and no sedation was used.
  - Basic scanning time was ~1minute per dynamic loop (~1 image/second)
  - 2 - 8 loops acquired either all parallel or mixture of orthogonal orientations as possible

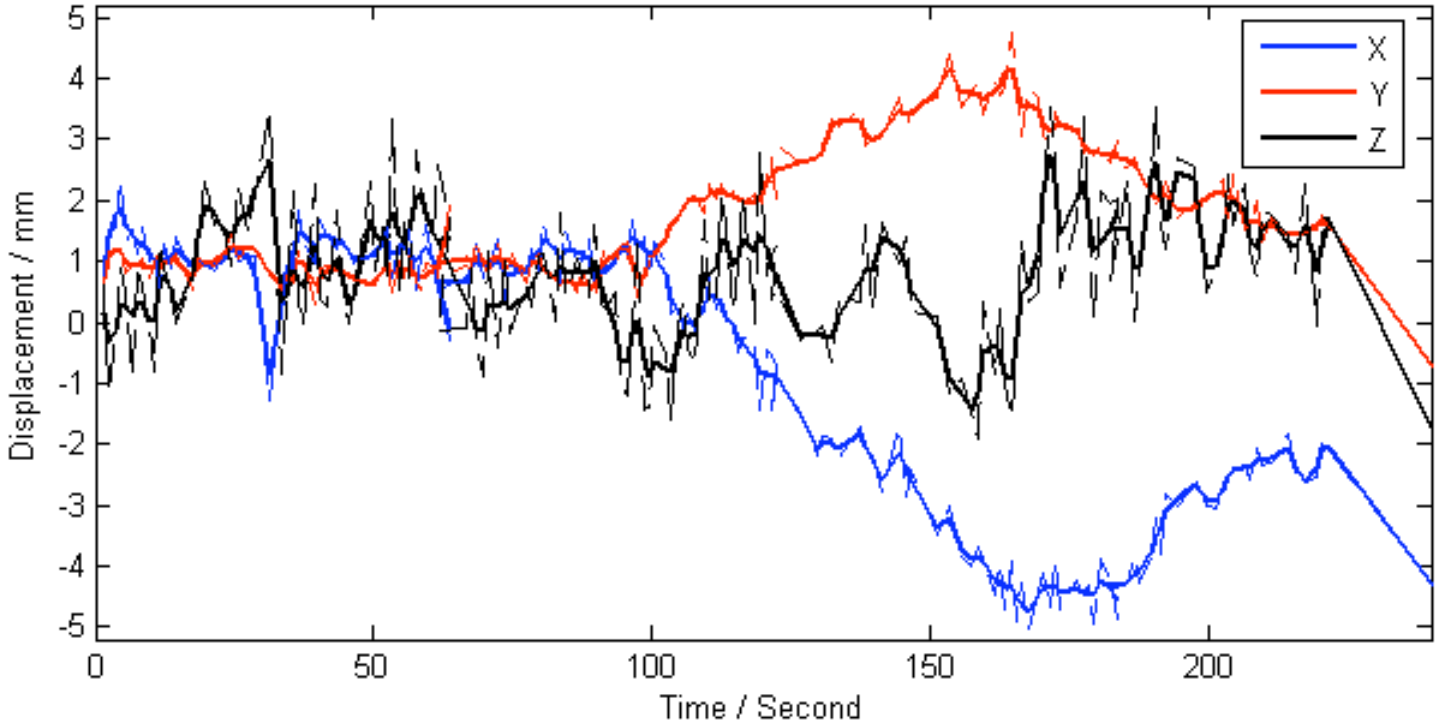
- All examinations successfully reconstructed

