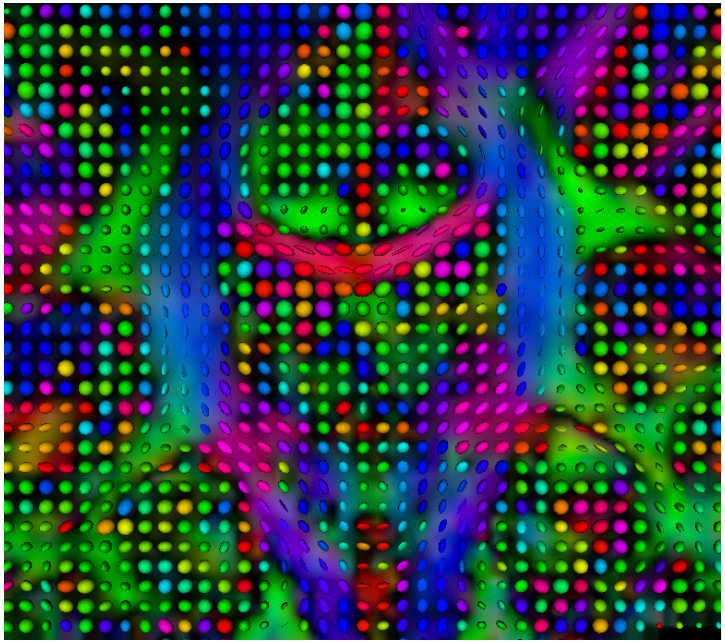


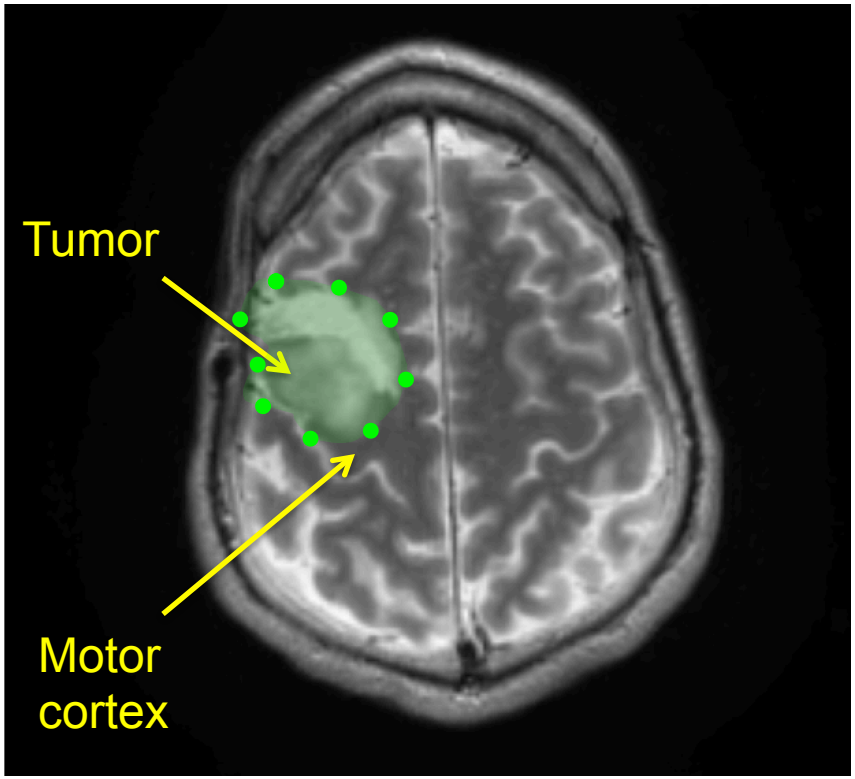
Mapping white matter pathways with Diffusion MRI

Sonia Pujol, Ph.D.

Brigham and Women's Hospital,
Harvard Medical School

spujol@bwh.harvard.edu

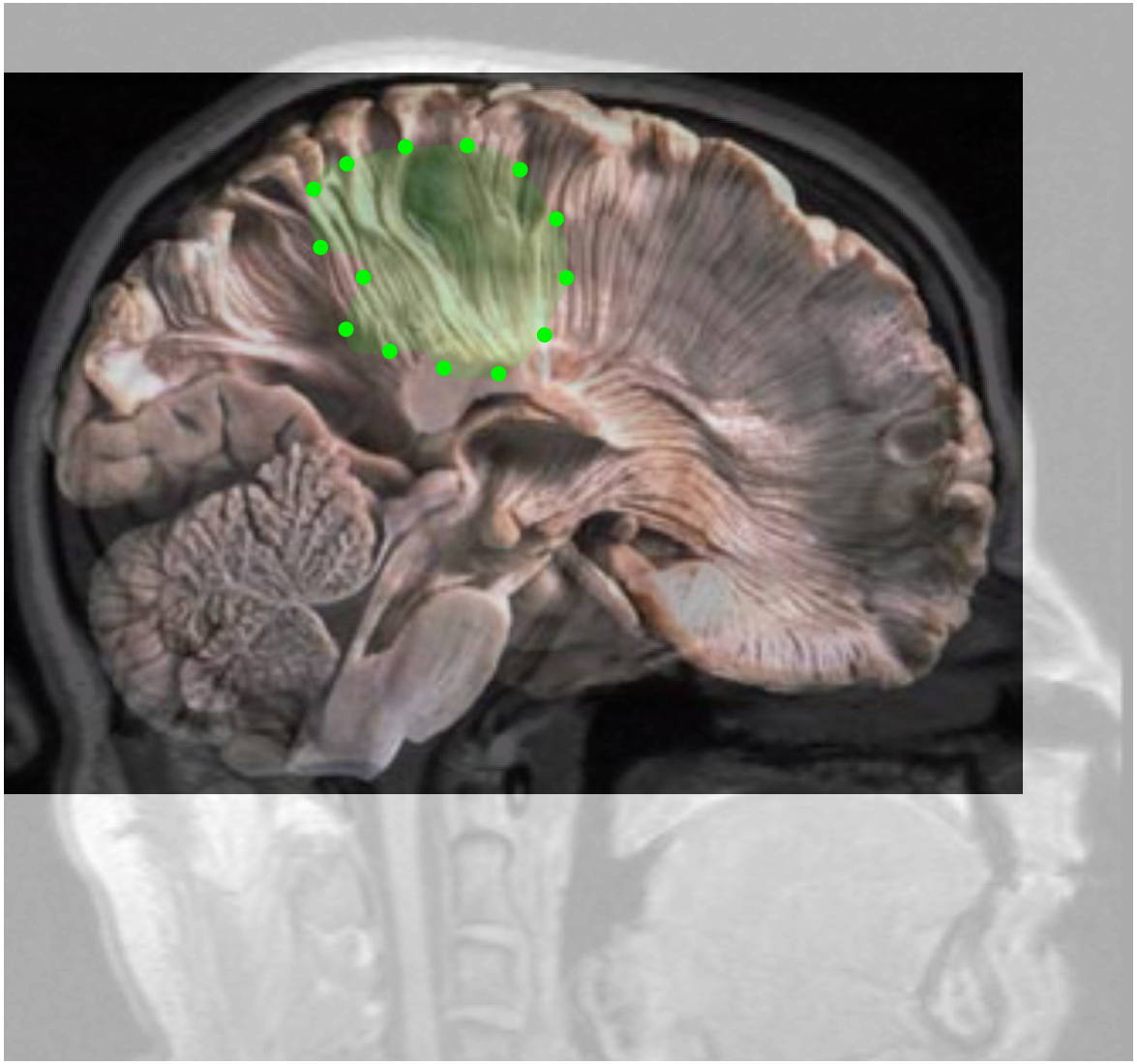
Clinical Case



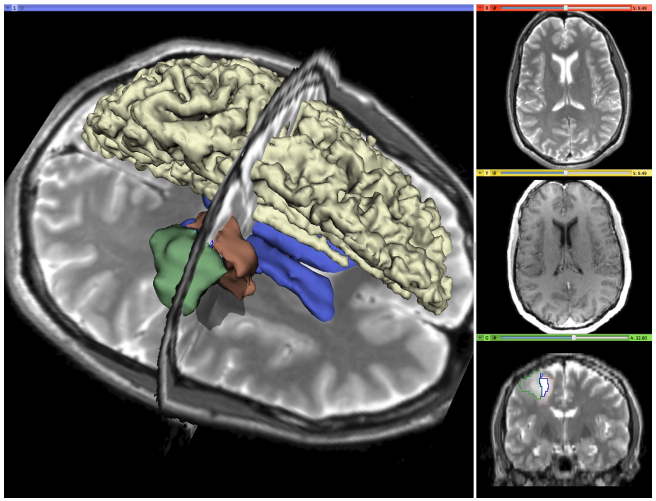
Clincal case courtesy of Dr. Alexandra Golby, Brigham and Women's Hospital, Harvard Medical School

- 47-y.o. golf professional
- Brain tumor resected in 1999
- Tumor recurrence in 2011

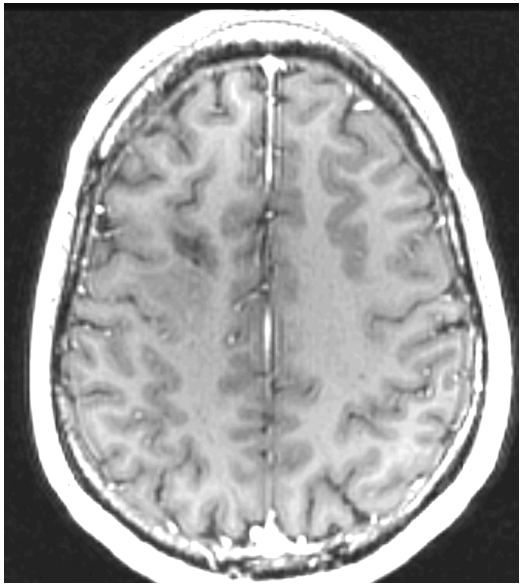
What does the surgeon want to see?



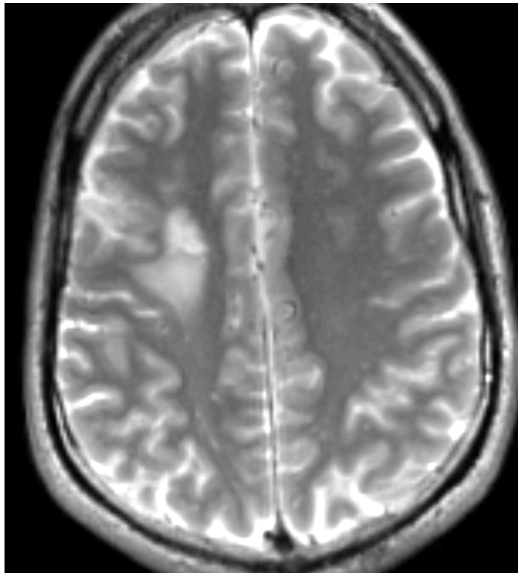
- Where are the tracts?
- Are they normal?
- Is anything missing?



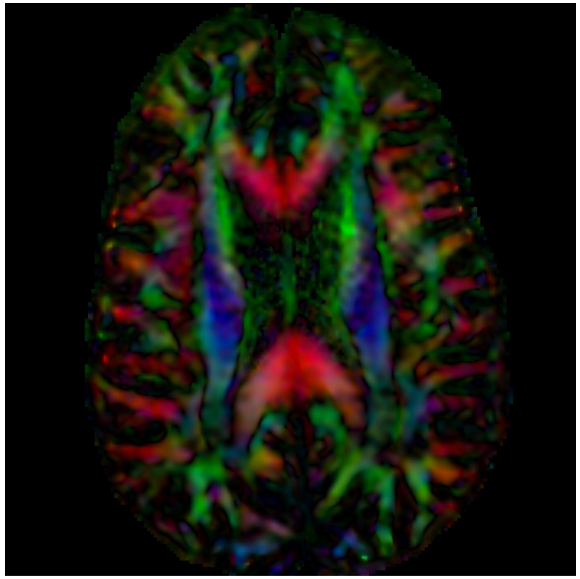
Pre-op Imaging



T1

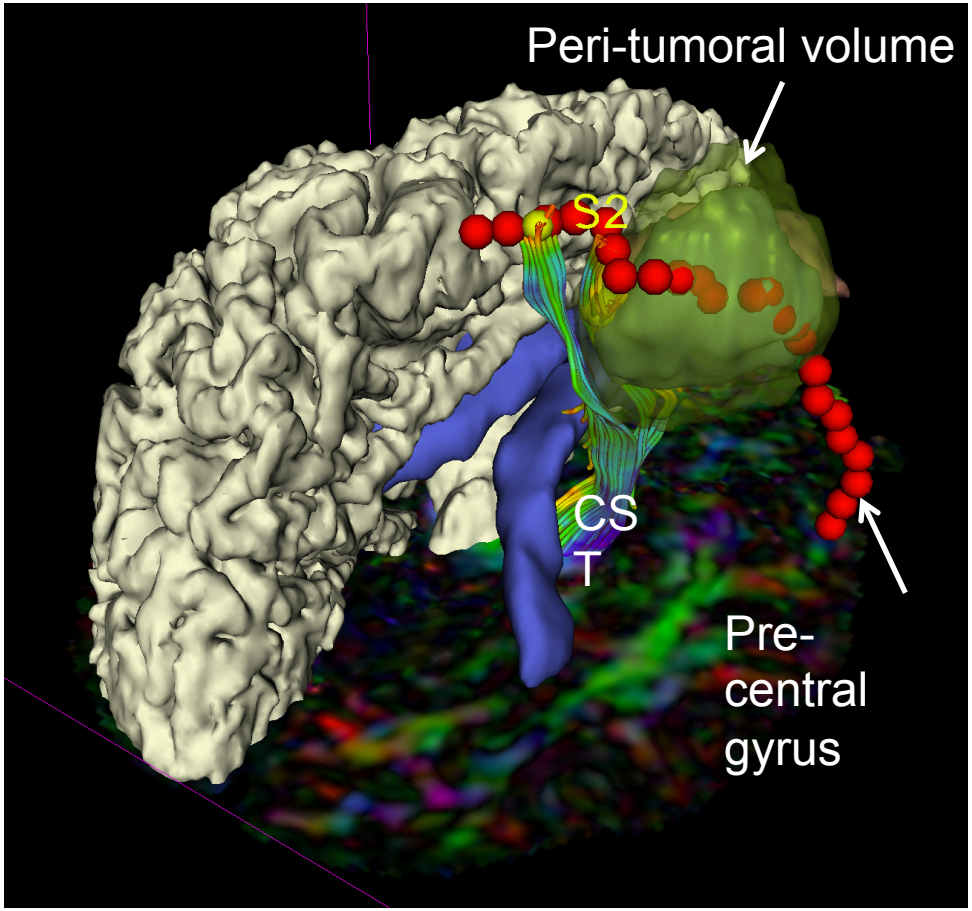


T2

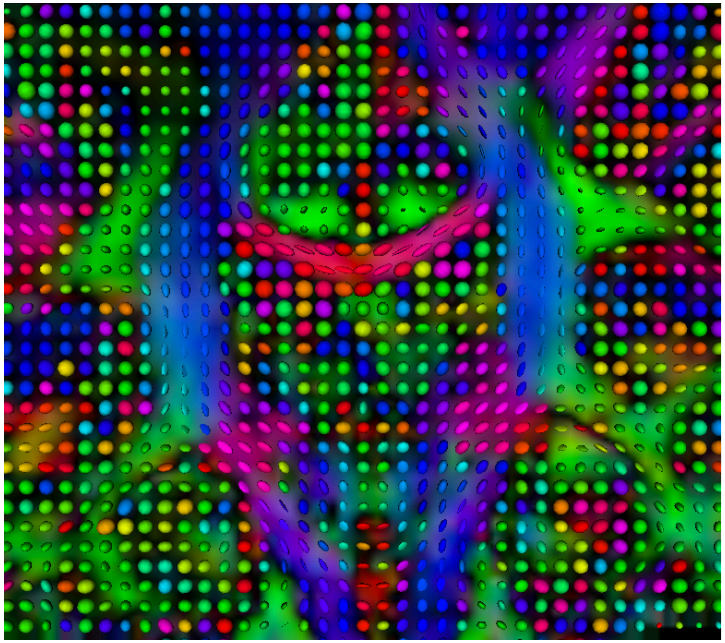


DWI

DTI Tractography for Brain Surgery

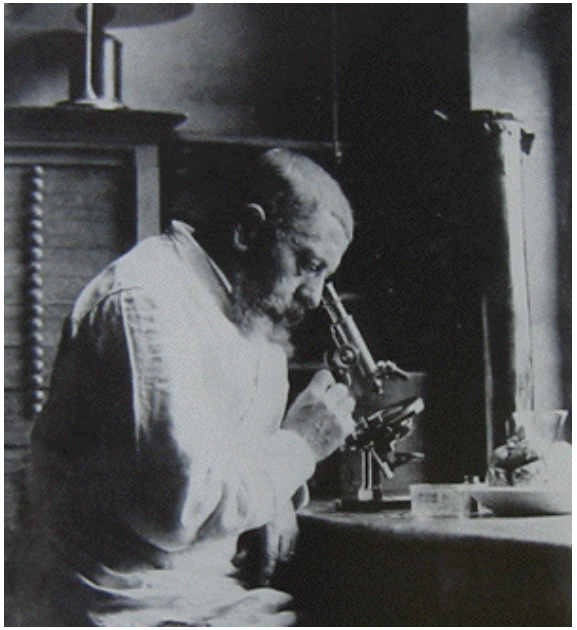


- Non-invasive 3D visualization of peritumoral white matter anatomy
- Spatial relationship of a tumor with tracts involved in motor, visual or language function
- A potentially clinically useful guide to the location of eloquent tracts for subcortical mapping



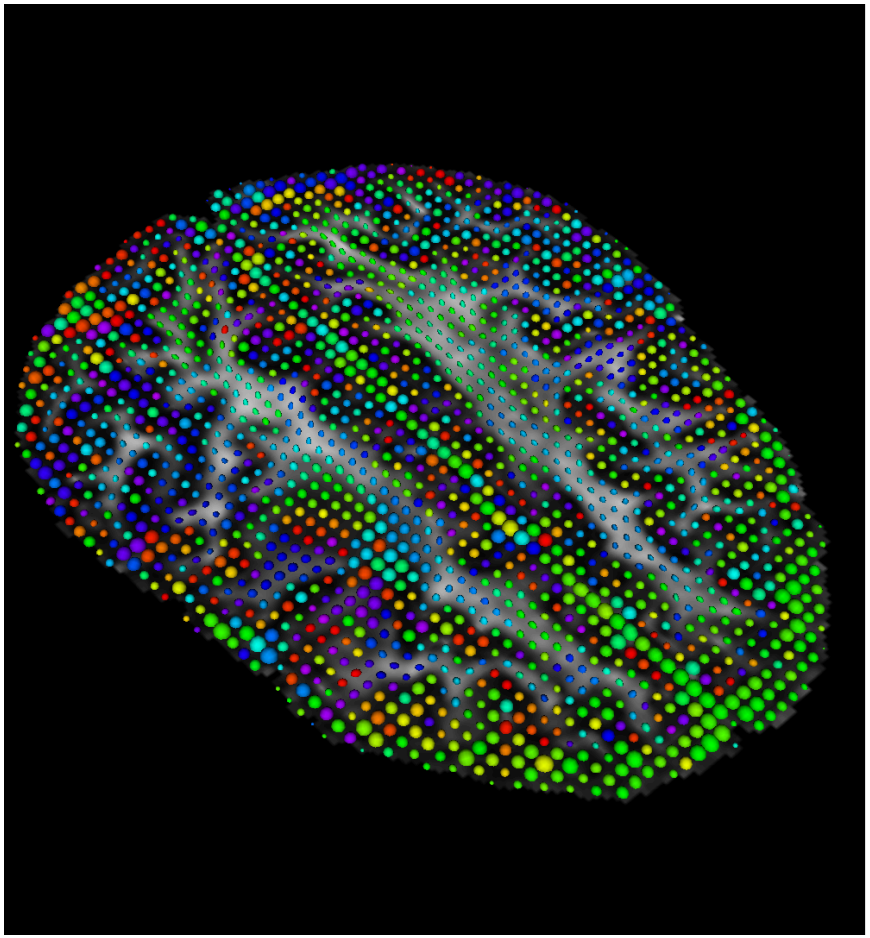
Part 1: An Introduction to Diffusion Tensor Imaging

White Matter Exploration



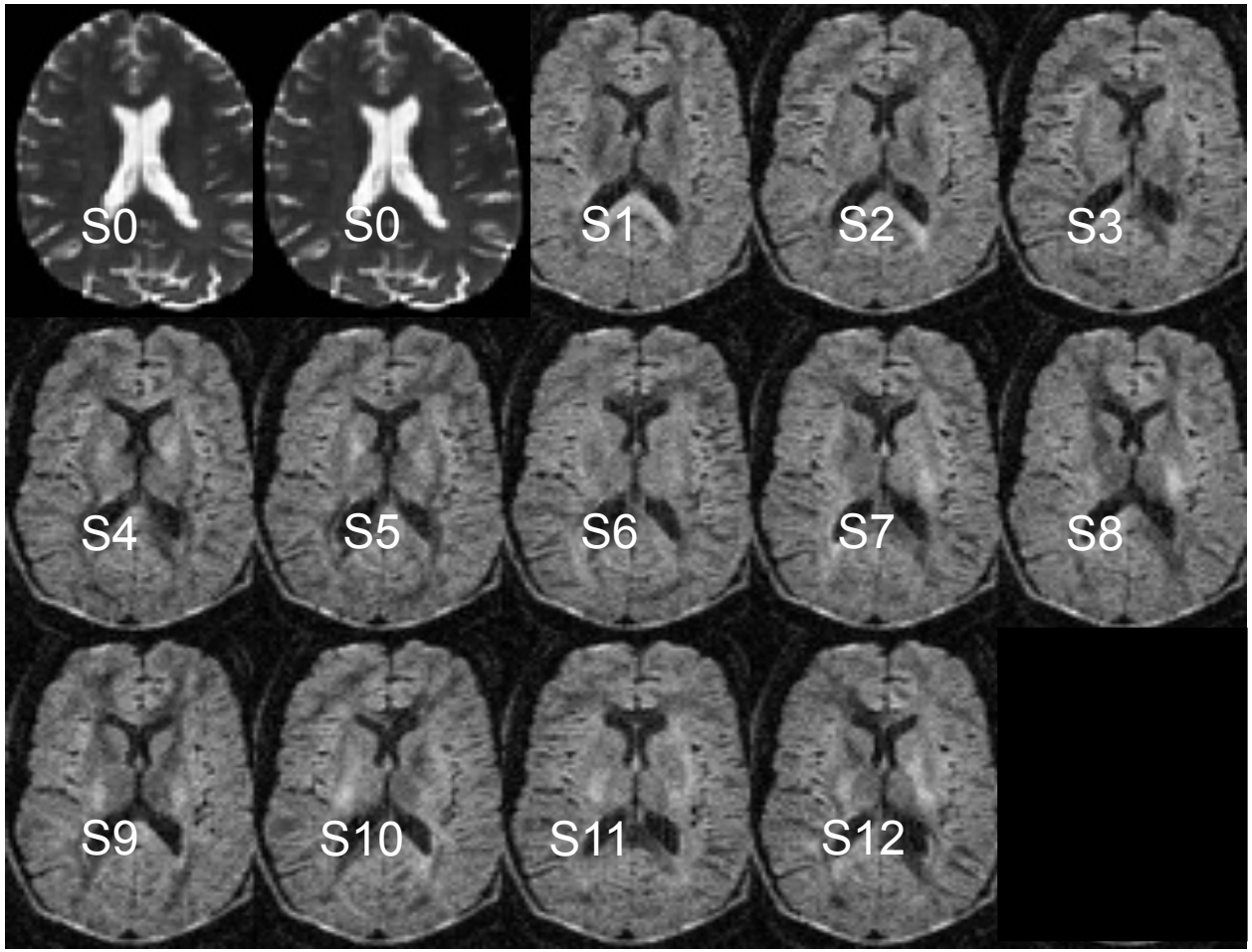
Jules Joseph and Augusta Dejerine (*Anatomie des centres nerveux* (Paris, 1890-1901)): Neuroanatomy atlas based on myelin stained preparation

Diffusion Tensor Imaging (DTI)



- First non-invasive window on white matter anatomy
- Measurement of the motion of water molecules using MRI techniques.
- Three-dimensional reconstruction of the trajectory of white matter bundles

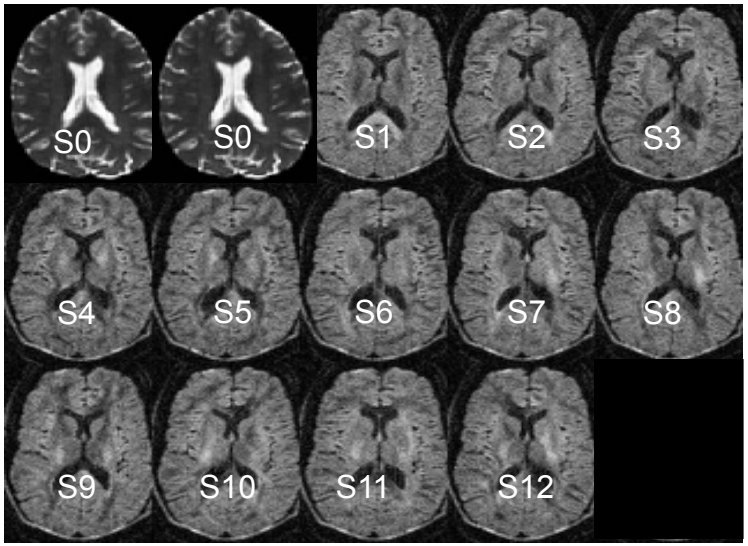
Diffusion Weighted Imaging (DWI)



In this example, the DWI scan was acquired with 12 diffusion sensitizing gradient directions (S1-S12) and 2 non-diffusion sensitizing gradients (S0)

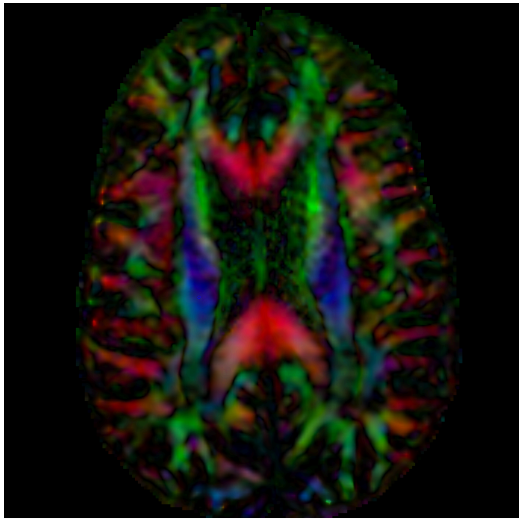
From DWI to DTI

DWI



DWI dataset

DTI



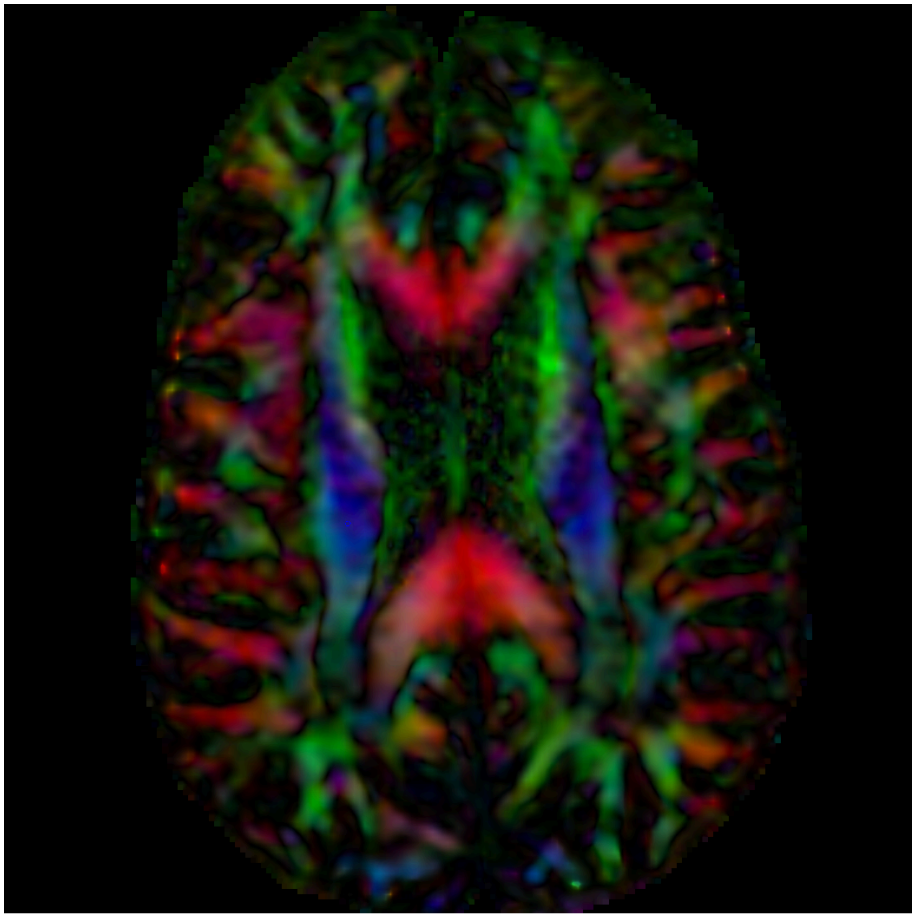
DTI dataset

$$S_i = S_0 e^{-b\hat{g}i^T \underline{D}\hat{g}_i}$$

Stejskal-Tanner (1965)

Si: DWI volume acquired with ith gradient
So: Baseline volume

DTI Color Map

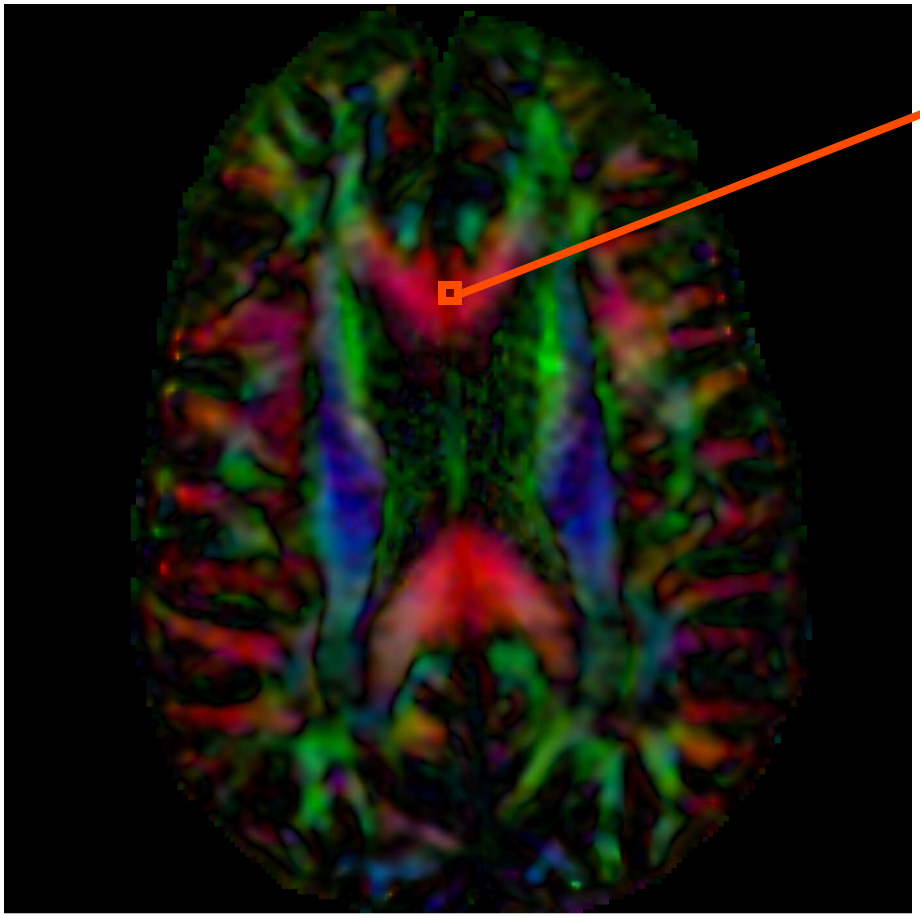


Red: left-right
(e.g. corpus callosum)

Green: anterior-posterior (e.g superior portion of cingulum)

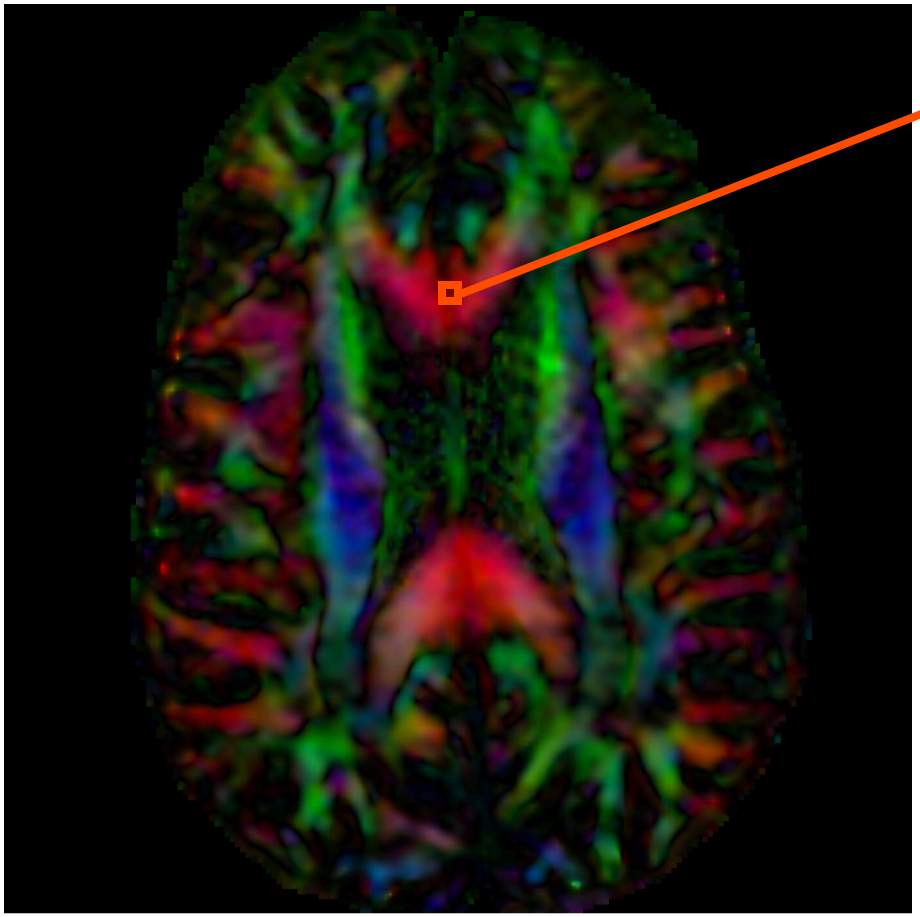
Blue: inferior-superior
(e.g. corticospinal tract)

