# Driving Biological Problem Huntington's Disease

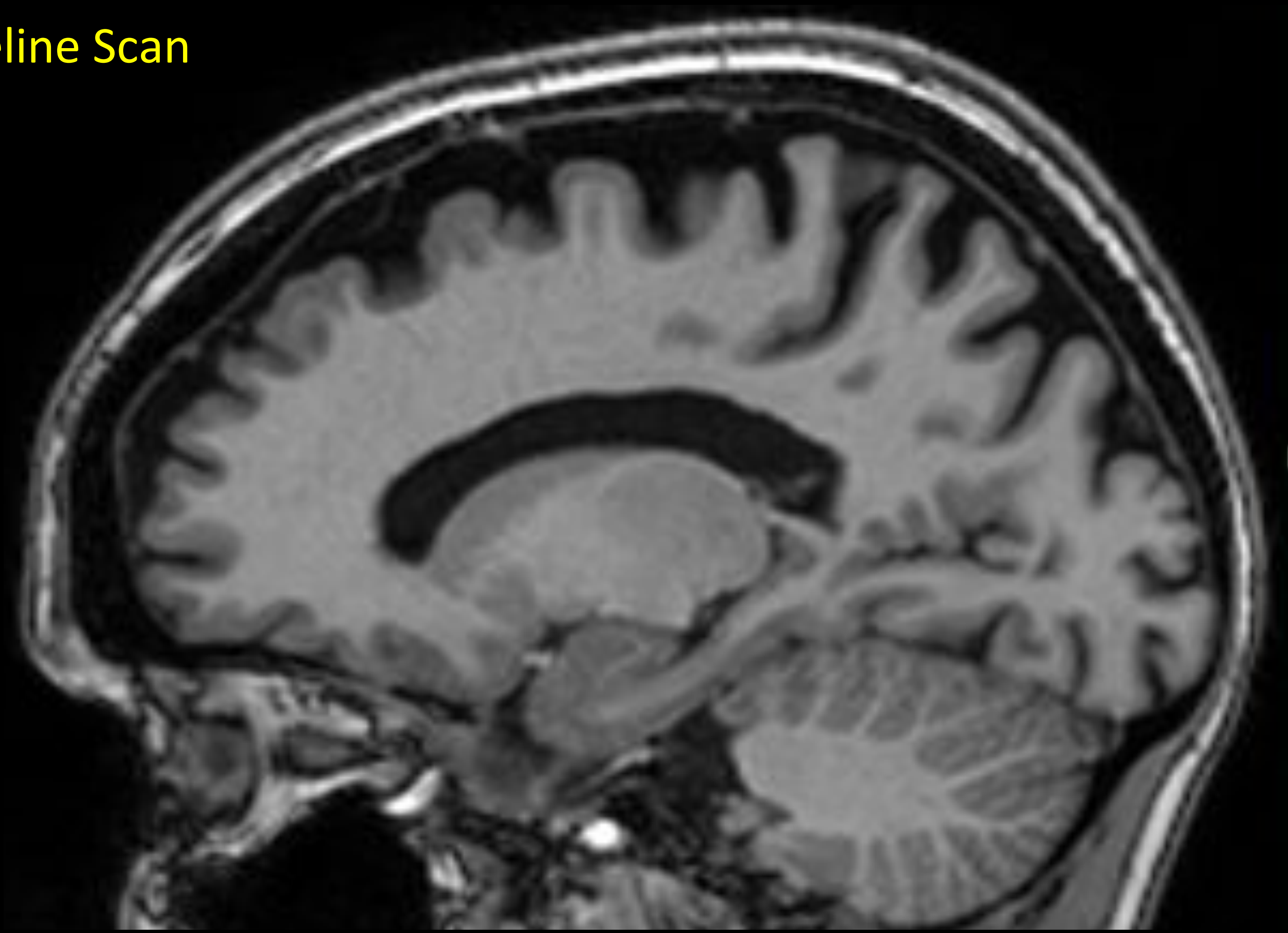
THE UNIVERSITY OF IOWA

# Builds on PREDICT-HD

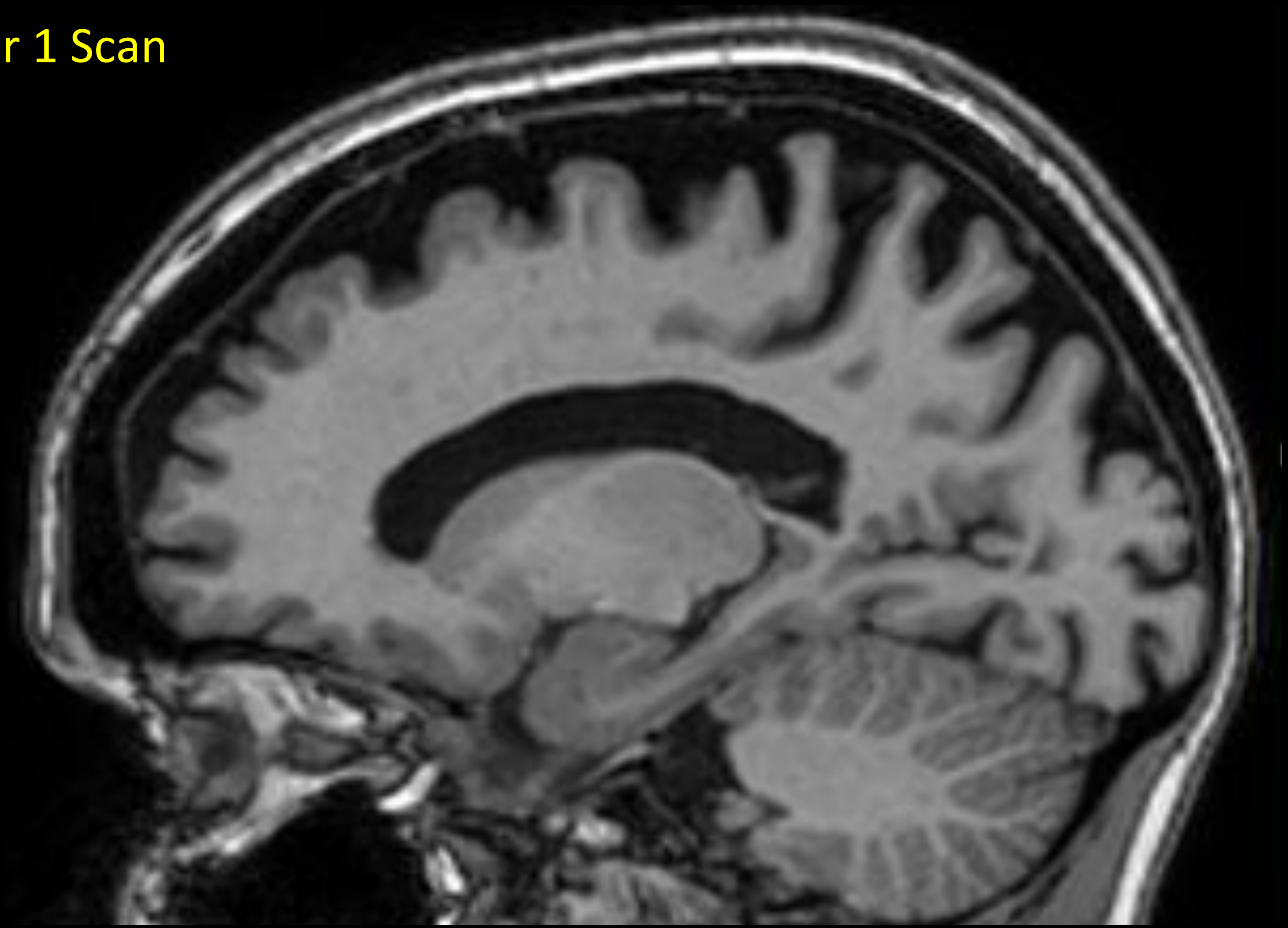
- The NIH-funded project "Neurobiological Predictors of Huntington's Disease" (PREDICT-HD) studies Huntington's disease (HD), a neurodegenerative genetic disorder that affects muscle coordination, behavior, and cognitive function, and causes severe debilitating symptoms by middle age.

