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# Quantitative Neuro-Anatomic and Functional Image Assessment

## **Recent progress on image registration and its applications**

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Guido Gerig

Sarang Joshi

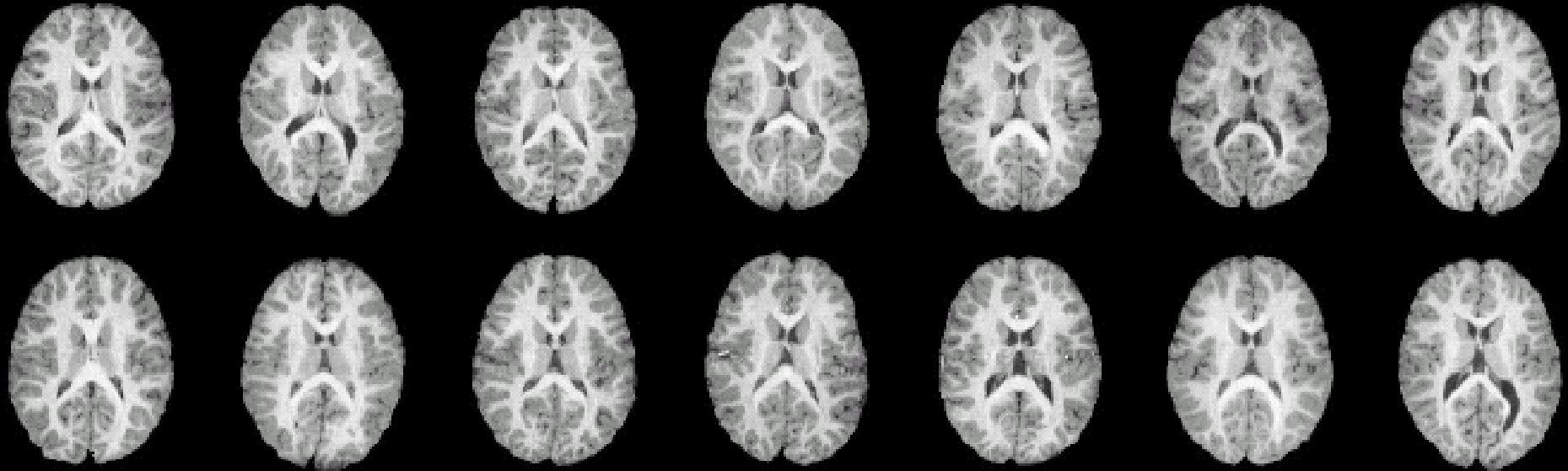
Tom Fletcher

# Applications of image registration in neuroimaging

- Atlas construction
  - Probabilistic atlases
  - Statistical atlases
  - Unbiased atlases
- Atlas-based segmentation
  - Atlases are used as prior knowledge
  - Tissue and/or anatomical segmentation
- Quantification of anatomical and functional differences
  - across time       $\Rightarrow$  longitudinal studies
  - across groups     $\Rightarrow$  cross-sectional studies

# Motivation: A Natural Question

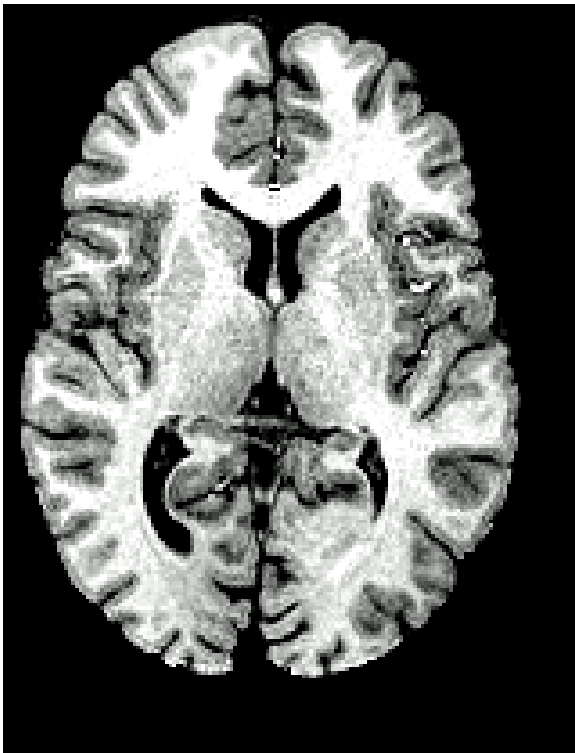
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- Given a collection of Anatomical Images what is the Image of the “Average Anatomy”.

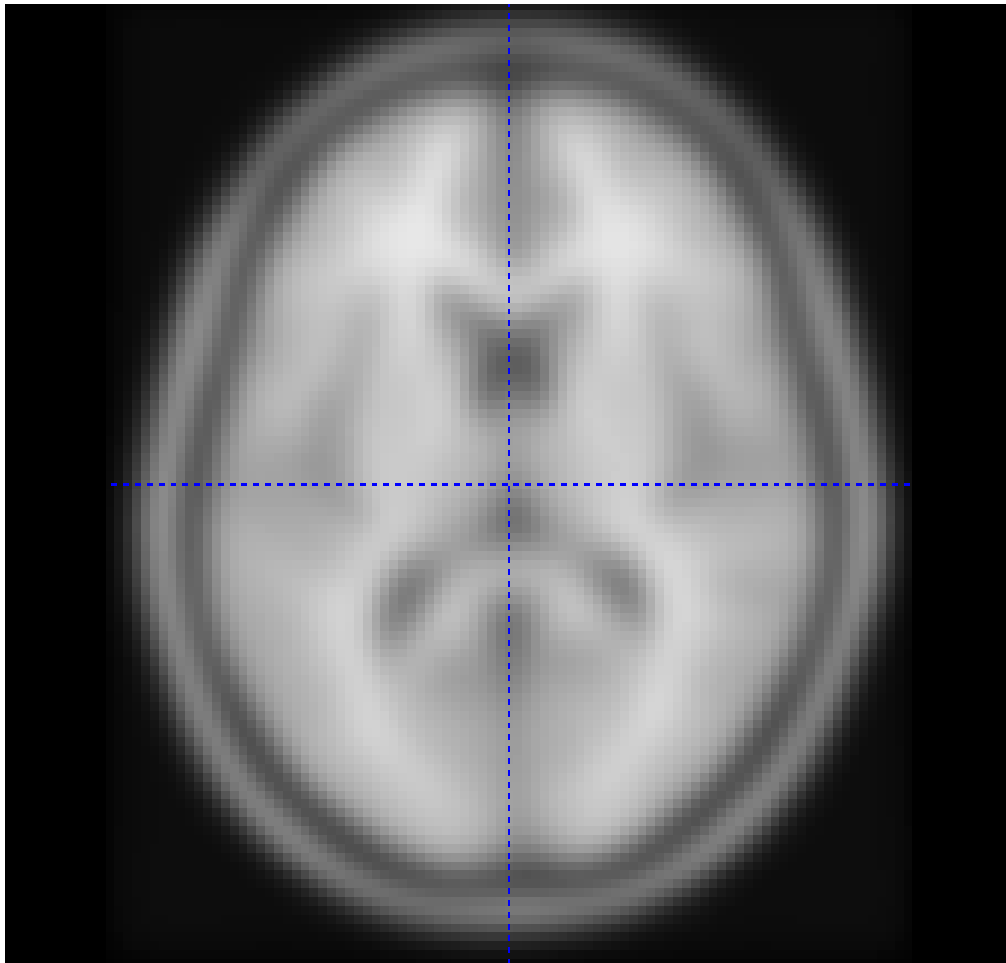
# Population Variability

- How to compare and measure structures across different subjects?



# Average after linear alignment (affine)

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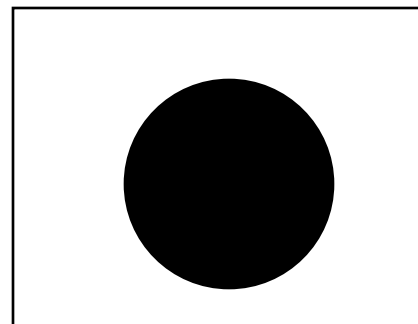
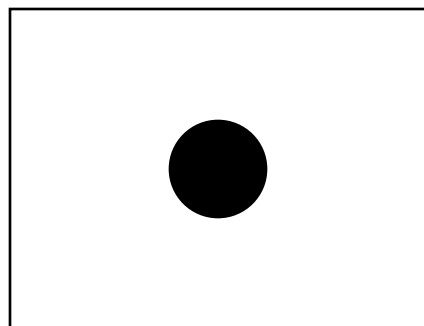
Adult brain MRI atlas  
(Montreal  
Neurological  
Institute):

- 152 adult subjects
- Affine registration
- Superposition
- Serves as probabilistic template for brain mapping
- **Blurry, does not look like a real image**

# Motivation: A Natural Question

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Consider two simple images of circles:

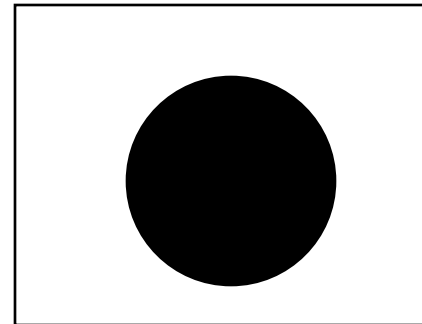
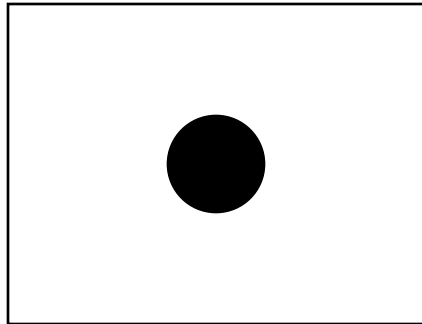


What is the Average?

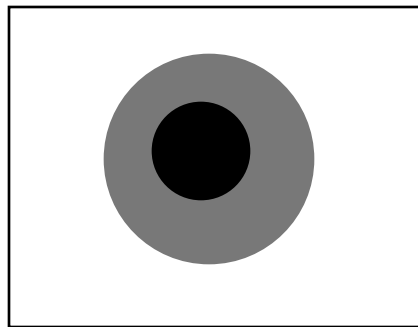
# Motivation: A Natural Question

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Consider two simple images of circles:

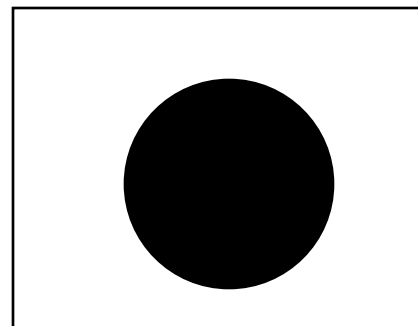
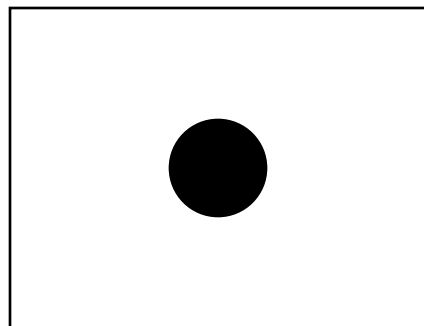


What is the Average?

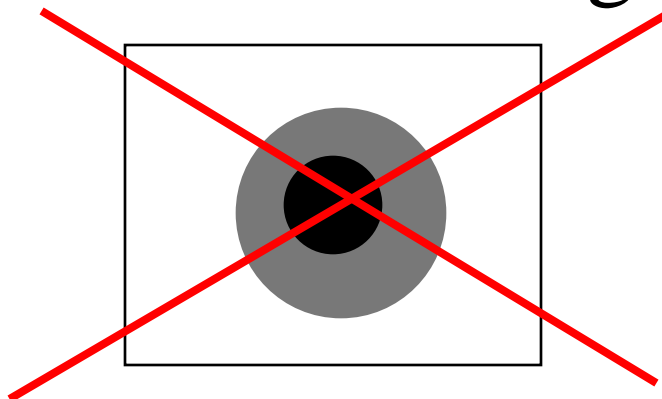


# Motivation: A Natural Question

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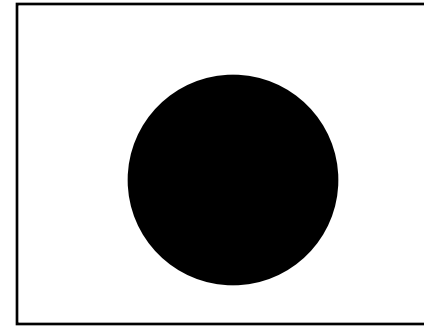
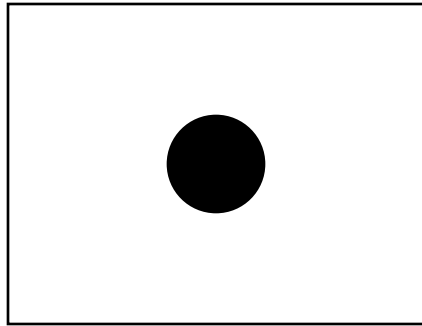
What is the Average?



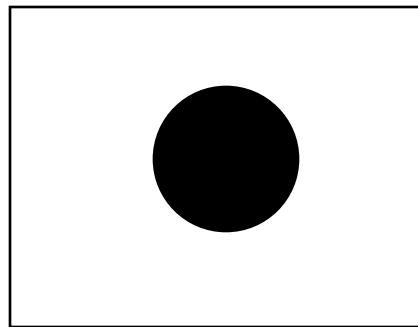


# Motivation: A Natural Question

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Average considering “Geometric Structure”



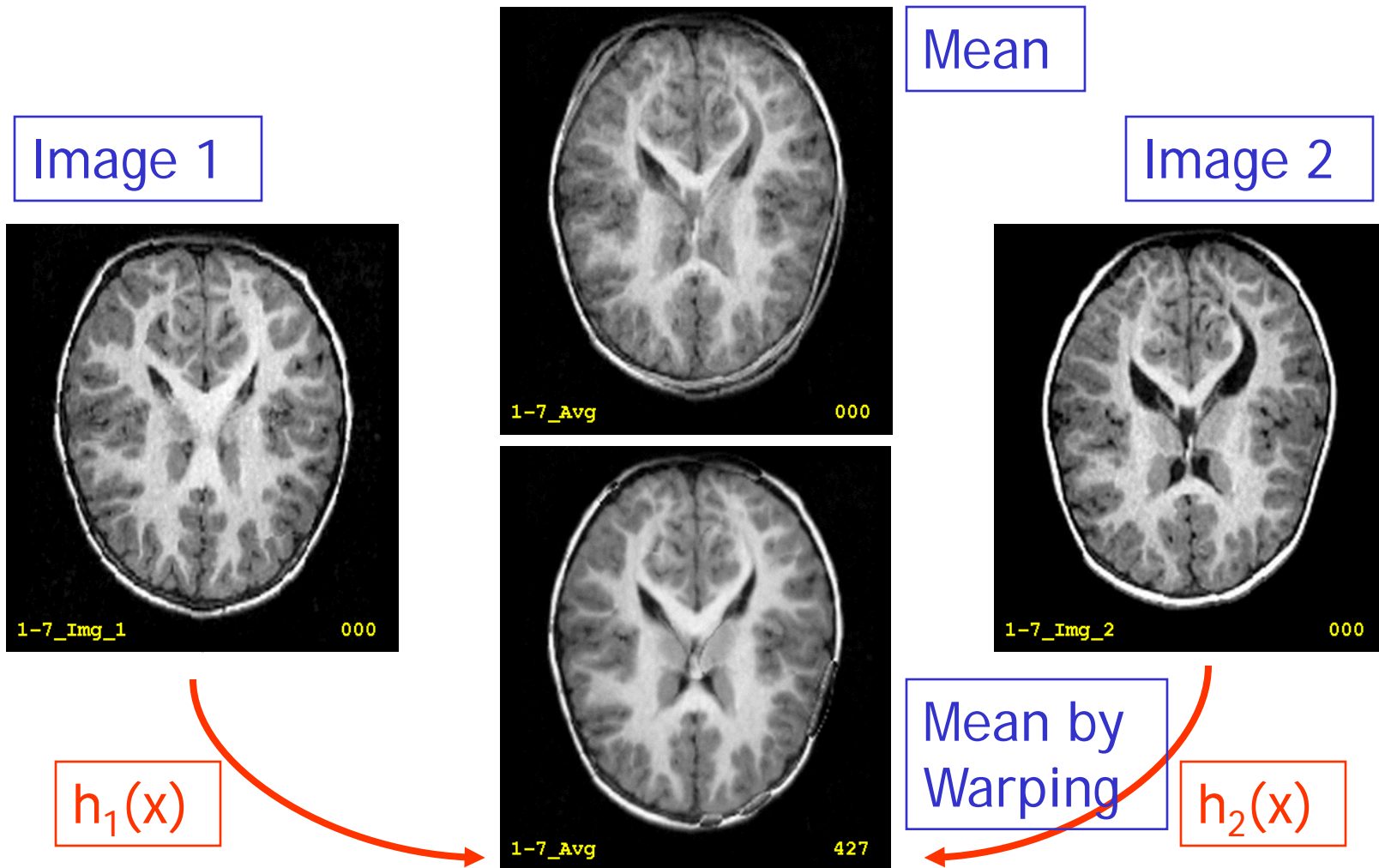
A circle with  
“average radius”

