

***Morphometry BIRN:  
Analysis,  
Visualization,  
Interpretation  
Update***

Steve Pieper, PhD



2005 mBIRN Retreat

# Overview

- Review of mBIRN AVI Overall Goals
- Specific Projects and Milestones
  - Segmentation
  - Shape Analysis
  - Diffusion Analysis
  - Integrated Visualization
  - Query Atlas
  - Machine Learning
- Interaction with Other Efforts in BIRN
- Interaction with Non-mBIRN Projects

# AVI Goals

- *Apply* Best Available Tools and Technology to Address mBIRN Testbed Aims
  - E.g. FreeSurfer for AD Analysis
- *Adapt* Tools to Work in mBIRN Environment
  - E.g. LDDMM on TeraGrid
- *Develop* New Tools when Needed for mBIRN-Specific Problems
  - E.g. BIRNDUP Pipeline for Data Sharing

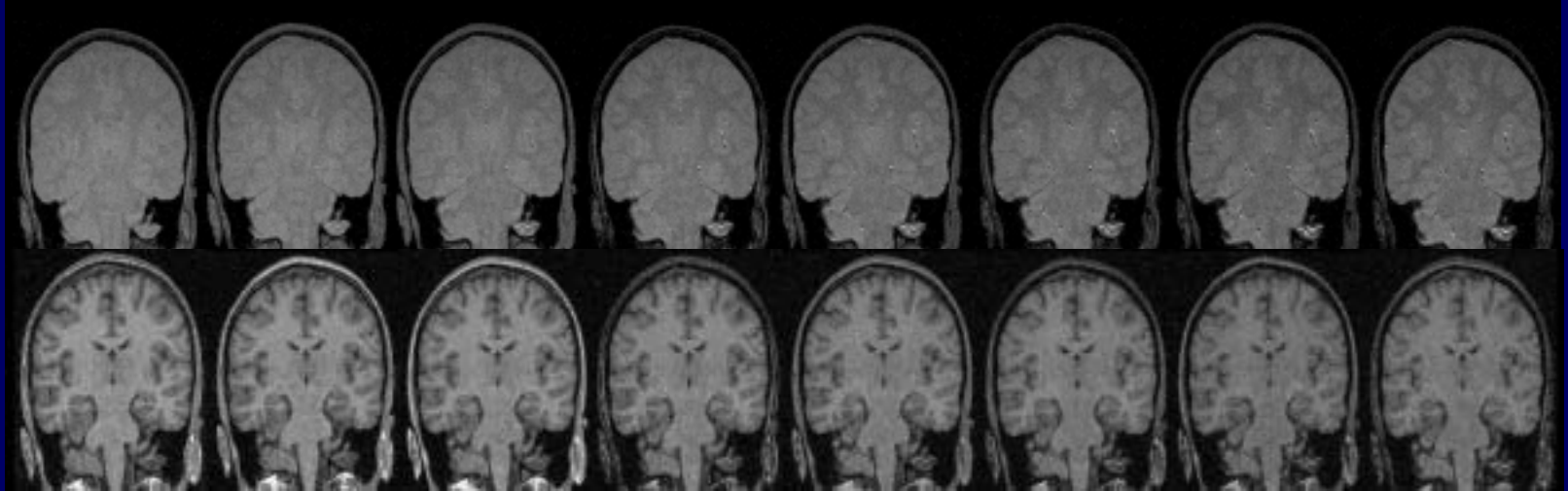
# AVI Milestones / Process

- Collected at October, 2004 AHM as Refinements of mBIRN Grant Plans
  - 6 Month Goals for April, 2005
  - 12 Month Goals for October, 2005
- Further Refined in AVI Conference Calls
- Project Status being Organized through the wiki
  - <http://www.na-mic.org/Wiki/index.php/Mbirn:AVI>

# Segmentation

- Protocol Specific
  - FreeSurfer-Based
  - Extensions to High Field Strength
  - Applied to Multi-Site AD
- Protocol Neutral
  - EMSegmentation-Based (Pohl, MIT; Slicer Team, BWH)
  - Applications to Wide Range of Data (MIRIAD Depression, MS, other)
- Skull Stripping
  - Best Practices Study
- Defacing
  - Recognition Study
  - Brain-Preserving
  - BIRNDUP Application for Redistribution

# Multi-echo FLASH Sequence



## Advantages:

- Less B0 distortion due to its high bandwidth, and less intensity variation
- Enables estimation of tissue parameters (T1, PD, T2\*)
- High CNR for more accurate subcortical segmentation

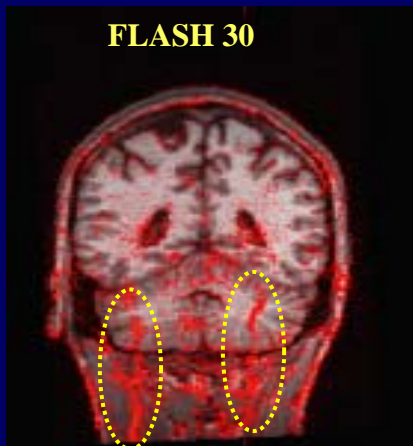
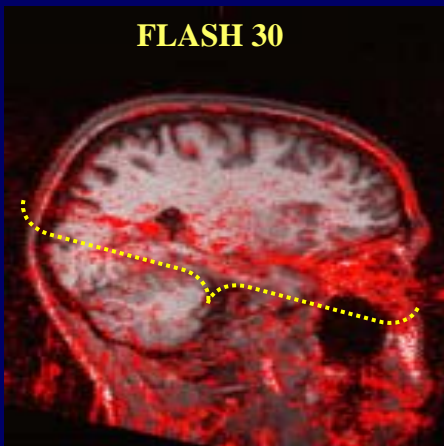
# Multi-echo FLASH Sequence

