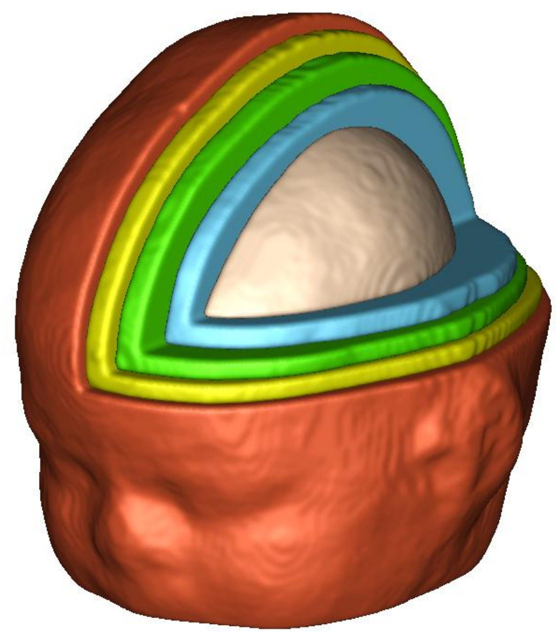
Growth trajectory of the early developing brain derived from longitudinal MRI/DTI data

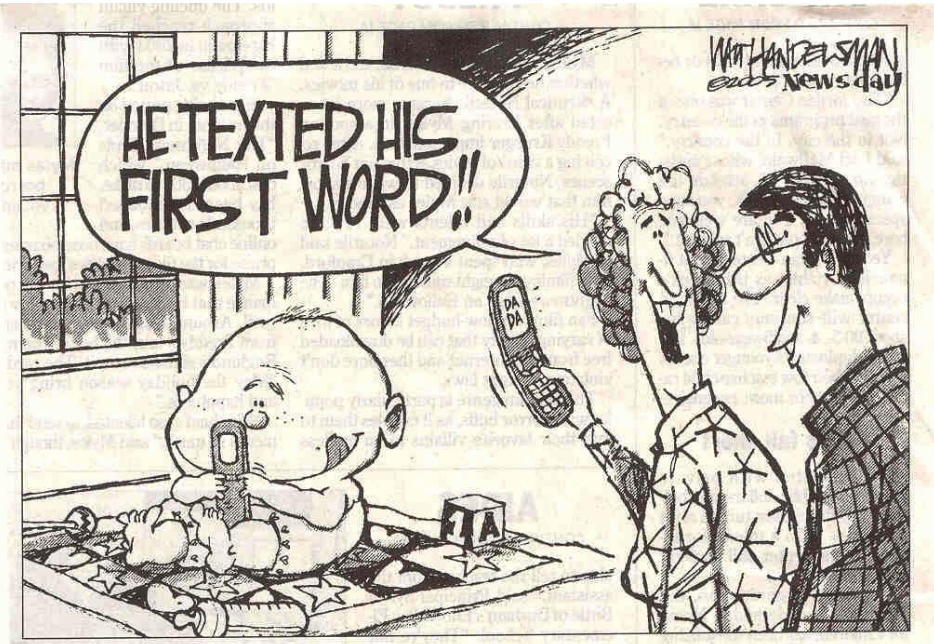
Guido Gerig

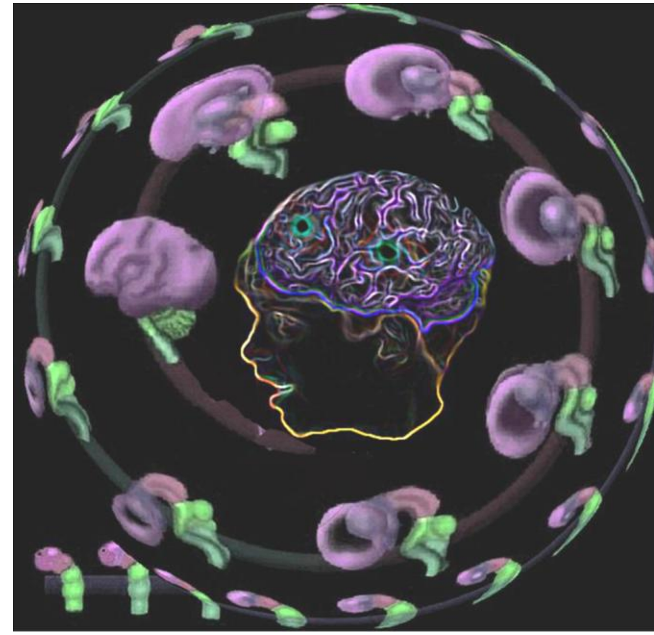
University of Utah

Scientific Computing and Imaging (SCI) Institute



Understanding early Development …





Brain Development in High Risk Children

- Understanding rate and variability of normal development
- Detect differences from typical development (autism, at risk, drug addiction,
- Early diagnosis → early therapy → better future for infants and families
- NIH funding: Increased support for "discovery science"

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Early Brain Development Studies

- John Gilmore, M.D.
  Principal Investigator
- Studies
- Investigators
- Image Analysis
- Progress/Publications
- Training Opportunities
- Links
- Contact Us

Early Brain Development Studies

Normal Controls

Twins

Mild Ventriculomegaly (MVM) (Brain)

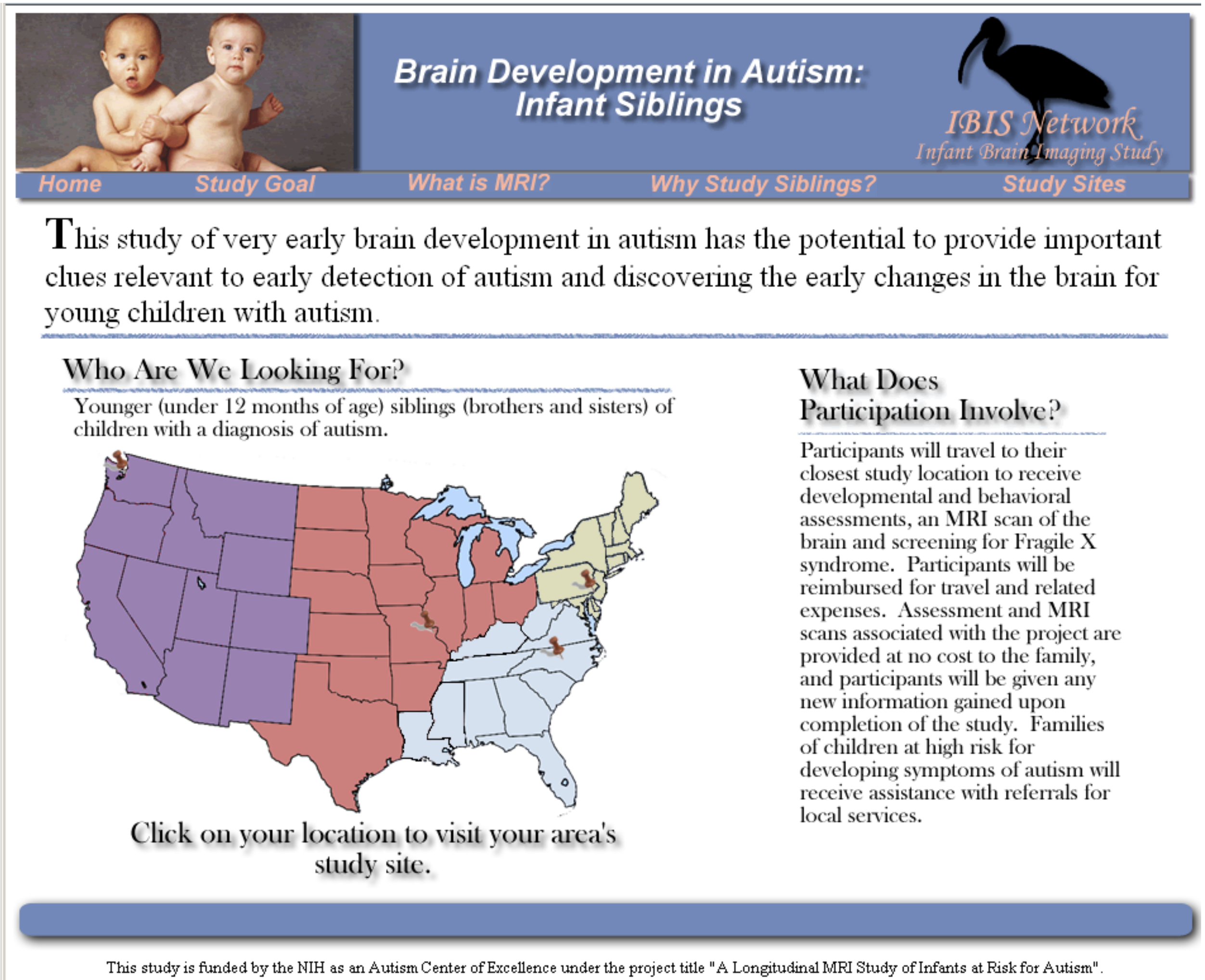
Babies of Mothers with Schizophrenia

Offsprings of cocaine-addicted mothers

Neonatal Brain Development in High Risk Children (J. H. Gilmore, MD)

- Understanding rate and variability of normal development
- Detect differences from typical development
- Early diagnosis → early therapy → help families

ACE: Autism Network of Excellence



PI Joseph Piven, UNC

Infants at risk 6mo to 2 years, longitudinal study

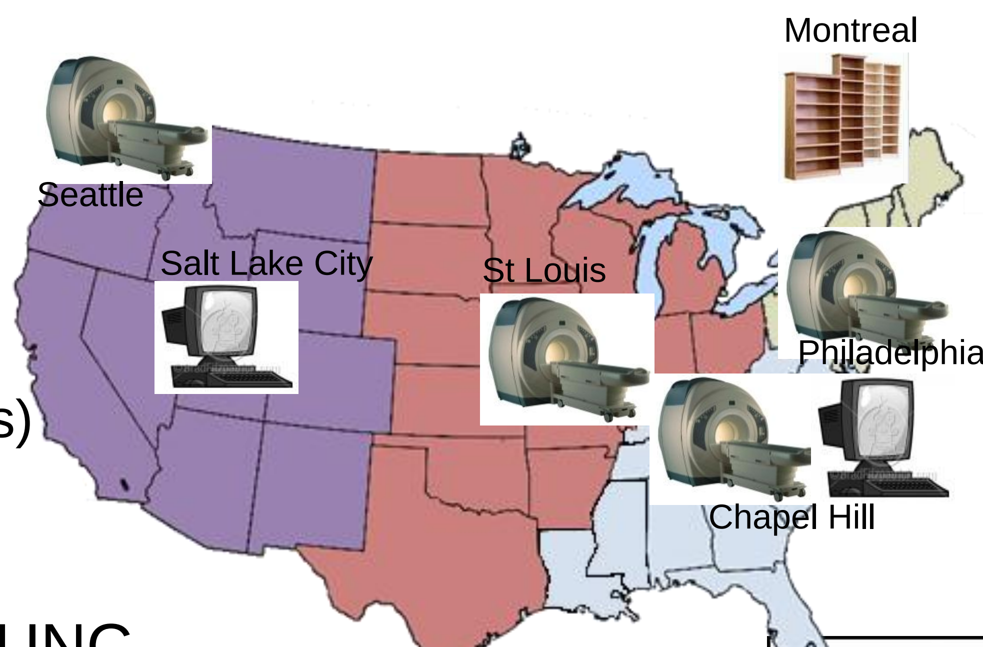
4 acquisition sites, DCC, processing Utah

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

ACE: Autism Network of Excellence Infant Brain Imaging Study IBIS

- P.I. Joseph Piven, UNC
- ACE grant: Autism center of excellence.
- Longitudinal study of infant siblings at risk for Autism scanned at 6mo, 1y and 2yr (total >600 MRI/DTI)
- 4 scanning sites:
  - Seattle
  - St Louis
  - Philadelphia
  - Chapel Hill (2 scanners)
- DCC: MNI Montreal
- Image analysis: Utah/UNC



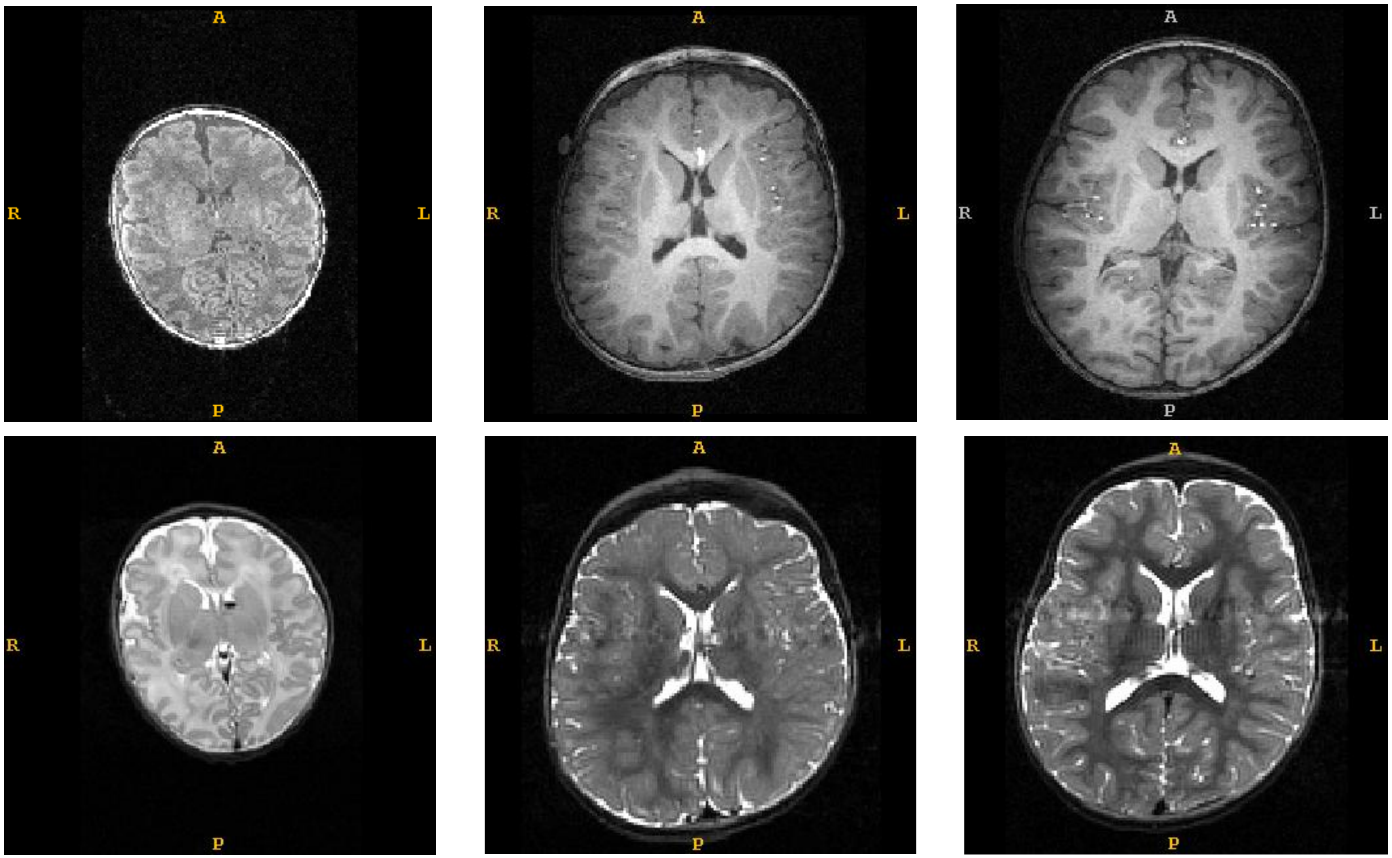
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Outline

1. Imaging Technology for Pediatric Imaging
2. Analysis of structural MRI
3. Image Registration
4. Population Studies of DTI
5. Results

High-Speed Imaging: Infant MRI at 3T



T1

T2

2 weeks | 1 year | 2 years

UNC Weili Lin: 3T Siemens Allegra
Total time: T1, T2hires, DTI 2x2x2: 15' total

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Training of “older” infants: Mock Scanner

- Old MRI scanner used for practice sessions (pictures Yale Univ.)
- Subjects learn to remain still for up to 30 minutes
- Head tracking coupled with video presentation (Duke)

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

UNC Scan Success Rate

Siemens 3T Allegra, Weili Lin & team

CONTE SZ Study, started 2002

Singletons	Neonates	Follow-up 1yr	Follow-up 2yrs
Controls	156	42	34
SZ & BP	33	15	9
MVM	34	12	2
Total	223	69	45
Attempted	251	110	77
Success Rate	89%	63%	58%

Twin Study started 2006

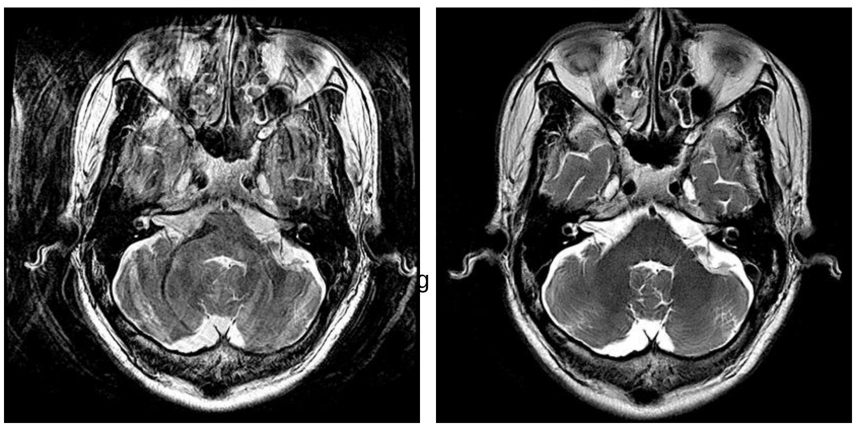
Twin Pairs	Neonates	Follow-up 1yr	Follow-up 2yrs
Controls MZ/DZ	67	28.5	12.5
Attempted	69	34	18
Success Rate	97%	84%	69%

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

New Technology: MRI Motion Correction

GE: PROPELLER* - Motion Correction Imaging (unique pattern of k-space filling that acquires data in radial "blades" rotating in sequence)



Siemens: Navigator pulse for online correction (Flash T1, courtesy of MGH).

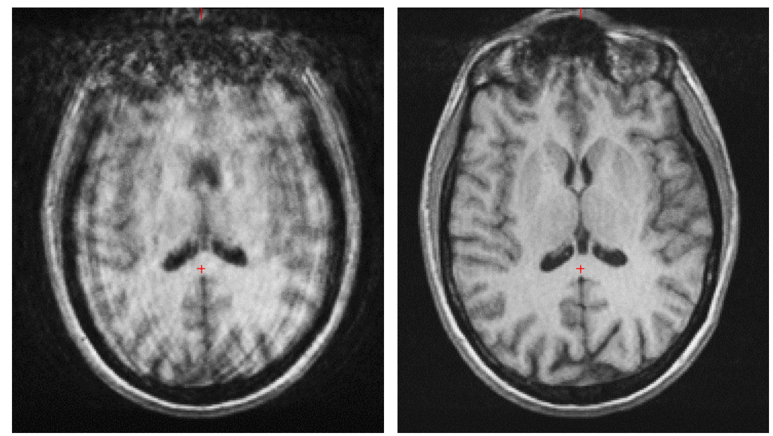
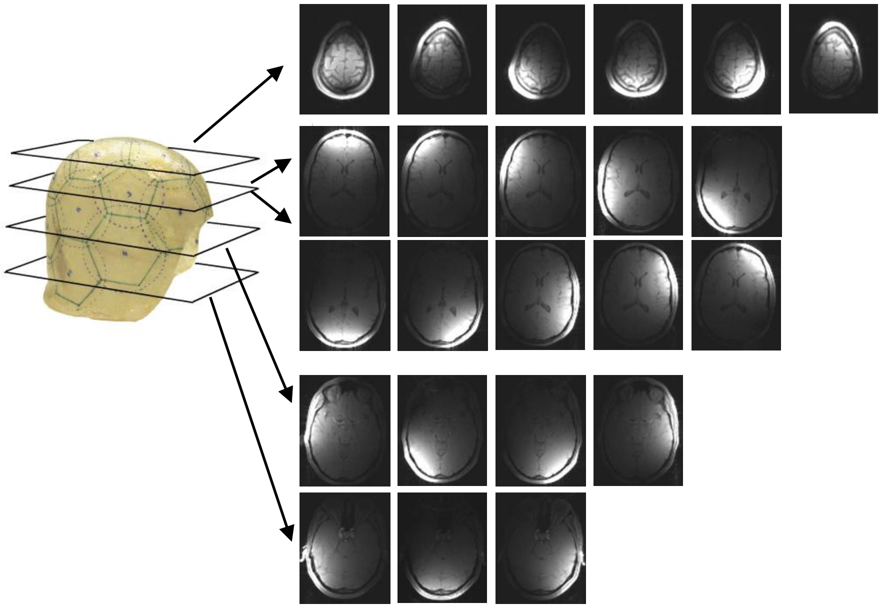


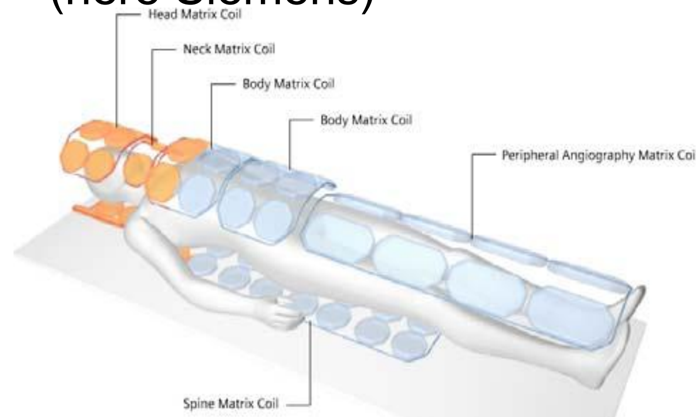
Fig C 14 Slice through average of 3 FLASH scans without motion correction (left) and 3 FLASH scans with motion correction (right).

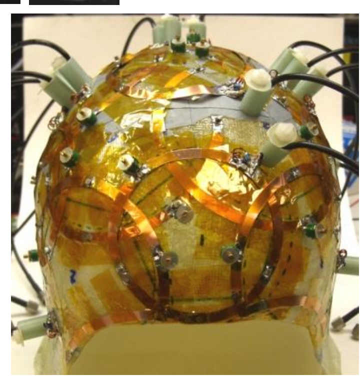
New emerging techniques: groups of Hajnal, Studholme, Warfield

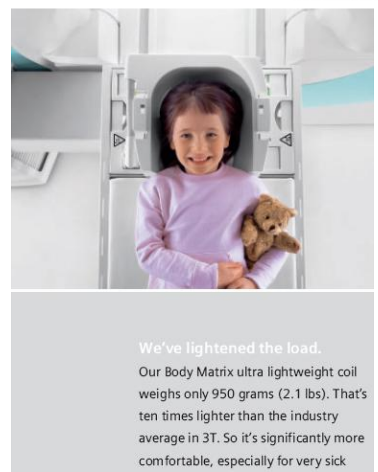
Parallel Acquisition with Matrix Coils



Parallel imaging & matrix coils (here Siemens)







23 channel prototype array at 1.5T – Gram Wiggins and Larry Wald, MGH

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

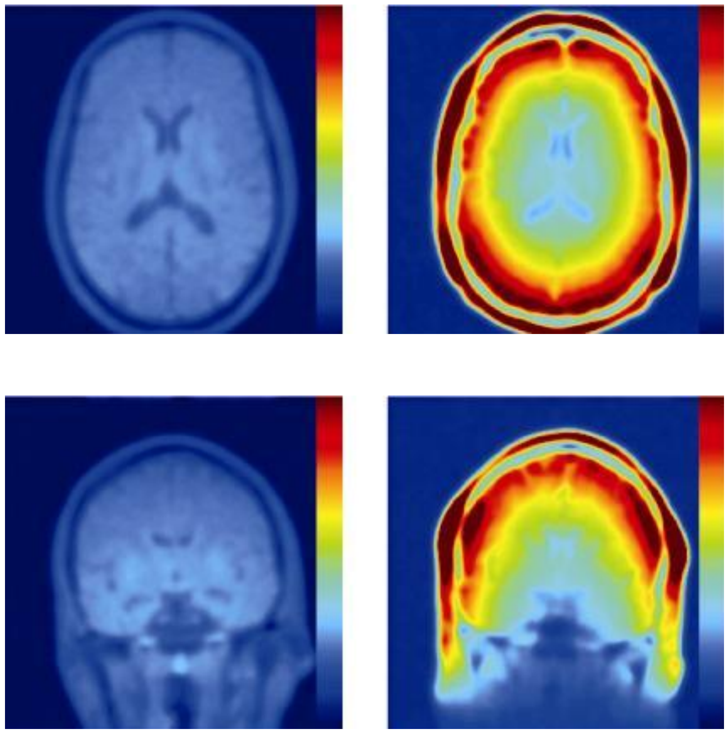
SCI INSTITUTE

23 channel array for 1.5T

SNR Maps
Grad. Echo

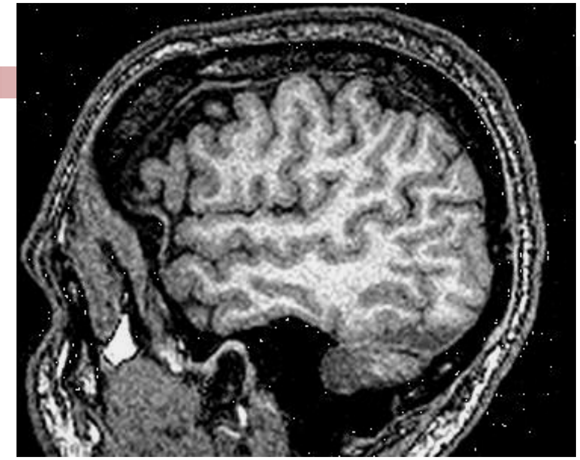
Normalized to volume coil average (=1.0)

SNR gain:
- 4 fold in cortex
- 1.75x in corpus callosum

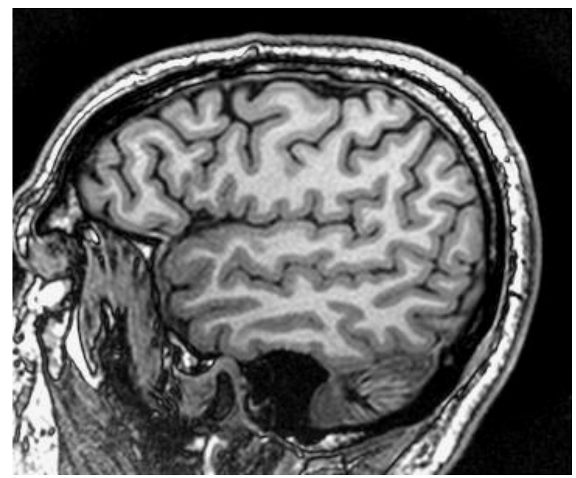


Siemens volume coil

23 channel array



Volume coil



23 Channel “Bucky”

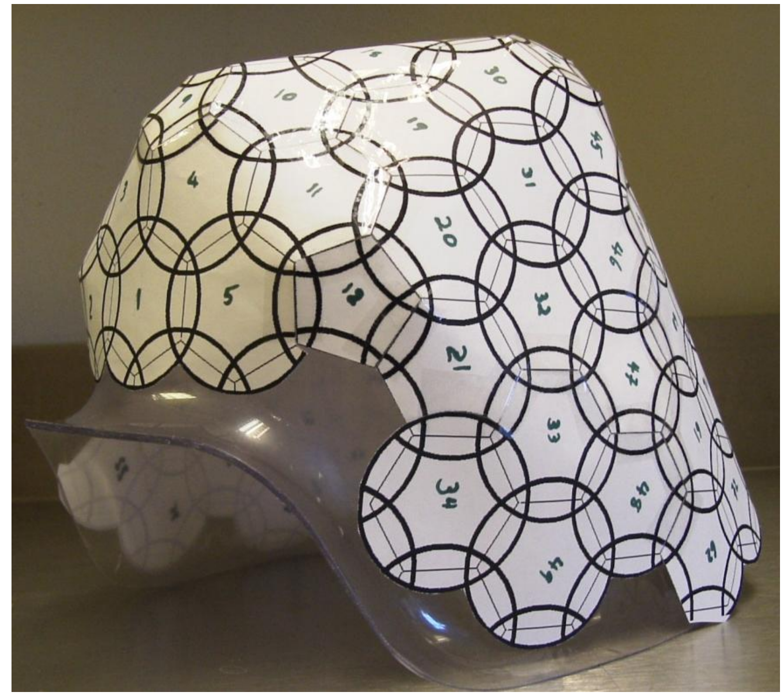
Courtesy Bruce Rosen, MGH

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Optimal coils for infants?

