HST.583 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis
Fall 2008

Spatial Normalization of Images

HST.583 Fall 2008
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Image Registration

- Image alignment, matching
- Establishing dense spatial correspondence
- Multi-modal (e.g. MRI to Ultrasound, structural MRI to fMRI)
- Multi-subject

Roadmap

- Image Registration: Theory
- Three types:
  - Function to anatomy
  - Inter-subject
  - Subject to atlas
- Conclusion

Formulation

$$I_1(\vec{x}) \xleftrightarrow{Match} I_2(\Phi_{21}(\vec{x})), \quad \vec{x} \in \Re^3, \quad \Phi_{21} : \Re^3 \rightarrow \Re^3$$

$$I_1(\Phi_{12}(\vec{x})) \xleftrightarrow{Match} I_2(\vec{x}), \quad \vec{x} \in \Re^3, \quad \Phi_{12} : \Re^3 \rightarrow \Re^3$$

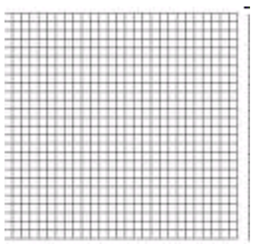
- Inverse Consistency:

$$\Phi_{12}{}^{-1} = \Phi_{21}$$

Interpolation

- Assume we know Φ_{12}
- Note: images live on a discrete grid.

$$I_1(\vec{x}), \quad \vec{x} \in \Omega_d$$



- In general, mapped points don't lie on the grid.

$$I_1(\Phi_{12}(\vec{x})), \quad \vec{y} = \Phi_{12}(\vec{x}) \notin \Omega_d$$

- Need to "interpolate."
  - Nearest Neighbor, (Bi-, Tri-) Linear, Polynomial, Spline-based, …

Re-sampling

- Sampling grid:
  - One of the two images (fixed image)
  - Another grid, e.g. atlas frame.

$$\vec{y} = \Phi_{12}(\vec{x})$$

$$\vec{z} = \Phi_{2A}(\vec{y}) = \Phi_{2A}(\Phi_{12}(\vec{x}))$$

for any one-to-one mapping Φ_{2A}

- The sampling grid is somewhat arbitrary.
- Be very careful when reporting results on the geometry (e.g. area, volume, shape).

Pairwise Image Registration

$$\arg\max_{\Phi}\Big(\mathrm{Sim}\big(I_1(\vec{x});I_2(\Phi(\vec{x}))\big)-\mathrm{Reg}(\Phi)\Big)$$

Similarity between images

Regularization of warp

Typical Registration Algorithm

- Warp space: e.g. rotate around image center
- Alignment measure: e.g. mean absolute difference
- Optimization: e.g. exhaustive search