EYE MOTION

FLOW

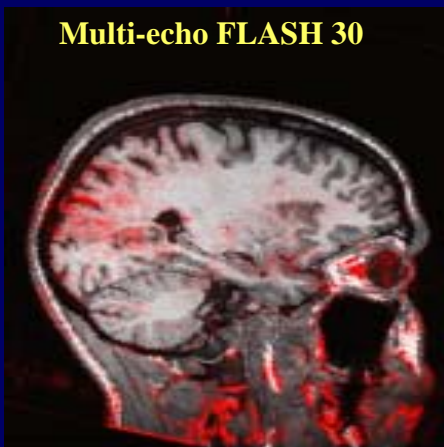
FLASH 30

FLASH 30



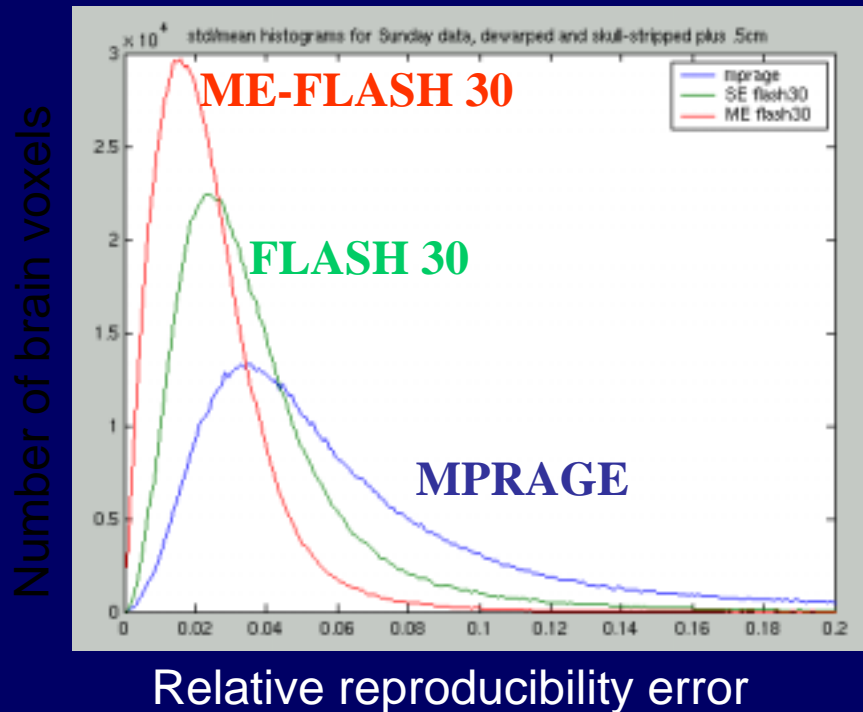
Multi-echo FLASH 30

Multi-echo FLASH 30



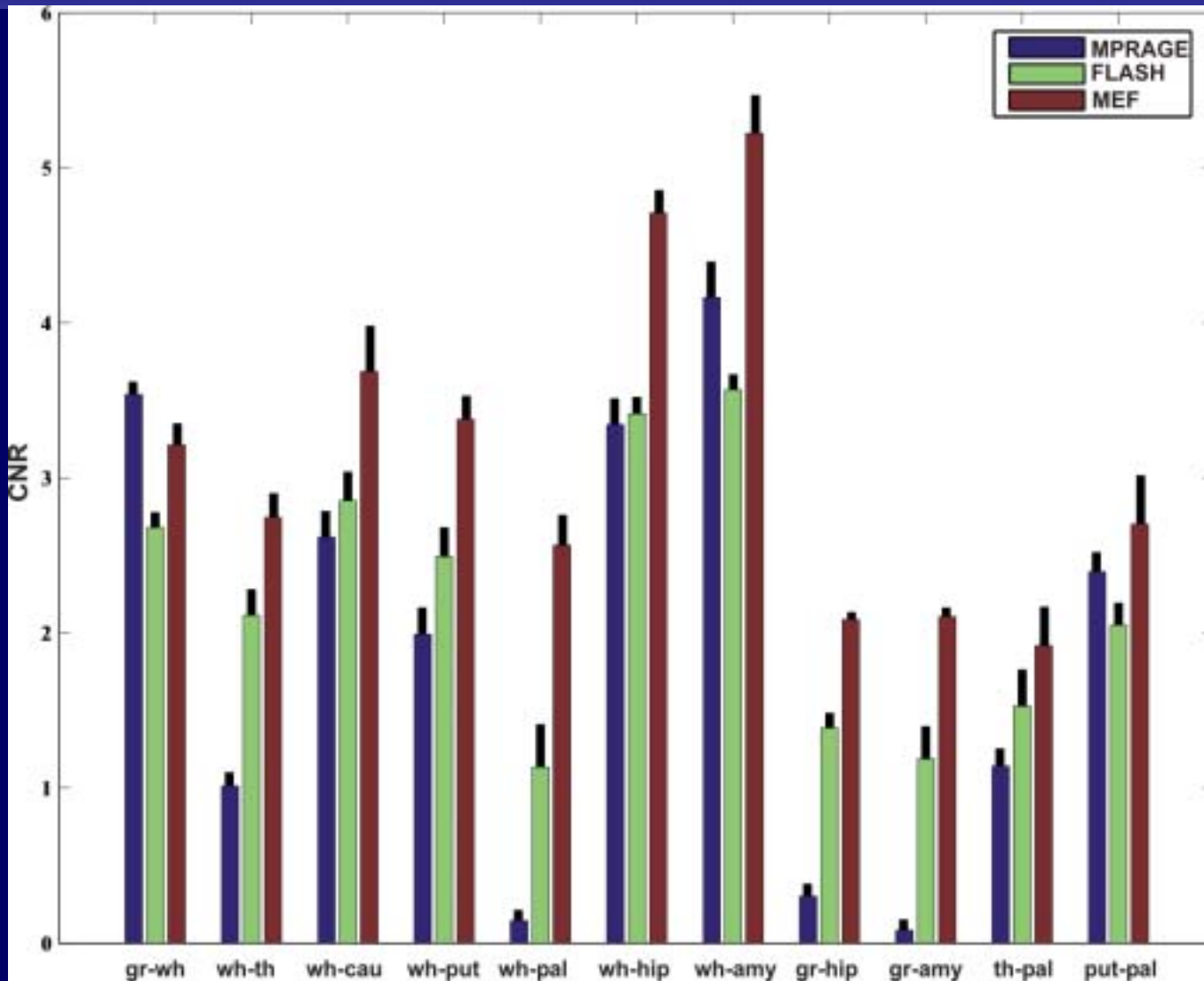
Overlay threshold: 8%

Image intensity histogram of relative test-retest variability



Improving within site, within session reproducibility

# Multi-echo FLASH Sequence

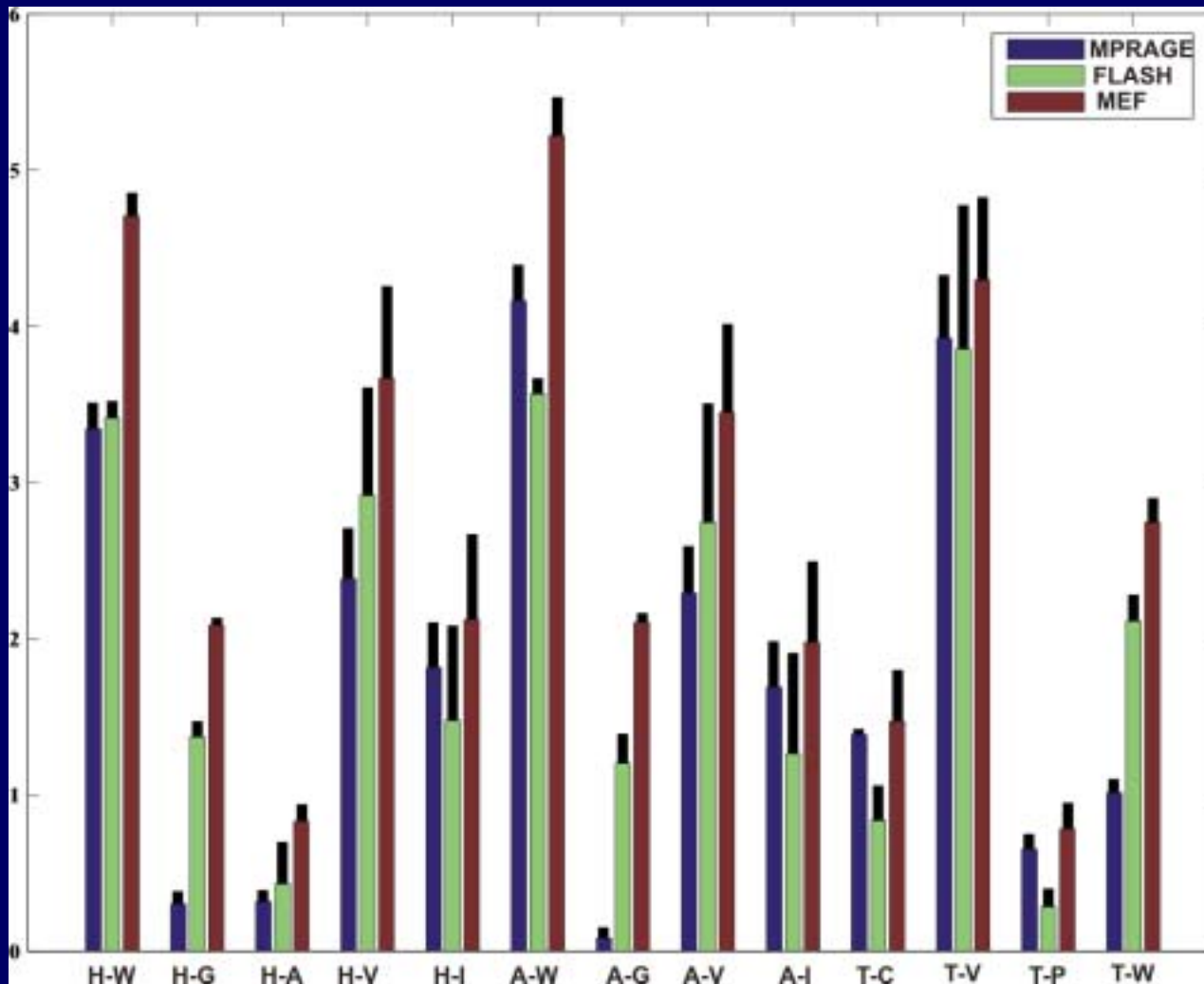


gr: Gray Matter  
wh: White Matter  
th: Thalamus  
cau: Caudate  
put: putamen  
hip: Hippocampus  
amy: Amygdala  
pal: Pallidum

MEF provides higher CNR for subcortical structures



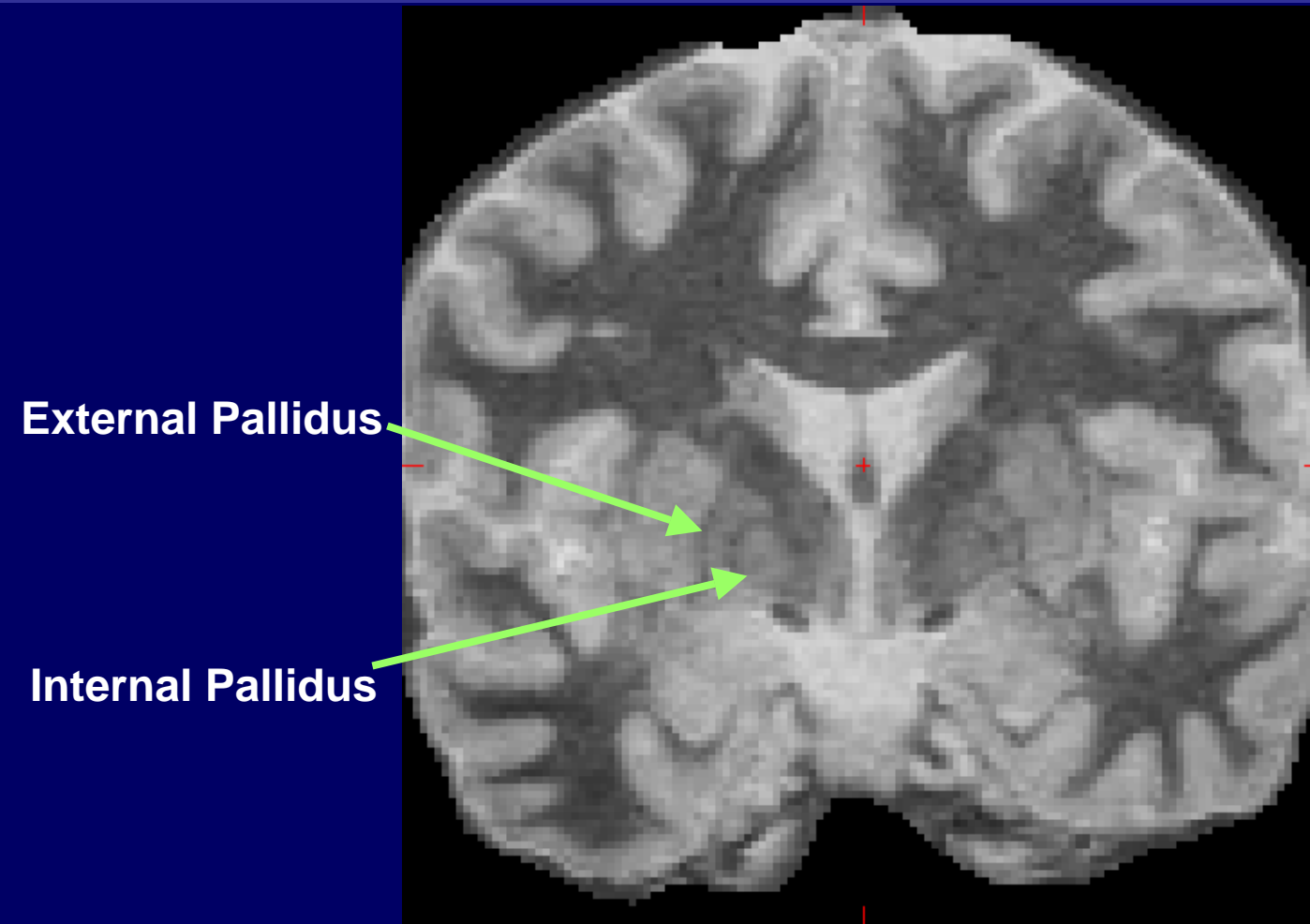
# Multi-echo FLASH Sequence



**W: White Matter**  
**G: Gray Matter**  
**H: Hippocampus**  
**A: Amygdala**  
**T: Thalamus**  
**V: Lateral Ventricle**  
**I: Inf. Lat. Ventricle**  
**C: Caudate**  
**P: Pallidum**

MEF provides higher CNR for subcortical structures

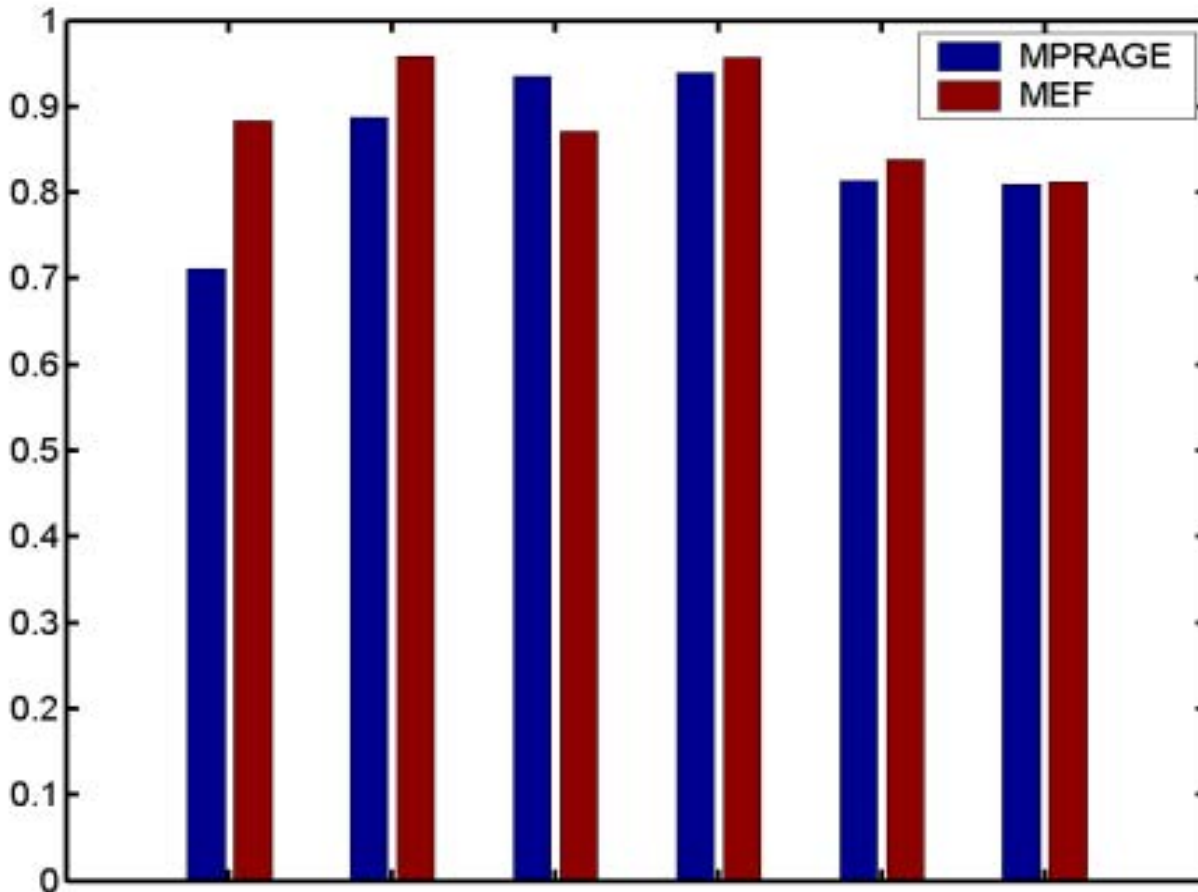
# Multi-echo FLASH Sequence



Optimal image can be synthesized from original echo images for better visualization of subcortical structures