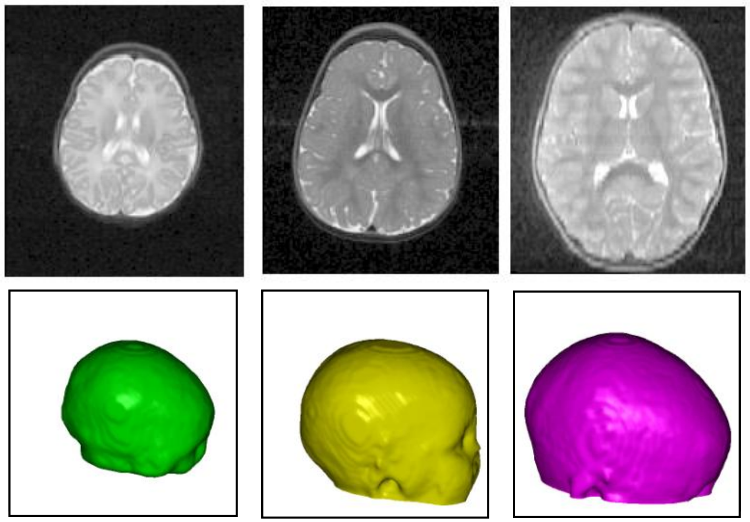
- Challenge: Parallel coils have to be placed close to head/brain
- Infant brain shows rapid growth: Adult coil not optimal
- Need: Helmets adapted to infant head sizes
- How many helmets do we need?



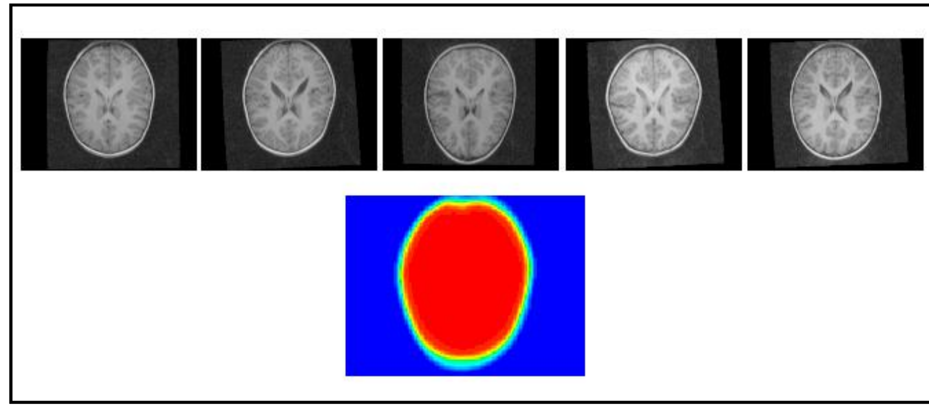
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

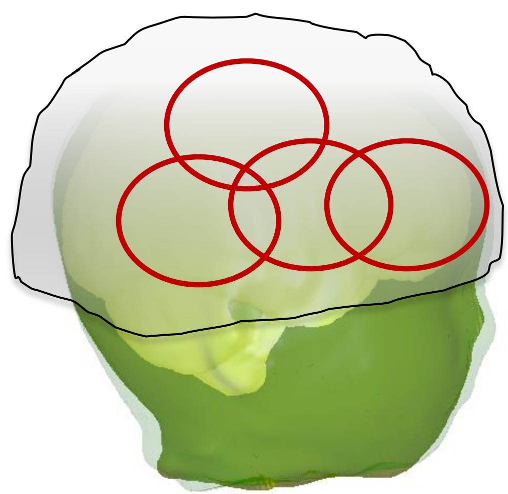
Modeling Head Shapes for Infant Coil Design



Statistical head shape model



Statistical modeling of head shapes for infant matrix coils: UNC-MGH-Utah Collaboration (Larry Wald, Weili Lin, G. Gerig)



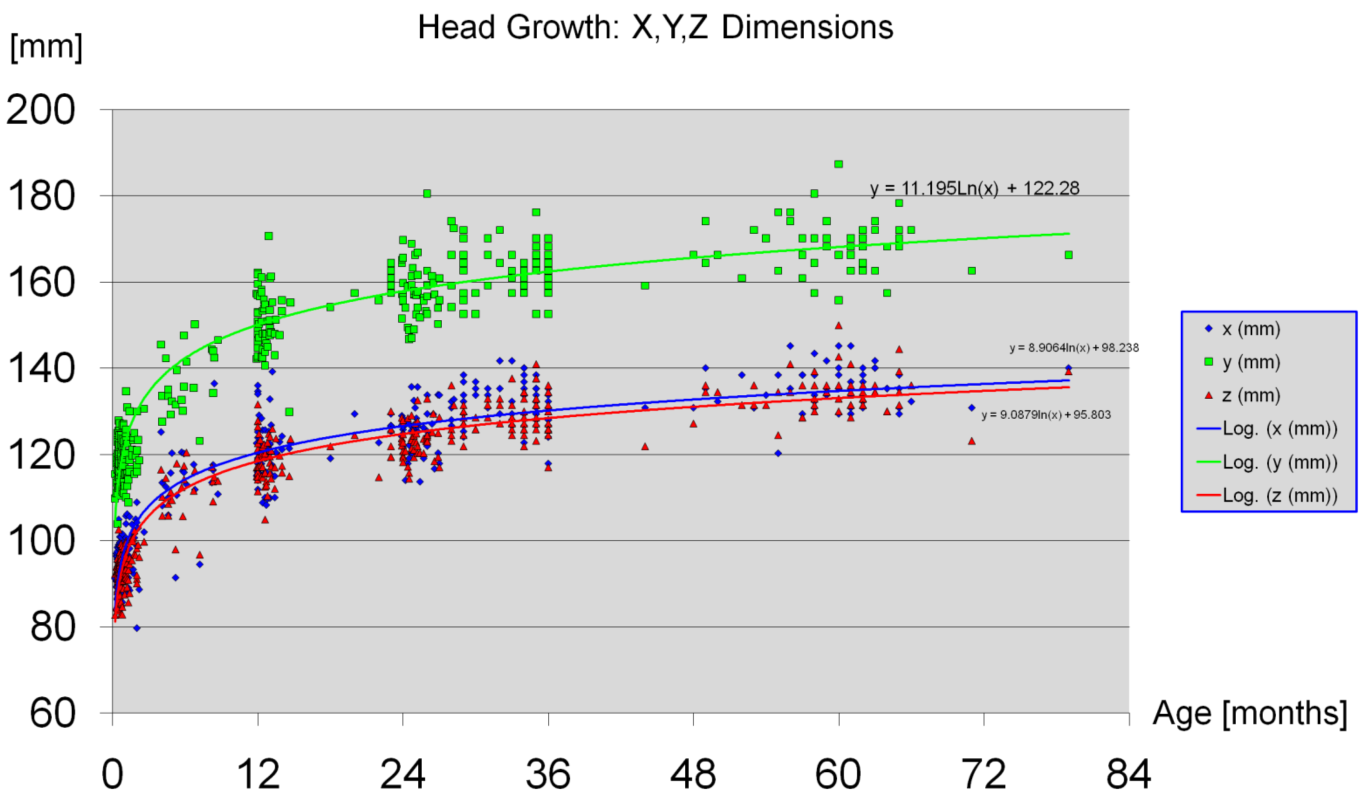
Example: 95% head and brain size for 2yr group.

Optimal placement of coils w.r.t. brain

I INSTITUTE
SITY OF UTAH

SCI INSTITUTE

Modeling Head Shapes for Infant Coil Design



Longitudinal modeling of head size (N=411) based on MRI

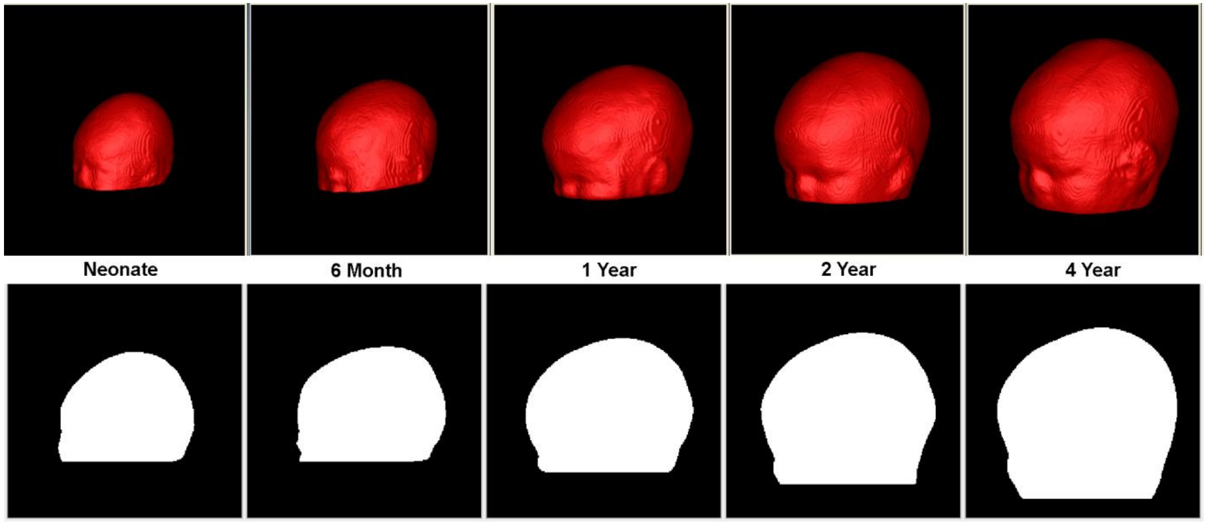
So far:
Models & coils for neonates, 6months, 1yr and 2yrs

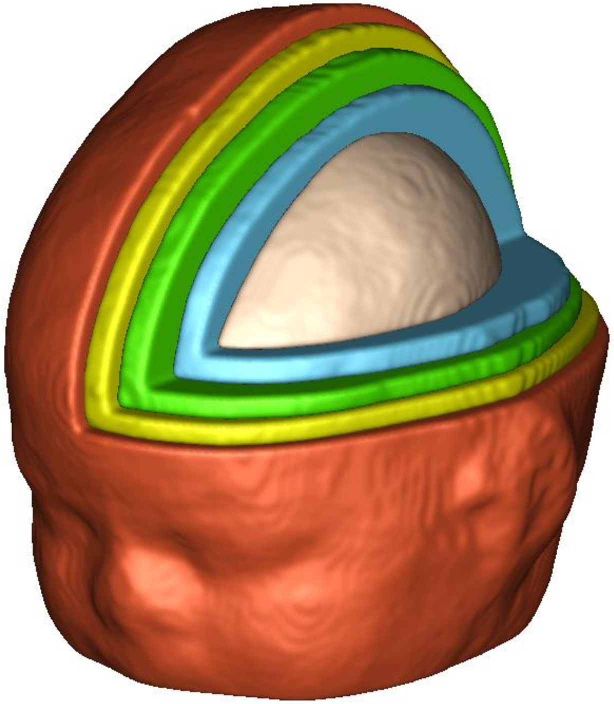
Currently:
Calculate optimal set of "equally spaced" shape models

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Modeling Head Shapes for Infant Coil Design





Collaboration Weili Lin, UNC and Larry Wald, MGH: Design of Dedicated Parallel Coils for Infants

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Modeling Head Shape Growth

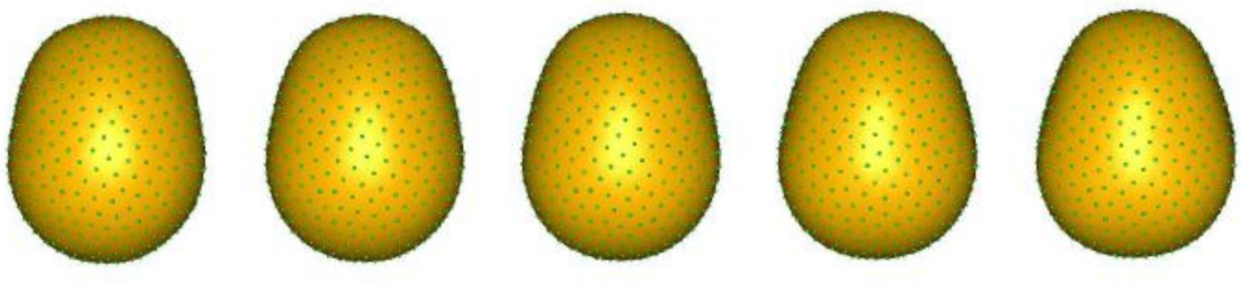


Fig. 3. Overview of head shape regression: Changes in head shape with age

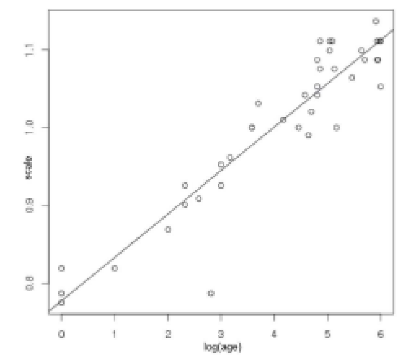
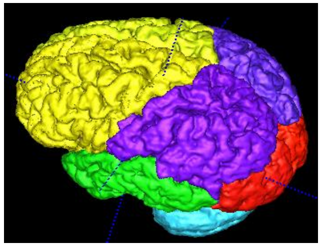


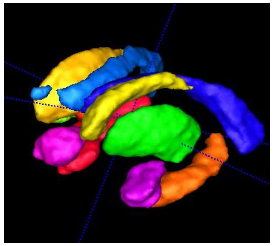
Fig. 2. Changes in head size with age

Link to Movie

Datar, Cates, Fletcher, Gouttard, Gerig, Whitaker, MICCAI 2009

Currently: Application to brain structures





THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

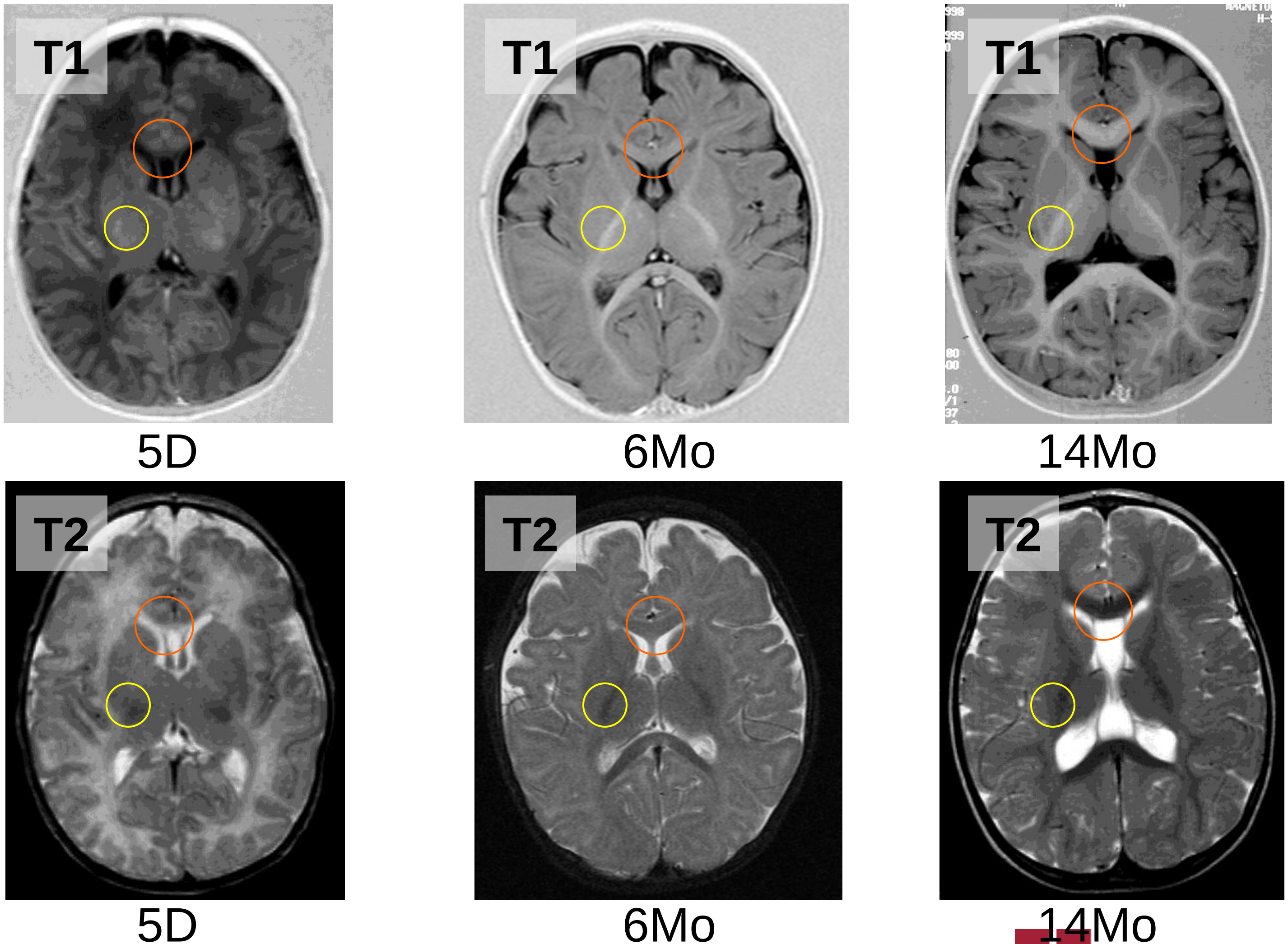
SCI INSTITUTE

Outline

1. Imaging Technology for Pediatric Imaging
2. Analysis of structural MRI
3. Image Registration
4. Population Studies of DTI
5. Results

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Contrast changes in early development



Myelinated during 1st yr

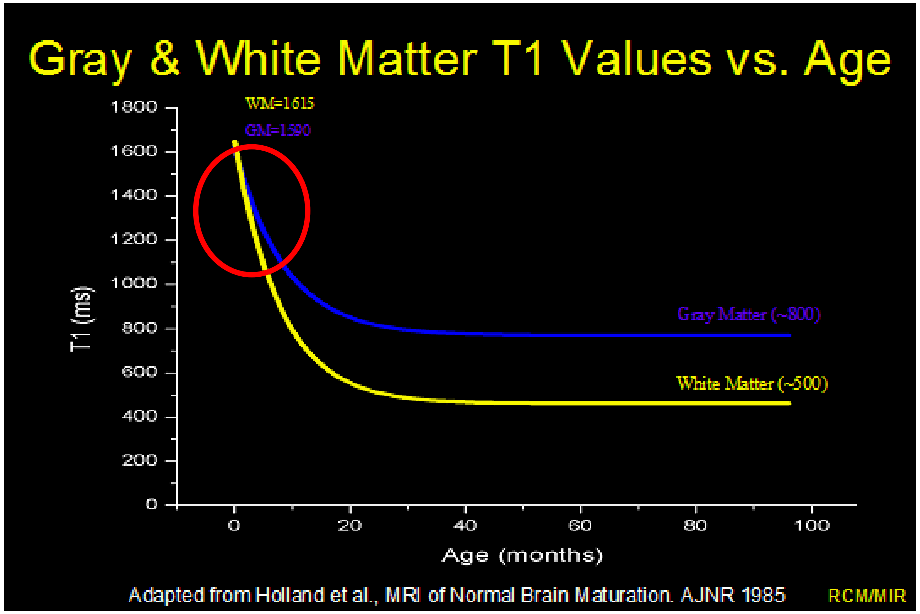
Early myelination

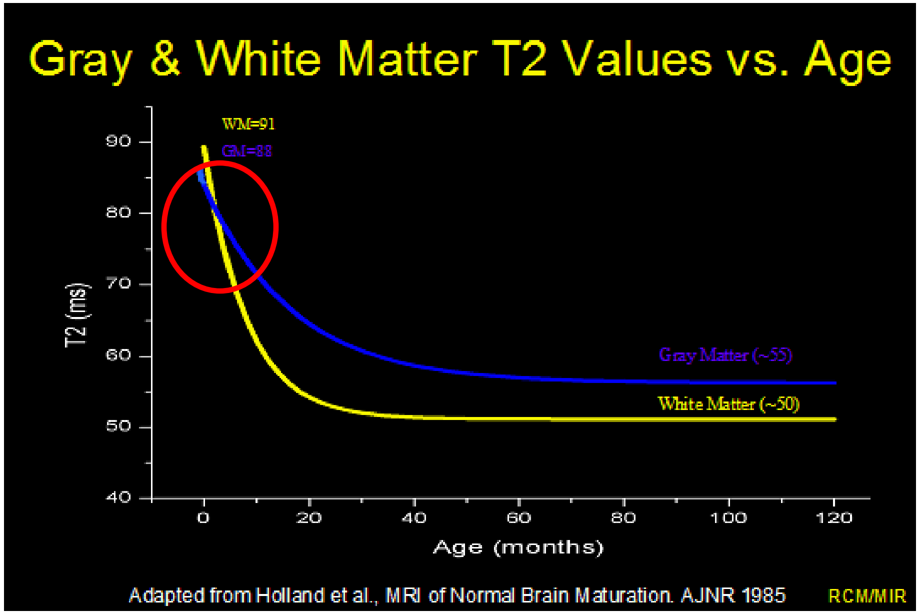
Courtesy Keith Smith, UNC Radiology

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

MRI parameters vs. age





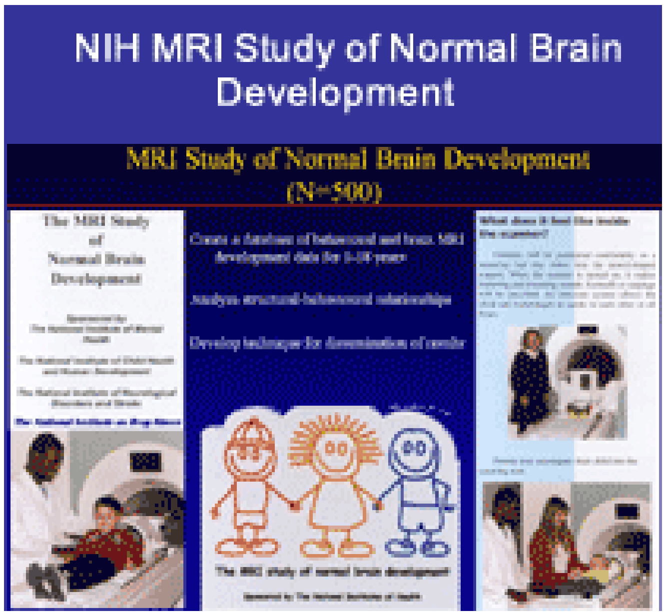
Contrast flip in T1 and T2 during first year

Courtesy Bob McKinstry, Washington University

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Normative Pediatric MRI Database (MNI A. Evans+ Consortium)



[Movie](#)

A. MRI of the Developing Brain from Birth through 3 Years

Fig. 3

0-3 months

3-6 months

6-12 months

12-18 months

24-36 months

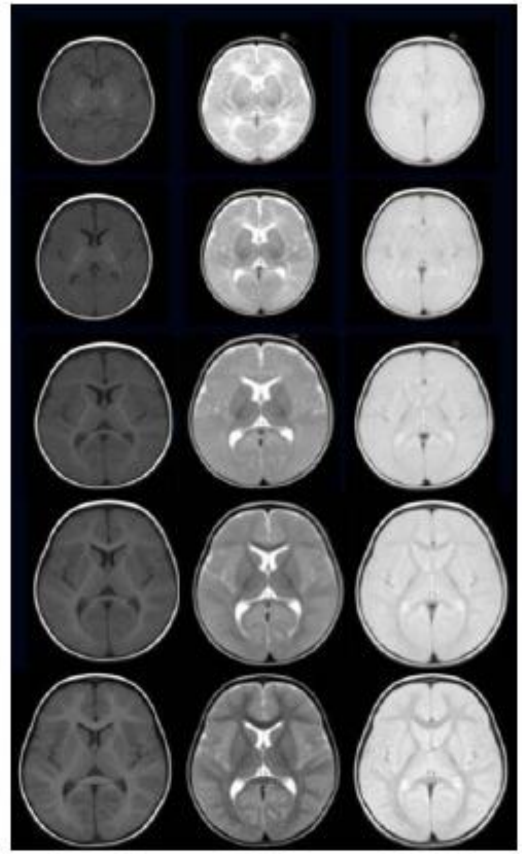
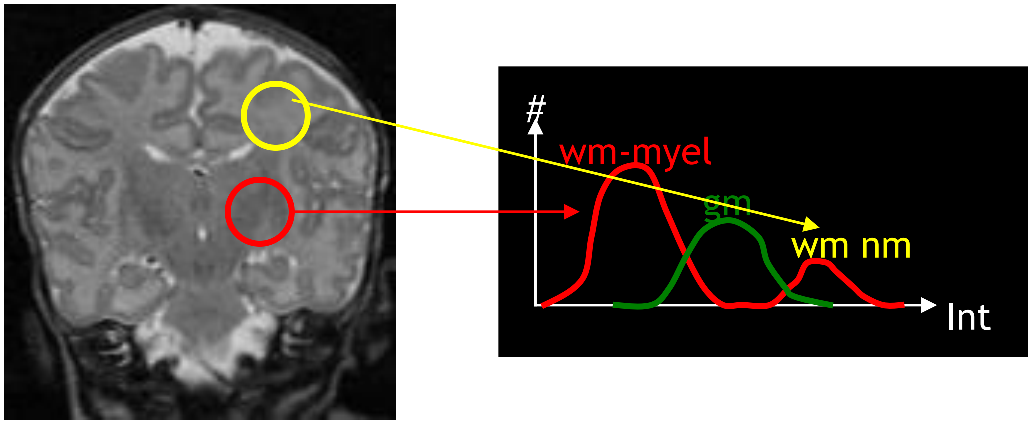
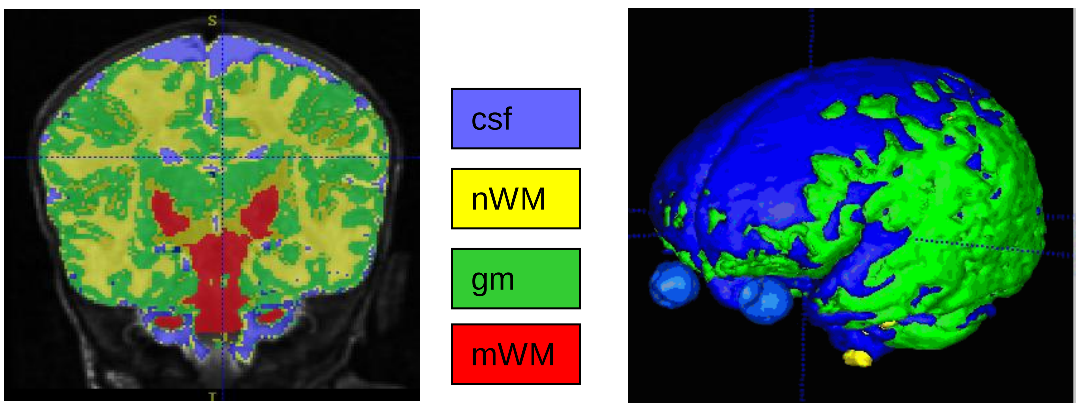


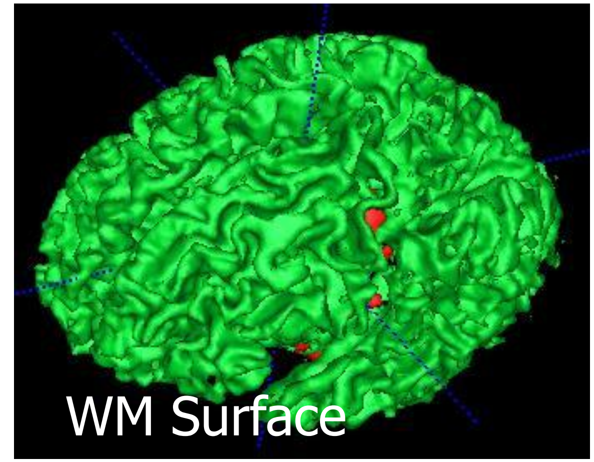
Fig 3 shows MRI data from the NIH MRI Study of Normal Development (NIHPD), from 50 children aged 10 days to 4 years (some scanned as many as 9 times). Note the dramatic myelination that occurs between 6 and 18 months (lighter in T_1 (left), darker in T_2 (middle)and PD (right)); with almost no gray-white contrast at $\leq$ 6 months.

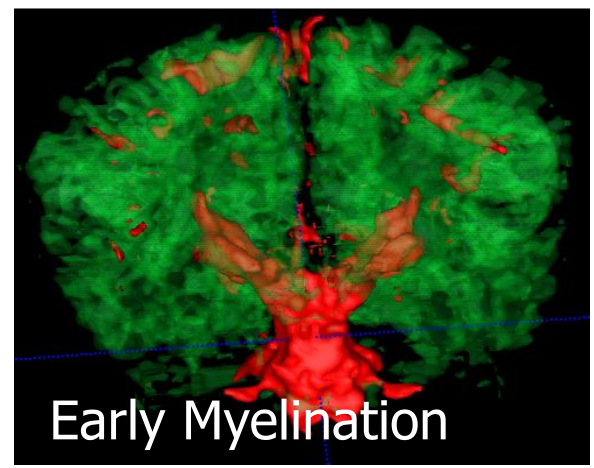
Frames here are extracted from a video (see CD in Appendix V or: www.bic.mni.mcgill.ca/users/alan/ACE obj2model2.avi) of this cross-lagged longitudinal MRI data from 200 MRI studies. The individual datasets were spatially re-sampled into stereotaxic space (without overall size scaling). Scans from selected epochs were then averaged for each MRI sequence (T_1, T_2, PD).