Diffusion Tensor Imaging



$$S_i = S_0 e^{-b\hat{g}i^T \underline{D} \hat{g}_i}$$

Diffusion Tensor Imaging

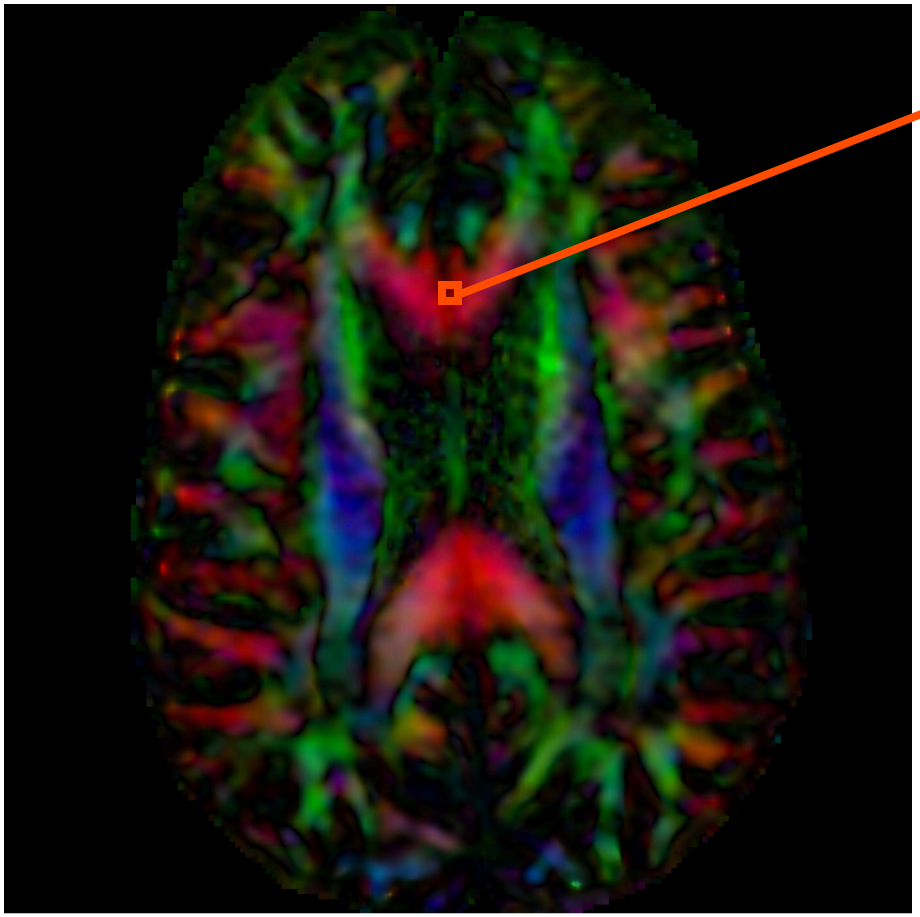


$$S_i = S_0 e^{-b\hat{g}i^T \underline{D} \hat{g}_i}$$

$$\downarrow$$

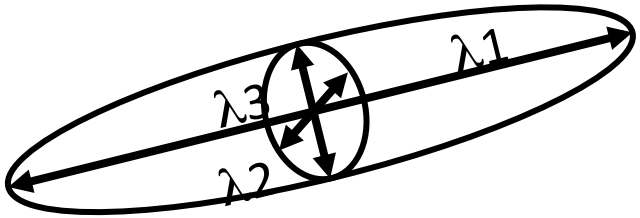
$$\underline{\mathbf{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

Diffusion Tensor Imaging

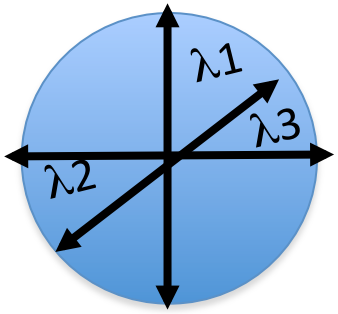


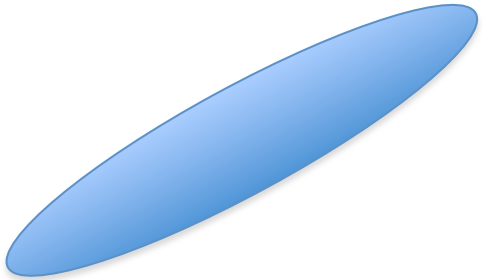
$$S_i = S_0 e^{-b\hat{g}i^T \underline{D} \hat{g}_i}$$

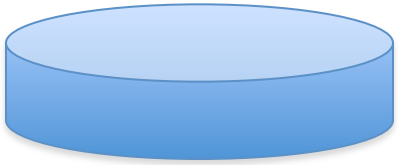
$$\underline{\mathbf{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$



Diffusion Tensor Shape







$\lambda 1 = \lambda 2 = \lambda 3$

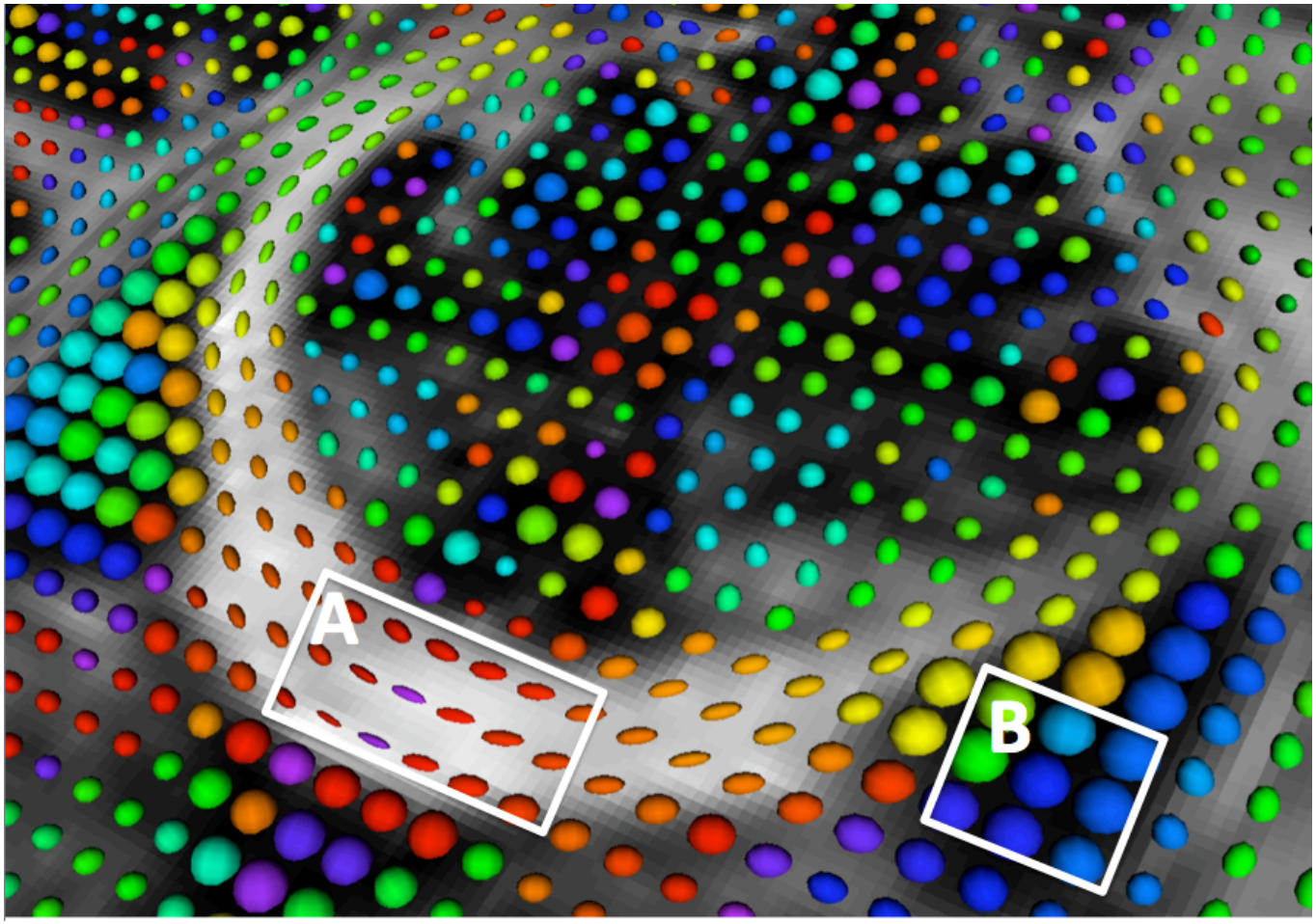
$\lambda 1 >> \lambda 2, \lambda 3$

$\lambda 1 \sim \lambda 2 >> \lambda 3$

Isotropic media
(CSF, gray matter)

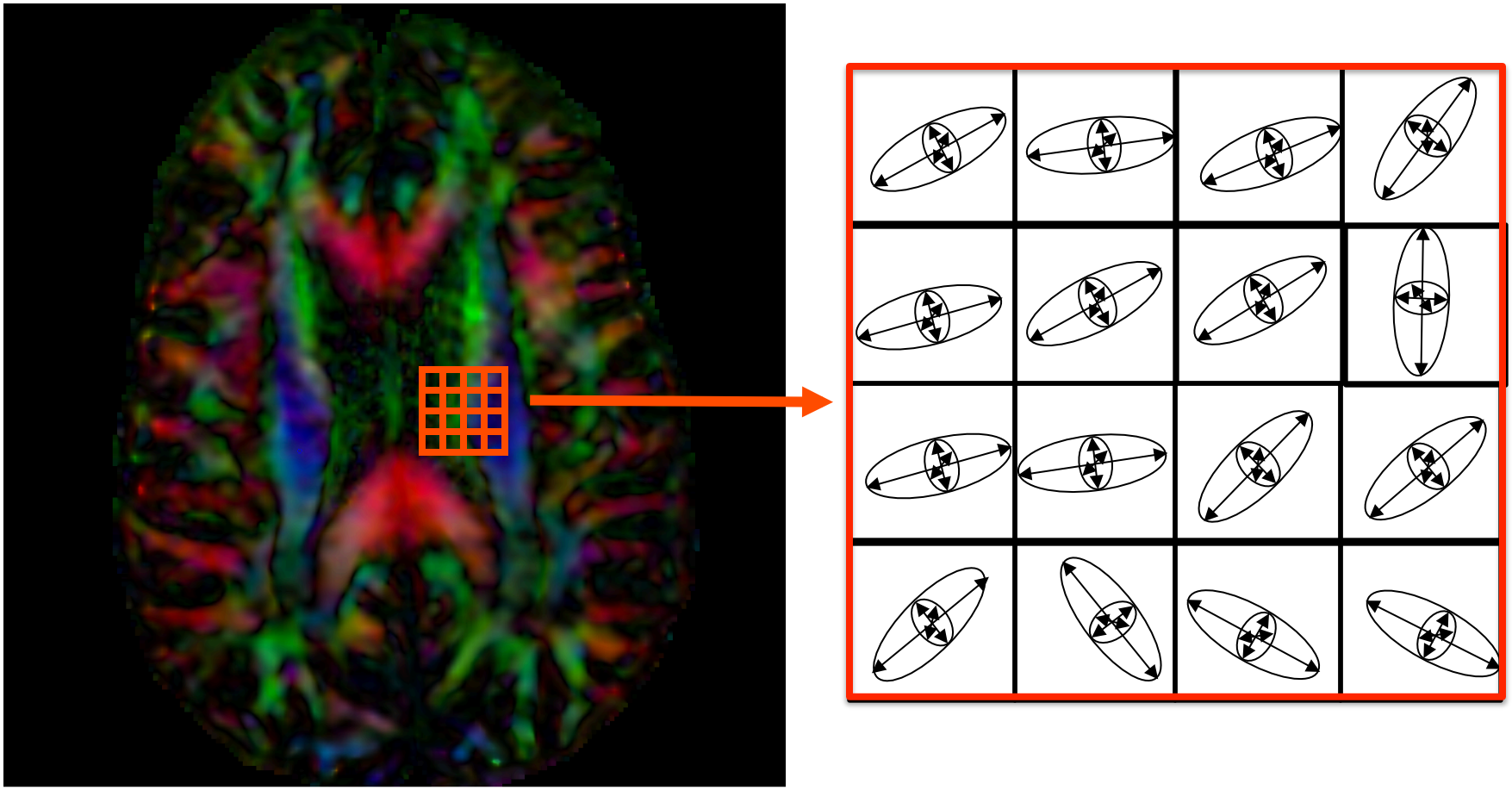
Anisotropic media
(white matter)

Diffusion Tensor Imaging (DTI)

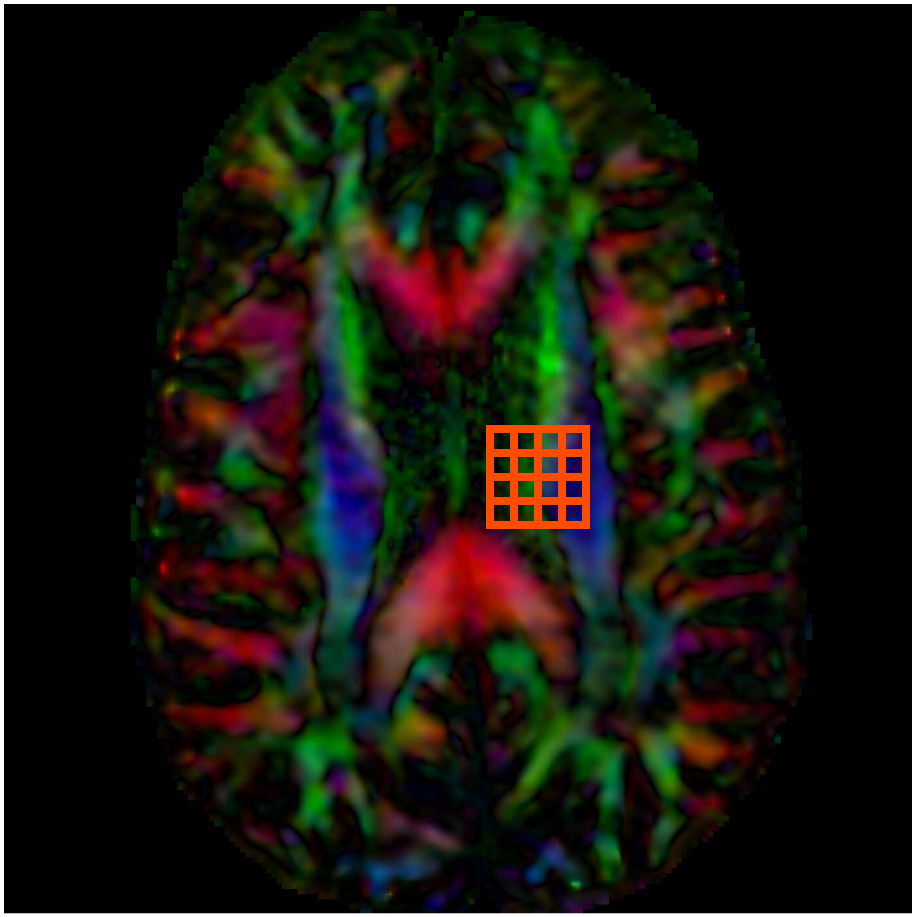


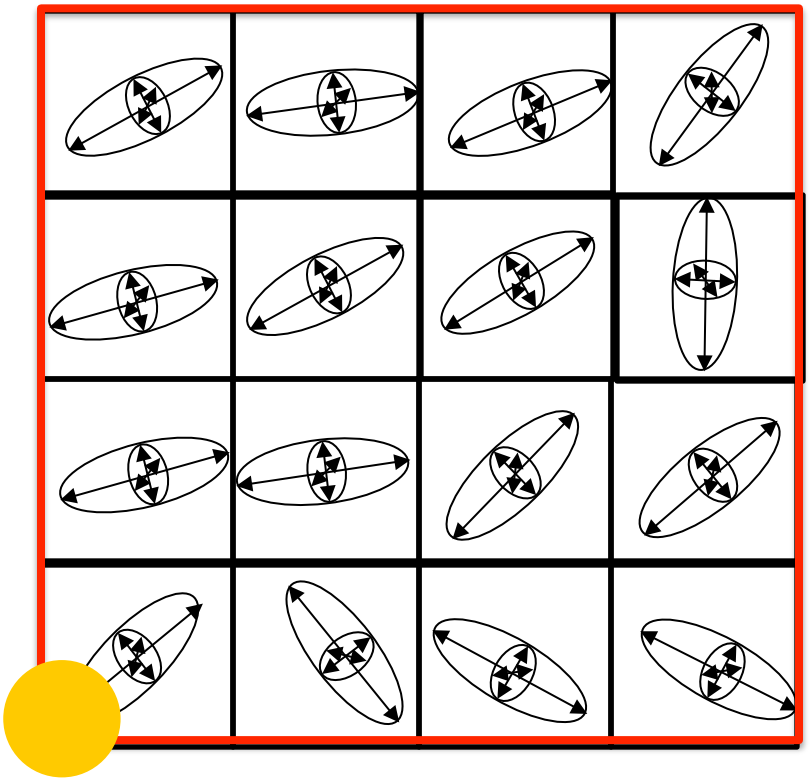
A: Anisotropic; B: Isotropic

DTI Tractography



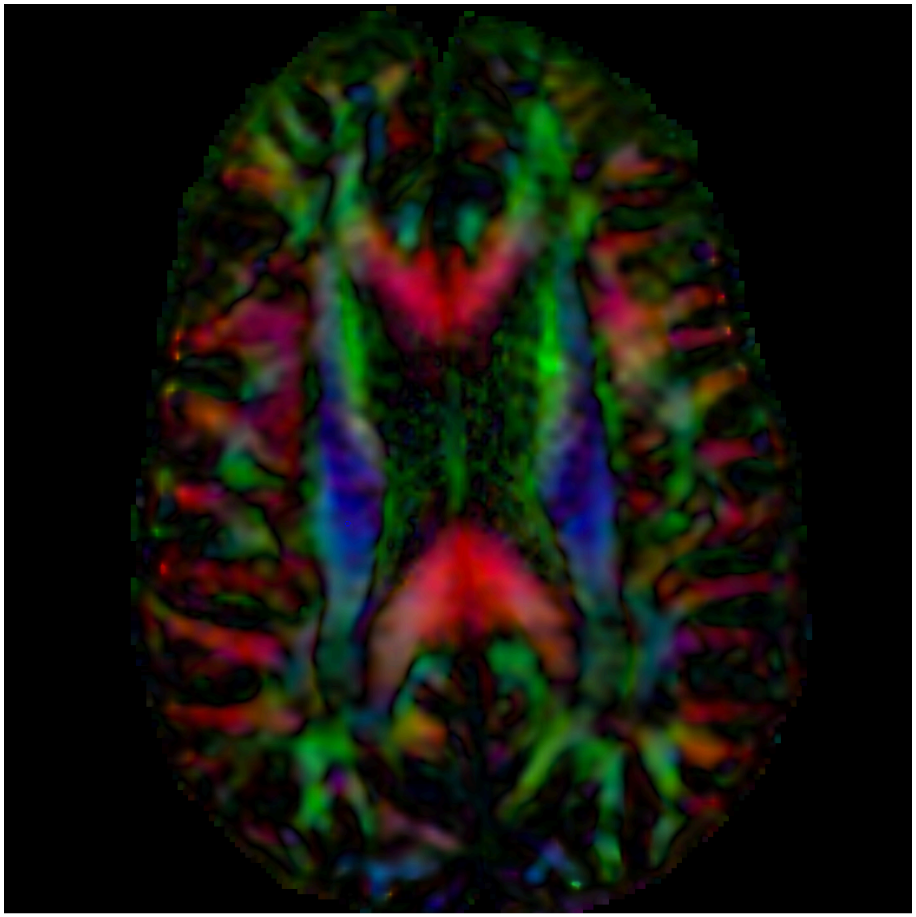
DTI Tractography

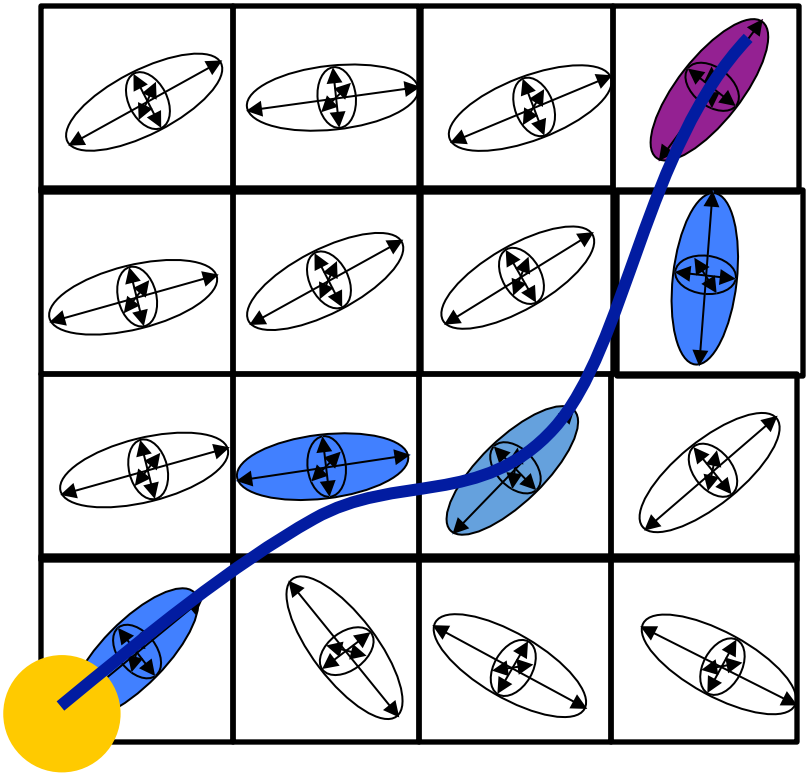




Seed Point

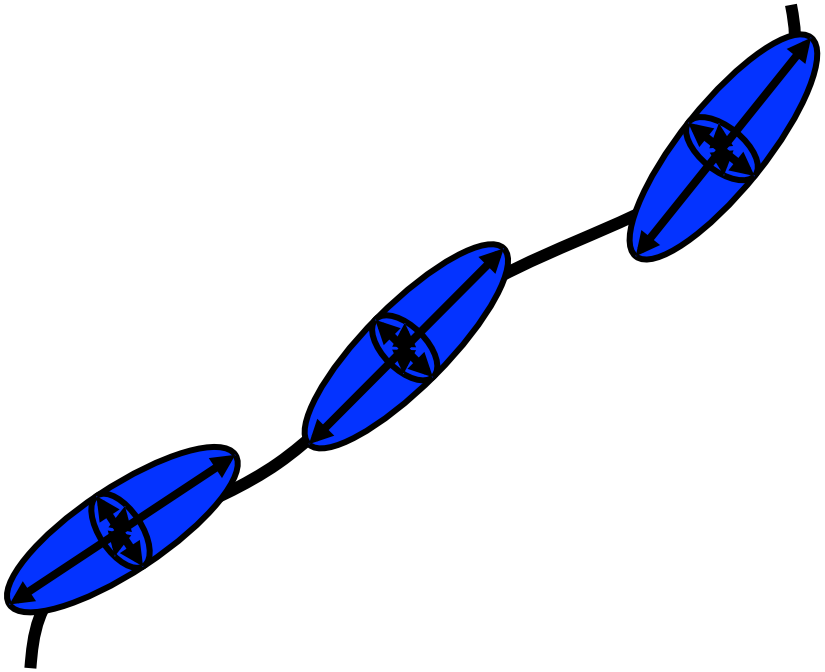
DTI Tractography

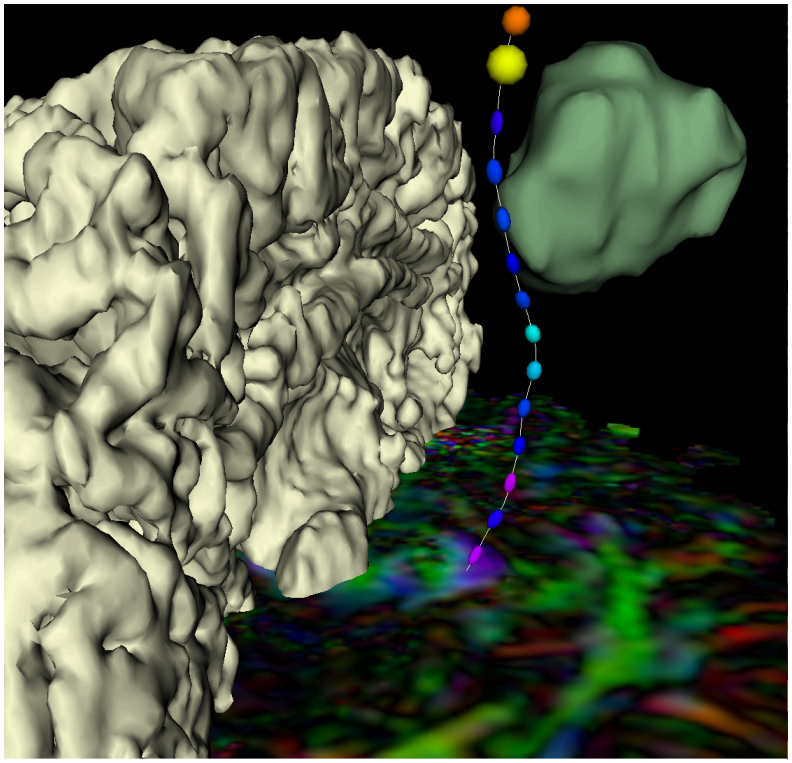




Seed Point

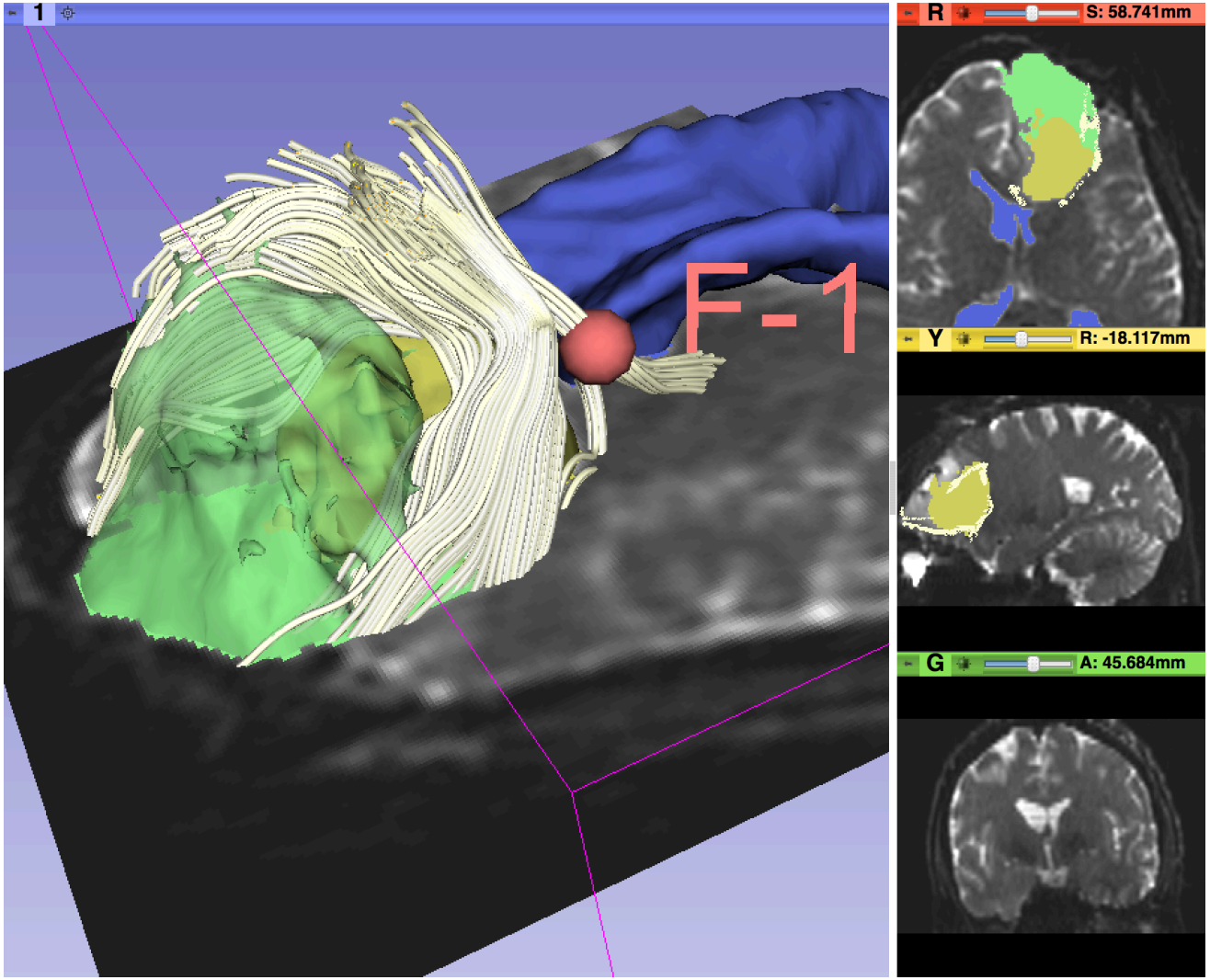
DTI Tractography



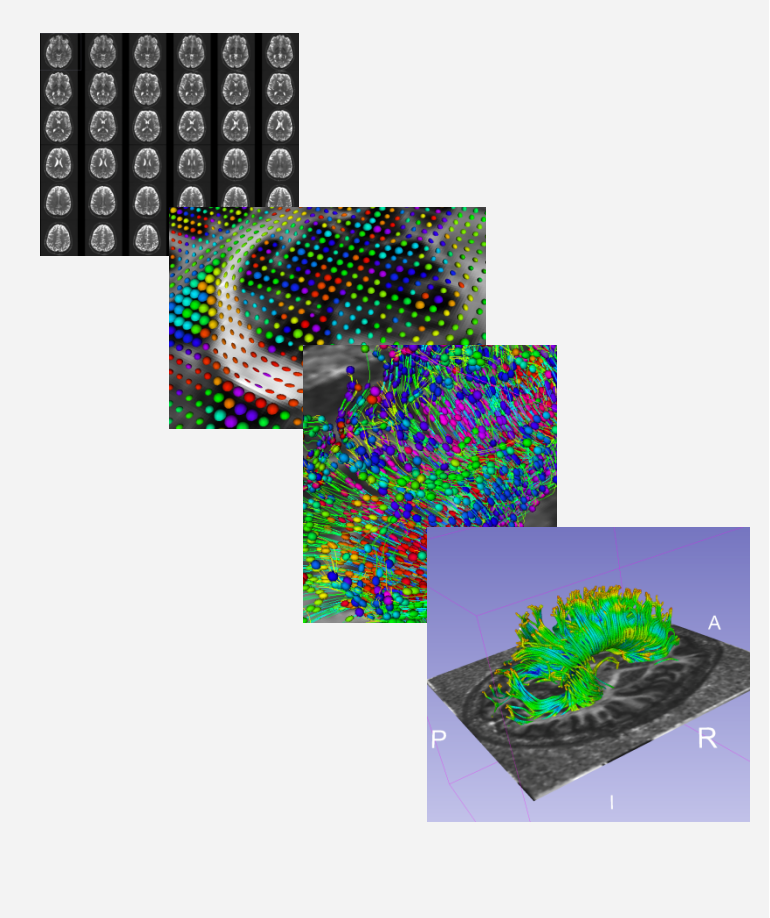


DTI tractography provides 3D reconstruction of the trajectory of white matter pathways

Brain Mapping for Neurosurgery



Tutorial Outline



This tutorial is an introduction to the fundamentals of Diffusion MRI analysis, from the estimation of diffusion tensors to the interactive 3D visualization of tracts.