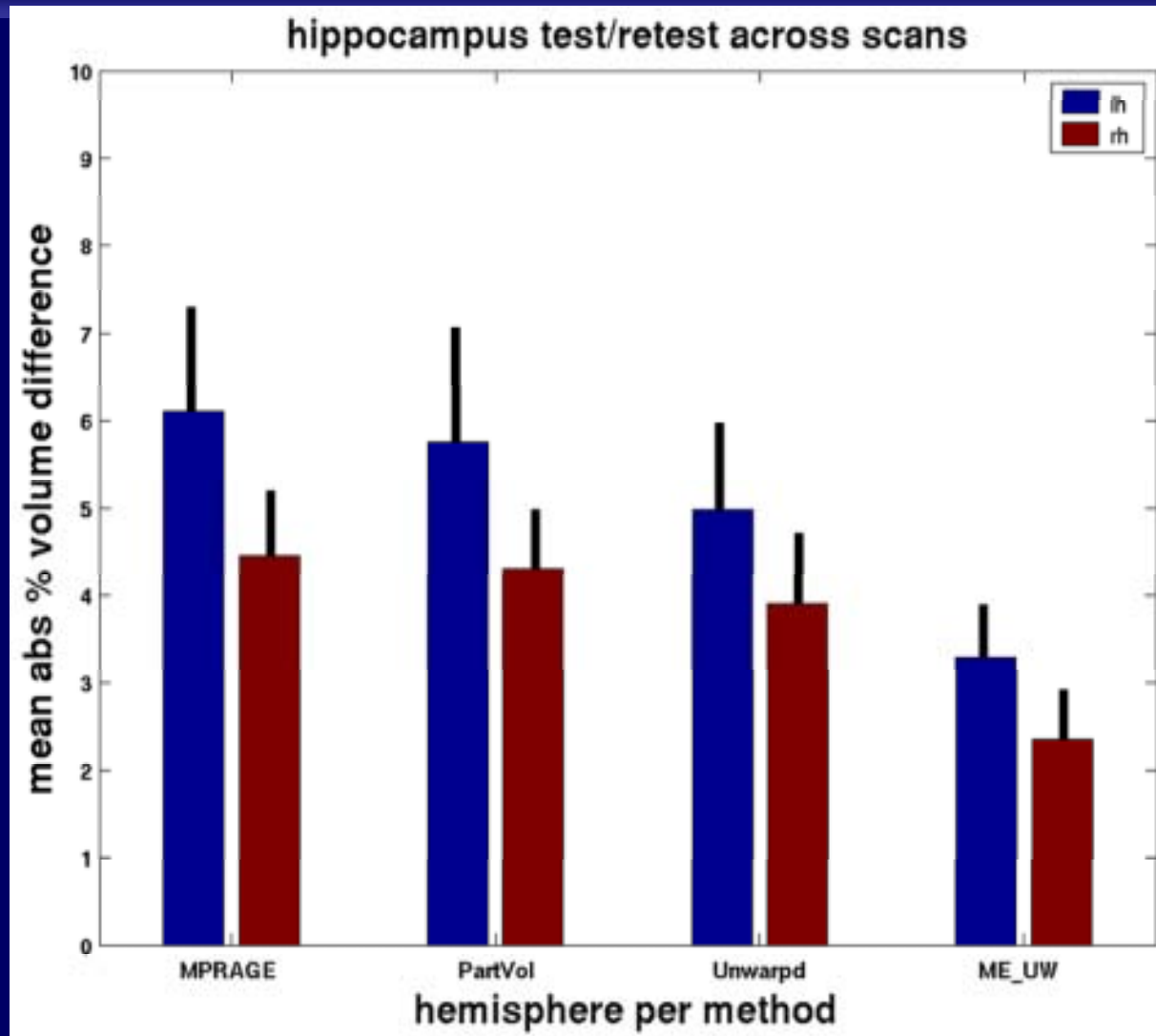
# Multi-echo FLASH Sequence

Intra-class Correlation coefficients across repeated scans



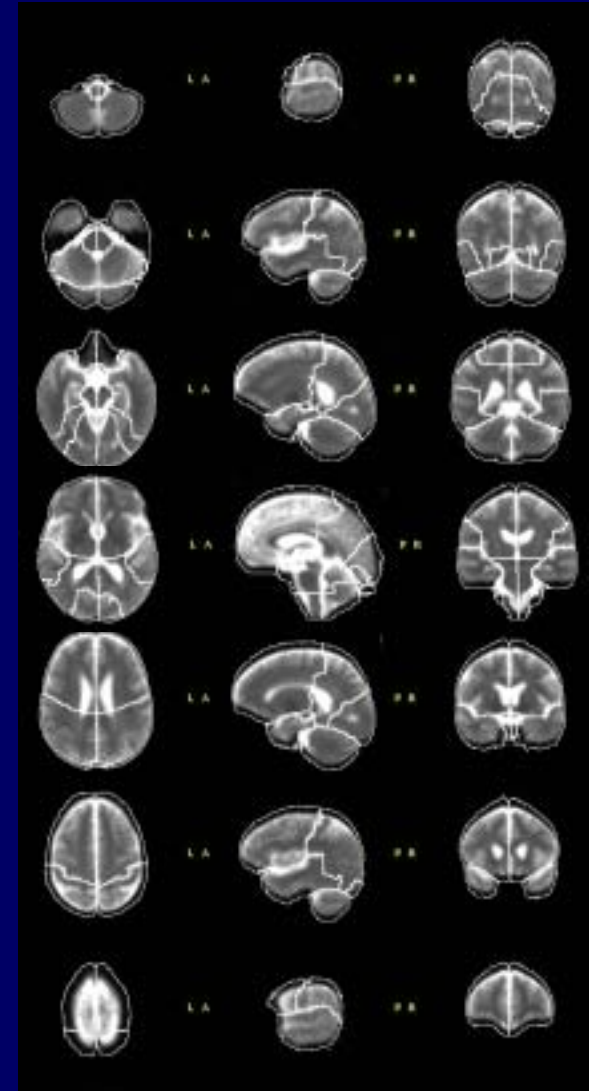
MEF gives better subcortical segmentation reproducibility

# Multi-echo FLASH Sequence



MEF gives better subcortical segmentation reproducibility

- MIRIAD Clinical Paper in Final Stages of Preparation
  - MacFall et al
  - Describes Application of mBIRN Systems (LONI Lobar Atlas) to Duke Longitudinal Depression Study
  - Found Greater White Matter Lesion Volume in Temporal Lobes in Depressed vs. Controls



# Protocol Neutral Plans

- Apply Newly Developed EMSegmentation from MIT / BWH Collaboration (NAC P41)
  - Improved Atlases and Techniques
  - Integrated Registration with Segmentation
- Continue Work with BWH Center for Neurological Analysis (C. Guttman, L. Liu)
  - Draw on CNI Radiological and Neurological Expertise in White Matter Lesion Segmentation
  - MIRIAD Processing Stream is being Tested on MS Data Sets
    - Initial results indicate that MIRAD can work on difficult cases where previous approach failed
    - Improved Pipeline and General Parameters in 6 months
    - A Formal Comparison will be done over the next 12 months
  - Integrate Tool for Multiple Applications

# CNI Lesion Analysis of MS

- Simon Warfield, et. al. “Automatic Identification of Grey Matter Structures from MRI to Improve the Segmentation of White Matter Lesions” the Second Annual International Symposium on Medical Robotics and Computer Assisted Surgery, November 4-7, Baltimore, USA.
- Warfield S, Robatino A, Dengler J, Jolesz F, Kikinis R. Nonlinear registration and template-driven segmentation. In: Toga AW, editor. Brain warping. San Diego: Academic Press; 1999. p 67–84.
- Wei et al. [Quantitative Analysis of MRI Signal Abnormalities of Brain White Matter With High Reproducibility and Accuracy](#). J. Magn. Reson. Imaging, 2002; 15:203-209.

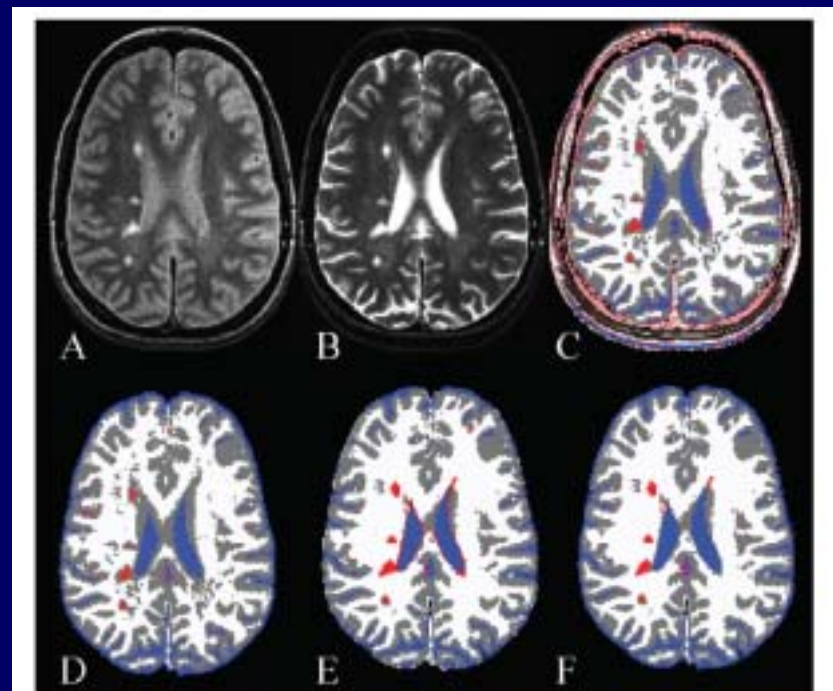
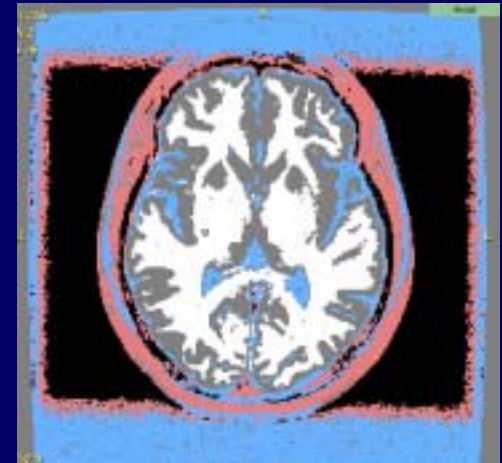
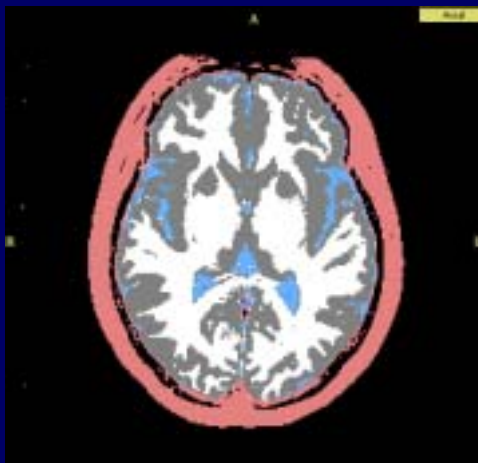
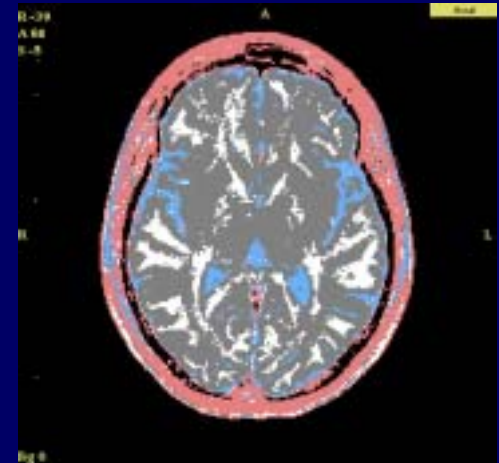
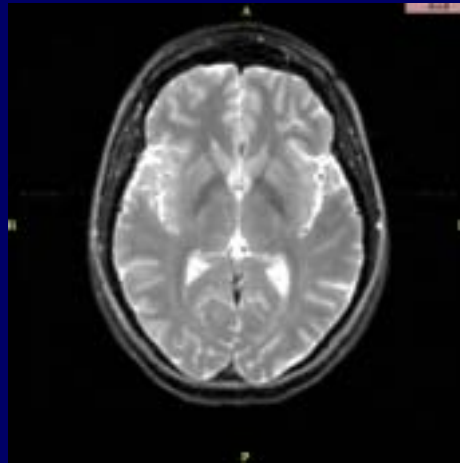
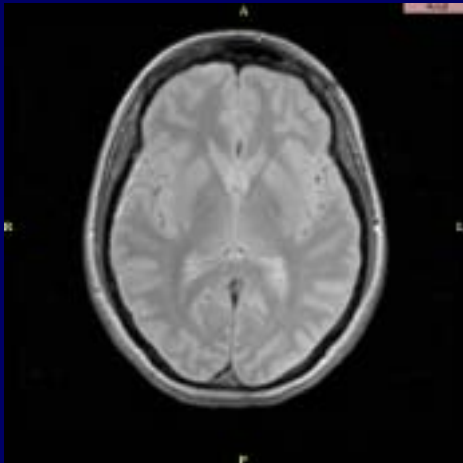


Figure 1. Segmentation of WMHA. Proton-density-weighted (A) and T2-weighted (B) images at the level of the lateral ventricles of the brain of a clinically definite MS patient. WMHA are visible in the right centrum semiovale. Corresponding segmented images obtained by three-dimensional EM segmentation (C), PNEC pipeline (D), TDS pipeline (E), and TDS+ pipeline (F) show labels: gray matter = gray, white matter = white, WMHA = red, CSF = black. The EM segmentation algorithm generated a preliminary segmentation of gray matter, white matter, WMHA, and CSF. Spurious WMHA were found at the boundaries between CSF and brain parenchyma (type I misclassifications), while a large part of the WMHA were classified as gray matter (type 2 misclassifications) (C). PNEC eliminated most type I misclassifications (D), whereas TDS corrected type II misclassifications and part of type I misclassifications (E). While a few spurious WMHA persisted, the TDS+ pipeline corrected most of the two kinds of error, and generated much better segmentations of WMHA (F).

