Goals

1. Describe surface-based analysis procedures
2. Describe work applying these techniques to the study of age and Alzheimer associated brain alterations
3. Describe some of the caveats associated with MR studies of neurodegeneration
Why use MRI?

• Non invasive technique to obtain indirect measures of neural anatomy and integrity
• Multiple contrast mechanisms allow for obtaining measures that are differentially sensitive to a variety of anatomic and pathologic properties
• Image analysis procedures to obtain numerous measures from a single image
FreeSurfer: MR Image Analysis Software

- Freely Distributed Tools
  - fMRI Analysis
  - Morphometry:
    - Cortical Thickness
    - Cortical Volume
    - Cortical Surface Area
    - Subcortical structural volume
- Tools on the Horizon
  - Diffusion tensor analysis
  - Callosal morphometry
  - Diffusion informed segmentation
  - Whole brain white matter parcellation (from T1 images)
FreeSurfer Resources

• Most items can be found on the FreeSurfer webpage:
  – [http://surfer.nmr.mgh.harvard.edu](http://surfer.nmr.mgh.harvard.edu)

• Journal Articles- Dale, Fischl, Sereno
  – Surface reconstruction
  – Coordinate system
  – Thickness
  – Applications

• Documentation: Freesurfer Wiki
  – Manuals
  – Tutorials
  – Downloads
  – Software Help Files

• E-mail List:
  – [Majordomo@surfer.nmr.mgh.harvard.edu](mailto:Majordomo@surfer.nmr.mgh.harvard.edu) subscribe freesurfer in body
Surface Studies of Aging and AD
Aging and AD: Global and Regional Degeneration: Prior non-MR Work

- Cortical atrophy is apparent with normal aging and Alzheimer’s disease.
- *Age-related* global cortical atrophy is minimal early on and accelerated during the sixth and seventh decades, while *early AD* shows cortical atrophy and may accelerate with increasing disease severity.
- Greatest and earliest age-related changes suggested to be in association areas (e.g., prefrontal) and later changes in primary sensory regions.
- Early and profound degeneration in medial temporal and parietal cortex with AD.
- Until recently, there was limited information about regional patterns of atrophy in aging and AD (most studies just examined whole brain).
PFC Gray and White Matter Volumes

Manual tracing of each slice
PFC Subregional Measures

Manually intensive, regionally arbitrary, subjective: Automated measures needed
Automated Cortical Reconstruction


Averaged Hi-Res Scans → Intensity Normalized

Brain Isolated → White Matter Isolated
Hemispheres Separated and Tesselated

Gray/White Border

Gray/CSF Border
Gray/CSF Deformation

Gray-White Boundary

Outer Cortical Surface

Dale and Sereno, 1993; Dale et al., Dale et al., 1999; Fischl et al., 1999; Fischl et al., 2000; Fischl et al., 2001
Optimal Surface Placement

Gray-White Boundary

Outer Cortical Surface
Uses information about WM curvature and surrounding tissue
Cortical Thickness

Shown slice here, but this is a whole ribbon process.
Thickness must consider entire ribbon

Cortex is not 10 mm thick
Cortical thinning in aging and AD

Questions:

How early can age-related cortical atrophy be detected?

What are the regional patterns of age-related cortical atrophy?

Do patterns of cortical atrophy differ in AD compared to healthy aging?
Participants

- Younger Participants (YP; n = 31; mean age 22.8)
- Middle-aged Participants (MP; n = 18; mean age 49.4)
- Older Participants (OP; n = 58; mean age 77.1)
- Patients with Alzheimer’s disease (AD; n = 57; matched to OP)

- Scans collected through WUSTL ADRC in collaboration with Drs. Randy Buckner and John Morris
Visualization: Surface Inflation

Dale and Sereno, 1993; Dale et al., Dale et al., 1999; Fischl et al., 1999; Fischl et al., 2000; Fischl et al., 2001
Thickness Maps

- Thinning (shift from yellow to red) apparent in individual participants with increasing age
Aging: Global Volume

- Total volume correlated with age across all participants
- Total volume reduced in MP and OP compared to YP, and OP compared to MP
- No sex differences when volumes corrected for head size

Volume is calculated from thickness by surface area: Can be decomposed
How to align different cortical surfaces?
Talairach averaging

Single subject

Average of 40
Surface-Based Spherical Coordinate System
Spherical Averaging

Inflated Surface

Transformed Surface
Automated Cortical Labeling Demonstrates the Power of Spherical Averaging
Effect of Spherical Averaging

Repetition Effect (Novel vs. Repeated Words)

Talairach Average

Spherical Average
Thinning from Young to Old Age

- Thinning in primary as well as association areas
Aging v AD Brain

Do patterns of cortical atrophy differ in AD compared to healthy aging?

Alois Alzheimer described in 1906

Staging: Ball, Braak, Hyman
Regional Thinning: Aging v AD

**OP > AD**
Left Hemisphere Right Hemisphere

**YP > OP**
Left Hemisphere Right Hemisphere

*Cortical loss in AD seems to be primarily thickness, not surface area*
Thickness Summary

- Global thinning is apparent with early aging (earlier than we expected)
- Age-related thinning is regionally widespread including association cortex as well as primary sensory/motor regions (more widespread than we expected)
- Regional thinning differs in AD compared to healthy aging with greater thinning in medial temporal and parietal cortex in AD, consistent with pathology studies
- Thickness measures may be useful clinically (e.g., diagnostically)
What else can we do with surfaces?
Additional Properties of Interest:
Amount of ‘Stretching’ to Match Atlas

Individual Subject

Average (Target)
Cortex
Æ
White matter

"Twinkie Model"

Can be used to inform subcortical labeling

Twinkie Model
Why use WM Parcellation?

1. Could provide information about WM associated with specific cortical regions
2. T1 data is far more abundant than DTI data
3. May provide unique information about WM degeneration
MR Anatomy Caveats

• Dependent on data quality
  – Contrast to noise
  – Signal to noise
  – Voxel resolution

• MR Artifacts
  – MR susceptibility
  – MR distortions

• Variations in MR tissue parameters across regions of the brain and are altered in different populations

• Most problems can be reduced if acknowledged, and potentially be strengths

• What is the biological basis of morphometric changes?
Multimodal 1: Diffusion Tensor Imaging

- Contrast dependent on molecular self diffusion of water
- Diffusion highly influenced by myelinated axons
  - Questions about biophysics in health and disease
- Index of various aspects of tissue microstructure
  - Myelination
  - Orientation
Association Between FA and Cortical Thickness

Right

Lateral

Medial

Frontal/Occipital

Left

OA < AD

p < .001  p < .01  p < .05

OA > AD

p < .05  p < .01  p < .001

p < .001 in all participants
p < .005 in AD alone