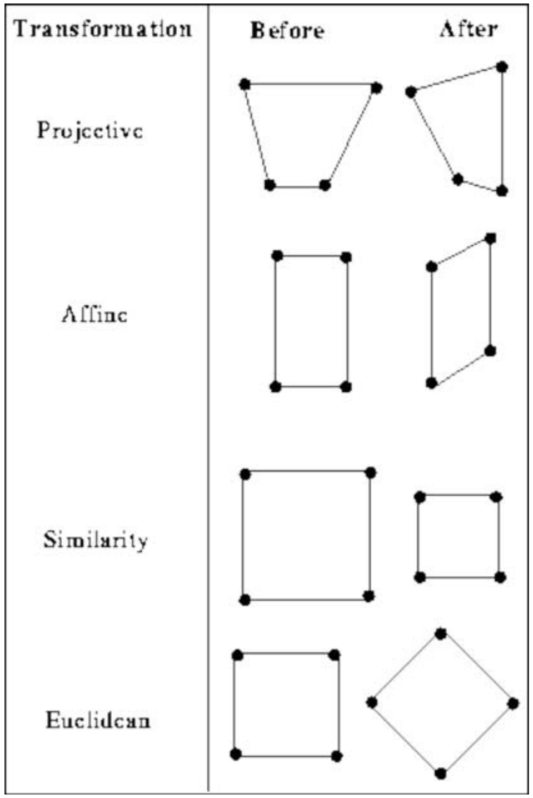
Fixed Image

Floating Image

Absolute Difference

Geometric Warps

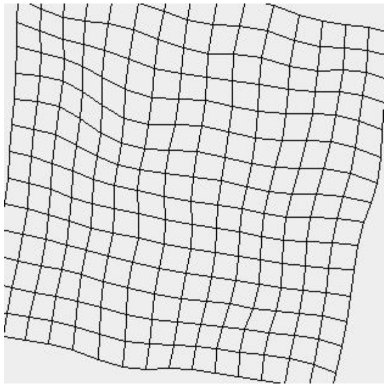
- Rigid-body (Euclidean):
  - 6 parameters in 3D (rotation and translation).
  - Preserve angle, length and area.
  - Models orientation variation.
- Affine:
  - 12 parameters in 3D (rotation, translation, scaling, shearing)
  - Preserve co-linearity and relative size.



http://homepages.inf.ed.ac.uk/rbf/HIPR2/figs/affhei.gif

Geometric Warps (2)

- Piecewise Affine:
  - Chop grid into blocks – each block is warped using an affine transformation model.
  - For invertibility, we can use boundary conditions.
- Parametric Non-linear Models:
  - Polynomial, Radial-basis functions



- Non-parametric Models:
  - Dense deformations, Diffeomorphisms

Geometric Warps (3)

- Understand what we are modeling:
  - Inter-image geometric variation
- Sources of variation:
  - Scanner orientation
  - Image resolution
  - Physics of image acquisition, e.g. EPI distortion
  - Physical deformation, e.g. post-op MRI, tumor
  - *Inter-subject variability of anatomy*

Geometric Warps (4)

- Common modeling strategies:
  - Warp should be invertible
  - Warp should be spatially smooth
  - Use physical deformation models

  } Regularization
- Inter-subject variability:
  - No ground truth!
  - Evaluate quality of warp by measuring landmark alignment

Alignment Measure

- Objective measure: quality of alignment.
- Two strategies:
  - Landmark-based
  - Landmark-free (image-based)
    - E.g. sum-of-squared differences, mutual information

Alignment Measure (2)

- Design depends on the context
- If we have robust landmarks, then landmark-based
- If we care about alignment everywhere, then image-based
- If single modality: e.g. sum-of-squared differences
- If multi-modal: e.g. mutual information (entropy) of pixel intensity values

Optimization

- Searching for the best warp.
- Usually iterative, numerical optimization.
- More parameters leads to slower algorithm.
- Gradient-based approaches yield faster methods.
- Smoother alignment measures are better.
- Multi-resolution pyramid to speed up.

Registration Instances

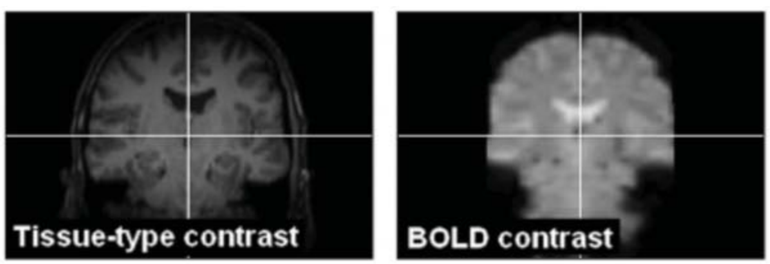
- Functional-to-anatomical
- Inter-Subject
- Subject-to-Atlas

Functional-to-Anatomical

- Before: PET to CT/MRI
- Today: fMRI to anatomy (T1, T2*, PD)
- Mutli-modal, intra-subject registration
- Fact: There is one-to-one correspondence
- Sources of geometric variation:
  - Scanner orientation
  - Motion
  - Imaging physics, e.g. EPI distortion
  - Resolution