# Mathematical Foundations of Computational Anatomy

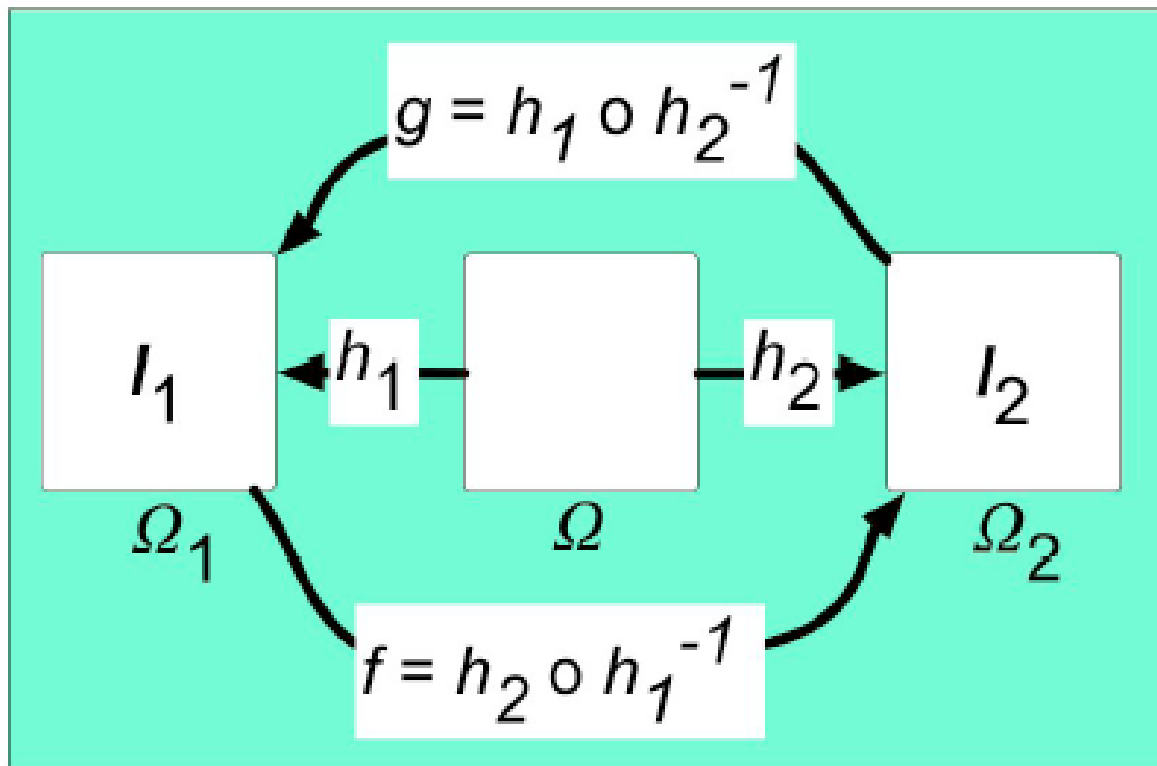
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- Structural variation within a population represented by transformation groups:
  - For circles simple multiplicative group of positive reals ( $\mathbb{R}^+$ )
  - Scale and Orientation: Finite dimensional Lie Groups such as Rotations, Similarity and Affine Transforms.
  - High dimensional anatomical structural variation: Infinite dimensional **Group of Diffeomorphisms.**

# Unbiased Diffeomorphic Atlas Construction for Computational Anatomy (Joshi, Davis, Lorenzen)



# Atlas Formation: Symmetric Registration



**Symmetric Registration Framework**

$$f \circ g = h_2 \circ h_1^{-1} \circ h_1 \circ h_2^{-1} = \text{Id}$$

# Averaging Anatomies'

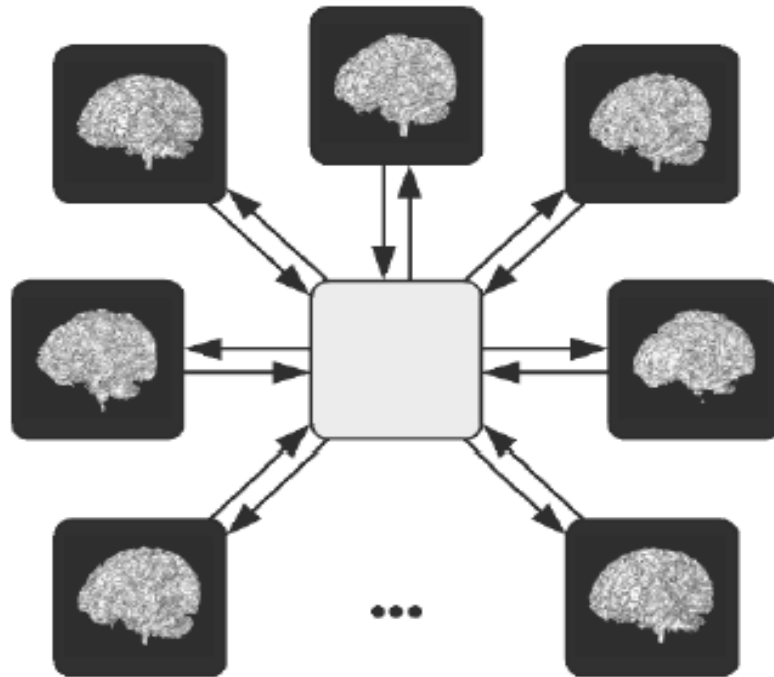
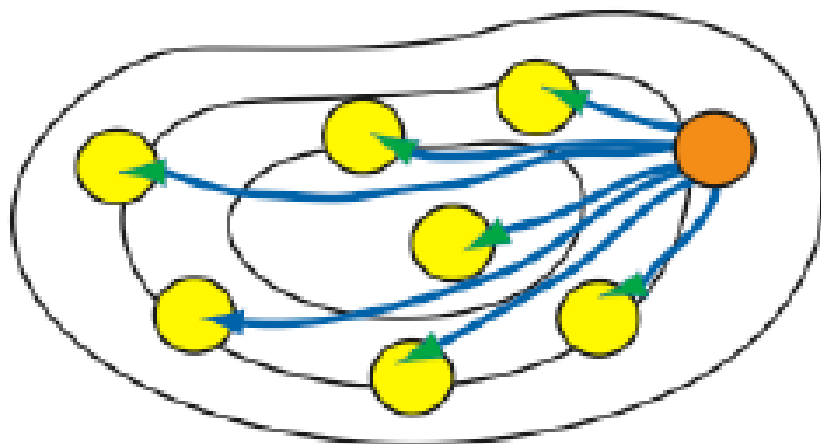


Figure 1. Template Construction Framework

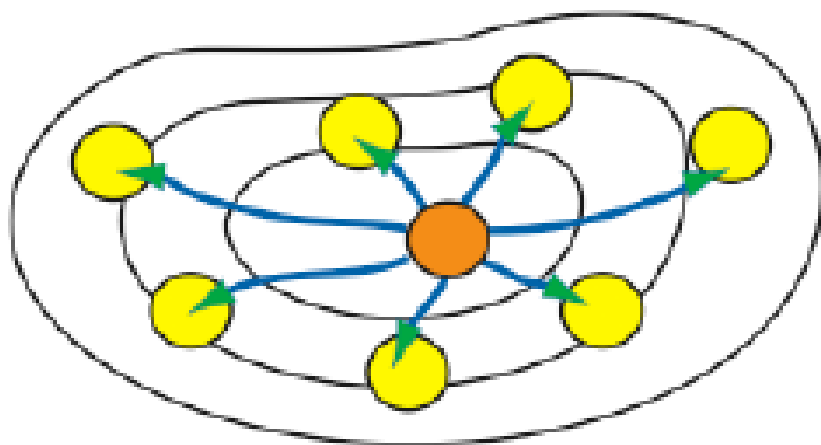
## Motivation:

- Map population into common coordinate space
- Learn about normal variability
- Describe difference from normal
- Use as normative atlas for segmentation

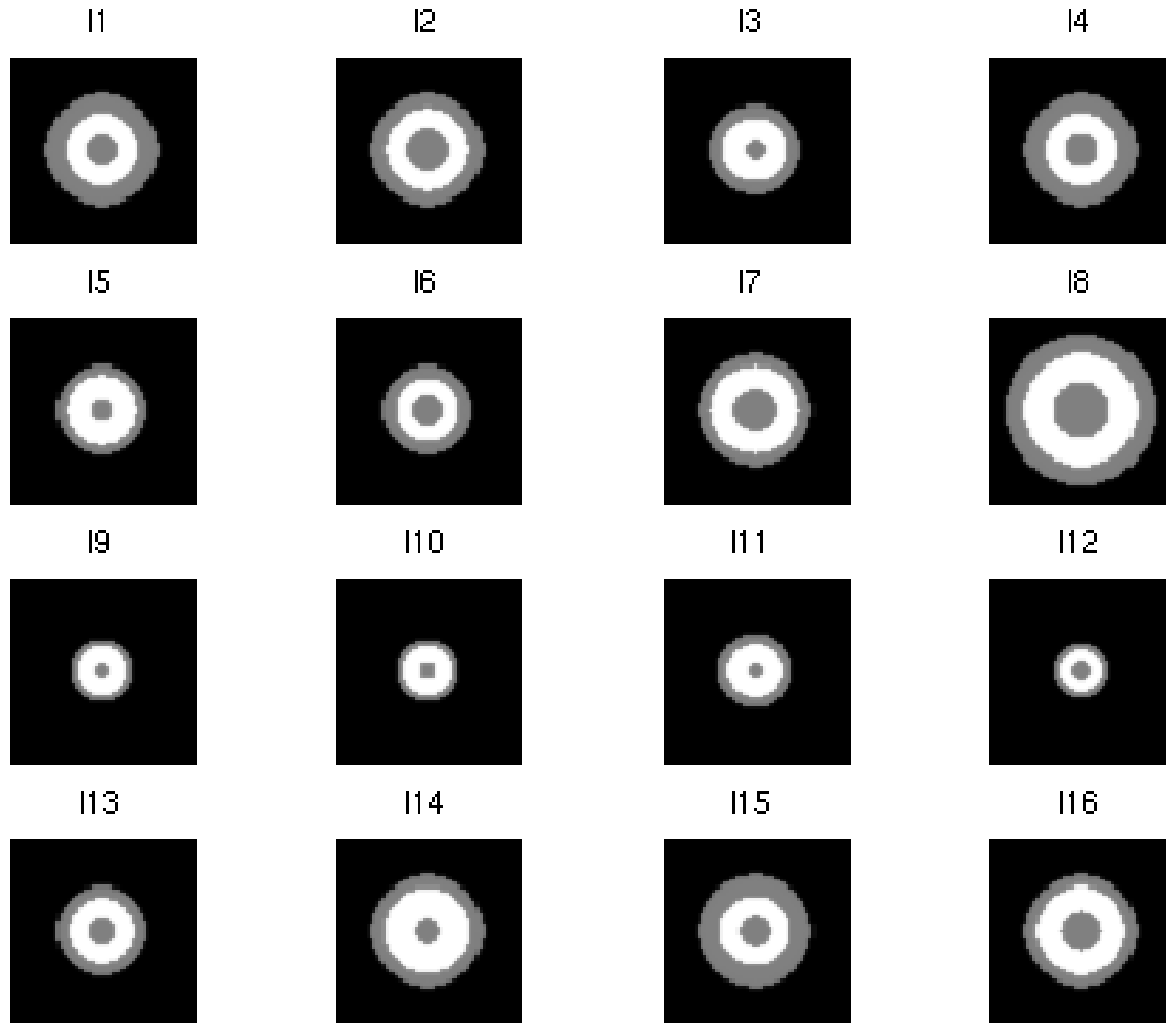
# Group-wise Atlas Building



Minimize total distance  
between population  
and template  
(Gee & Avants,  
Joshi&Fletcher)