# TRACK-HD Stage 1 HD Subject

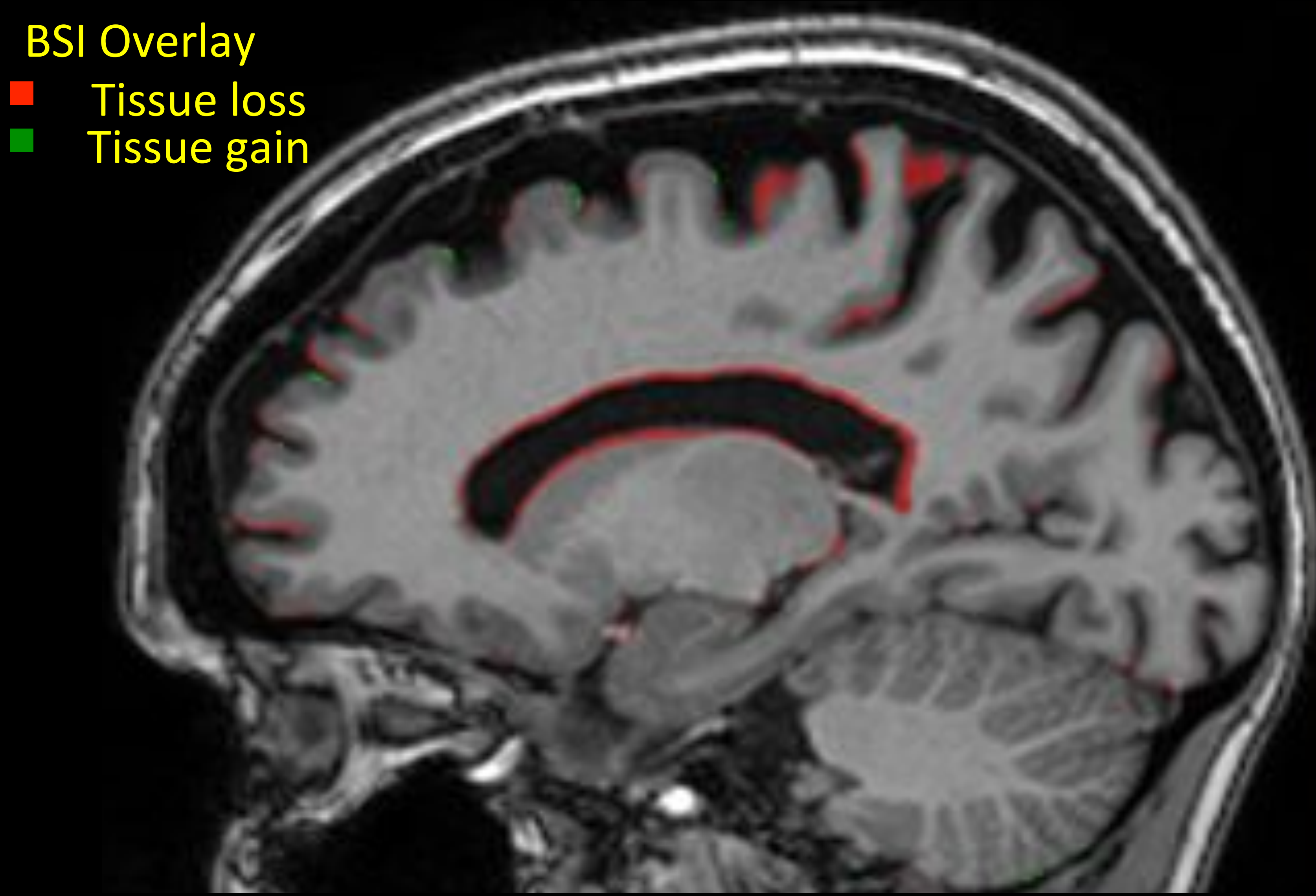
Baseline Scan



# TRACK-HD Stage 1 HD Subject



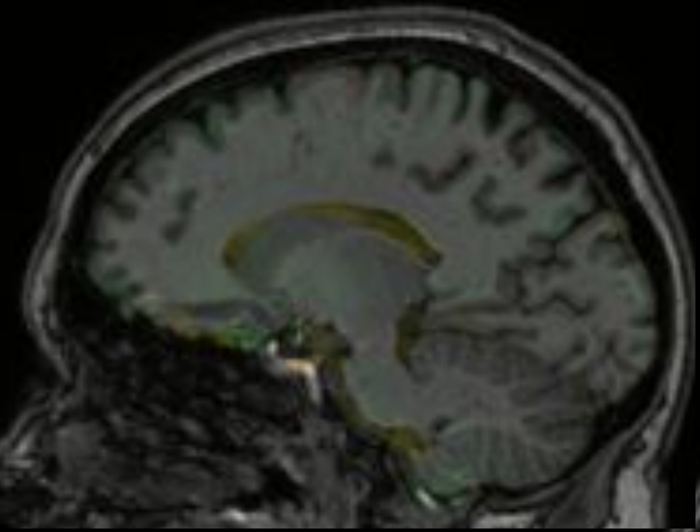
# TRACK-HD Stage 1 HD Subject



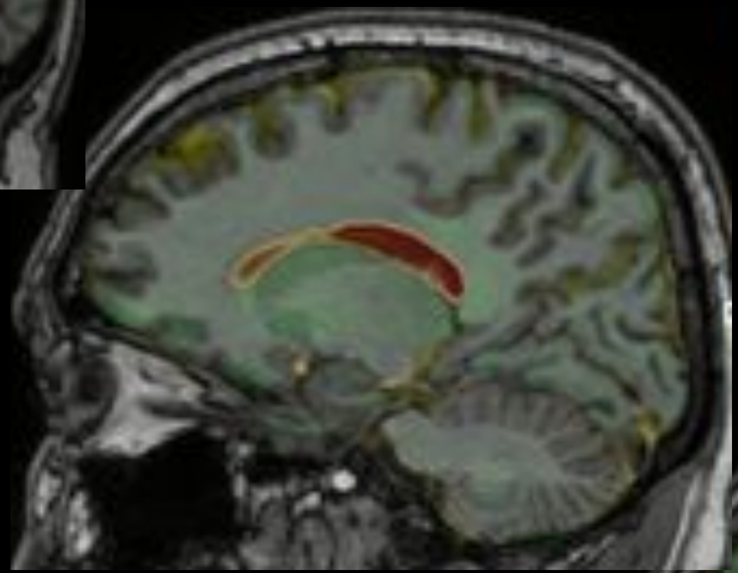

Atrophy Rate: 1.9%     Premanifest Rate: 0.7%     Control Rate: 0.2%

# 24-month voxel-compression mapping

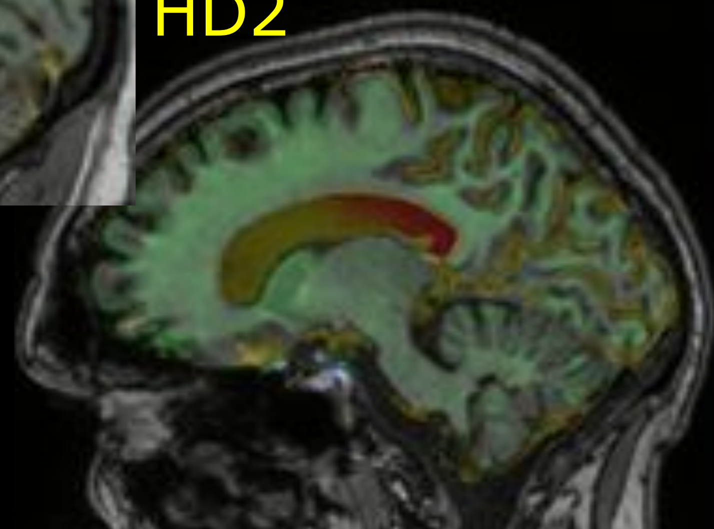
Control



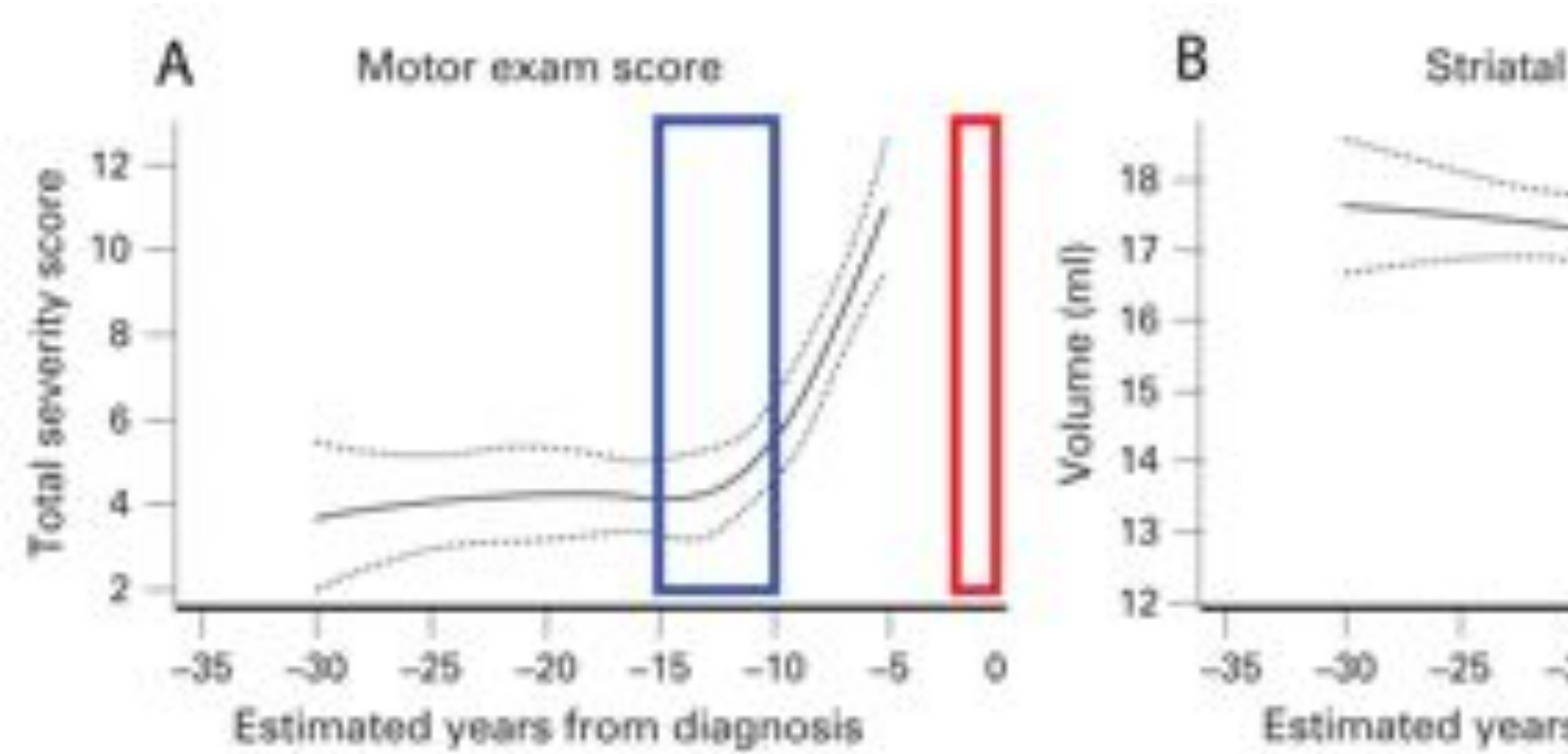
PreA



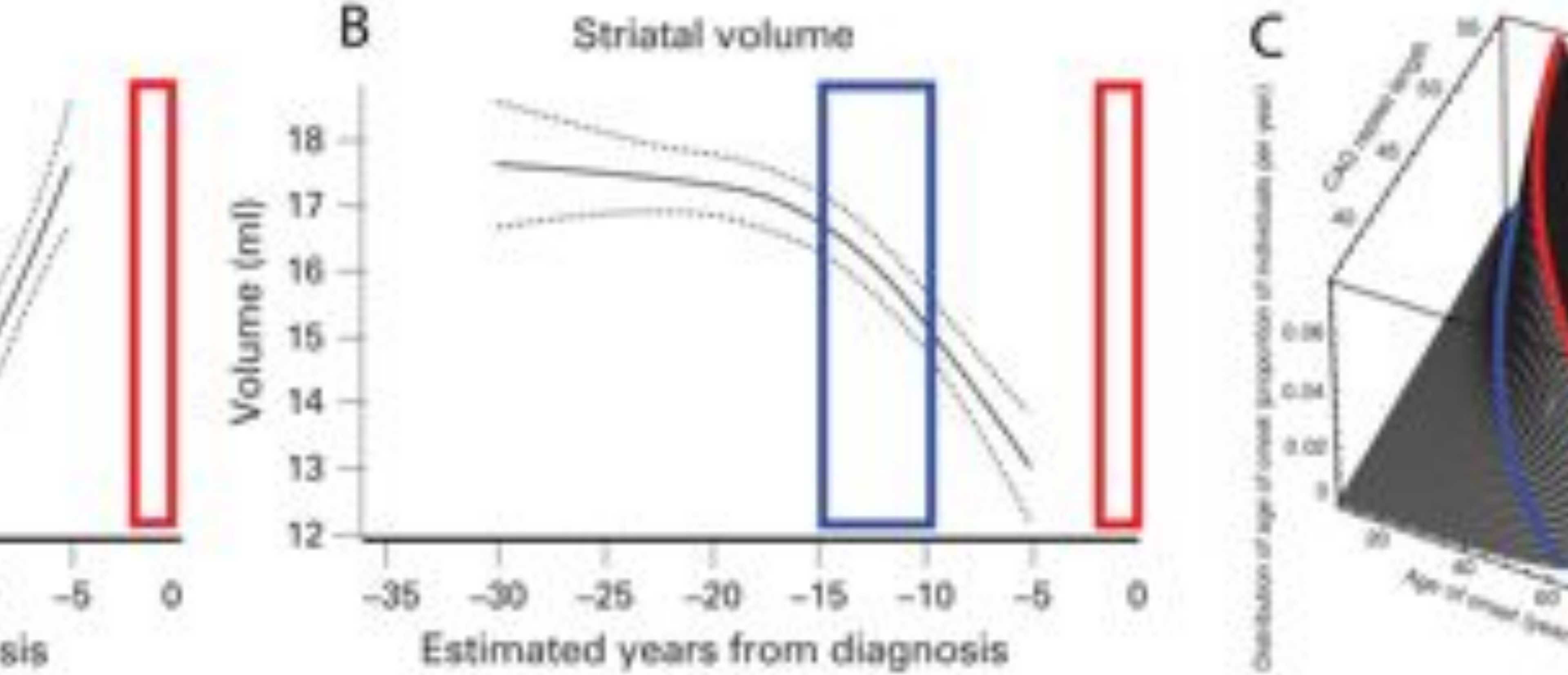
HD2



# HD Background



# HD Background



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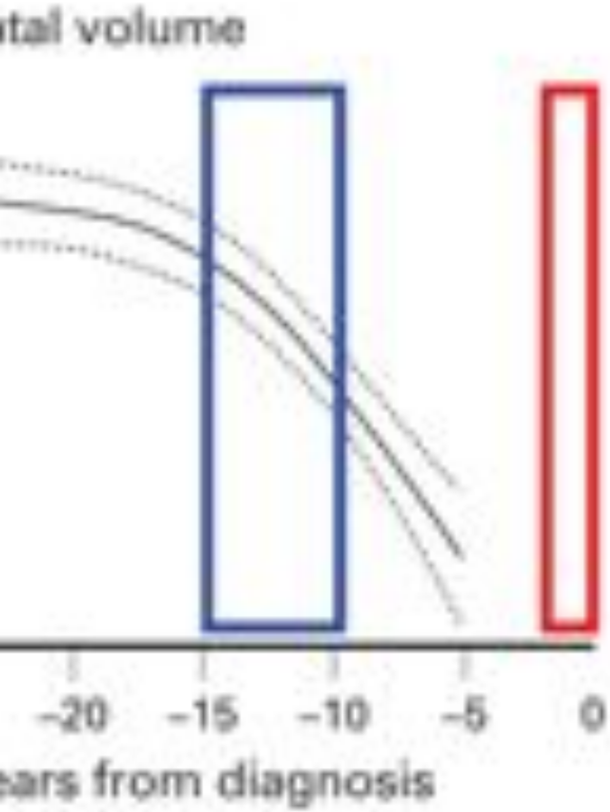


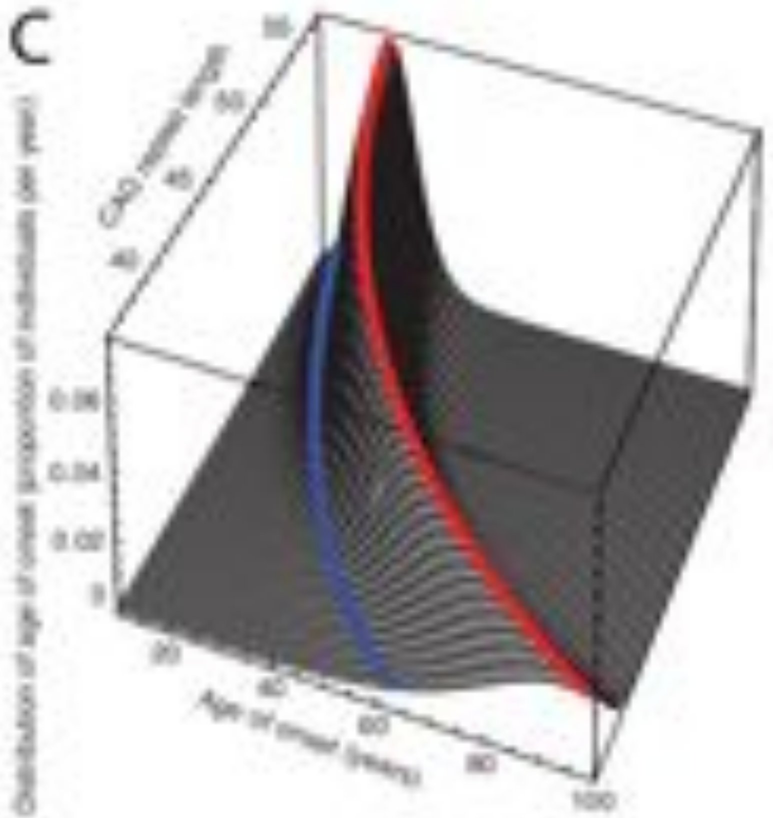

# Specific Aims

- Perform individualized longitudinal shape change quantification from multi-modal data.
- Complete full brain Diffusion Tensor Imaging tractography analysis.
- Deploy extensible tools for sharing source data, derived data, algorithms and methods to multi-site analysis teams.