# Parameter Sensitivity

- MIRIAD Segmentation Applied to MS Data



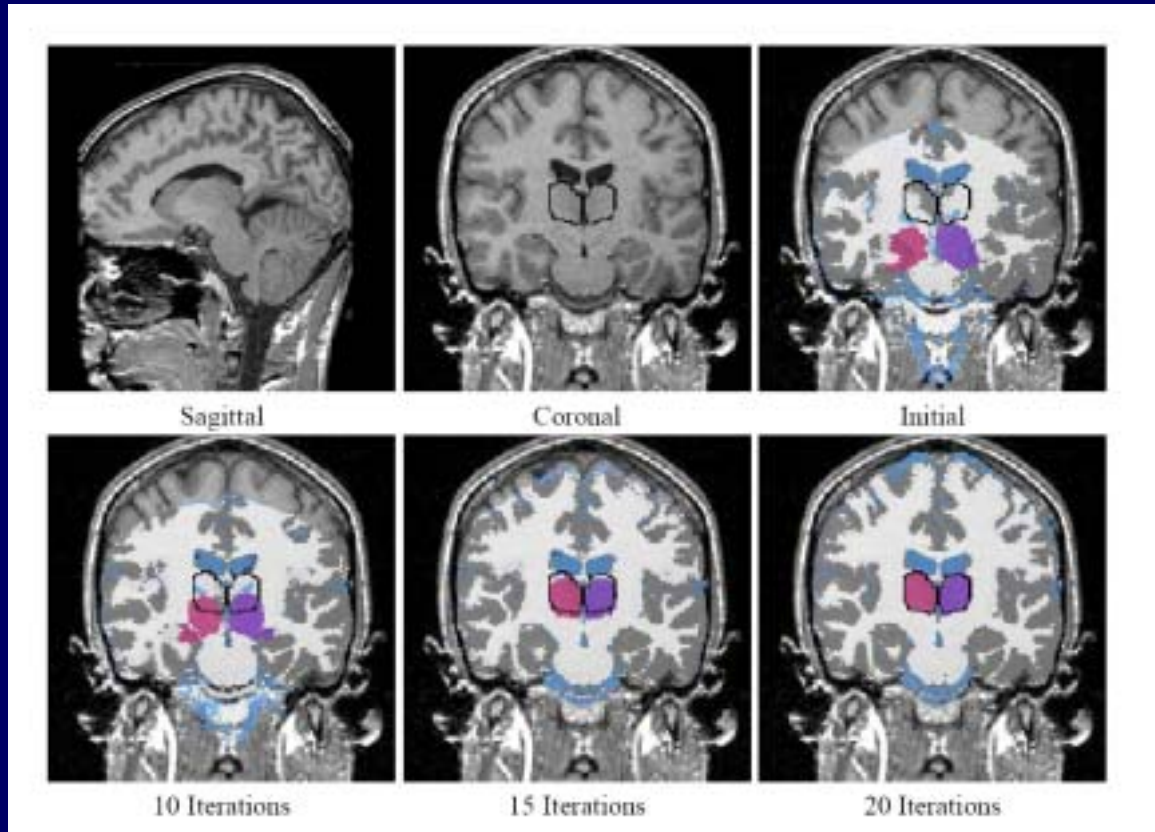


# CNI Challenges

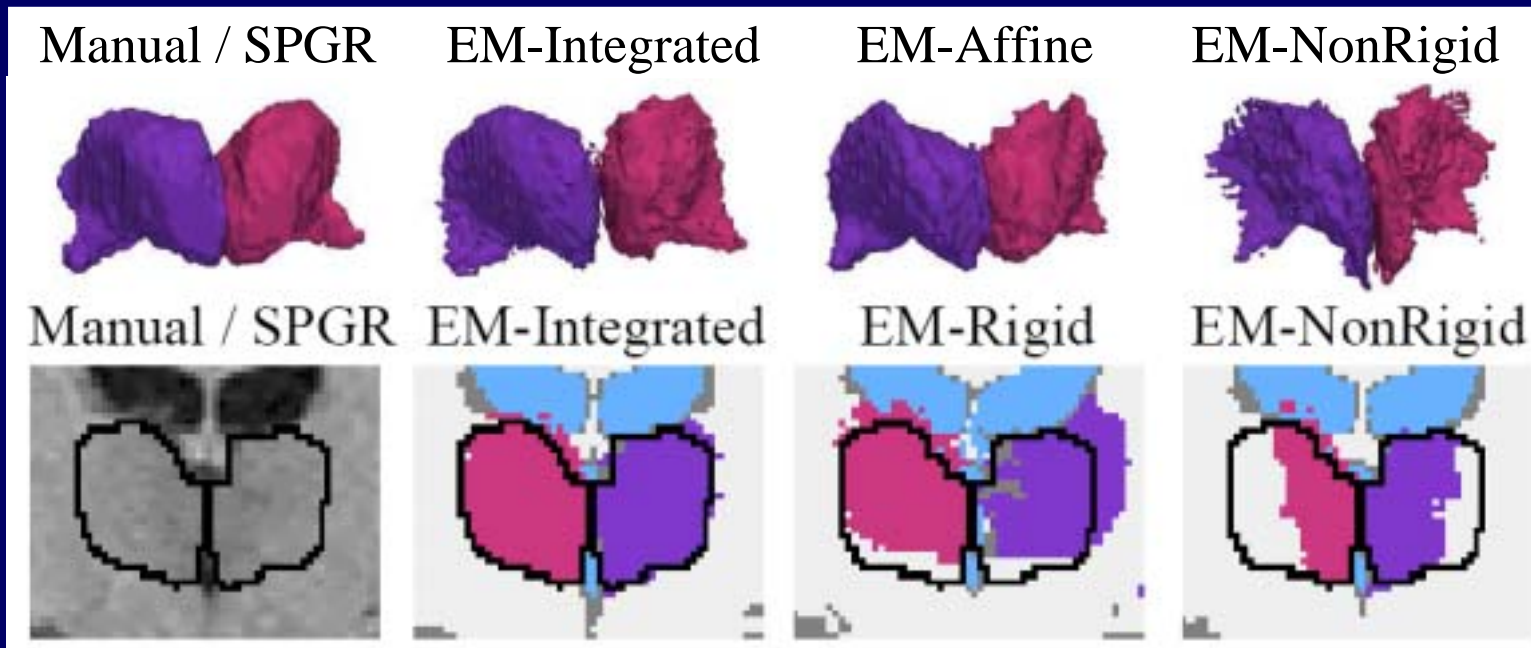
- Different scanners may have differences in the gain field, signal intensity range, and signal/noise ratio.
- Tissue intensity inhomogeneity among different levels of the brain slices.
- Background ( eyes, skin and bones ) may be misclassified when adjusting weights of atlas for different tissues.
- Comparison with gold standards and just view by experts?
- Atlas may not fit for all age people and diseases.

# New EMSegment Technique

- Pohl (MIT)
  - Address limitations of Atlas Registration
  - Single Statistical Formulation for Registration and Segmentation
  - Promising Initial Results in a 30 Subject Study

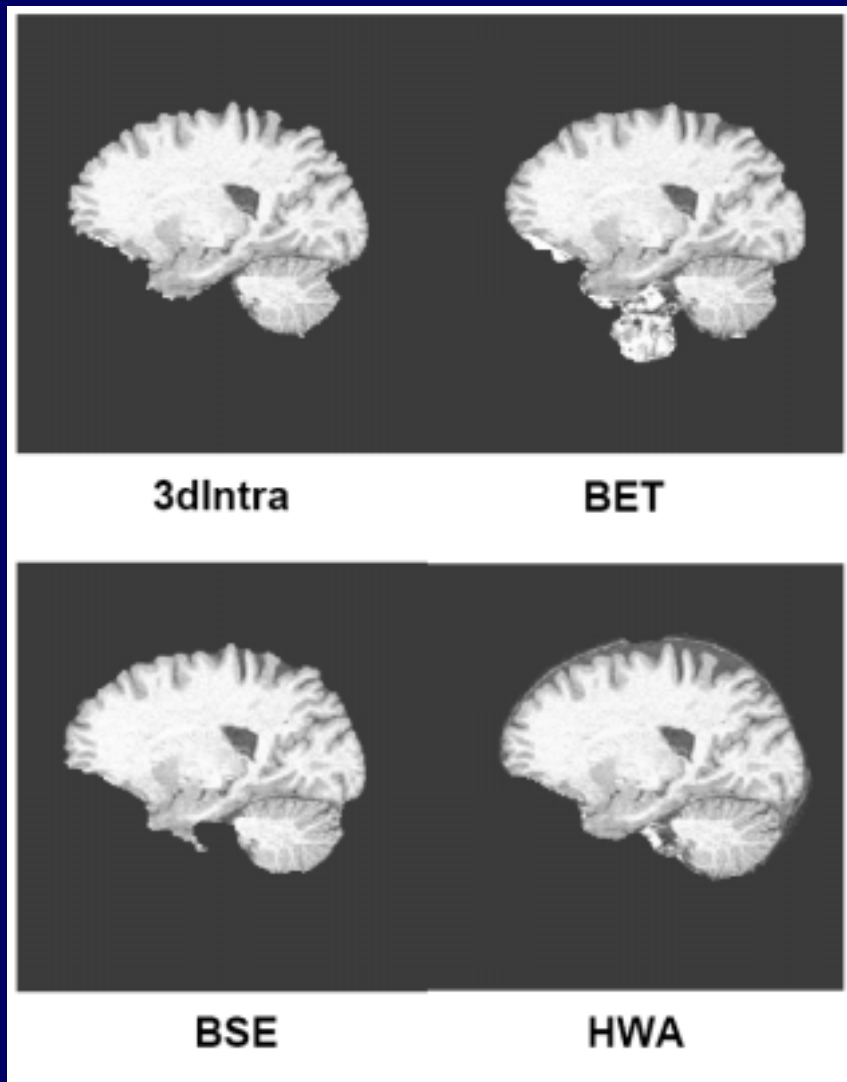


# Integrated Registration Example



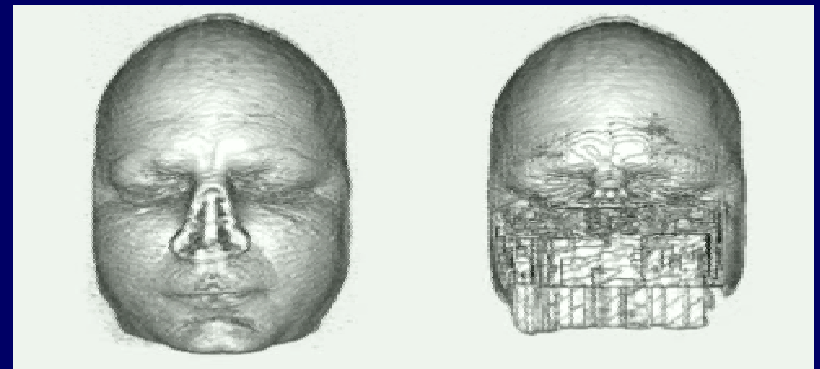
# Skull Stripping

- Comparison of 4 Techniques as Byproduct of the Deidentification Research
- Publication in Final Stages of Preparation
  - Manuscript Accepted for Publication at HBM
  - Fennema-Notestine et al.