Neonatal MRI Segmentation







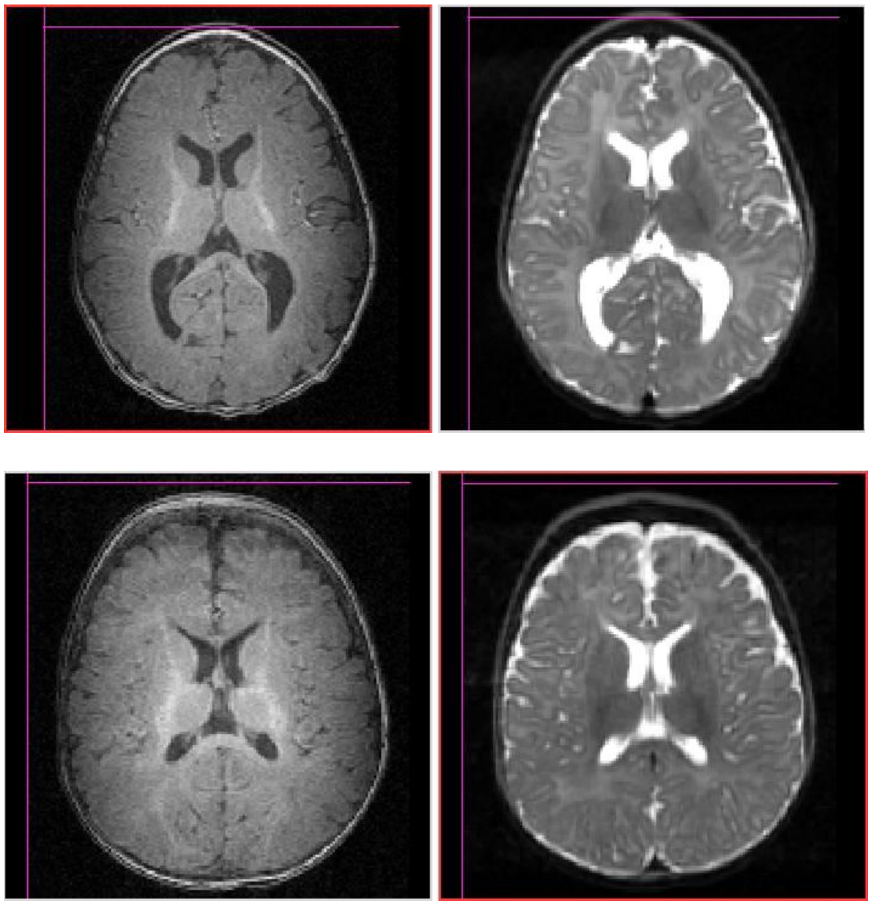


Marcel Prastawa, John H. Gilmore, Weili Lin, Guido Gerig, Automatic Segmentation of MR Images of the Developing Newborn Brain, (MedIA). Vol 9, October 2005, pages 457-466

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

4 and 6 month old subjects



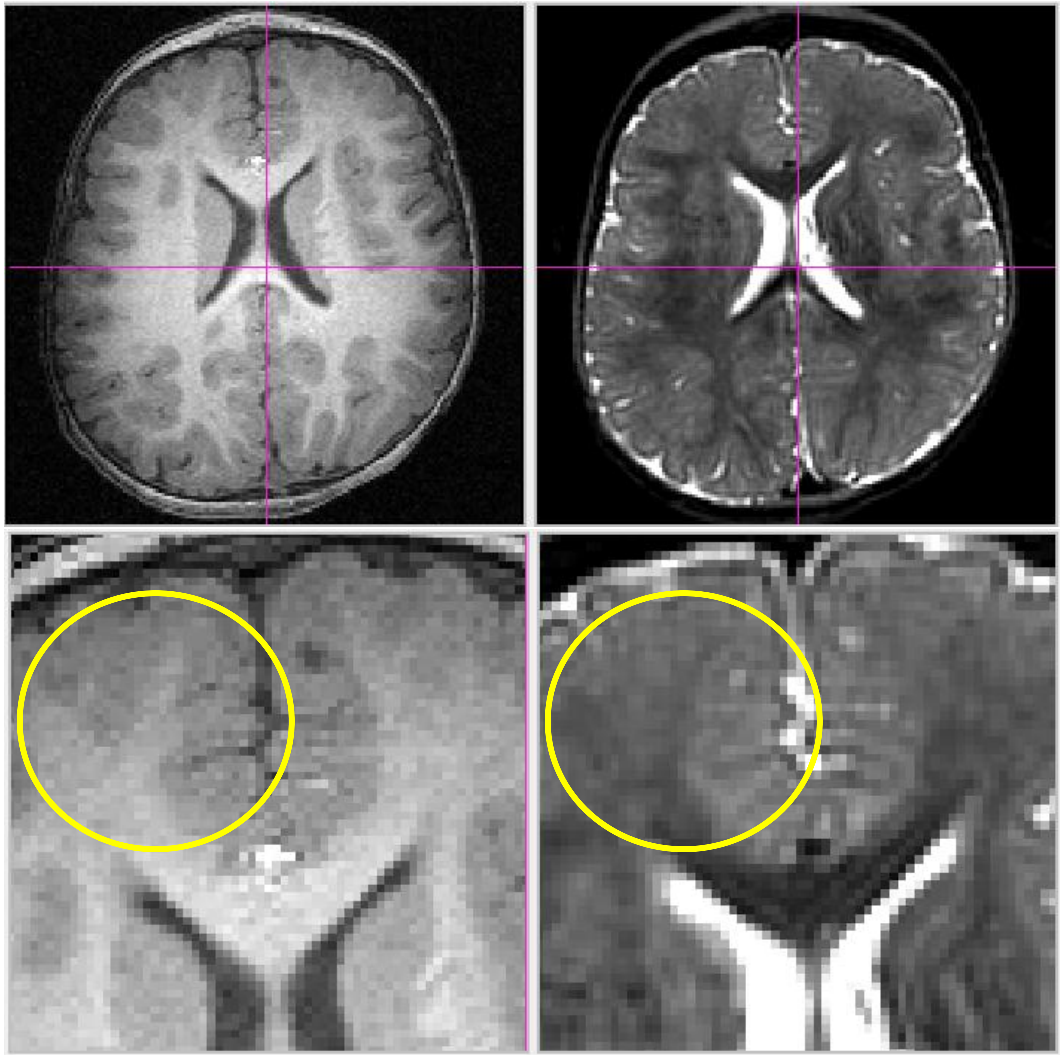
Intermediate stage of contrast flip between white and gray, with no differentiation in T1w at 4-6 mt and in T2 at 6-8 mt.

T1 and T2 are not in sync w.r.t. tissue contrast

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Challenge in Segmentation of 1years olds



T1w axial and zoomed T2w axial and zoomed

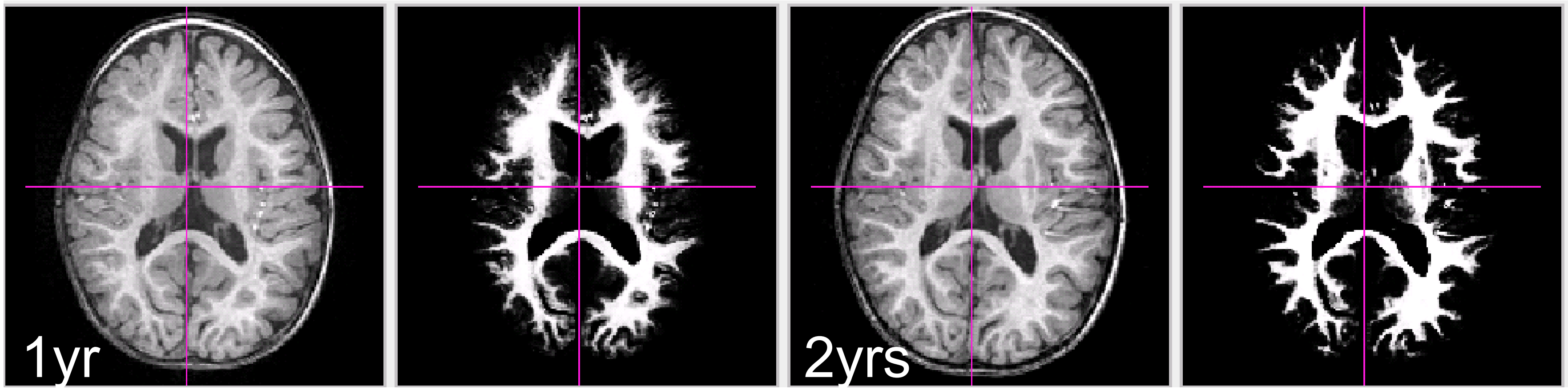
Difficulties for tissue segmentation:

- Strong bias inhomogeneity
- Gradual degree of myelination decreasing from central to peripheral regions
- Very low contrast in cortical white/gray
- T2 lags behind T1 in its ability to depict wm contrast and therefore even shows less contrast.

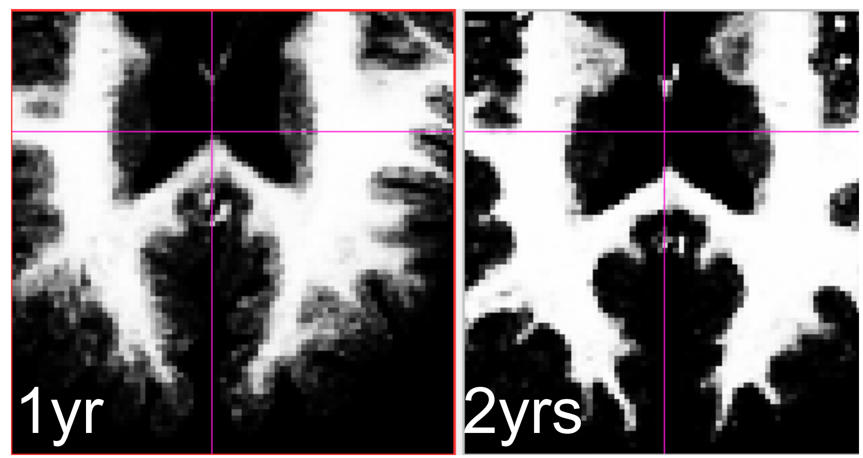
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Follow-up: Hi-res T1 (Weili Lin, UNC)

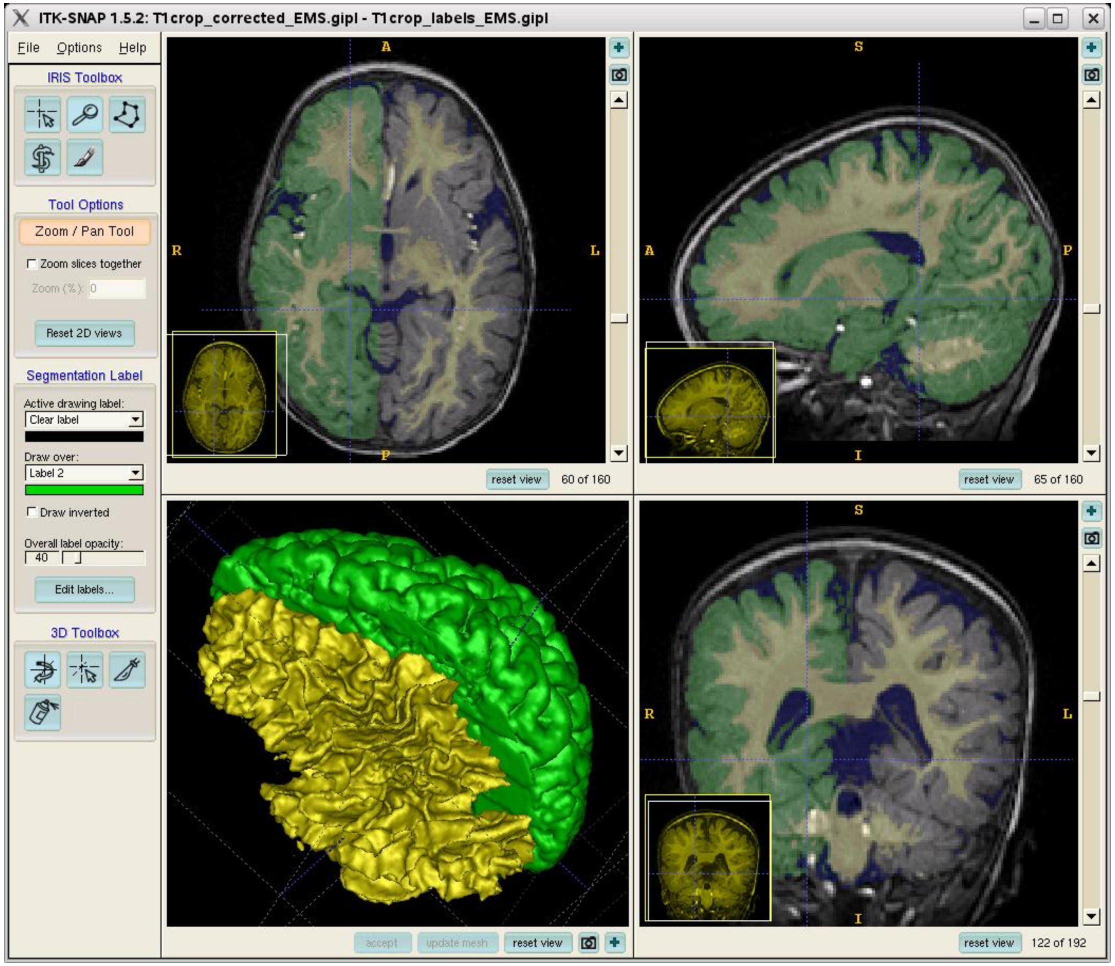


T1 MRI of same child at 1yr and 2yrs with wm probability maps: wm/gm boundary more fuzzy at 1yr.



THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Brain Segmentation 1year old

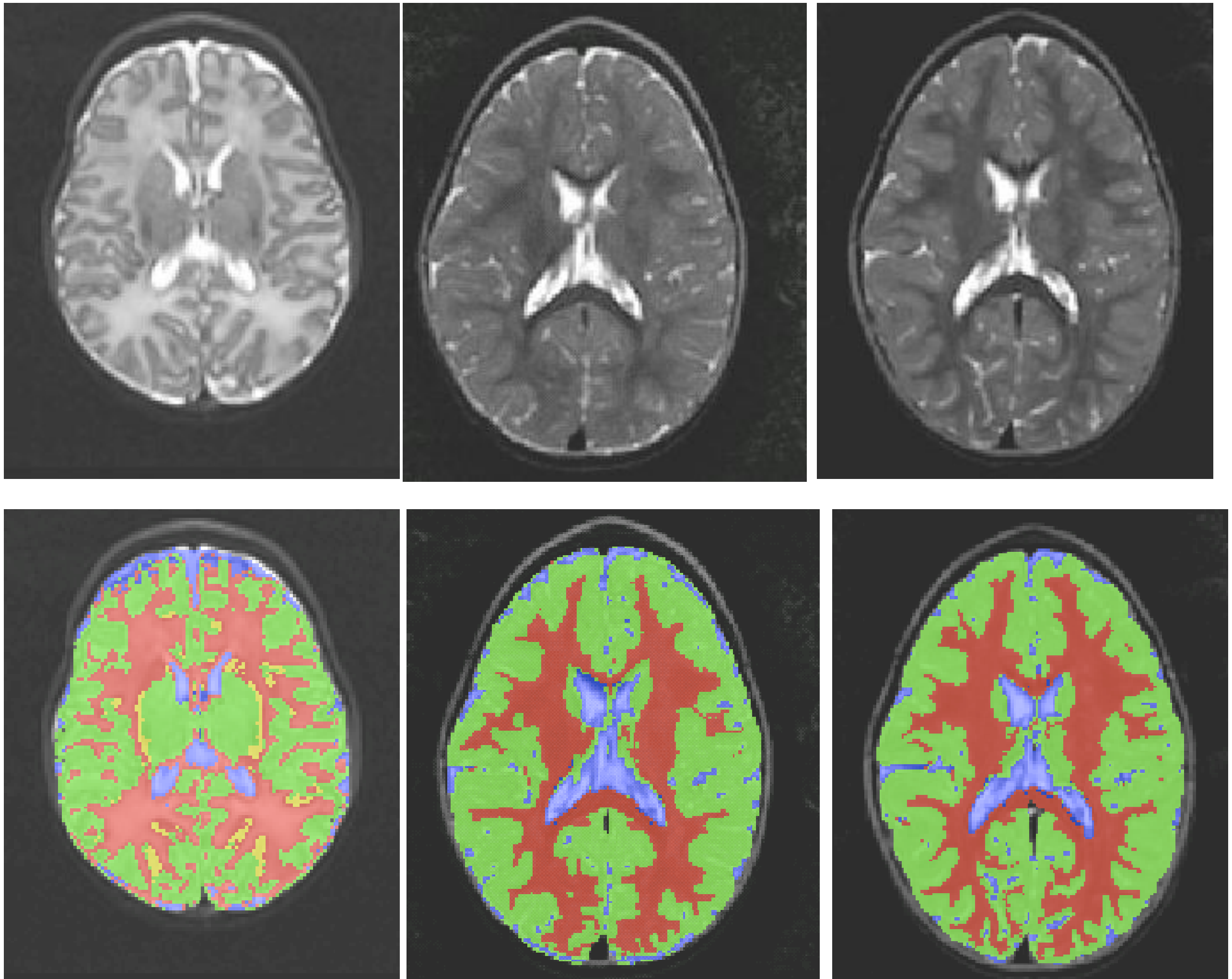


- Advanced version of expectation-maximization segmentation (M. Prastawa)
- Prior: Age-specific atlas
- Nonlinear registration of atlas to subject
- Robust, nonparametric clustering
- Parametric bias field correction

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Current Solution: Individual Tissue Segmentation at each time point



0.7 months   13.4 months   24.2 months

Segmentation procedures:

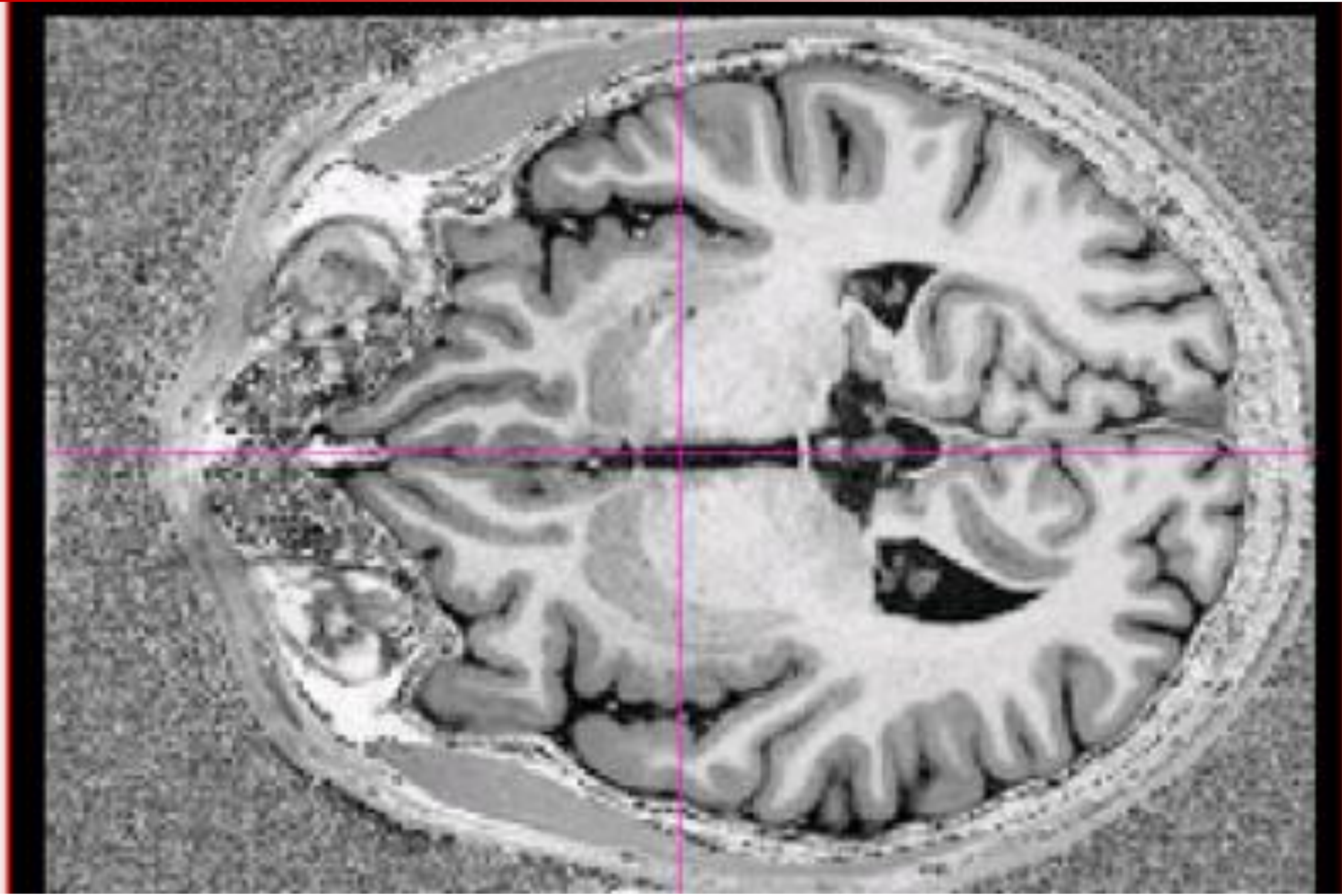
Prastawa et al.,

GM

WM

CSF

Pitfall: Bias inhomogeneity correction alters age-related contrast changes

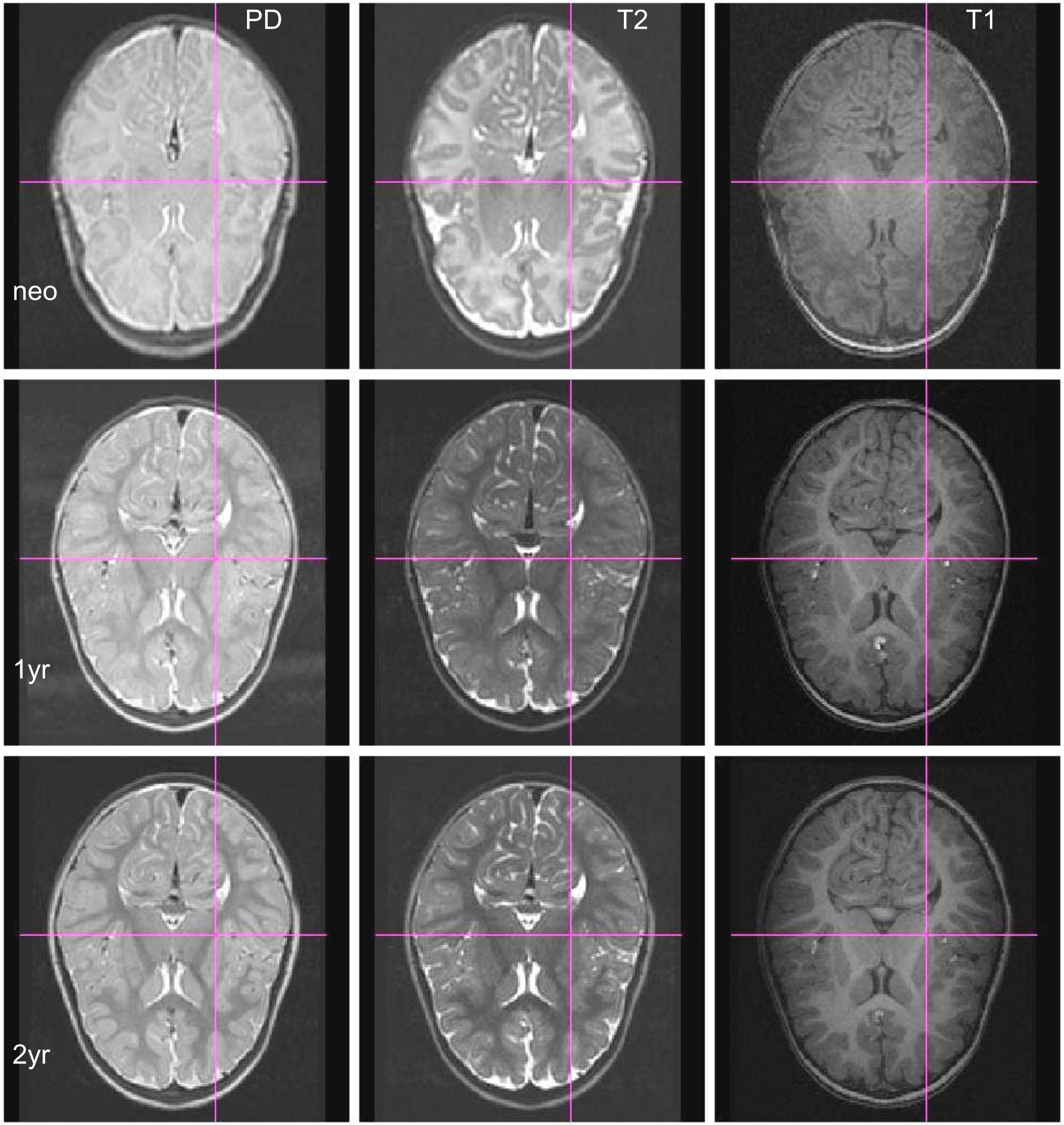


Outline

1. Imaging Technology for Pediatric Imaging
2. Analysis of structural MRI
3. Image Registration
4. Population Studies of DTI
5. Results

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

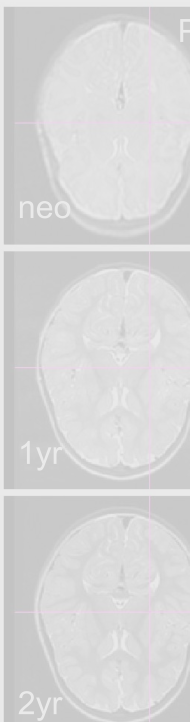
'rajectory

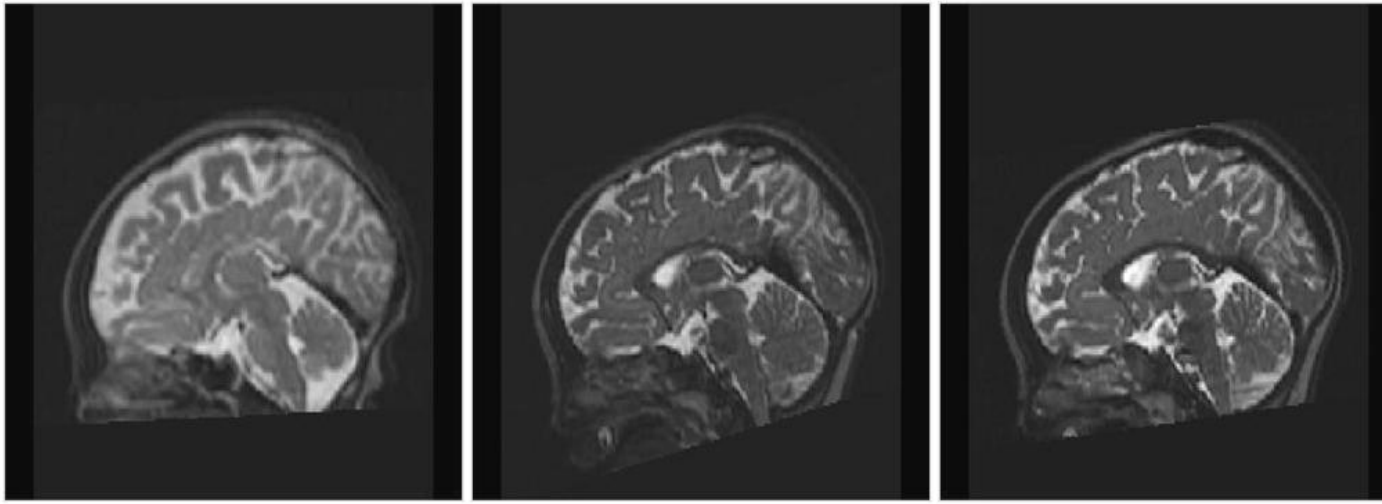


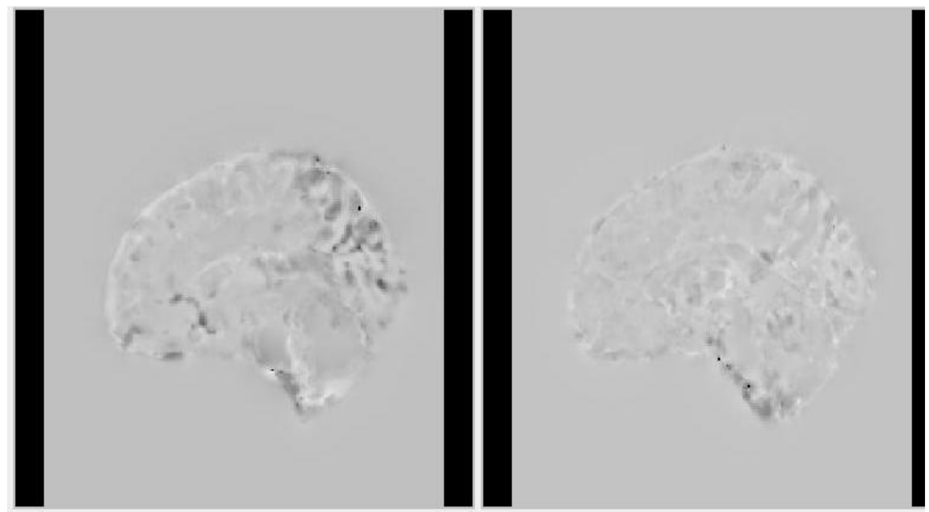
HE BRAIN INSTITUTE
HE UNIVERSITY OF UTAH

Goal: A

- Stabili
  nonline
- Analyz



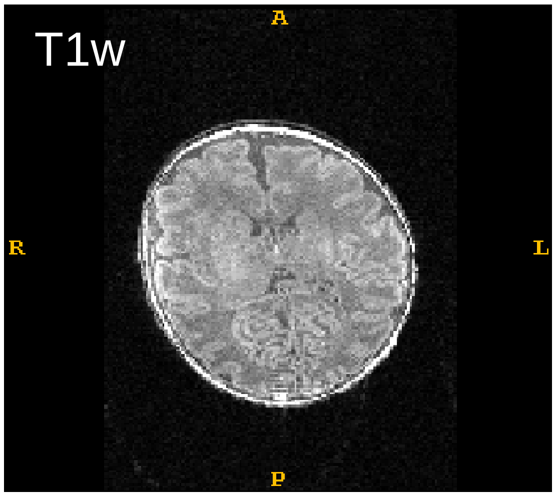




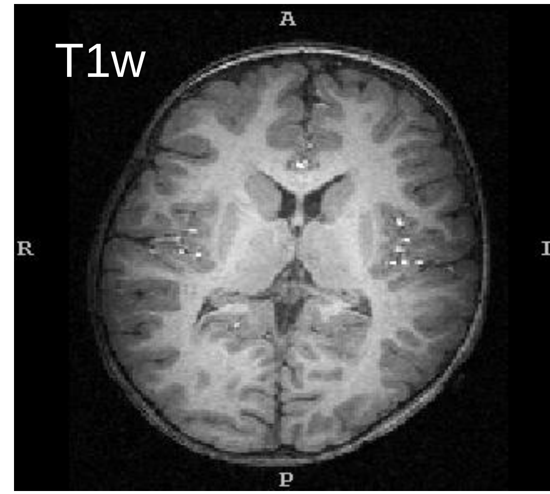
Log(|Jac|)

See work by Rueckert et al., Studholme et al. on deformation analysis

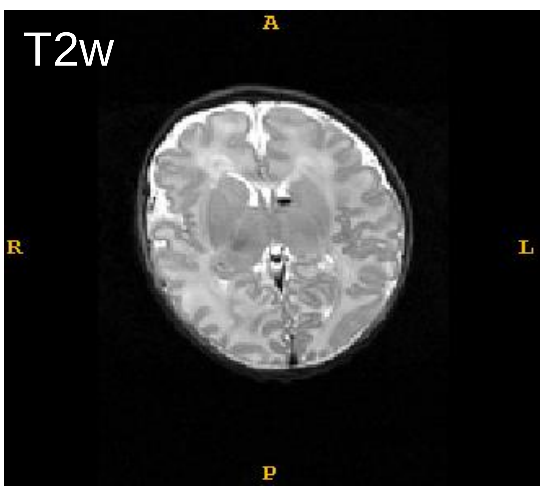
Atlas-building with changing contrast?