# Sharing HD Data

http://www.na-mic.org/Wiki/index.php/2011_Summer_Project_Week

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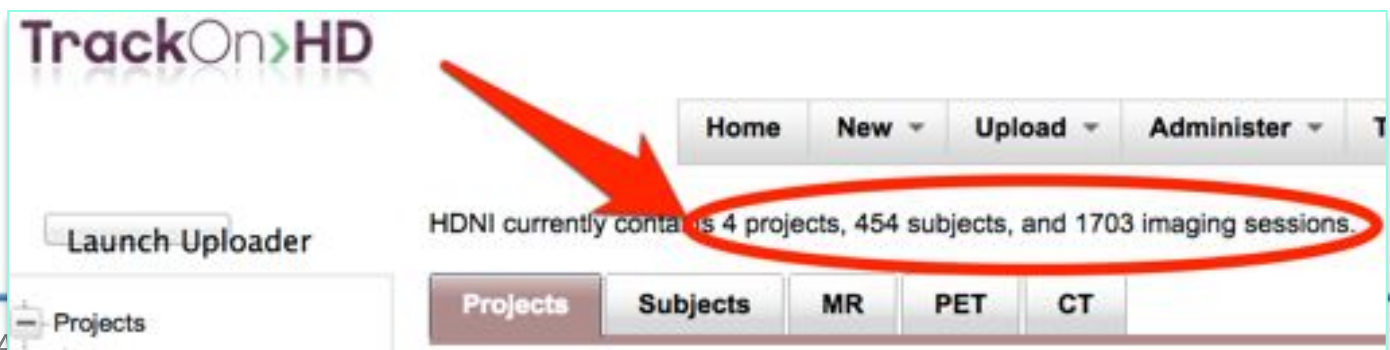
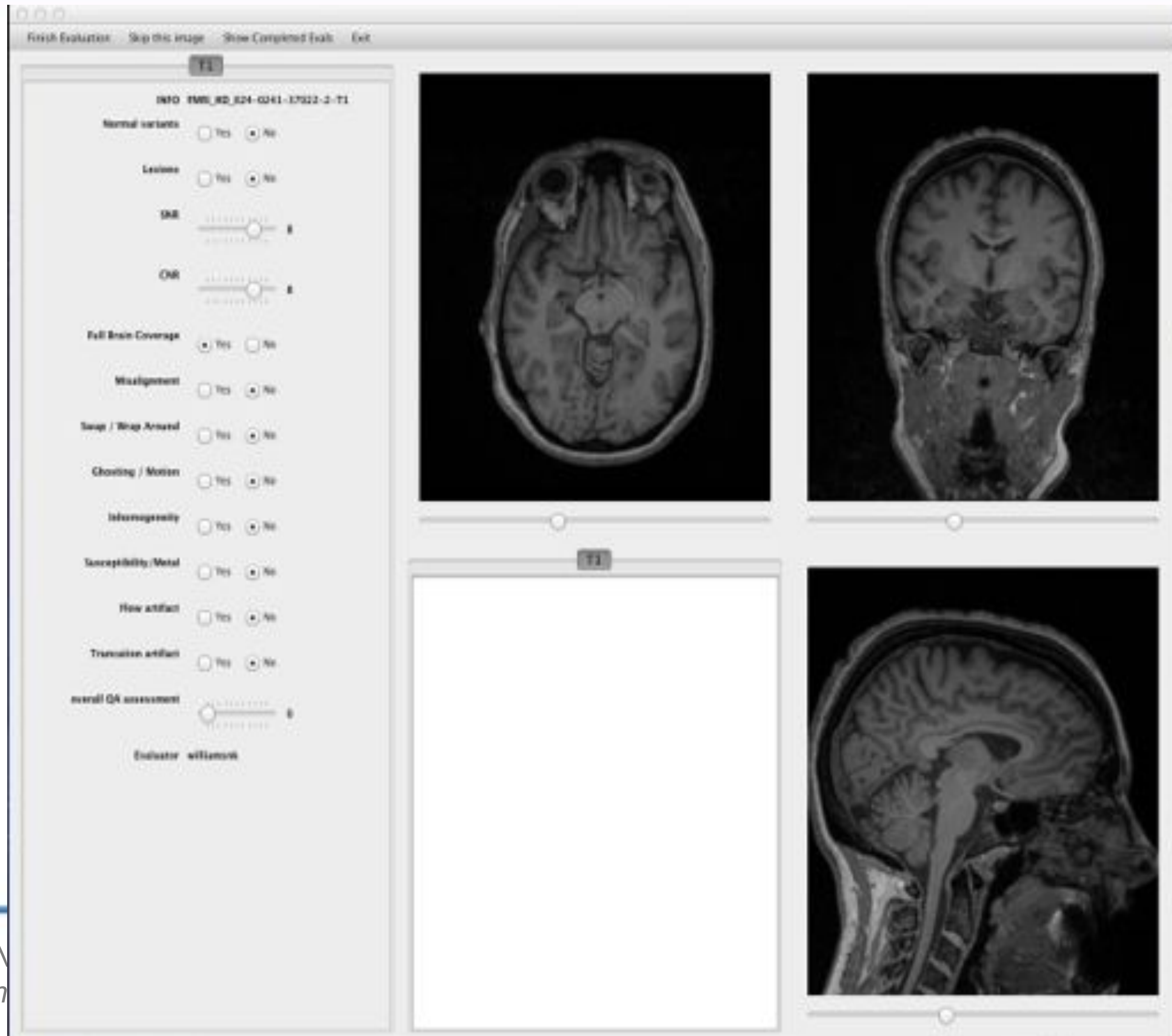
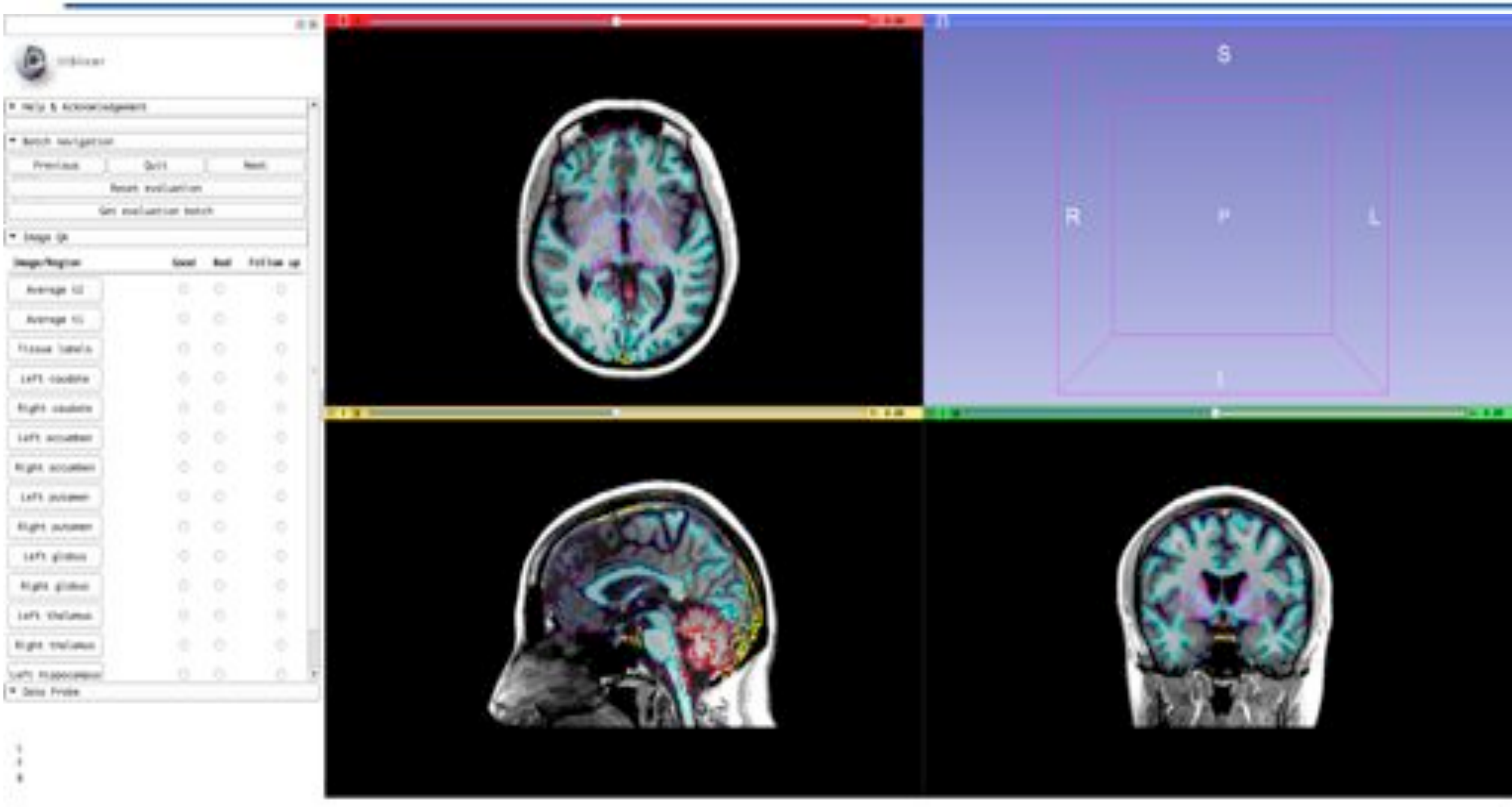


# Quality Assurance tools



# Quality Assurance tools



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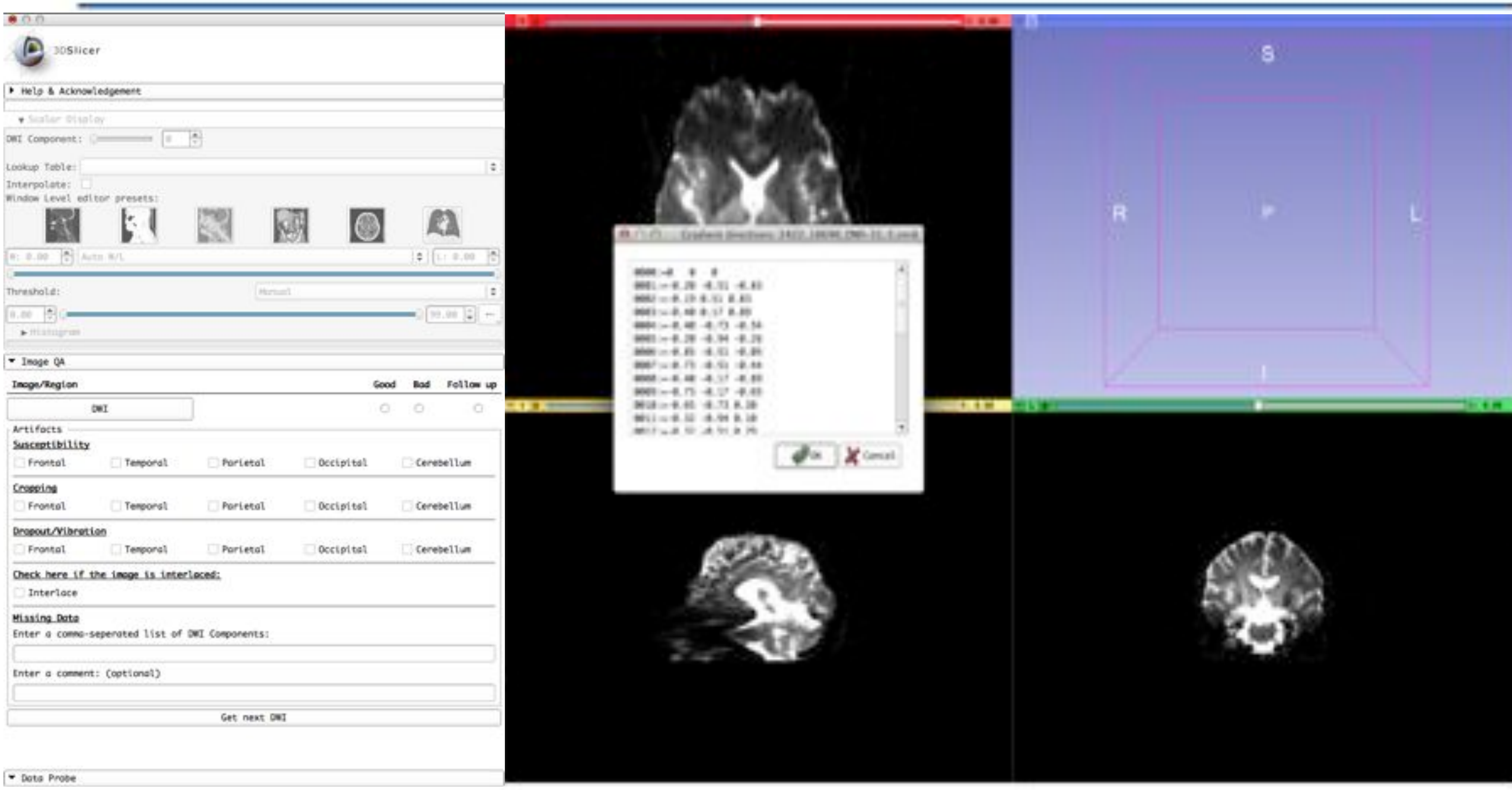
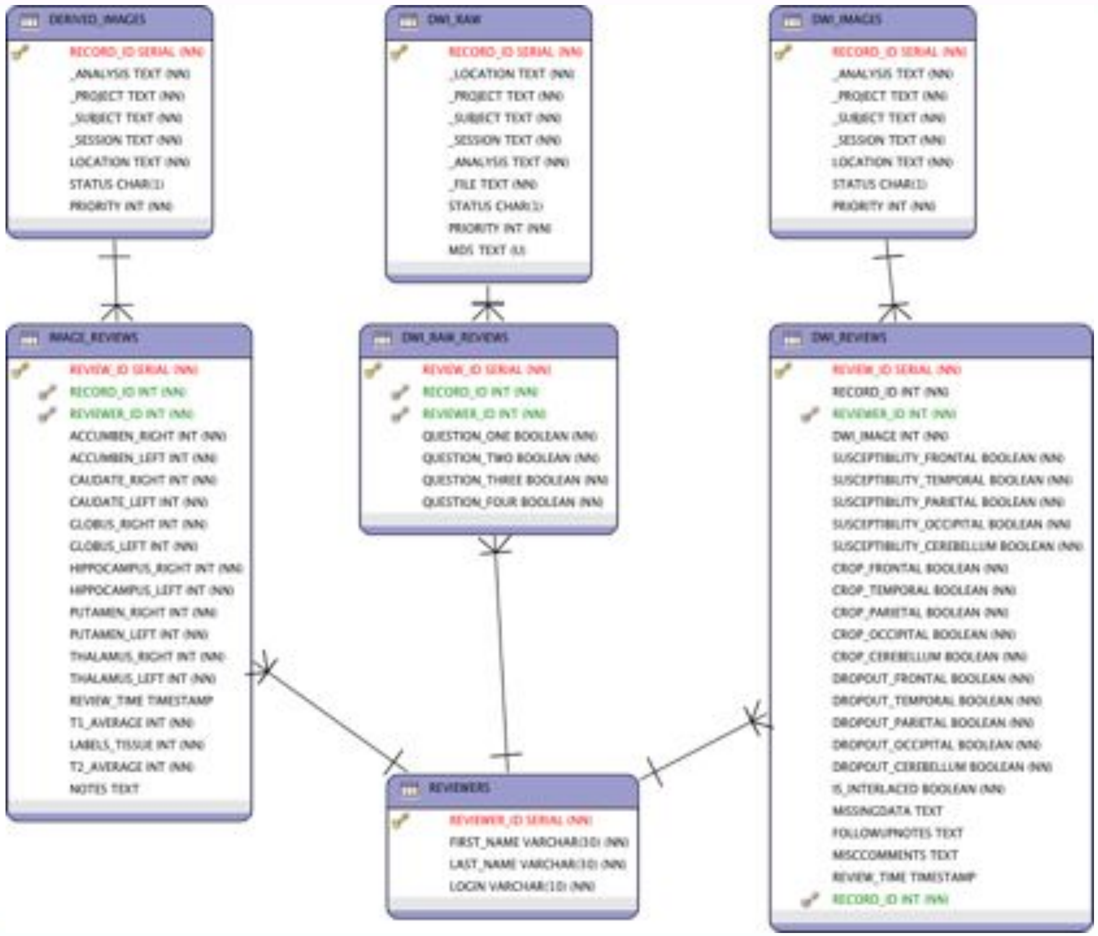
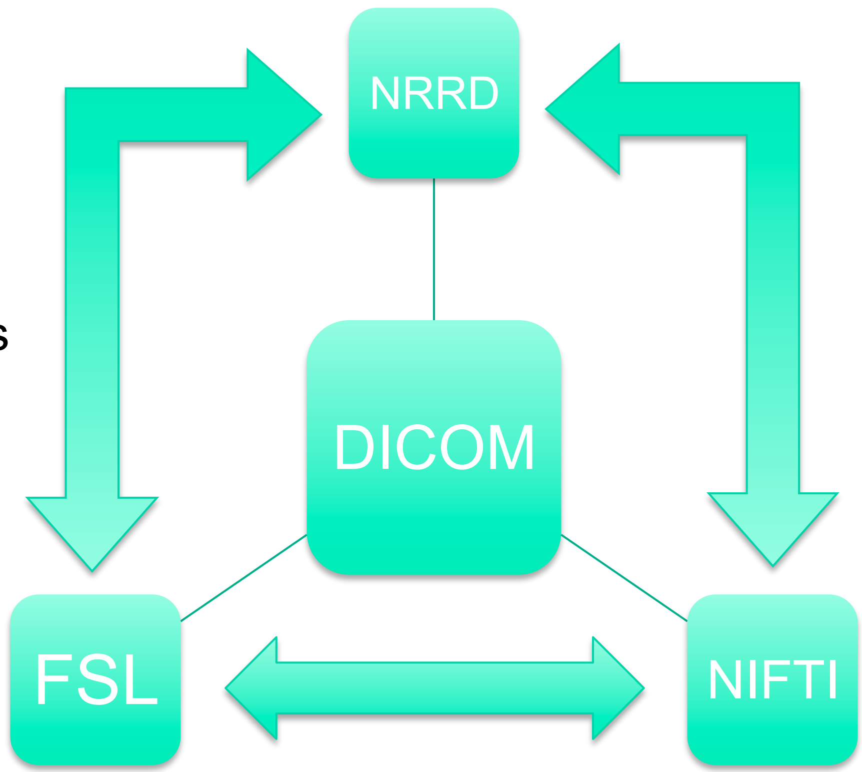