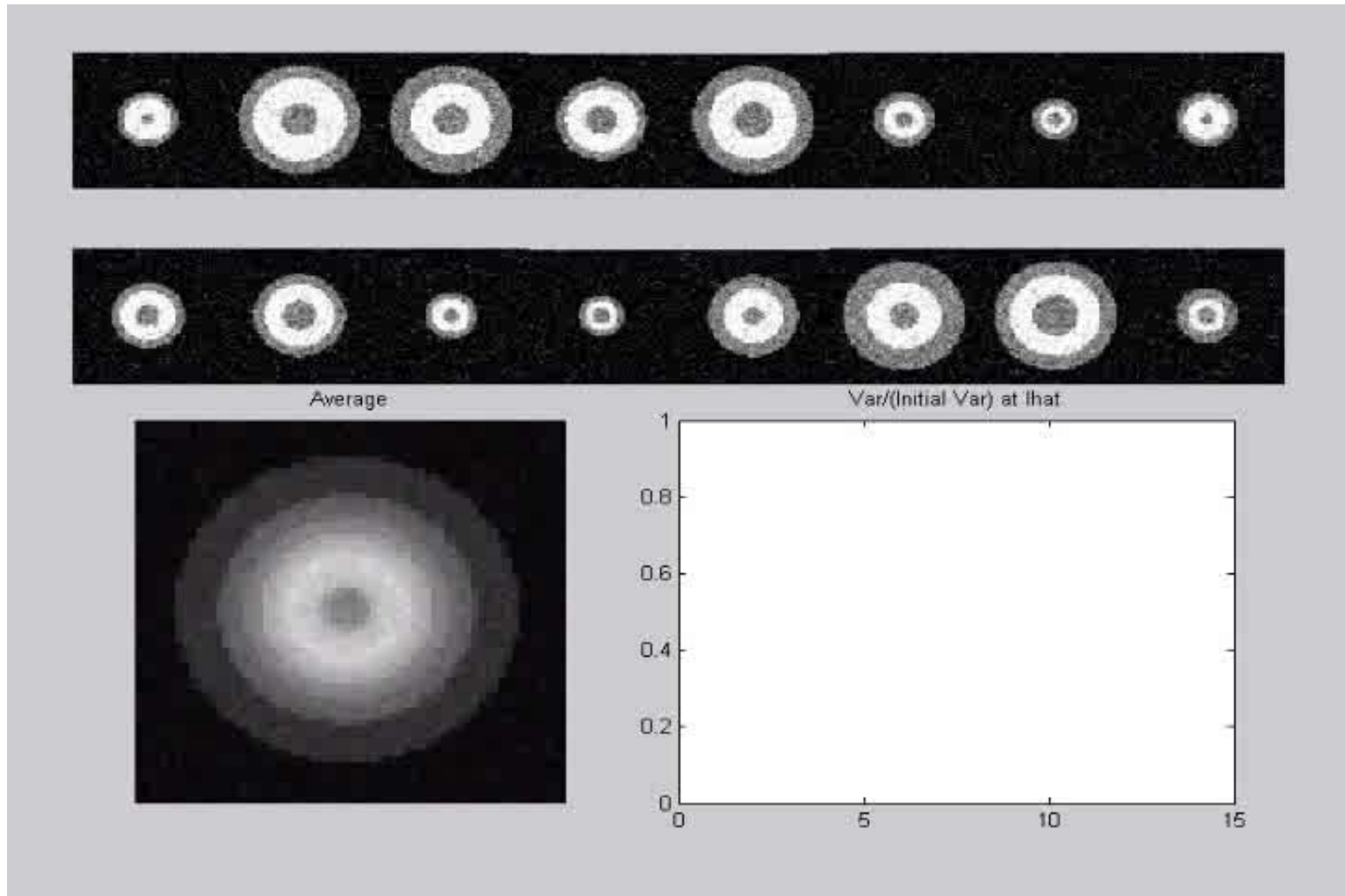


# More than Pairs: Sample of 16 Bull's eye Images



Courtesy S. Joshi

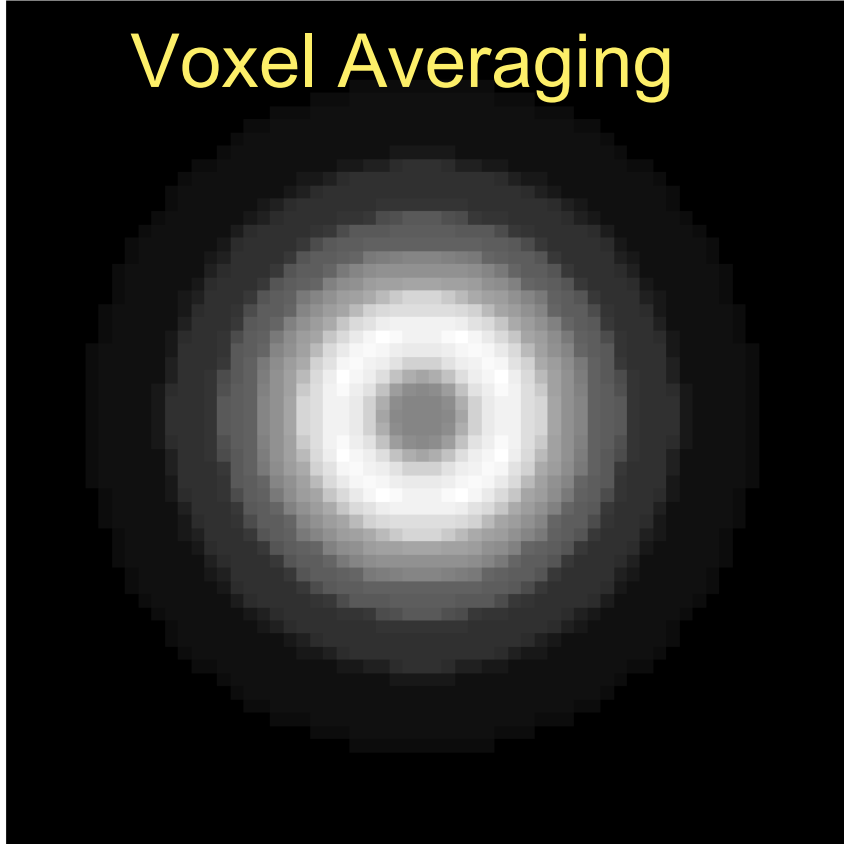
# Group-wise Image Averaging



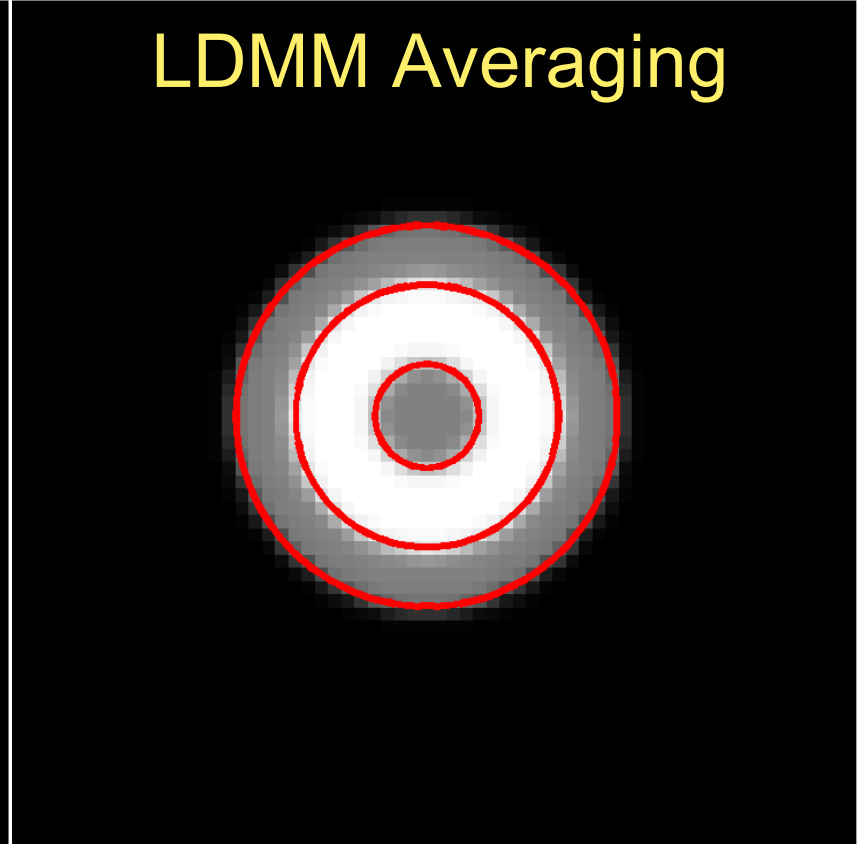


# Averaging of 16 Bull's eye images

Voxel Averaging



LDMM Averaging



○ Numerical geometric average of the radii of the individual circles forming the bulls eye sample.

# Averages in Metric Spaces

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- Recall the linear average:

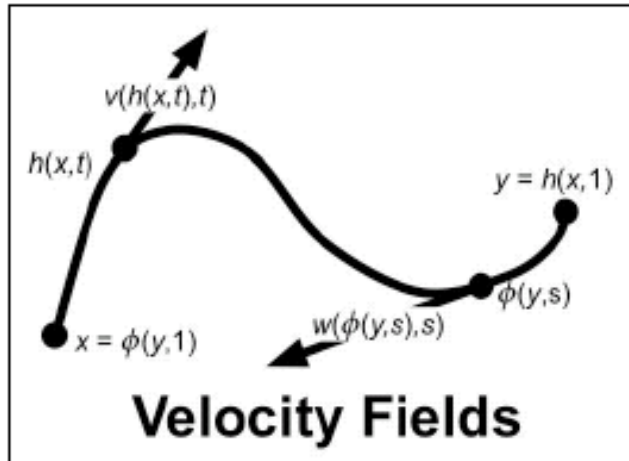
$$\mu = \frac{1}{N} \sum_{i=1}^N x_i$$

- The space of diffeomorphisms is not a vector space
- Need a more general notion of “average”
- Frechet mean: 
$$\mu = \operatorname{argmin}_{x \in \mathcal{M}} \sum_{i=1}^N d(x, x_i)^2$$

# Large deformation diffeomorphisms.

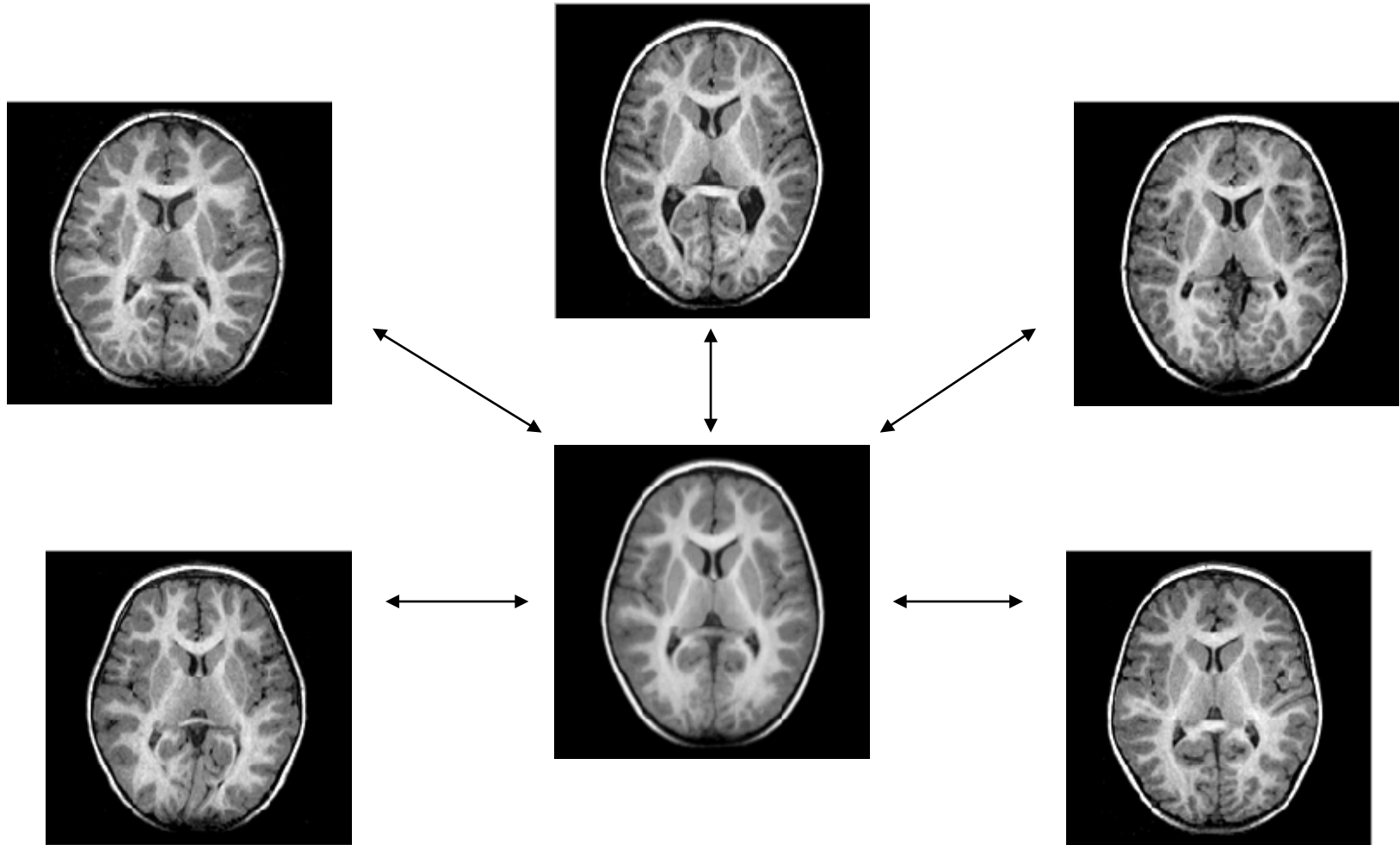
- $Diff(\Omega)$  infinite dimensional “Lie Group”.
- Tangent space: The space of smooth vector valued velocity fields on  $\Omega$ .
- Construct deformations by integrating flows of velocity fields.
- Induce a metric via a differential norm on velocity fields.

$$\frac{d}{dt}h(x, t) = v(h(x, t), t) \quad h(x, 0) = x.$$

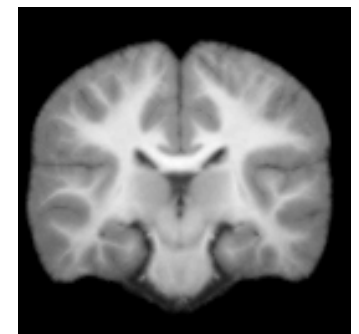
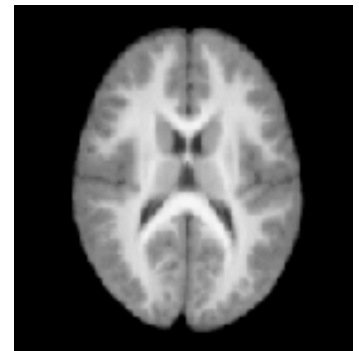
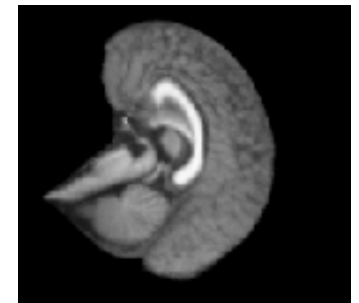
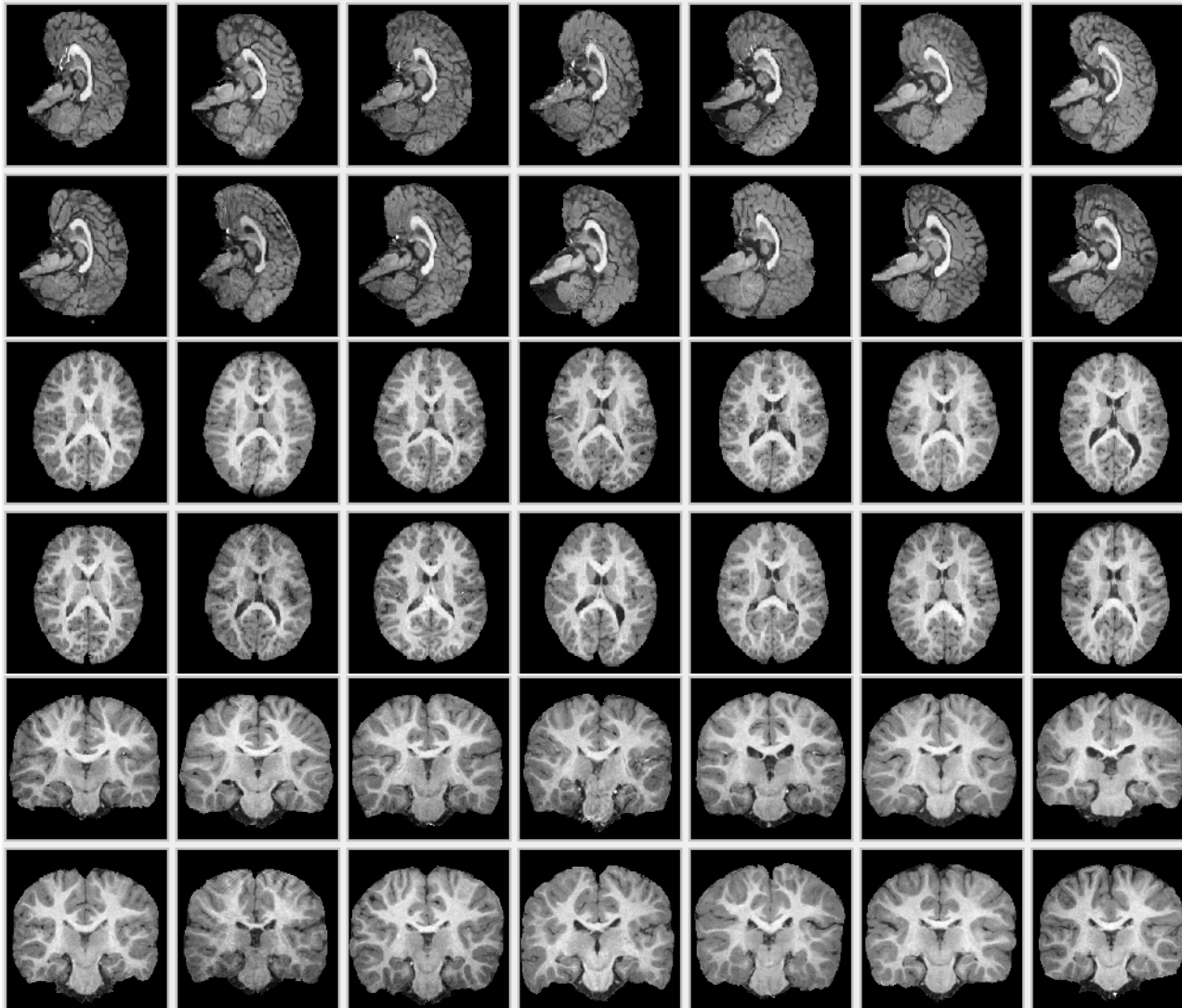


$$y = h(x, 1) = x + \int_0^1 v(h(x, \tau), \tau) d\tau$$
$$x = \phi(y, 1) = y + \int_0^1 w(\phi(y, \tau), \tau) d\tau$$