2 weeks



2 years



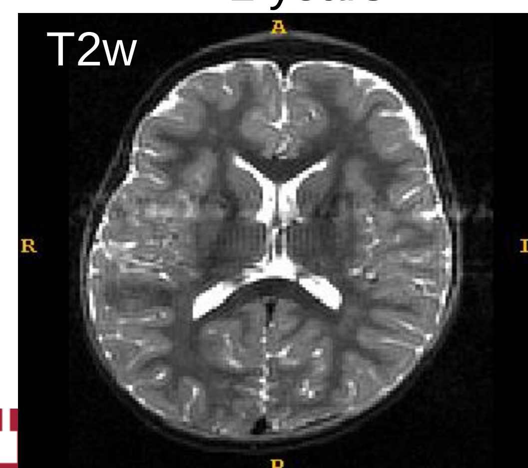
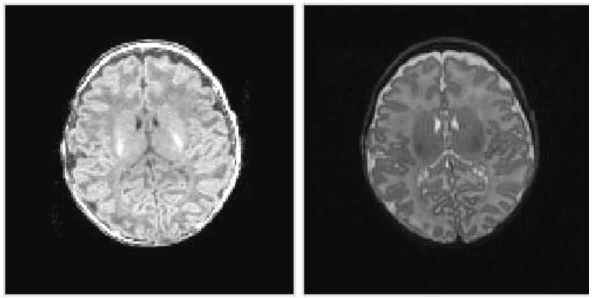
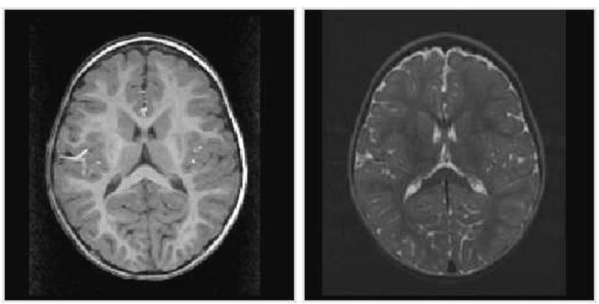


Image registration with changing contrast and structures



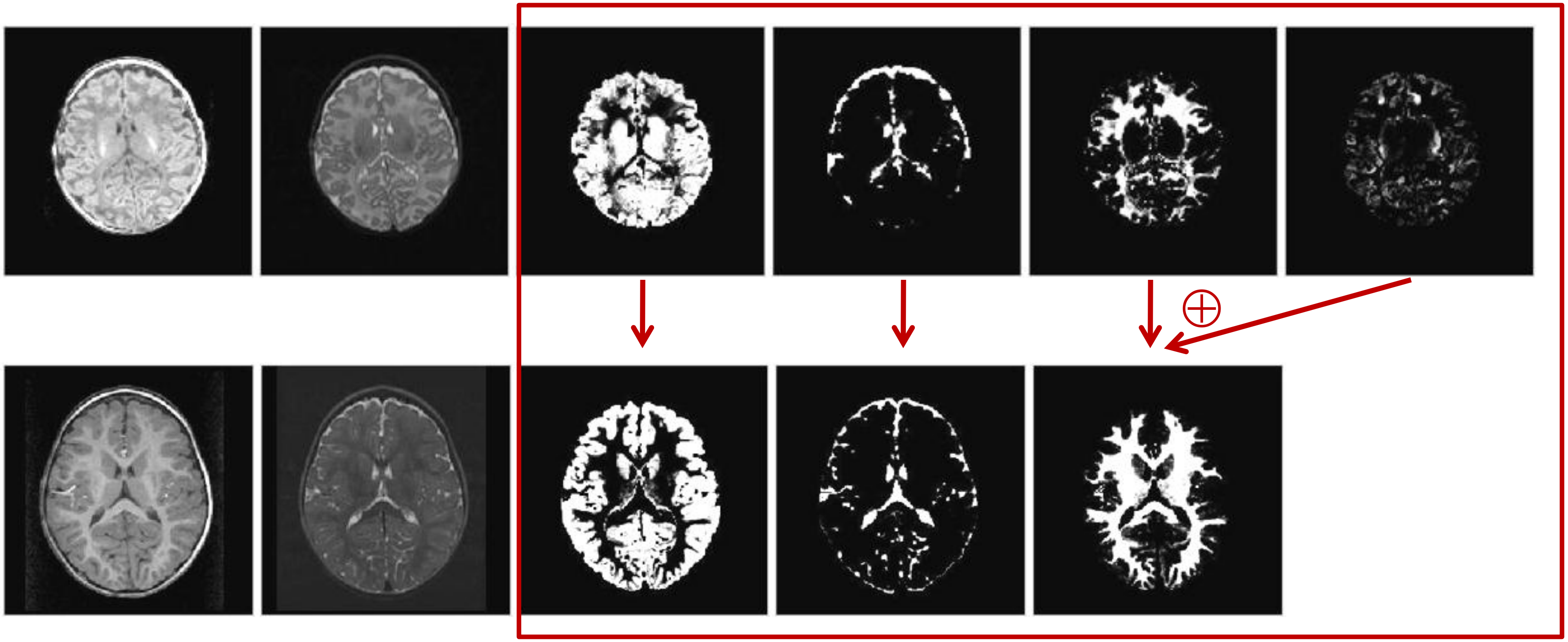


Direct registration
of multi-channel
MRI: Difficult

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Image registration with changing contrast and structures

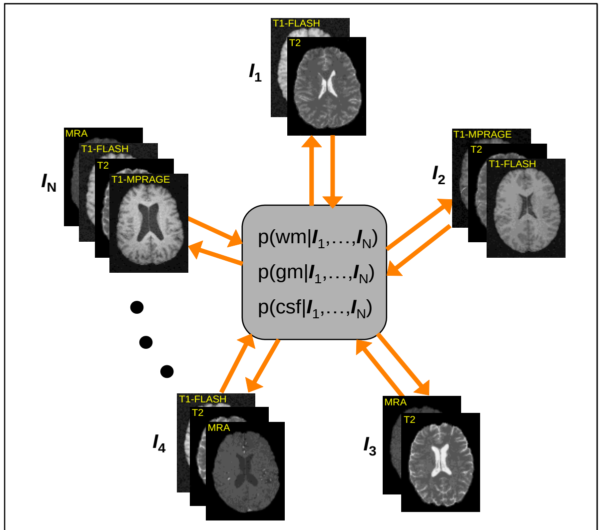


Direct registration of multi-channel MRI: Difficult

- Registration via sets of tissue probabilities
- Kullback-Leibler Divergence

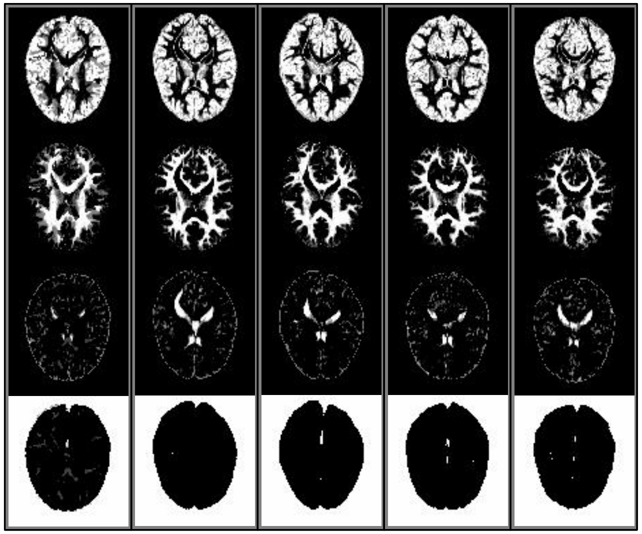
Atlas-building for multi-modality MRI and images of changing contrast:

Multi-class Posterior Atlas Formation (Lorenzen PhD)

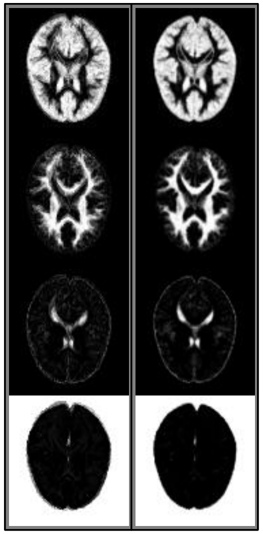


Template Estimation Framework

The template image requires the smallest amount of transformation energy



Five class posteriors each with four class structures

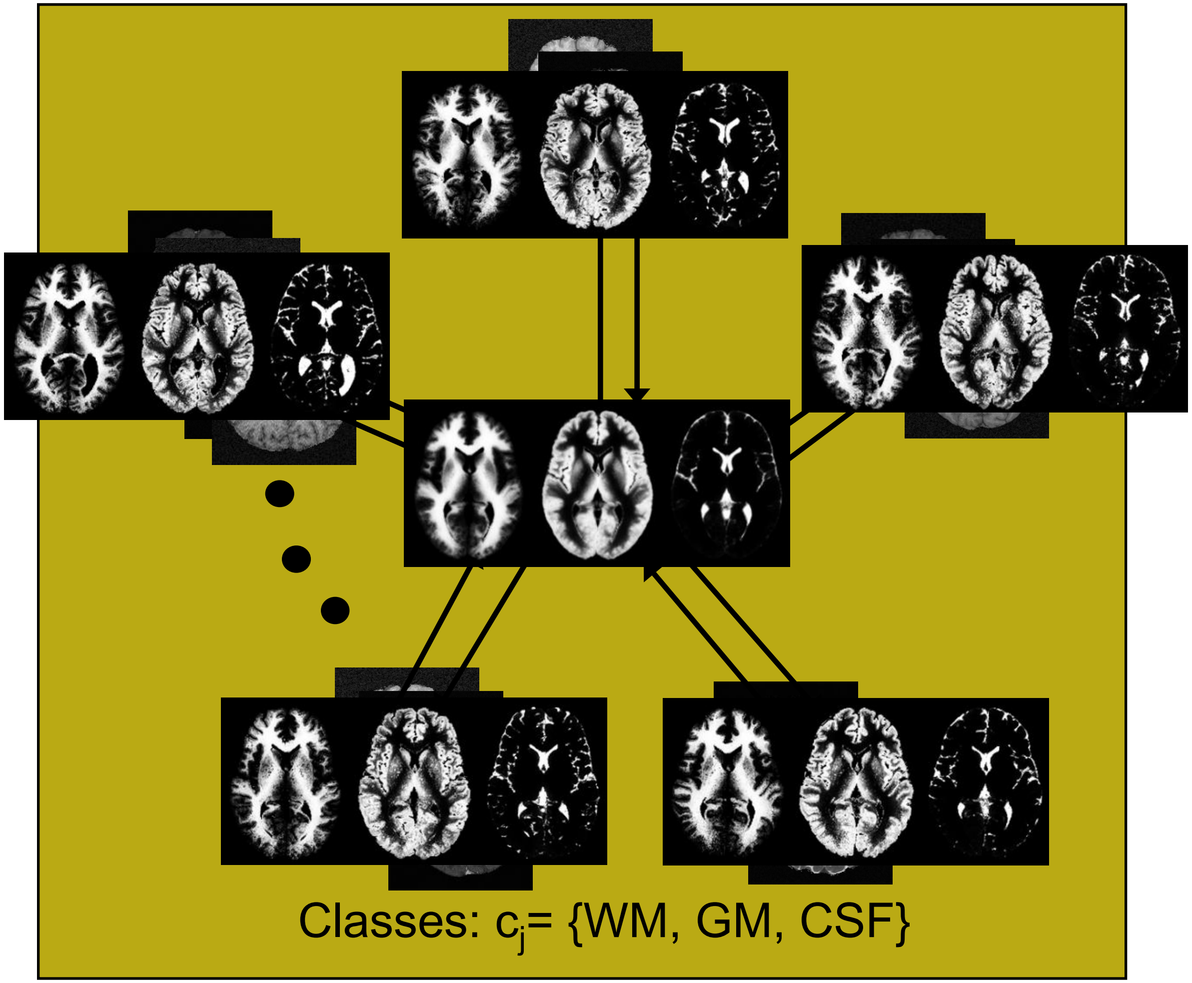


Initial *Final*
Template Estimation

Peter Lorenzen, Marcel Prastawa, Brad Davis, Guido Gerig, Elizabeth Bullitt, and Sarang Joshi, *Multi-Modal Image Set Registration and Atlas Formation*, Medical Image Analysis MEDIA, Elsevier, 2006

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Multi-Class Posterior Atlas Formation



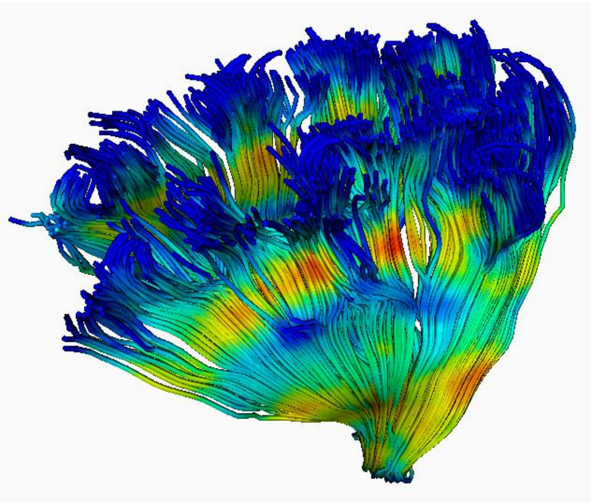
See also MICCAI'09 by Piotr A Habas, Kim, Rousseau, Studholme. Spatio-temporal atlas …

P. Lorenzen, M. Prastawa, B. Davis, G. Gerig, E. Bullitt, and S. Joshi, *Multi-Modal Image Set Registration and Atlas Formation*, Medical Image Analysis MEDIA, 2006

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

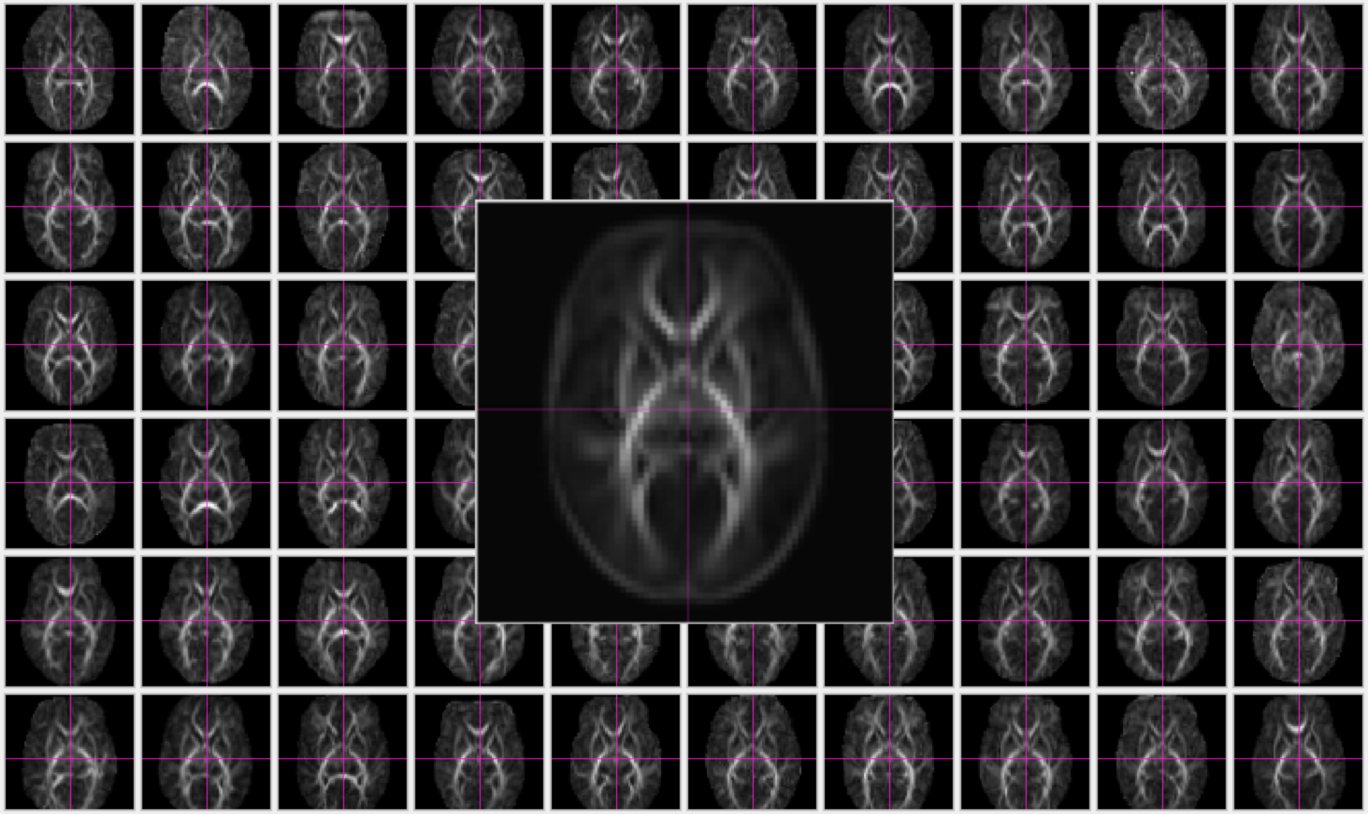
Outline

1. Imaging Technology for Pediatric Imaging
2. Analysis of structural MRI
3. Image Registration
4. Population Studies of DTI
5. Results



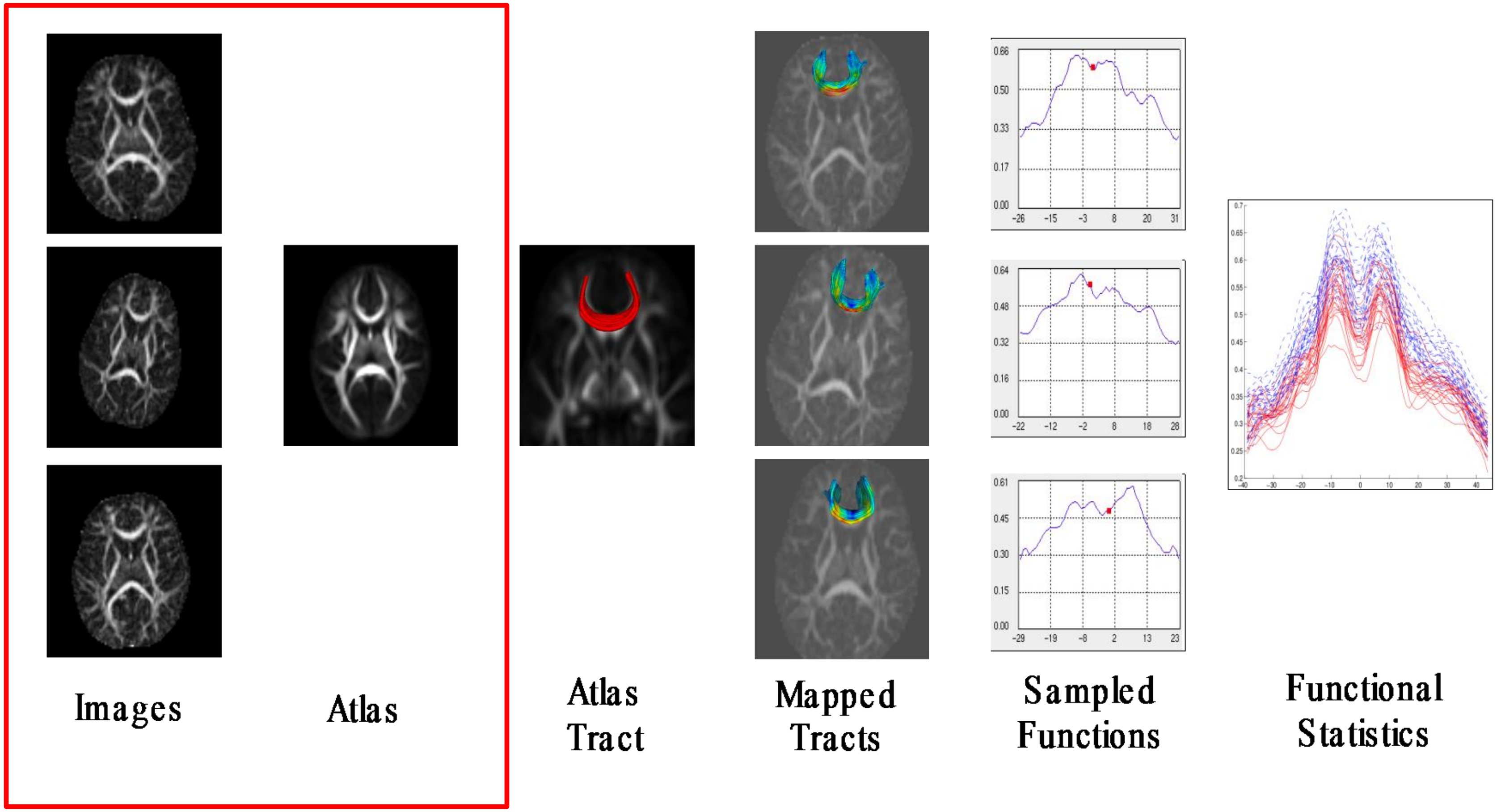
Population-based analysis of fiber tracts

Example: 150 neonate DTI mapped to unbiased atlas



Casey Goodlett, Sarang Joshi, Sylvain Gouttard, Guido Gerig, SCI Utah (MICCAI'06, MICCAI'08, NeuroImage (in press)

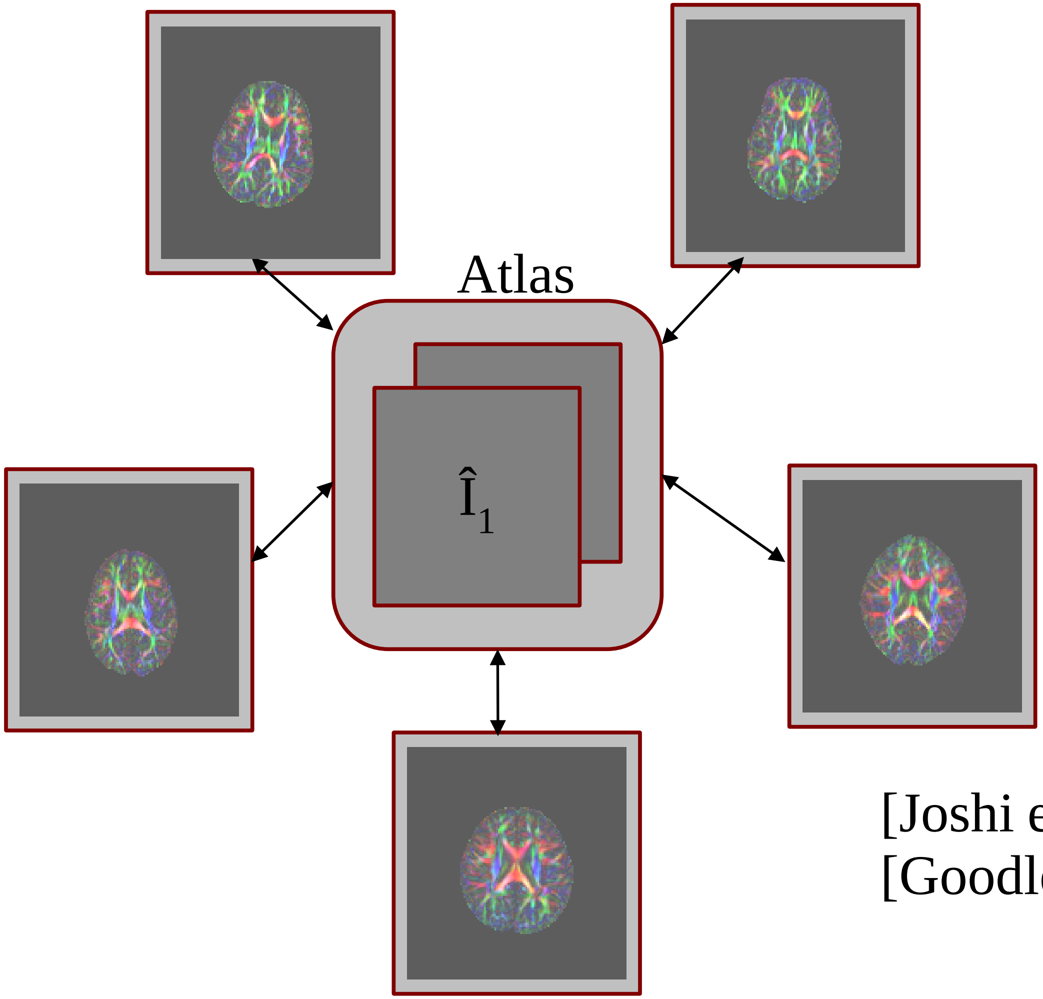
Concept: Group statistics of fiber tracts