# Quality Assurance tools



# DWIConvert

- Replacement for DicomToNrrdConverter
- ~4 months of effort
  - Help from NAMIC Team
  - Help from Scanner Manufactures
  - Help from MR Physicist
- Built on ITKv4
- Depends on DCMTK
  - Removed GDCM



# Improve DICOM conversion

**How we improved conversion from DICOM**

- Found **differences in DICOM metadata** for different data types in THP data
- Expanded compatibility of program **DicomToNrrdConverter** to correctly convert 42 varieties of DICOM data to NRRD file format
  - Still some data could not be converted
- COMPLTELY REWROTE TO DWIConvert
  - 2012 Revealed 2 new incantations of diffusion data from DICOM
  - DWIConvert is more modular and easier to incorporate new rules
  - DWIConvert is built against ITKv4 and DCMTK allowing the reading of multiframe data
    - DCMTK support is not also part of ITKv4
  - Public and private element tag metadata compatibility
  - Devised a method to calculate missing diffusion gradient direction coordinates from private data in some scanners

# Improve DICOM conversion

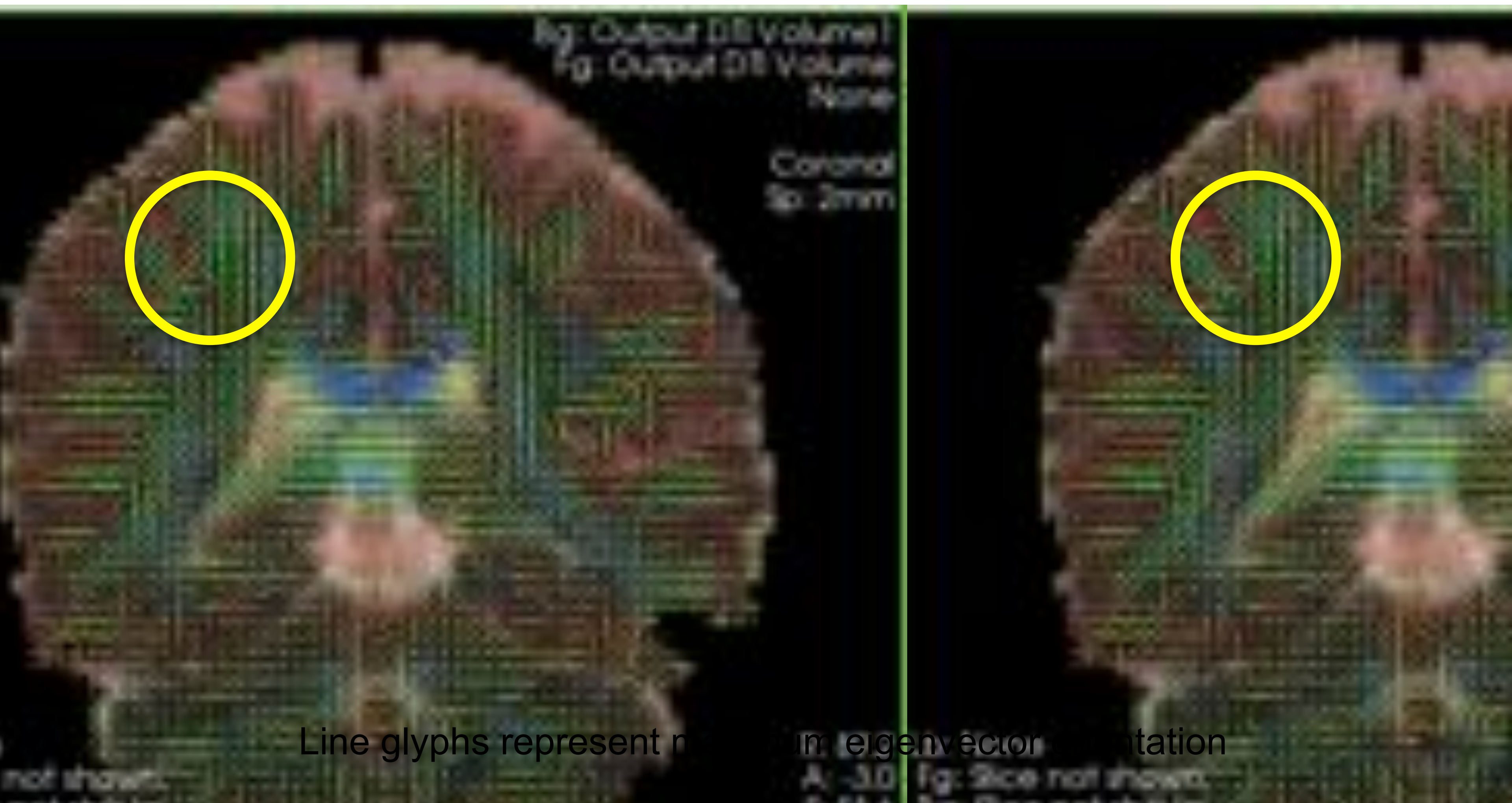
Traveling Human Phantom (THP) Data Set

(Shared With NAMIC, 17 external groups using it)

- Designed to overcome compatibility issues with multi-site data
- 5 healthy subjects
- Each subject imaged at 8 sites in 1 month
  - 5 Siemens scanners, 3 Philips scanners
  - 4 different scanner software versions
- T1- and T2-weighted images
- Diffusion-weighted images
  - 30/32 direction scan (4 repeats per site)
  - 71 direction scan (2 repeats per site)

# Improve DICOM conversion

Incorrect Correct




Line glyphs represent m[illegible]im eigenvector [illegible]tation

# Improve DICOM conversion

Many different locations (element tags) of metadata important to DWI data analysis

| Element tag | GE (Signa) | Siemens (Trio Tim) | Siemens (Verio) | Philips (Achieva) |
|---|---|---|---|---|
| B value | 0043,1039 | 0029,1010 | 0029,1010 | 2001,1003 |
| Gradient vector coordinates | 0019,10BB ($x$)<br>0019,10BC ($y$)<br>0019,10BD ($z$) | 0029,100E | 0029,100E | 2001,1004 |
| Mosaic size parameters | | 0051,100B<br>0029,100A | 0051,100B<br>0051,100B | |
| Measurement frame | | 0020,0032 | 0020,0032 | 0020,0032 |
| B matrix | | 0019,100E | | |

Software revision used to determine when estimation from B matrix is needed

# Improve DICOM conversion

Calculate missing (or incorrect) diffusion gradient direction coordinates by using **b** matrix coordinates in private element tag

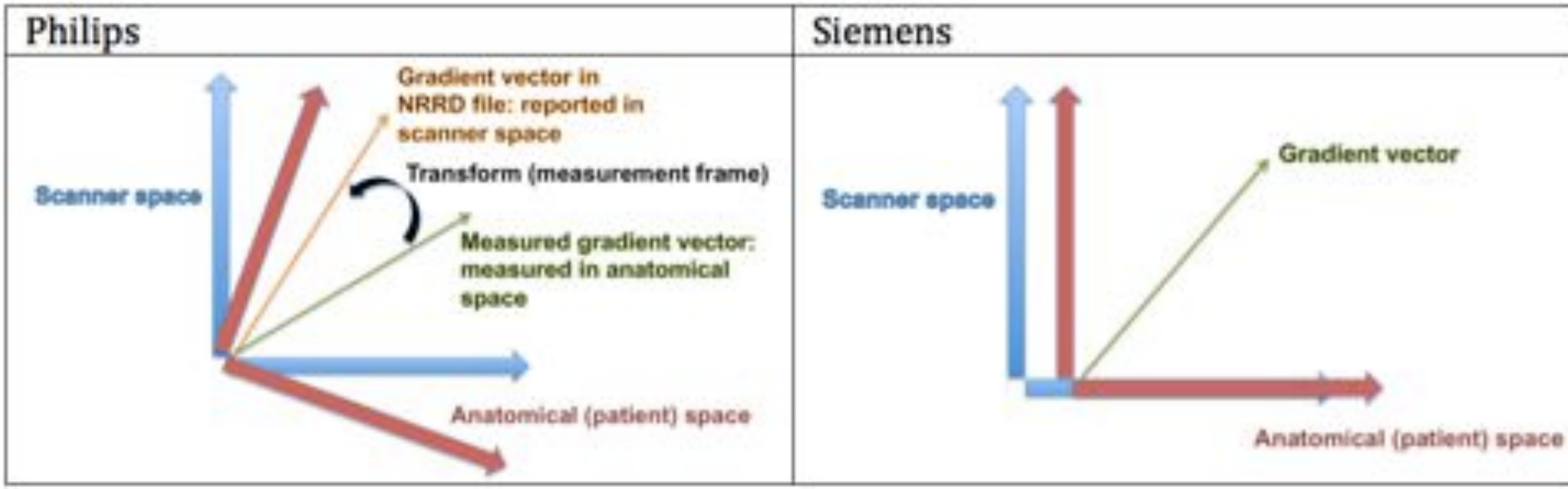
**Missing gradient direction coordinates**

$$\boldsymbol{g} = \boldsymbol{G}_n \boldsymbol{G}_n^T = \begin{pmatrix} g_x \\ g_y \\ g_z \end{pmatrix} \begin{pmatrix} g_x & g_y & g_z \end{pmatrix} = \begin{pmatrix} g_x^2 & g_x g_y & g_x g_z \\ g_y g_x & g_y^2 & g_y g_z \\ g_z g_x & g_z g_y & g_z^2 \end{pmatrix}$$

$$\boldsymbol{b} = b\boldsymbol{g}$$

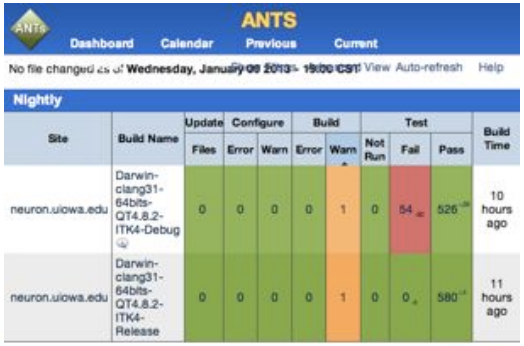
6 elements of symmetric matrix given in private element tag → SVD → b-value for gradient

# Improve DICOM conversion



# Contribute to many NA-MIC family tools

- ITKv4 Contributions
- Many contributions to Slicer to prepare for ITKv4 update, add new modules, improve end-user experience, replace legacy/broken modules with compliant functionality
- Wrap tools needed for processing in Slicer Execution Model(SEM)
- Developed converter for SEM to nipype for automatic wrapping
- Updated tools to ITKv4
- Updated tools to consistent "SuperBuild"
- Many, many contributions to the "Advanced Normalization Toolkit (ANTS)" (Wrap in nipype, ITKv4 compiliant, SuperBuild, Testing Suite)

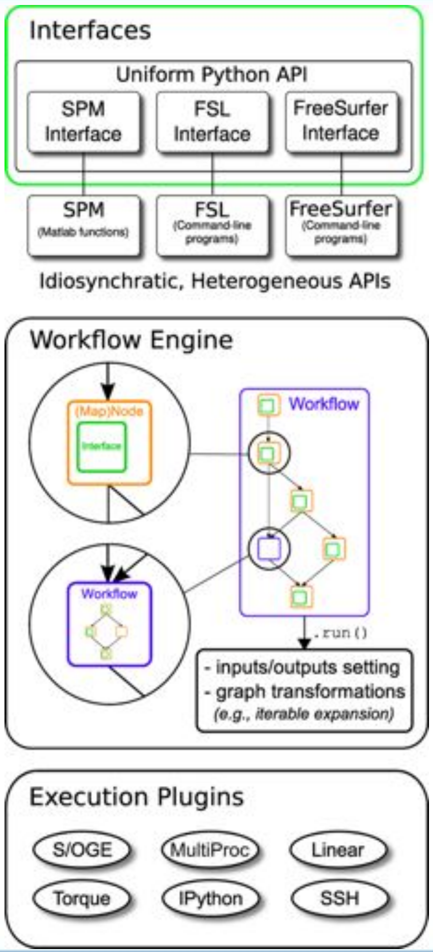



| Site | Build Name | Update | Configure | | Build | | Test | | | Build Time |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Files | Error | Warn | Error | Warn | Not Run | Fail | Pass | |
| neuron.uiowa.edu | Darwin-clang31-64bits-QT4.8.2-ITK4-Debug | 0 | 0 | 0 | 0 | 1 | 0 | 54 | 526 | 10 hours ago |
| neuron.uiowa.edu | Darwin-clang31-64bits-QT4.8.2-ITK4-Release | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 580 | 11 hours ago |

# Improving shared derived data processing

- Convert brains2 internal tools auto workup into fully NA-MIC compliant tool suite
  - (DONE)Convert major applications to SEM compliance (Decouple SEM from Slicer)
  - (DONE)Use SimpleITK to replace brains2 basic image processing building blocks
  - (In Progress)Transition Slicer to ITKv4
  - (DONE)Define workflows in NiPype (Thanks Satra Ghosh)

# NiPype: Large catalog of tools with a uniform interface

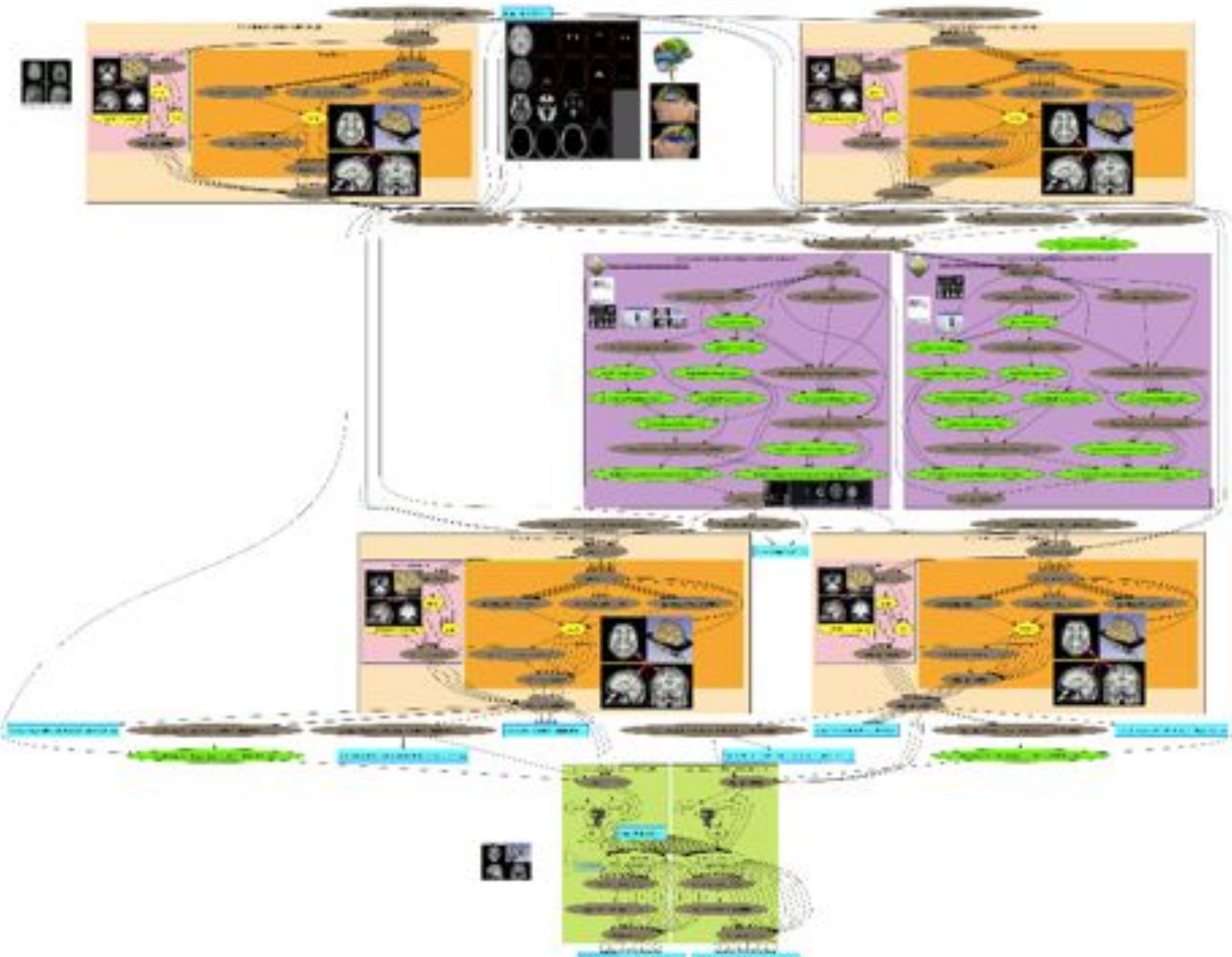



- **Batch processing**
  - Distributed processing plugins
  - Reruns affect updated/edited node connections <u>ONLY</u>!
- Uniform node creation
  - Stable and consistent API
  - Nipype's Function node allows easy integration of CLI tools
- **Pipeline complexity**
  - Iterables, MapNodes
  - Nested workflows