Learning Objectives

Following this tutorial, you'll be able to

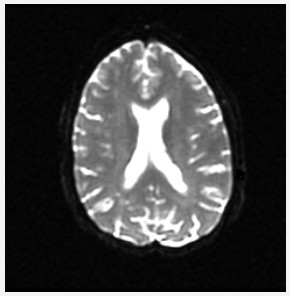
1) Estimate a tensor volume from a set of Diffusion Weighted Images

2) Understand the shape and size of the diffusion ellipsoid

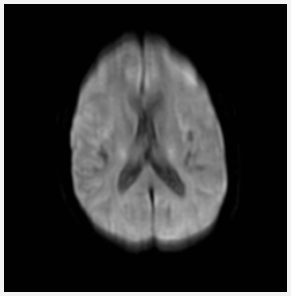
3) Reconstruct DTI tracts from a pre-defined region of interest

4) Interactively visualize DTI tracts seeded from a fiducial

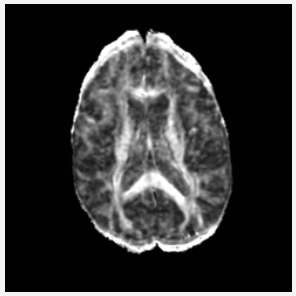
MR Diffusion Analysis Pipeline



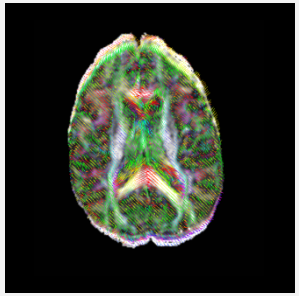
DWI
Acquisition



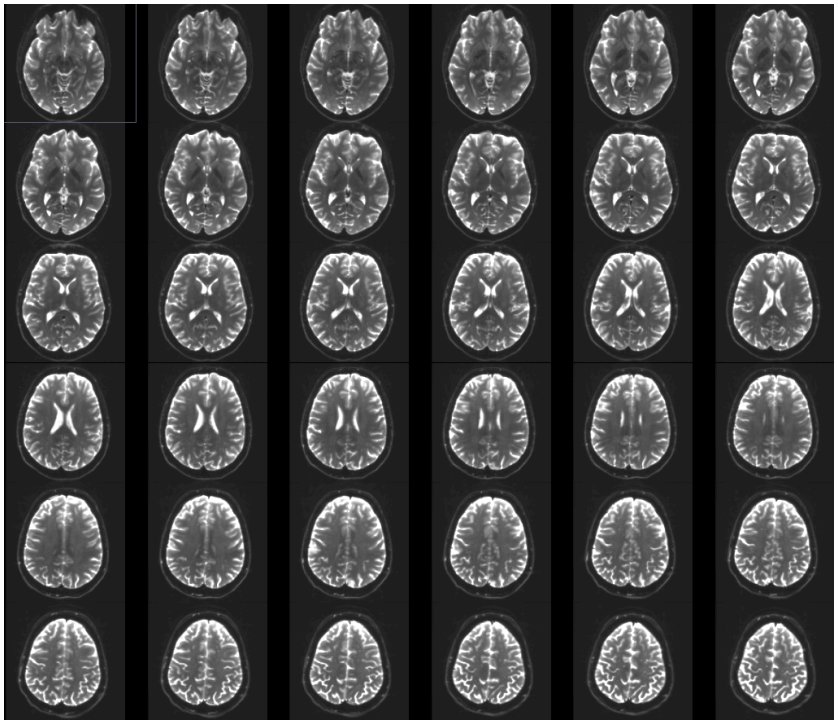
Tensor
Calculation



Scalar
Maps

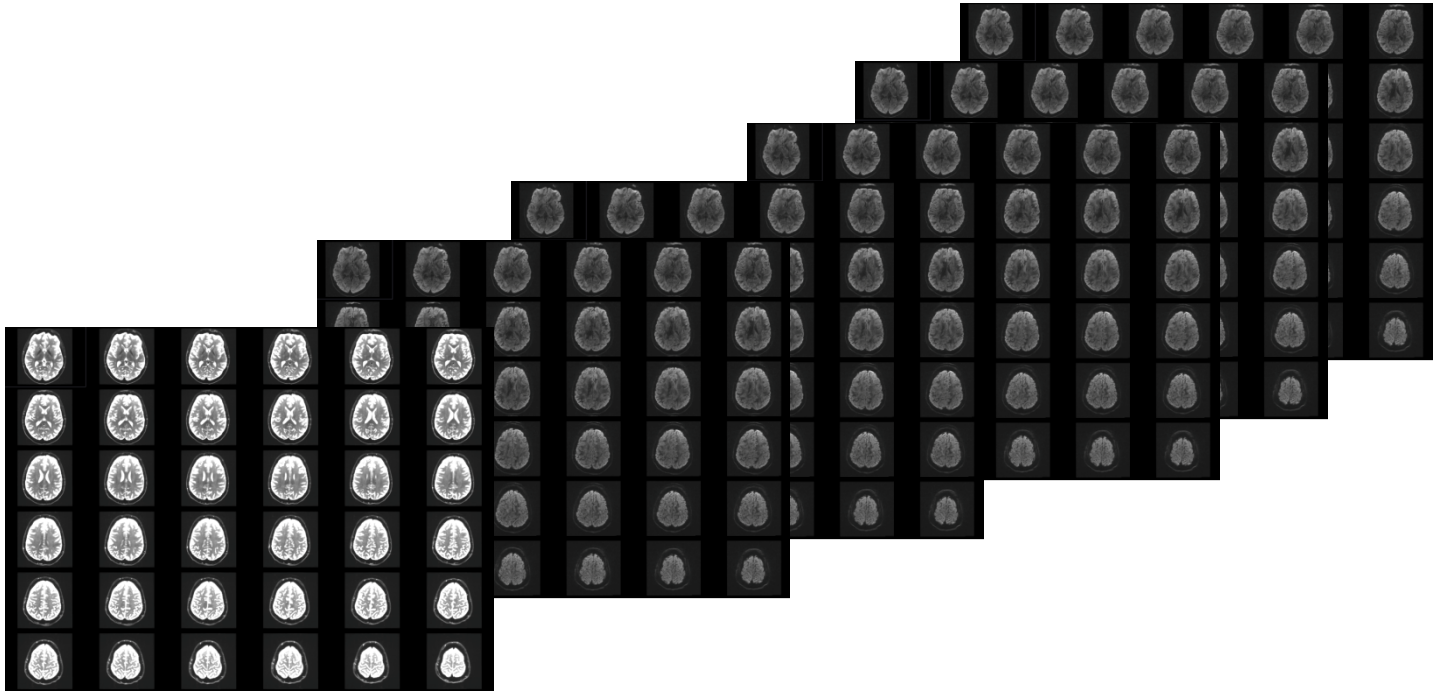


3D
Visualization



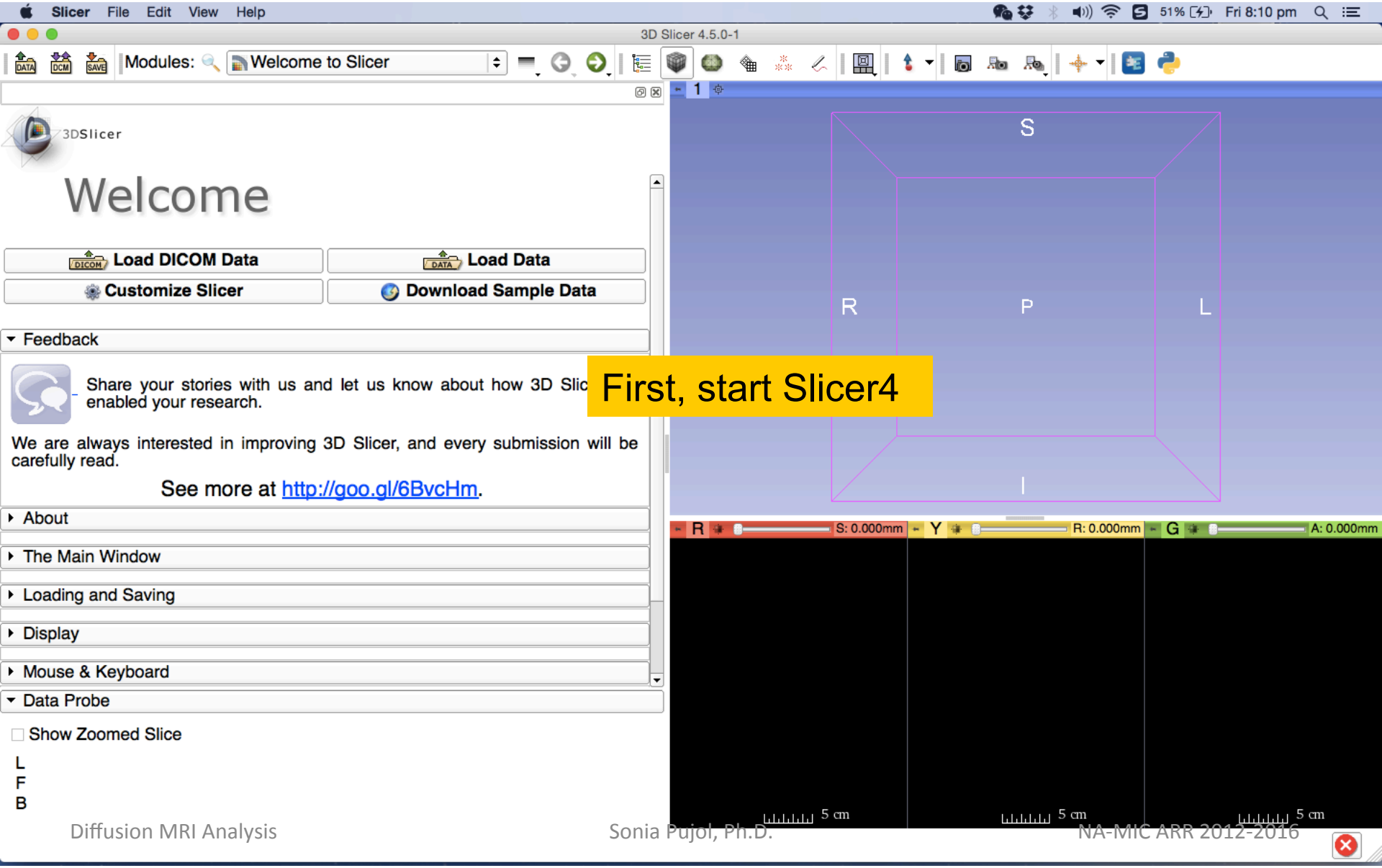
Part 1: From DWI images to Tensors

Understanding the DWI Dataset



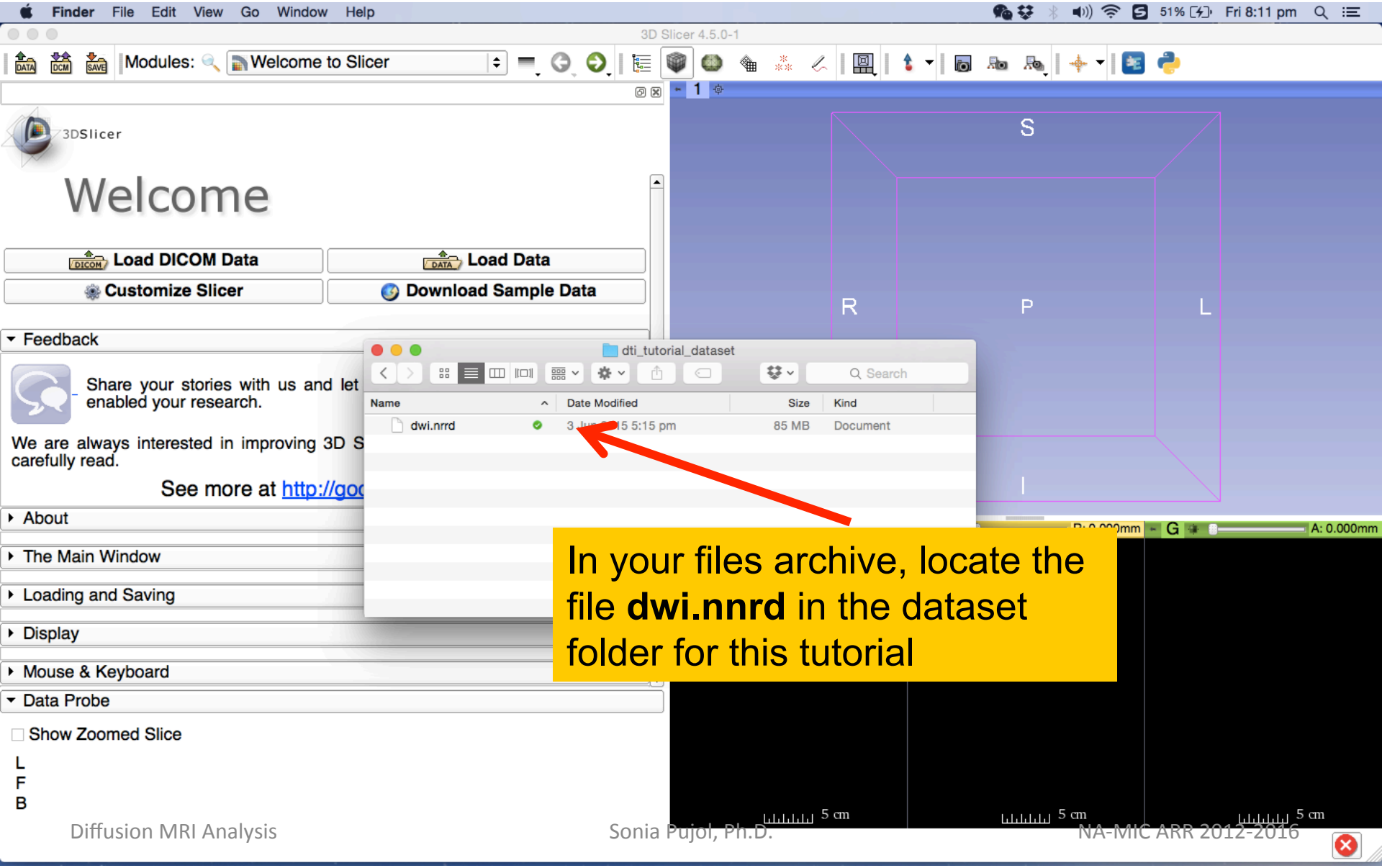
The Diffusion Weighted Imaging (DWI) dataset is composed of 48 volumes acquired with 41 different diffusion-sensitizing gradient directions, and 7 baseline image acquired without diffusion weighting.

Loading the DWI Dataset



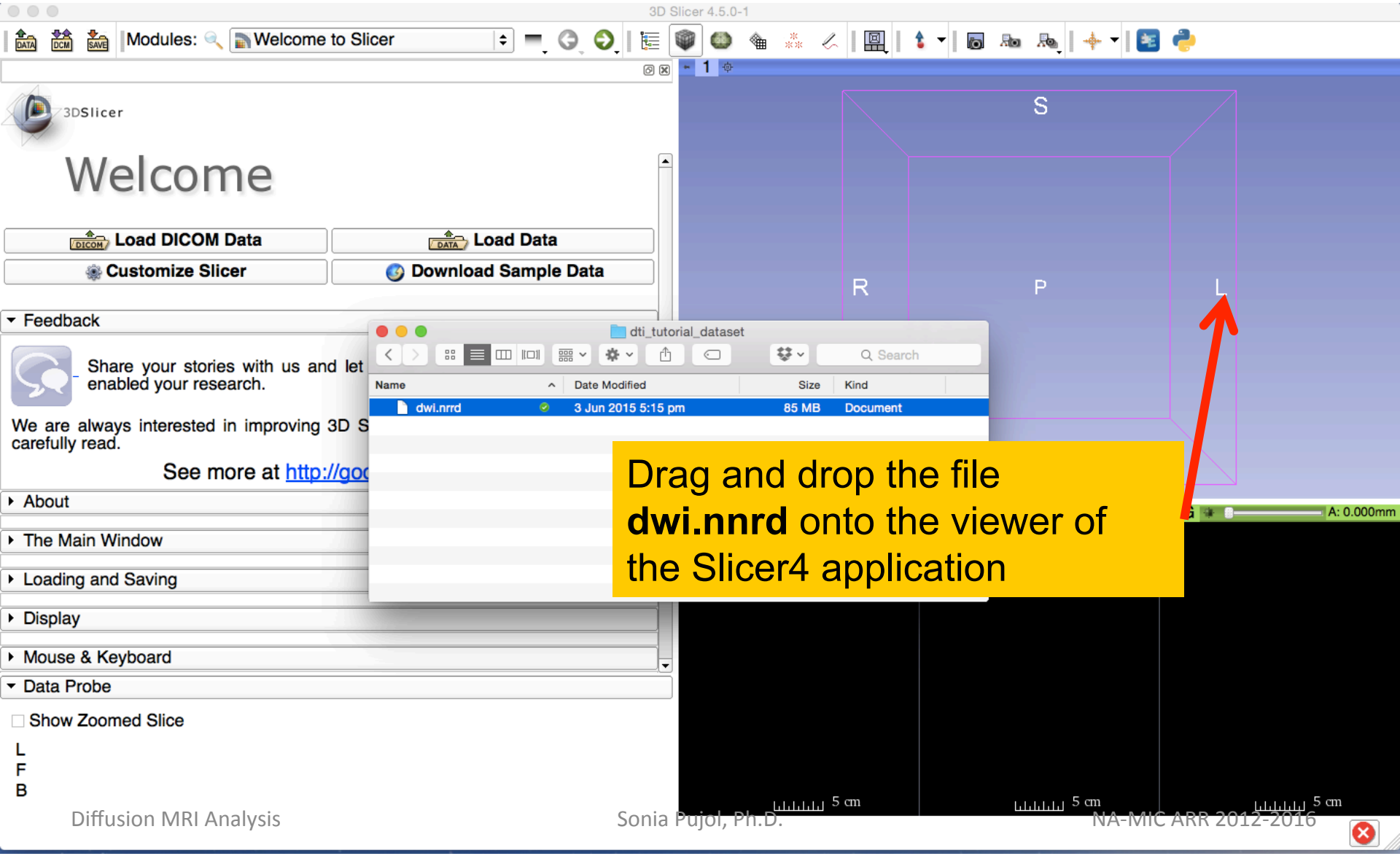
First, start Slicer4

Loading the DWI Dataset



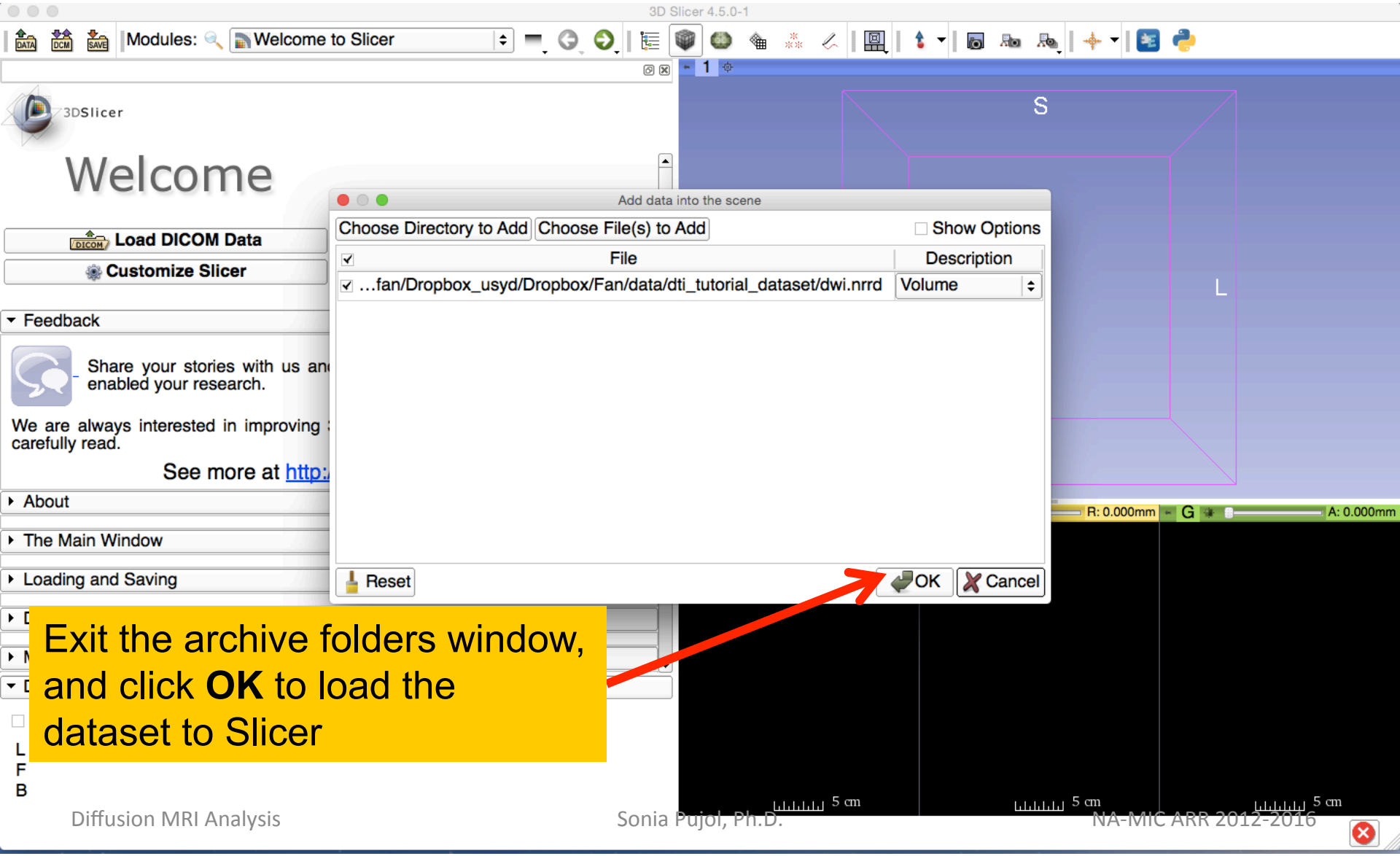
In your files archive, locate the file **dwi.nnrd** in the dataset folder for this tutorial

Loading the DWI Dataset



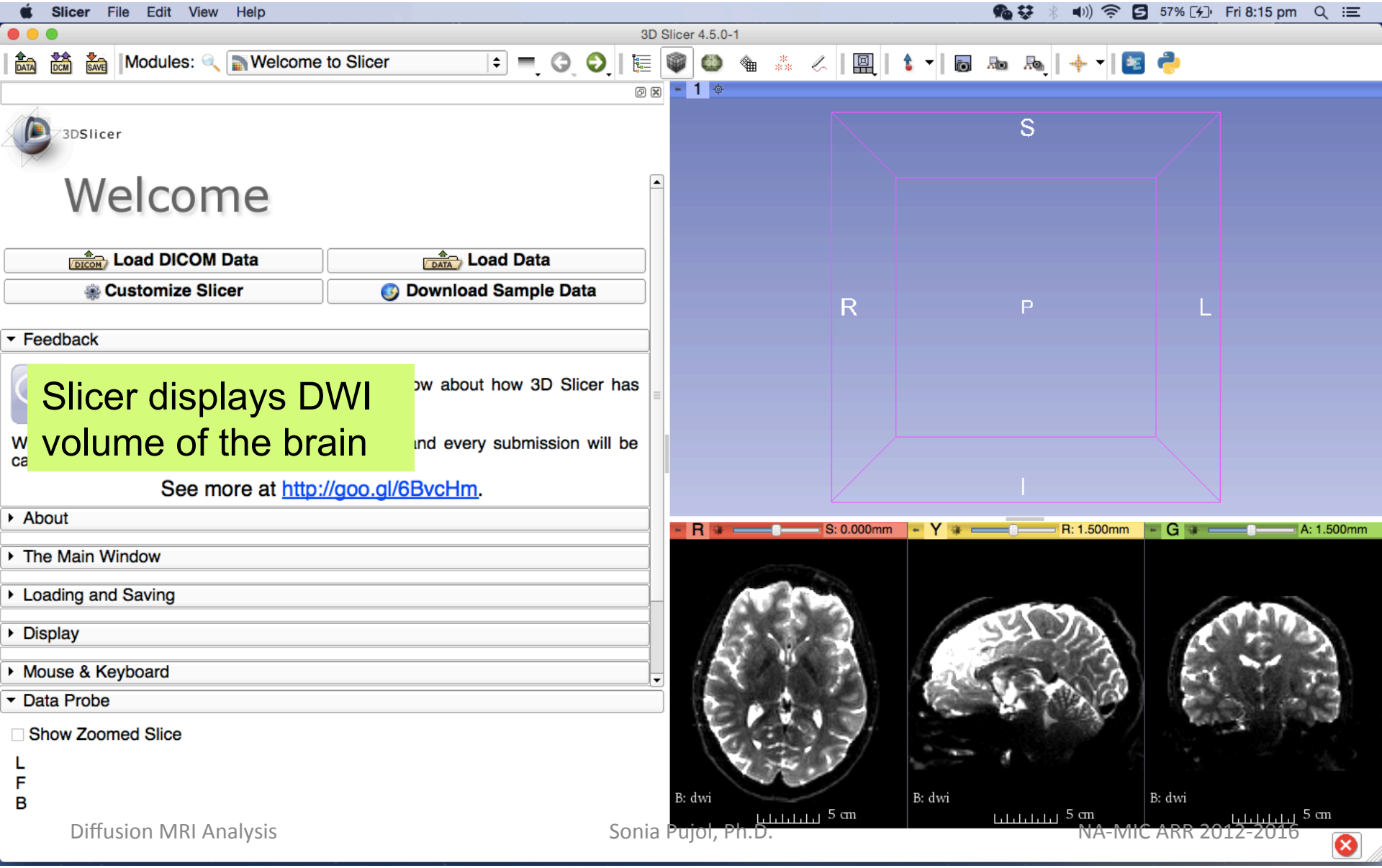
Drag and drop the file **dwi.nnrd** onto the viewer of the Slicer4 application

Loading the DWI Dataset

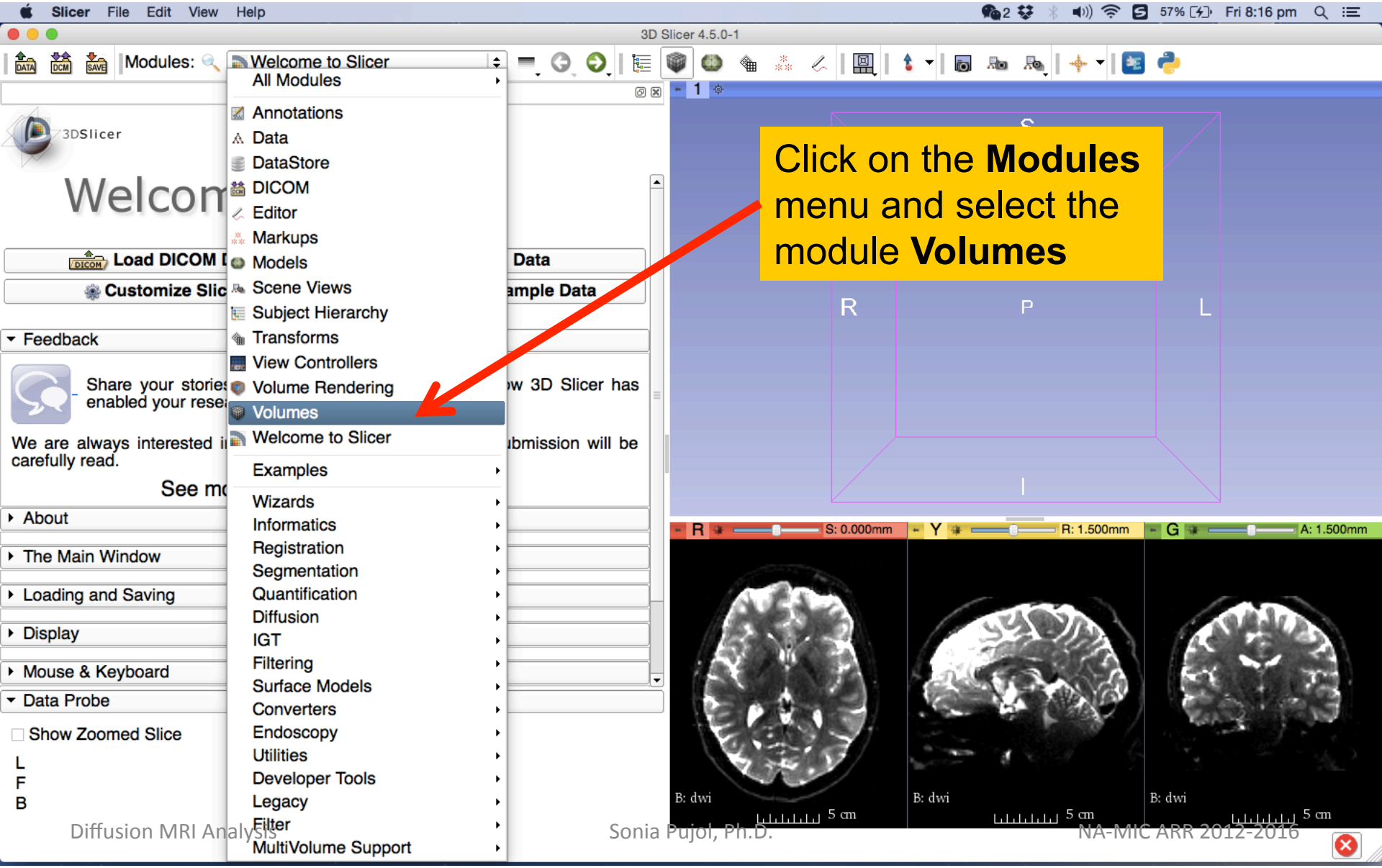


Exit the archive folders window, and click **OK** to load the dataset to Slicer

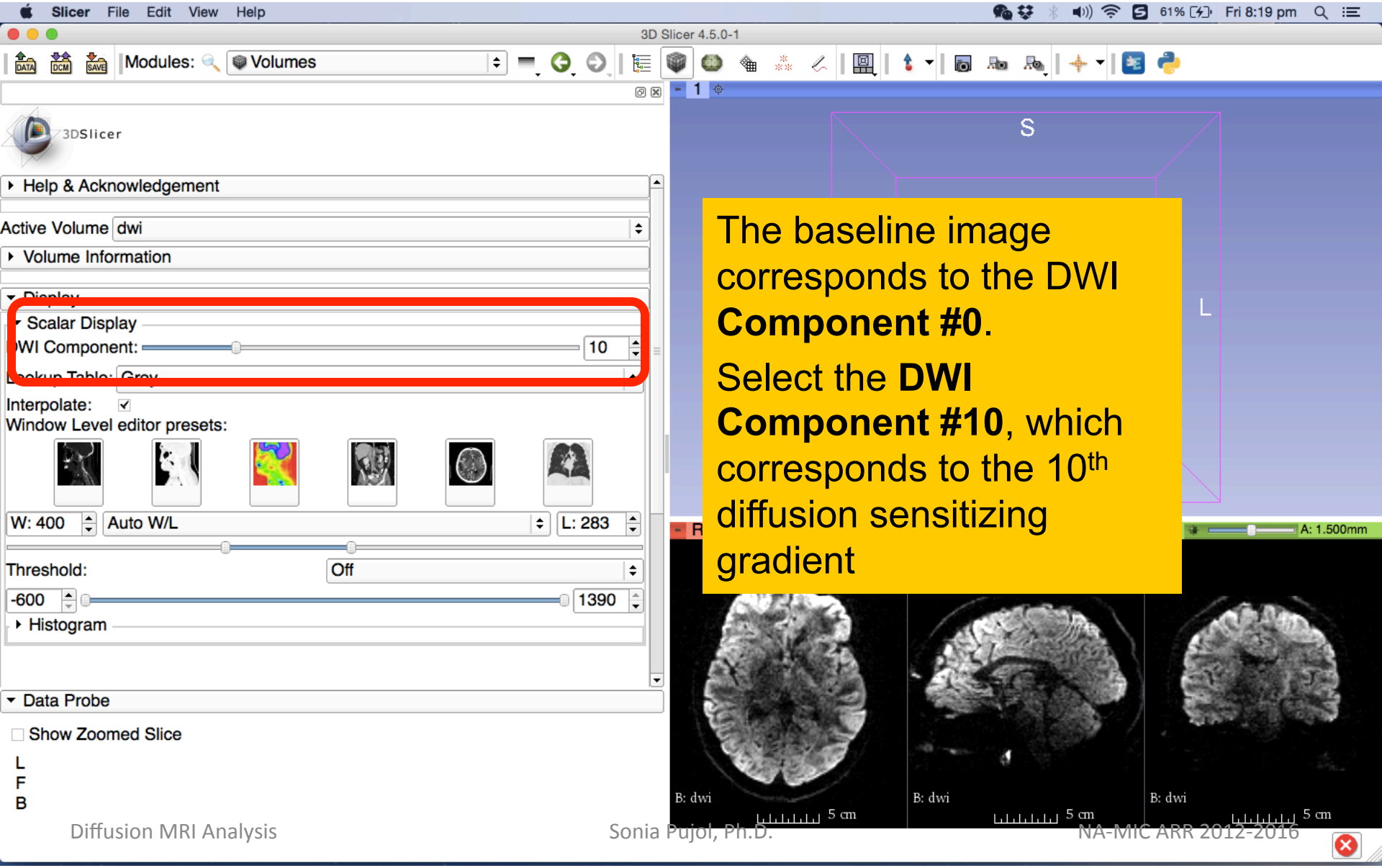
Loading the DWI Dataset



Loading the DWI Dataset



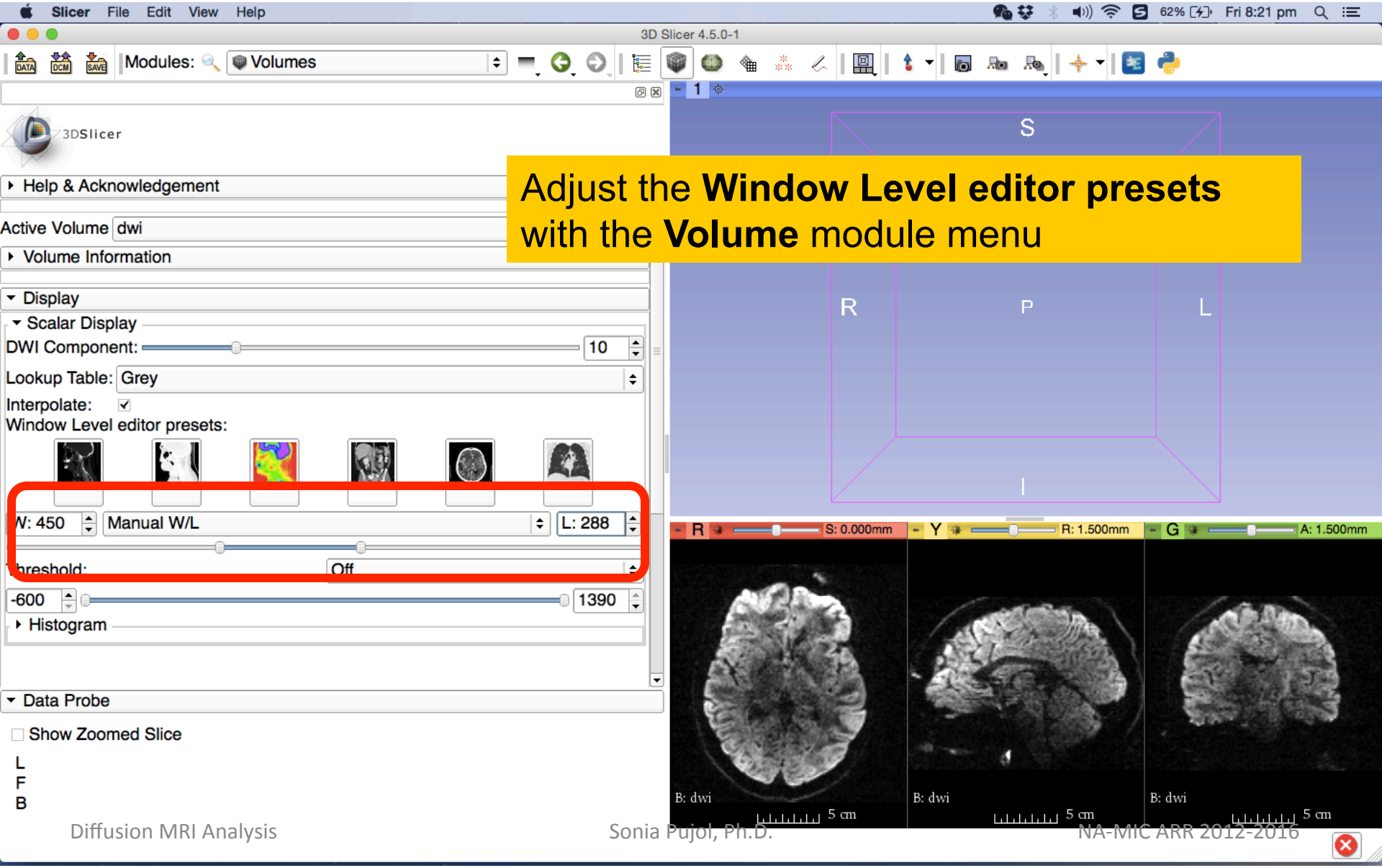
Loading the DWI Dataset



The baseline image corresponds to the DWI **Component #0**.