Goodlett et al., MICCAI'08, NeuroImage in print

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

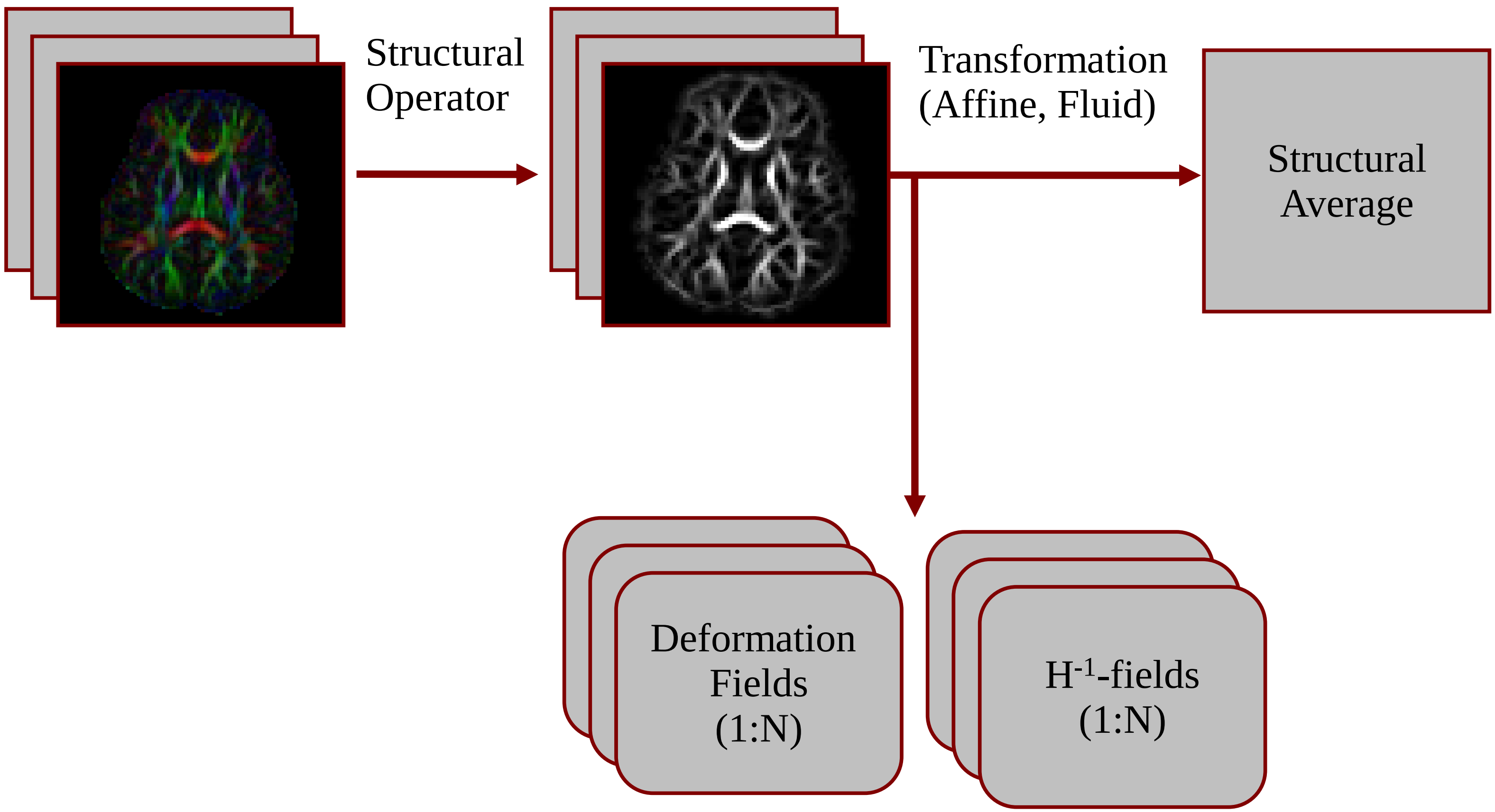
Atlas Building



[Joshi et al 2004]
[Goodlett et al 2006]

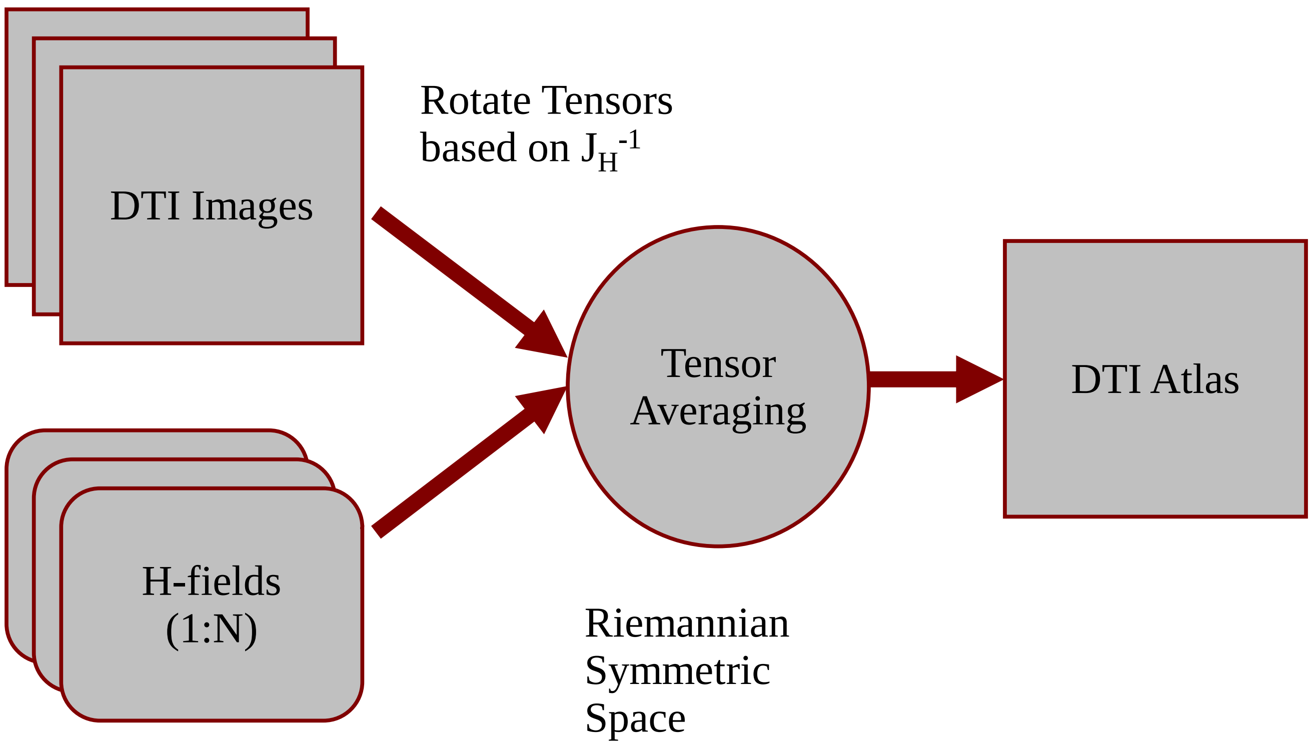
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Estimation of coordinate transformations



THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

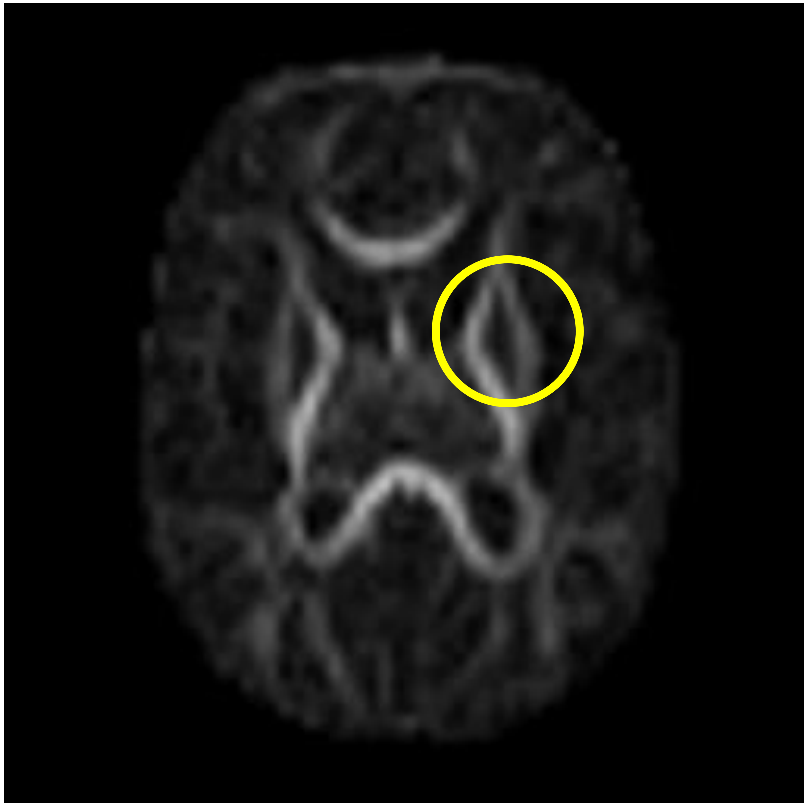
Computation of mean tensor images



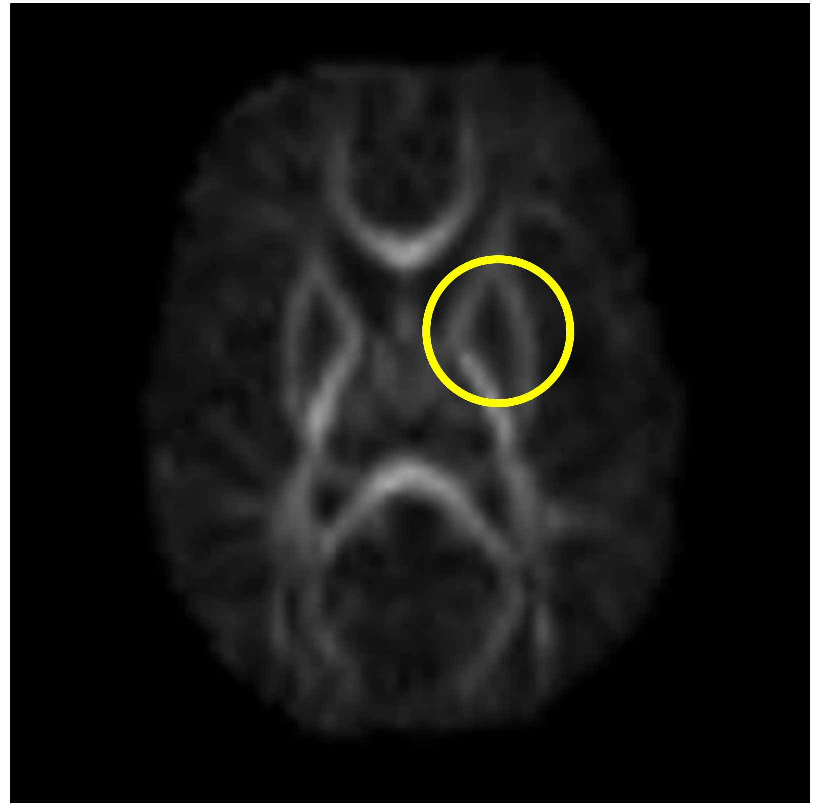
- Reorientation of tensors (Alexander, Jones)
- Interpolation of DWI or tensors (Fletcher, Arsigny, Westin&Kindlman)

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Co-registration: From linear to nonlinear



Linear registration (affine)

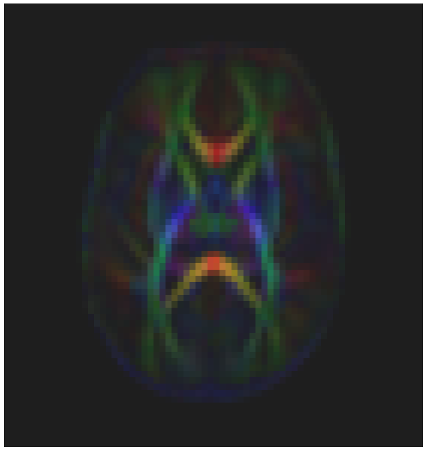


Nonlinear registration (fluid)

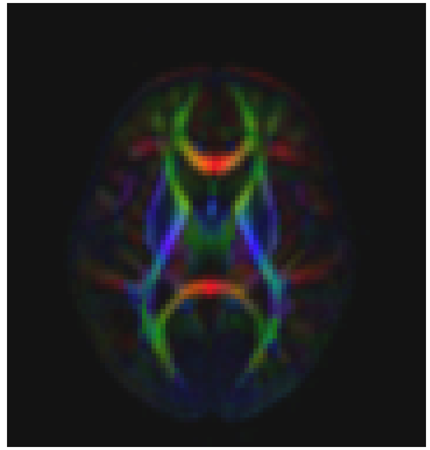
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

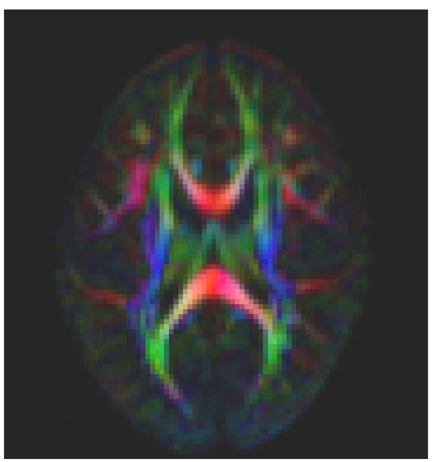
Application: Neurodevelopmental Statistical Atlases



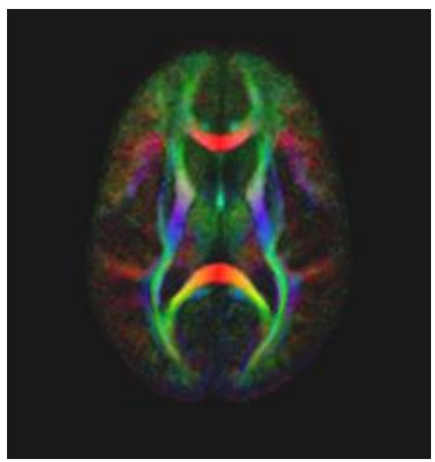
Neonate (N=95)



1 year (N=25)



2 year (N=25)



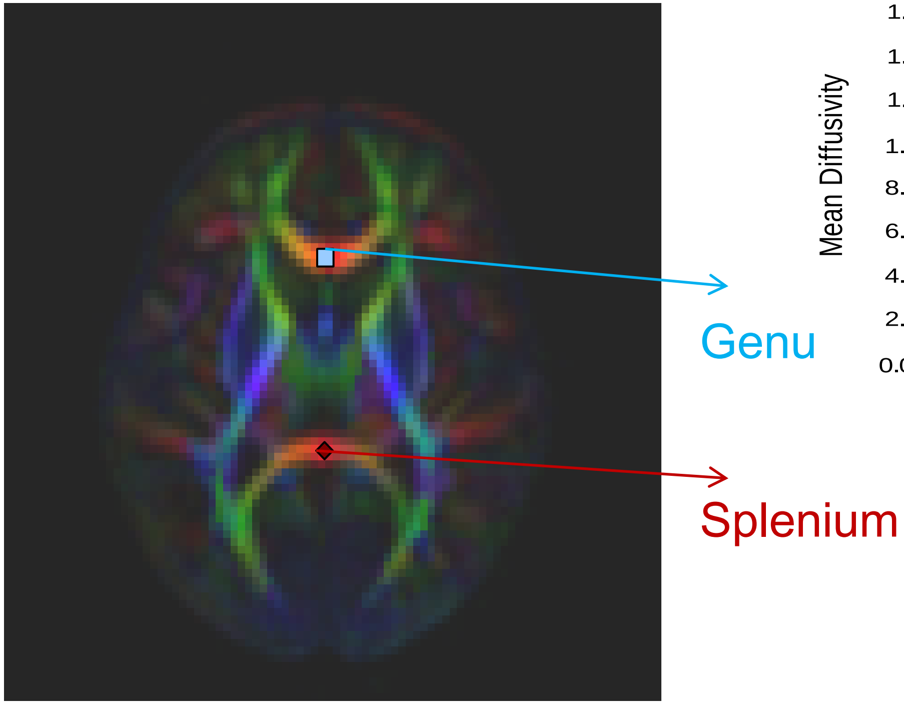
Adult (N=24)

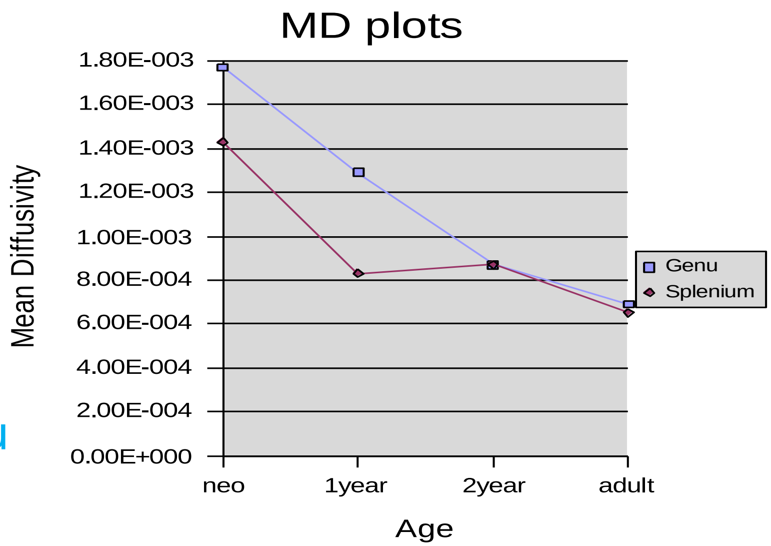
Collaborative research on studying the early developing brain with John H. Gilmore and Weili Lin, UNC Chapel Hill

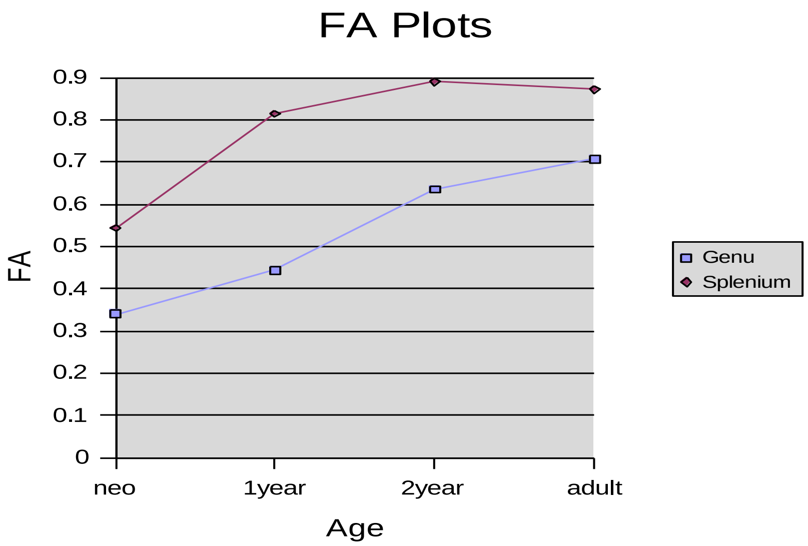
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Sample Quantitative Statistics

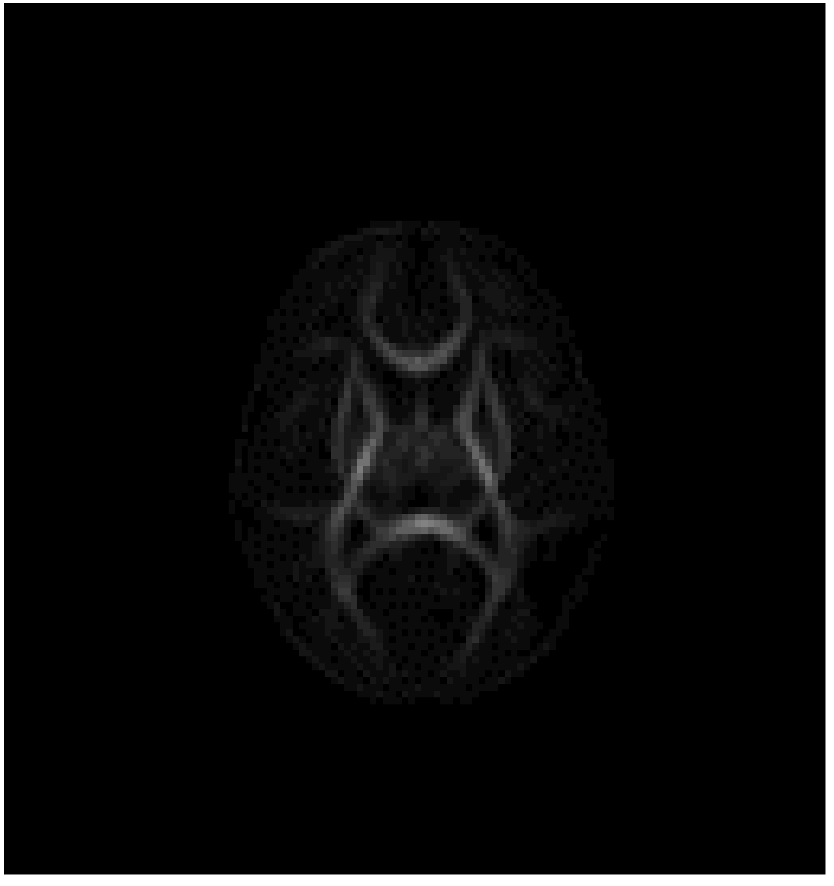


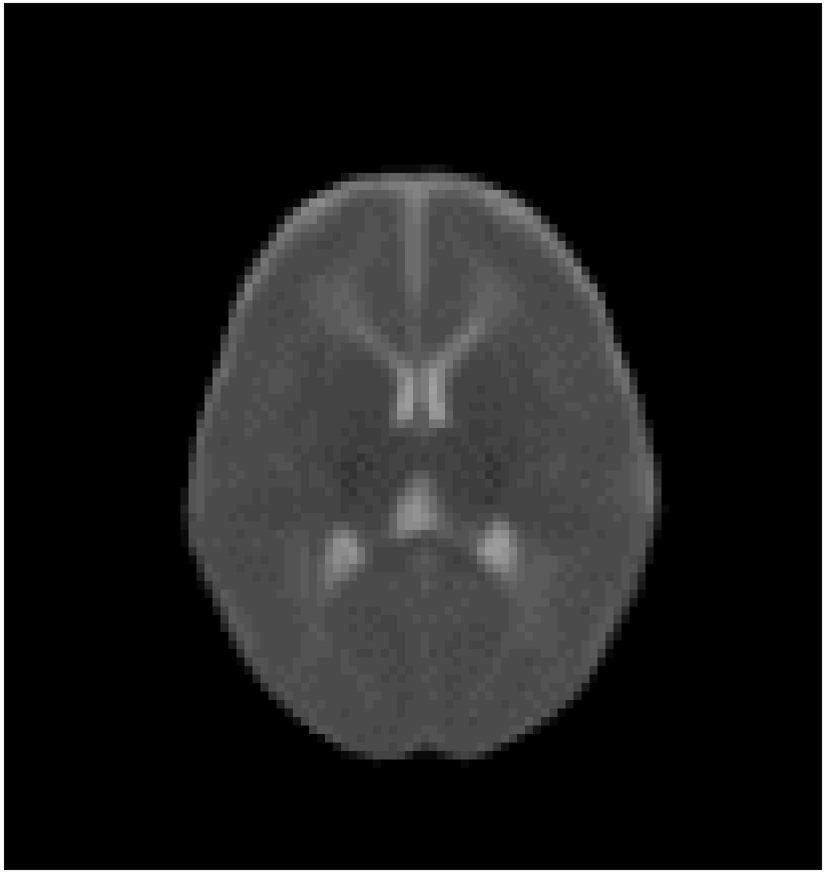




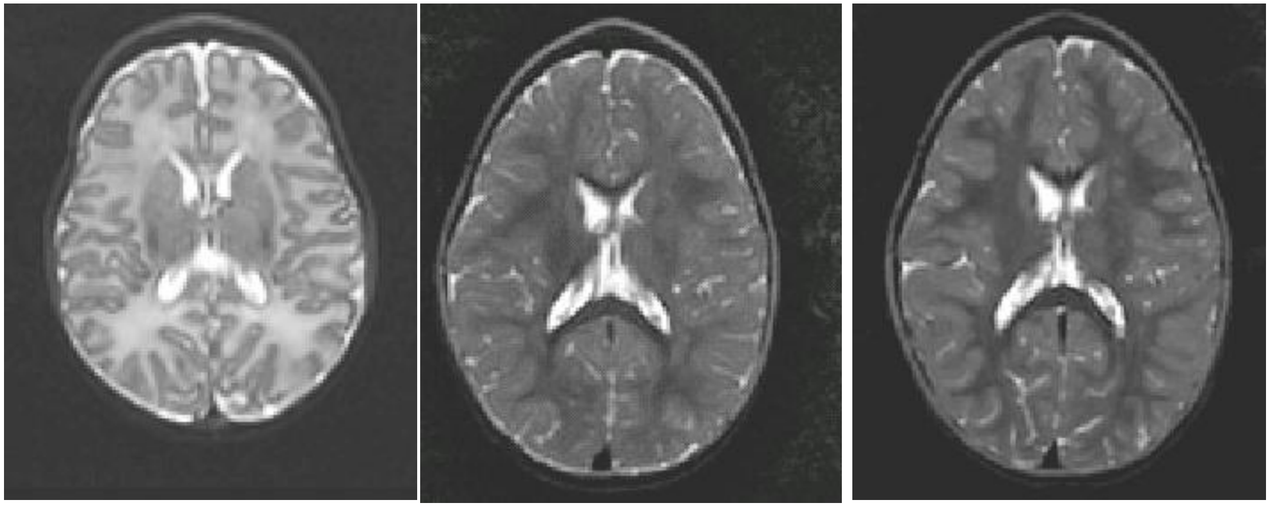
See also: I seminal work by Dubois, Manging, LeBihan et al.

Neurodevelopmental atlas

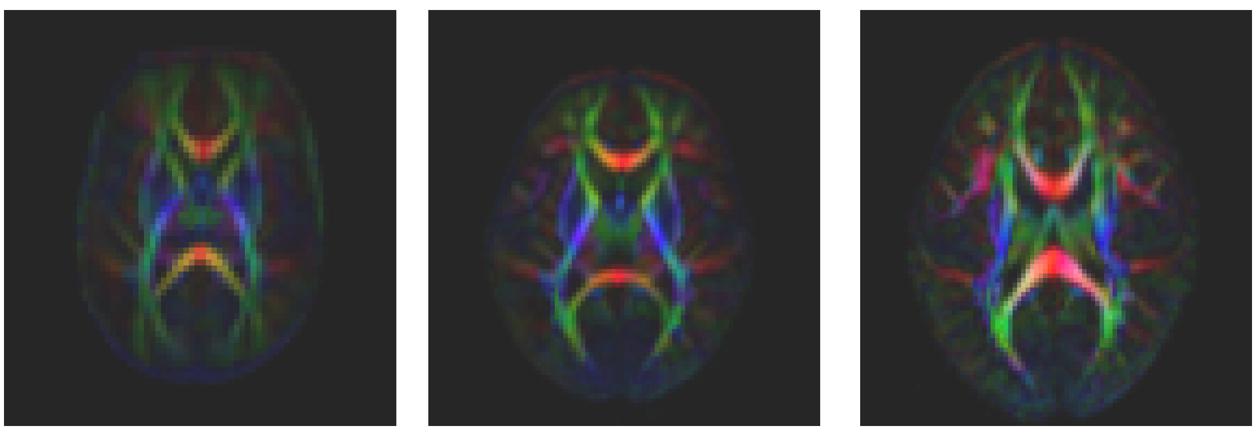




Neurodevelopment in sMRI and DTI



neonate 1 year 2 years



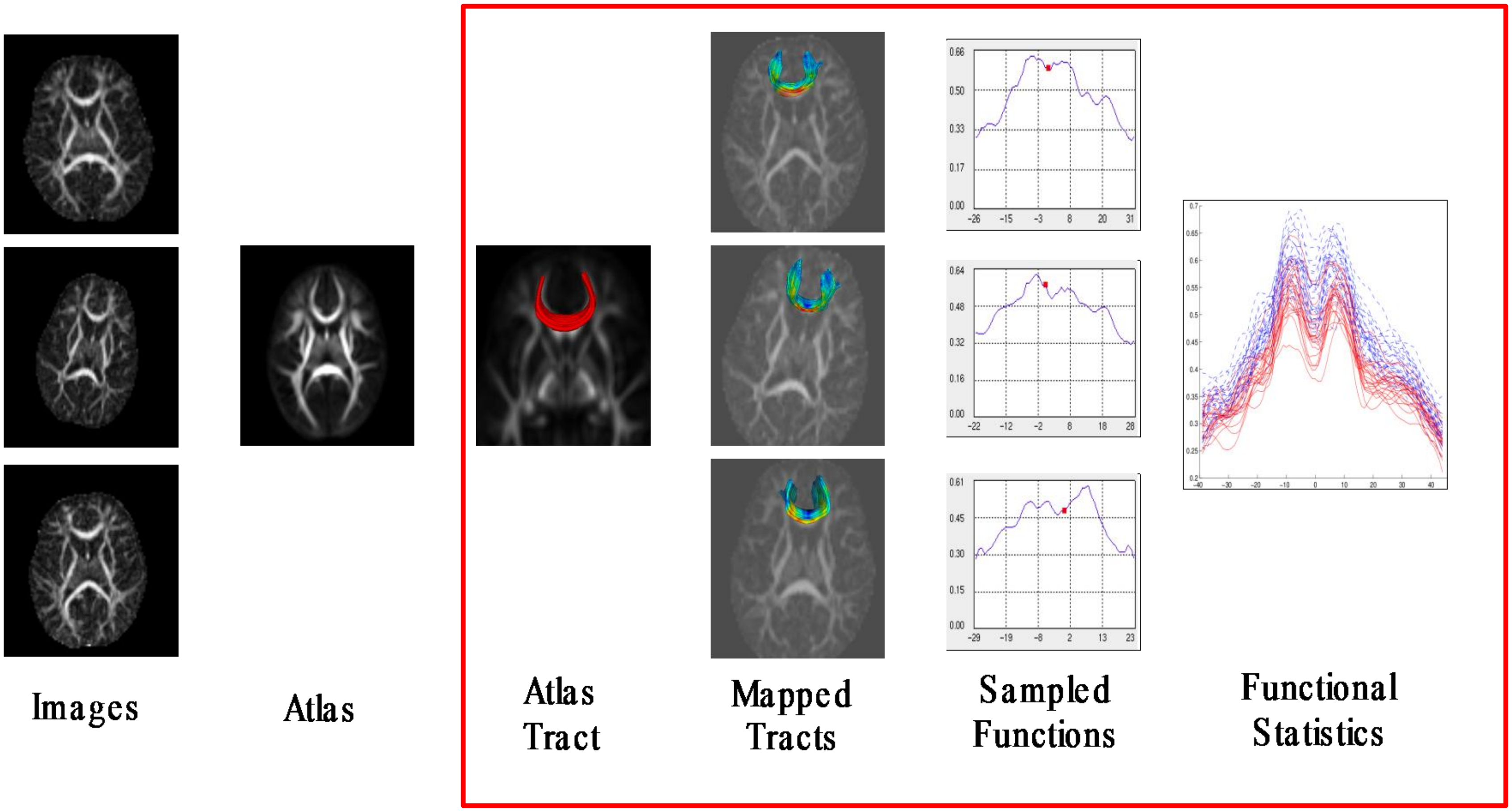
Structural MRI shows contrast flip due to wm structuring.