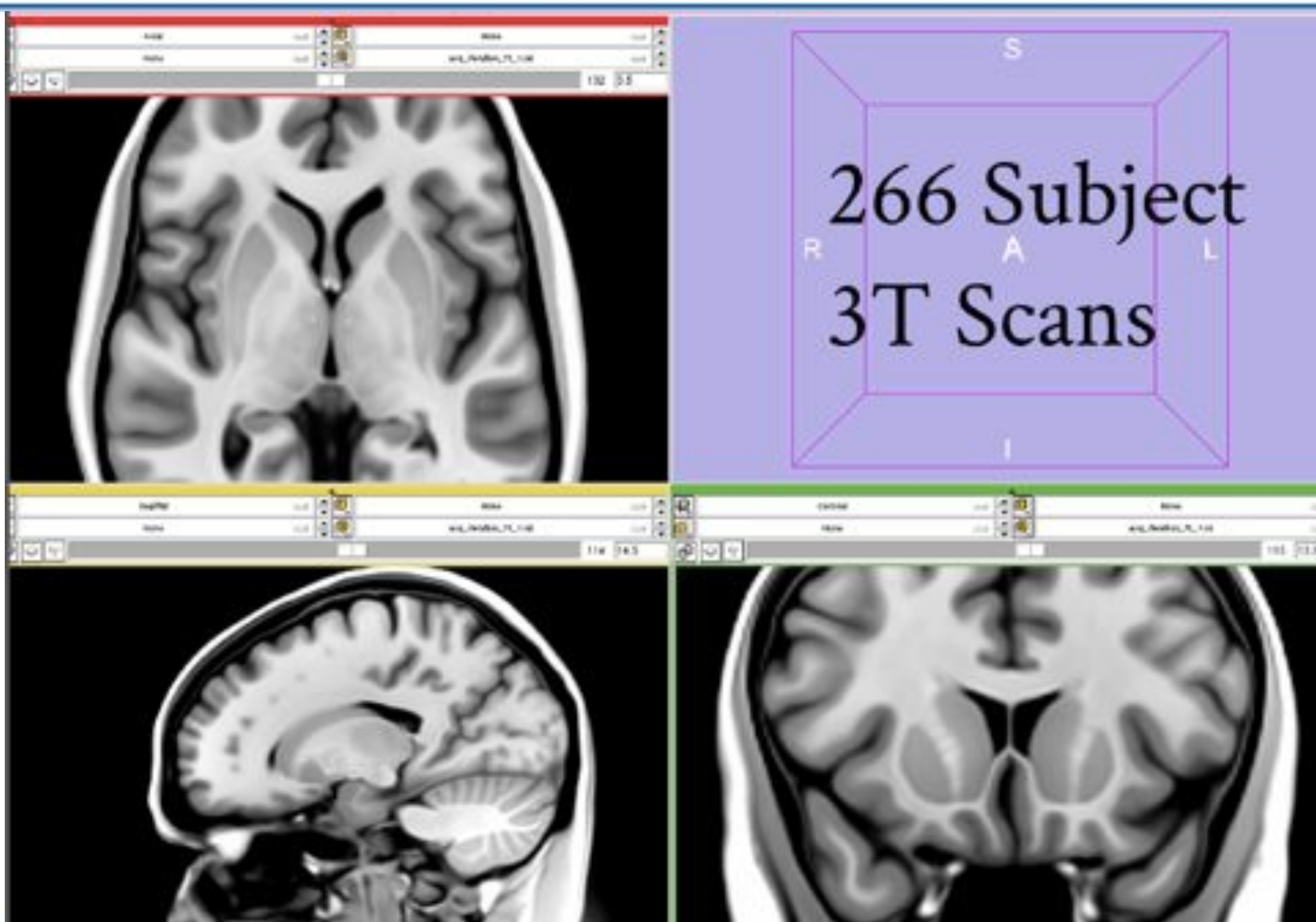


Image source: Gorgolewski K *et al.,* (2011) Nipype: a flexible, lightweight and extensible neuroimaging data processing framework in Python. Front. Neuroinform. 5:13.

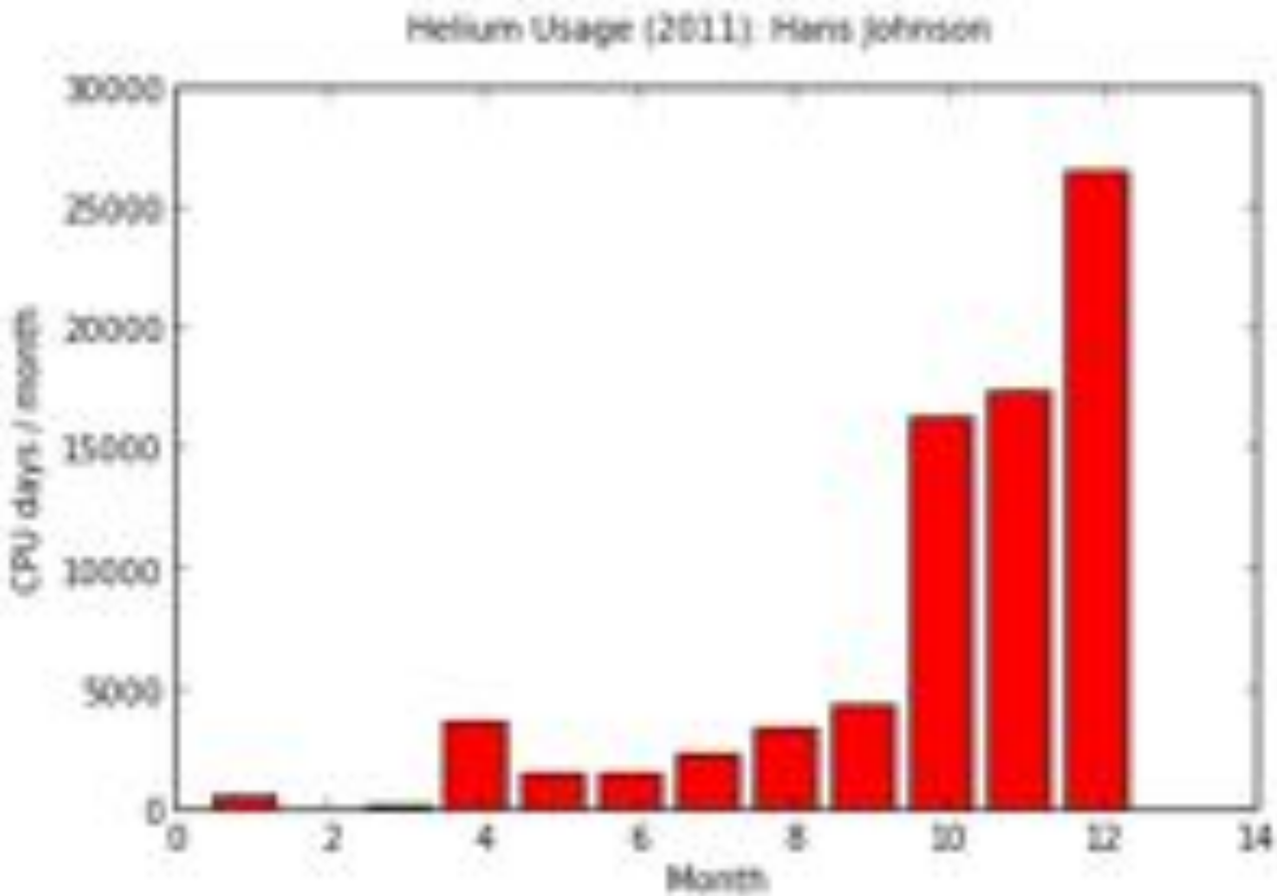
# Diagram of Longitudinal Processing Pipeline



# Improved Template Building with ANTS



# Cost of Longitudinal Analysis

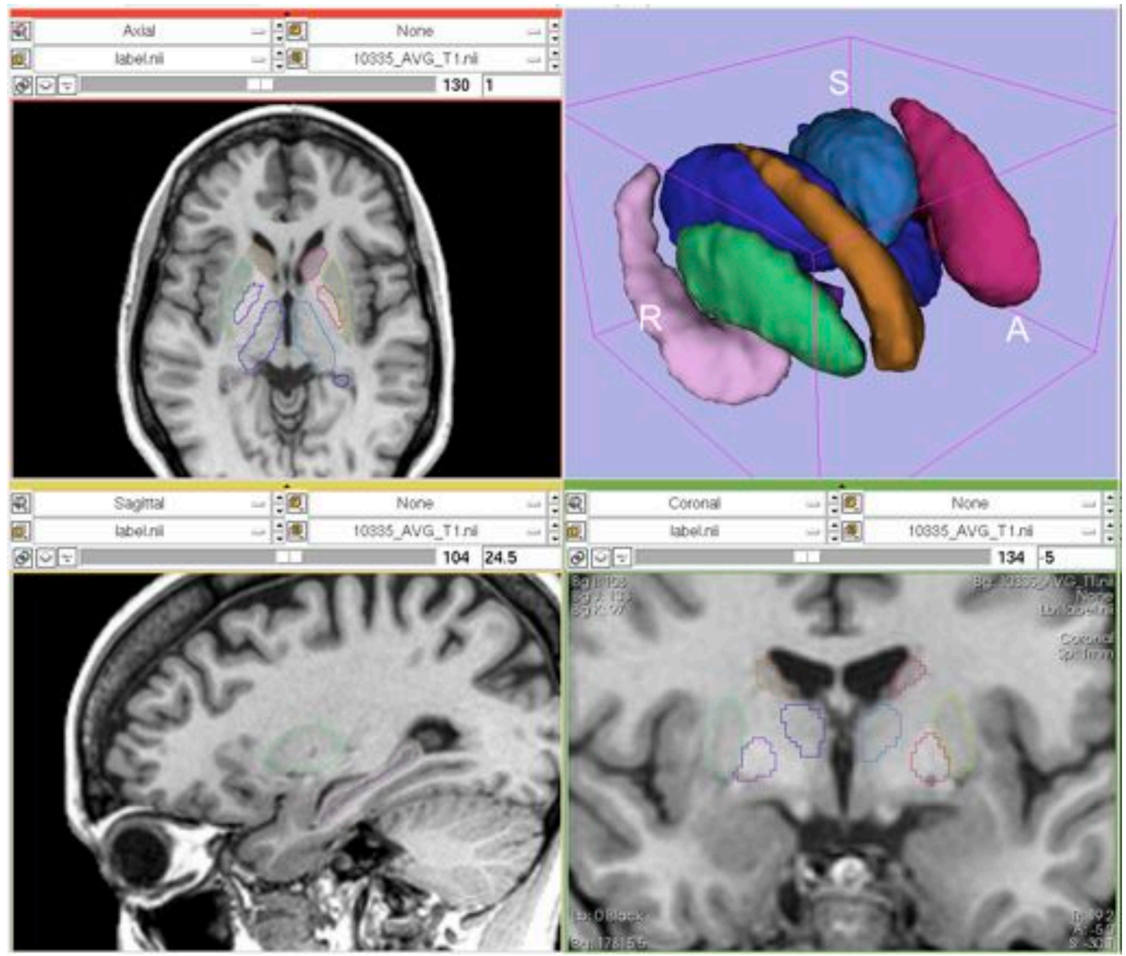


# Brain Sub-Cortical Structures:
## BRAINSCut (Longitudinal estimation)

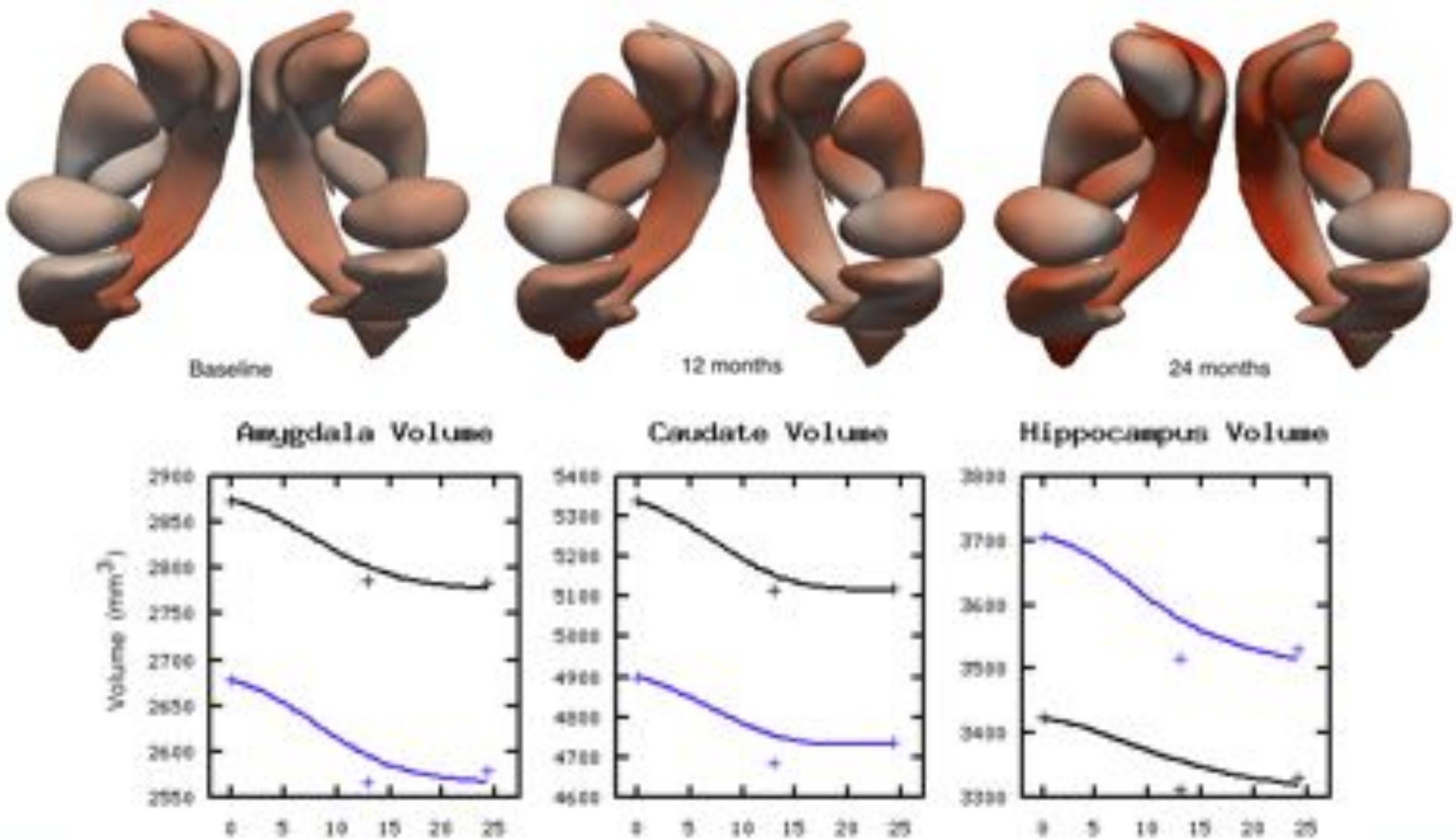
Developed
- Caudate
- Putamen
- Thalamus