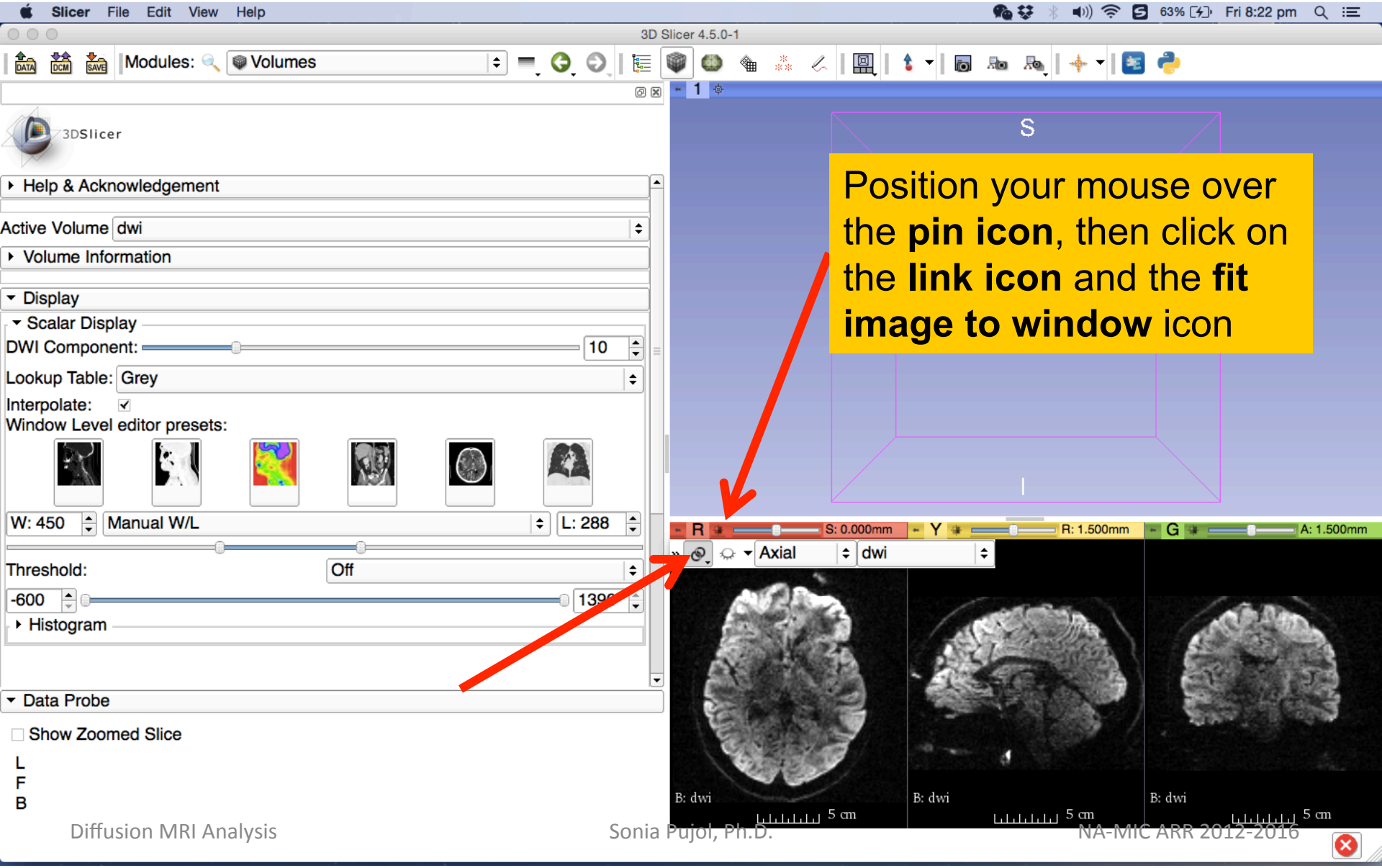
Select the **DWI Component #10**, which corresponds to the 10th diffusion sensitizing gradient

Loading the DWI Dataset



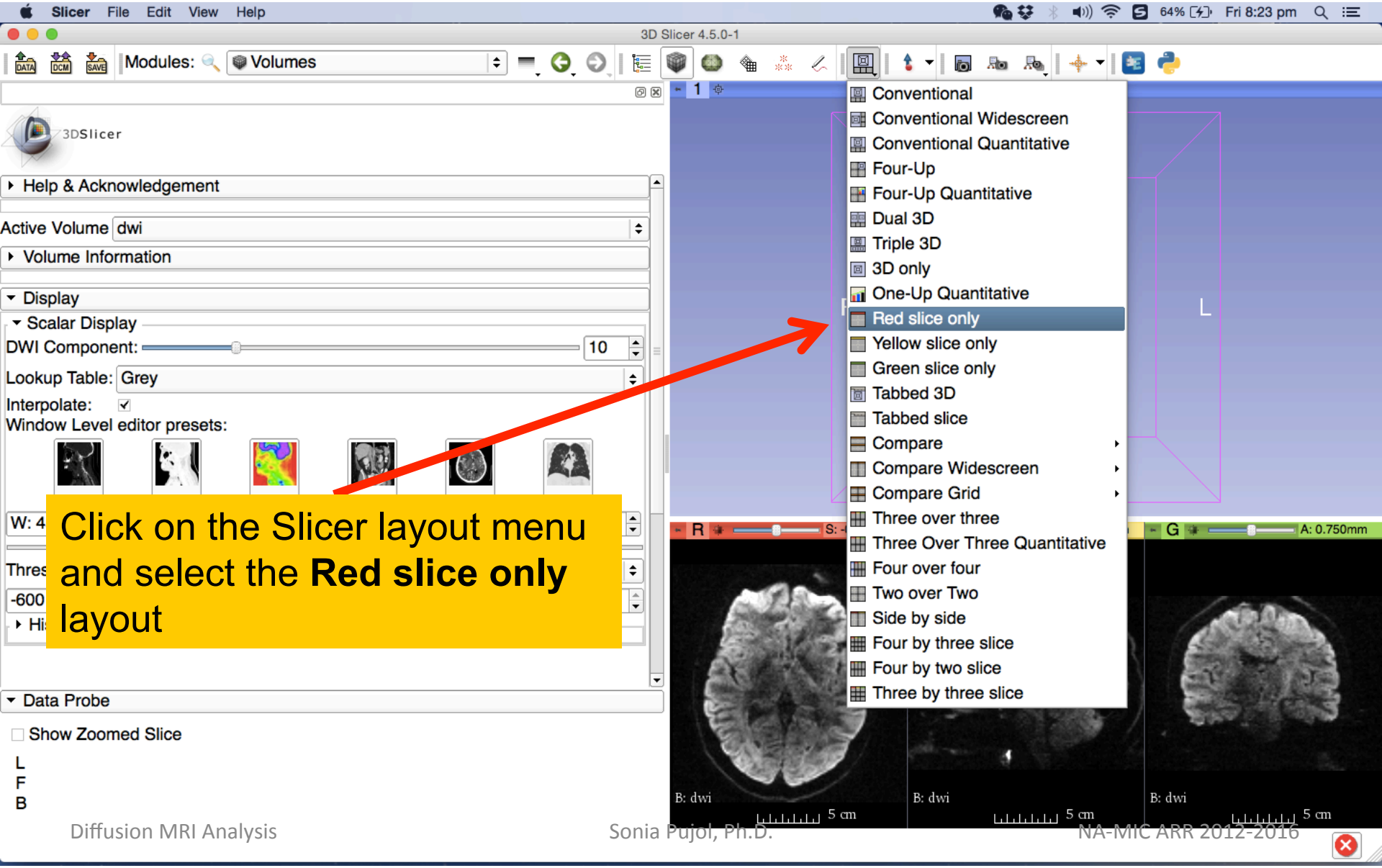
Adjust the **Window Level editor presets** with the **Volume** module menu

Loading the DWI Dataset



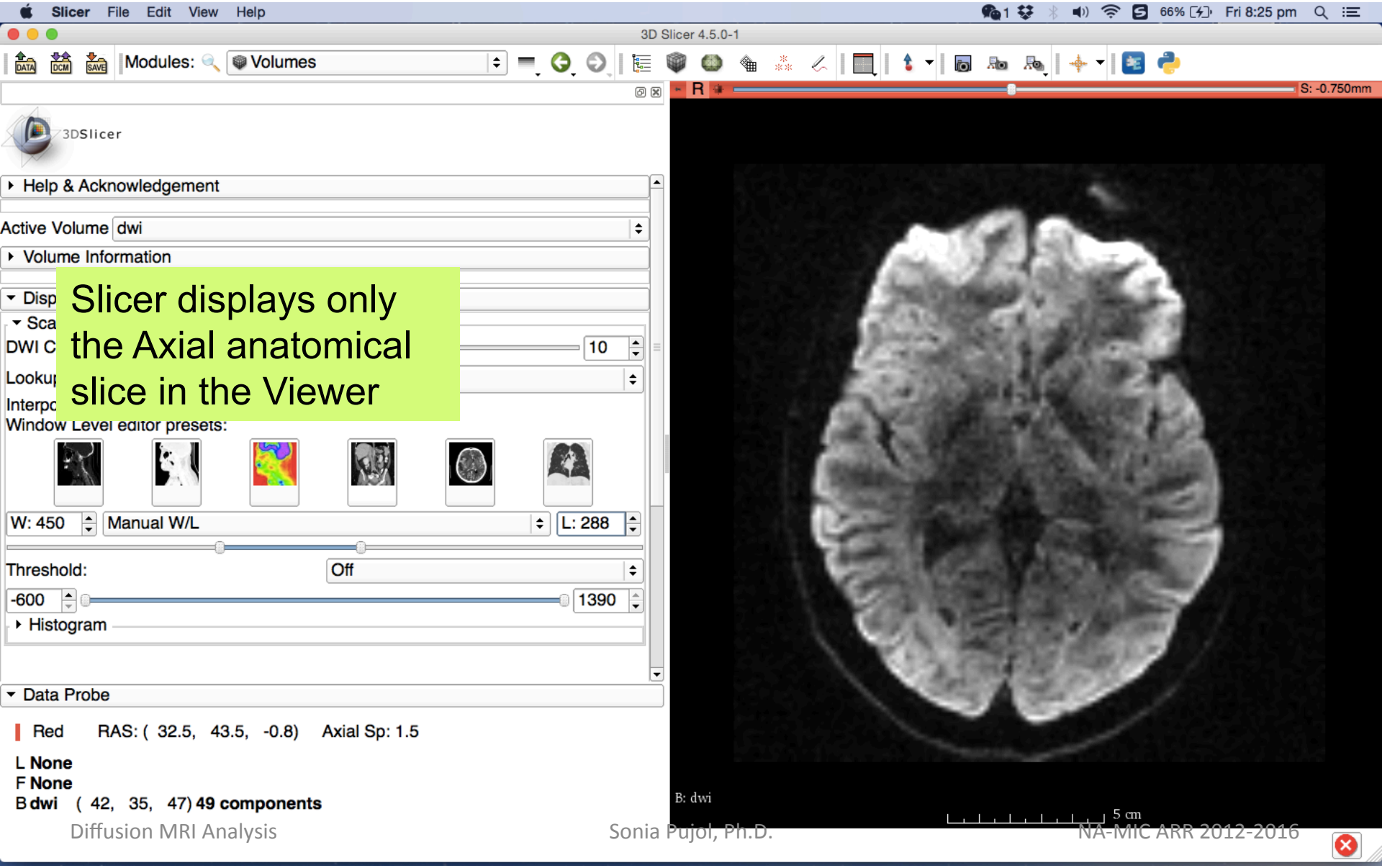
Position your mouse over the **pin icon**, then click on the **link icon** and the **fit image to window** icon

Loading the DWI Dataset

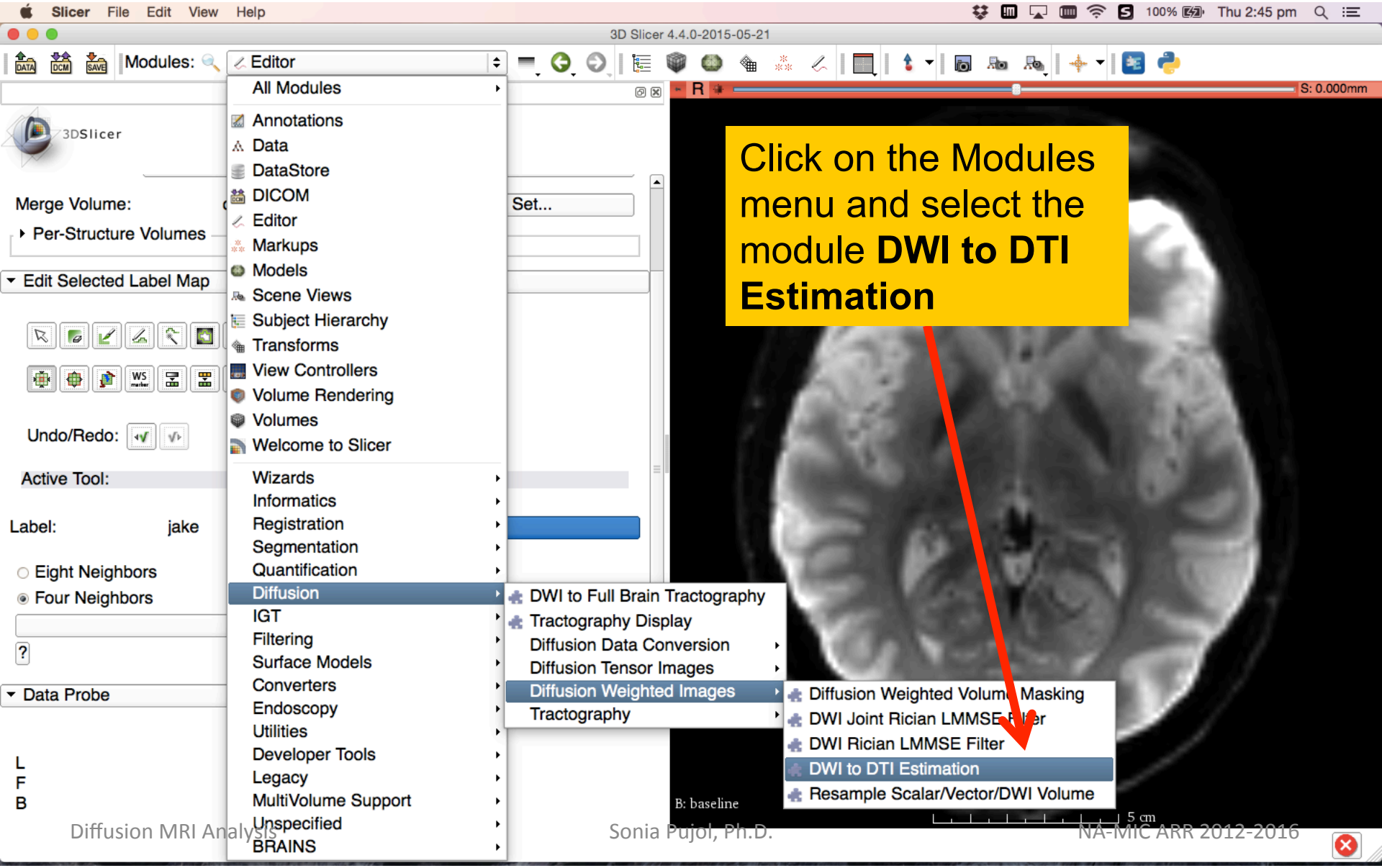


Click on the Slicer layout menu and select the **Red slice only** layout

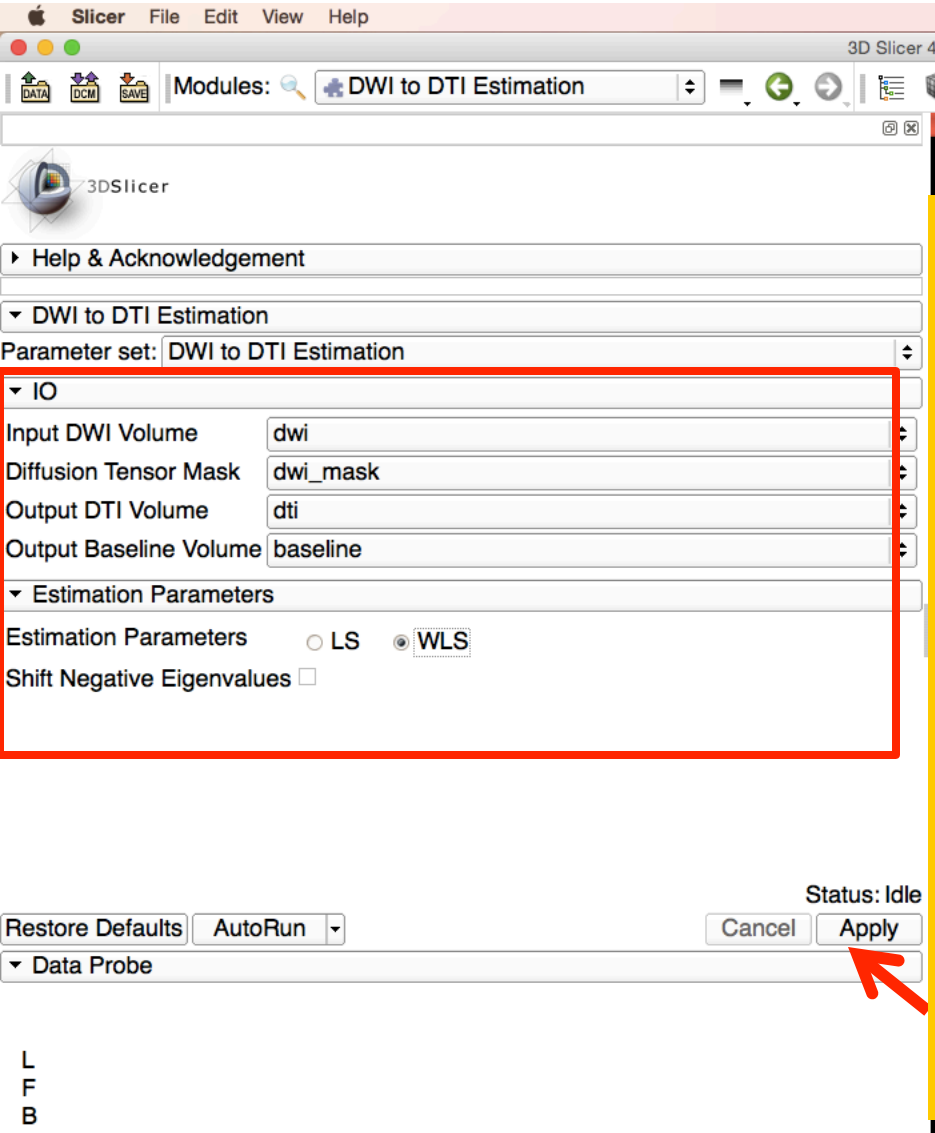
Loading the DWI Dataset



Estimating the tensor



Estimating the tensor



Select the module **DWI to DTI Estimation** in the modules menu:

-Set the **Input DWI volume** to '**dwi**'

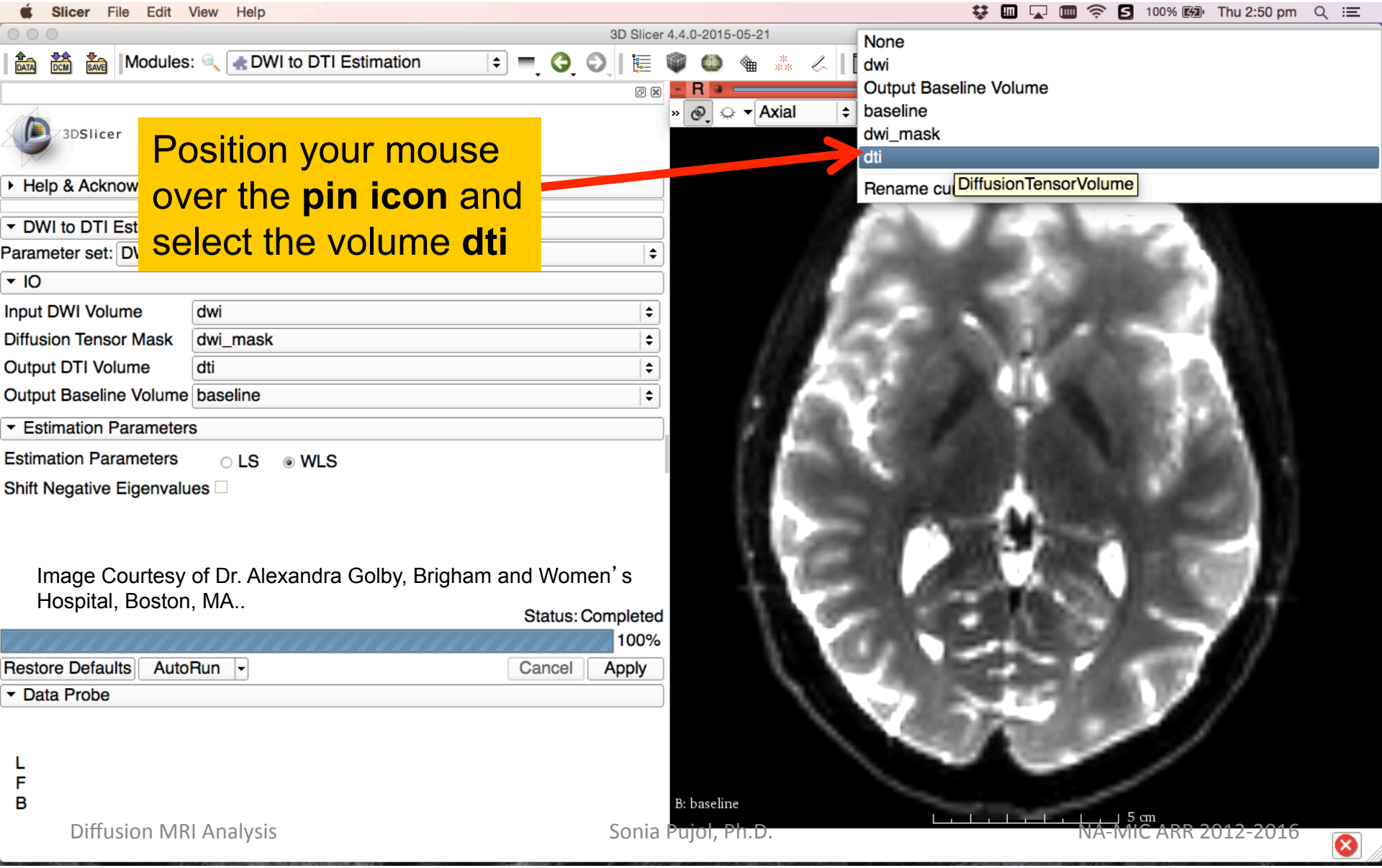
-Set the **Diffusion Tensor Mask** to '**None**'

- Select **Output DTI Volume** '**Create and Rename New Volume**', and rename it '**dti**'

-Set **Output Baseline Volume** to '**baseline**'

-Select the **Estimation Parameters** **'WLS'** (Weighted Least Squares) and click on **Apply**.

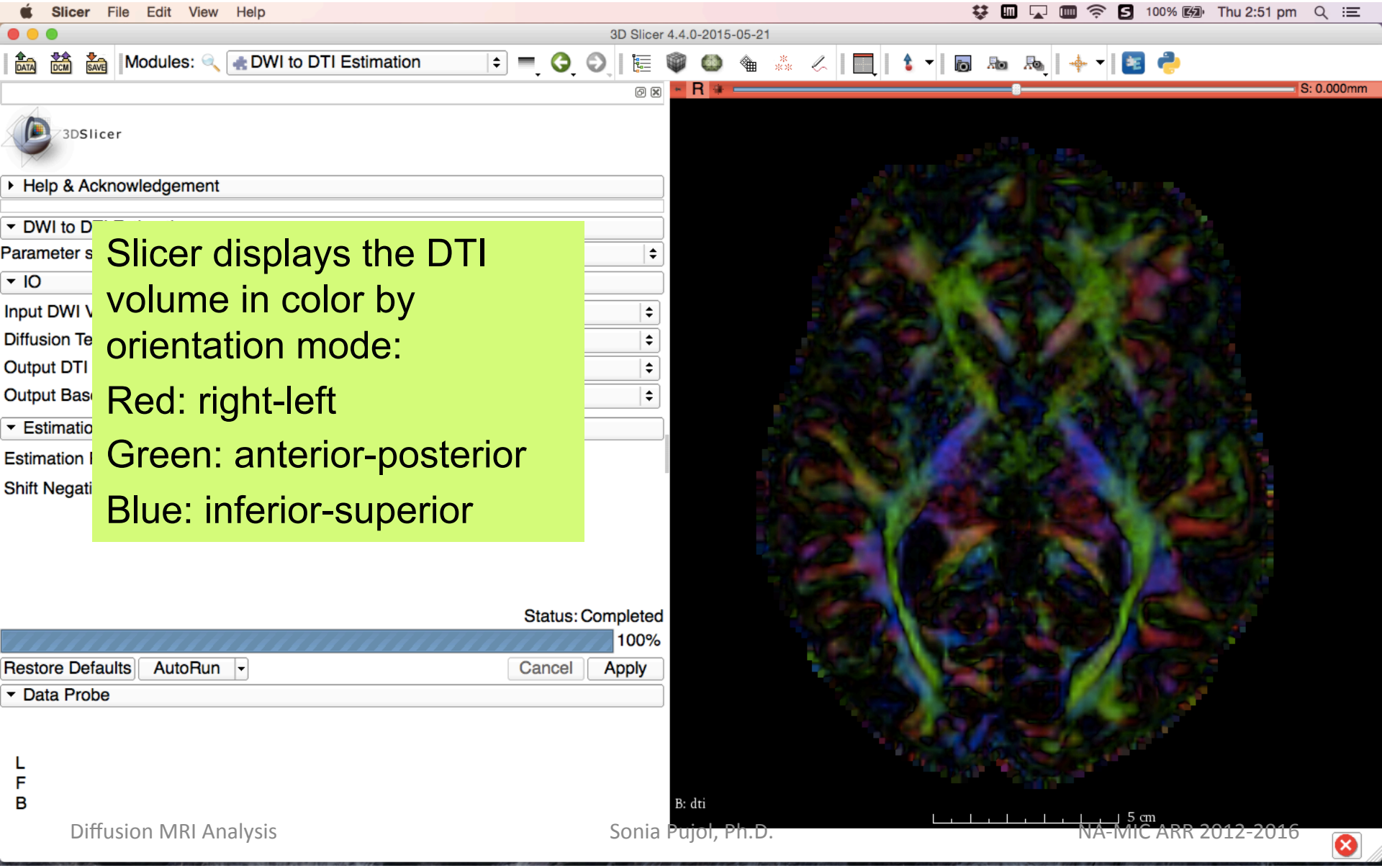
Estimating the tensor



Position your mouse over the **pin icon** and select the volume **dti**

Image Courtesy of Dr. Alexandra Golby, Brigham and Women's Hospital, Boston, MA..

Exploring the DWI Dataset



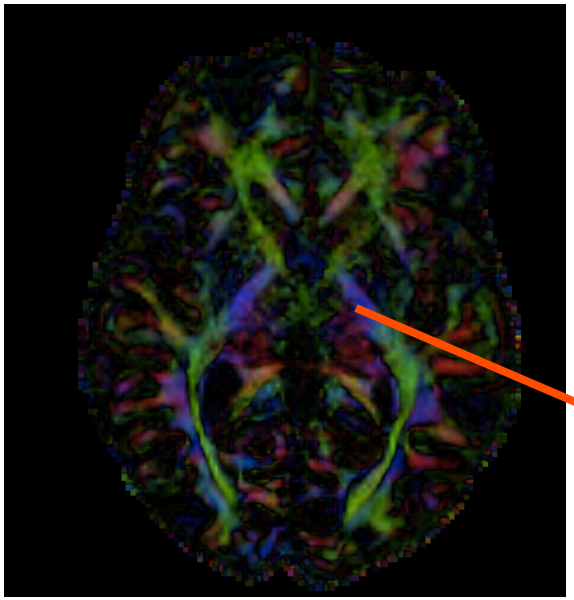
Slicer displays the DTI volume in color by orientation mode:

Red: right-left

Green: anterior-posterior

Blue: inferior-superior

Diffusion Tensor Data



$$S_i = S_0 e^{-b\hat{g}i^T \underline{D}\hat{g}_i}$$

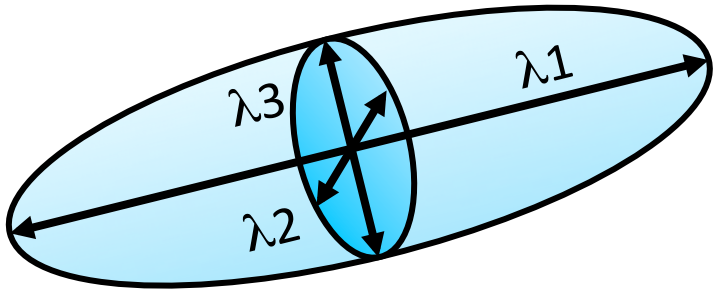
Stejskal-Tanner equation (1965)

$$\underline{\mathbf{D}} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

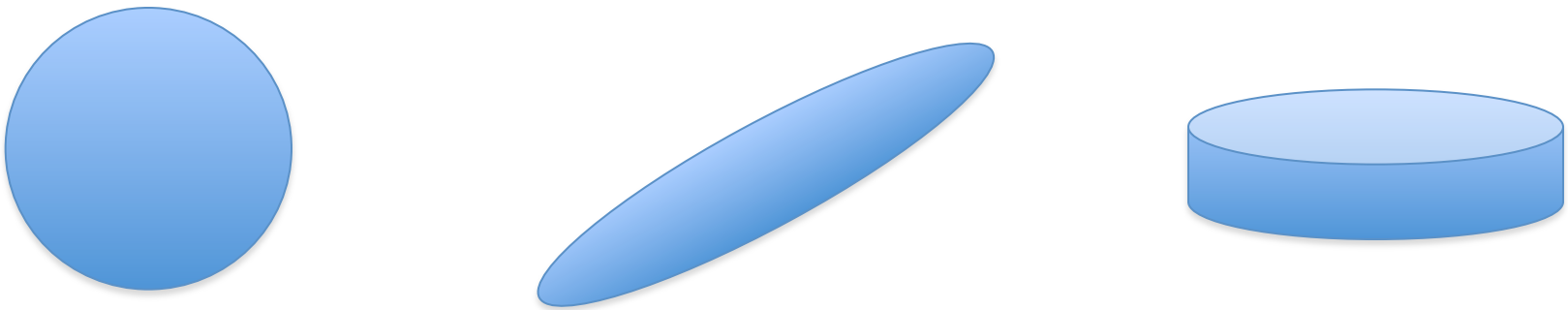
The diffusion tensor <u>D</u> in the voxel (I,J,K) is a 3x3 symmetric matrix.

Diffusion Tensor

- The diffusion tensor D in each voxel can be visualized as a diffusion ellipsoid, with the eigenvectors indicating the directions of the principal axes, and the ellipsoidal proportional to the square root of the eigenvalues defining the
- Scalar maps can be derived from the rotationally invariant eigenvalues λ1, λ2, λ3 to characterize the size and shape of the diffusion tensor.