DTI shows a type of continuous maturation process.

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Concept: Group statistics of fiber tracts

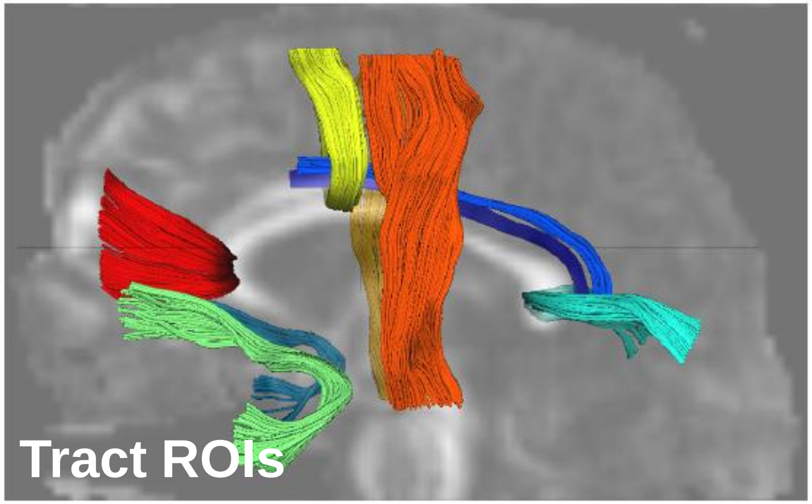


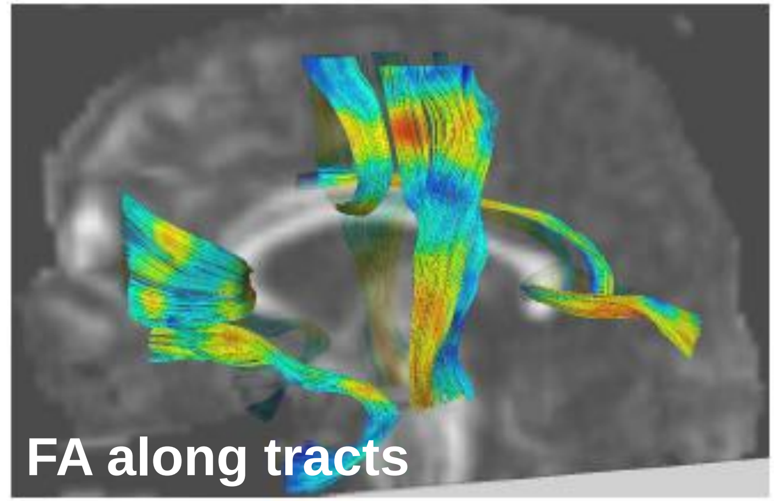
Goodlett et al., MICCAI'08, NeuroImage in print

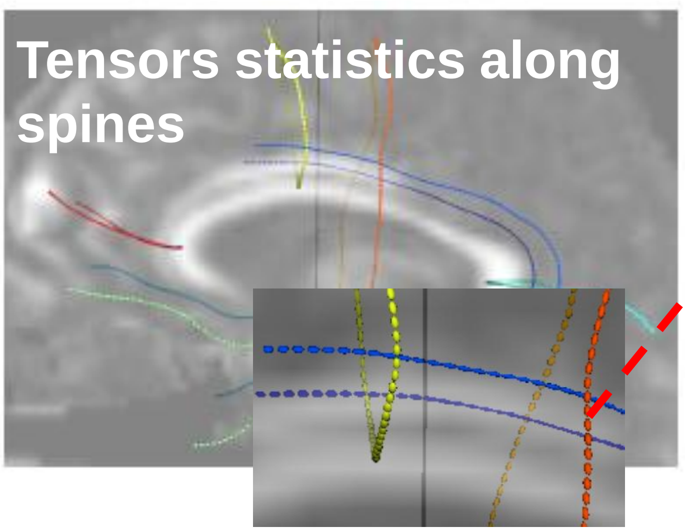
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

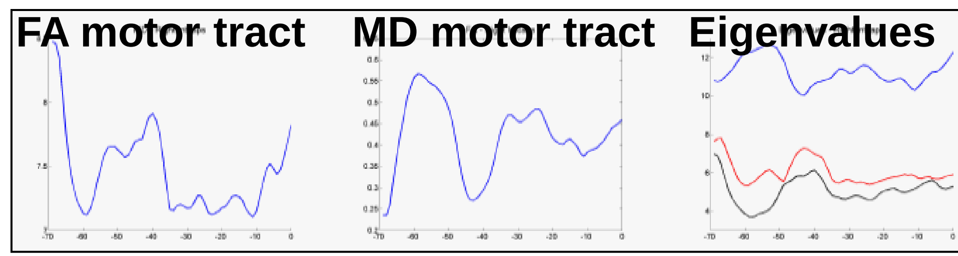
SCI INSTITUTE

Quantitative Tractography





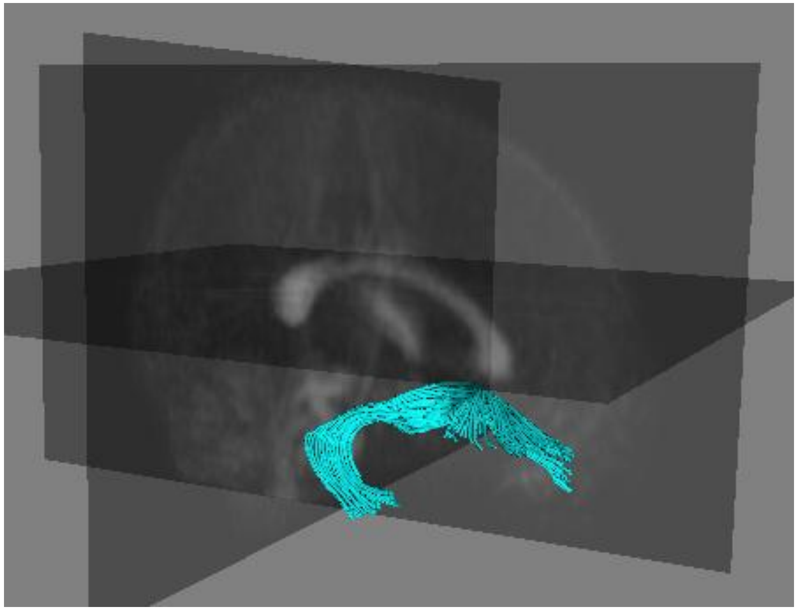


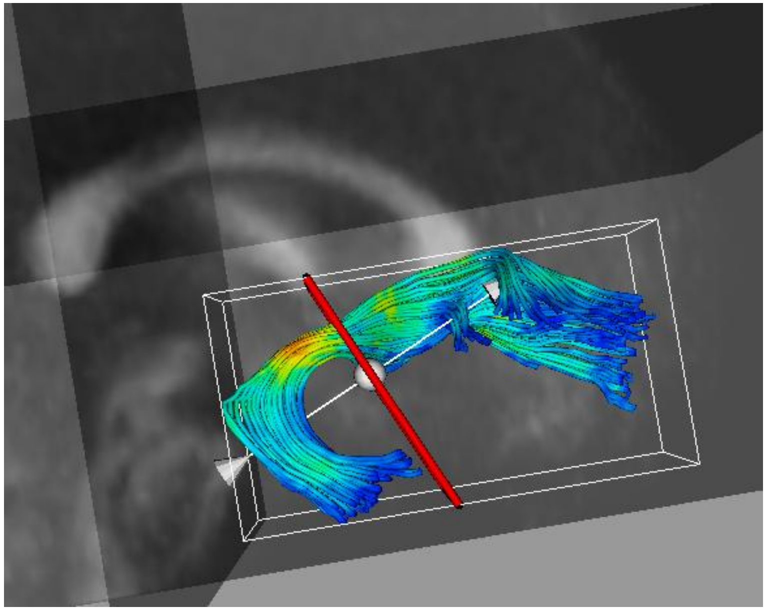


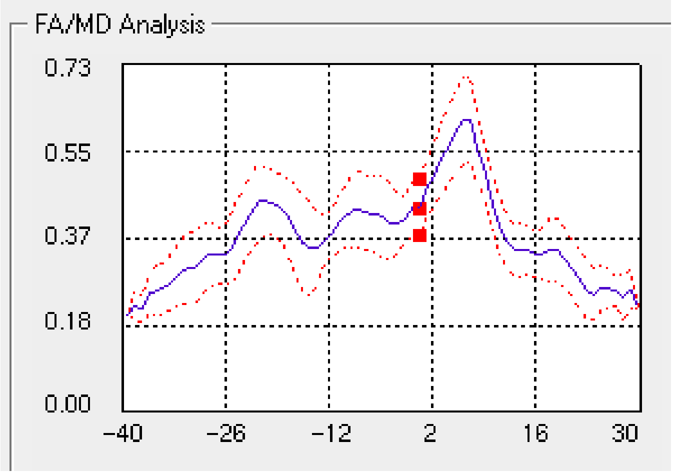
- Tractography for ROI definition
- Tensor analysis for statistics along tracts
- Corouge, Gouttard, Gerig, MedIA'06

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Example Uncinate Fasciculus

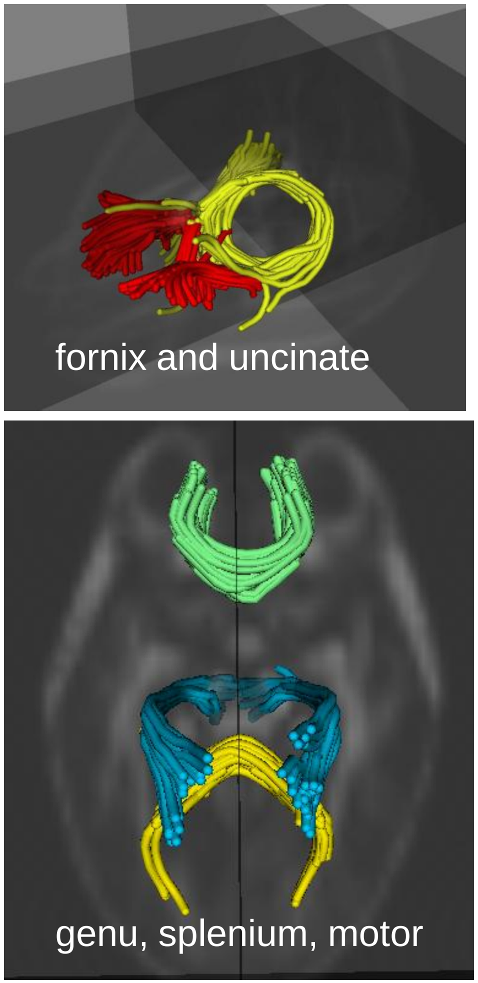




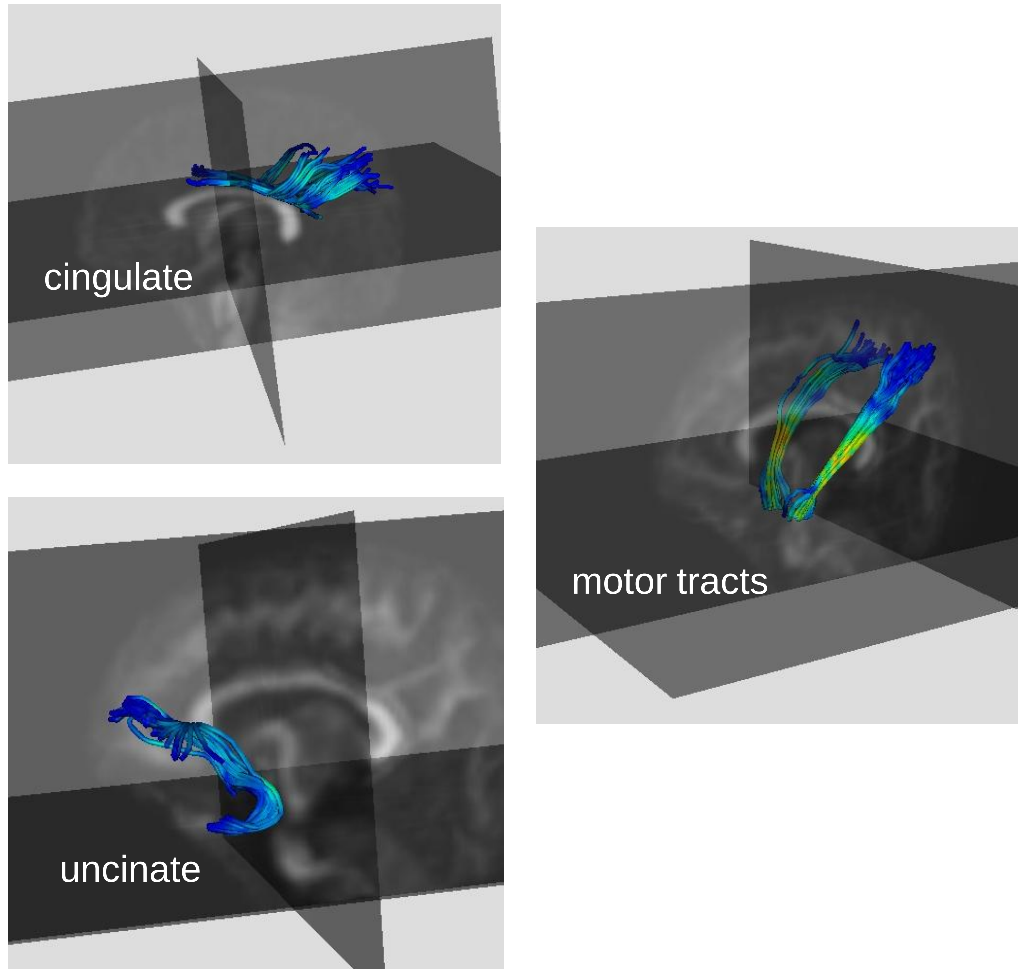


Corouge et al. *Fiber tract-oriented statistics for quantitative diffusion tensor MRI analysis*. Medical Image Analysis 2006.
FiberViewer software - http://www.ia.unc.edu/dev/

Fiber Tractography via Atlases



Neonate atlas DTI

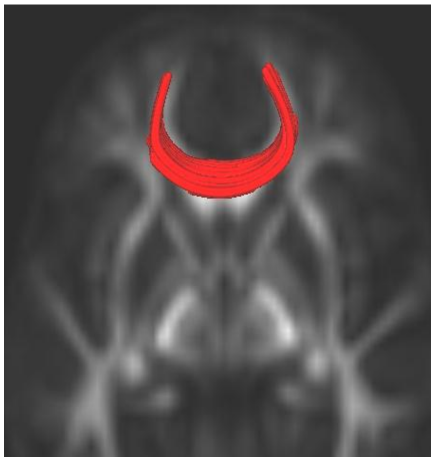


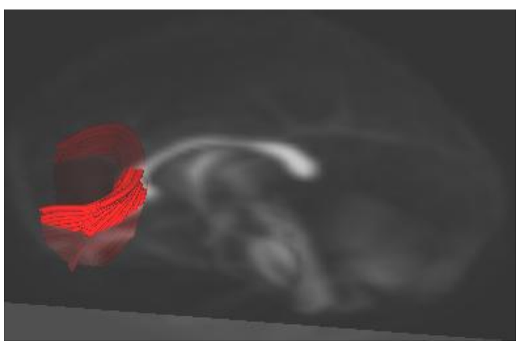
1yr atlas DTI

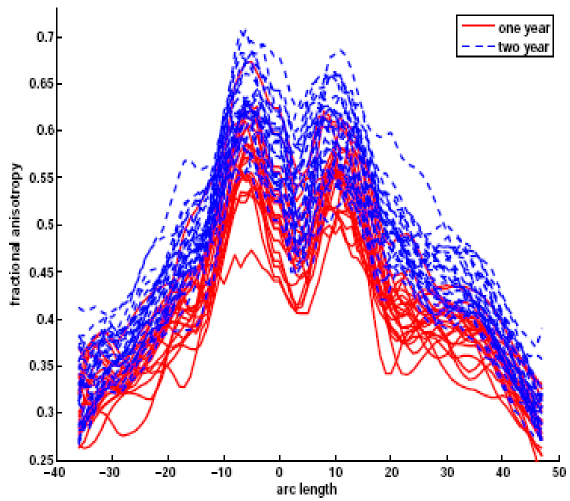
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

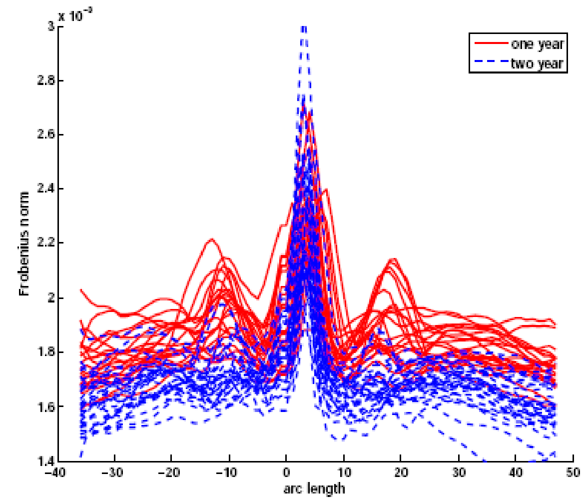
Pediatric Example: Genu Tract 1-2yrs







(b) All FA curves



(c) All norm curves

- Working example of 1 year vs. 2 year subjects
- Significance expected
- Discrimination provides interpretation

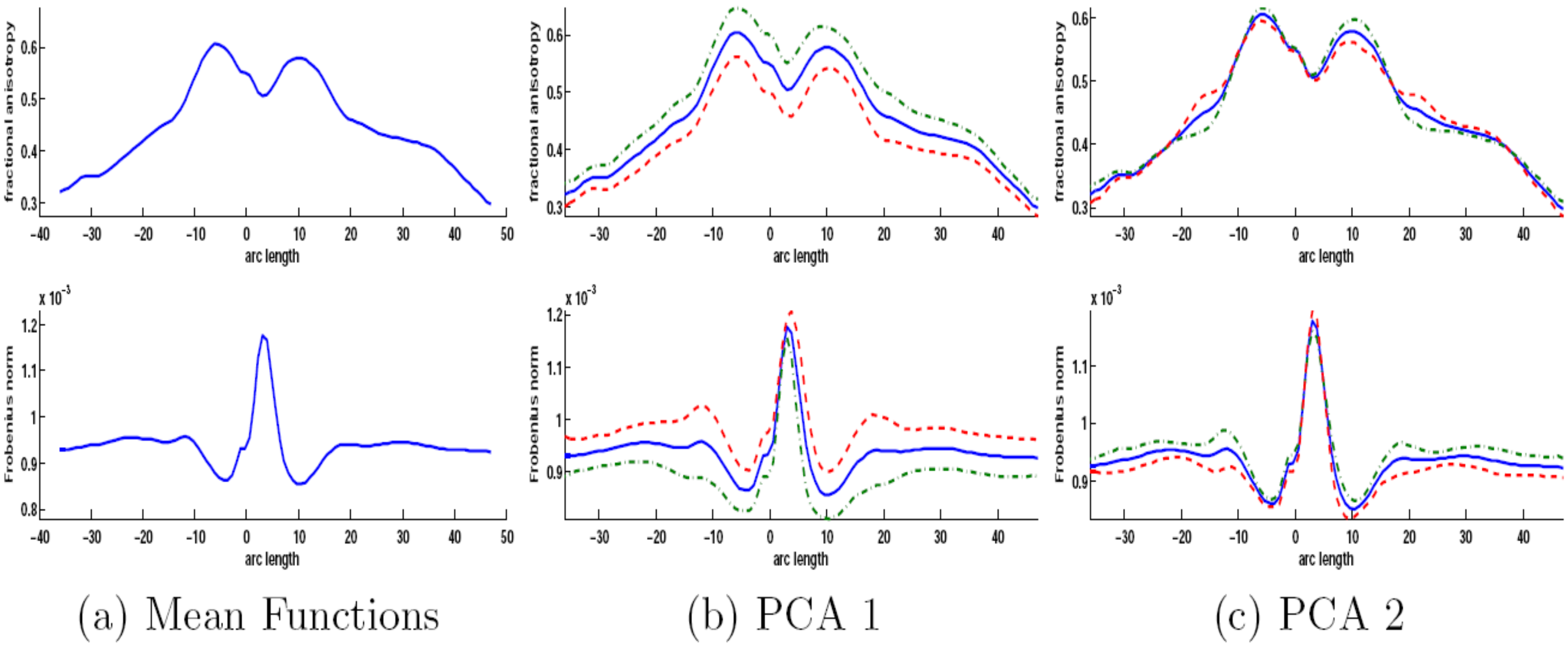
THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Functional Data Analysis

- Underlying biology of measurements is continuous
- Tract analysis samples from the continuous biology
- Global vs. point-wise statistics
  - Smoothing
  - Dimensionality Reduction
- Ramsay and Silverman 2002
- Functional Statistics: $\bar{f}(t) = \frac{1}{N} \sum_{i=1}^{N} f_i(t),$

$$v(s,t) = \frac{1}{N-1} \sum_{i=1}^{N} (f_i(s) - \bar{f}_i(s))(f_i(t) - \bar{f}_i(t)).$$

Functional PCA



Hypothesis testing and discrimination

- Permutation test using T^2 statistics

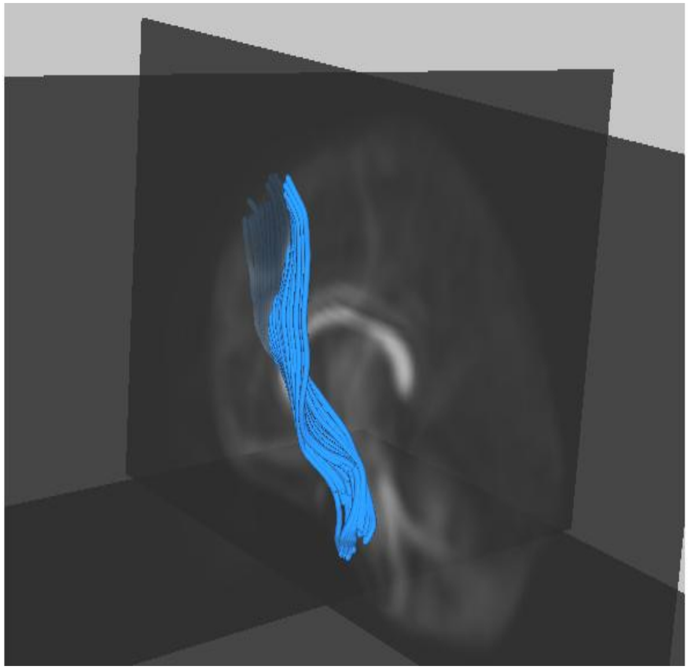
$$T^2 = \frac{n_x n_y}{n_x + n_y} (\bar{\mathbf{x}} - \bar{\mathbf{y}}) \mathbf{S}^{-1} (\bar{\mathbf{x}} - \bar{\mathbf{y}})^T$$

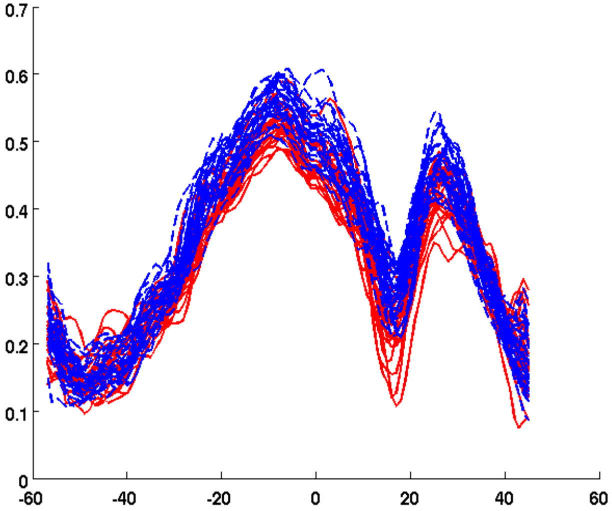
- Linear discriminant embedded in T^2

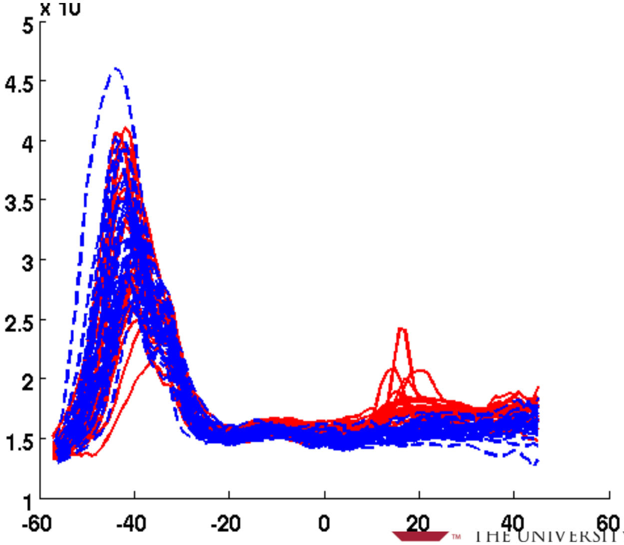
$$\omega = \mathbf{S}^{-1} (\bar{\mathbf{x}} - \bar{\mathbf{y}})^T.$$

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Pediatric Example – Left motor tract



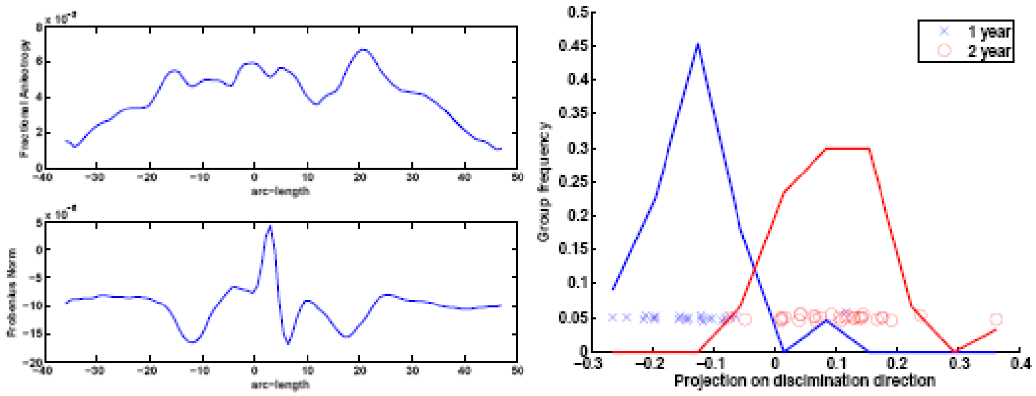




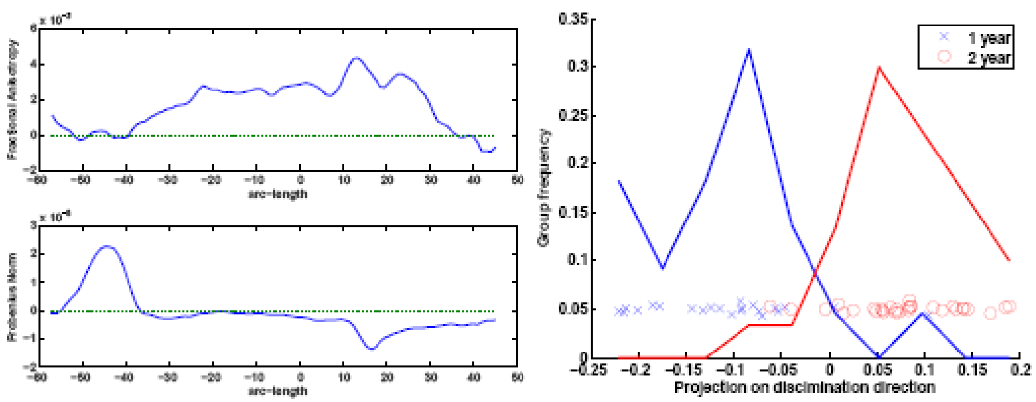
TITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Statistical analysis of tracts as 1-D curves: Functional data analysis (FDA)



(a) Genu discriminant functions (b) Data functions projected on FLD

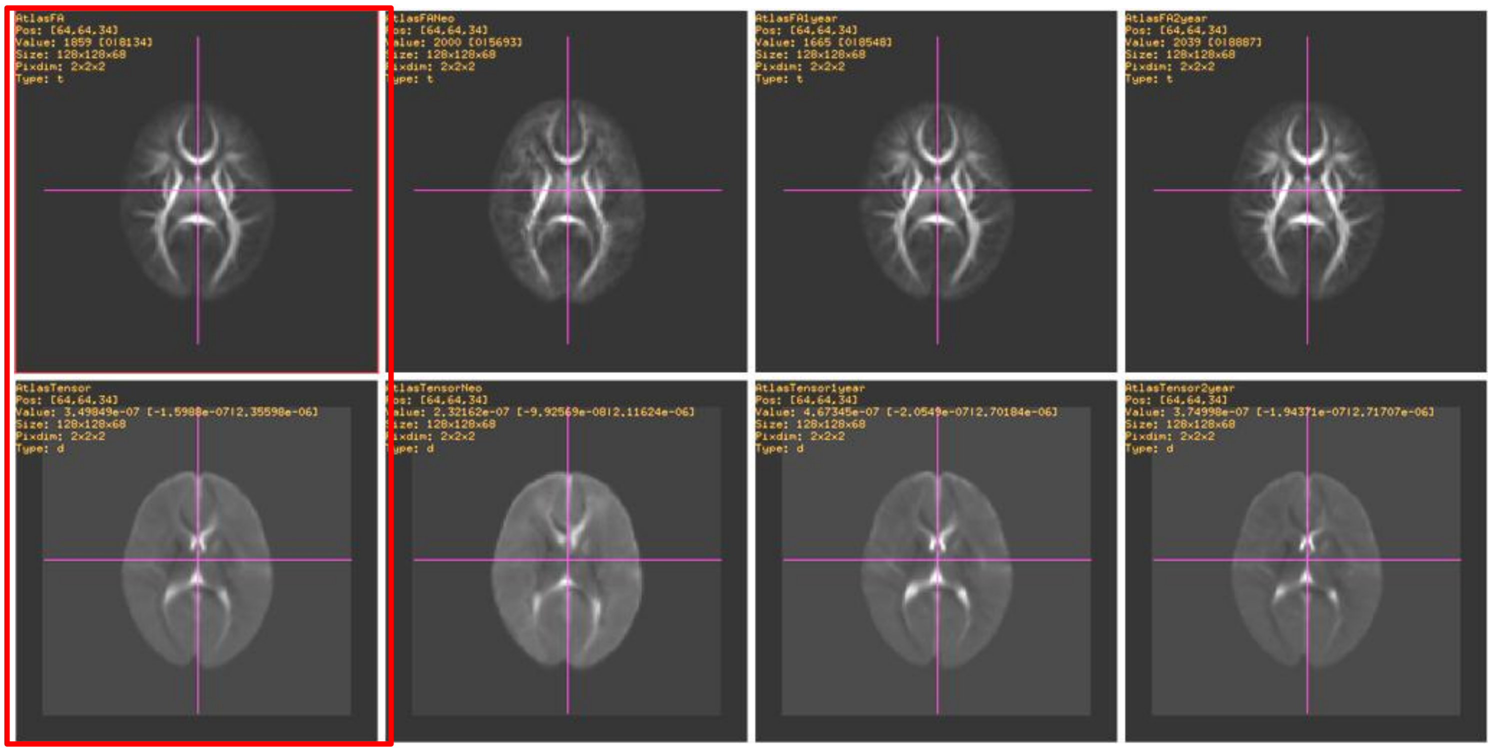


(c) Motor tract discriminant functions (d) Data functions projection on FLD

"Group Statistics of DTI Fiber Bundles Using Spatial Functions of Tensor Measures" Casey Goodlett, P. Thomas Fletcher, John Gilmore, and Guido Gerig, MICCAI 2008, NeuroImage 2009

Hypothesis testing and discriminant analysis on first k PCA modes (Hotelling T^2)
→ Type and Location of group differences.