Functional-to-Anatomical (2)

- Similarity Measure:
  - Extrinsic: based on fiducials, e.g. stereotaxic frame screwed on the skull.
  - Intrinsic:
    - Landmark-based: e.g., surfaces, points, …
    - Image-based: e.g. mutual information, local correlation-ratio, joint entropy



Gholipour et al. "Brain Functional Localization: A Survey of Image Registration Techniques", IEEE TMI, April 2007

Functional-to-Anatomical (3)

- Warp space:
  - EPI Distortion -> Non-linear geometric variation due to interaction between motion and field inhomogeneity. Particularly severe along the phase-encoding direction and around air-pockets e.g. sinuses.

Two Strategies:

- Explicitly model the physics of EPI distortion
- Use generic multi-modal non-linear registration

Inter-subject Registration

- Population Analysis, Multi-subject studies
- Objectives:
  - Pool data from subjects
  - Compare individual results
  - Report results in a standard coordinate system
- Main source of geometric variation:
  - Anatomical Variability

Inter-subject Registration (2)

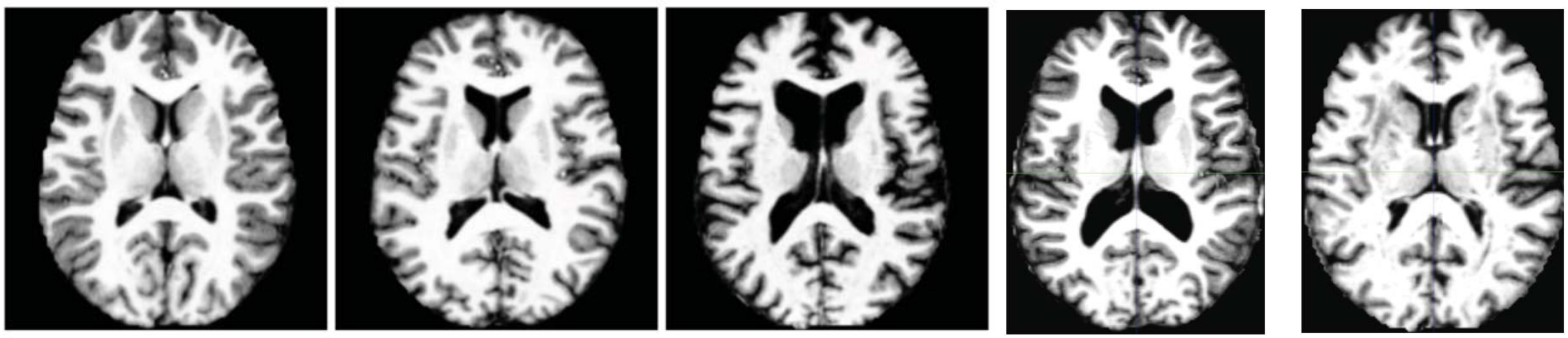
- Different levels of anatomy:
  - Macro-anatomy: structural MRI
  - Micro-anatomy: Histology
  - Functional anatomy: fMRI, EEG, MEG
  - Connectivity: Diffusion MRI
- What is spatial correspondence across subjects?
- Historically in MRI it is based on macro-anatomy encoded in hi-res structural MRI.

Inter-subject Registration (3)

- Alignment measure:
  - Based on landmarks (Talairach and Tournox)
  - Based on image features (e.g. intensities, attribute vectors)
- Intensity-based measures are usually naive:
  - E.g. sum of squared differences between image intensity values.
- We know they are optimized at good alignment – but the solution is non-unique.
- Regularization is typically achieved via warps!

Inter-subject Registration (4)

- The anatomy is enormously variable



24 yr, healthy female | 52 yr, healthy female | 76 yr, male w/ probable AD | 25 yr, healthy male | 74 yr, healthy female

- Dense correspondence is hard!
- We don’t even know if it’s one-to-one: Probably not!