Diffusion Tensor Shape



$\lambda 1 = \lambda 2 = \lambda 3$

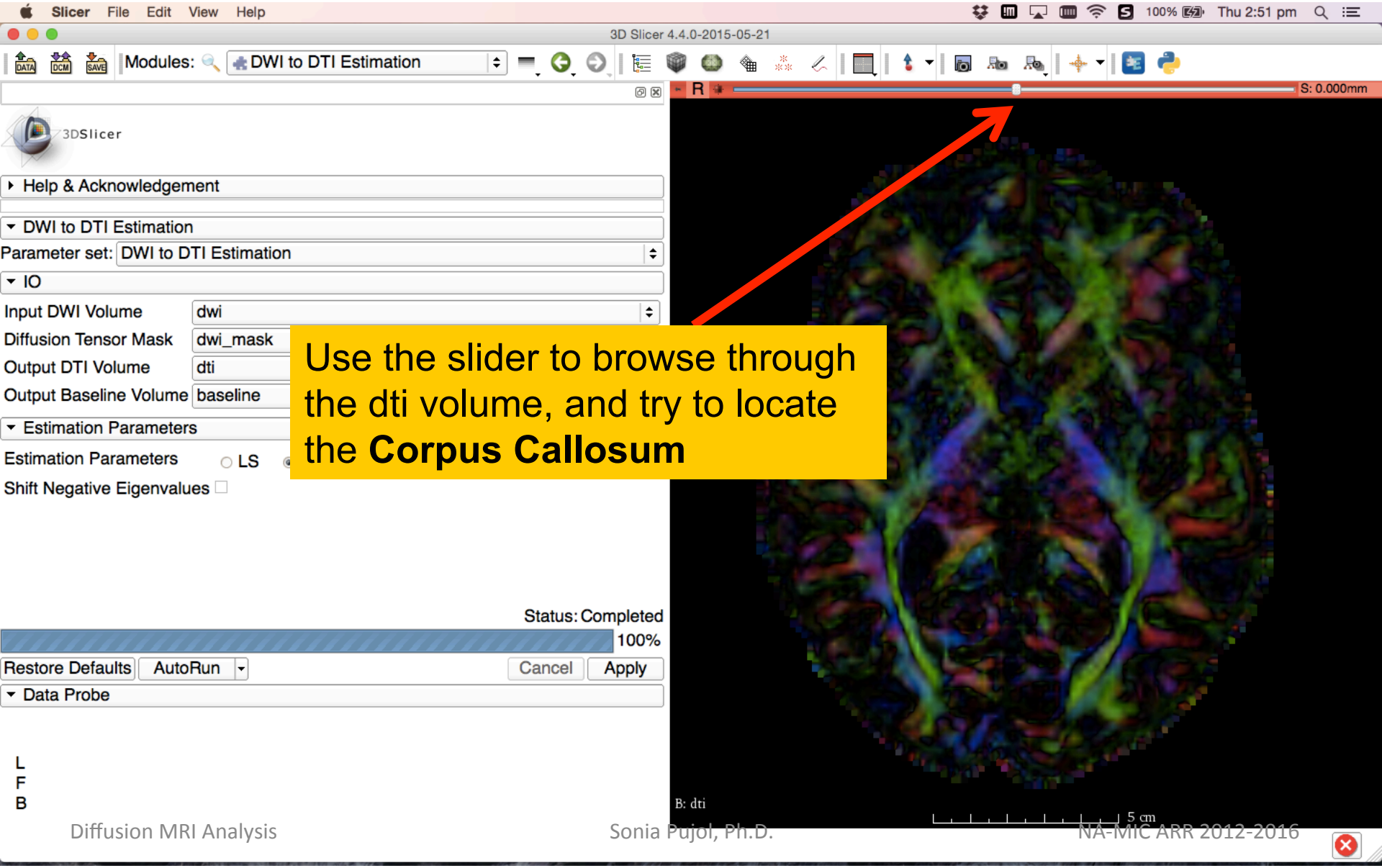
$\lambda 1 >> \lambda 2, \lambda 3$

$\lambda 1 \sim \lambda 2 >> \lambda 3$

Isotropic media (Cerebrospinal Fluid, gray matter)

Anisotropic media (white matter)

Exploring the DWI Dataset



Use the slider to browse through the dti volume, and try to locate the **Corpus Callosum**

Corpus Callosum

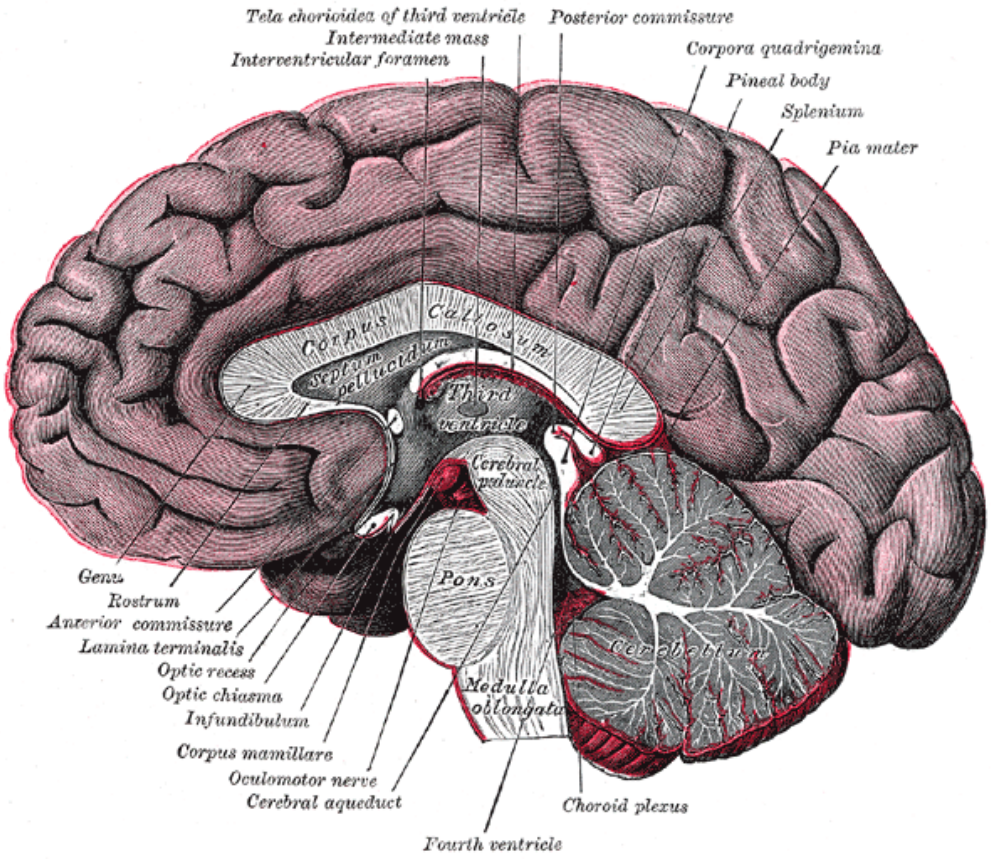


Image from Gray's Anatomy

The corpus callosum is a broad thick bundle of dense myelinated fibers that connect the left and right hemisphere. It is the largest white matter structure in the brain

Corpus Callosum

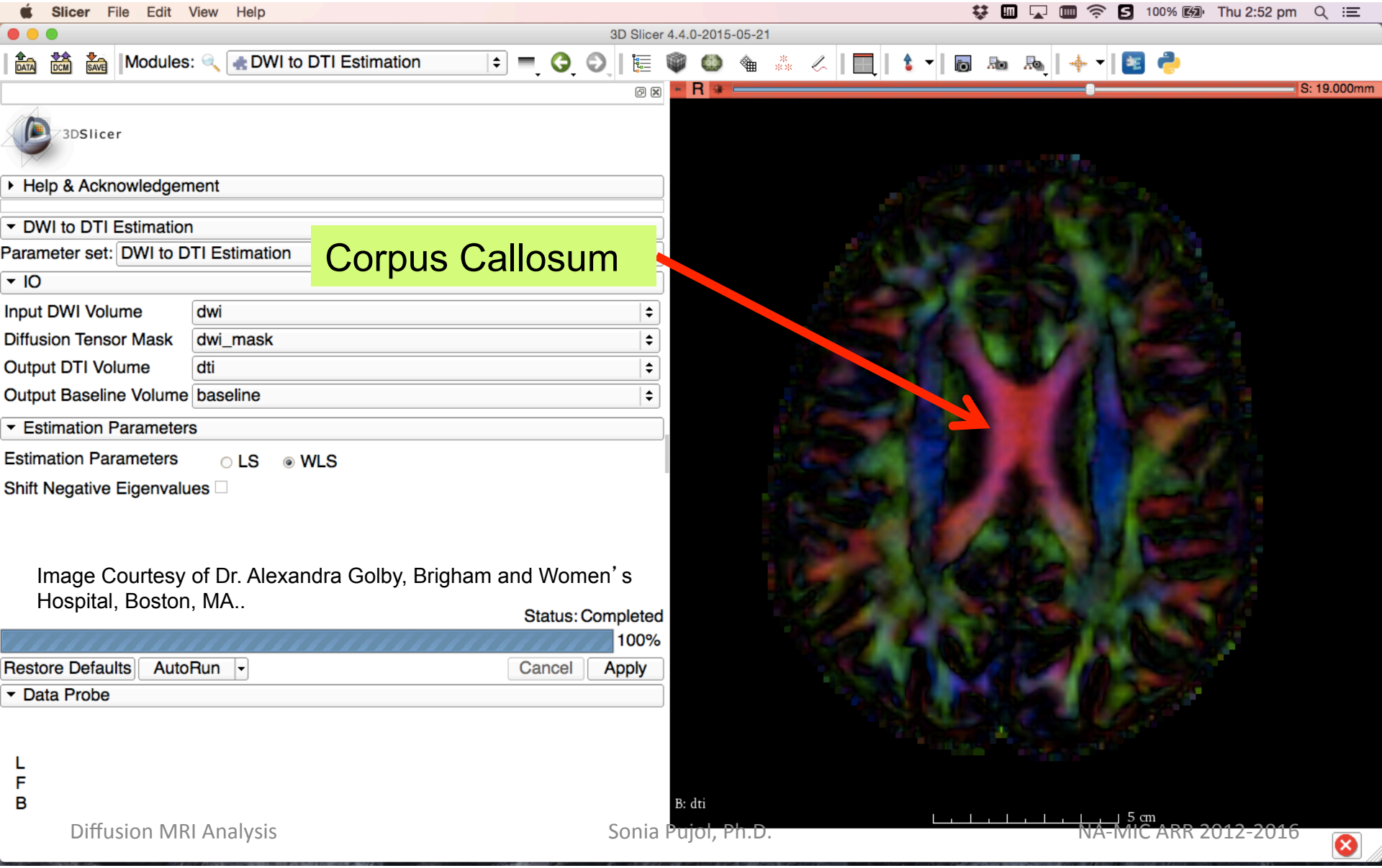


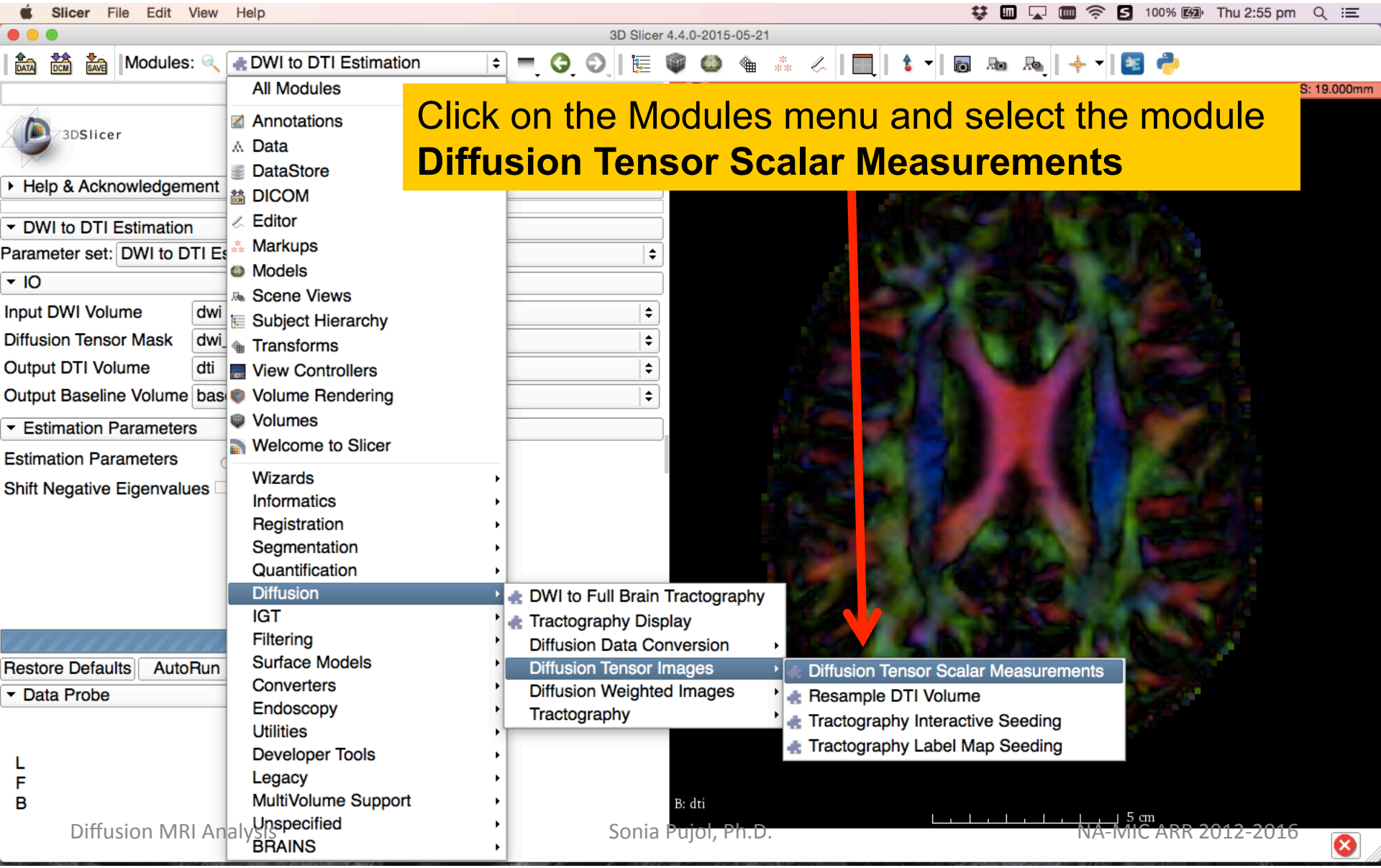
Image Courtesy of Dr. Alexandra Golby, Brigham and Women's Hospital, Boston, MA..

Characterizing the Size of the tensor: Trace

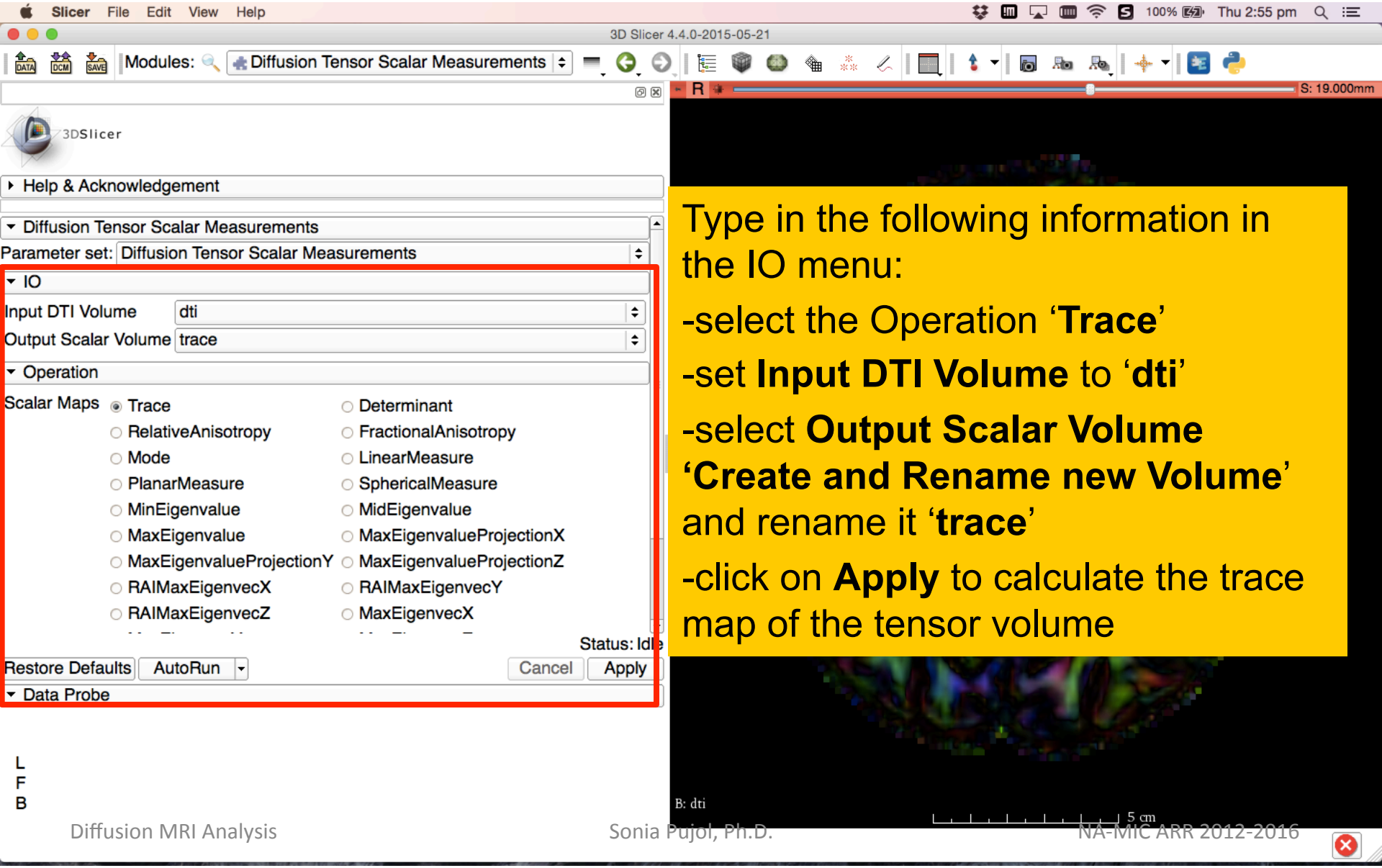
$$\text{Trace}(D) = \lambda 1 + \lambda 2 + \lambda 3$$

- Trace(D) is intrinsic to the tissue and is independent of fiber orientation, and diffusion sensitizing gradient directions
- Trace(D) is a clinically relevant parameter for monitoring stroke and neurological condition (degree of structural coherence in tissue)
- Trace(D) is useful to characterize the size of the diffusion ellipsoid

Trace


Click on the Modules menu and select the module
Diffusion Tensor Scalar Measurements
Slicer File Edit View Help
3D Slicer 4.4.0-2015-05-21
Modules:
DWI to DTI Estimation
All Modules
Annotations
Data
DataStore
DICOM
Editor
Markups
Models
Scene Views
Subject Hierarchy
Transforms
View Controllers
Volume Rendering
Volumes
Welcome to Slicer
Wizards
Informatics
Registration
Segmentation
Quantification
Diffusion
IGT
Filtering
Surface Models
Converters
Endoscopy
Utilities
Developer Tools
Legacy
MultiVolume Support
Unspecified
BRAINS
DWI to Full Brain Tractography
Tractography Display
Diffusion Data Conversion
Diffusion Tensor Images
Diffusion Weighted Images
Tractography
Diffusion Tensor Scalar Measurements
Resample DTI Volume
Tractography Interactive Seeding
Tractography Label Map Seeding
Help & Acknowledgement
DWI to DTI Estimation
Parameter set:
IO
Input DWI Volume
Diffusion Tensor Mask
Output DTI Volume
Output Baseline Volume
Estimation Parameters
Estimation Parameters
Shift Negative Eigenvalues
Restore Defaults
AutoRun
Data Probe
B: dti
5 cm

Trace



Type in the following information in the IO menu:

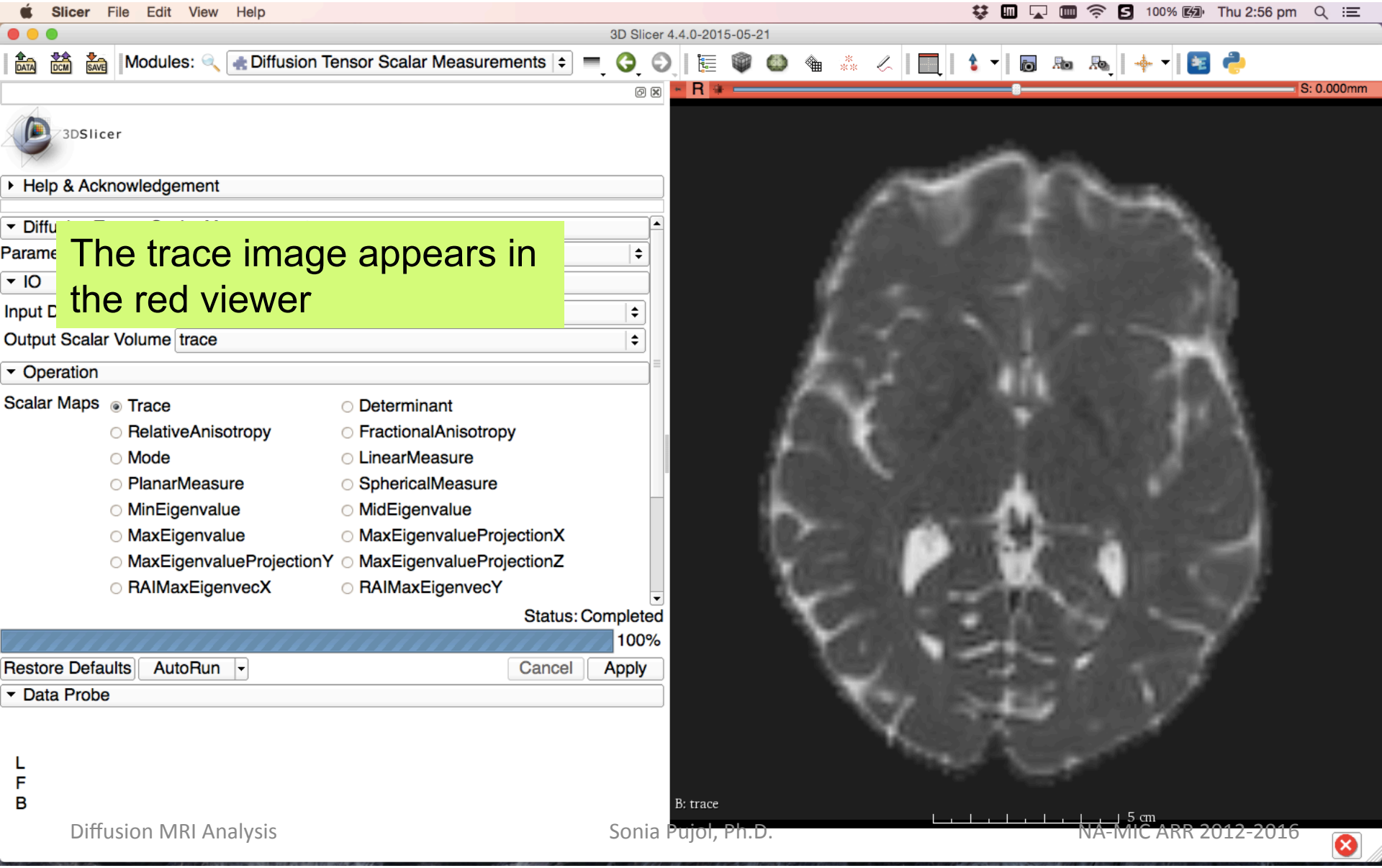
-select the Operation '**Trace**'

-set **Input DTI Volume** to '**dti**'

-select **Output Scalar Volume** '**Create and Rename new Volume**' and rename it '**trace**'

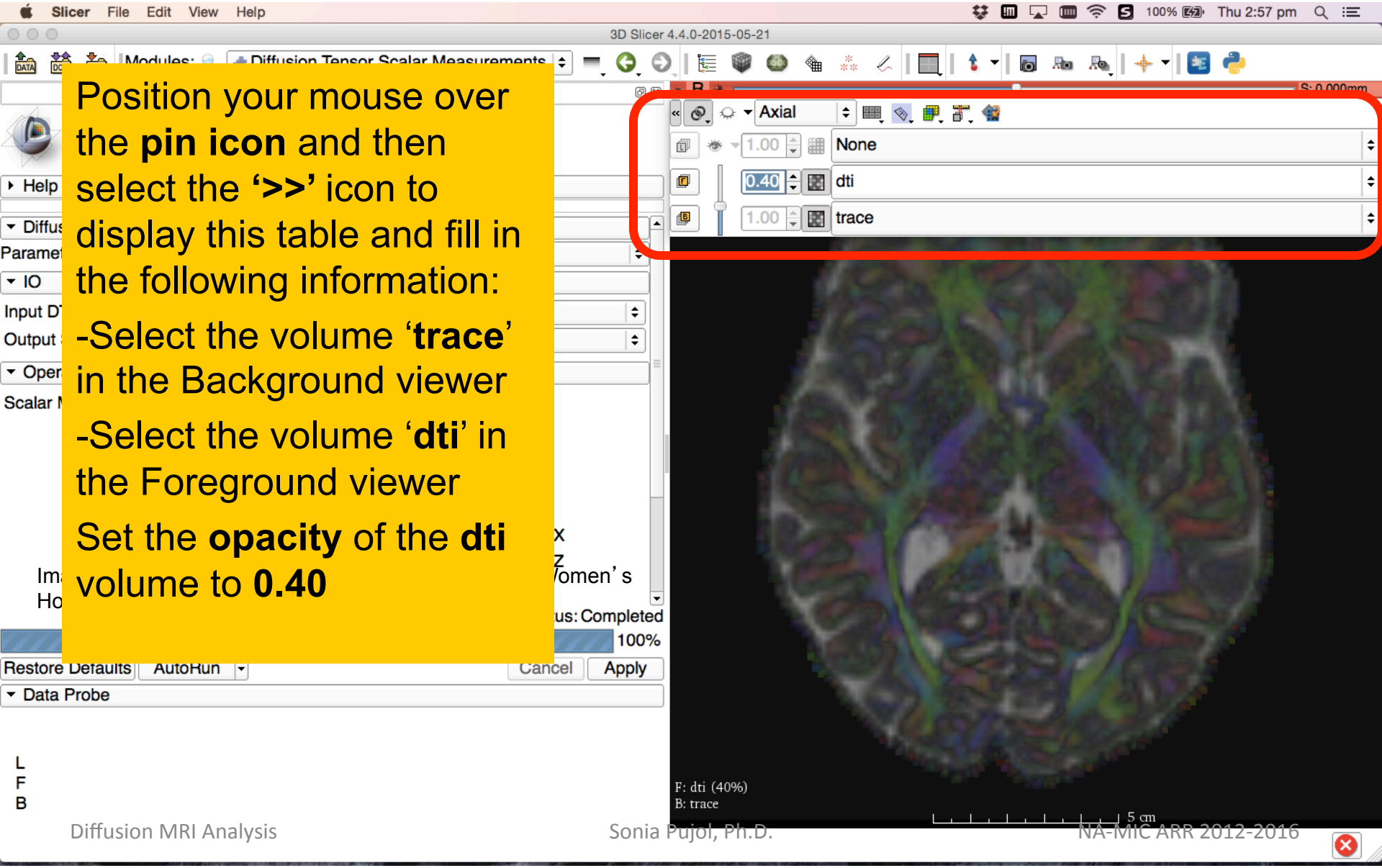
-click on **Apply** to calculate the trace map of the tensor volume

Trace



The trace image appears in the red viewer

Trace



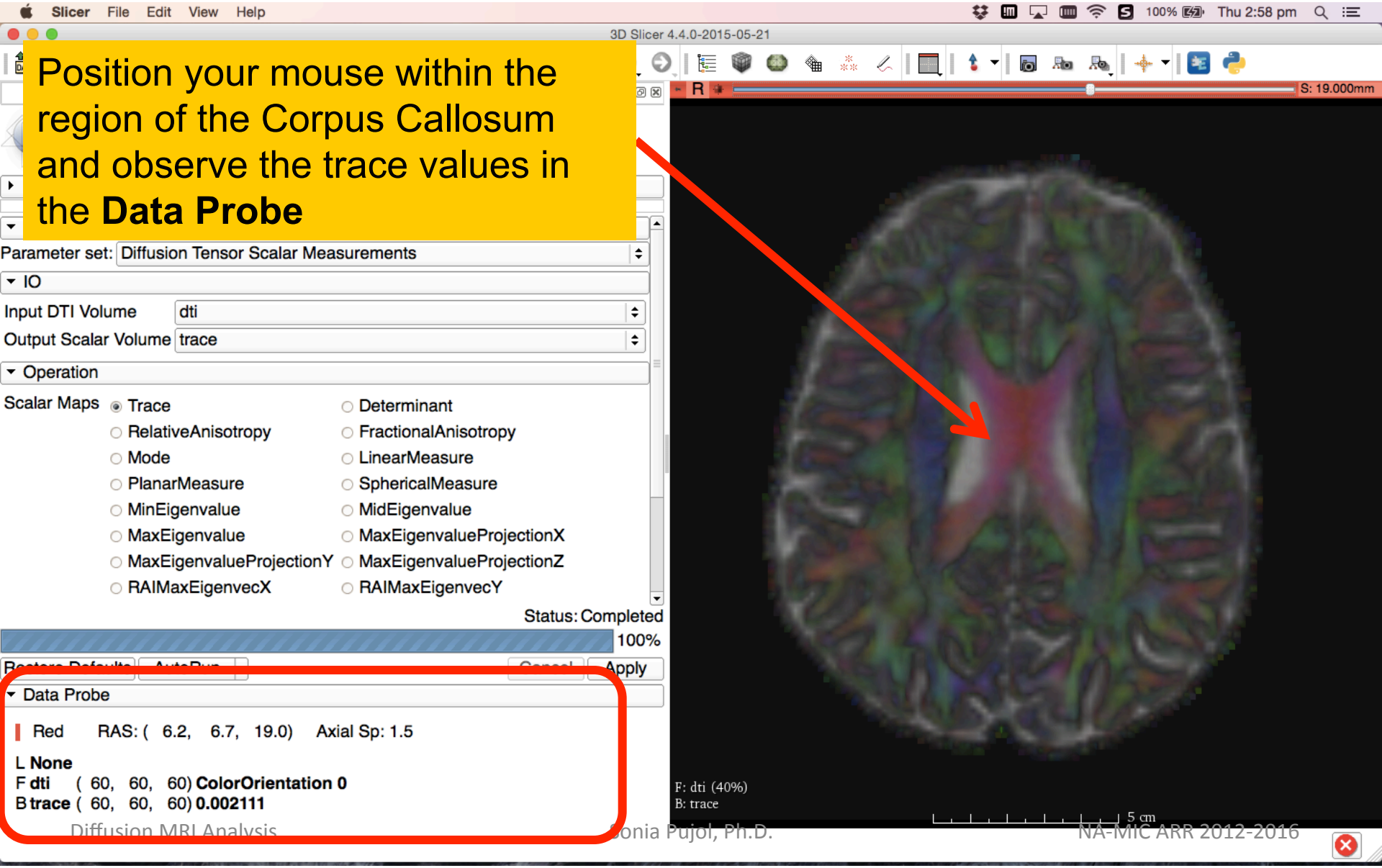
Position your mouse over the **pin icon** and then select the **'>>'** icon to display this table and fill in the following information:

-Select the volume '**trace**' in the Background viewer

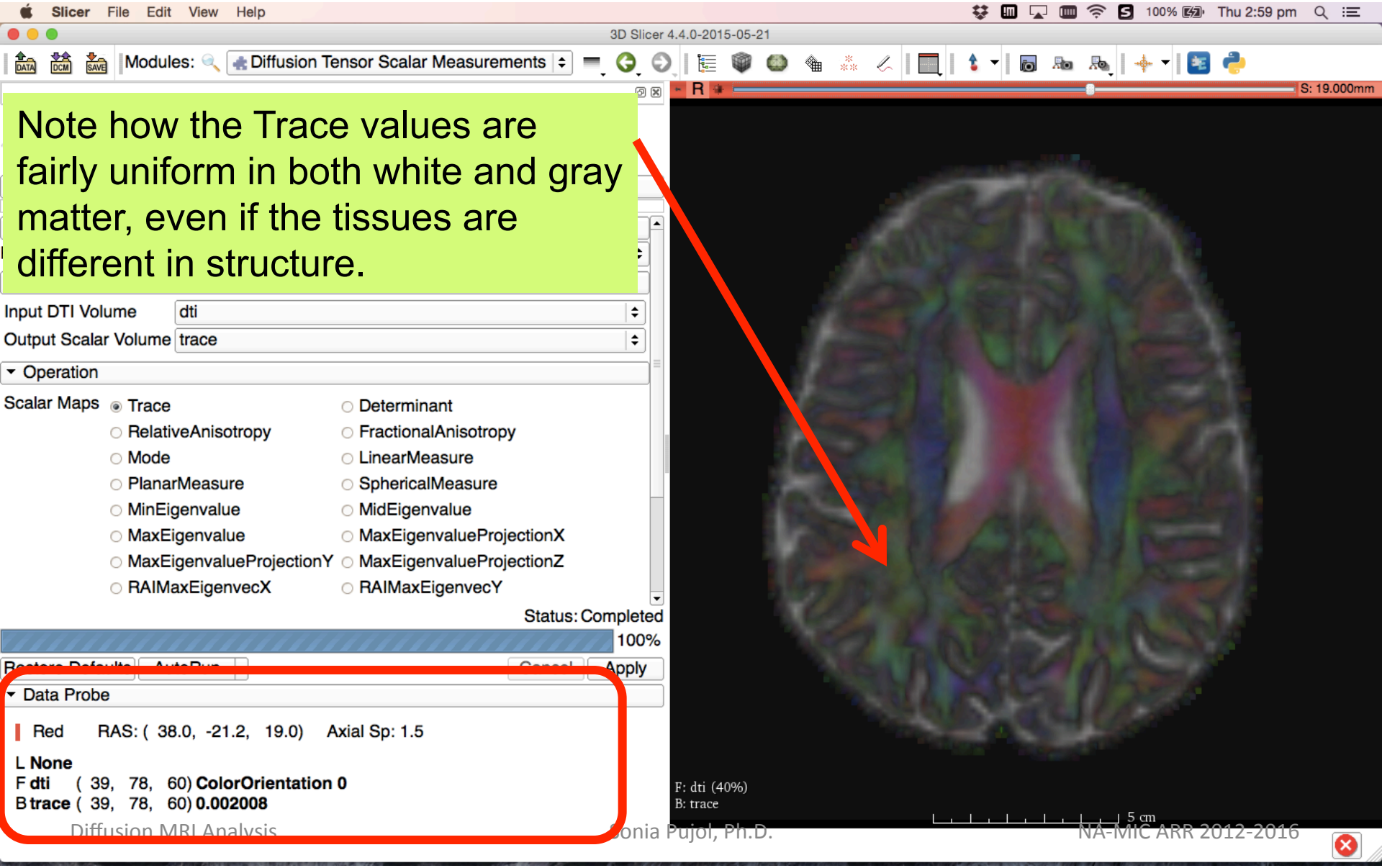
-Select the volume '**dti**' in the Foreground viewer

Set the **opacity** of the **dti** volume to **0.40**

Trace


Slicer File Edit View Help
3D Slicer 4.4.0-2015-05-21
Position your mouse within the region of the Corpus Callosum and observe the trace values in the **Data Probe**
Parameter set: Diffusion Tensor Scalar Measurements
IO
Input DTI Volume dti
Output Scalar Volume trace
Operation
Scalar Maps
Trace
Determinant
RelativeAnisotropy
FractionalAnisotropy
Mode
LinearMeasure
PlanarMeasure
SphericalMeasure
MinEigenvalue
MidEigenvalue
MaxEigenvalue
MaxEigenvalueProjectionX
MaxEigenvalueProjectionY
MaxEigenvalueProjectionZ
RAIMaxEigenvecX
RAIMaxEigenvecY
Status: Completed
100%
Apply
Data Probe
Red RAS: (6.2, 6.7, 19.0) Axial Sp: 1.5
L None
F dti (60, 60, 60) ColorOrientation 0
B trace (60, 60, 60) 0.002111
S: 19.000mm
F: dti (40%)
B: trace
5 cm