Towards longitudinal analysis: White Matter Growth Trajectory

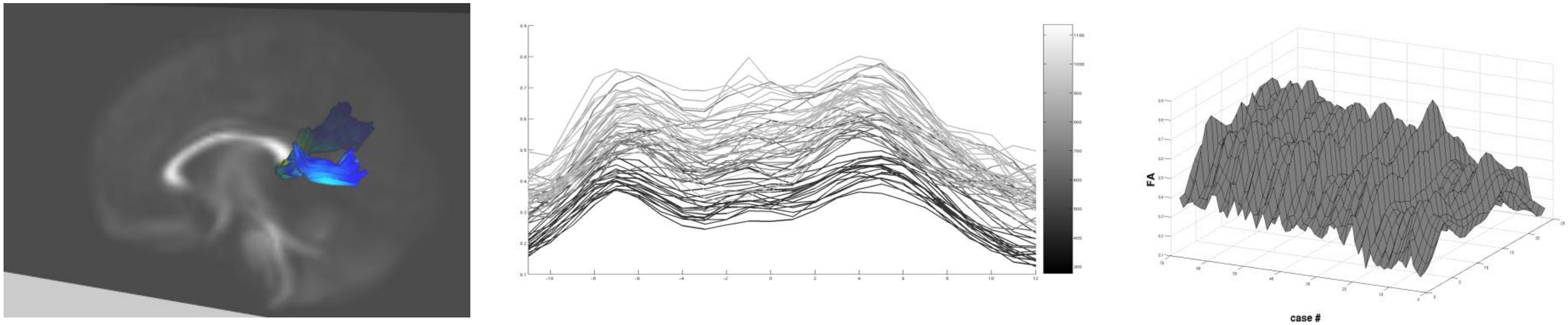


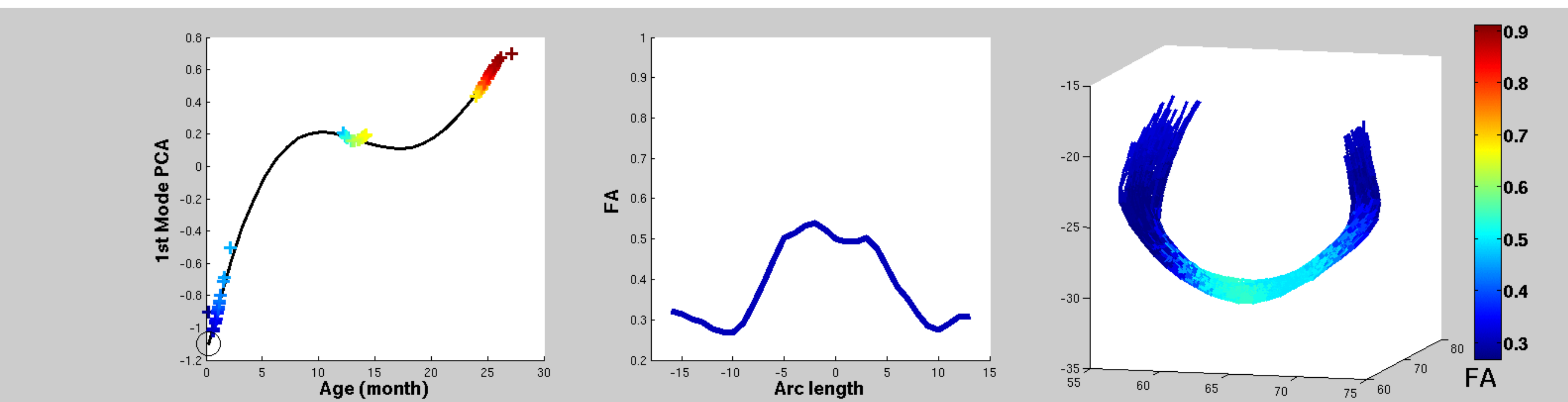
All subjects (N=70) Neonates (N=20) 1year (N=22) 2years (N=28)

Gouttard et al., Constrained Data Decomposition and Regression for Analyzing Healthy Aging from Fiber Tract Diffusion Properties, MICCAI 2009

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Trajectory of development via longitudinal analysis





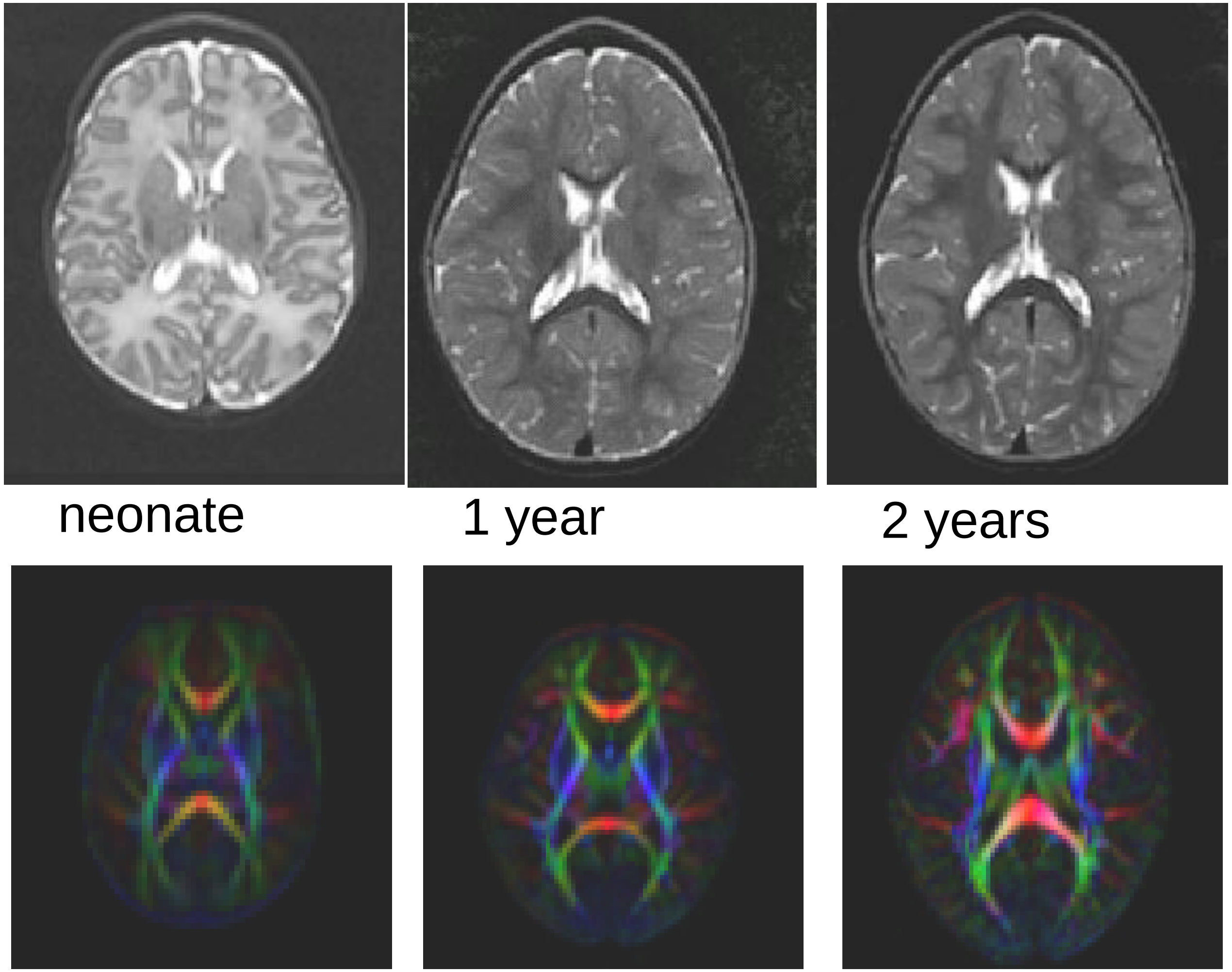
Gouttard et al., MICCAI 2009

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

DWI does only partially explain white matter development

Neurodevelopment in sMRI and DTI



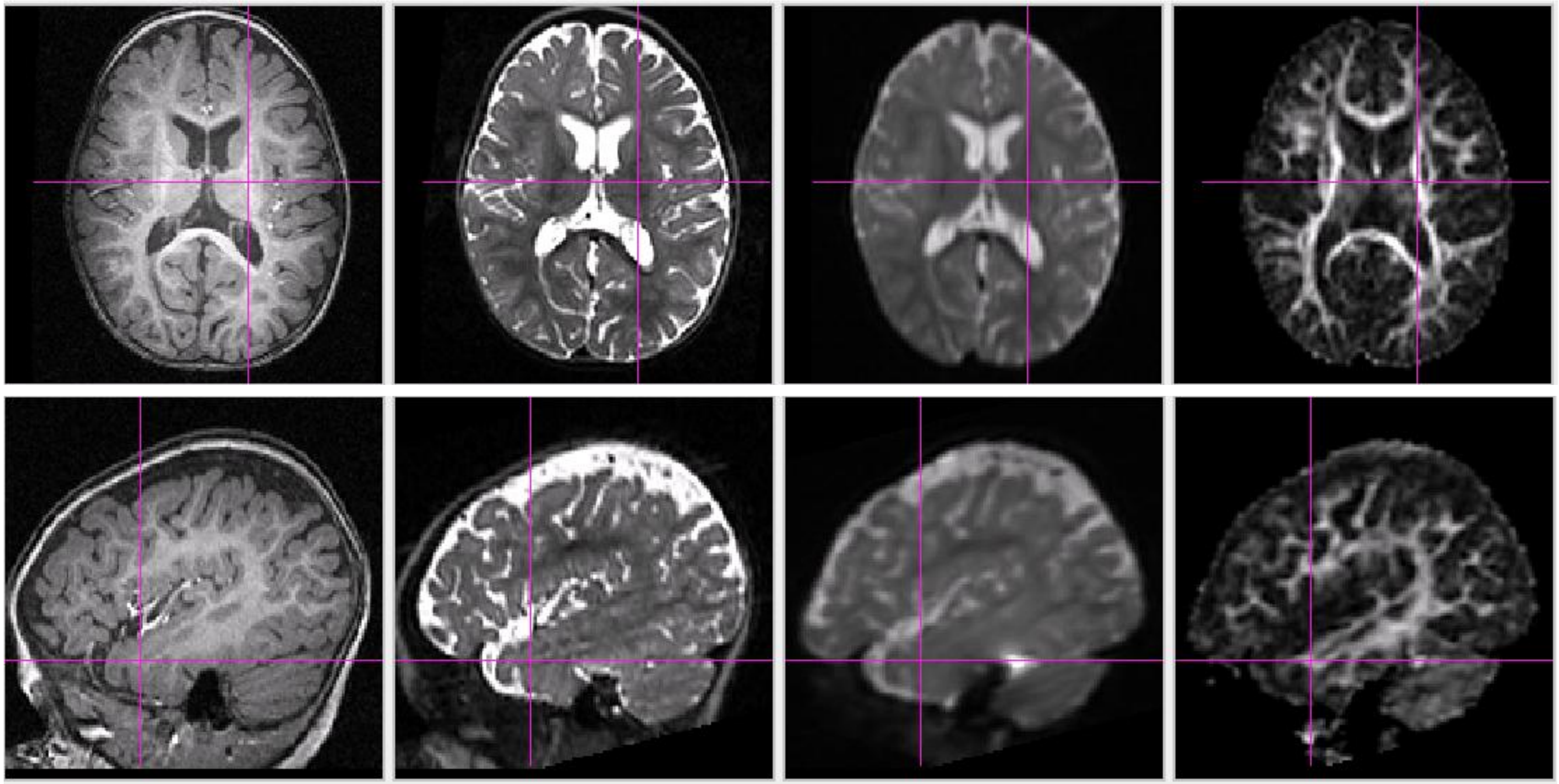
Structural MRI shows contrast flip due to wm structuring.

DTI shows a type of continuous maturation process.

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

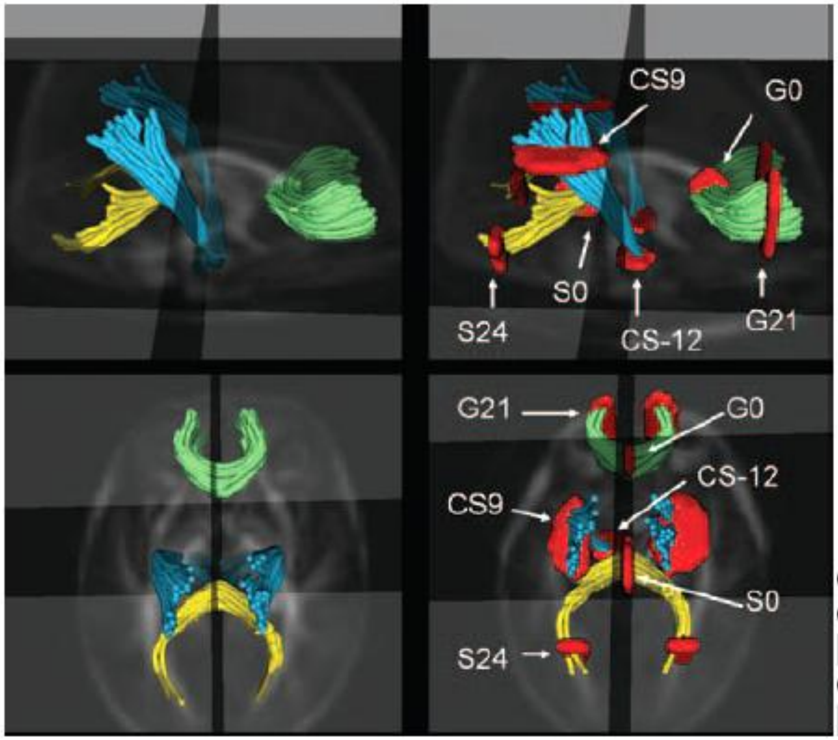
SCI INSTITUTE

DTI is part of multi-modal MRI protocol

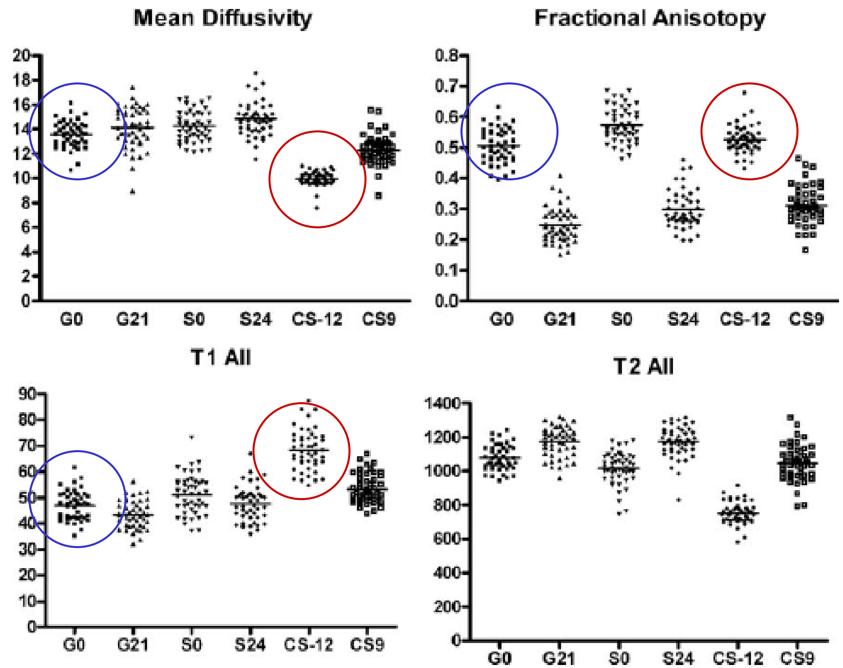


T1 MPRage. T2 3D TSE, MD, FA (2yrs old. Weili Lin, UNC)

Quantitative Tractography to study early wm development

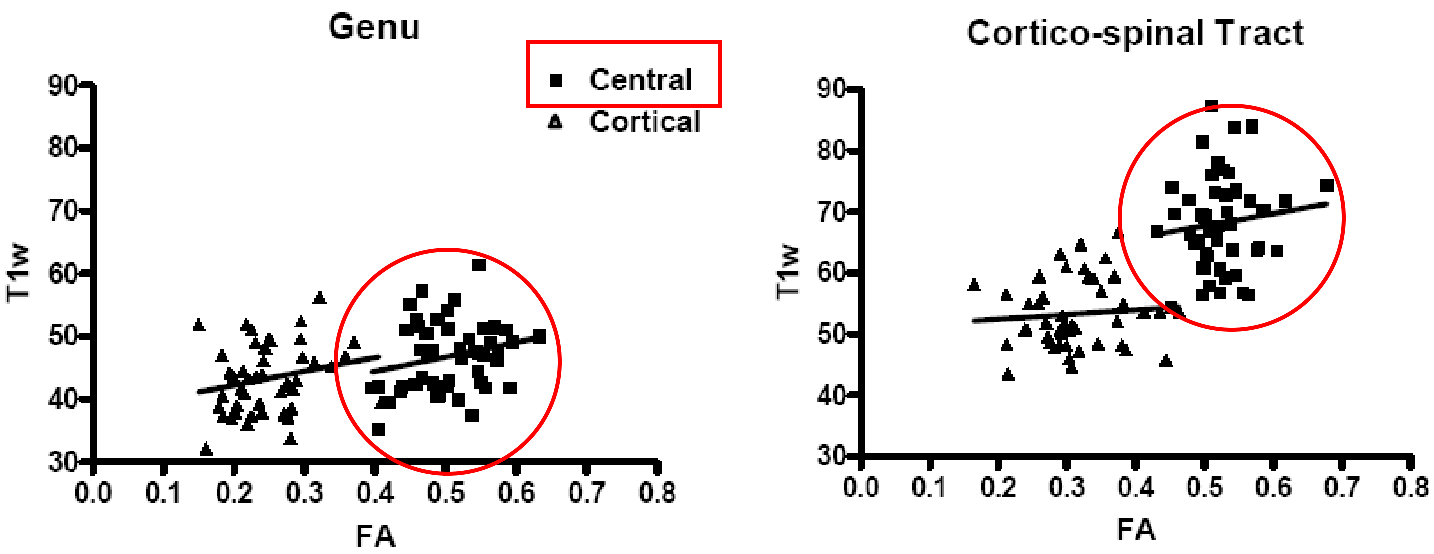


John H. Gilmore et al., Early Postnatal Development of Corpus Callosum and Corticospinal White Matter Assessed with Quantitative Tractography, AJNR Nov. 2007



- FA does not explain degree of myelination but structuring
- → Joint use of DTI, T1w and T2w in multivariate analysis

Early postnatal development of white matter



Joint analysis of structural MRI and DTI:

Genu at center (non myelinated) versus internal capsule (myelinated)

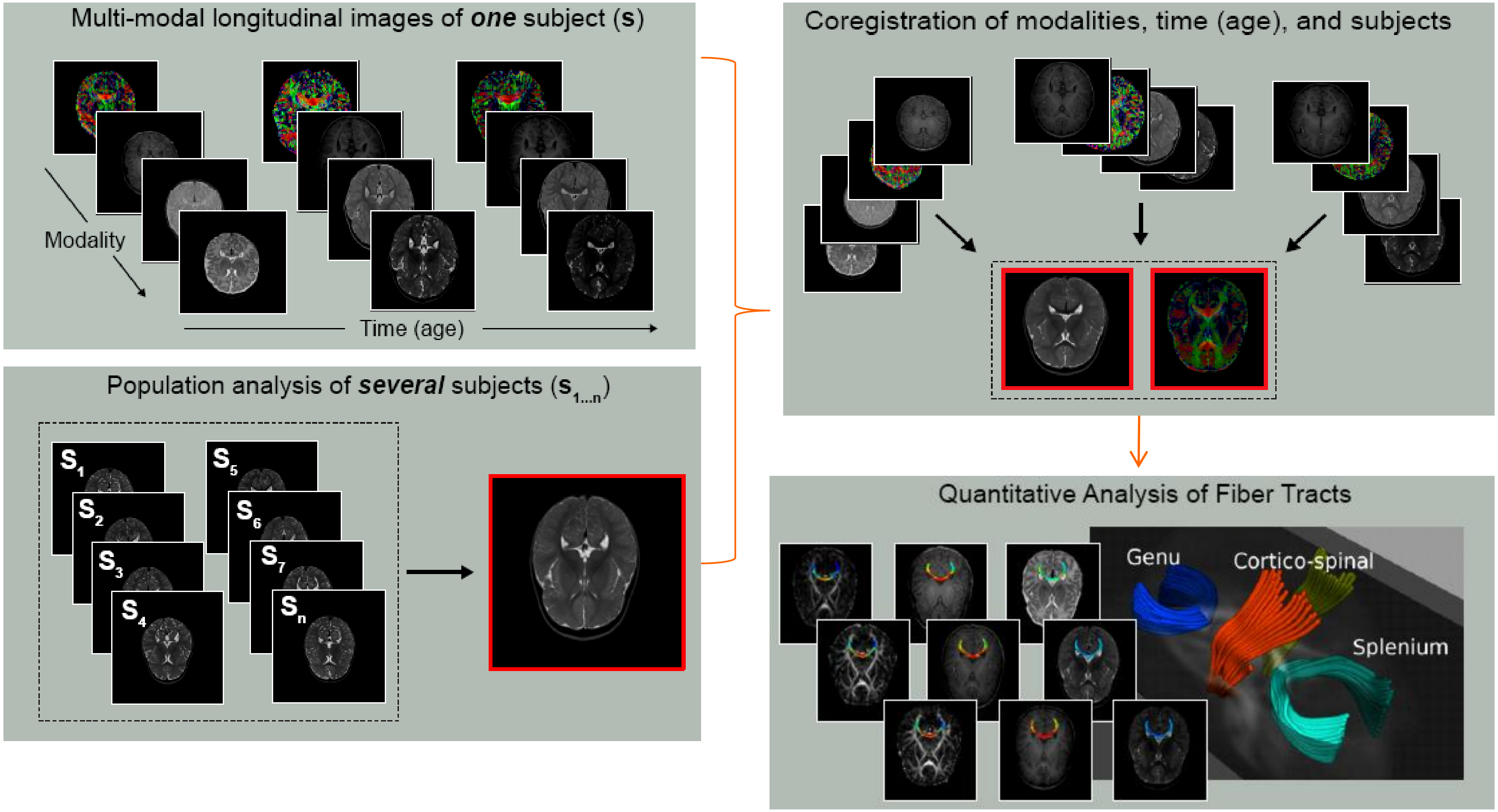
- FA genu ≈ FA intcaps
- T1w genu >> T1w intcaps

Analysis detects differences between dense structuring and early myelination

Procedure to be used to measure maturation process

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Towards multimodal spatio-temporal analysis

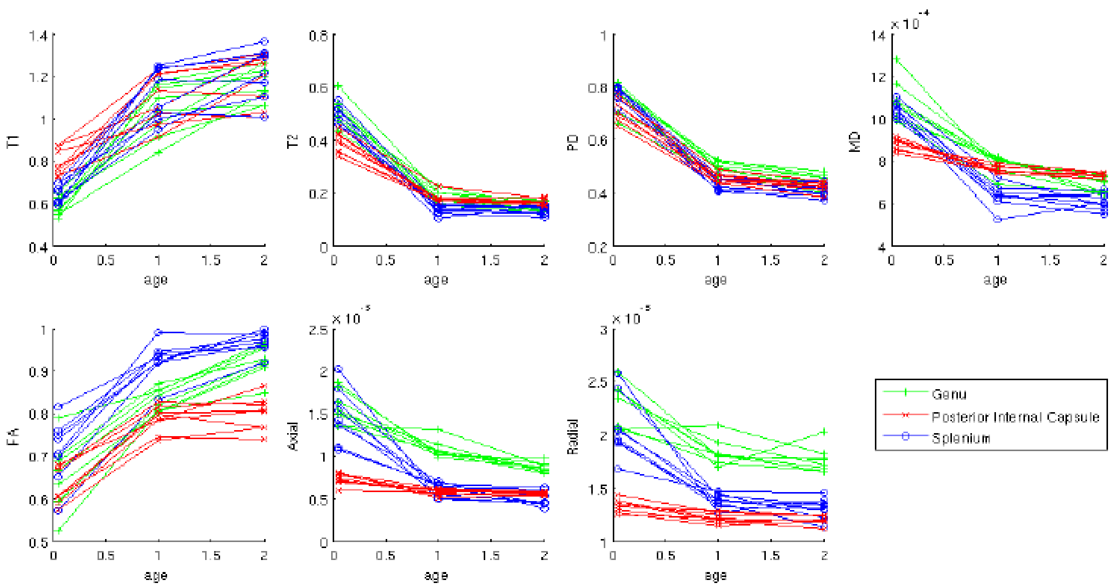


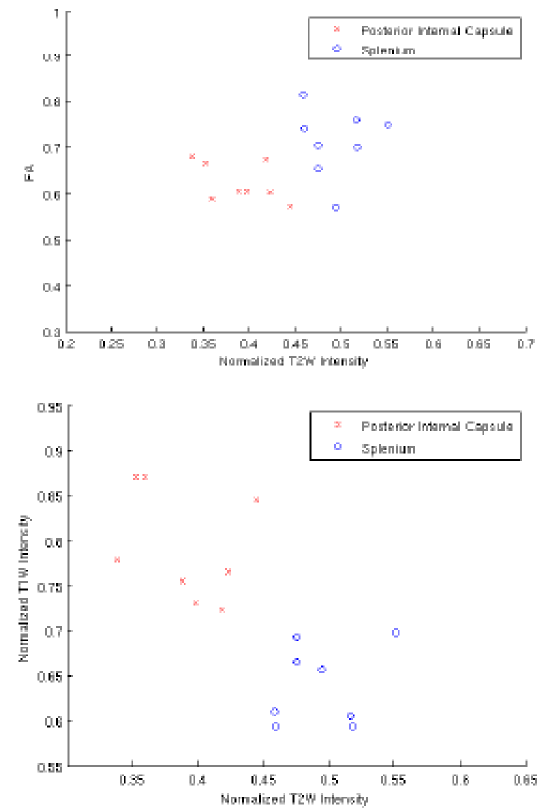
Neda Sadhegi, PhD project Utah, work in progress

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Towards multimodal spatio-temporal analysis





Growth trajectory, T2, PD, AD, RD, and increase in T1 and FA. changes related to age such as decrease in MD

FA not strongly correlated with myelination!