Data from: http://www.oasis-brains.org

Inter-subject Registration (5)

- Warp models:
  - Piece-wise affine (Tailarach [25], ANIMAL [198])
  - Polynomial warps (Woods et al. [193])
  - Harmonic basis functions (SPM [196])
  - Dense/Non-parametric (Demons [197], LDDMM [200], HAMMER [207])
  - Spline-based (RPM [208], Rueckert et al.**)
  - Cortical surface based (FreeSurfer***)

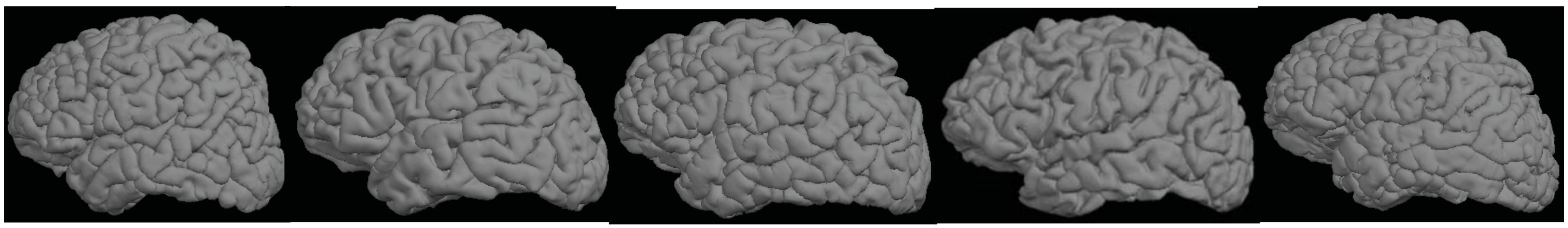
•Reference numbers are from Gholipour et al. “Brain Functional Localization: A Survey of Image Registration Techniques,” IEEE TMI 2007

** Rueckert et al. “Nonrigid registration using free-form deformations: Application to breast MR images,” IEEE TMI 2003

***http://surfer.nmr.mgh.harvard.edu/

Inter-subject Registration (6)