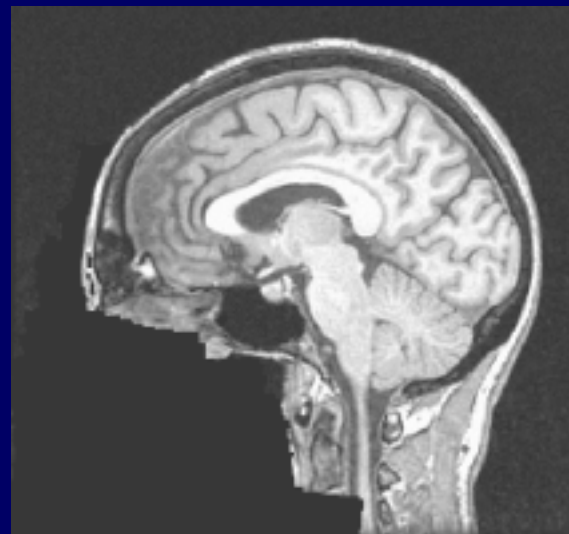
# Defacing Algorithm: Method

- Defacing uses models of non-brain structures for removing potentially identifying facial features from T1-weighted volumes (*Fischl, MGH*).
  - Facial features of 10 subjects were manually labeled; an optimal linear transform was used to build a face membership atlas.
  - When a novel image is presented, the optimal linear transform is computed for the input volume (*Fischl et al 2002*).
  - A brain mask is constructed by summing the prior probabilities at each image location of all brain tissue and then morphologically dilated to yield a mask indicating the presence of brain within x mm of each voxel.
  - Finally, all voxels outside mask with a non-zero probability of being a facial feature are set to 0.



# Defacing: Brain Untouched

- Tested 244 datasets: depressed, Alzheimer's, elderly and young control groups (*UCSD Bischoff-Grethe, Fennema-Notestine, Morris, Ozyurt, Clark, Brown; Bischoff-Grethe et al. 2004 HBM abstract*)
  - Qualitative visual inspection of the defaced images showed none had brain tissue removed.
  - Preliminary quantitative analyses examined 16 datasets that were conservatively<sup>1</sup> skull-stripped (*Segonne et al., 2004*).
    - $0.03 \pm 0.07\%$  of voxels in skull-stripped volume were removed by defacing.
  - Overall, results suggest that the automatic defacing algorithm is robust and efficiently removes non-brain tissue that would have similarly been removed via skull-stripping.
  - Methodology and statistical manuscript is in preparation (*Bischoff-Grethe, Fischl et al.*).



<sup>1</sup>based on *Fennema-Notestine et al. (Accepted)*

# Defacing: Truly De-identified?

- Present work focuses on a behavioral paradigm to assess the effectiveness of defacing MR volumes in leaving the data truly un-identifiable:
  - Stimuli include photographs and 2D views of rendered, defaced T1-weighted volumes from a group of local individuals; images will be presented in  $\frac{3}{4}$  view.
  - Subjects will participate in a matching task to assign photographs to defaced MR views and to rate the level of familiarity with faces.
  - Data will be collected from two participant groups, one group familiar with individuals pictured in the study and another group unfamiliar with these same individuals. This is crucial since familiarity influences an individual's approach to recognition (*Clutterbuck & Johnston, 2002*).

# Shape Analysis

## ■ Large Scale Computation

- Successfully used TeraGrid and BIRN SRB. Completed LDDMM processing through collaboration (storing data at different physical locations)
- Morphometry BIRN - scaled run of 45 subjects (30,000 CPU hours, 4 TB data)
- Mouse BIRN – Fragile X mouse data (3,000 CPU hours, 0.47 TB data)
- Large scale testing of SRB with BIRN CC
- LDDMM Optimization: studying algorithms to identify potential optimization
- Benchmarking: work in progress to improve LDDMM code performance

## ■ Statistical Metrics

- Completed analysis of scaled run of 45 subjects. Results to be presented at Human Brain Mapping 2005.
- Dr. Miller to elaborate on findings at Miami meeting Plenary talk.

## ■ Visualization Integration

- Generated script to extract and visualize Atlas/Target/Metric Distance data located on SRB (MayaVi)

## ■ Standardized Representation

- Collection of tools will reside on BIRN 2.0. Standard location of Freesurfer, LDDMM and Slicer makes integration possible

## ■ Haystack/LDDMM

- Identified resource to begin LDDMM data conversion to Haystack

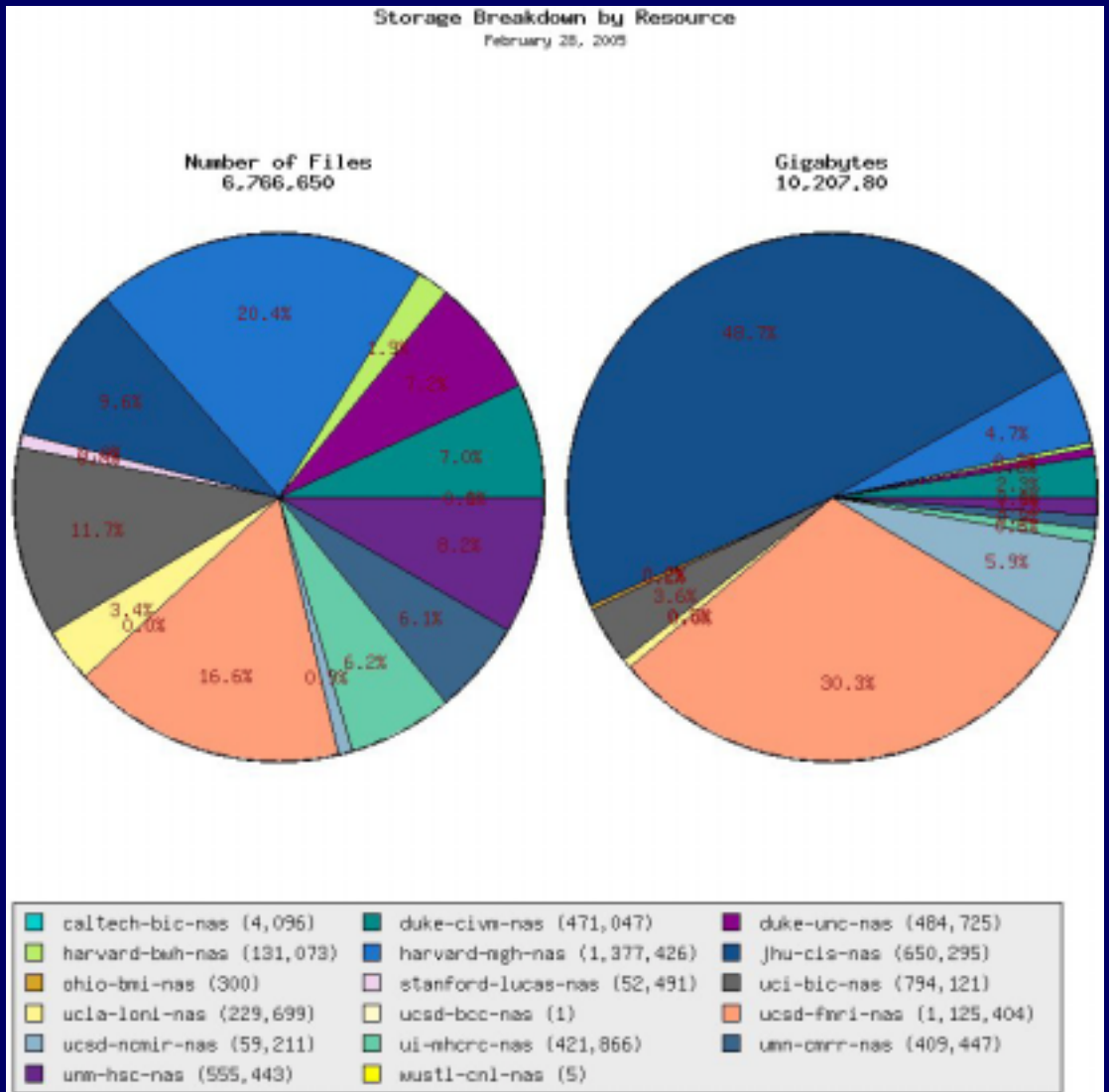
## ■ Near Future Plans

- Define LDDMM table for HID
- Review directory structure of SRB (ensure directory structure adaptable to multiple LDDMM runs with varying parameters)
- LDDMM portal processing to make use of BIRN clusters
- Add 12TB storage to JHU BIRN rack
- Identify file formats used by BIRN tools (LDDMM, Slicer, Freesurfer, Haystack)



# Shape Analysis Data Processing

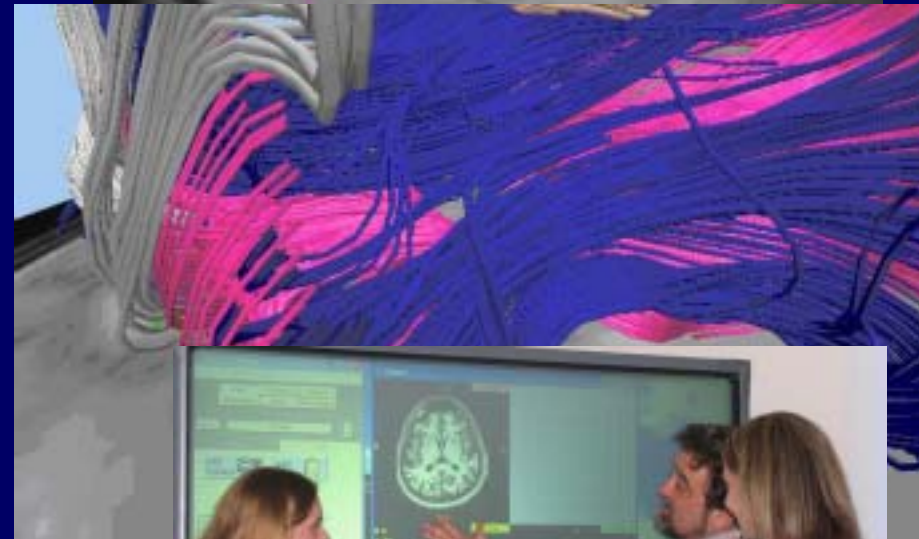
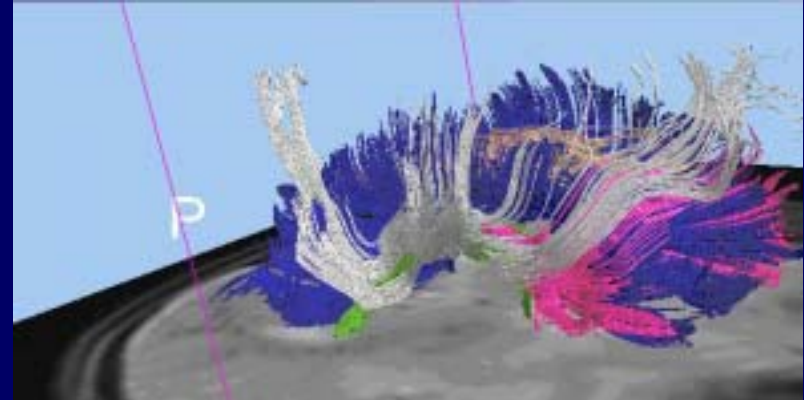
- Successful Collaboration of Large Deformation Metric Mapping using the Storage Resource Broker



- Year 1 Goals
  - Build Interfaces to “Standard” DTI Images
  - Develop Common File Interoperability
- Standard DTI Data Sets
  - mBIRN Sites: MGH, Duke, JHU, BWU, UCSD
  - fBIRN Sites: UNM, Ulowa (others expected)
- Common Import Routine in 3D Slicer
  - Protocols defined by: #Baseline, \$Gradient, Directions, B-Value, Image Interleaving, etc.
  - Tested for GE and Siemens; BWH, MGH, UCSD
  - Other Site Protocols should work with Current Interface
  - File Format Evaluation Underway (Nifti, Nrrd, VTK, BXH...)
  - Ties into Visualization Goal