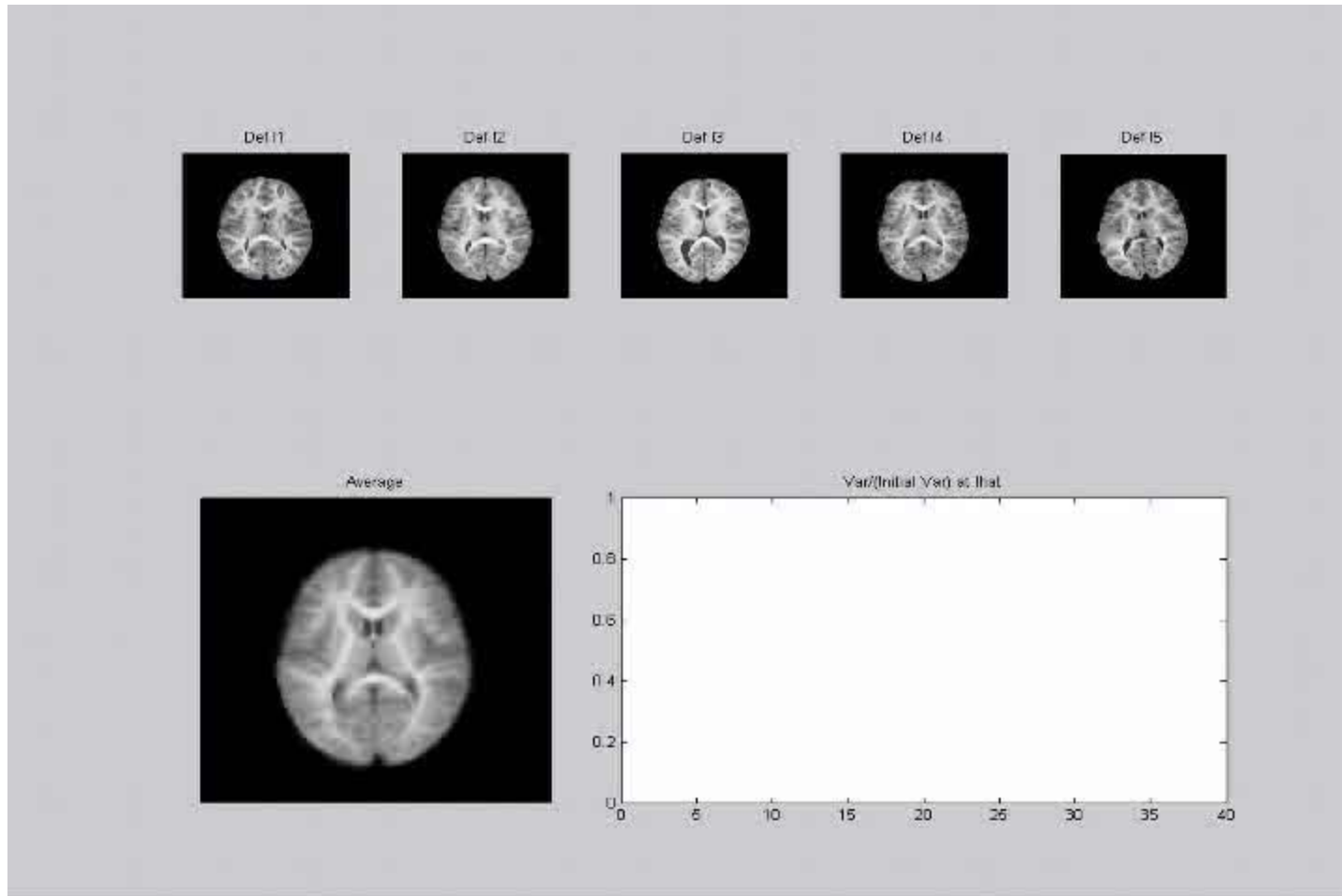
# Atlas Building – Population Average (Infant 2 yr)



# Atlas Builder – Atlas with 14 images

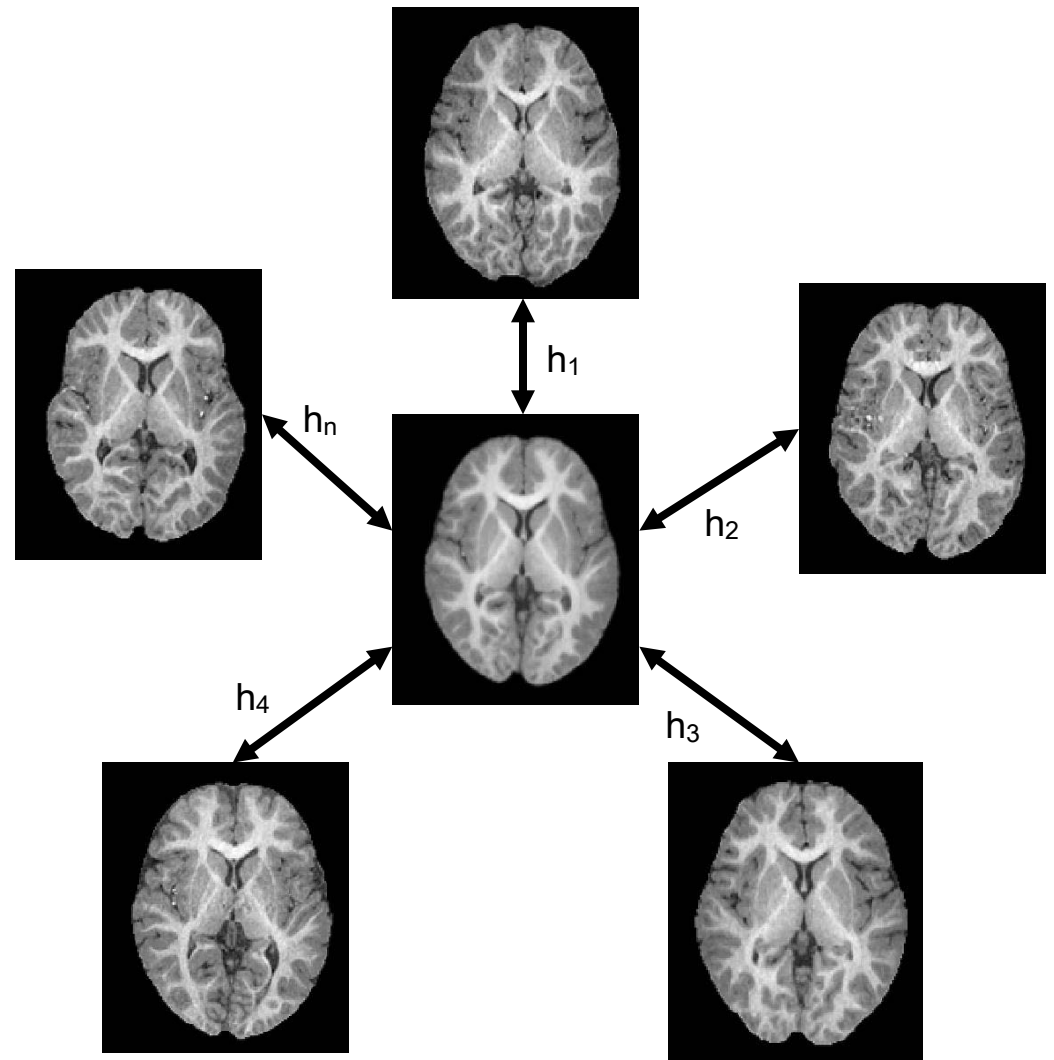


# Averaging Brain Images



# Motivation Atlas Building: Statistics of embedded Shapes

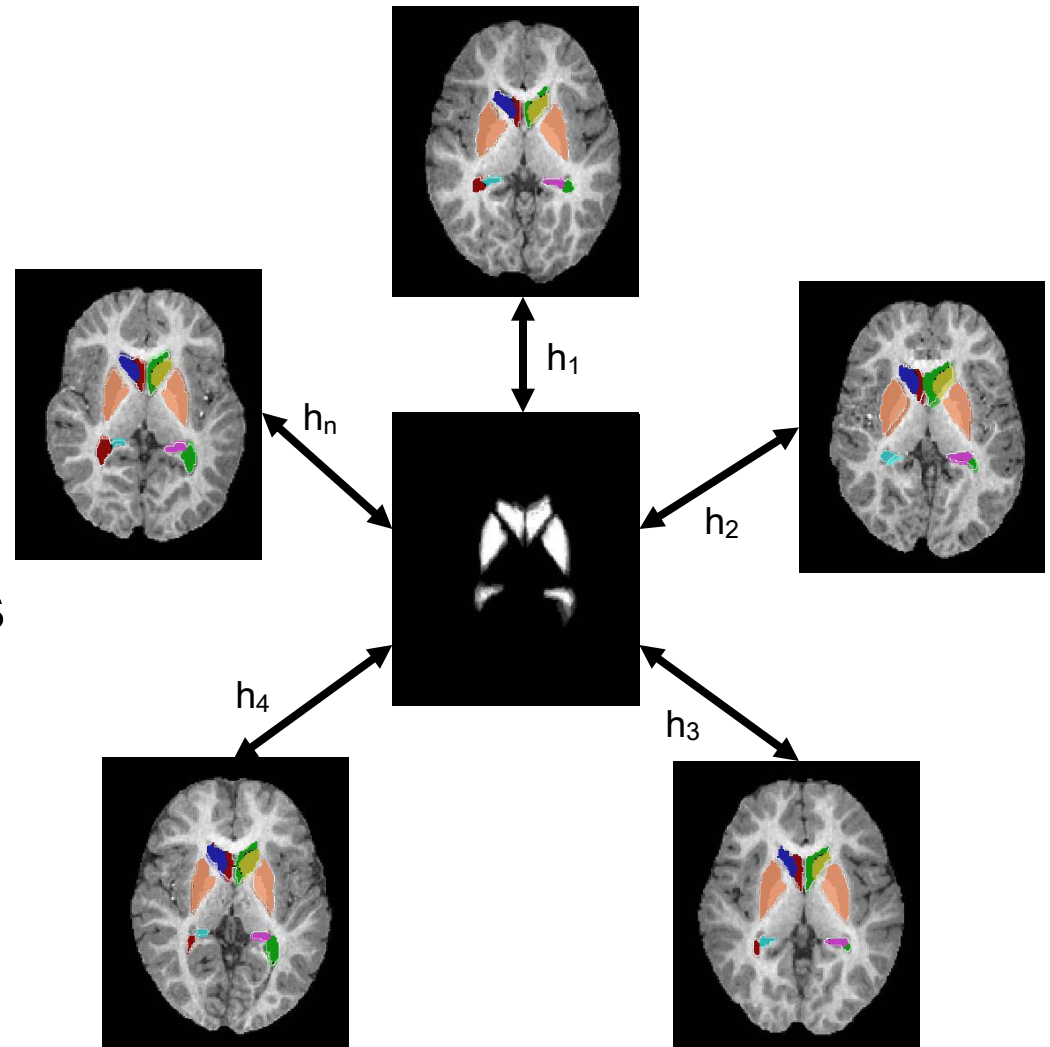
- Brain atlases is central to the understanding of the variability of brain anatomy.
- How to study statistical shape properties from nonlinear deformation fields of atlases?



# Embedded Objects: Voxel Representation

To evaluate shape variability

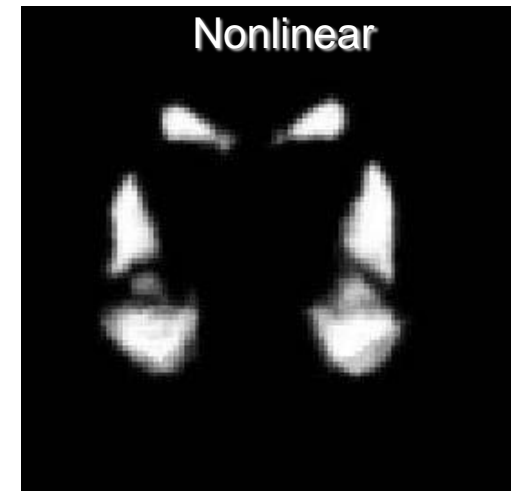
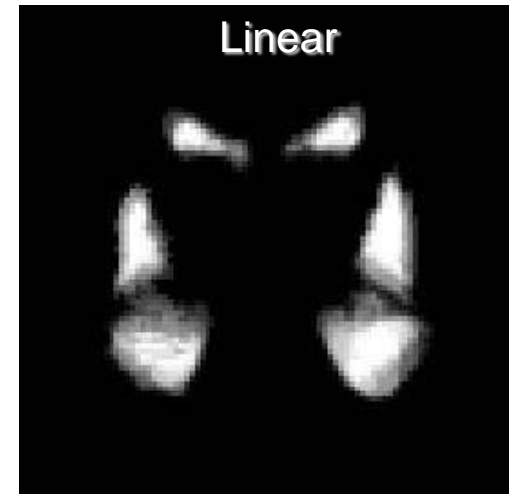
- reliable user-supervised voxel segmentations by geodesic snakes
- probability map in atlas space





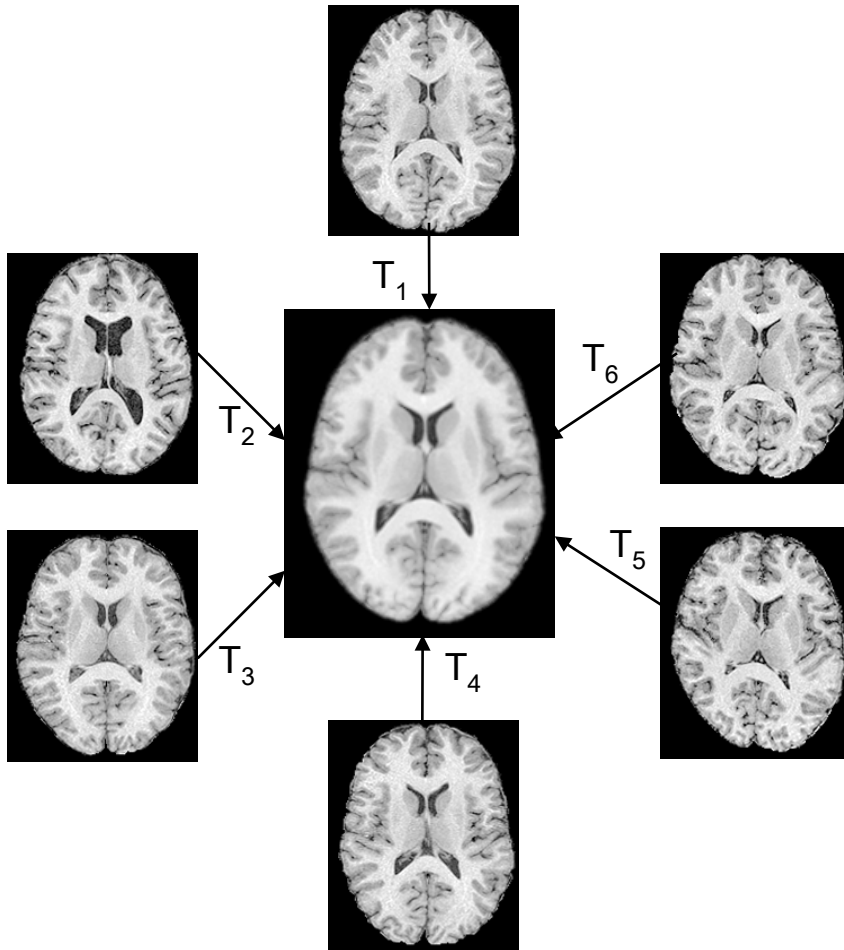
# Voxel-based Representation: Linear vs. Nonlinear Atlas