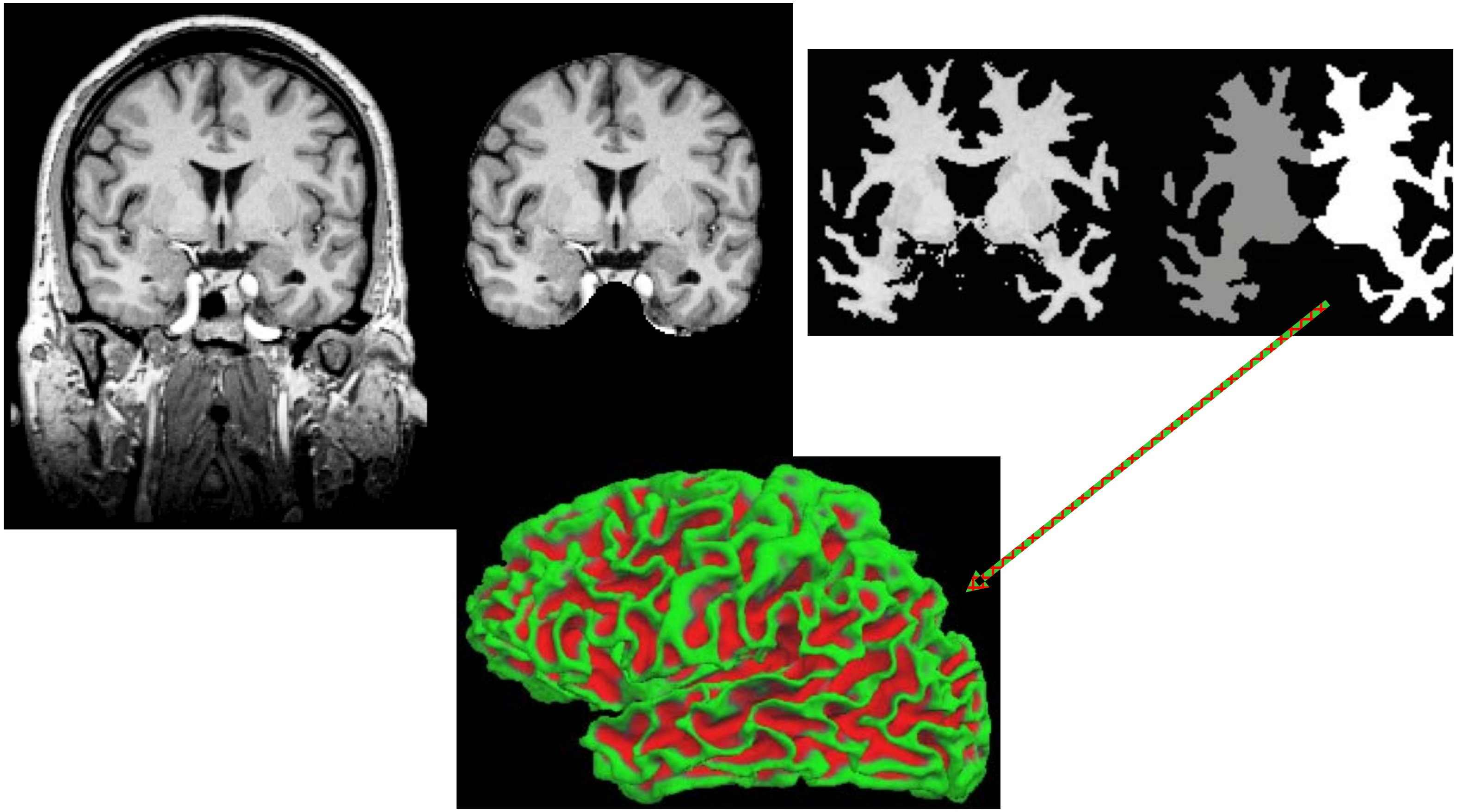
- Surface based methods



Cortical Surfaces (Courtesy of Bruce Fischl. Used with permission.)