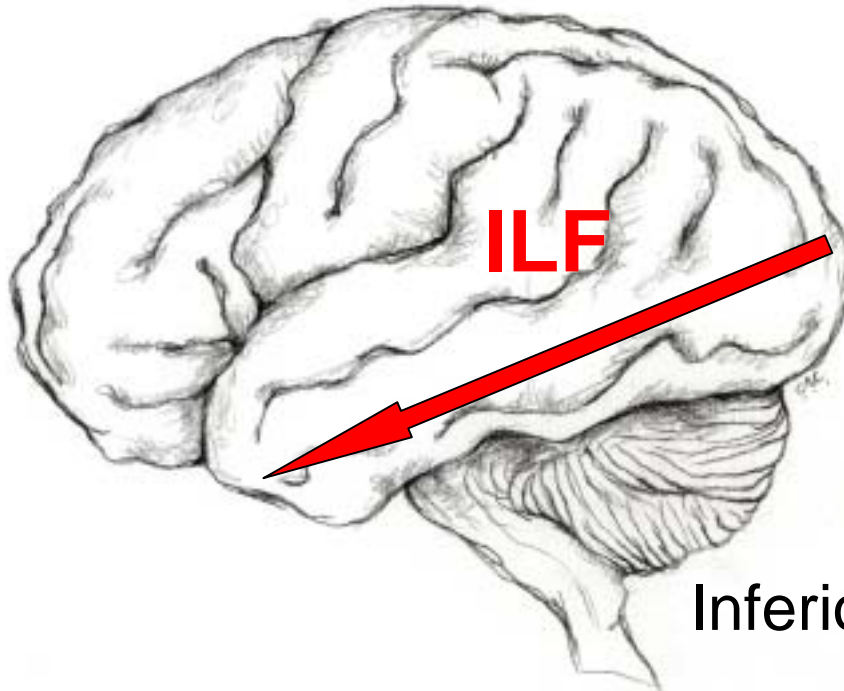
# White Matter Atlases

- Refining What We Need and What We Can Do (Fallon, UCI; Dale, Perry, UCSD; Estepar, Pieper, BWH)
  - Tractography Atlas
  - Label Map Atlas
- Developing Neuroanatomist-Friendly Tools for Atlas Building

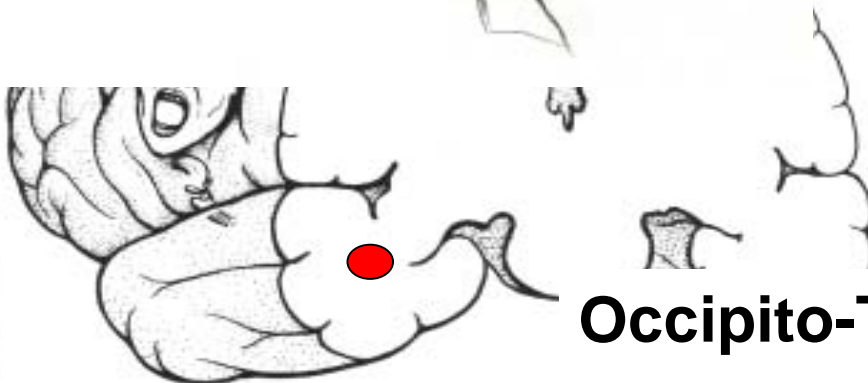


# Tractography Tools

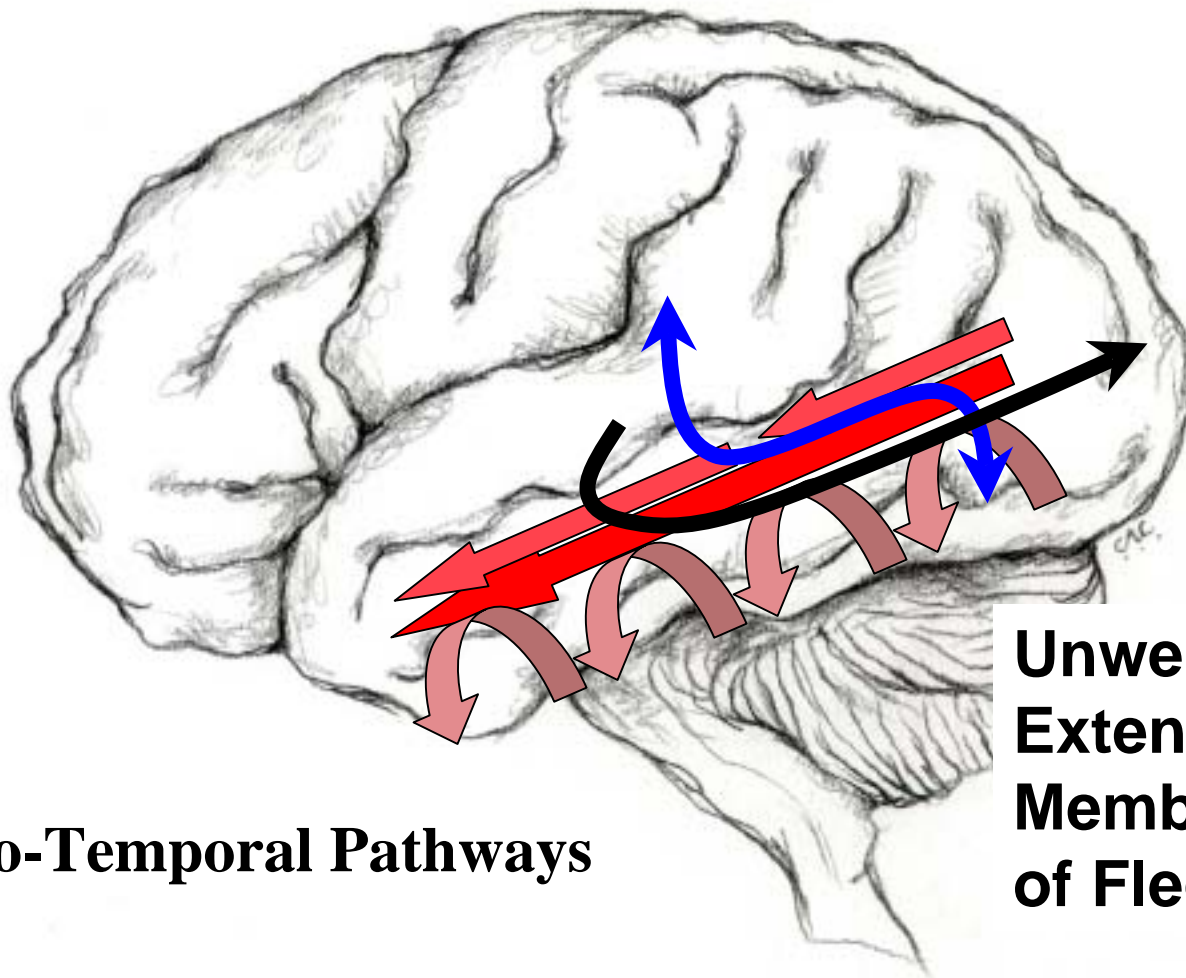
- **Fallon Requirements**
  - **Anatomical Accuracy**
  - **Integrated Data and Tractography**