Neda Sadhegi, PhD project Utah, work in progress

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Outline

1. Imaging Technology for Pediatric Imaging
2. Analysis of structural MRI
3. Image Registration
4. Population Studies of DTI
5. Outlook and Conclusions

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Towards Longitudinal Analysis

Fallacy of global versus local analysis: Nonlinear growth of human brain

Brain development during childhood and adolescence: a longitudinal MRI study

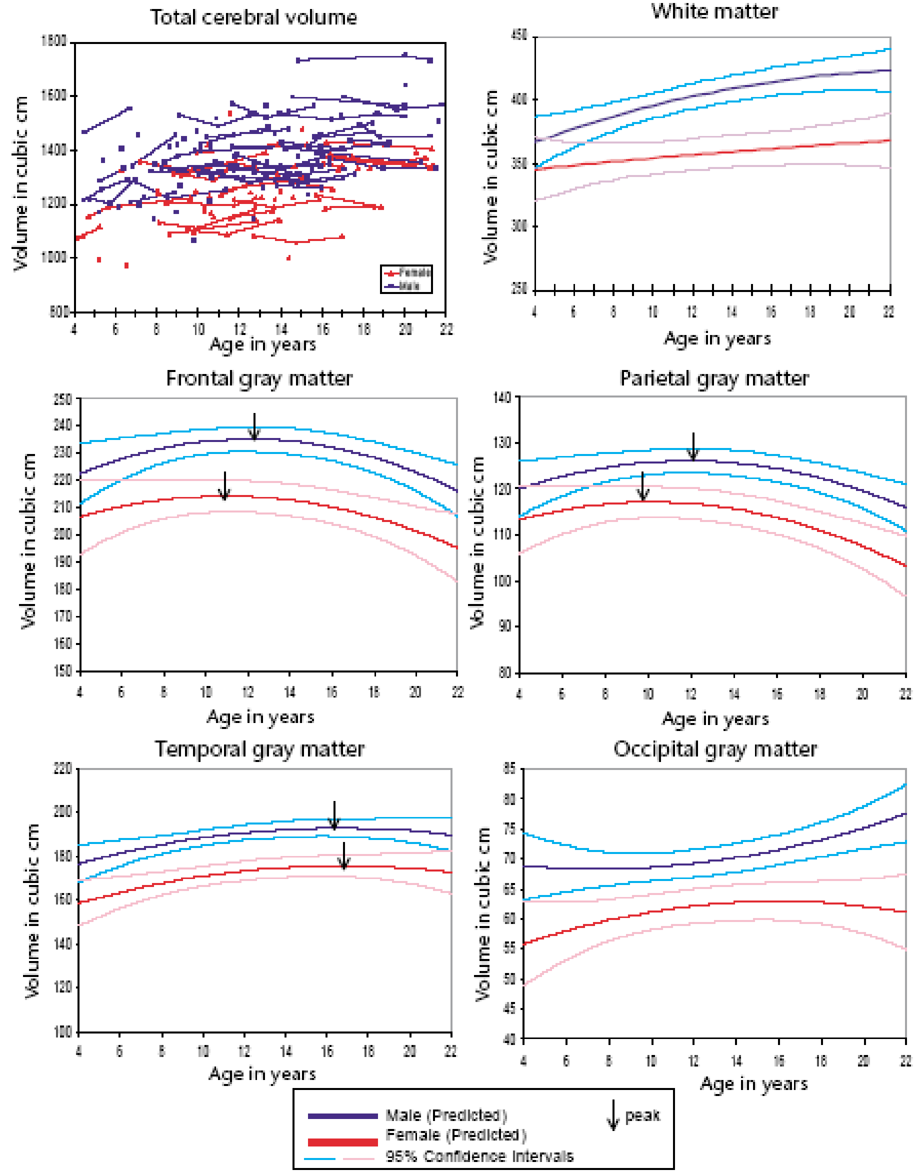
Jay N. Giedd[1], Jonathan Blumenthal[1], Neal O. Jeffries[2], F. X. Castellanos[1], Hong Liu[1], Alex Zijdenbos[3], Tomáš Paus[3], Alan C. Evans[3] and Judith L. Rapoport[1]

[1] *Child Psychiatry Branch, National Institute of Mental Health, Building 10, Room 4C110, 10 Center Drive, MSC 1367, Bethesda, Maryland 20892, USA*

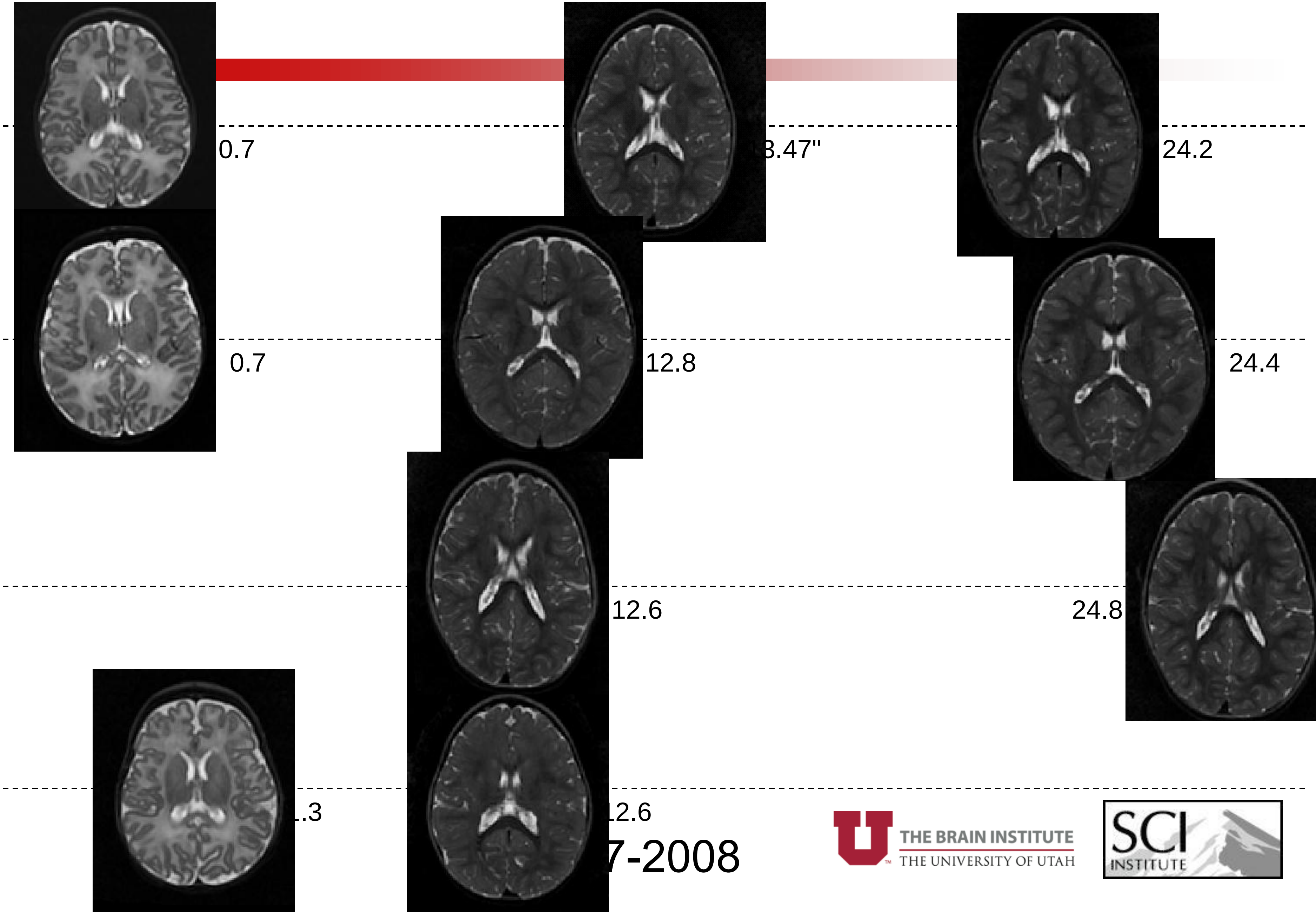
[2] *Biometry Branch, National Institute of Neurological Disease and Stroke, Federal Building, Room 7C06, 7550 Wisconsin Avenue, Bethesda, Maryland, 20892, USA*

[3] *Montreal Neurological Institute, McGill University, 3801 University Street, Montreal, Quebec H3A 2B4, Canada*

Correspondence should be addressed to J.N.G. (jgiedd@helix.nih.gov)



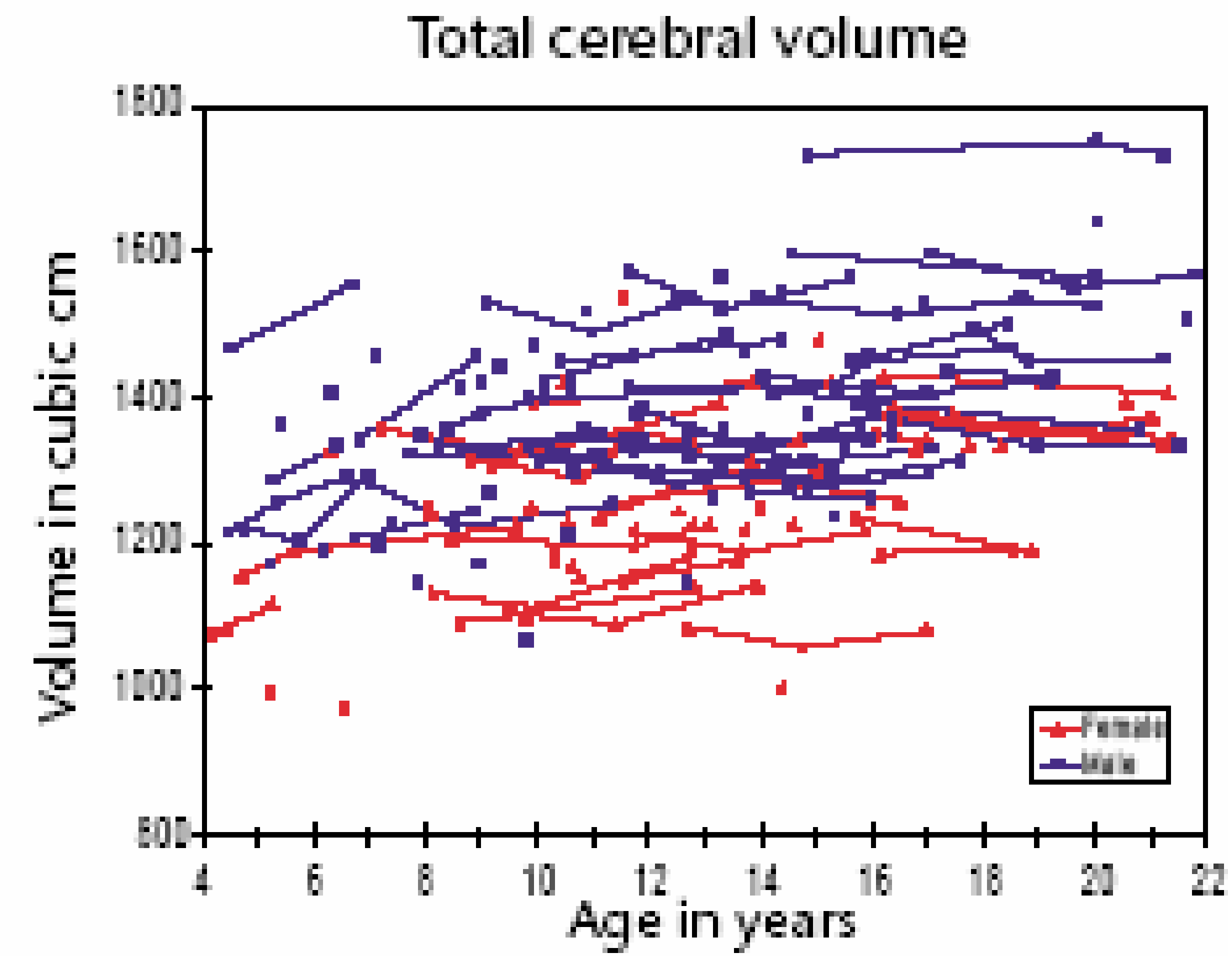
Longitudinal changes of MR images of population



THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Longitudinal Study Design: Normative NIH Brain Study

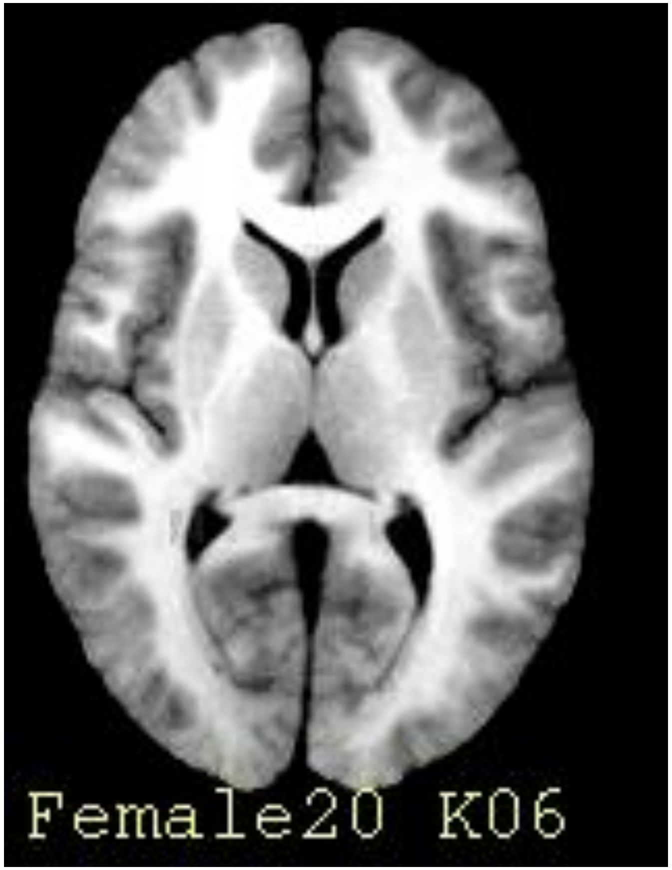


Challenges:

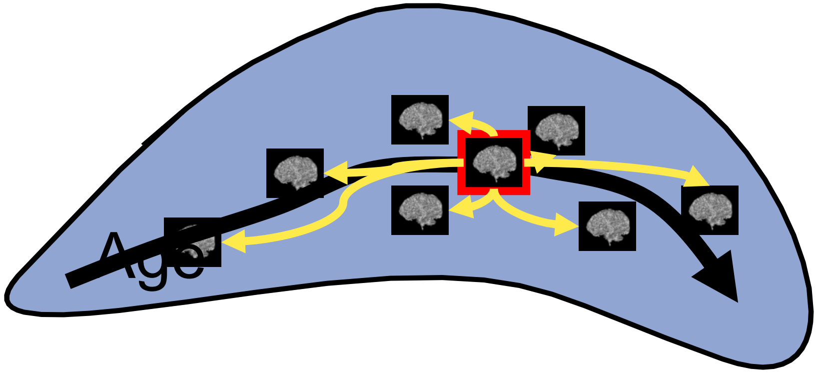
- Mixed Cross-sectional and longitudinal design
- Missing data (1, 2 or 3 data points per subject)

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH
SCI INSTITUTE

Aging Brain via Population Shape



Spatio-temporal 4D modeling:
Regression over image deformations



S. Joshi, T. Fletcher et al., Marr Prize, ICCV'07 best paper award

Properties of data

- Correlation, similarity between repeated MR scans
- Missing Data
- Unbalanced spacing, different time points
- Correlation between tissues, inter-subject variance, etc.
- Multivariate features: Dimensionality
- Regression not suitable

Challenge: Multivariate Longitudinal data analysis

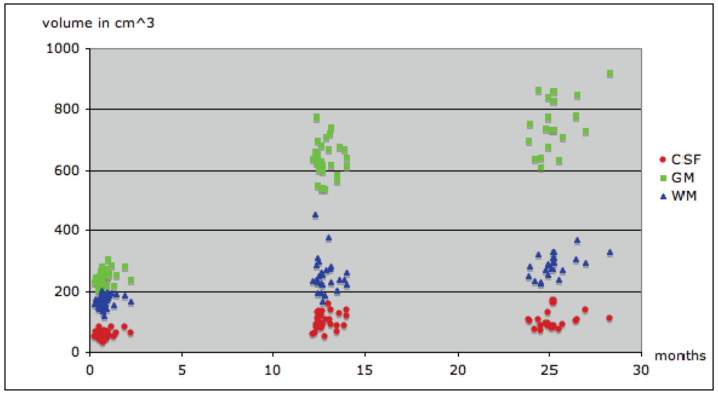


Figure 2. Scatter plot of our WM, GM, CSF data versus time. An illustration of irregular data that has uneven sampling at time axis for different subjects. CSF: red dot, GM: green box, WM: blue triangle.

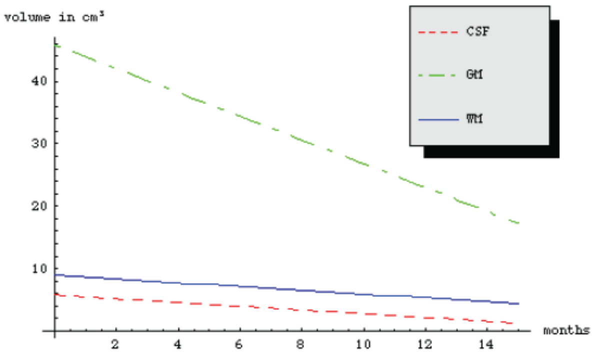


Figure 7. Derivatives of the parametric growth curves of three brain tissues. CSF: red dash line, GM: green dot-dash line, and WM: blue solid line.

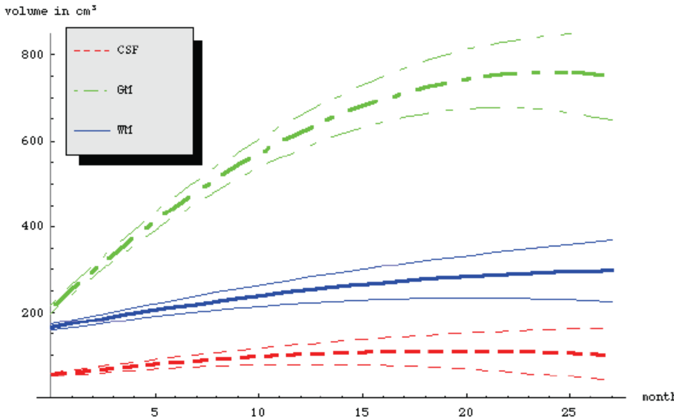


Figure 4. 95 % confidence interval of the growth curves of three brain tissues. CSF: red dash line, GM: green dot-dash line, and WM: blue solid line.

Multivariate Longitudinal Statistics for Neonatal-Pediatric Brain Tissue Development, Sh. Xu, M. Styner, J.H. Gilmore, G. Gerig, SPIE 2008

Multivariate Nonlinear Mixed Model to Analyze Longitudinal Image Data: MRI Study of Early Brain Development, Shu Xu et al., MMBIA 2008

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Challenge: Multivariate Longitudinal data analysis

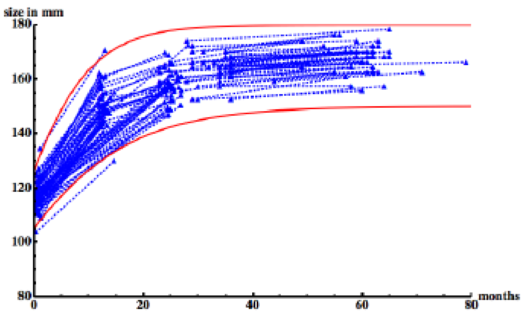


Figure 2. Illustration of individual growth trends. A spaghetti plot that connects repeated measurements of the same individual is shown. The two red upper and lower bound curves are generated by varying β_1 and β_3 only and with fixed β_2, which indicates population variance can be captured by varying only β_1 and β_3.

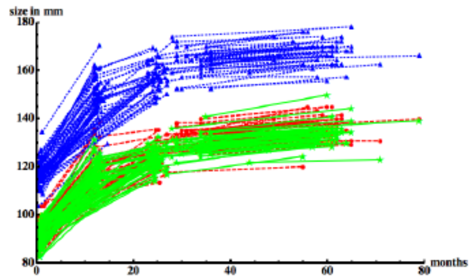


Figure 3. Illustration of individual growth trends. A spaghetti plot that connects repeated measurements of the same individual is shown. Multiple features that describe the three dimensional head size derived from each MRI brain image of neonates and young children is illustrated. X dimension: red dots connected by dashed lines; Y dimension: blue triangles connected by dotted lines; Z dimension: green stars connected by solid lines.

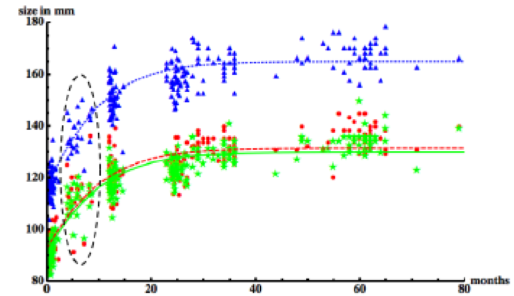


Figure 4. Population growth trajectories of head size dimension X, Y, Z plotted against the original data points ranged from age 0 to around 6 years old. A third population of 22 infants aged from 4 to 8 months old (in black dashed circle) are also plotted to validate the soundness of the average growth estimation. Symbols are the same as those in Fig. 3.

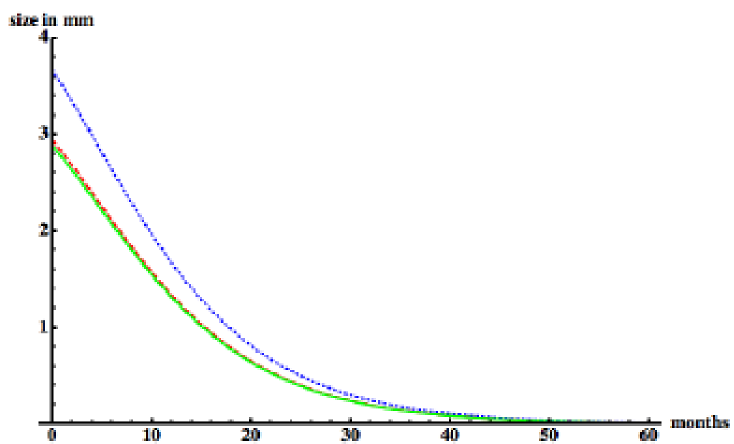


Figure 5. Growth rates of head size dimension X, Y, Z between birth to around 6 years old. X dimension: dashed red lines; Y dimension: dotted blue lines; Z dimension: solid green lines.

Multivariate Longitudinal Statistics for Neonatal-Pediatric Brain Tissue Development, Sh. Xu, M. Styner, J.H. Gilmore, G. Gerig, SPIE 2008

Multivariate Nonlinear Mixed Model to Analyze Longitudinal Image Data: MRI Study of Early Brain Development, Shu Xu et al., MMBIA 2008

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Spatio-temporal image/shape analysis

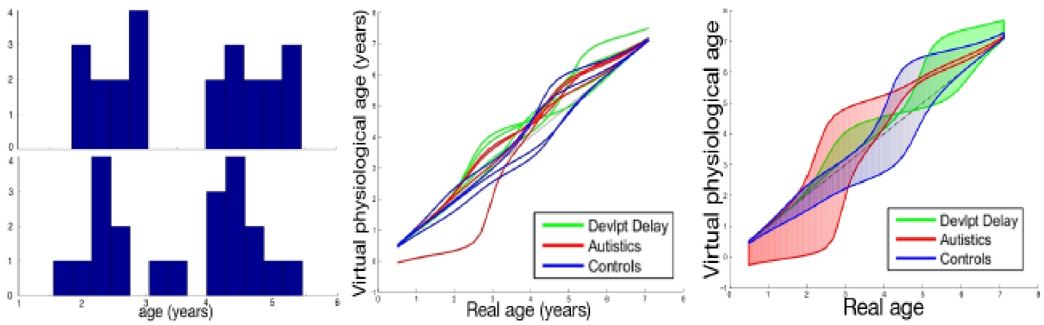
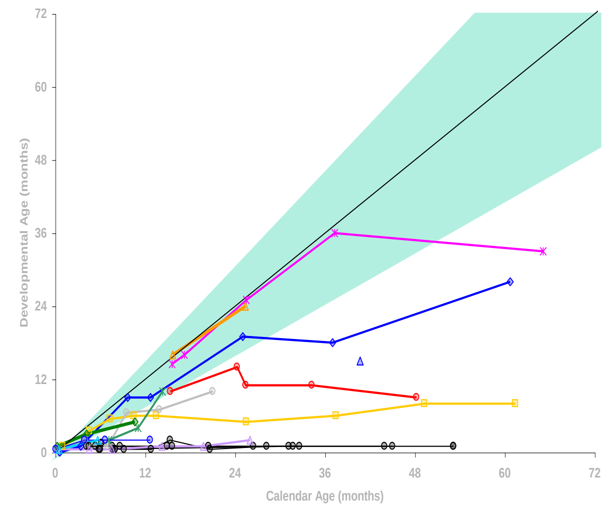


Fig. 5. Temporal deformation of the mean scenario Left: distribution of original (top) and registered (bottom) ages. Middle: time change functions for the 12 subjects. Right: First mode of variation at $\pm\sigma$ of the time change functions for each class. Autistics and controls show the same evolution pattern, but shifted in time.

Growth Phenotypes



Challenge: cross-sectional variation/deformation versus shift in age/time (Durrlemann et al, MICCAI 2009

Notion of normative model/atlas: Describe patients relative to population statistics of healthy development.

see also related work by Perperidis/Rueckert et al., Habas/Studholme et al., Peyrat/Ayache et al.

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Summary

Key topics related to imaging of early development:

- Imaging itself is great challenge
- Continuous contrast, size, shape changes:
  - Challenge for image registration
  - Challenge for image segmentation (thin cortex, very low contrast of subcortical structures)
  - Contrast flip wm/gm in anatomical images
- Myelination/Structuring: Continous appearance changes within tissue: Segmentation? Effect on registration?
- Longitudinal studies: Require study of temporal changes rather then cross-sectional differences

Conclusions

- **Pediatric Imaging & Image Analysis:**
  - Amazing progress of imaging technology
  - Image processing tools newly developed
  - Wealth of new results, but heterogeneous (bits and pieces)
  - Fascinating research area: Full of discoveries
  - **Potential impact: Better understanding → early detection → therapy**
- **Research field needs:**
  - Multidisciplinary research: Biology, anatomy, medicine, CS, statistics
  - Link between MRI findings and underlying neurobiology
  - Sharing of data and analysis tools
- **Fundamental computational and statistical problems:**
  - Everything changes: Contrast, size, shape, appearance
  - Statistics of growth of images and structures: 4D statistical atlases
  - (Longitudinal) multivariate statistics of imaging features & patient parameters
- **Significant progress over last few years**

THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE

Acknowledgements

Clinical Research Partners:

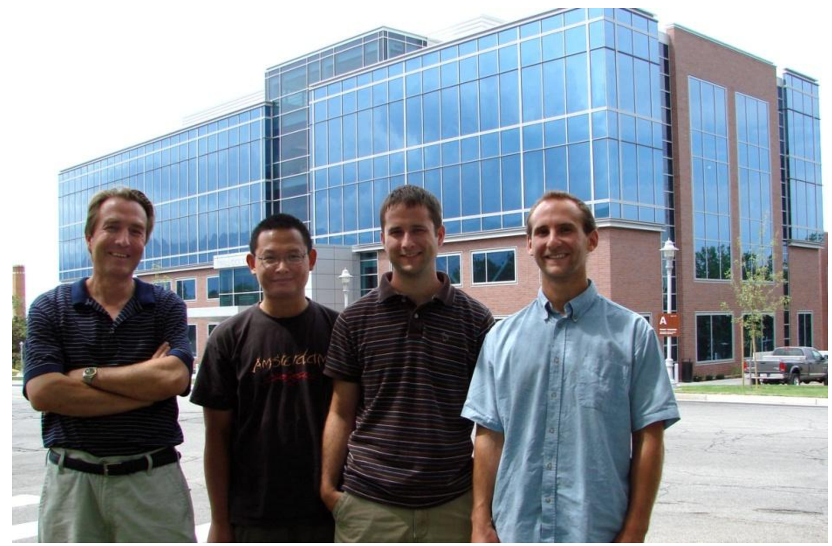
- Joseph Piven (UNC)
- John H. Gilmore (UNC)
- Janet Lainhart (Utah)
- Weili Lin (UNC)
- Larry Wald (MGH)

Computer Science Partners:

- Sarang Joshi (Utah)
- Tom Fletcher (Utah)
- Marcel Prastawa (Utah)
- Sylvain Gouttard (Utah)
- Casey Goodlett (Utah)
- Shu Xun (UNC)
- Martin Styner (UNC)
- Ron Kikinis (SPL Harvard)

Funding:

- NIH MH070890 (JHG)
- NAMIC U54 EB005149 (GG)
- NIMH Silvio Conte Center (JHG)



THE BRAIN INSTITUTE
THE UNIVERSITY OF UTAH

SCI INSTITUTE