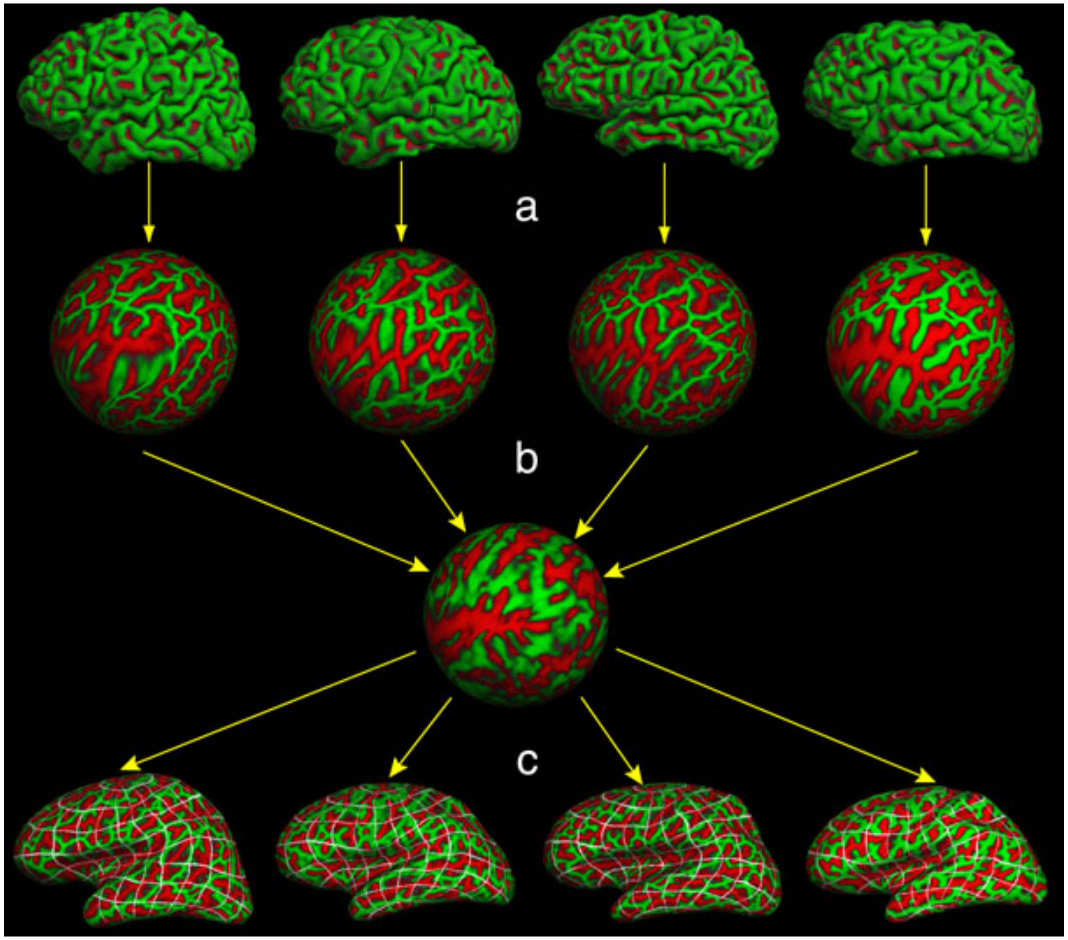
- Establish a 2-D coordinate system on cortical surface
  - One-to-one mapping between cortical hemisphere and a unit sphere.
  - The mapping tries to preserve distances.

Inter-subject Registration (7)



Courtesy of Bruce Fischl. Used with permission.

Inter-subject Registration (8)



Courtesy of Bruce Fischl. Used with permission.

Inter-subject Registration (9)

- No ground truth: so how to validate?
- To asses the optimizer:
  - Compute average across population and quantify sharpness
  - Compare the value of an objective alignment measure, e.g., mutual information
- To asses the algorithm:
  - Measure overlap/alignment of ROI's (e.g. sulci regions, tissue maps, etc.)

Subject-to-Atlas Registration

- A universal atlas-coordinate frame represented by a template image.
- Each subject is mapped to atlas space via pairwise registration with the template.
- Objectives:
  - Common coordinates to pool data
  - Perform atlas-based segmentation

Subject-to-Atlas Registration (2)

- Templates: Average images that summarize a population

Pair of brain images removed due to copyright restrictions.
"MNI 152 averate brain section from the SPM distribution,
next to the equivalent section of the Talairach atlas."