Inferior Longitudinal Fasciculus

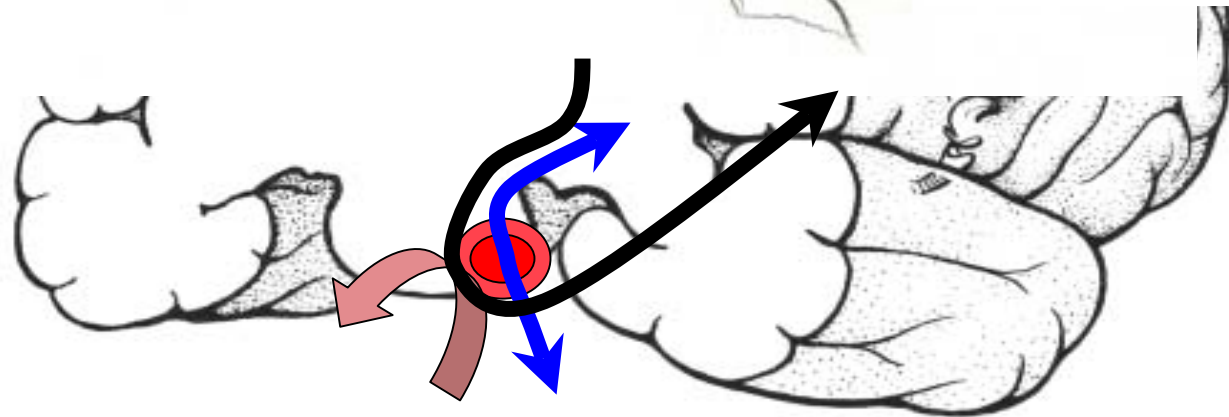


Occipito-Temporal Pathways

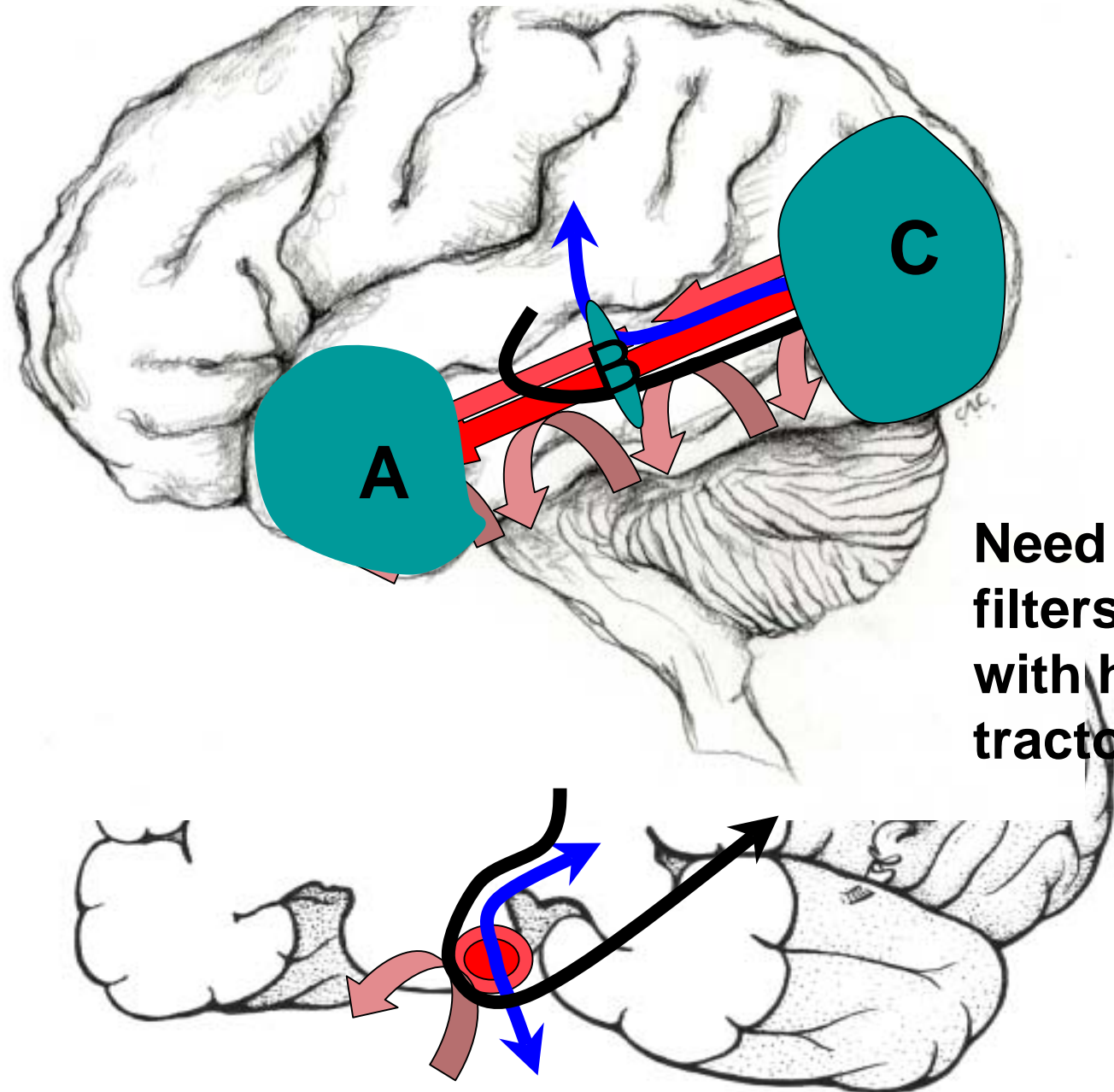


**Occipito-Temporal Pathways**

**Unwelcome  
Extended Family  
Members: Loop  
of Flechsig-Meyer**

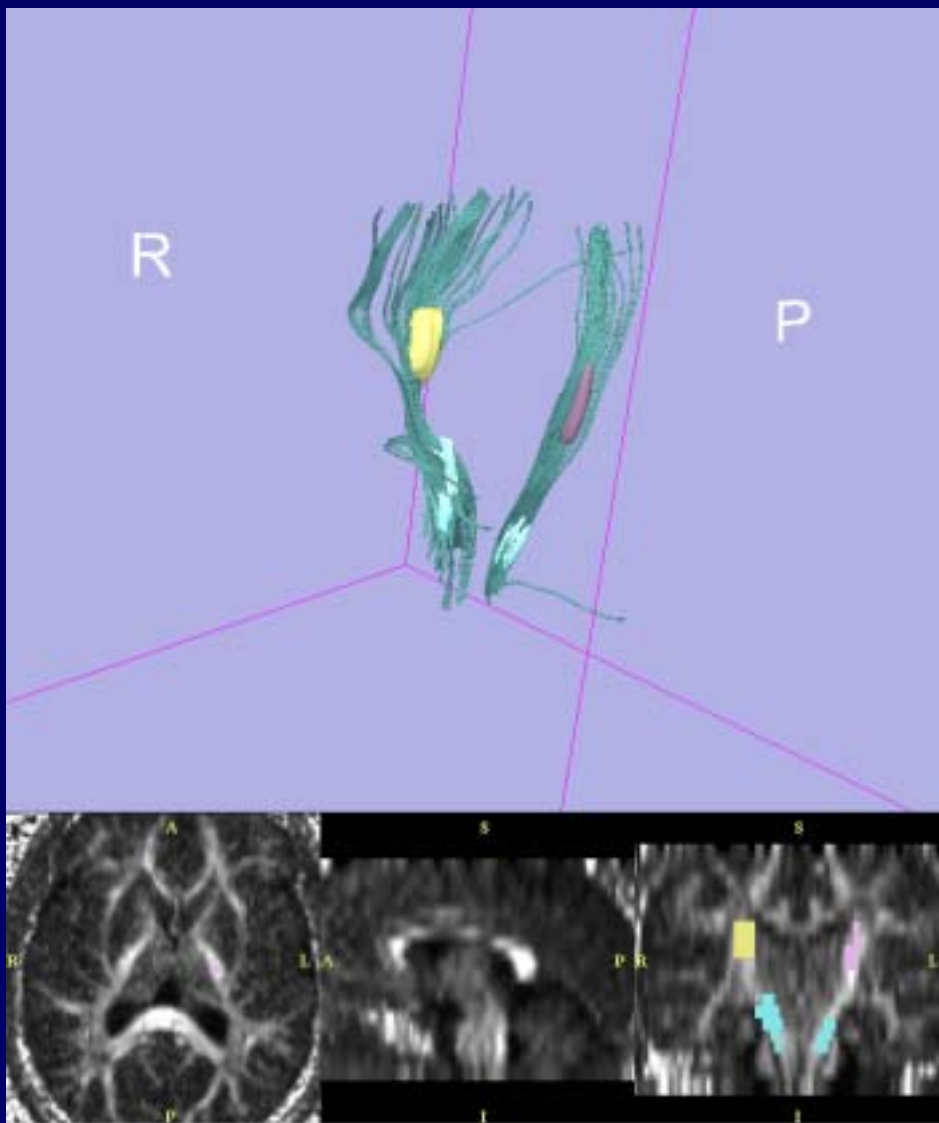


# Occipito-temporal pathways



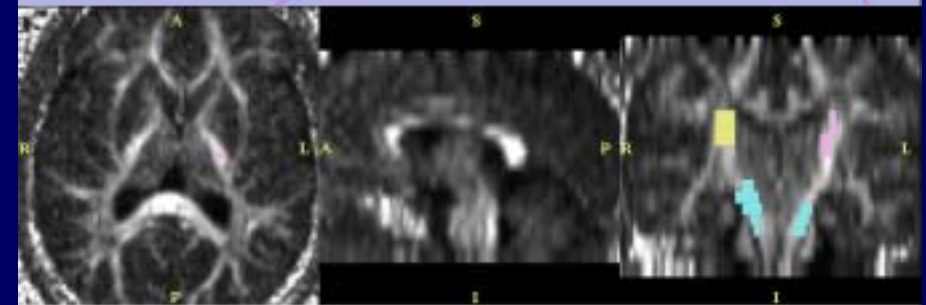
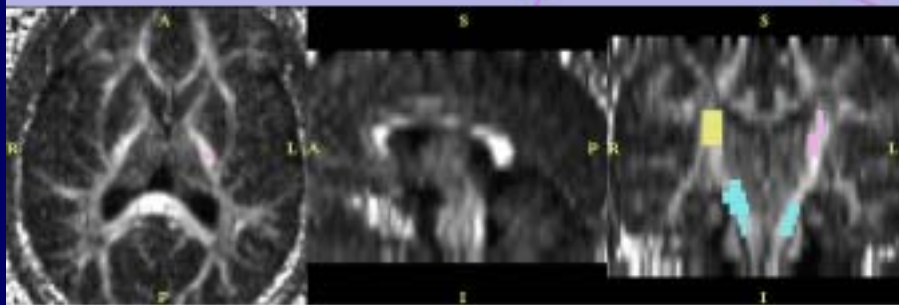
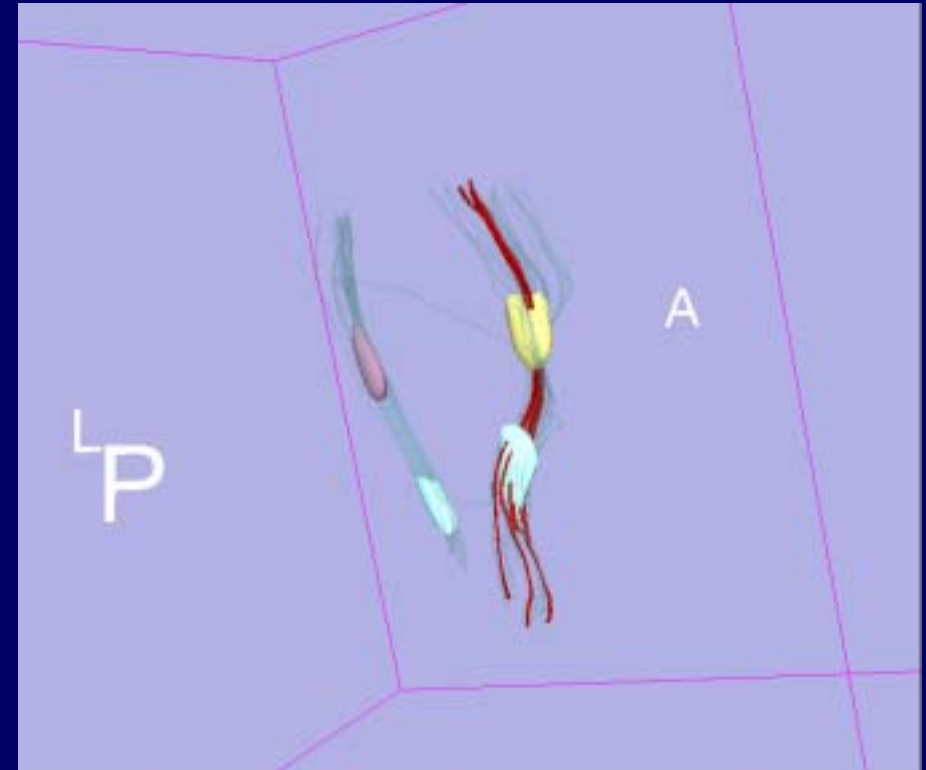
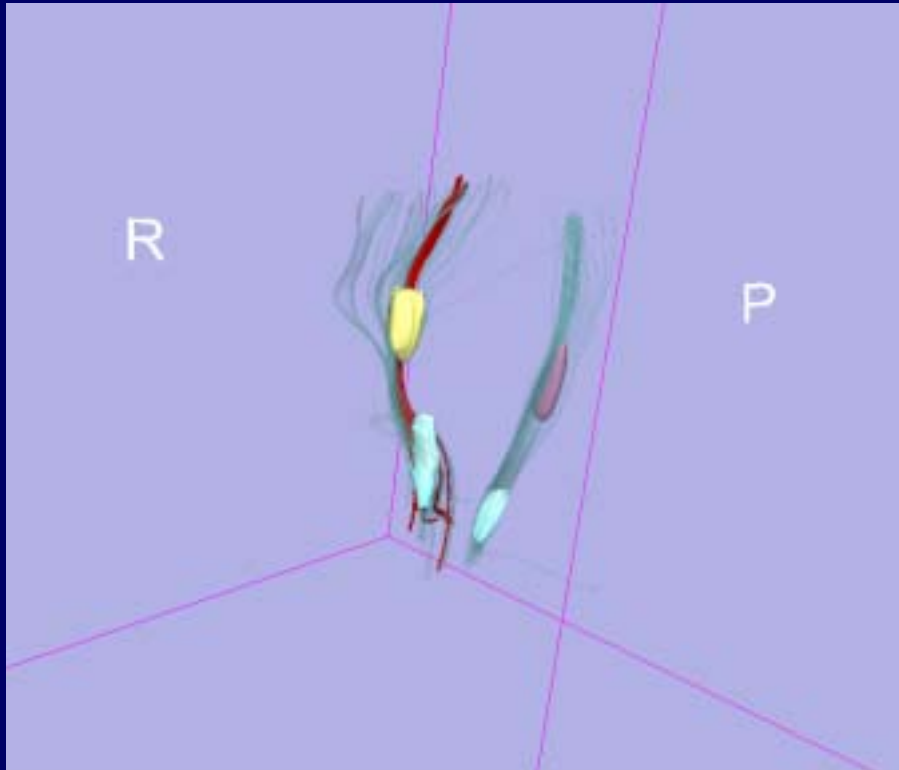
**Need for ABCD filters together with hand-made tractography**

# “Fallon ABC Tool”



Raul San Jose Estepar

# ROI Tract Localization





## ■ Interoperability

- **FreeSurfer / 3D Slicer (Tiech, MGH; Aucoin, BWH)**
  - vtkFreeSurferReaders to Load Volumes, Labels, Surfaces, Surface Field Data
  - Released in Slicer 2.4
  - Slicer Editor can be used in FreeSurfer Processing (Dickerson, BWH/MGH)
- **Being Applied to QA Review Process for AD Study**
  - Rapid Review QA Tools based on MIRIAD Review Tools used by MIT/Duke
  - Pre-Computed Movie Files and Live Visualization

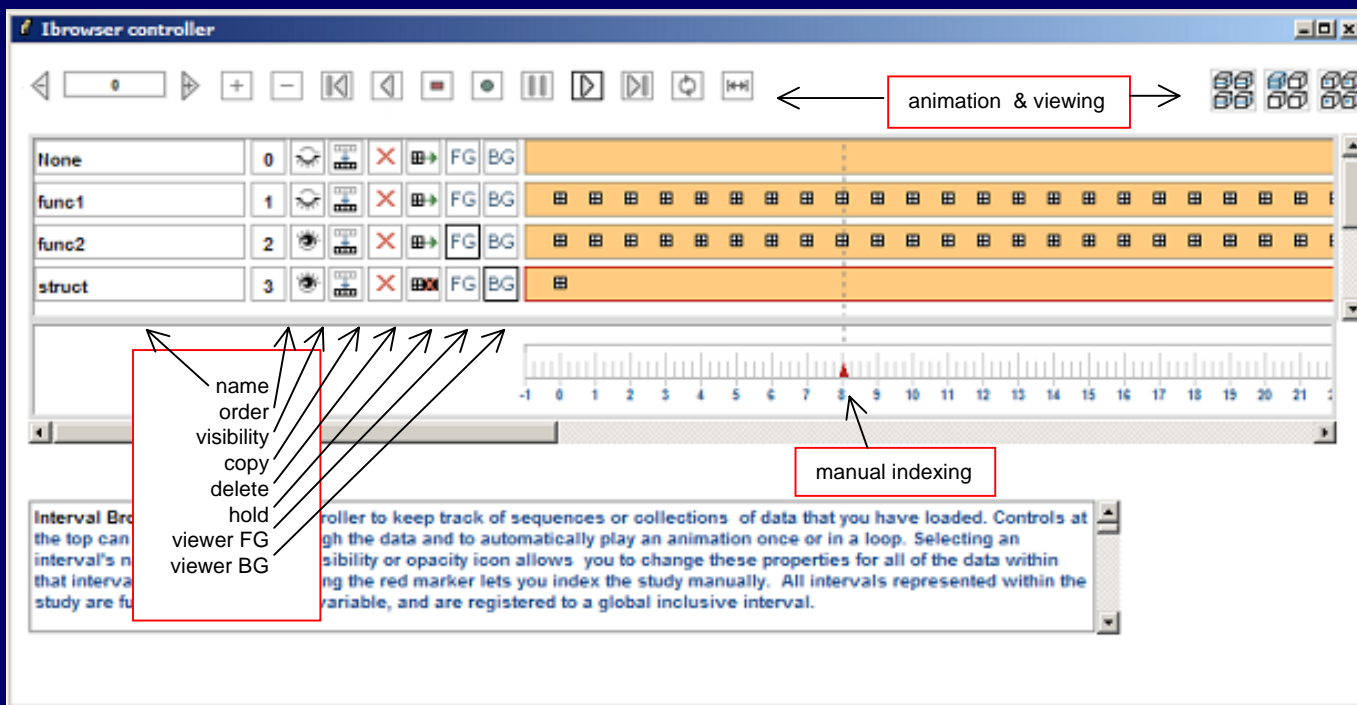
# Visualization: Grid Launch

- Grid Launch (Sacks, BWH)
  - Generalization of BIRN-CC Slicer Portal Launch
  - New Architecture for XNAT and Pipeline Compatibility
  