- Single population
- Linear averaging of voxel objects — blurry probability maps
- Nonlinear average appears sharper
- Notion of probabilistic label atlas: centered & population-based



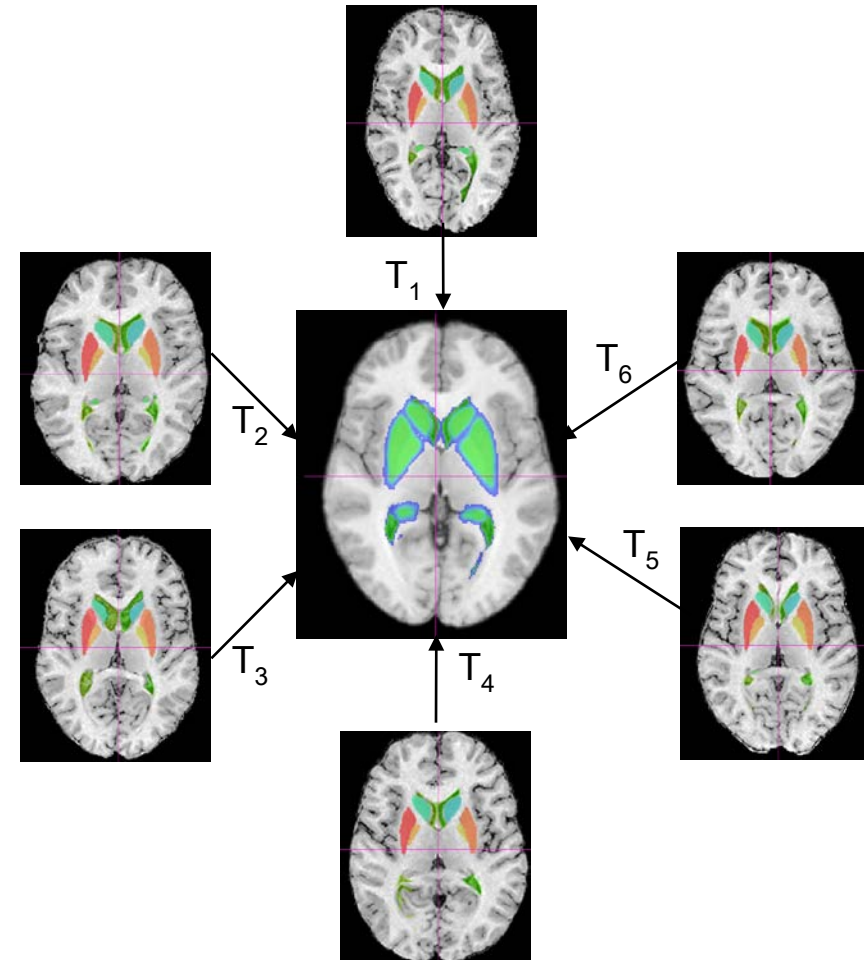
# Atlas-based segmentation: Atlas Building

Step 1



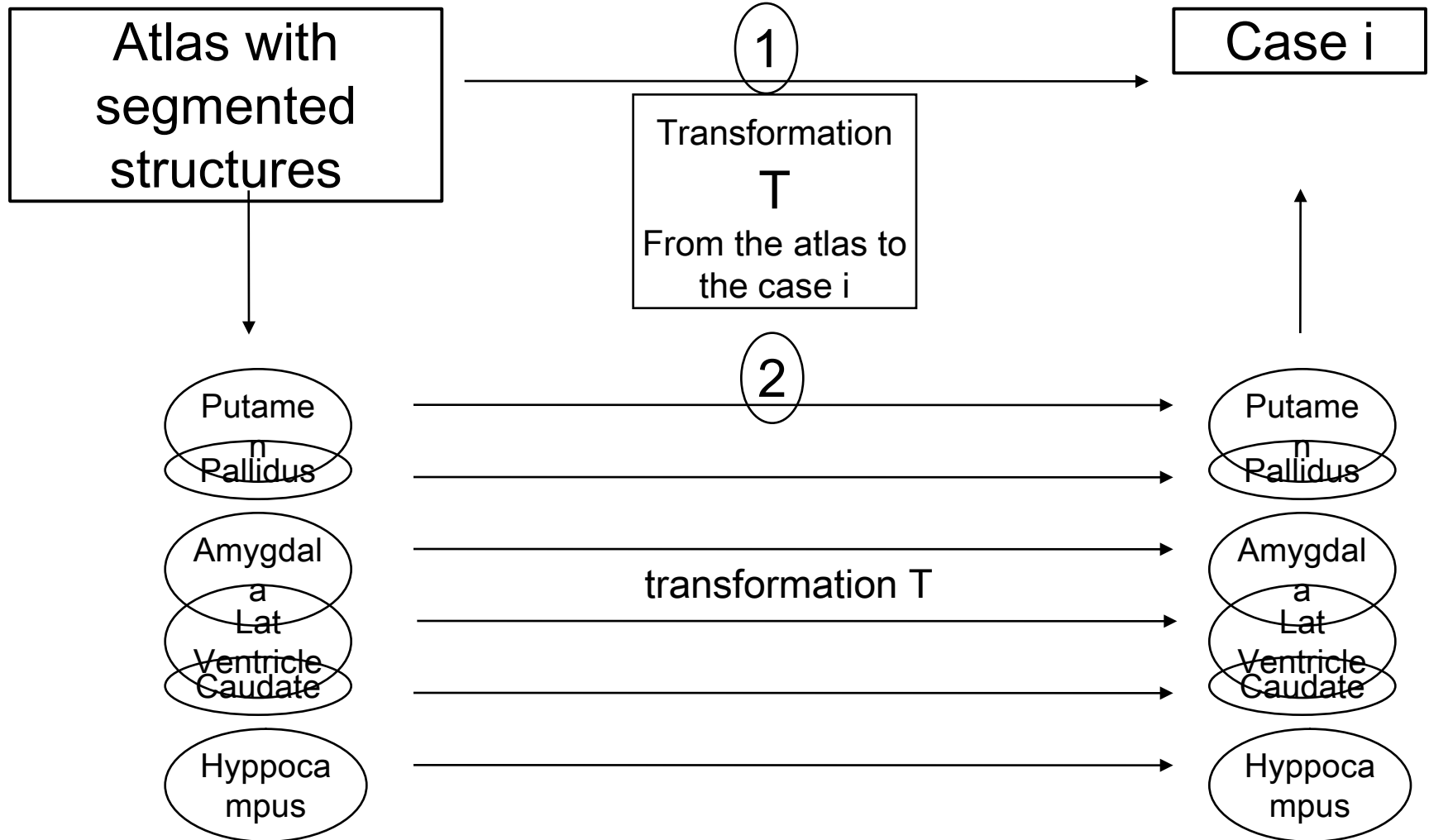
Template image created from several cases

Step 2



Probabilistic maps of the 12 ROIs

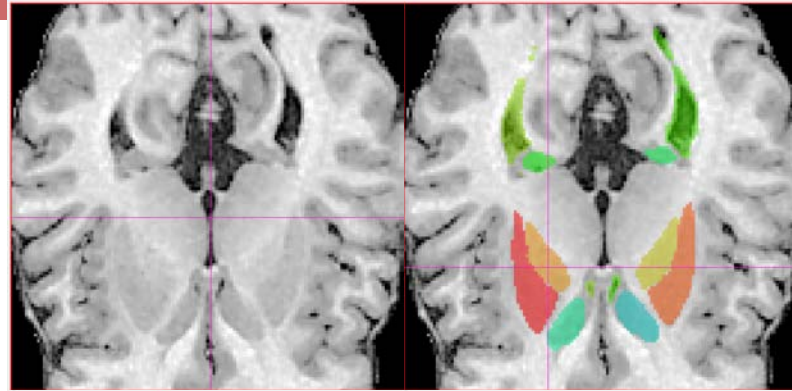
# Pipeline



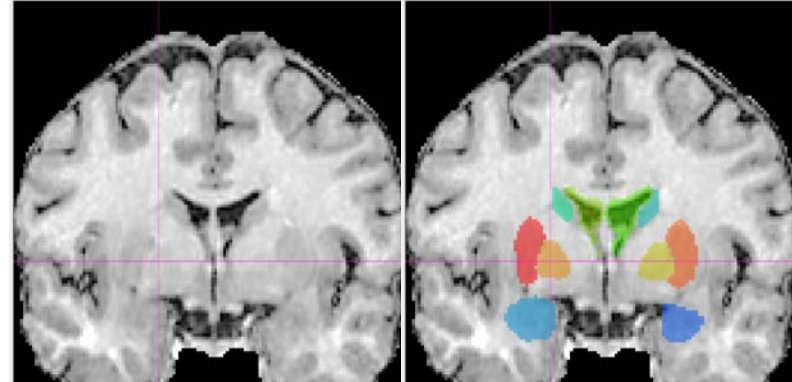
# Segmented ROIs

Segmented case  
Without ROIs      With ROIs

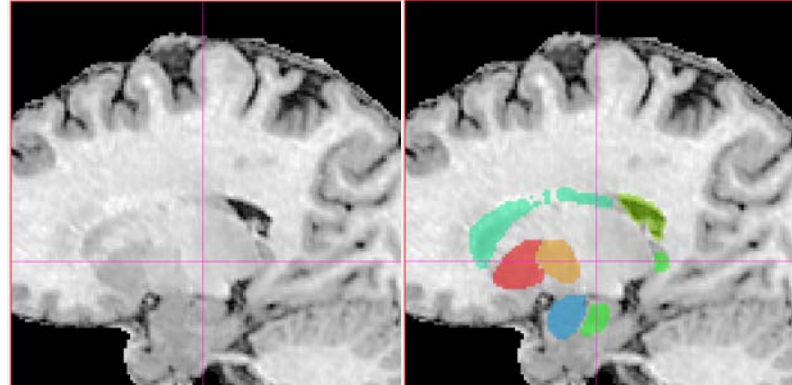
Axial View



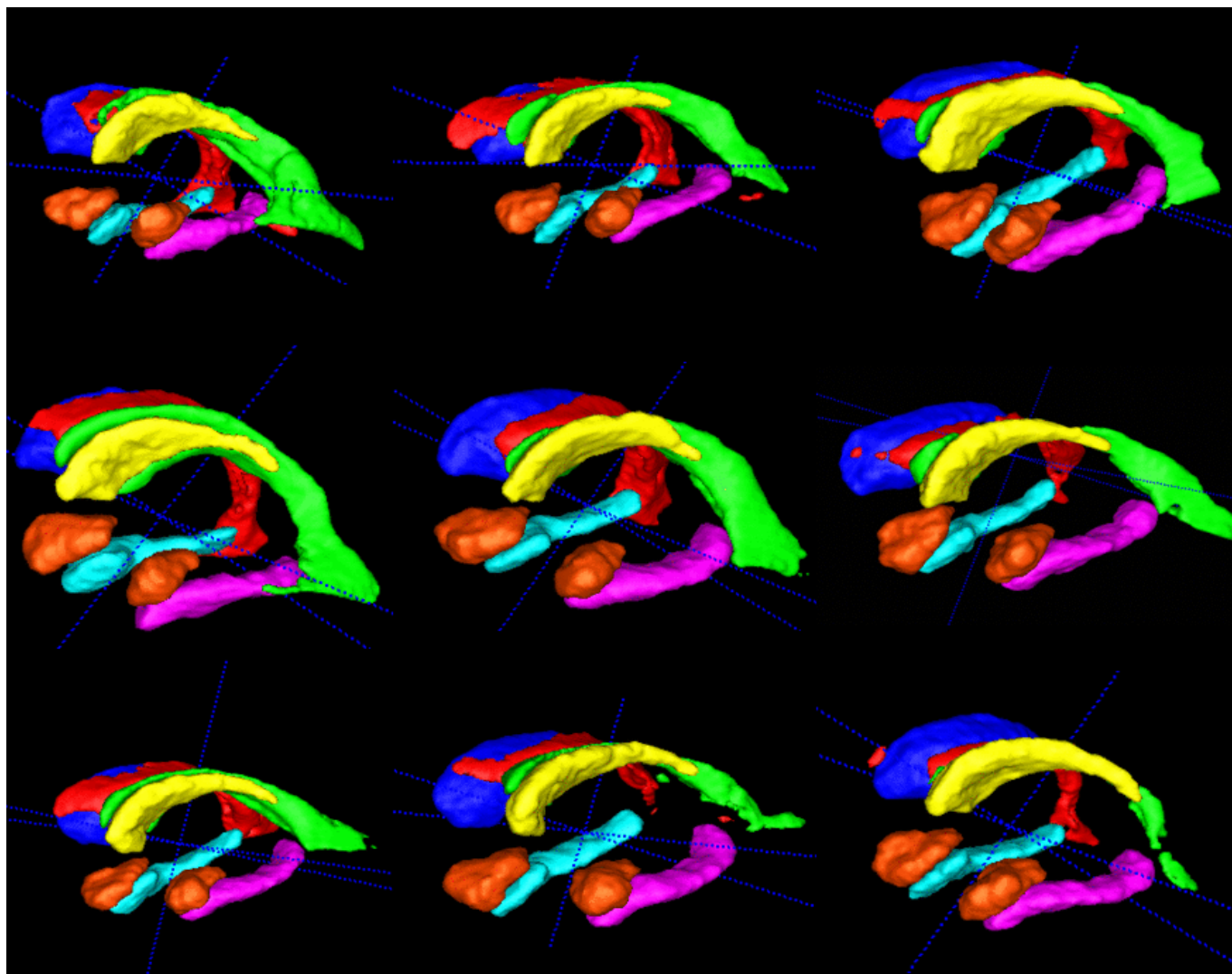
Coronal View



Sagittal View



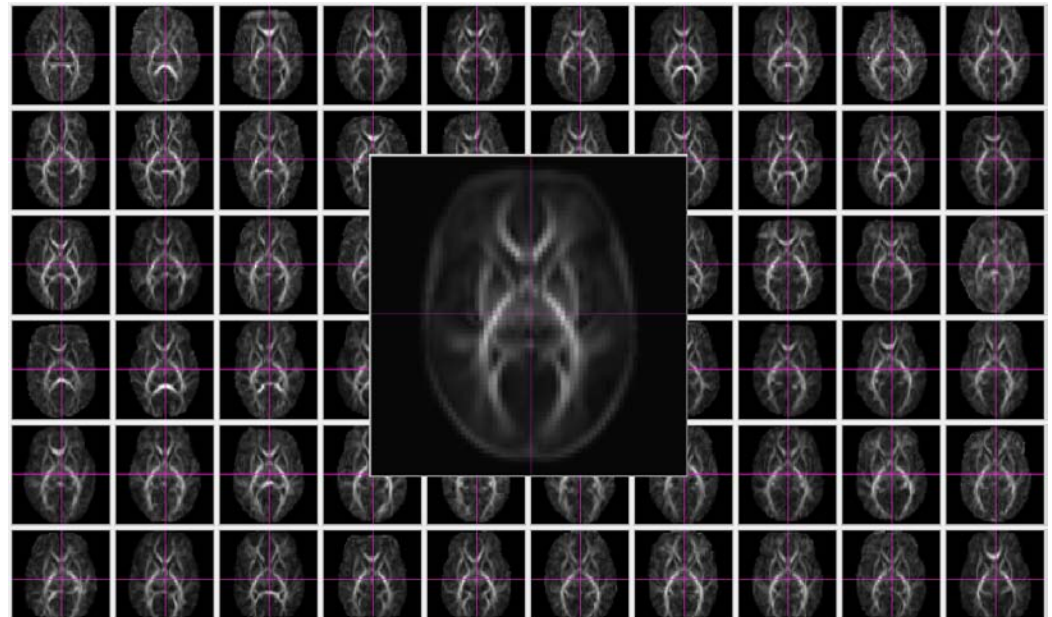
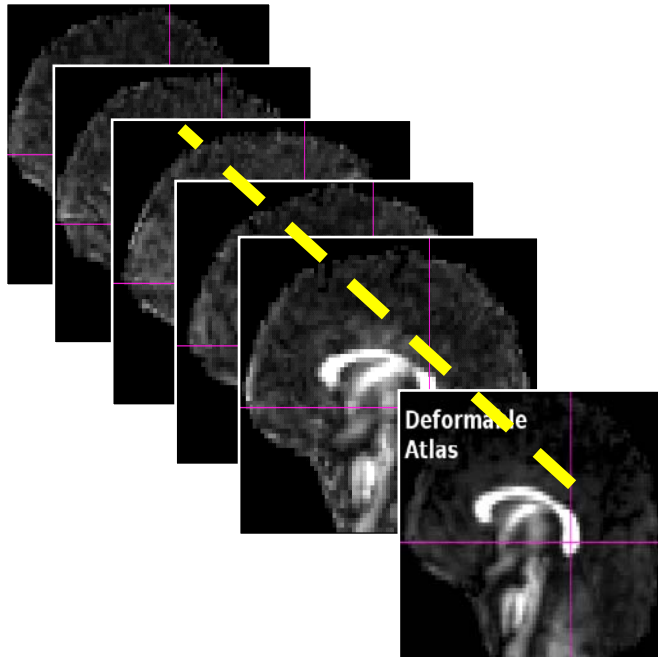
# Automatic segmentation (N=130)



UNC  
Chapel Hill  
pediatric  
autism  
study (J.  
Piven, H.  
Cody, G.  
Gerig et al.)