Trace

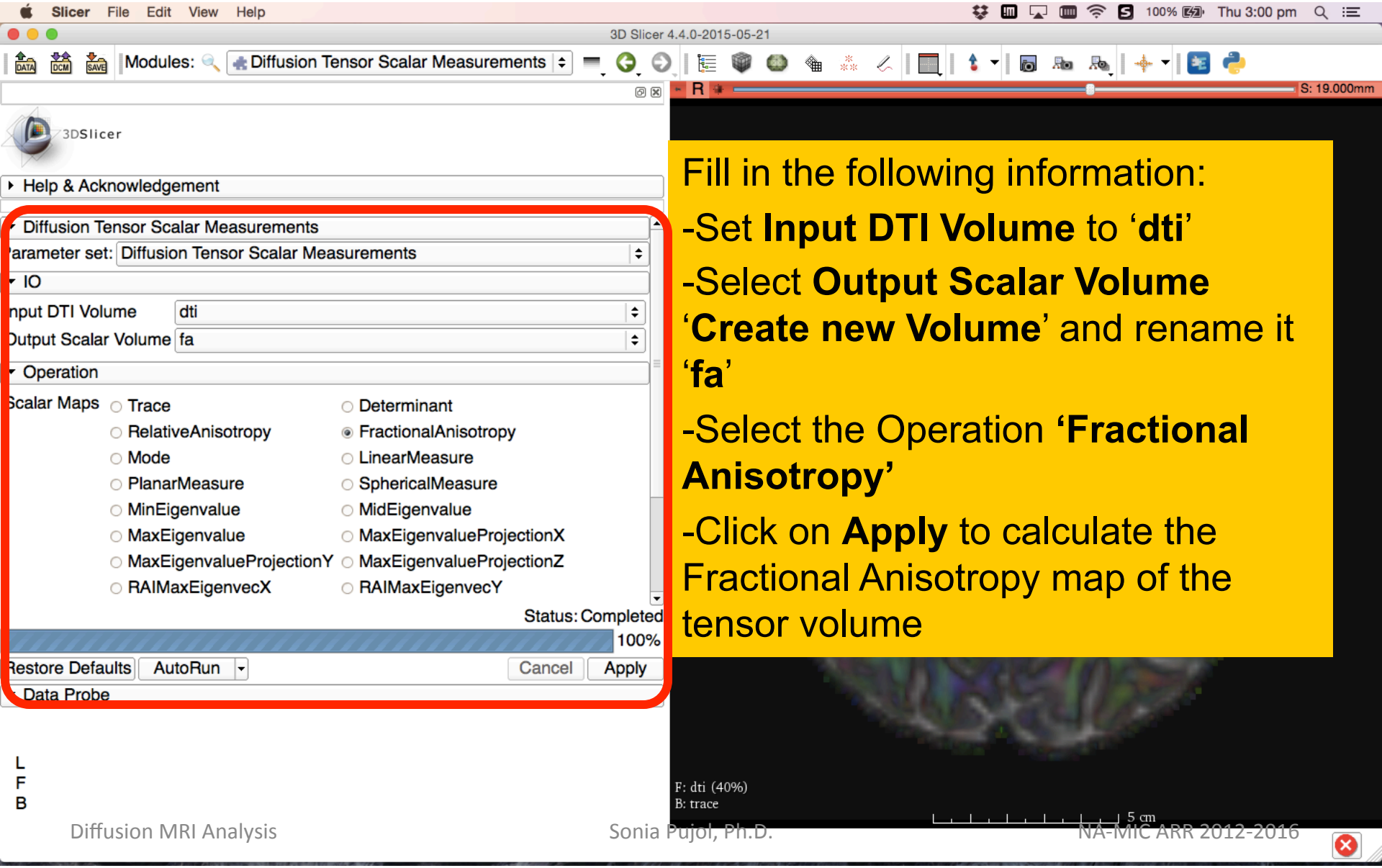

Slicer File Edit View Help
3D Slicer 4.4.0-2015-05-21
Modules: Diffusion Tensor Scalar Measurements
Note how the Trace values are fairly uniform in both white and gray matter, even if the tissues are different in structure.
Input DTI Volume dti
Output Scalar Volume trace
Operation
Scalar Maps
Trace
Determinant
RelativeAnisotropy
FractionalAnisotropy
Mode
LinearMeasure
PlanarMeasure
SphericalMeasure
MinEigenvalue
MidEigenvalue
MaxEigenvalue
MaxEigenvalueProjectionX
MaxEigenvalueProjectionY
MaxEigenvalueProjectionZ
RAIMaxEigenvecX
RAIMaxEigenvecY
Status: Completed
100%
Apply
Data Probe
Red RAS: (38.0, -21.2, 19.0) Axial Sp: 1.5
L None
F dti (39, 78, 60) ColorOrientation 0
B trace (39, 78, 60) 0.002008
S: 19.000mm
F: dti (40%)
B: trace
5 cm

Scalar Maps: Fractional Anisotropy

$$FA(D) = \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\sqrt{2}\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

- FA(D) is intrinsic to the tissue and is independent of fiber orientation, and diffusion sensitizing gradient directions
- FA(D) is useful to characterize the shape (degree of 'out-of-roundness') of the diffusion ellipsoid
- Low FA: → High FA:

Fractional Anisotropy



Fill in the following information:

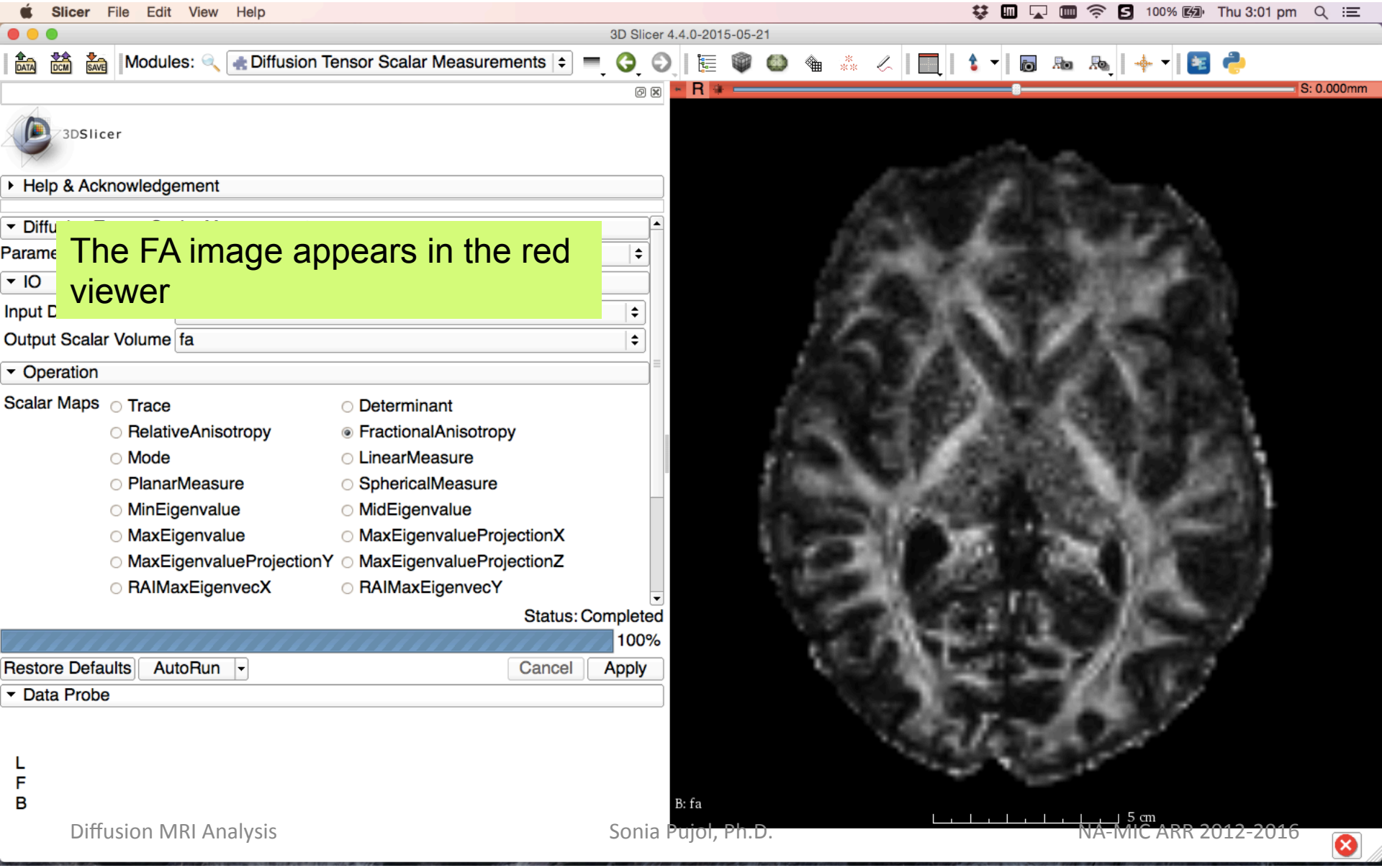
-Set **Input DTI Volume** to '**dti**'

-Select **Output Scalar Volume** '**Create new Volume**' and rename it '**fa**'

-Select the Operation **'Fractional Anisotropy'**

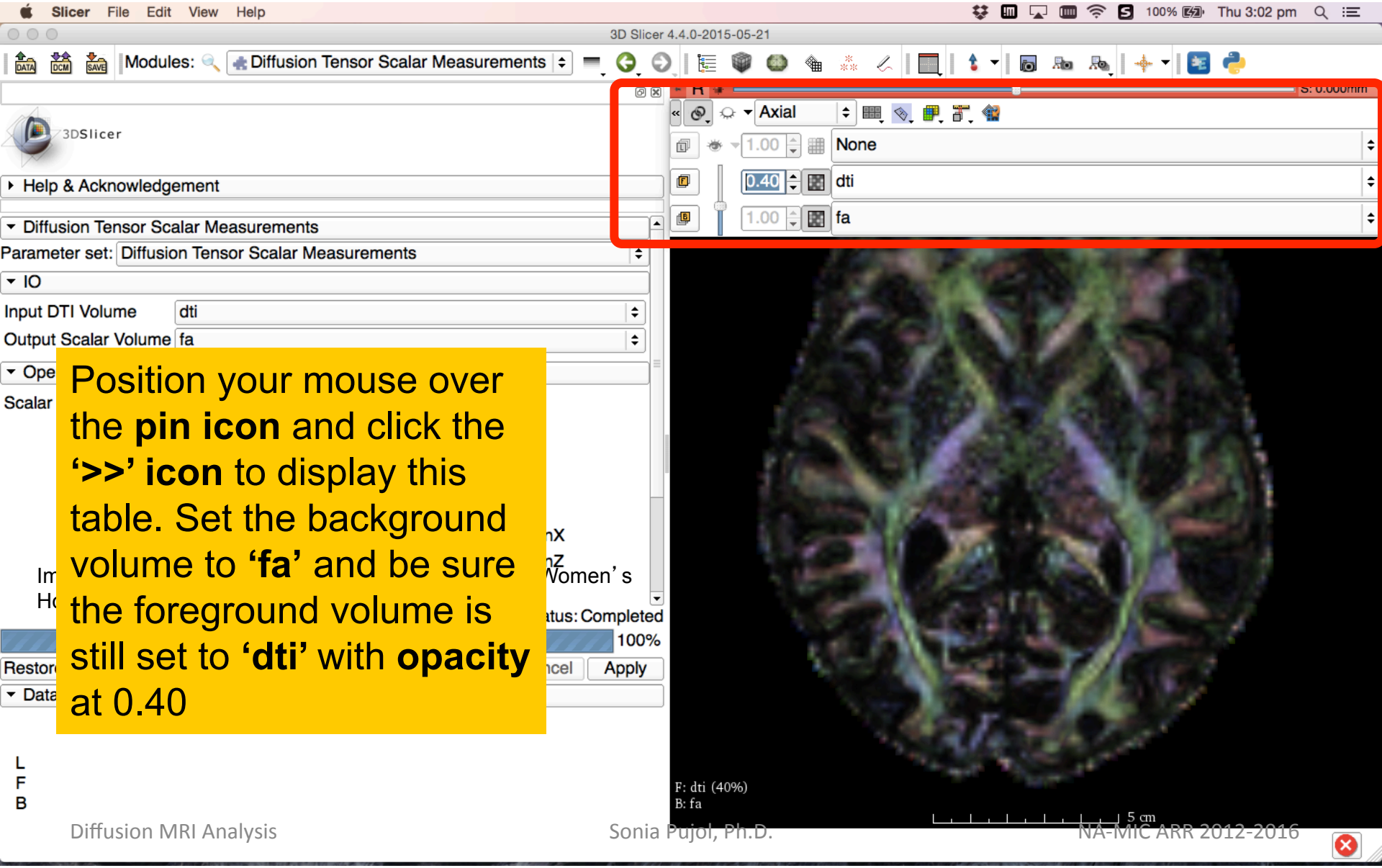
-Click on **Apply** to calculate the Fractional Anisotropy map of the tensor volume

Fractional Anisotropy



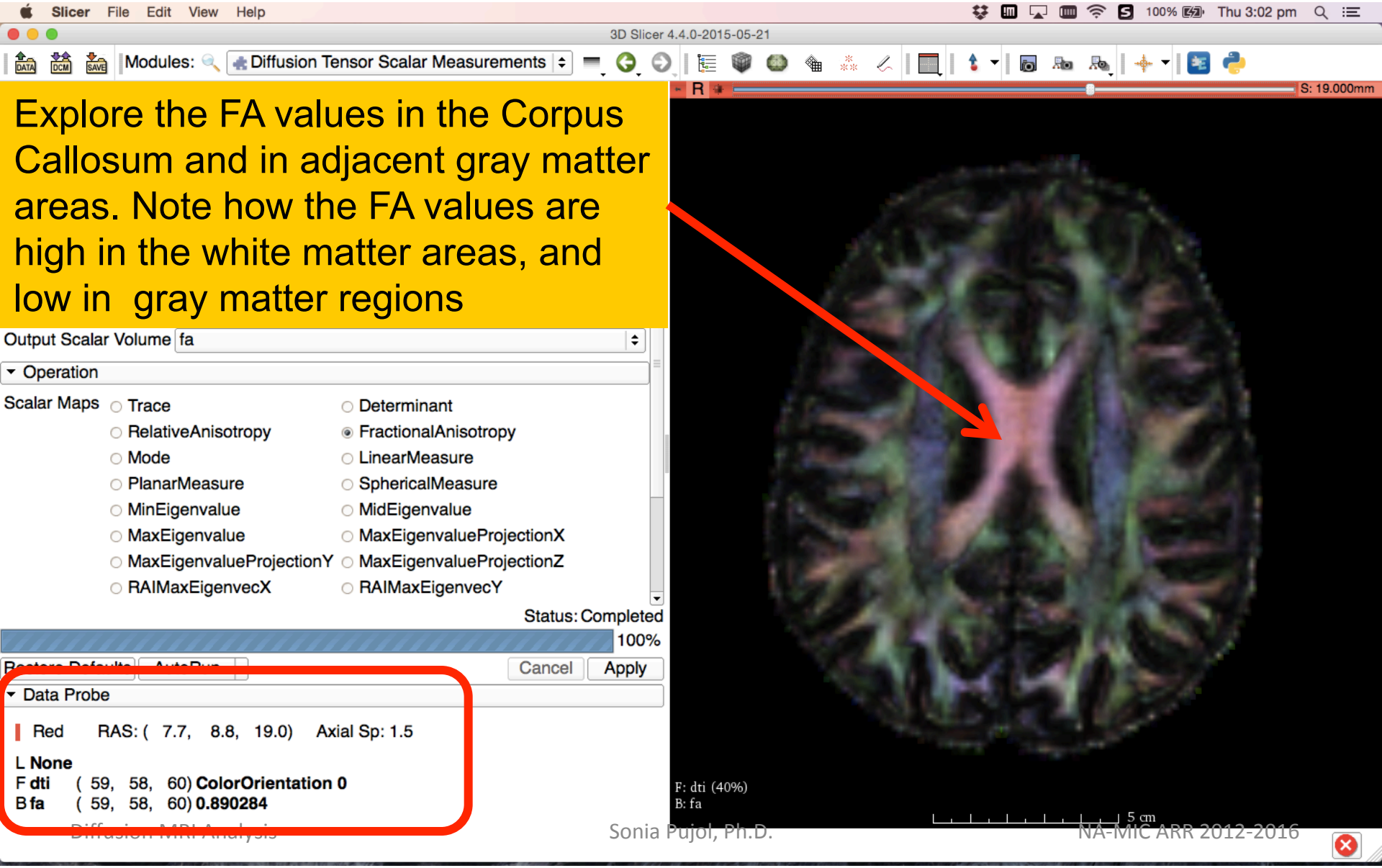
The FA image appears in the red viewer

Fractional Anisotropy



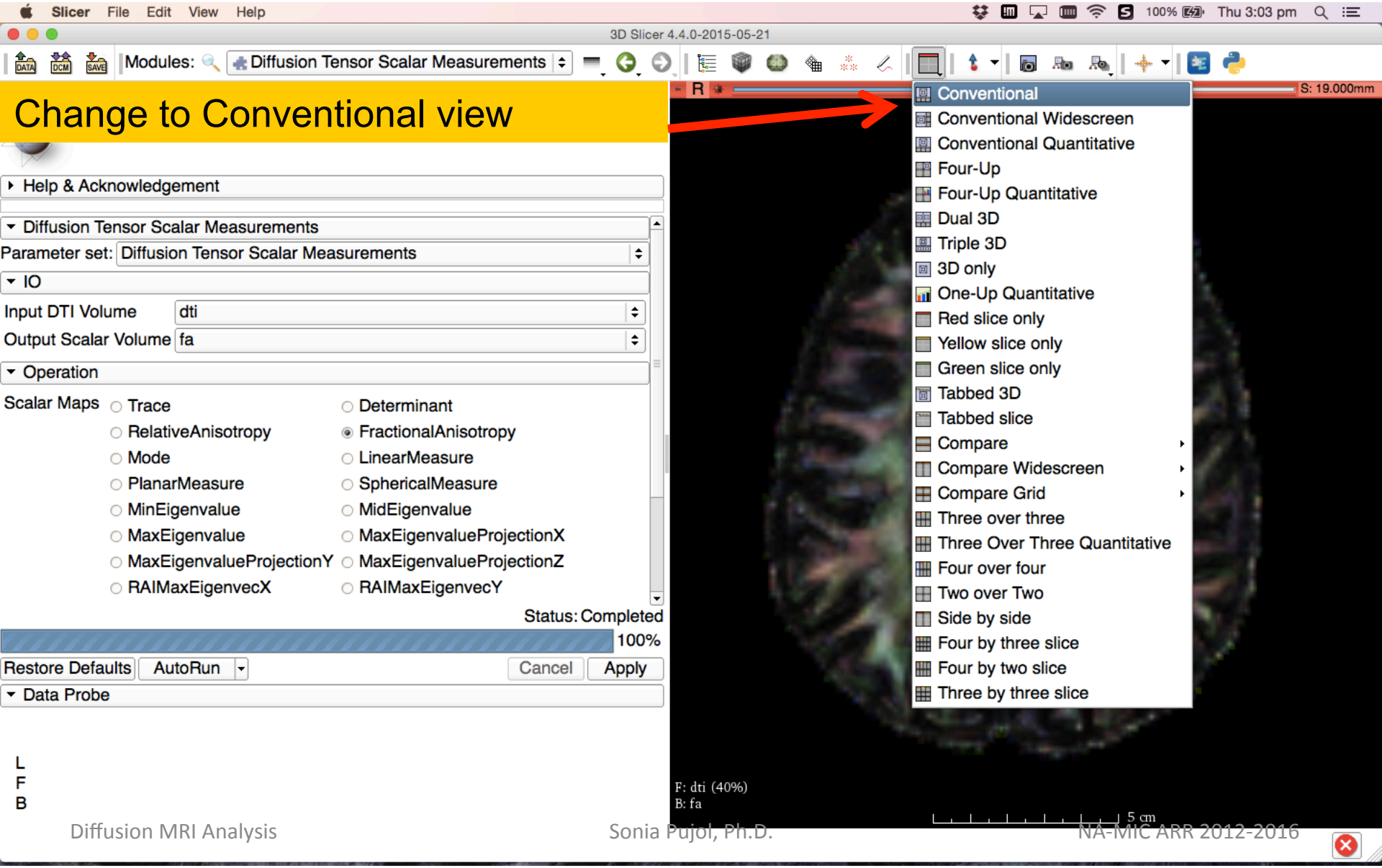
Position your mouse over the **pin icon** and click the **'>>' icon** to display this table. Set the background volume to **'fa'** and be sure the foreground volume is still set to **'dti'** with **opacity** at 0.40

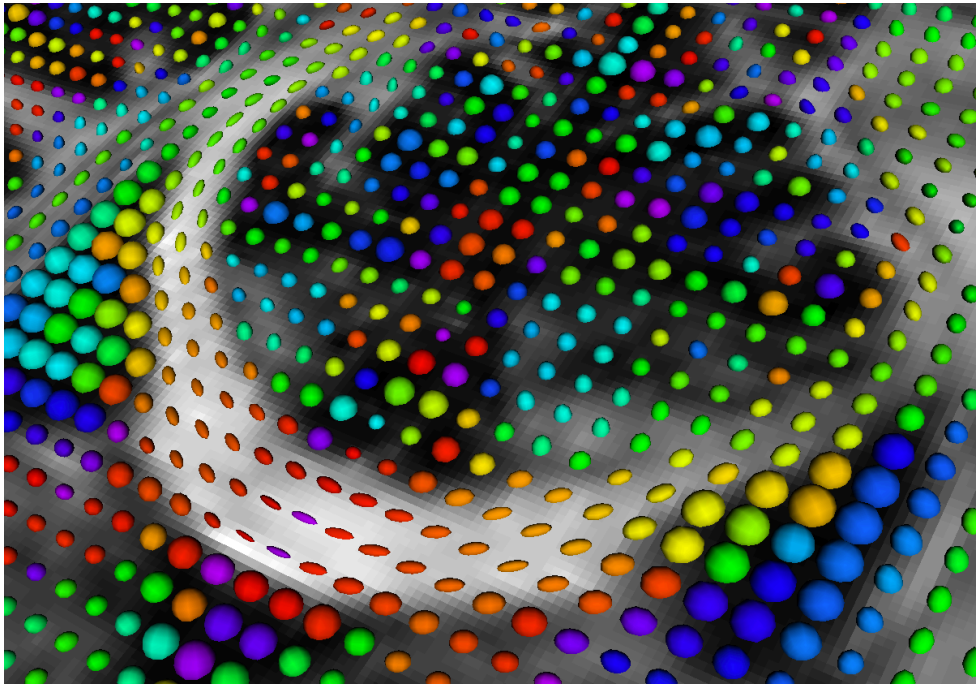
Fractional Anisotropy



Explore the FA values in the Corpus Callosum and in adjacent gray matter areas. Note how the FA values are high in the white matter areas, and low in gray matter regions

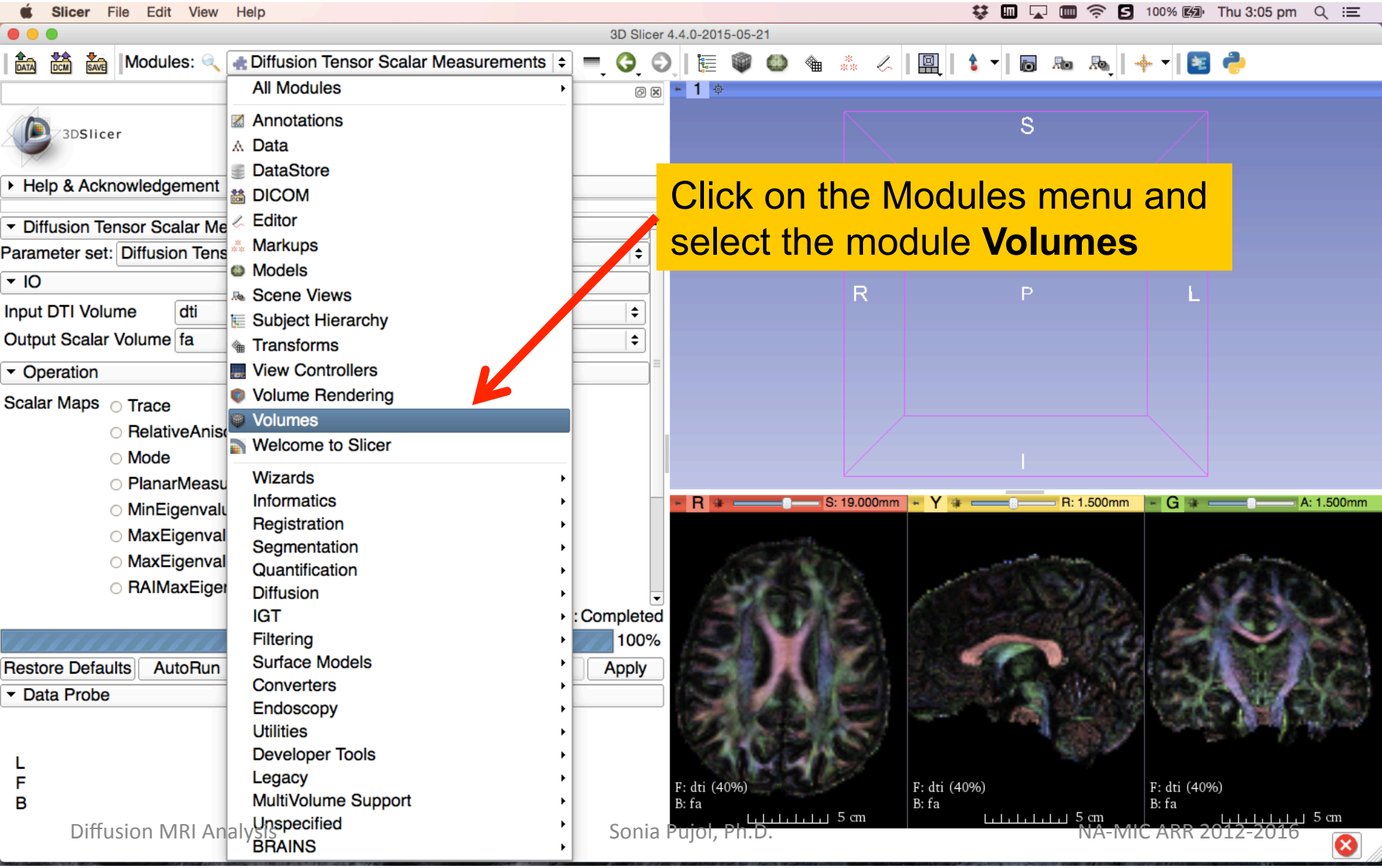
Fractional Anisotropy



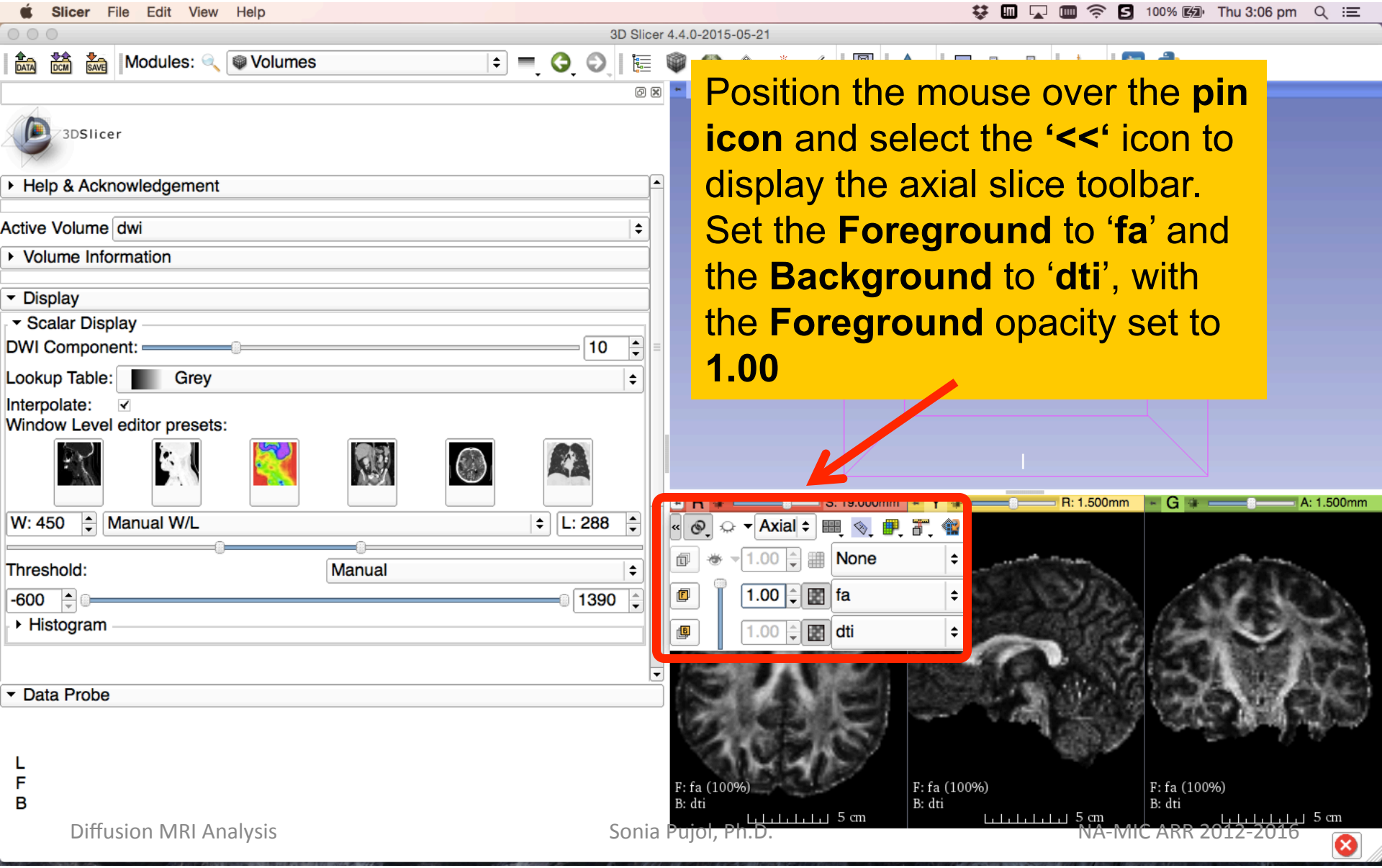


Part 2: Visualizing the tensor data

3D Visualization: Glyphs

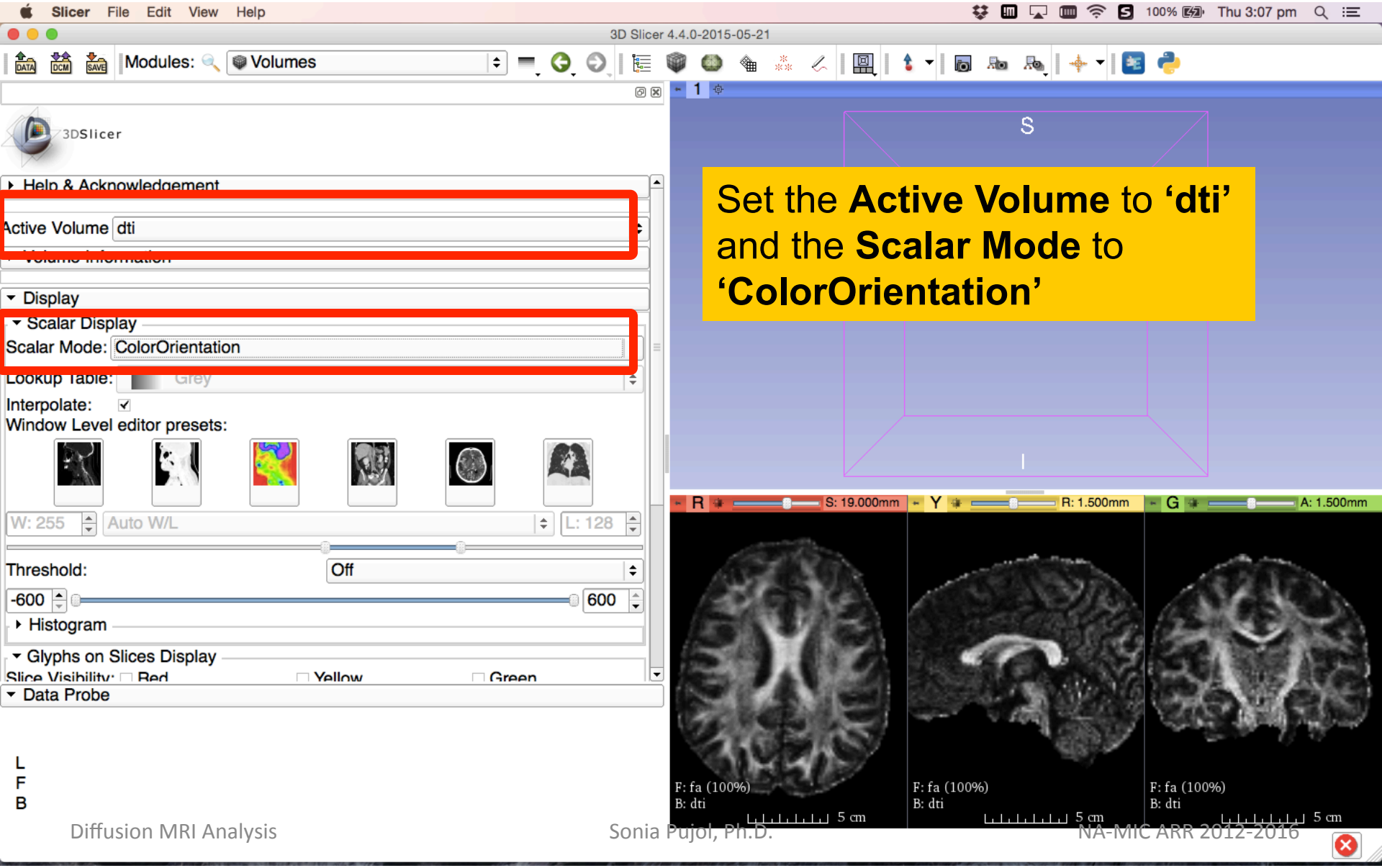


3D Visualization: Glyphs



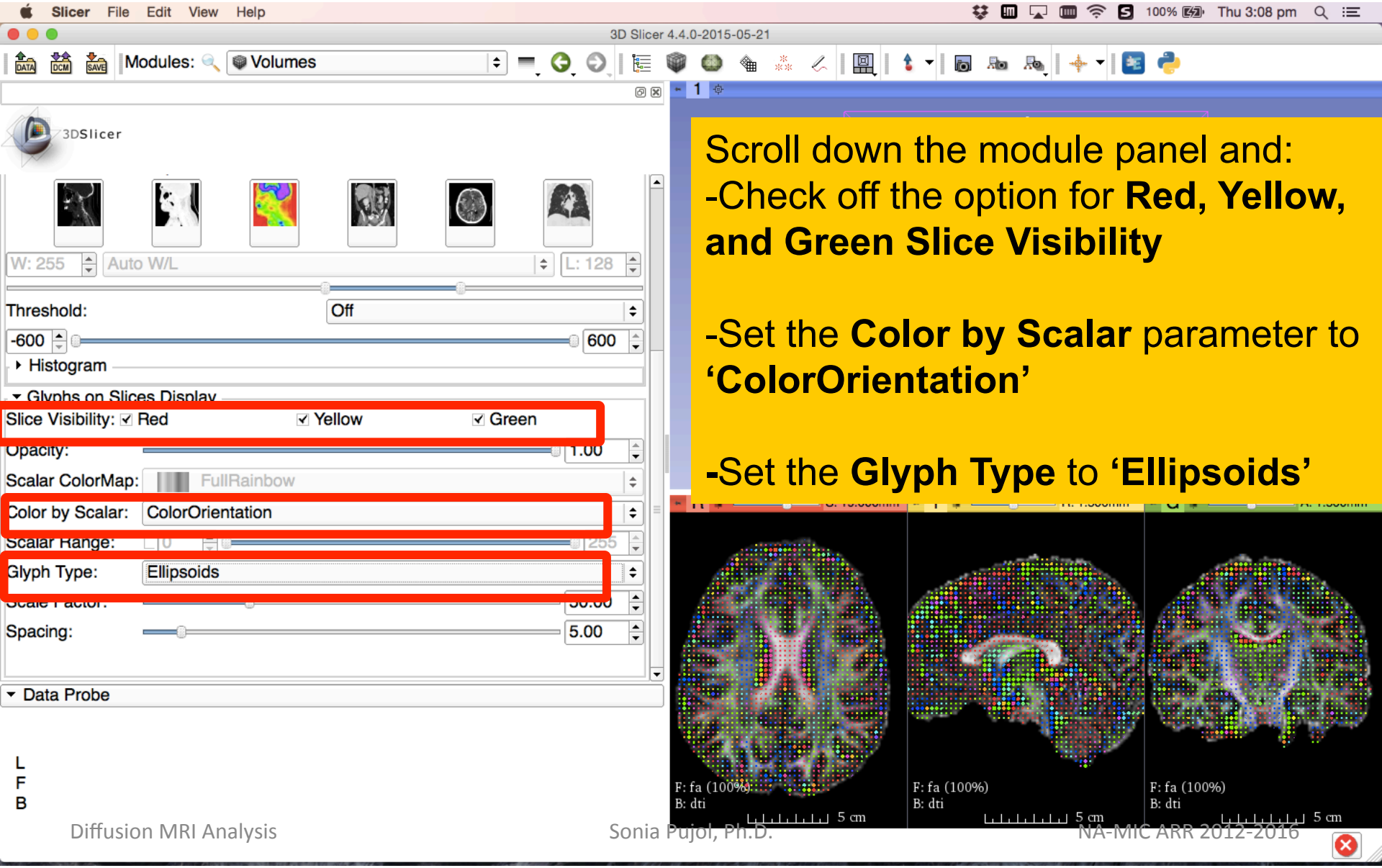
Position the mouse over the **pin icon** and select the **'<<'** icon to display the axial slice toolbar. Set the **Foreground** to '**fa**' and the **Background** to '**dti**', with the **Foreground** opacity set to **1.00**