Fetal MR imaging: Results

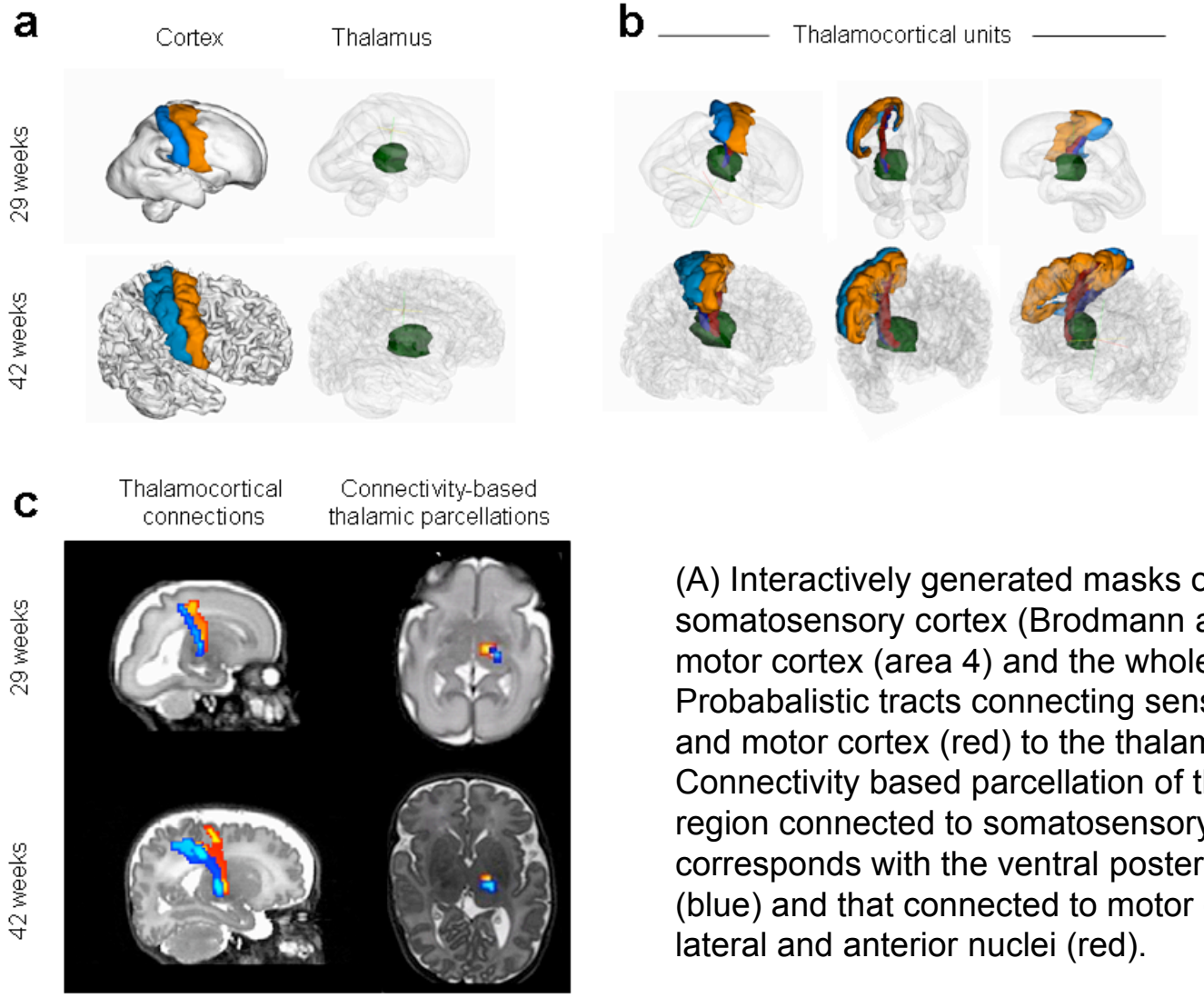


S. Jiang et al. MRI of moving subjects using multi-slice snapshot images with Volume Reconstruction. IEEE TMI, 2007.
Can also be done with DTI data (Jiang et al, MICCAI 2007)