Average of several hundred brains used in SPM

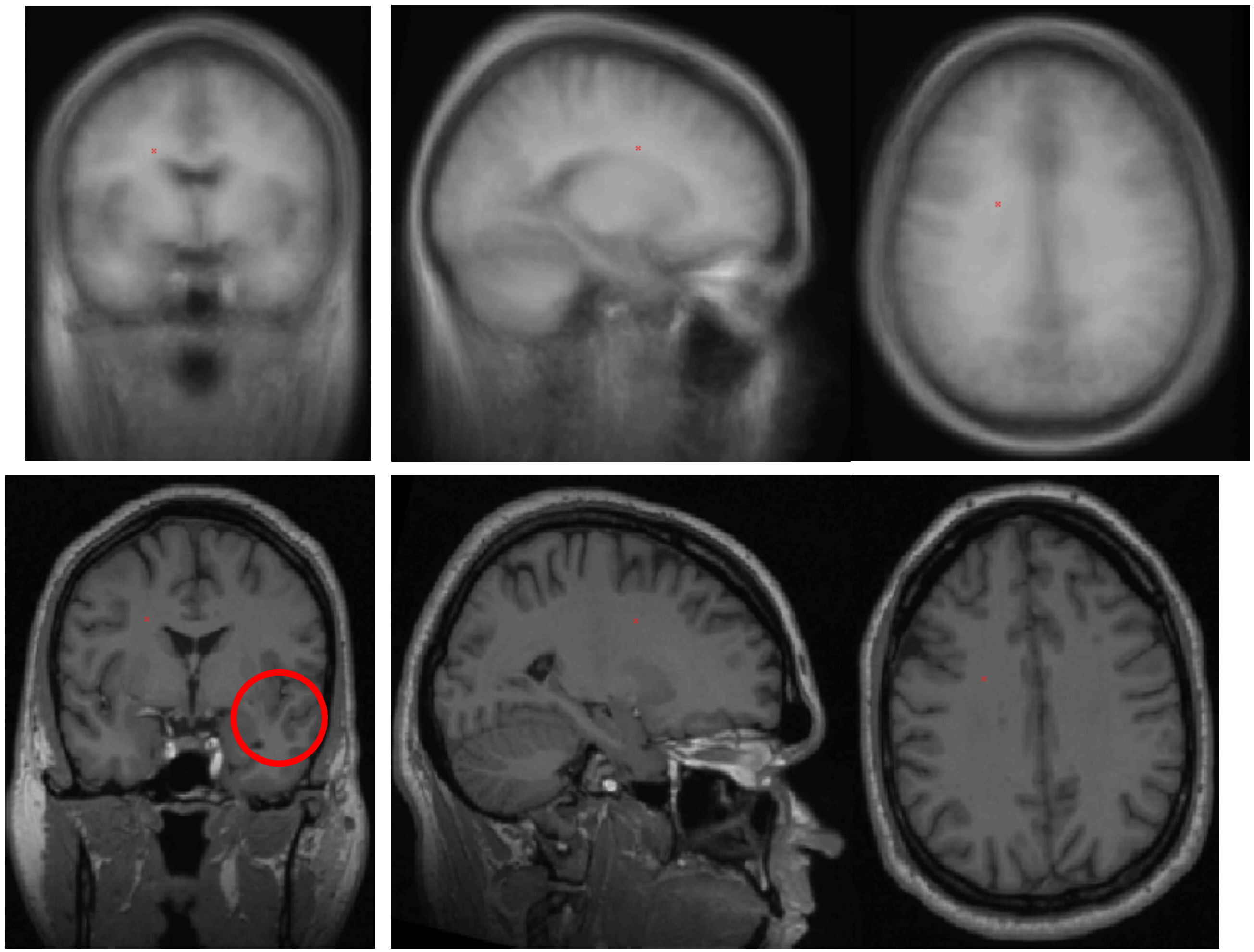
http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach

- Typically templates are "blurry" – this limits alignment accuracy and localization quality

Subject-to-Atlas Registration (3)

Average of 40

Single



Courtesy of Bruce Fischl. Used with permission.

Slide from Bruce Fischl

Subject-to-Atlas Registration (4)

- Sharp template is good, because:
  - It's an indication of how well we've modeled anatomical variability
  - Improves the alignment of the new subject
- Thus: template (atlas) sharpness + inter-subject alignment quality -> confidence in coordinates

Conclusion

- Two important points:
  - Worry about confidence in your correspondence
  - Don’t forget that registration warps your data, so results based on geometric properties (e.g. size, shape) should be interpreted delicately

Final Remark

- Acknowledge the variability across the different levels of anatomy.
- Inter-subject correspondence doesn’t have to be based on macro-anatomy.
  - DTI-based registration, fMRI based registration ...
- Even if we had a perfect method for structural alignment, our fMRI data would not be in perfect alignment due to the variability between structure and function.