3D Visualization: Glyphs



Set the **Active Volume** to **'dti'** and the **Scalar Mode** to **'ColorOrientation'**

3D Visualization: Glyphs



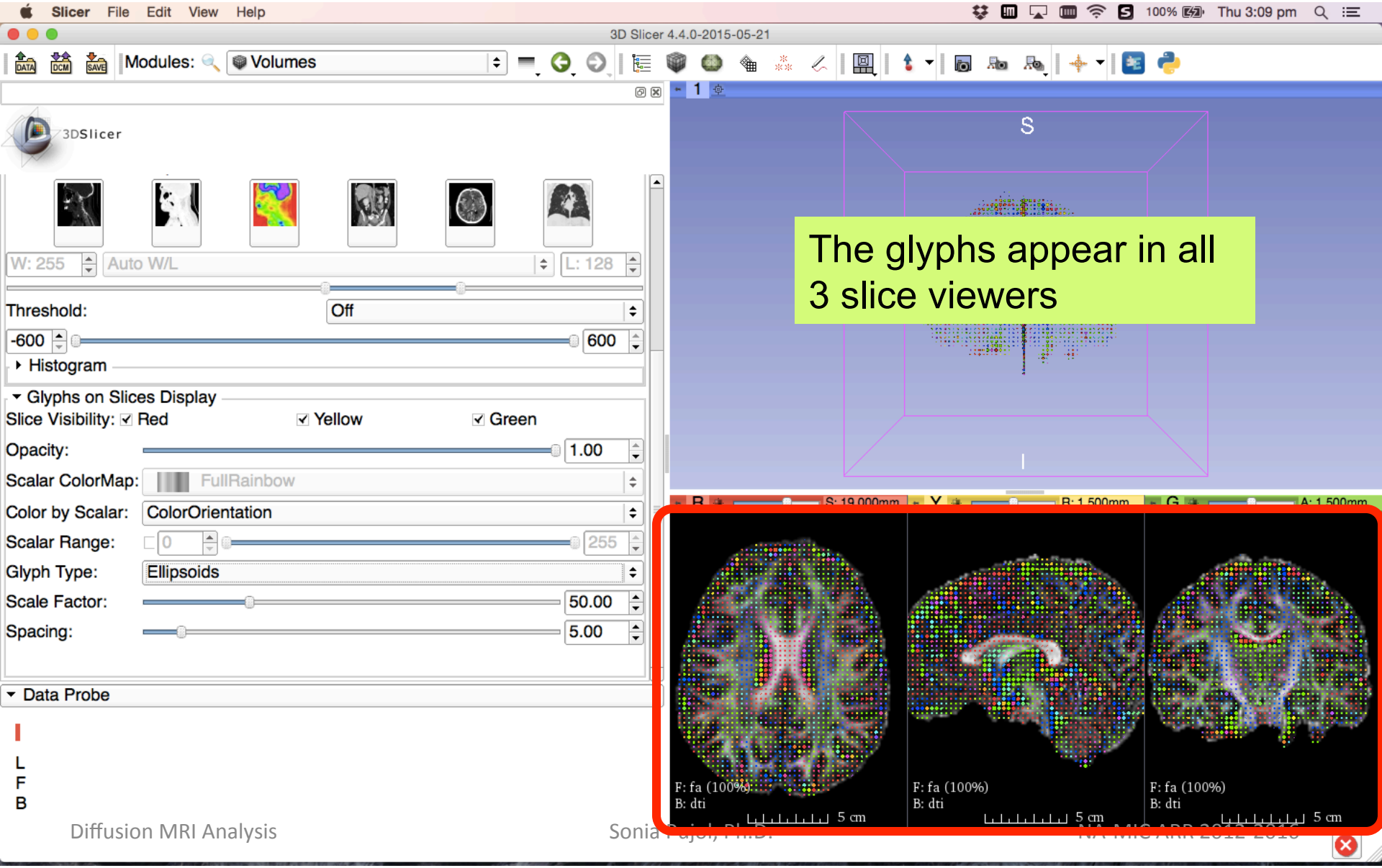
Scroll down the module panel and:

-Check off the option for **Red, Yellow, and Green Slice Visibility**

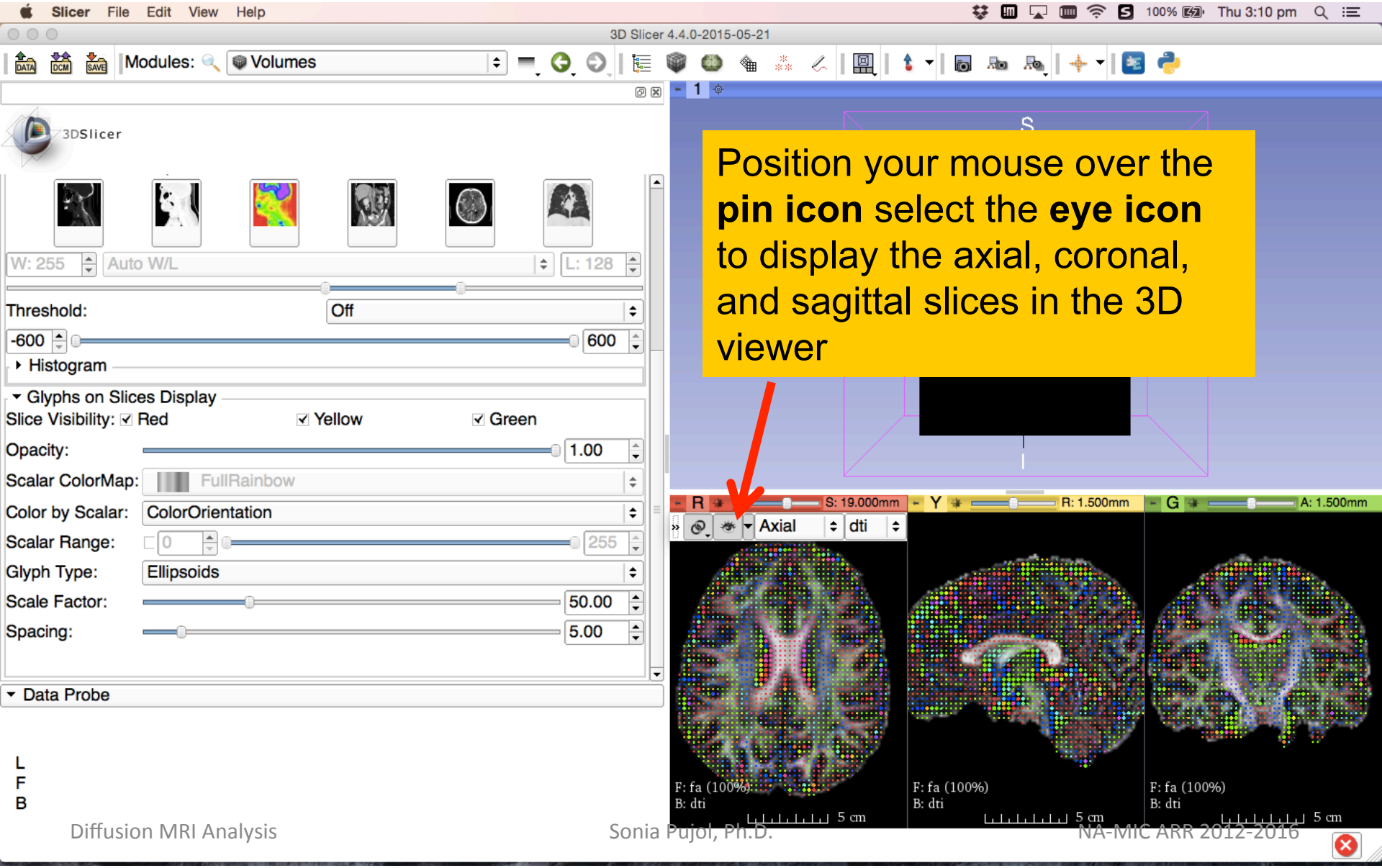
-Set the **Color by Scalar** parameter to **'ColorOrientation'**

-Set the **Glyph Type** to **'Ellipsoids'**

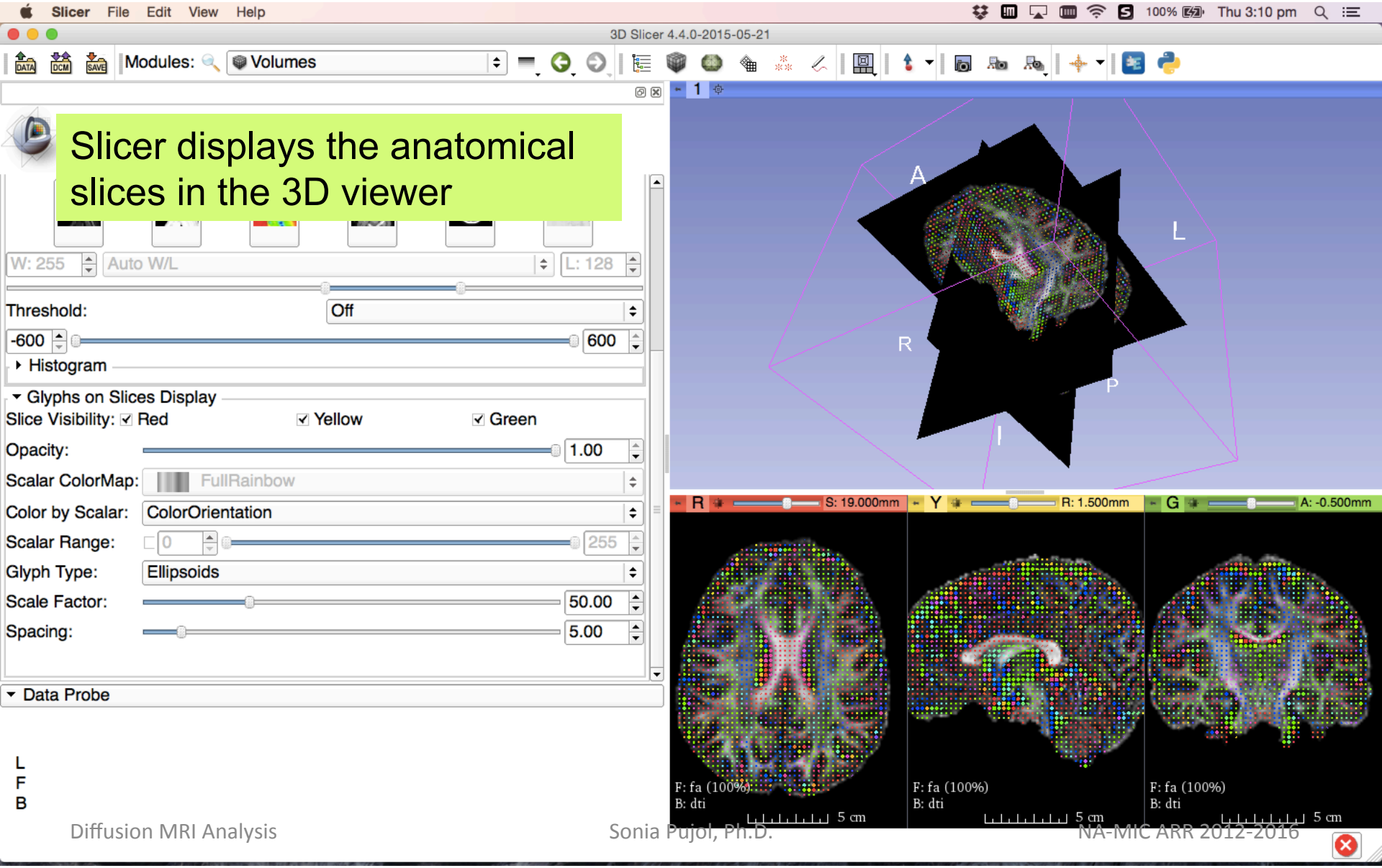
3D Visualization: Glyphs



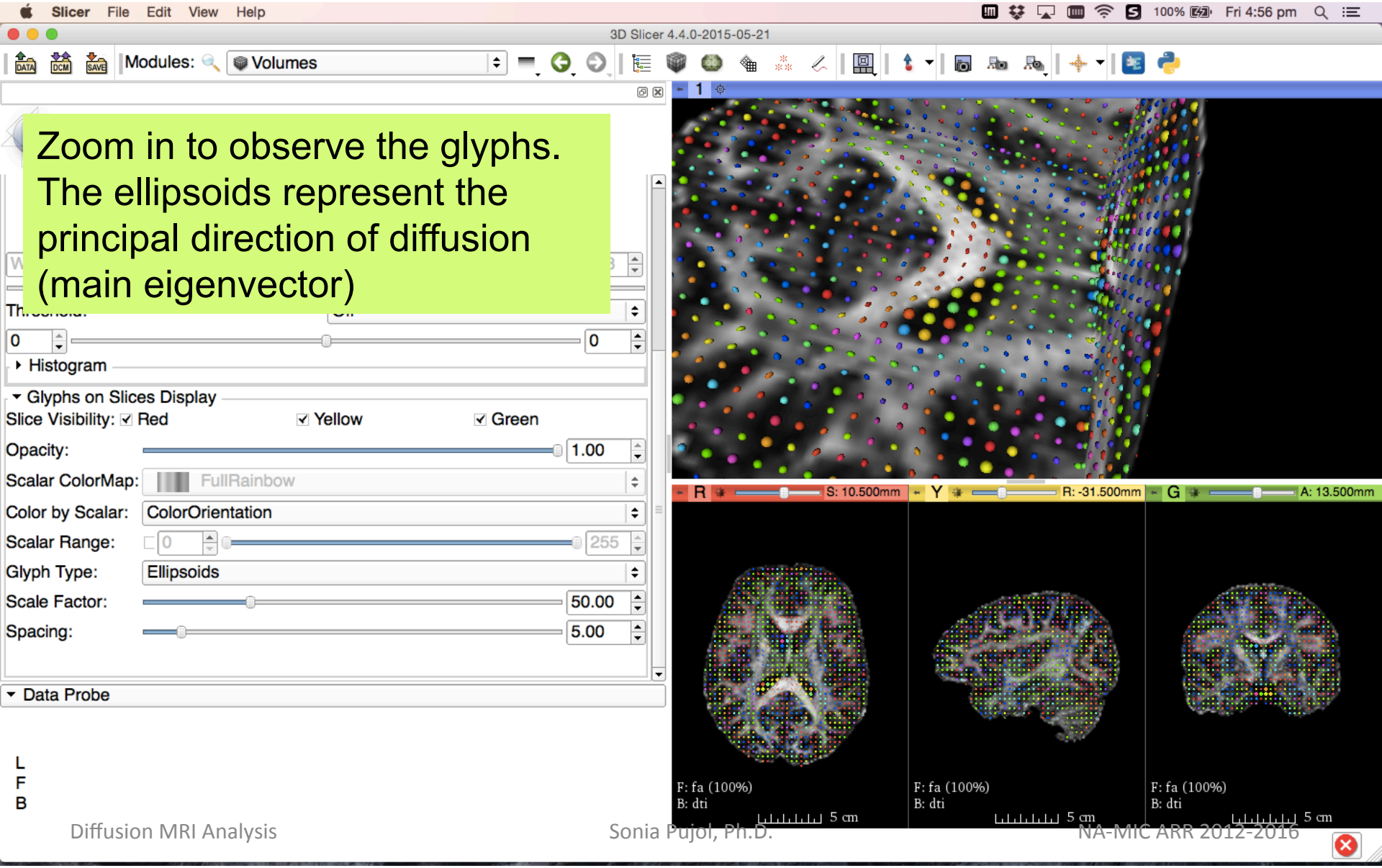
3D Visualization: Glyphs



3D Visualization: Glyphs

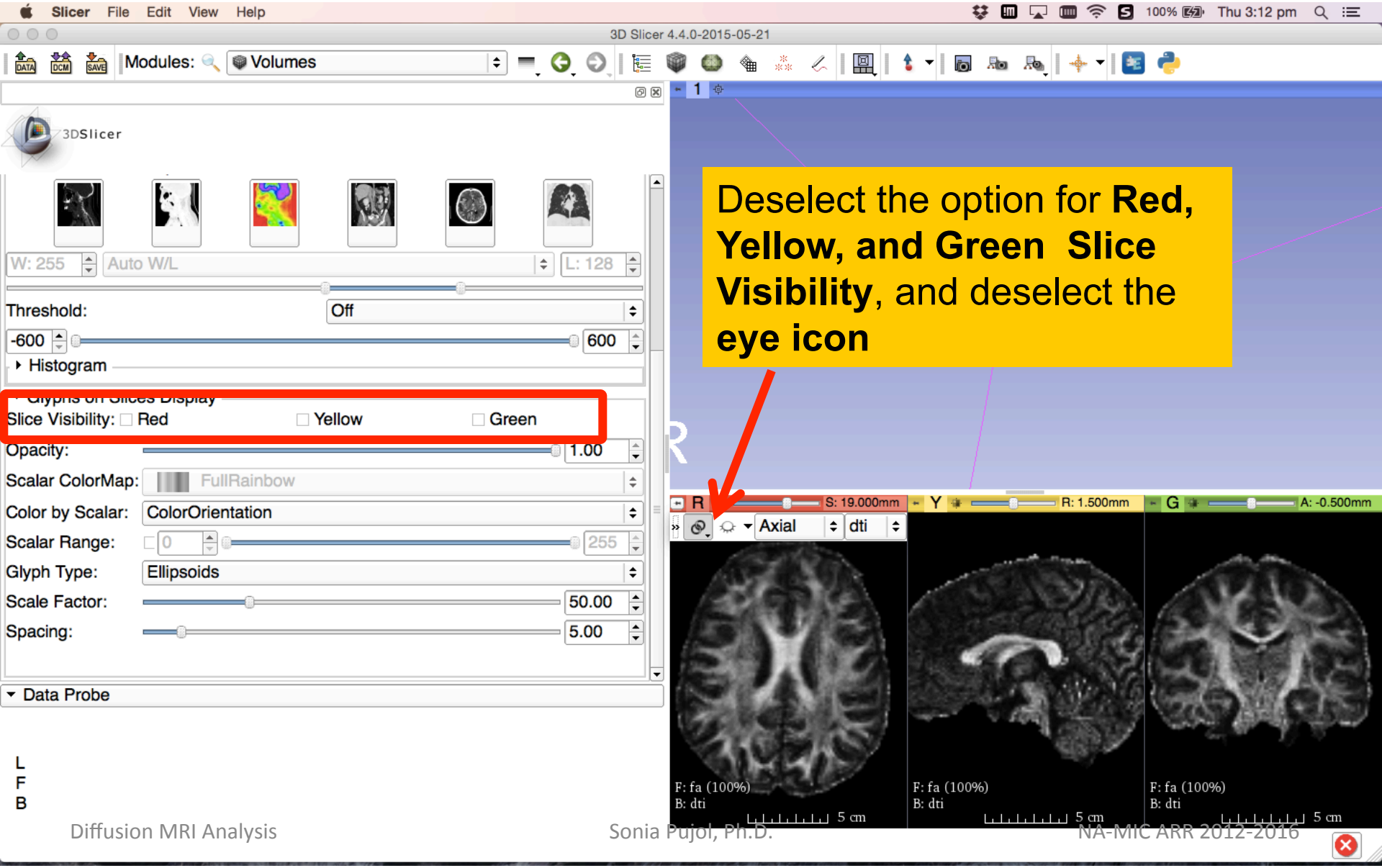


3D Visualization: Glyphs



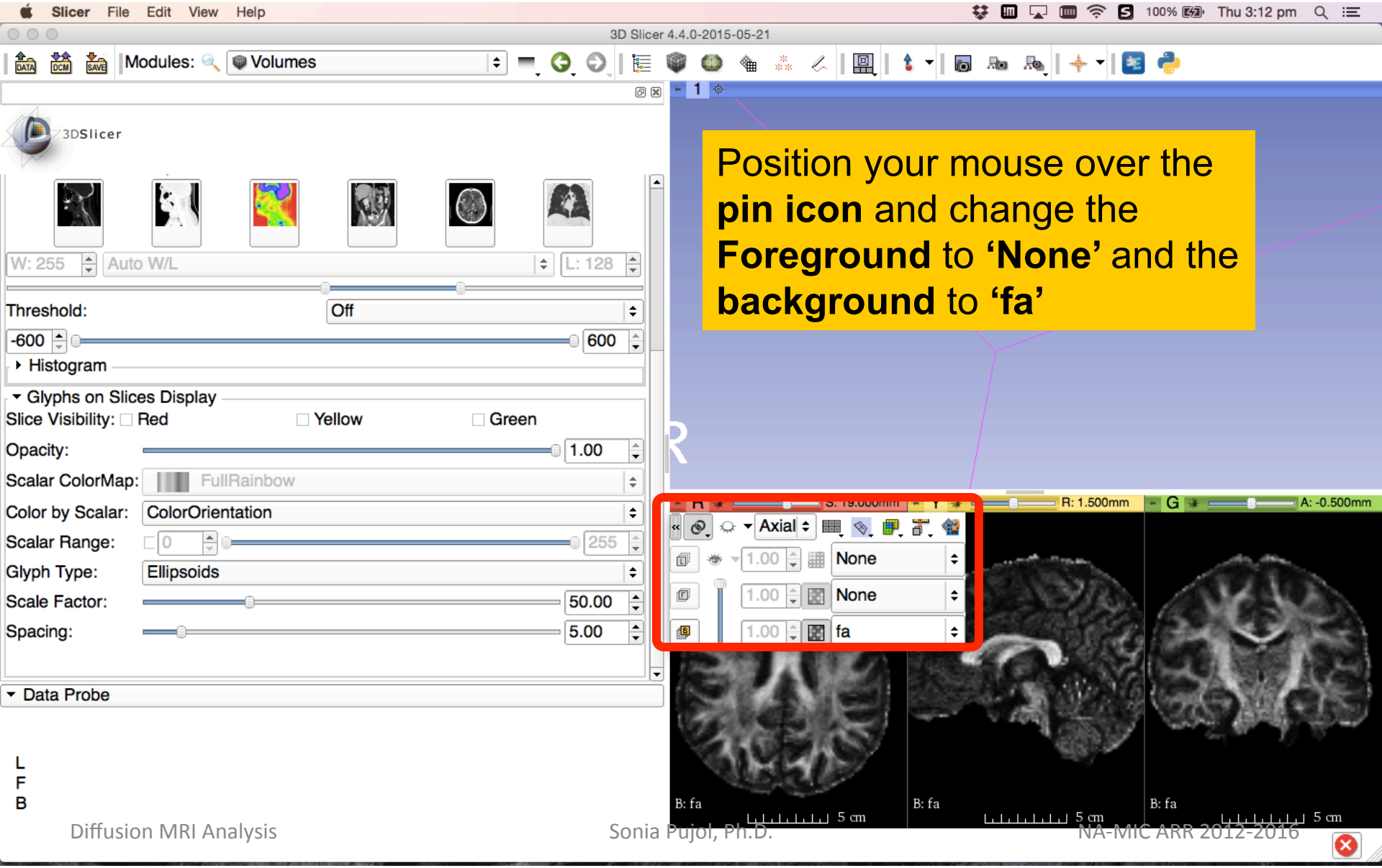
Zoom in to observe the glyphs. The ellipsoids represent the principal direction of diffusion (main eigenvector)

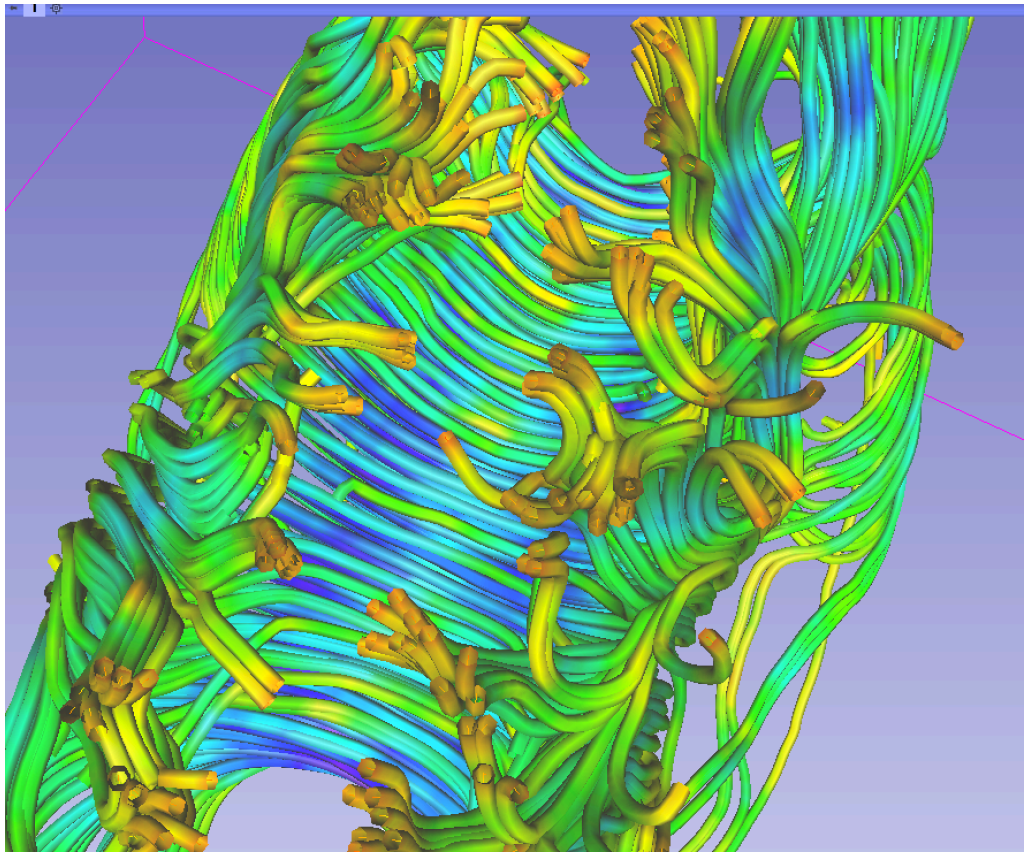
Diffusion MRI tractography



Deselect the option for **Red, Yellow, and Green Slice Visibility**, and deselect the **eye icon**

Diffusion MRI tractography



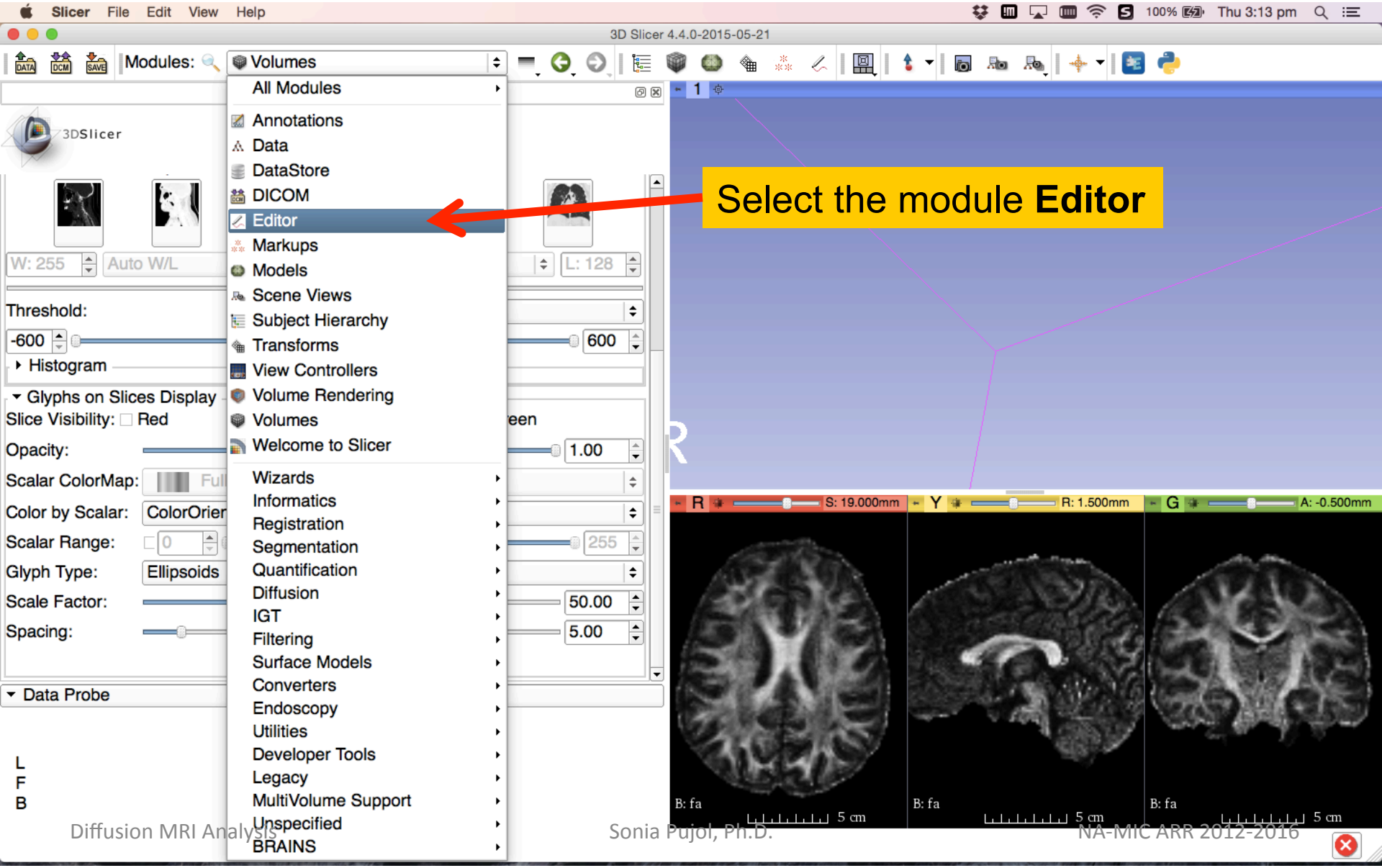


Part 3: From tensors to tracts

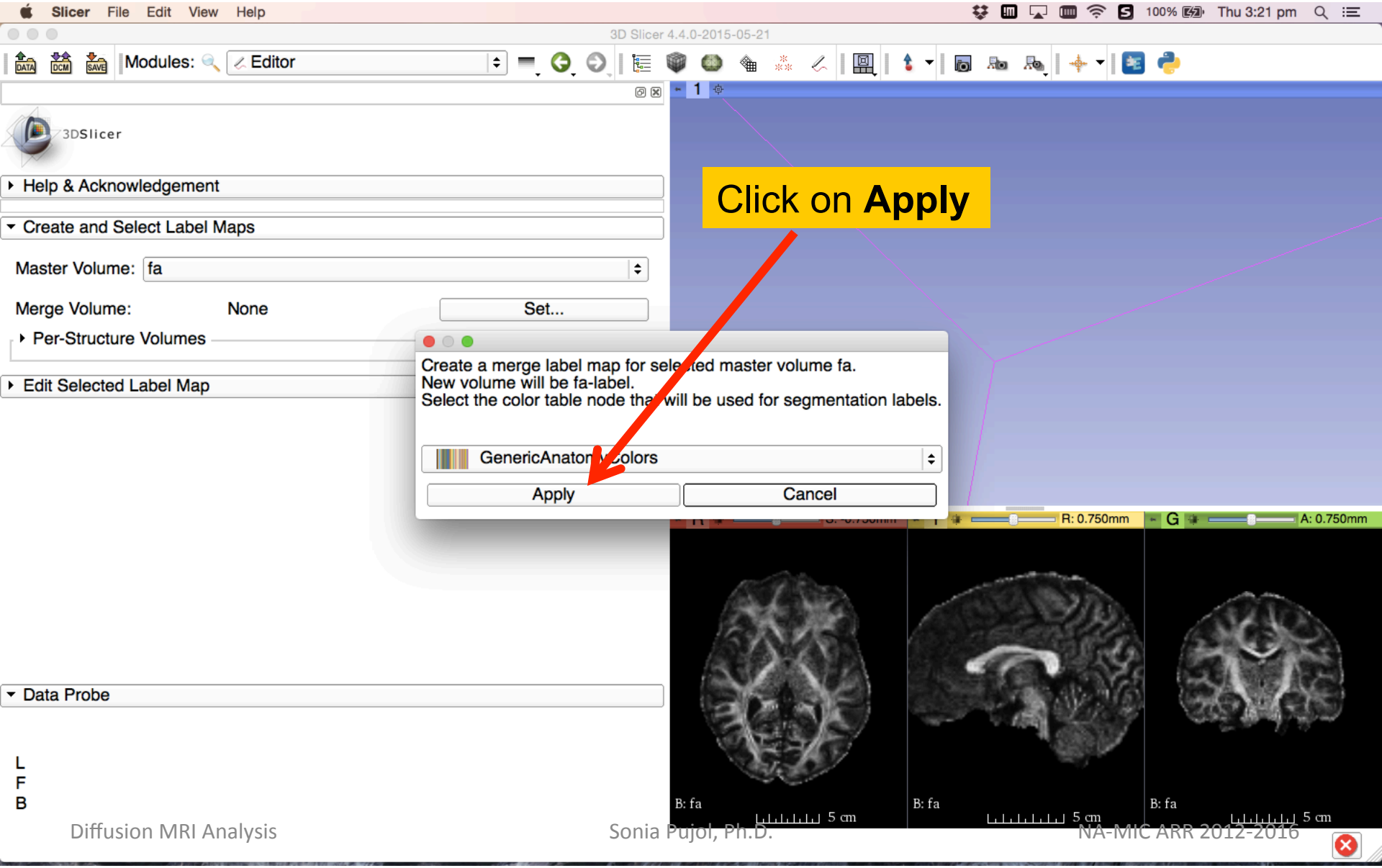
DTI tractography

- Definition of a region of interest (ROI) for seeding tract in an FA map (Editor module)
- Single-tensor tractography (Tractography Interactive Seeding module)
- Fiducial-seeding tractography (Tractography Interactive Seeding module)