# DTI: Population-based analysis of fiber tracts

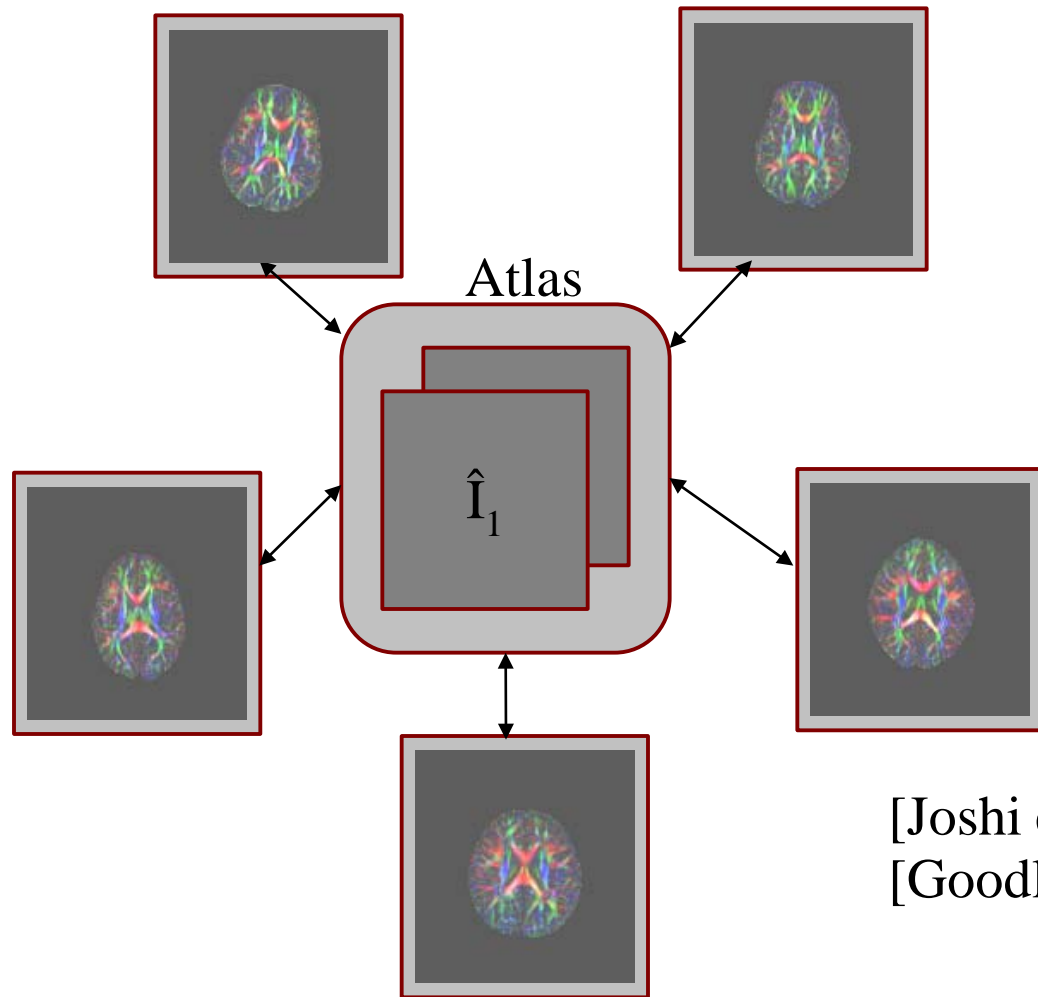
Example: 150 neonate DTI mapped to unbiased atlas



Casey Goodlett, Sarang Joshi, Sylvain Gouttard, Guido Gerig,  
(MICCAI'06, MICCAI'08, NeuroImage 2009)



# Atlas Building for DTI Tensor Fields

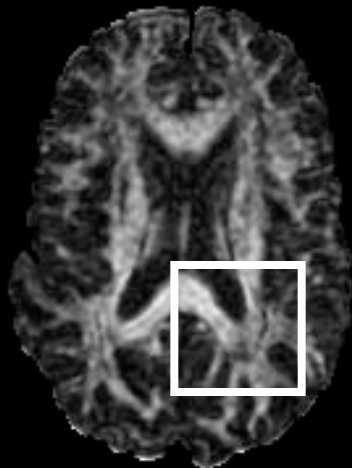


[Joshi et al 2004]

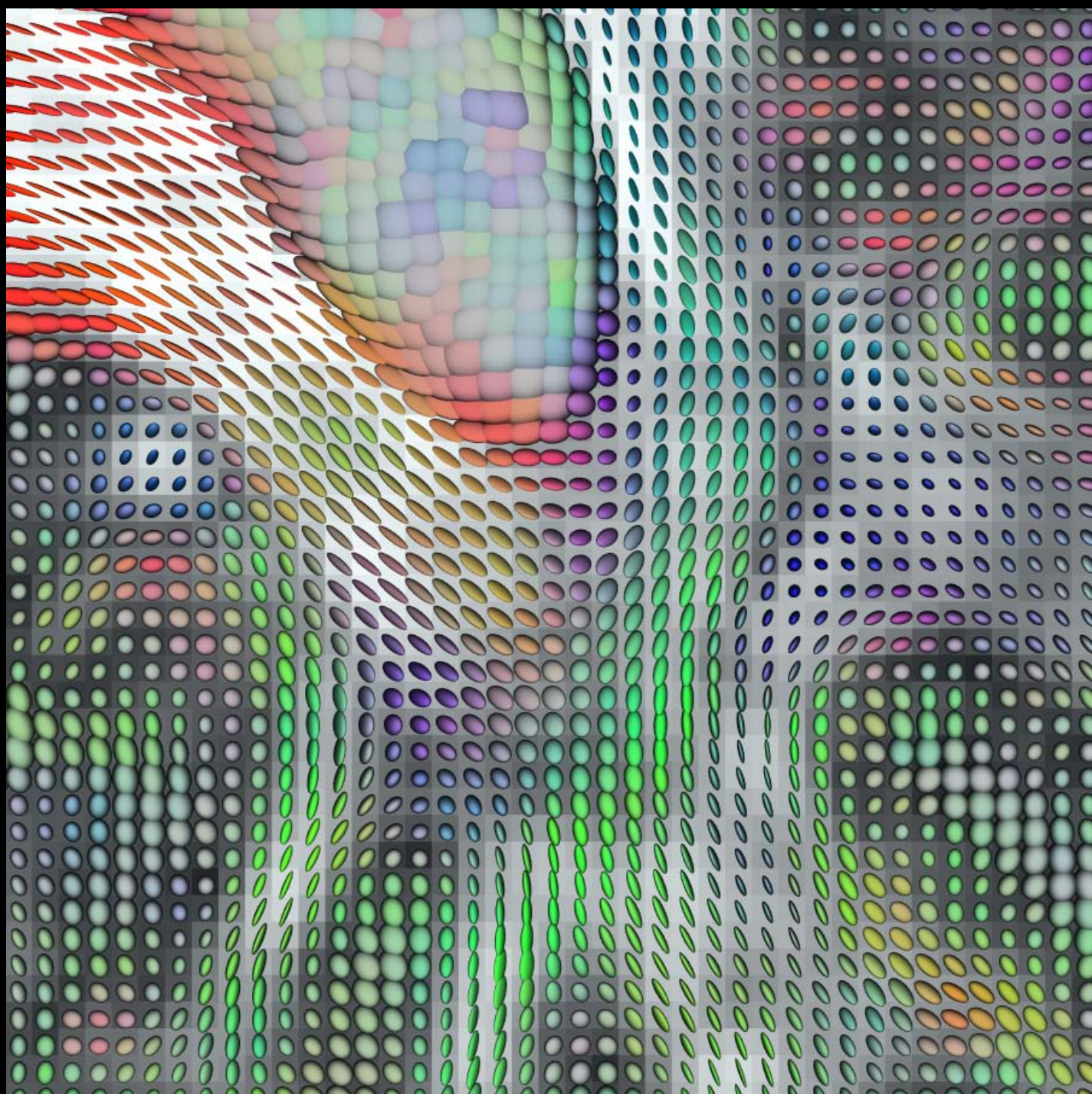
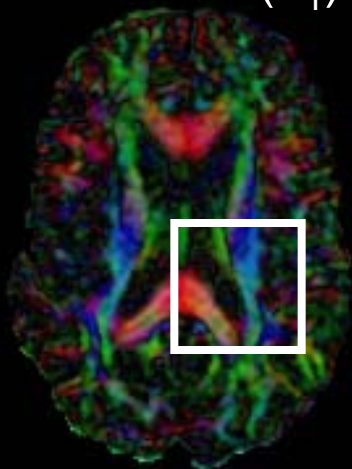
[Goodlett et al 2006, 2009]



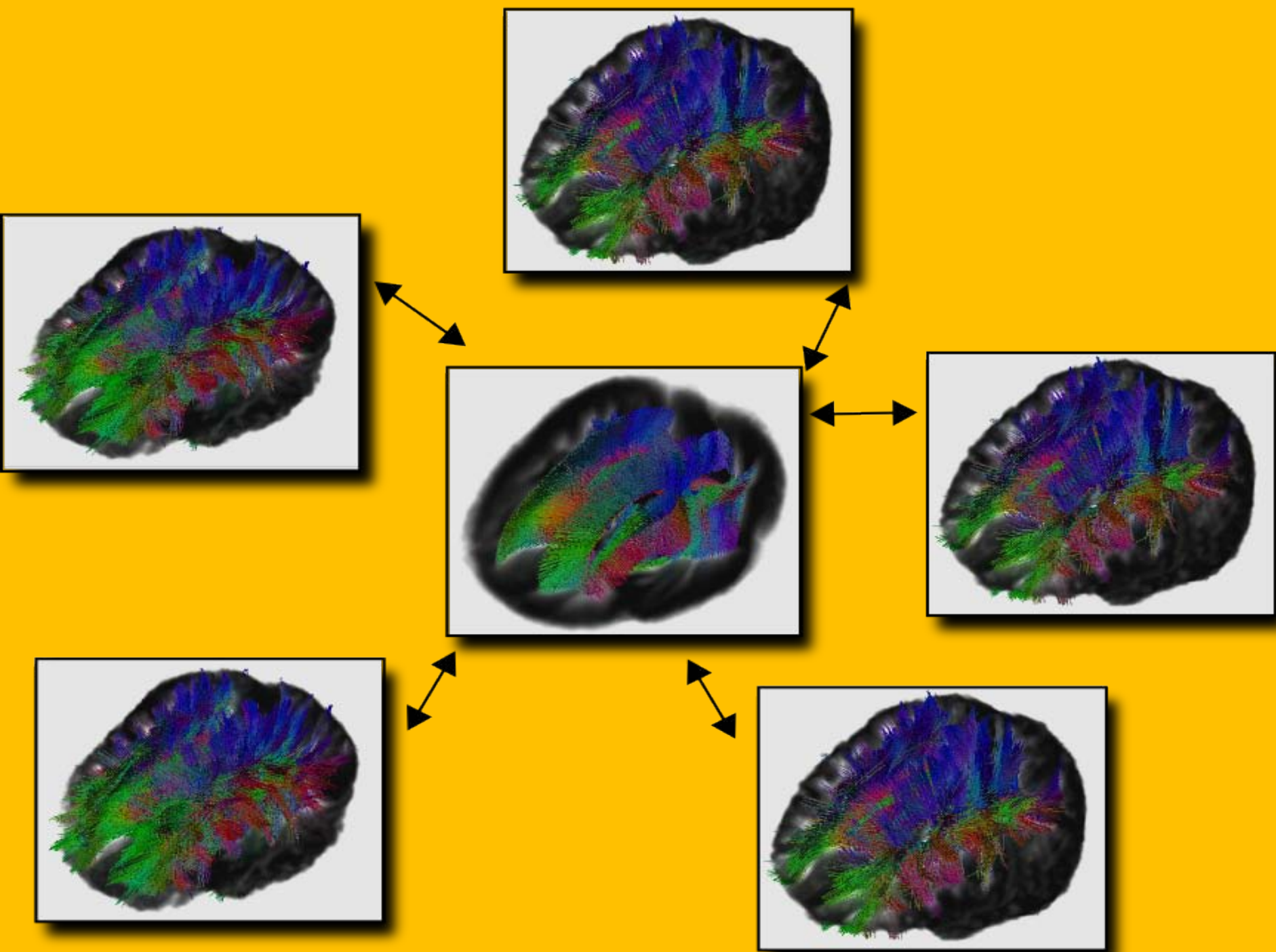
Backdrop: FA



Color: RGB( $\mathbf{e}_1$ )