- Working Closely with mBIRN Data Integration and Informatics Efforts

# Visualization: LDDMM

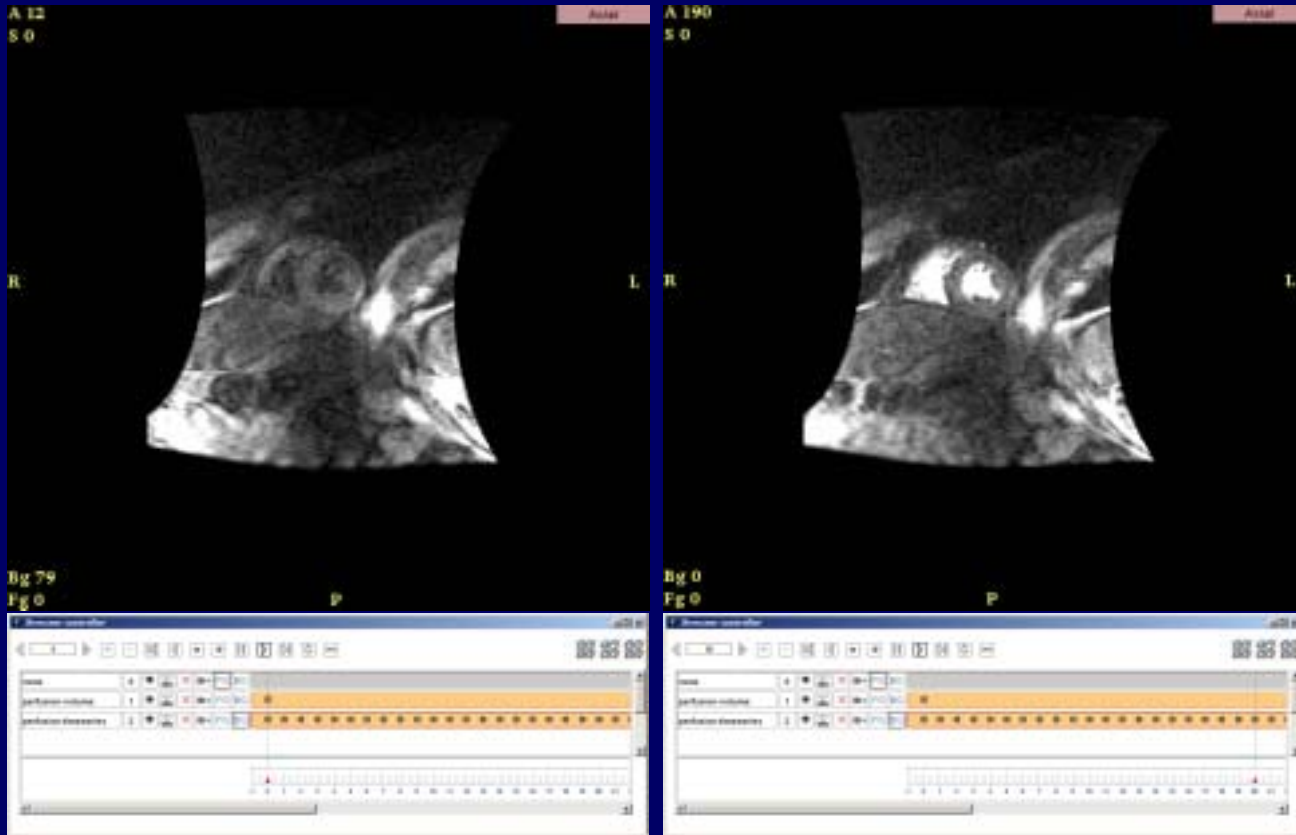
- Current LDMMViewer in Slicer
  - Released with Slicer 2.4
  - Customized for Current Shape Analysis Output
  - Can be used in Batch Mode or Interactively
- Next Generation Redesign
  - Leverage fBIRN-Developed Interval Browser Code for Time Series Volume Control
  - Integration Displacement Fields with Related Registration and Tensor-Valued Voxel Displays (e.g. DTMRI)

# ibrowser: time-series GUI



- \* GUI controls for indexing, animating, operating on sequences of volumes;
- \* GUI panel provides a graphical schematic of loaded volume sequences.

# ibrowser: other applications

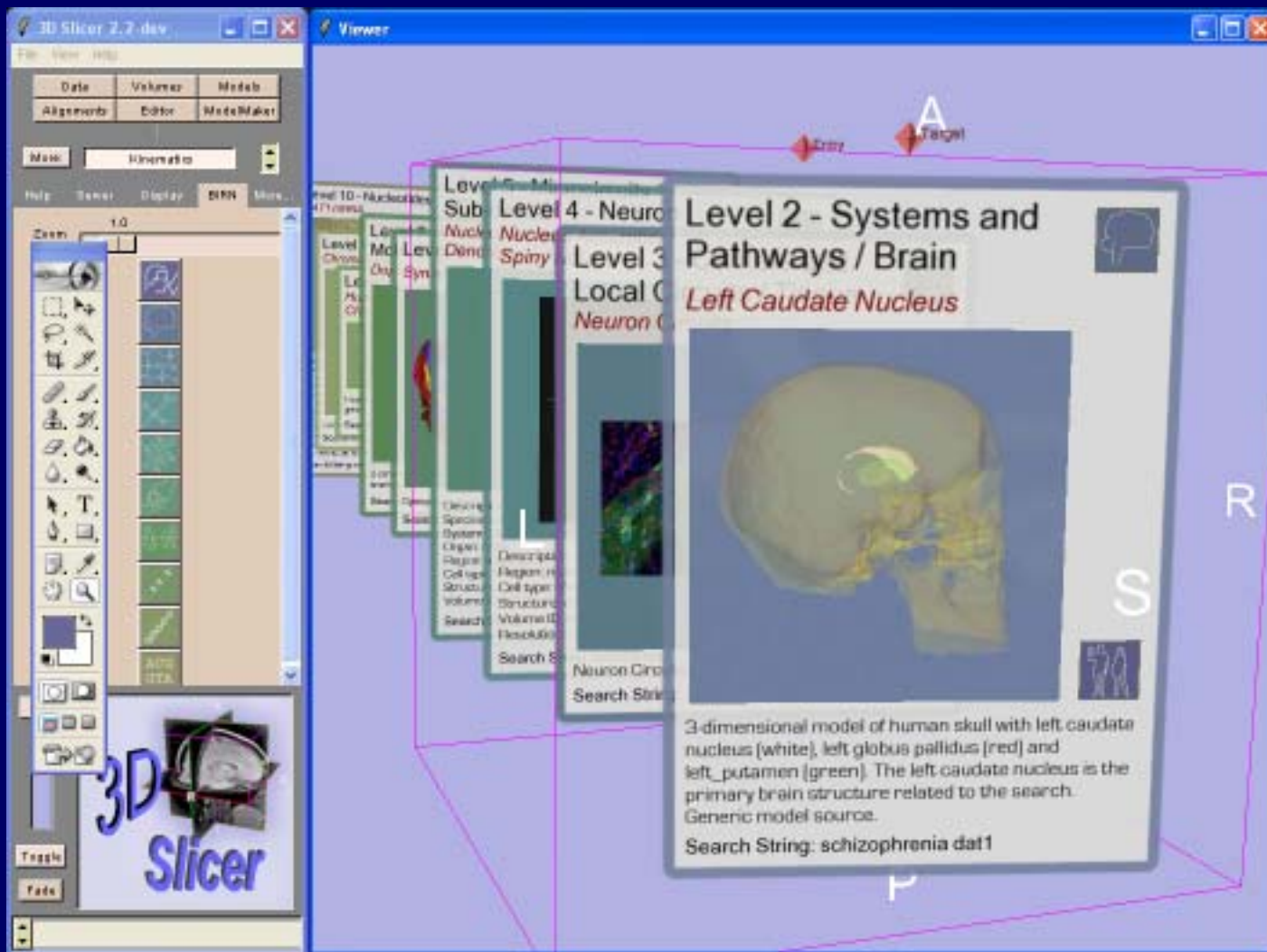


visualizing animated cardiac perfusion study

# Query Atlas

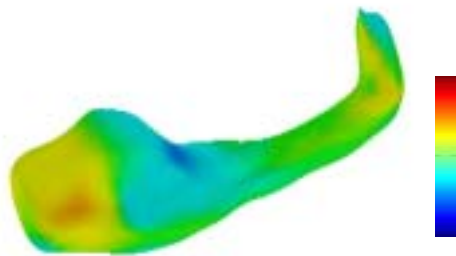
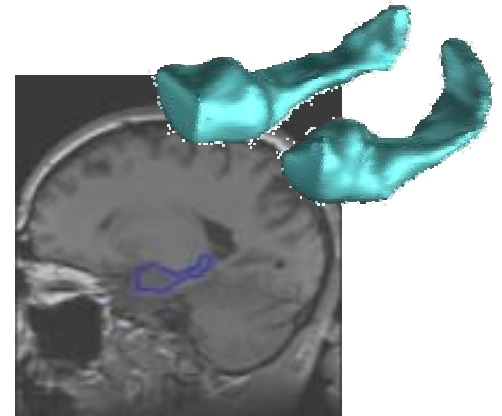
- Development Prototype Released with Slicer 2.4
  - FreeSurfer Labels
    - Cortical Surface Parcelations
    - Subcortical Label Maps
  - Form Compound Queries, Multiple Search Targets
- BIRNCard Interface Under Development
  - Native 3D Text and Image Display
  - Integration with VTK 3D Widgets for Greater Functionality

# BIRNCards Interface Prototype



Given two groups of subjects

- Train a classifier function
- Estimate its accuracy and statistical significance



- Create informative visualization of the detected differences



# Progress Report

- Identified integration path:
  - Application that runs locally on user data
  - Created jointly and supported at MGH
- Immediate goal:
  - Scripts for analysis of a selected data set
    - Hippocampus, longitudinal data, Alzheimer's study
  - With Bruce Fischl, MGH
- Longer term goal:
  - Convert the scripts into a GUI-based app



# Ties to Other BIRN Efforts

- Most mBIRN Sites have Ties to other BIRNs
  - Common Development Platforms
  - Shared Infrastructure
  - QueryAtlas Project has Aims in Both mBIRN and fBIRN; has links to Mouse BIRN Smart Atlas
- File Format Discussions and Interoperability Tools Benefit from Larger Group Participation
  - Data from Full Range of Scanners and Sequences
  - Awareness of Trends in the Community

# New Non-BIRN Collaborations

- National Centers for Biomedical Computation
  - NIH Roadmap Initiative
  - 4 Funded This Year, 3 More Next Year
- mBIRN Ties
  - National Alliance for Medical Image Computing (NA-MIC; Kikinis (PI), Ellisman, Toga, Pieper, Kennedy, Tuch, Gerig)
  - Center for Computational Biology (Toga, PI)
  - I2B2 (Murphy)

- Particularly Important Link for mBIRN AVI
  - Goals Include Open Source Infrastructure for Medical Image Computing
    - Based on ITK, VTK, and 3D Slicer
    - Emphasis on Software Engineering Methodologies
  - Initial Driving Biological Project:
    - Integration of Structural, Connectivity (DTI), and Functional Imaging with Genetics
    - Schizophrenia Research Target
- While mBIRN AVI *Applies and Adapts* Techniques, NA-MIC is Chartered to *Develop New* Algorithms, Processes, and Application Software
  - The Combination of mBIRN and NA-MIC Gives Critical Mass to Provide Comprehensive Solutions for the Research Environment