Registration results reveal fetal motion

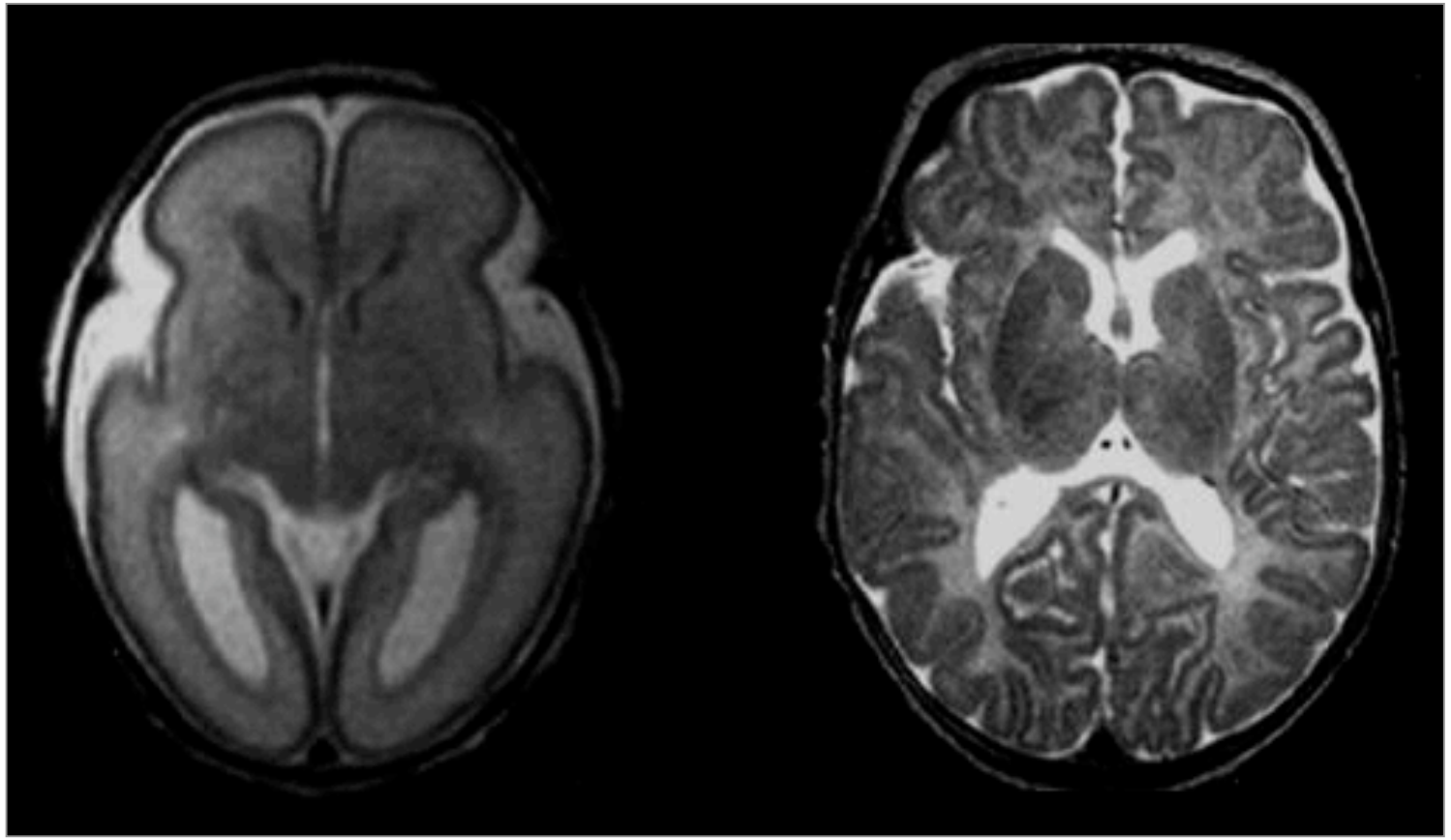


Current work work: Probabilistic tractography in preterm and term infants



(A) Interactively generated masks overlaying: primary somatosensory cortex (Brodmann areas 1-3); primary motor cortex (area 4) and the whole thalamus. (B) Probabalistic tracts connecting sensorimotor (blue) and motor cortex (red) to the thalamus. (C) Connectivity based parcellation of the thalamus. The region connected to somatosensory cortex corresponds with the ventral postero-lateral nucleus (blue) and that connected to motor cortex with ventral lateral and anterior nuclei (red).

Challenges and future work: Serial imaging of the developing brain



24 weeks gestation

Term (40 weeks gestation)

Acknowledgements

- Department of Computing, Imperial College London
  - P. Aljabar, K. K. Bhatia, H. Xue, M. Murgosova, A. Ericsson, E. Robinson, I. Gounasis
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  - J.P. Boardman, L. Srinivasan, M.A. Rutherford, L.E. Dyet, S. Jiang, R. Heckemann, S. Counsell, A. Hammers, A.D. Edwards, J.V. Hajnal