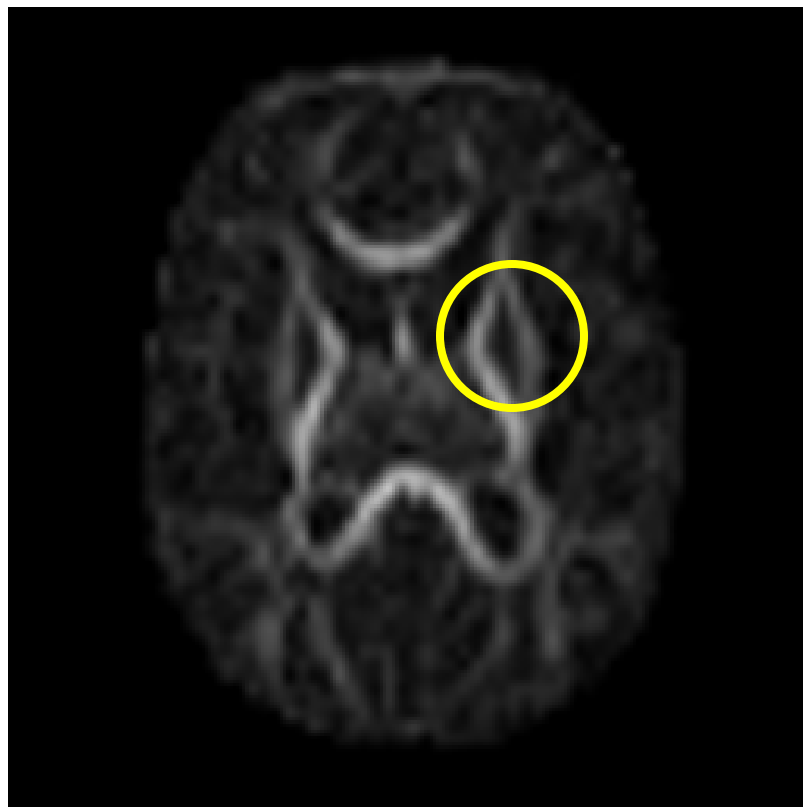




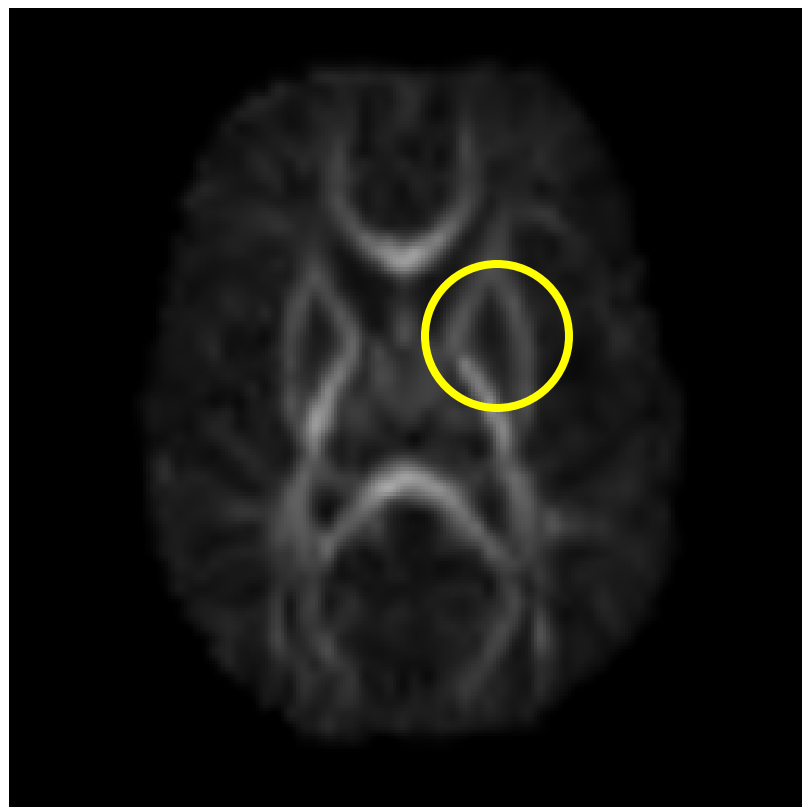


# Co-registration: From linear to nonlinear

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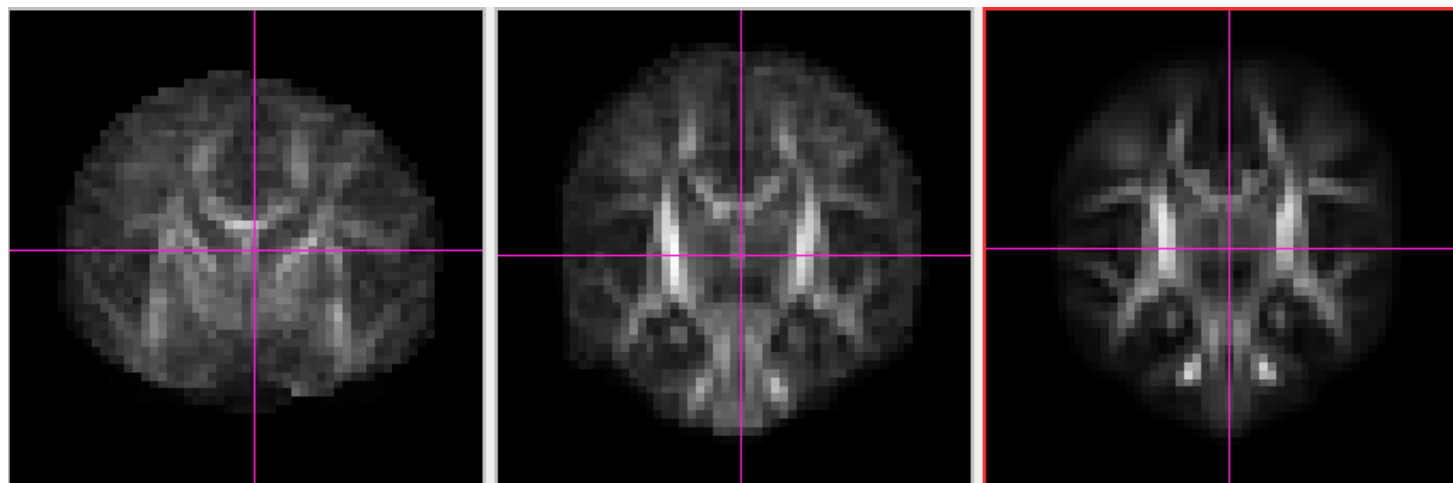
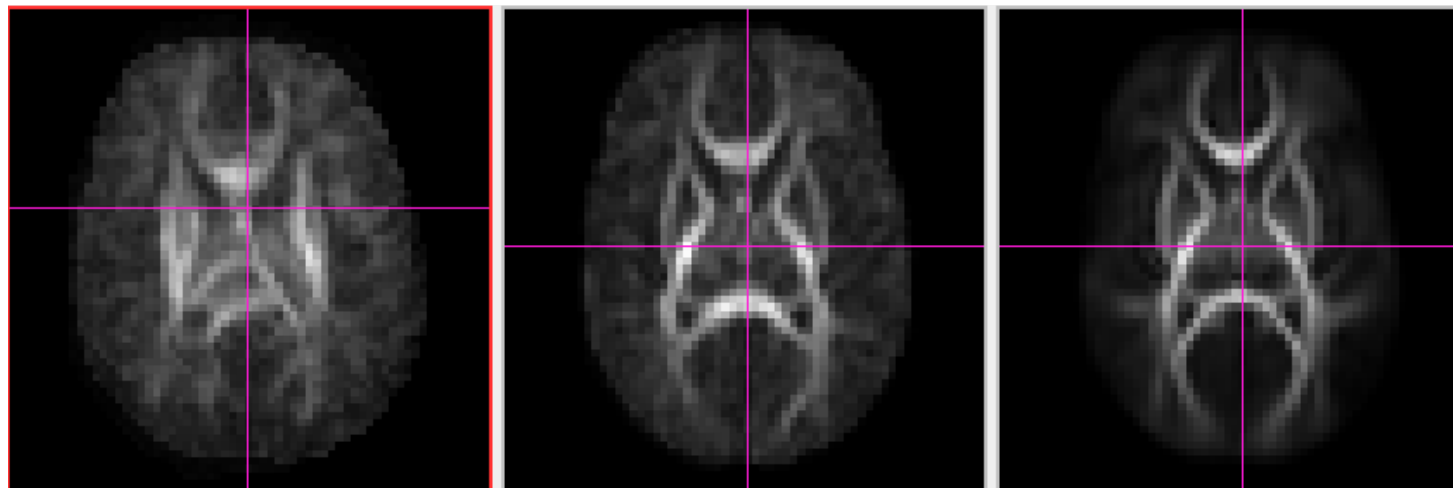


Linear registration (affine)



Nonlinear registration (fluid)

# Atlas Building: FA of average tensor field

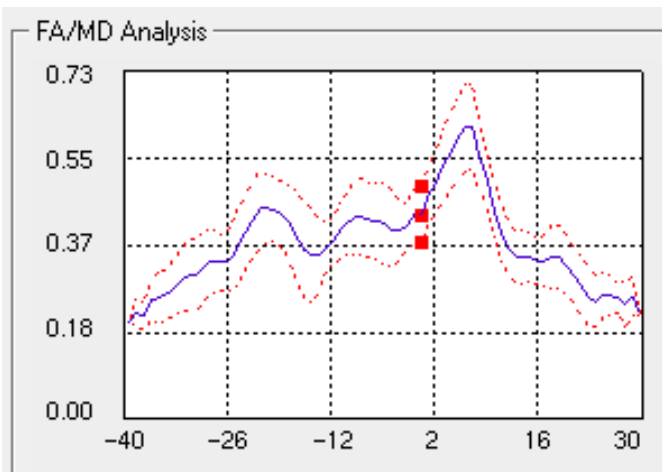
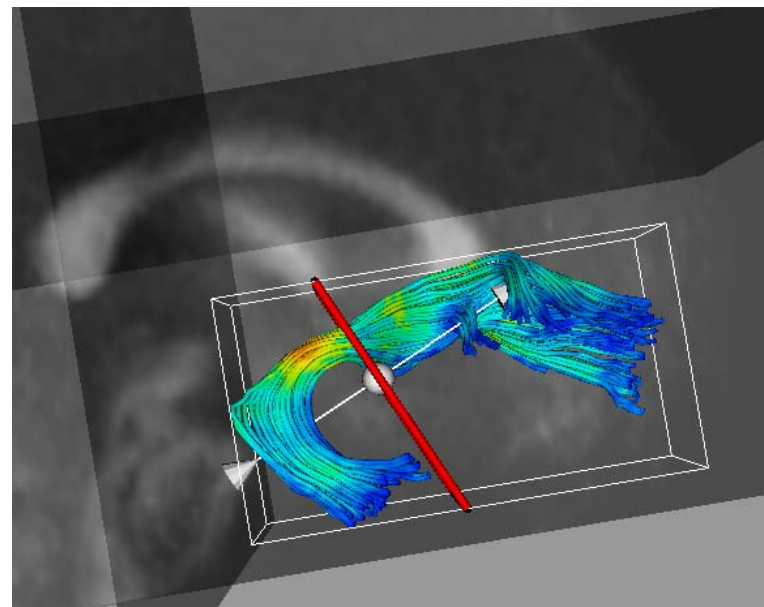
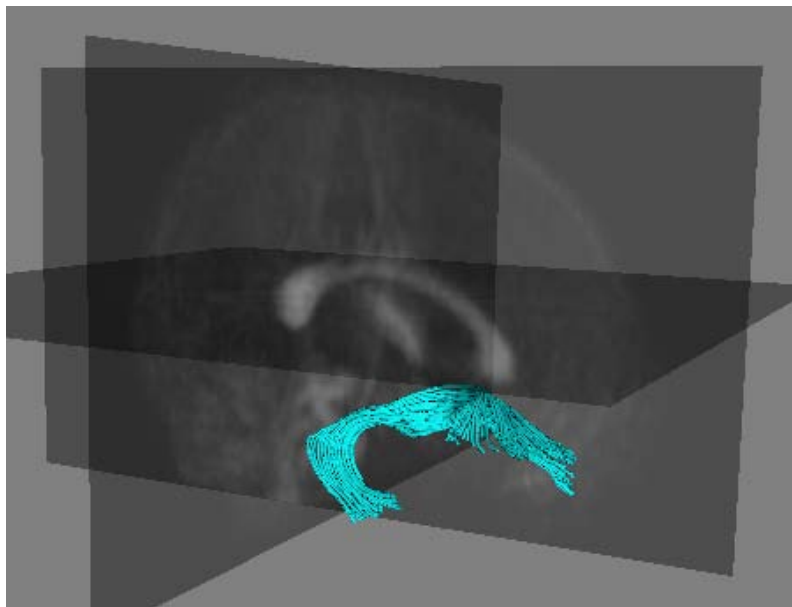


raw

linear

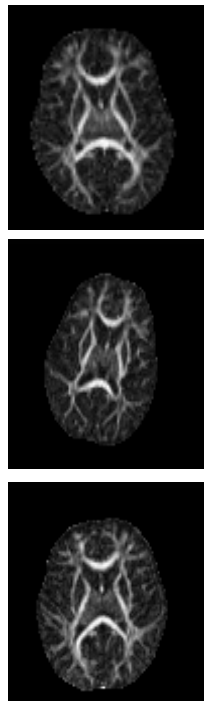
nonlinear

# Quantitative Fibertracking: Example Uncinate Fasciculus

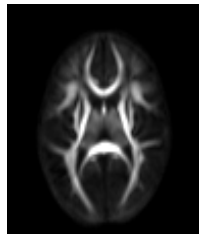


Corouge et al. *Fiber tract-oriented statistics for quantitative diffusion tensor MRI analysis*. Medical Image Analysis 2006.  
FiberViewer software - <http://www.ia.unc.edu/dev/>

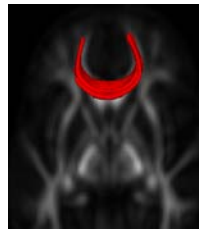
# Concept: Group statistics of fiber tracts



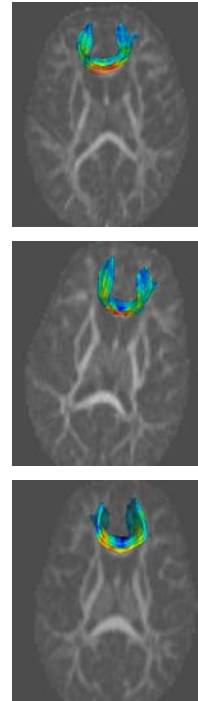
Images



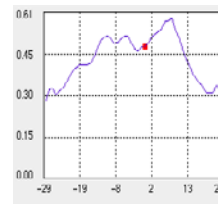
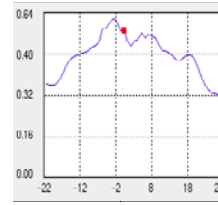
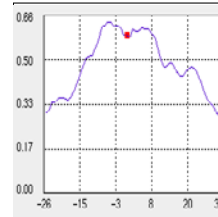
Atlas



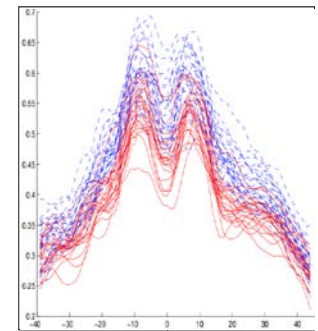
Atlas Tract



Mapped Tracts

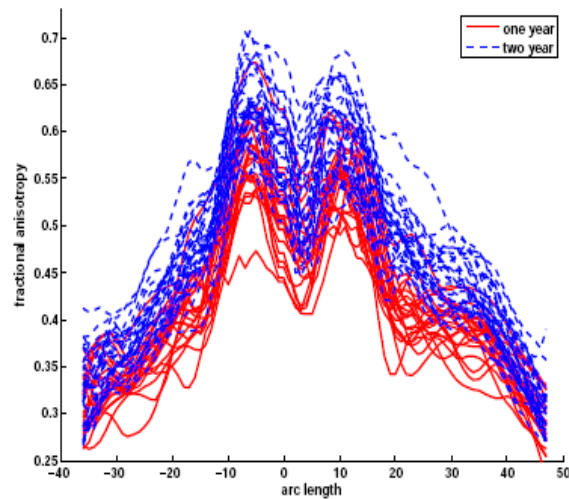
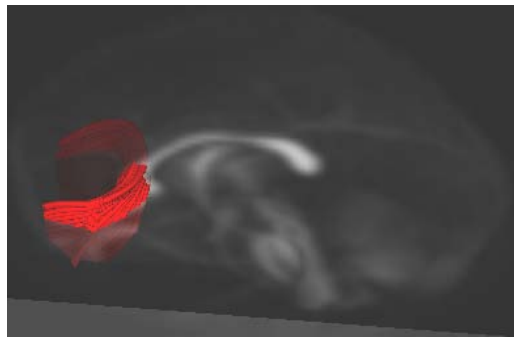
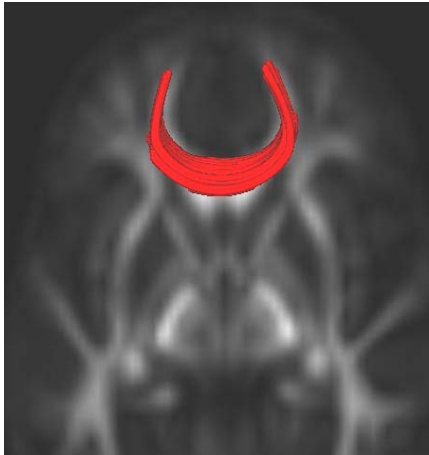