New structure
- Hippocampus

On going
- Globus
- Accumbens
- And more…



# Longitudinal Shape

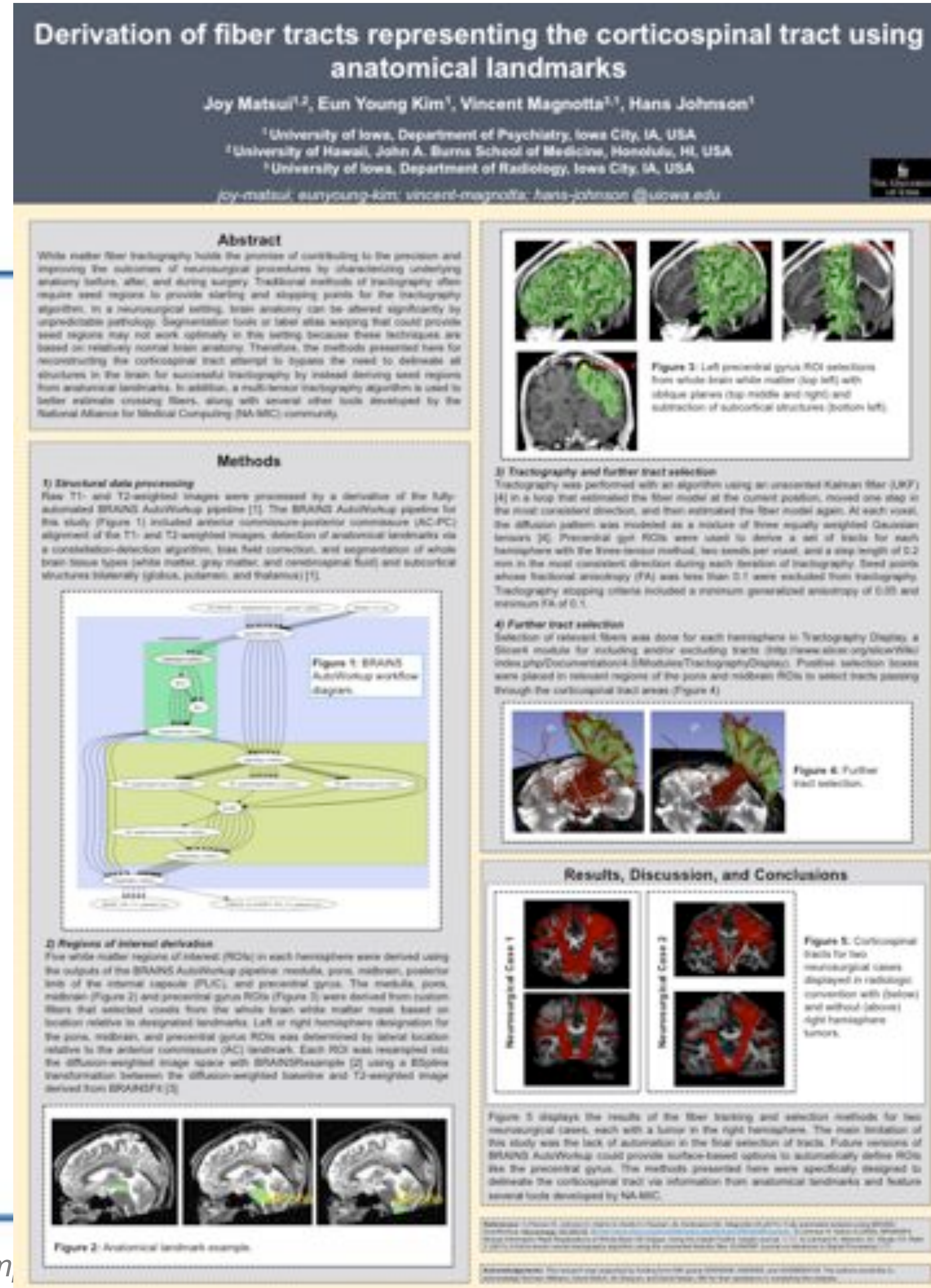





James Fishbaugh

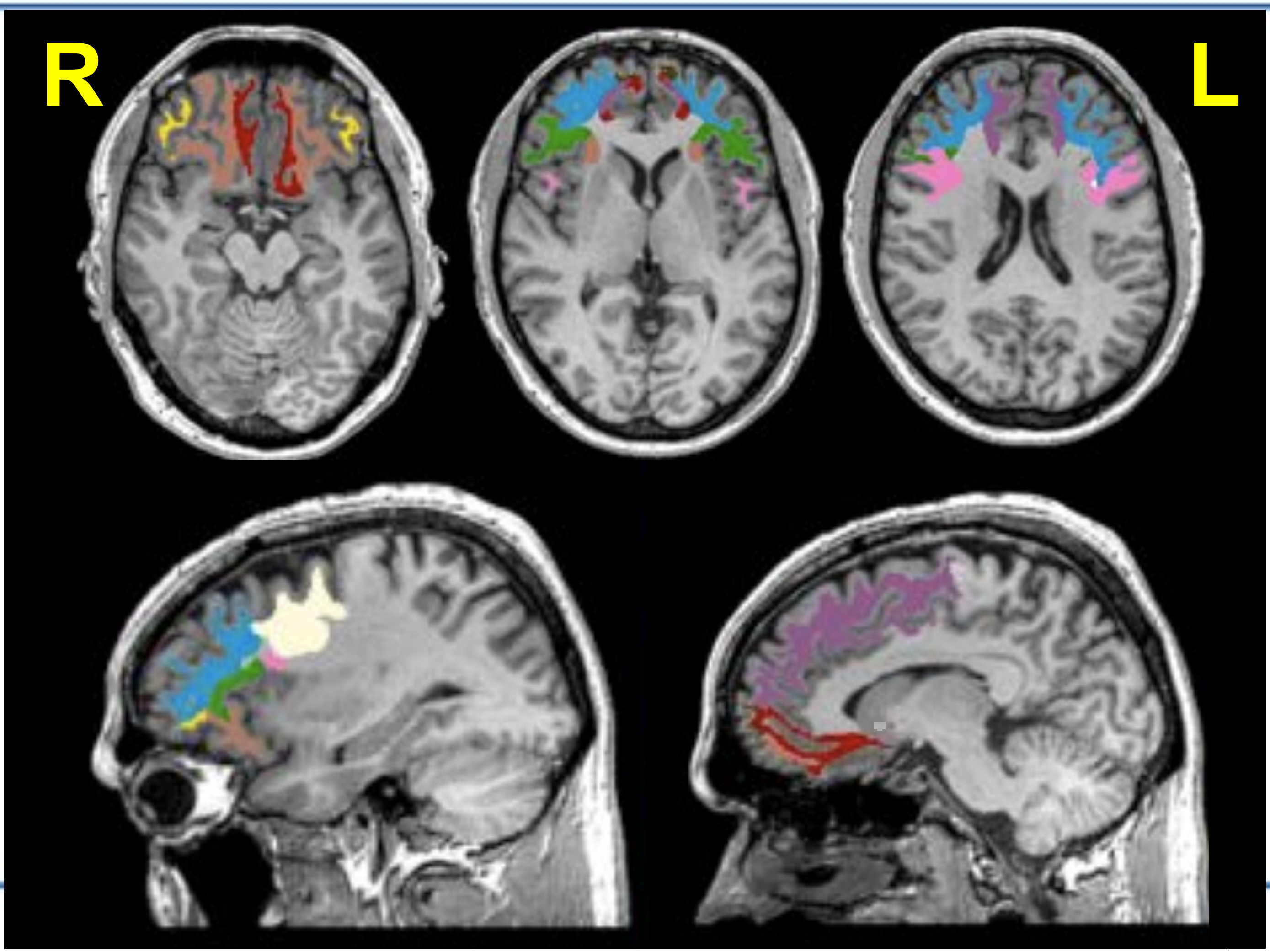
# MICCAI 2012

- Joy Matsui & Regina Kim participated in the DTI Challenge
- Joy participated in poster session

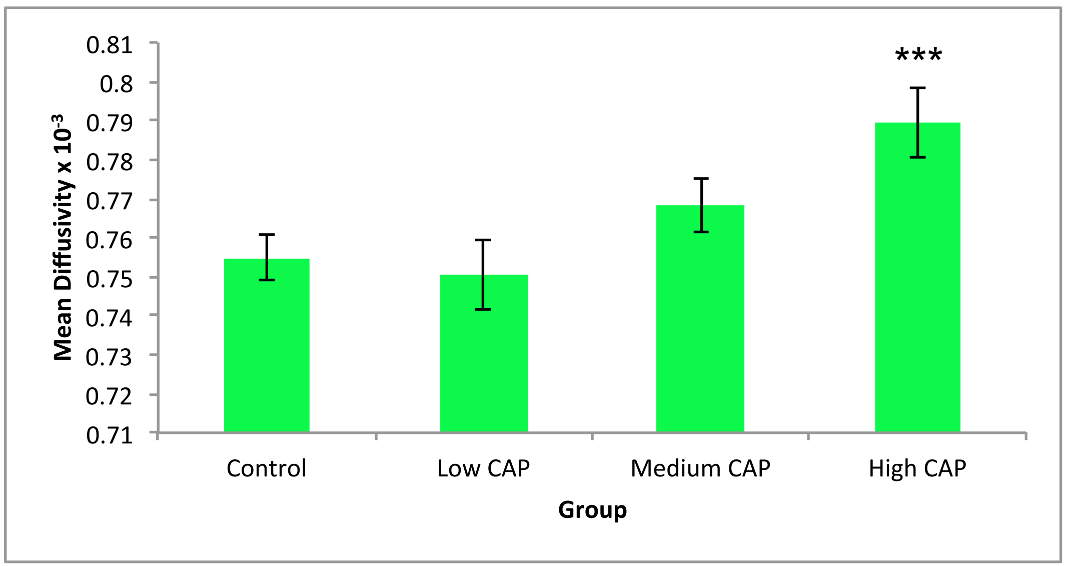


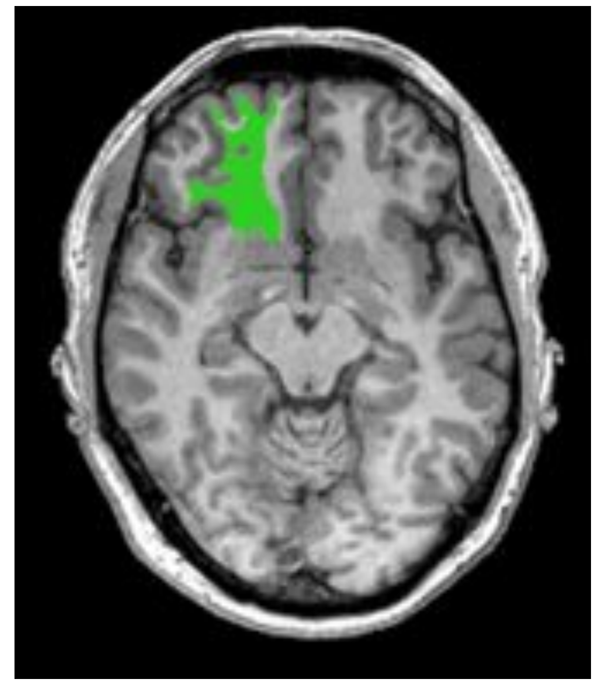
# Diffusion weighted imaging of prefrontal cortex in prodromal Huntington's disease

[Submitted Human Brain Mapping Oct 2012]

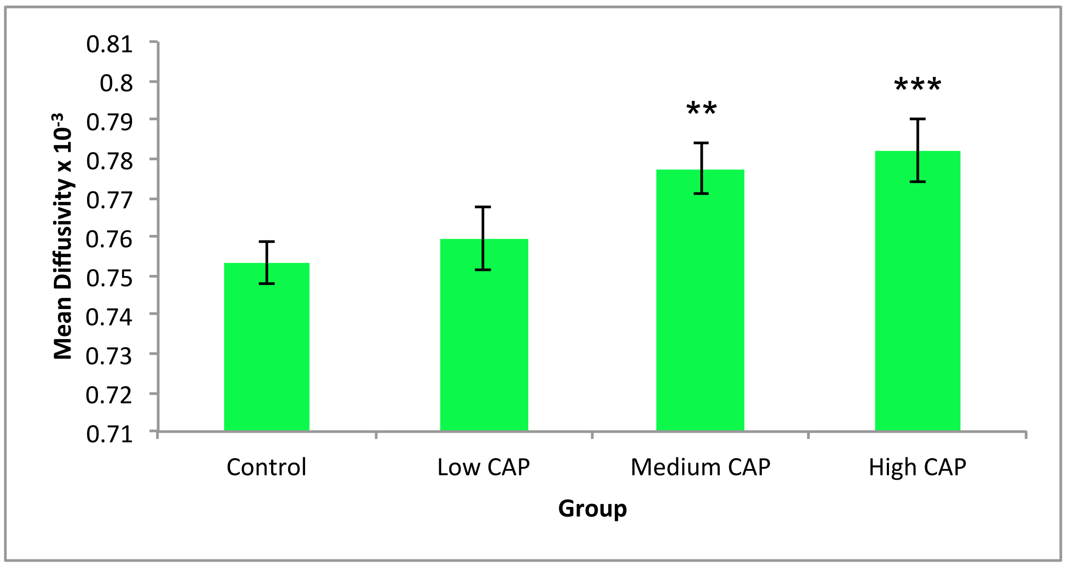


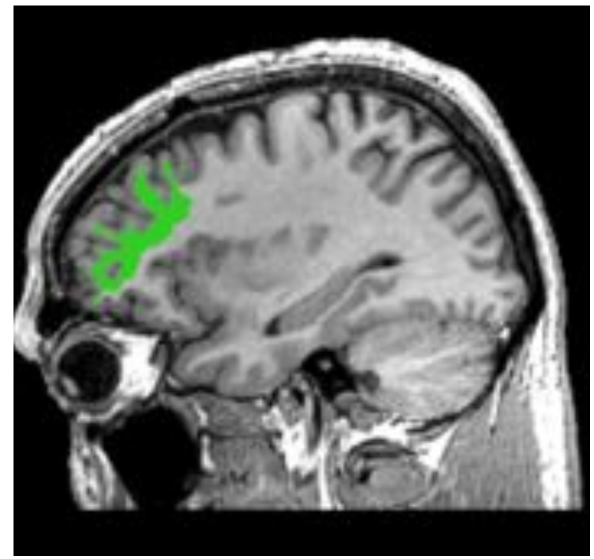
## Mean Diffusivity in the Right Lateral Orbitofrontal Region by Group