Sampled Functions

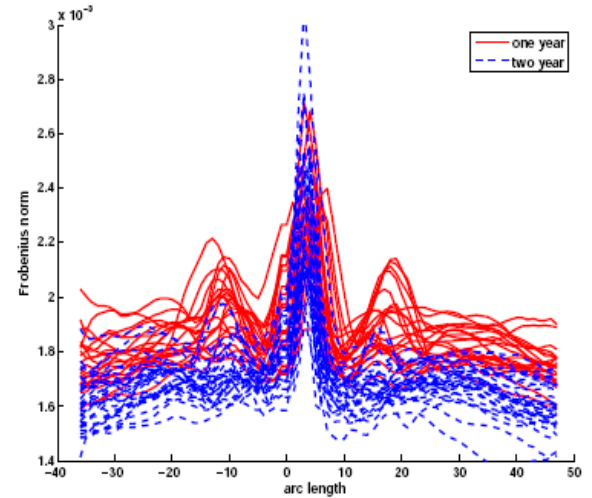


Functional Statistics

# Pediatric Example: Genu Tract 1-2yrs



(b) All FA curves



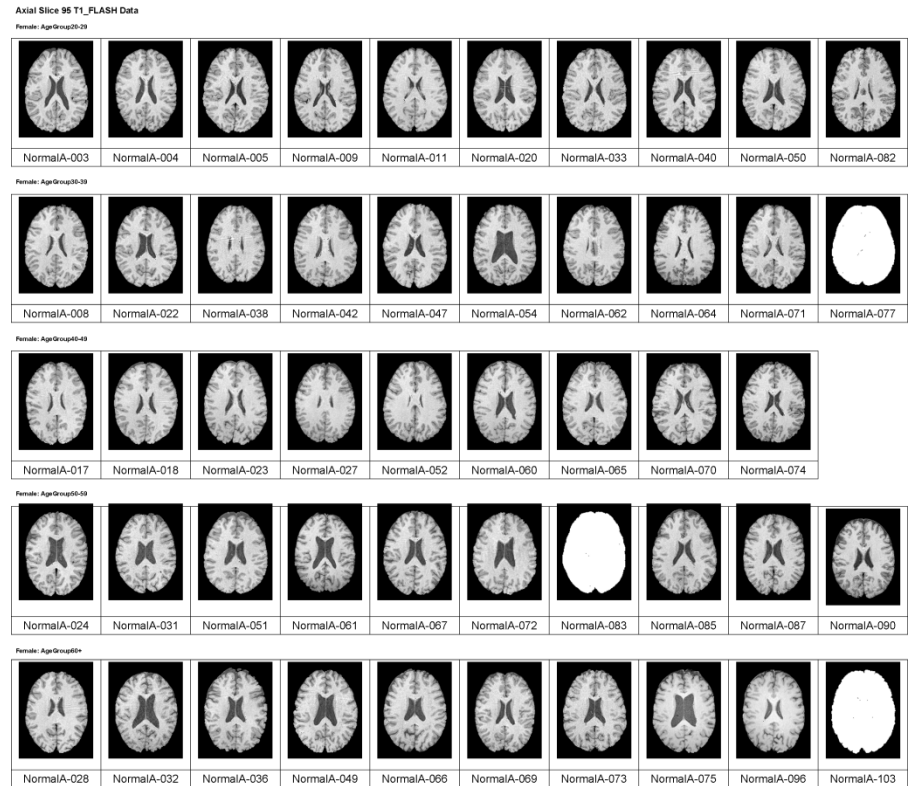
(c) All norm curves

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

# Towards 4D Atlases: Study of Healthy Aging

## Elizabeth Bullitt, UNC

- ◆ MRI Aging Study
- ◆ 100 volunteers (50 male, 50 female). 20 subjects, equally divided by sex, were imaged by decade (20-29, 30-39, 40-49, 50-59, and 60-72).
- ◆ Images (T1 and T2 sequences) 3T MR
- ◆ Automatic EM Segmentation (Marcel Prastawa, Gerig)
- ◆ Atlas formation (Peter Lorenzen, Sarang Joshi, Brad Davis)

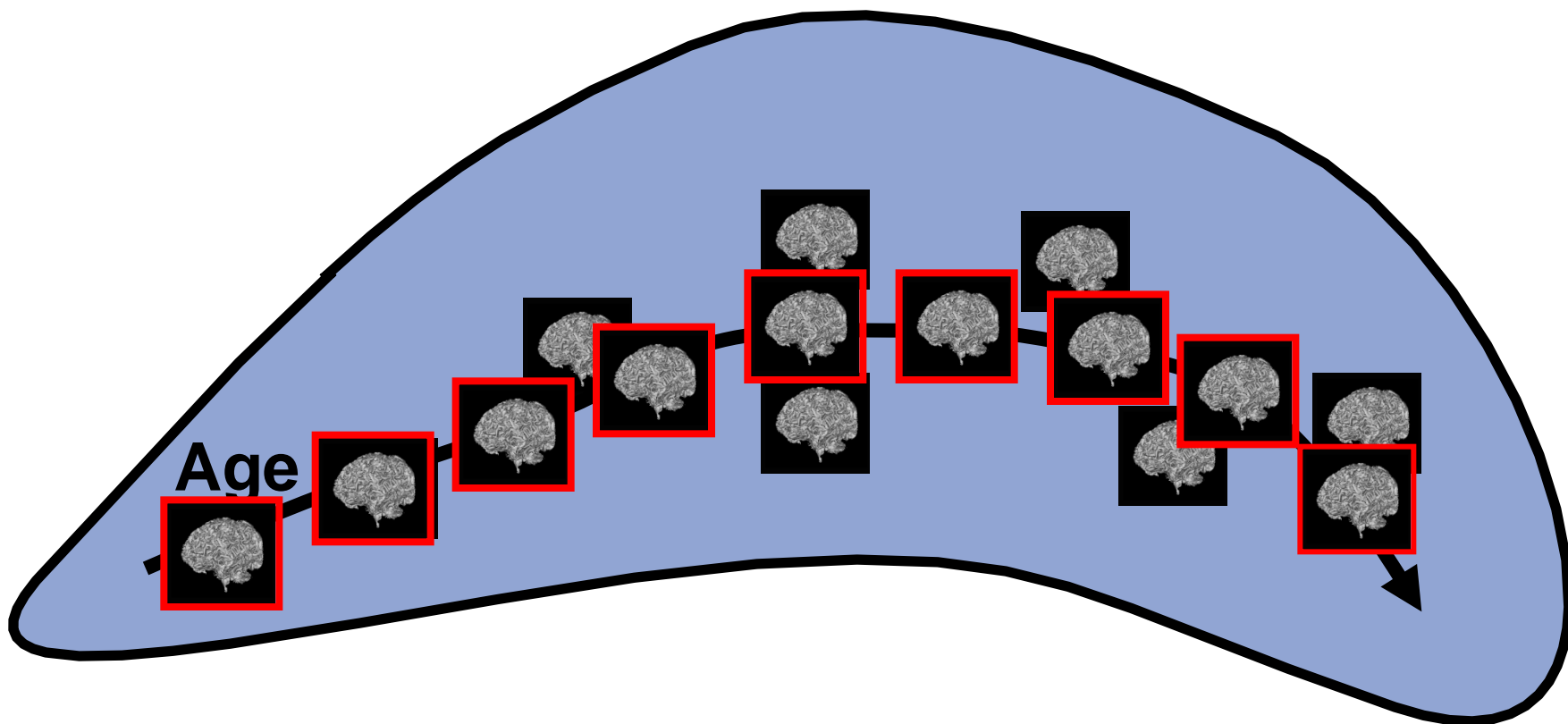


T1 of female subjects, per decade



# Manifold Kernel Regression (B. Davis)

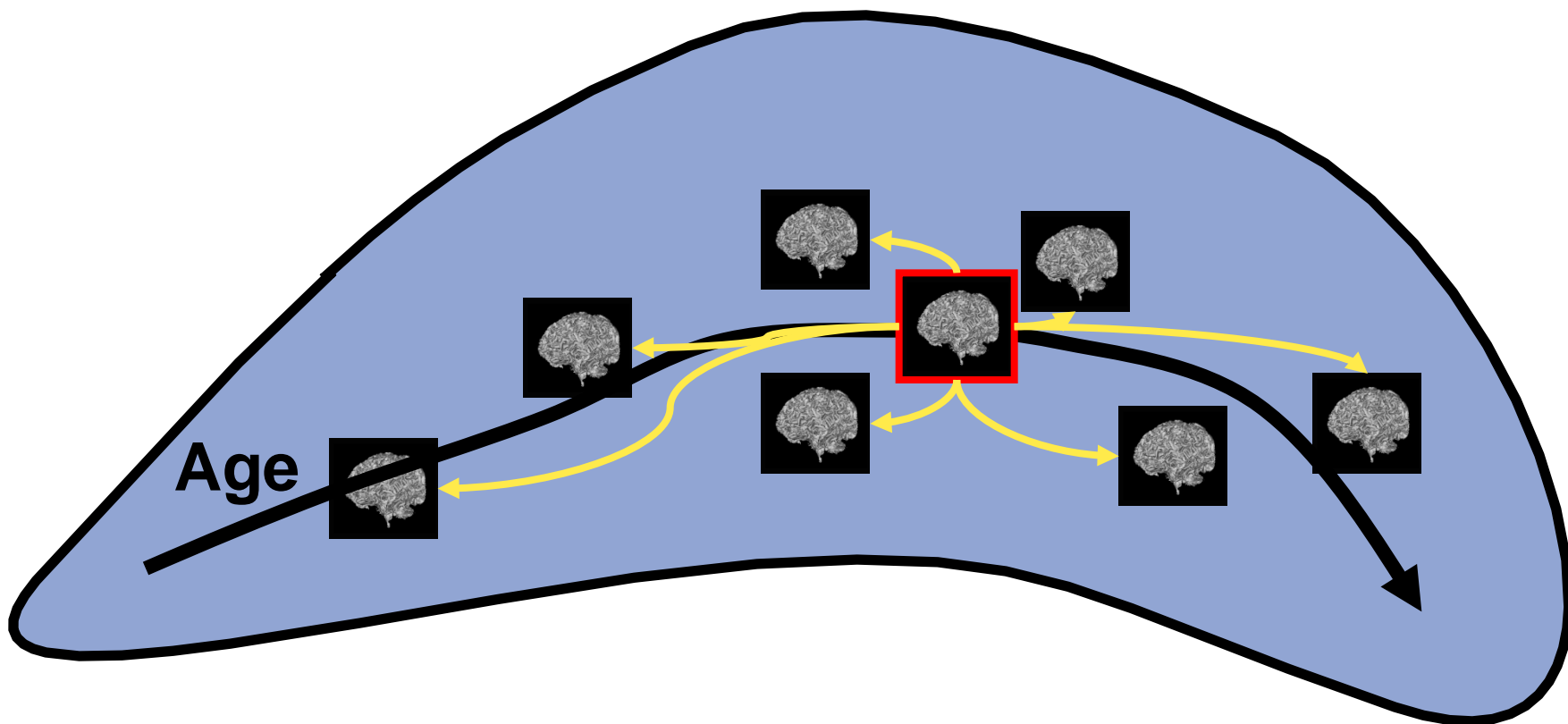
- What are we looking for: A weighted Fréchet mean image as a function of age!
- Weights depend on the age



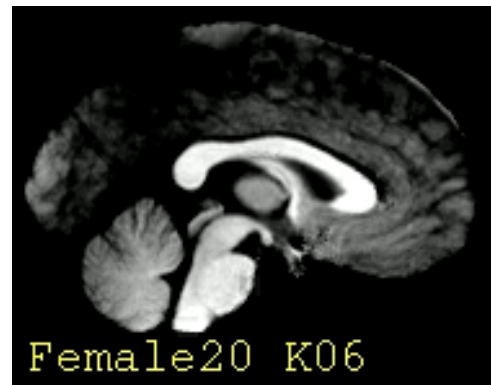
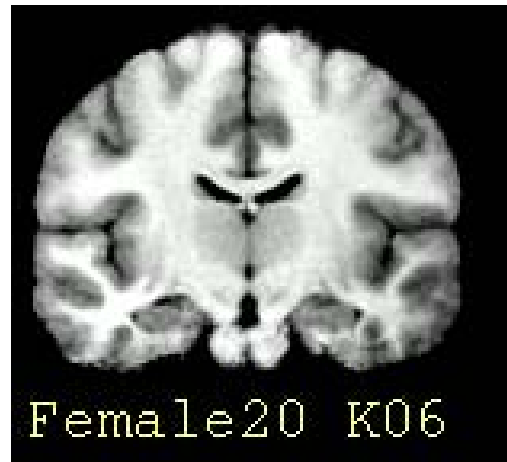
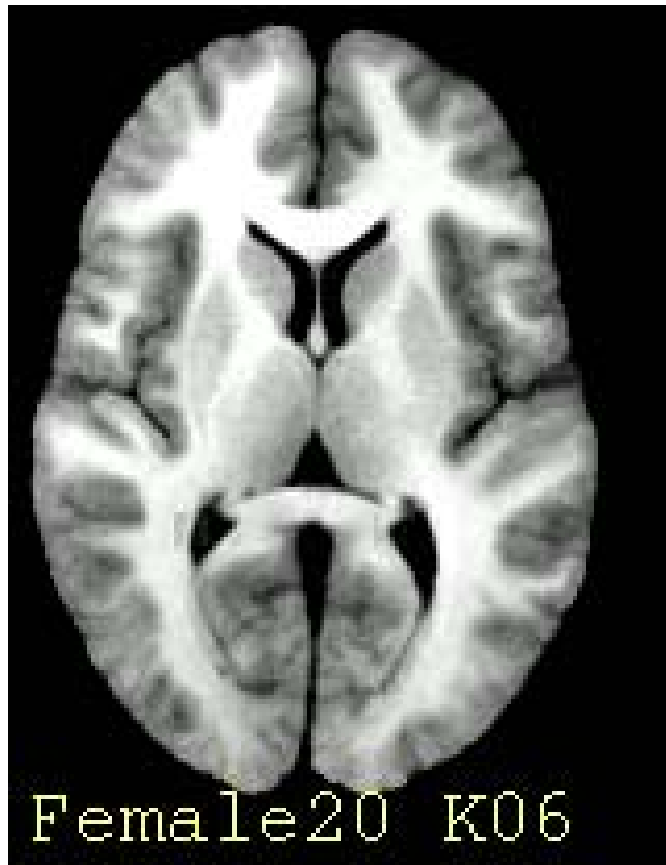


# Manifold Kernel Regression (B. Davis)

- What are we looking for: A weighted Fréchet mean image as a function of age!
- Weights depend on the age



# Aging Brain via Population Shape: Manifold Kernel Regression



- B. Davis, E. Bullitt, (UNC)
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- D. Marr Prize, ICCV'07 best paper award

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# Conclusions

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- Image registration has become one of the most important tools for medical image analysis
- Powerful packages available to the scientific community:
  - RVIEW, ITK, Demons, SPM, AIR, FSL, FreeSurfer, SLICER-3, etc.
- Important issue: Choice of appropriate methodology (linear versus nonlinear, type of nonlinear method, image match metric, cascading of transformations)
- Community needs: Platform for validation and cross-method comparison -> Users can choose most appropriate, best techniques