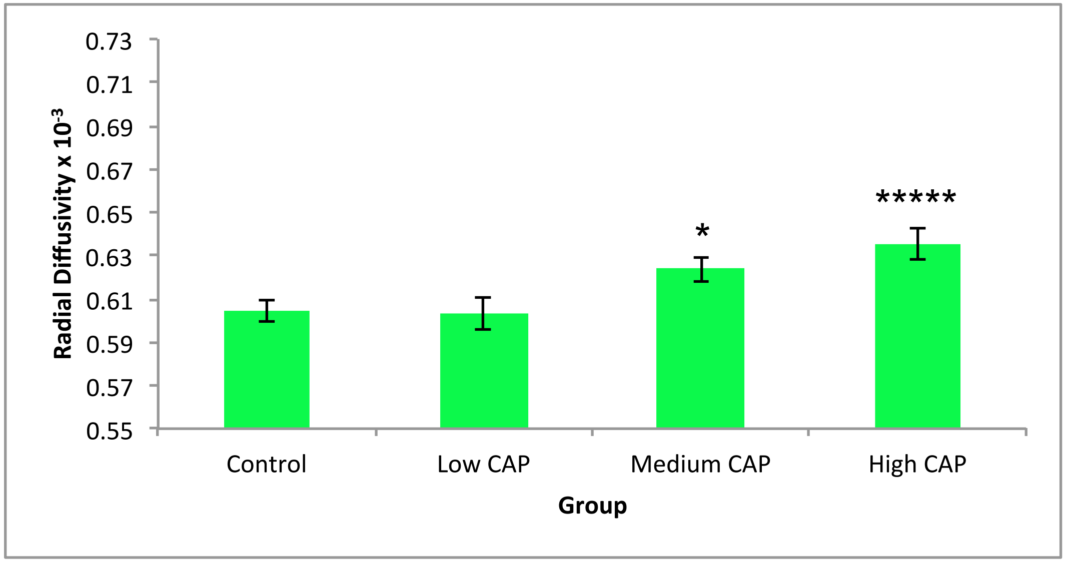



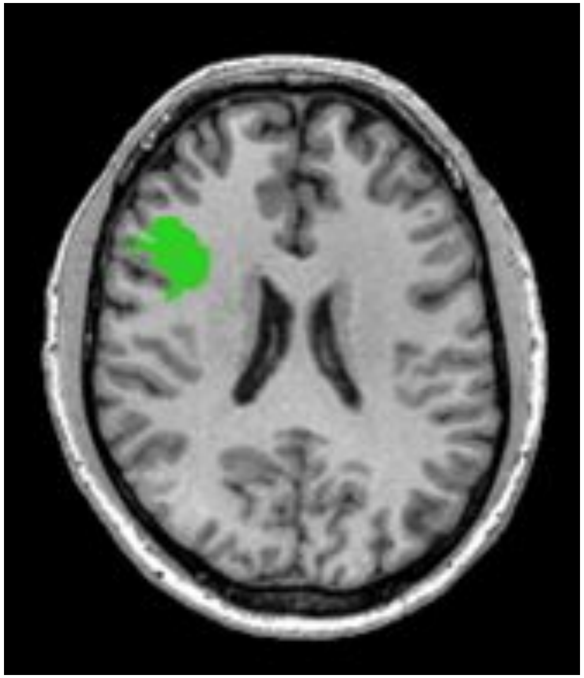
## Mean Diffusivity in the Left Rostral Middle Frontal Region by Group



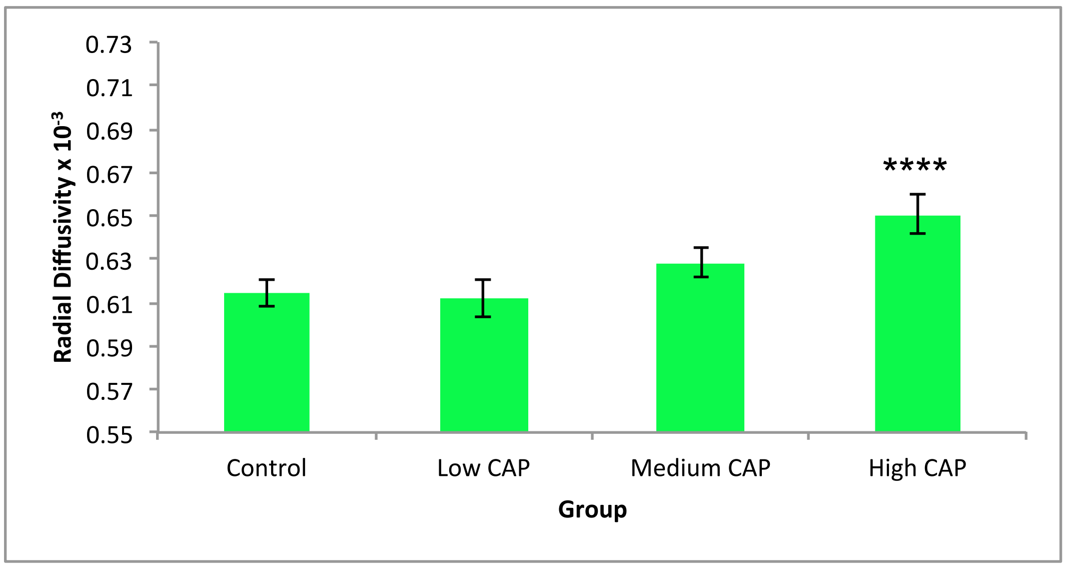



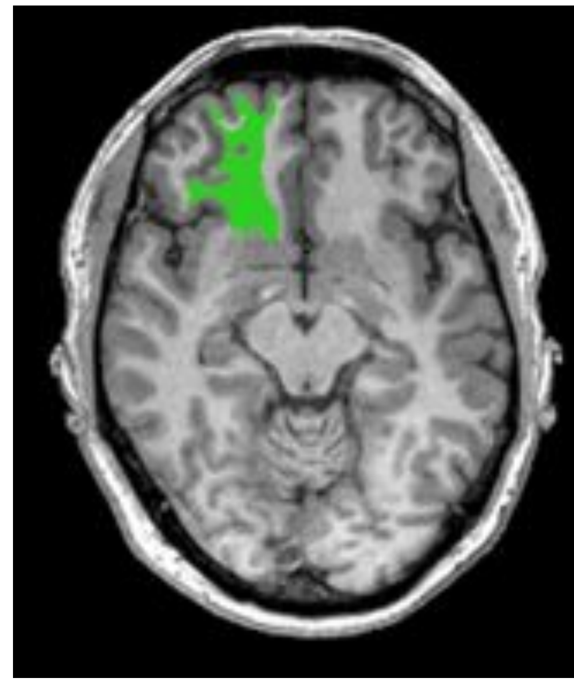
# Radial Diffusivity in the Right Pars Opercularis Region by Group



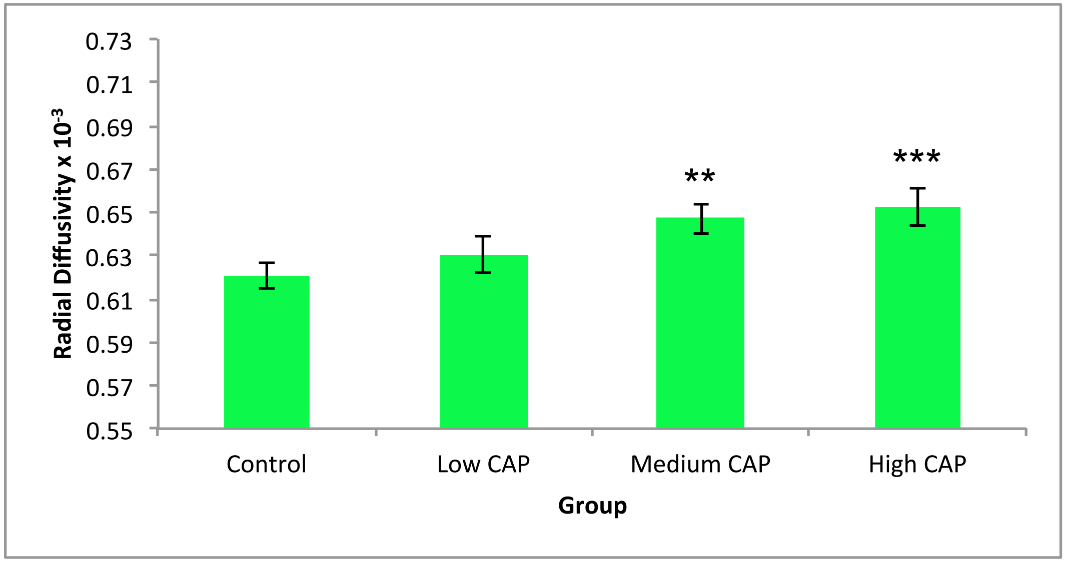



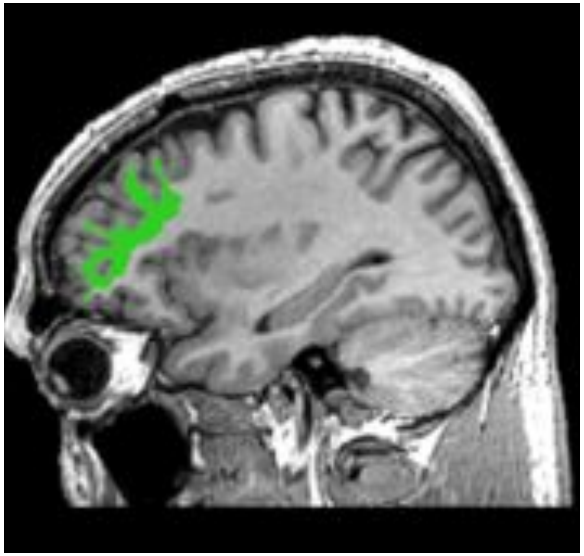
## Radial Diffusivity in the Right Lateral Orbitofrontal Region by Group



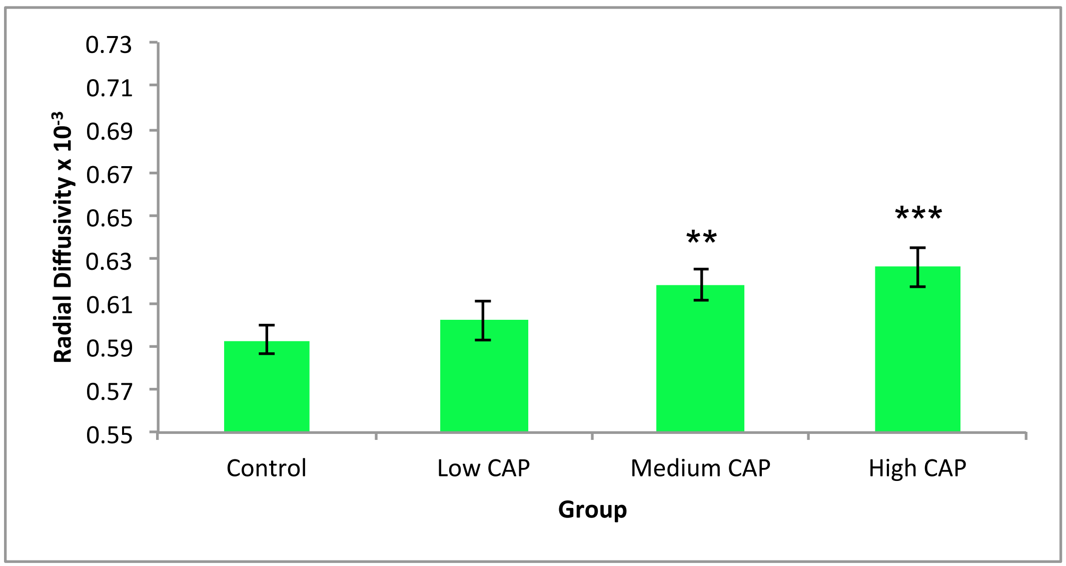



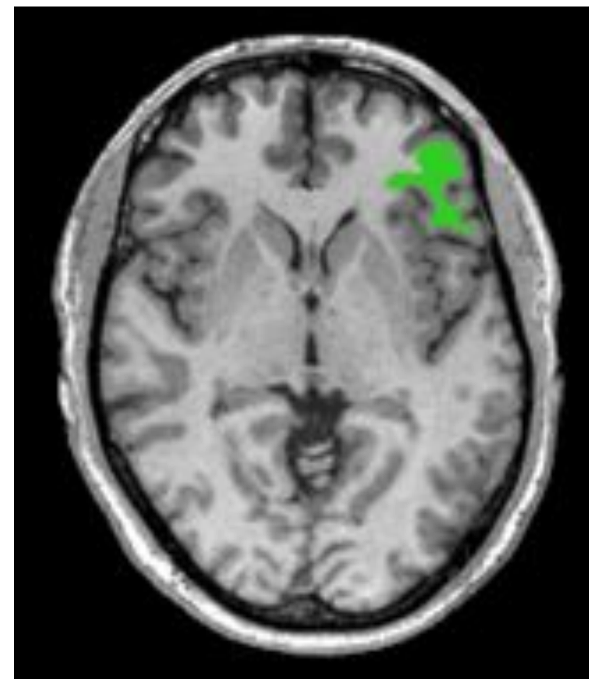
## Radial Diffusivity in the Left Rostral Middle Frontal Region by Group

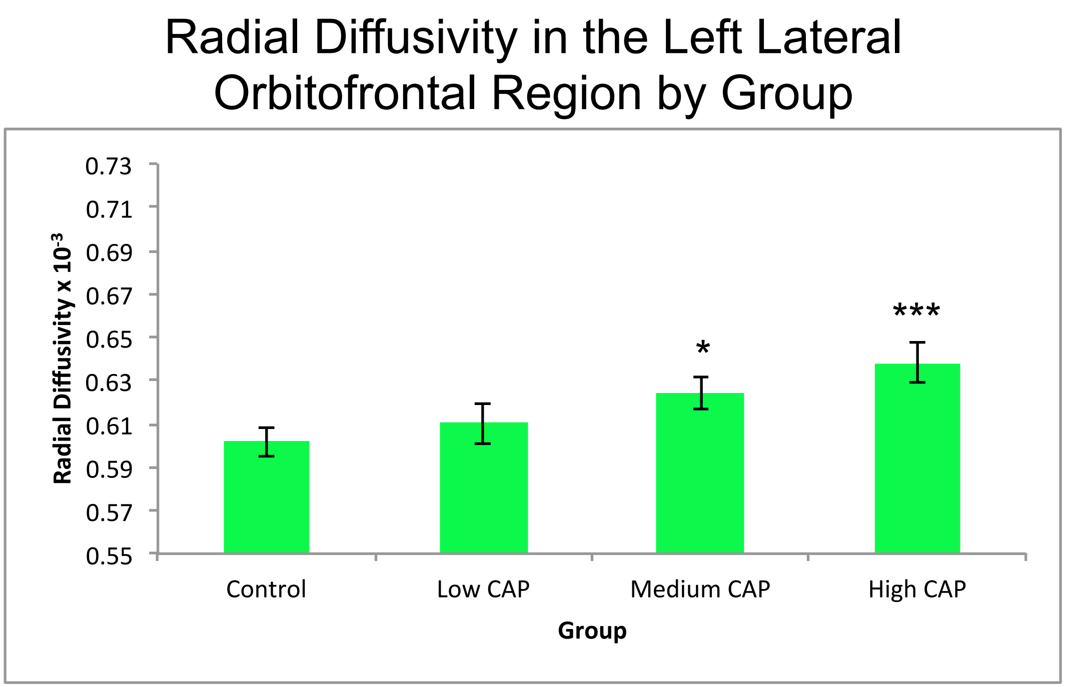


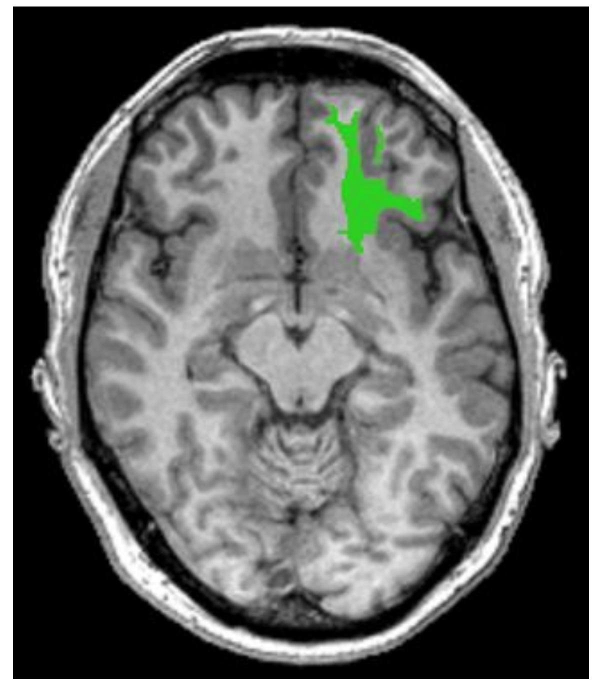



## Radial Diffusivity in the Left Pars Triangularis by Group

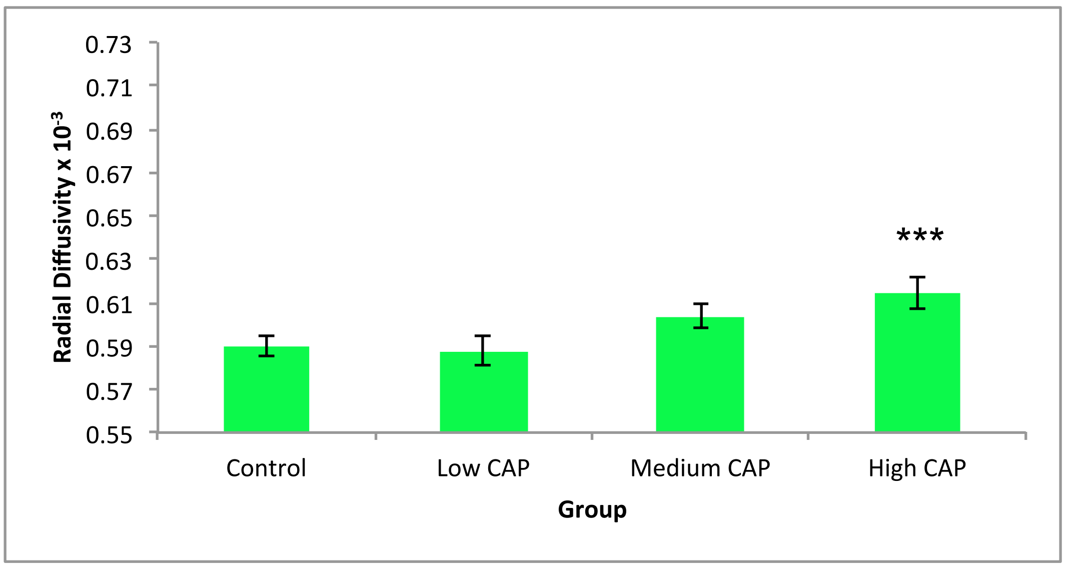


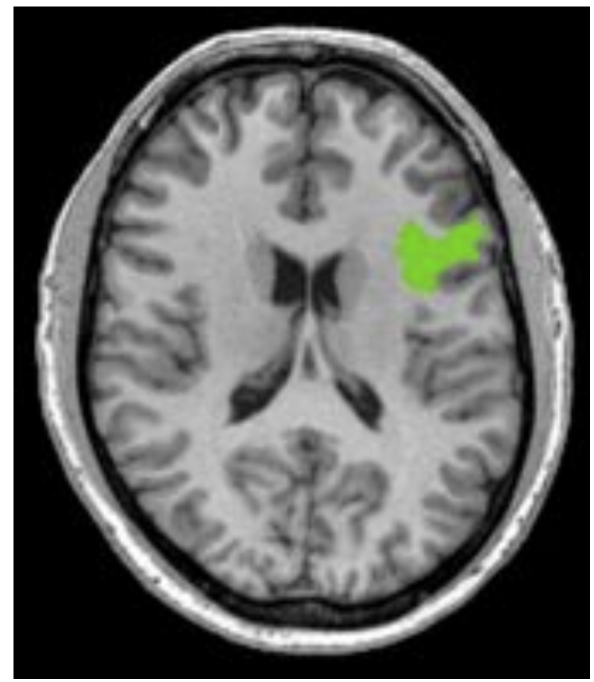



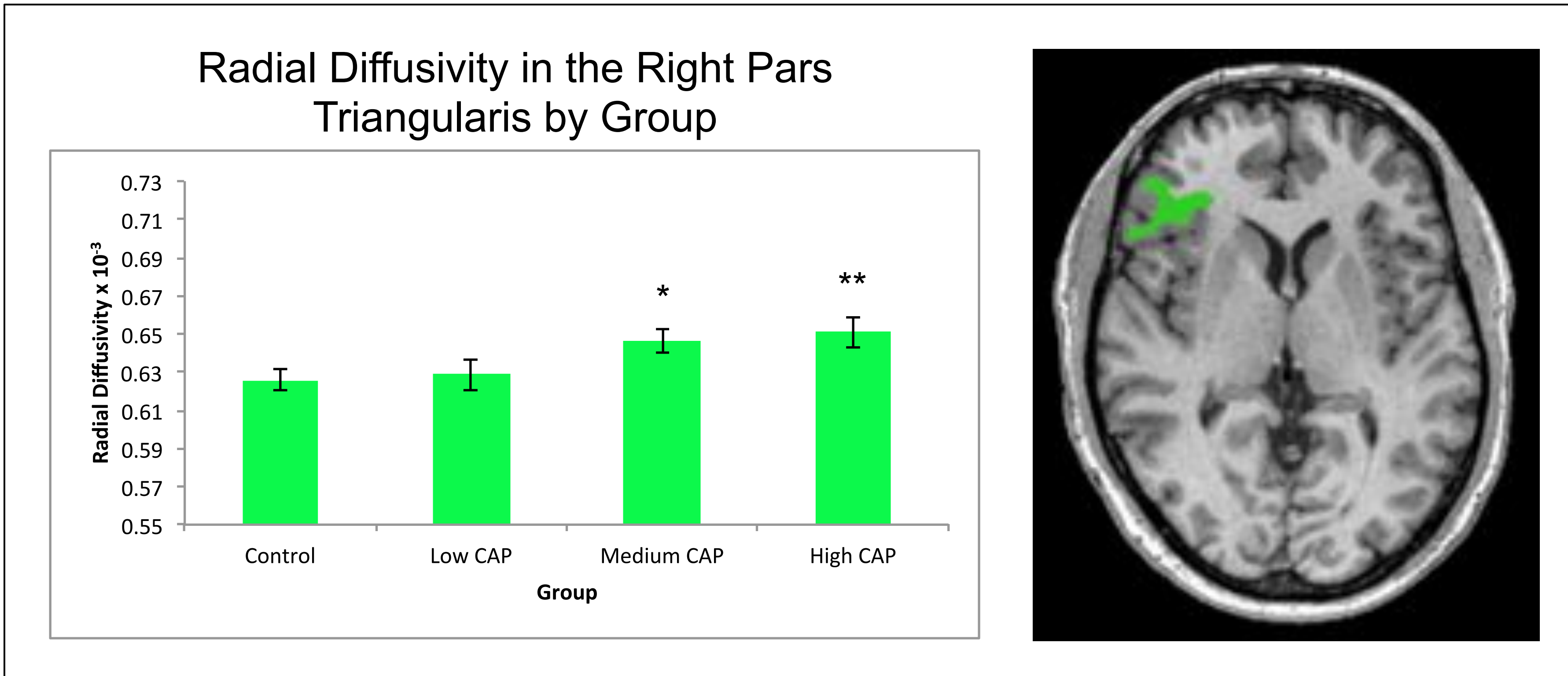

Radial Diffusivity in the Left Lateral Orbitofrontal Region by Group
Radial Diffusivity x 10-3
0.73
0.71
0.69
0.67
0.65
0.63
0.61
0.59
0.57
0.55
*
***
Control
Low CAP
Medium CAP
High CAP
Group

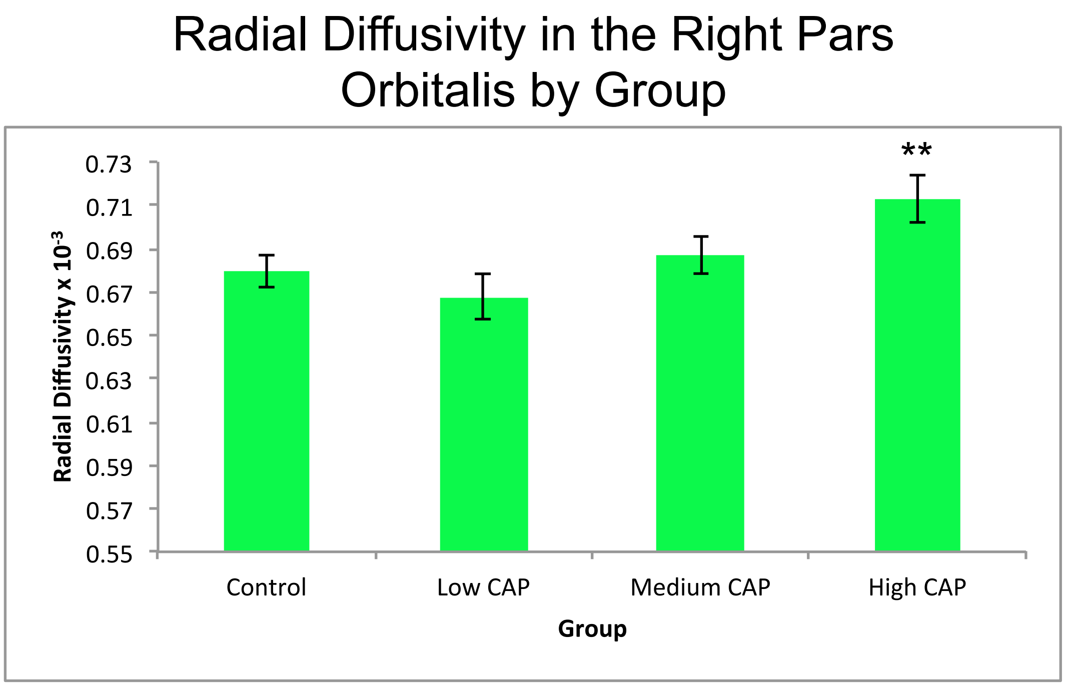


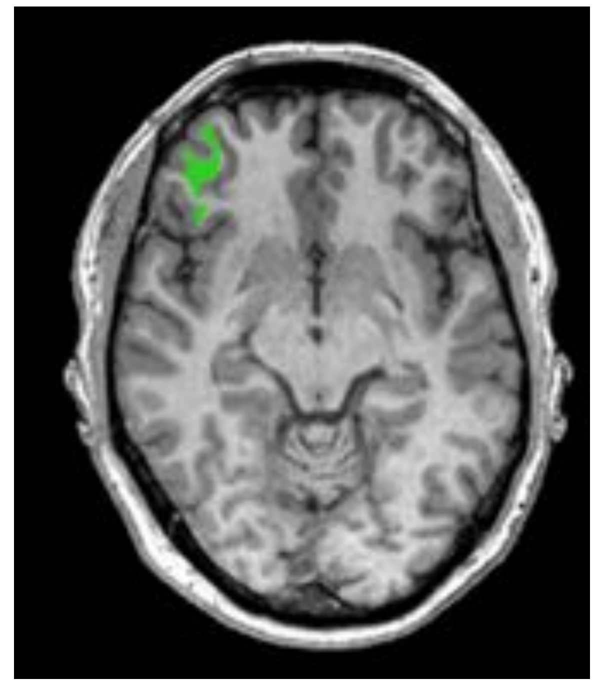
## Radial Diffusivity in the Left Pars Opercularis by Group




Radial Diffusivity in the Right Pars Triangularis by Group
0.73
0.71
0.69
0.67
0.65
0.63
0.61
0.59
0.57
0.55
Radial Diffusivity x 10-3
*
**
Control
Low CAP
Medium CAP
High CAP
Group


Radial Diffusivity in the Right Pars Orbitalis by Group
0.73
0.71
0.69
0.67
0.65
0.63
0.61
0.59
0.57
0.55
Radial Diffusivity x $10^{-3}$
**
Control
Low CAP
Medium CAP
High CAP
Group



# Future

- Seminar Series Spring 2013
- BRAINSCamp 2013
- EHDN DWI Imaging Meeting (Sept 2013)
- Continue Integration of UNC/Utah/MGH in processing tools as they mature
- Deploy on 1000’s of data sets
- Export QC Review Tools for closer Slicer Integration

# Thank You!

- Questions?