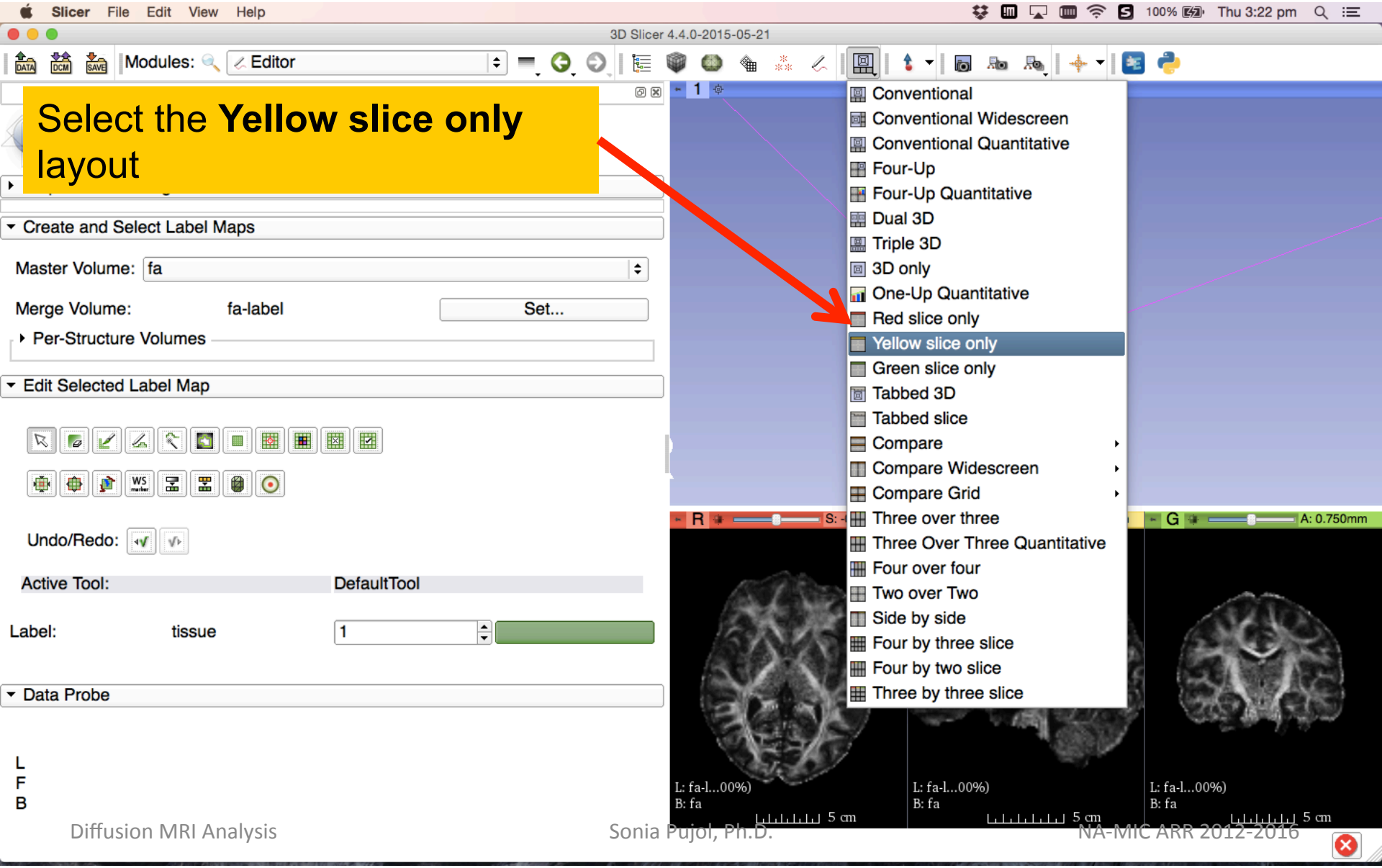
Diffusion MRI tractography



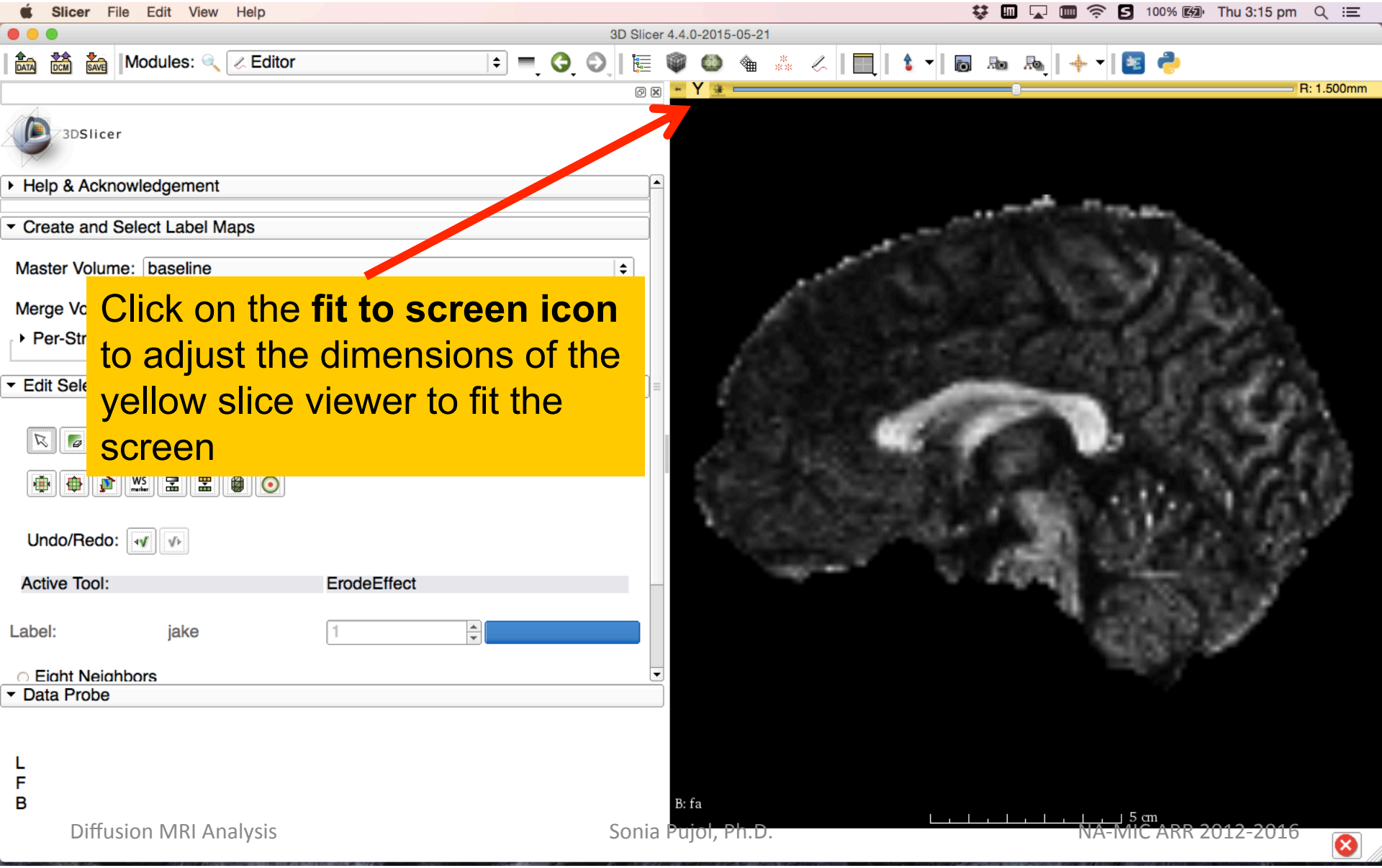
Diffusion MRI tractography



Diffusion MRI tractography

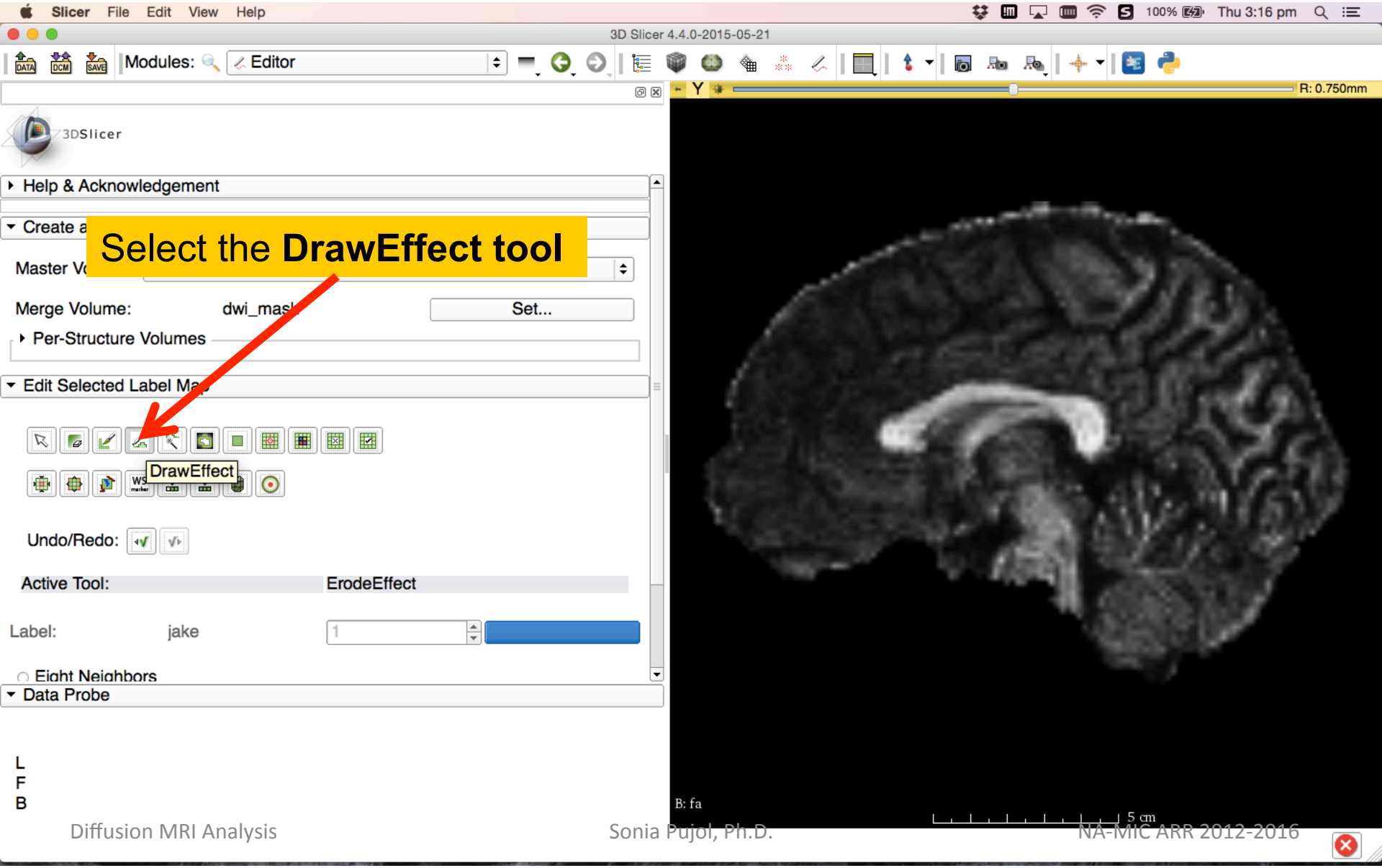


Diffusion MRI tractography

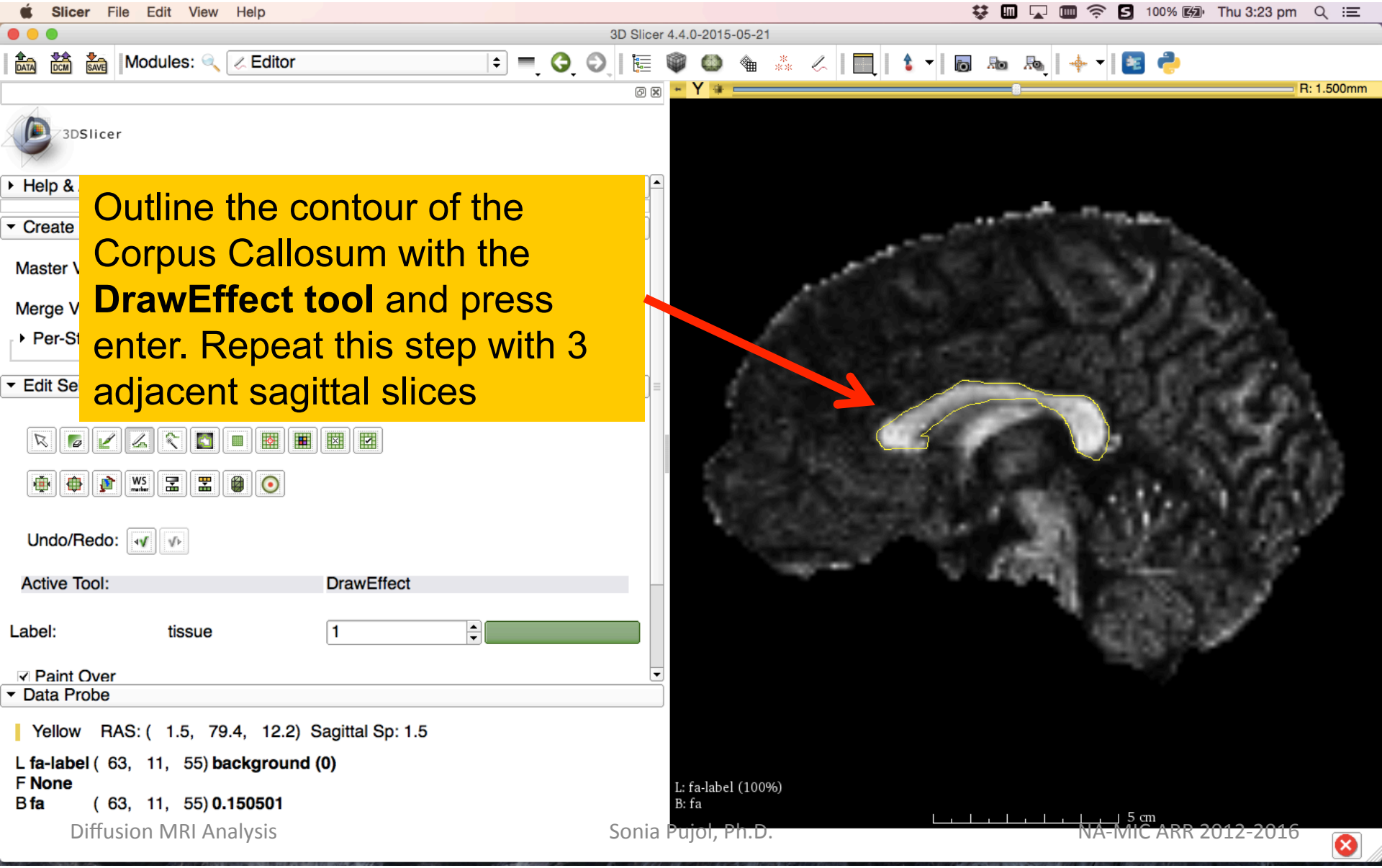


Click on the **fit to screen icon** to adjust the dimensions of the yellow slice viewer to fit the screen

Diffusion MRI tractography

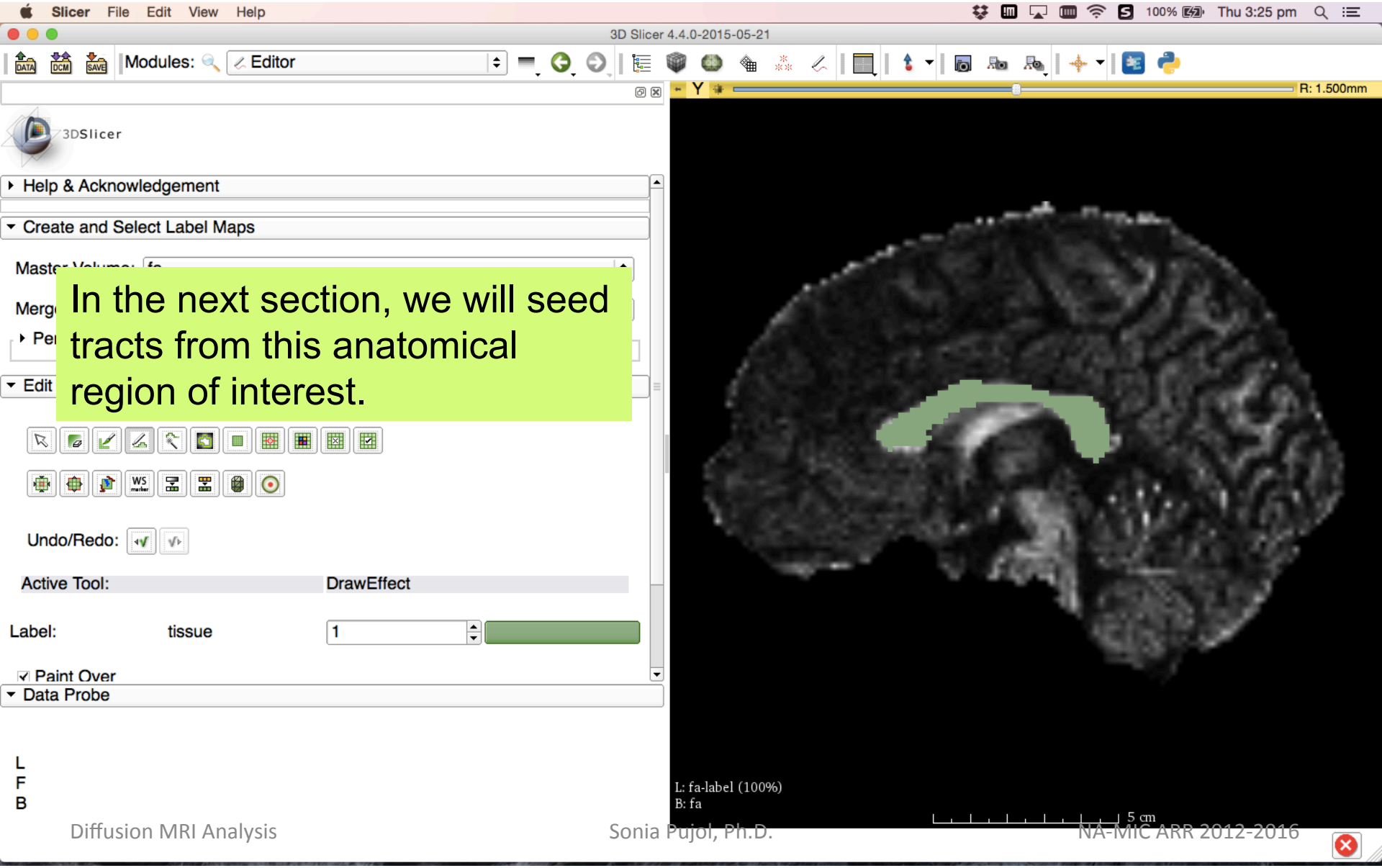


Diffusion MRI tractography



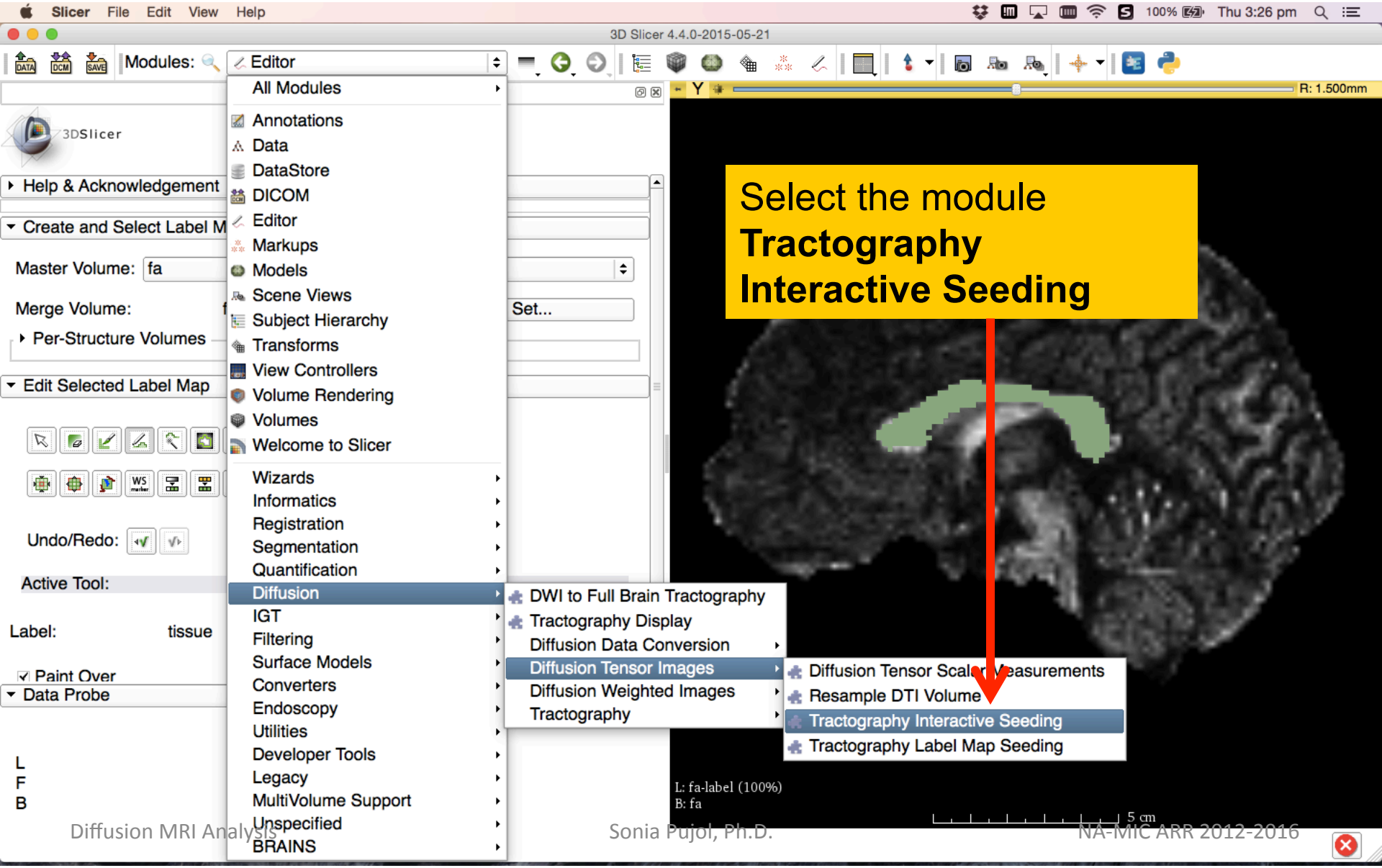
Outline the contour of the Corpus Callosum with the **DrawEffect tool** and press enter. Repeat this step with 3 adjacent sagittal slices

Diffusion MRI tractography

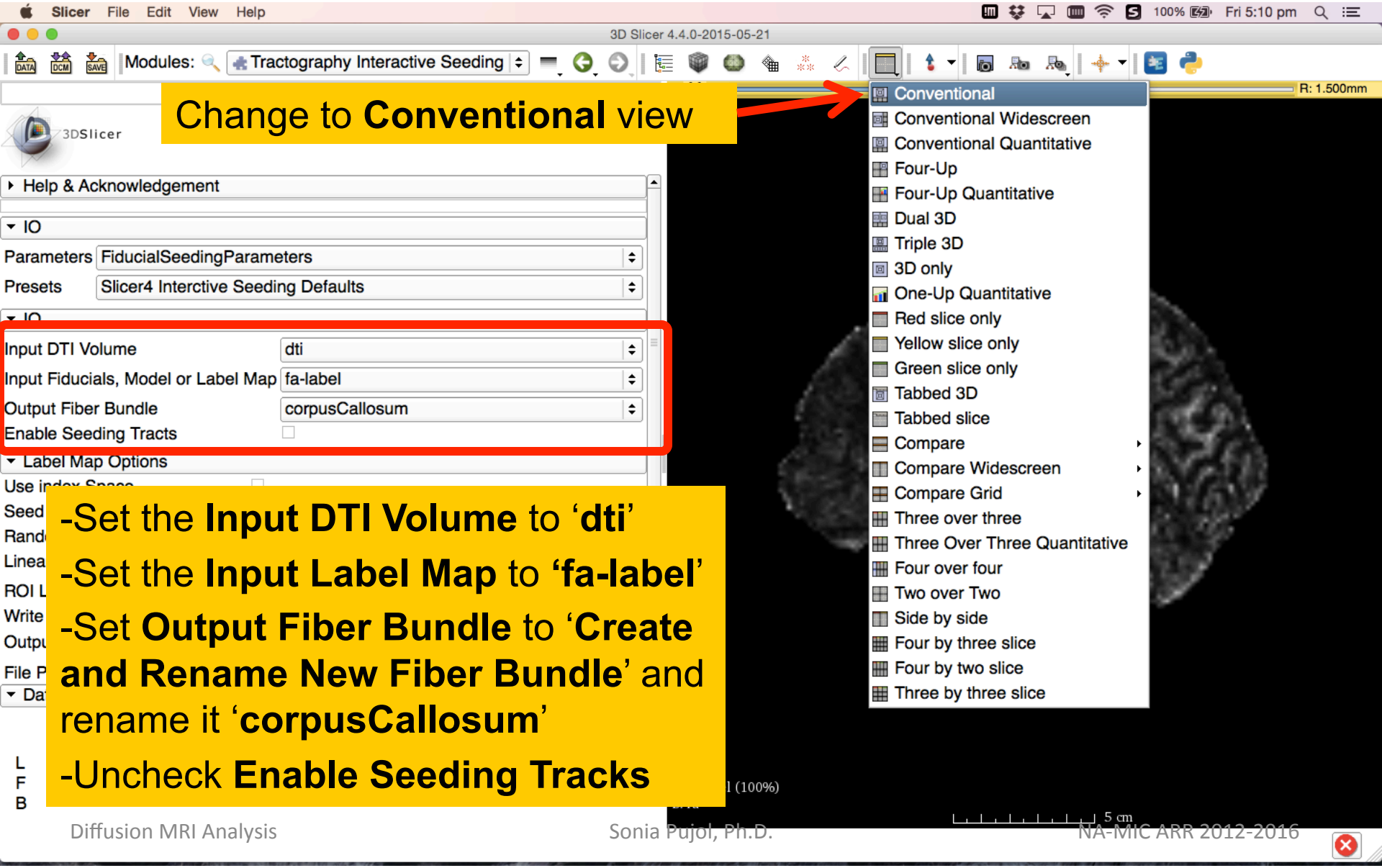


In the next section, we will seed tracts from this anatomical region of interest.

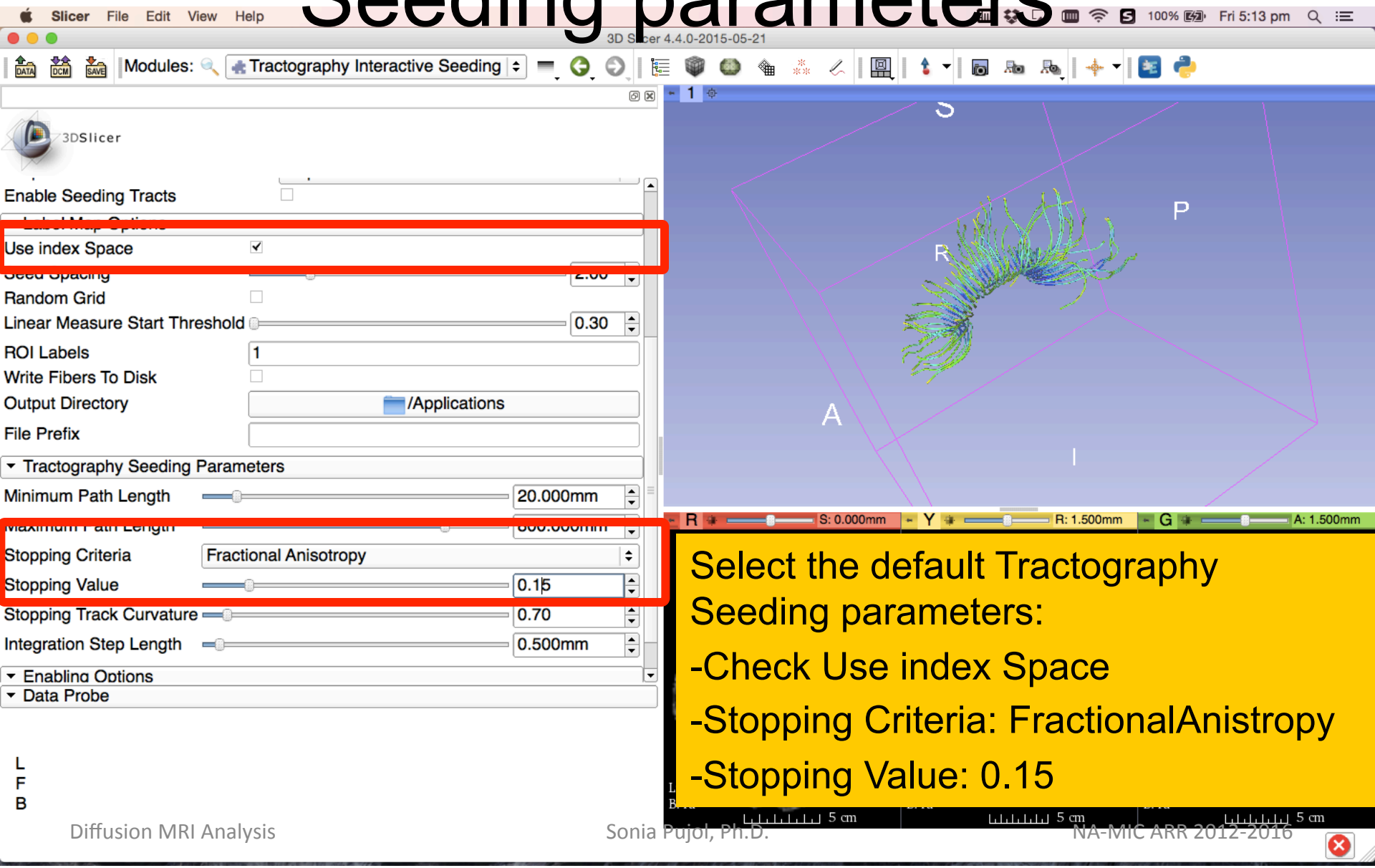
Diffusion MRI tractography



Labelmap Seeding: Step1: I/O



LabelMap Seeding: Step 2: Seeding parameters



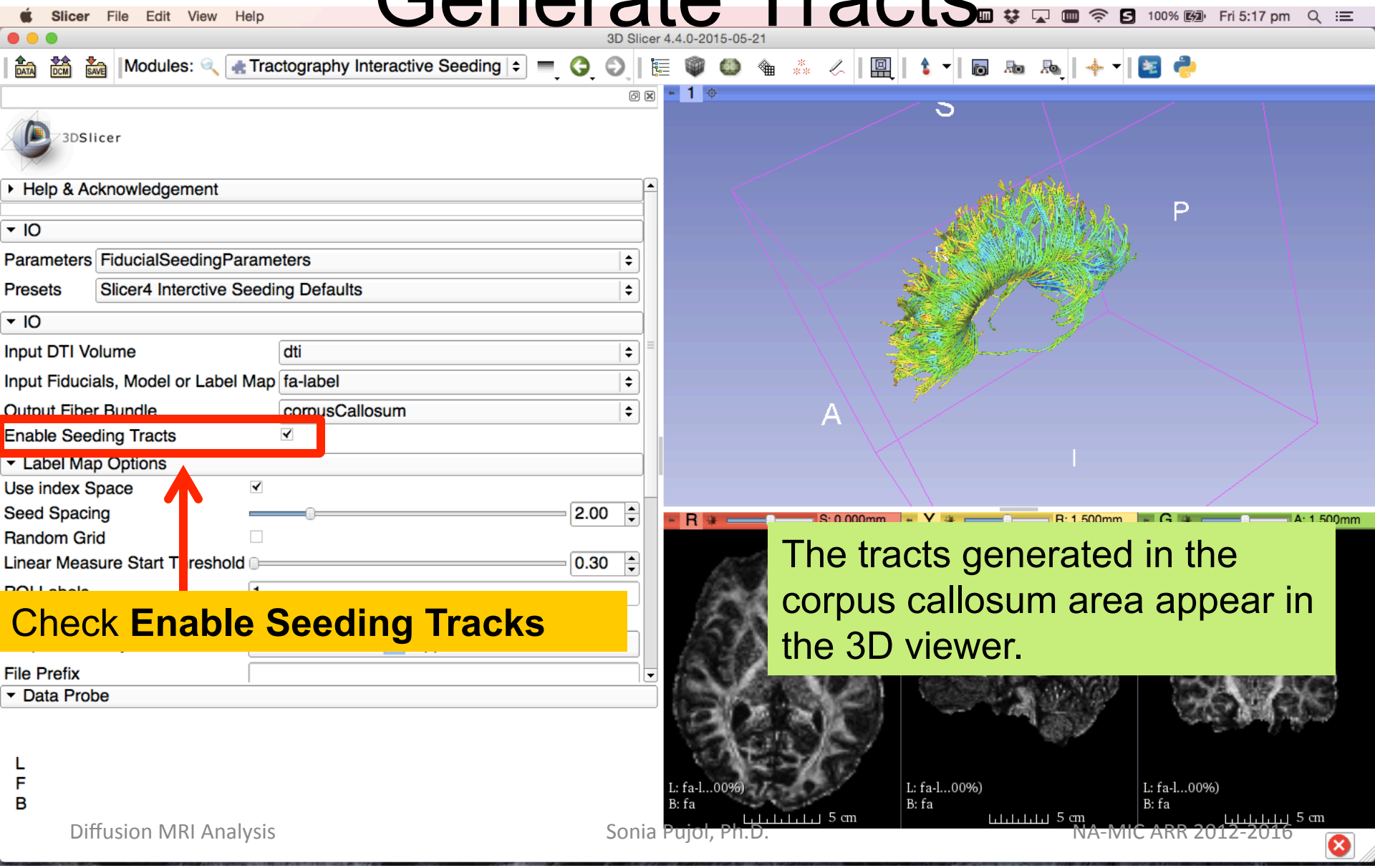
Select the default Tractography Seeding parameters:

-Check Use index Space

-Stopping Criteria: FractionalAnistropy

-Stopping Value: 0.15

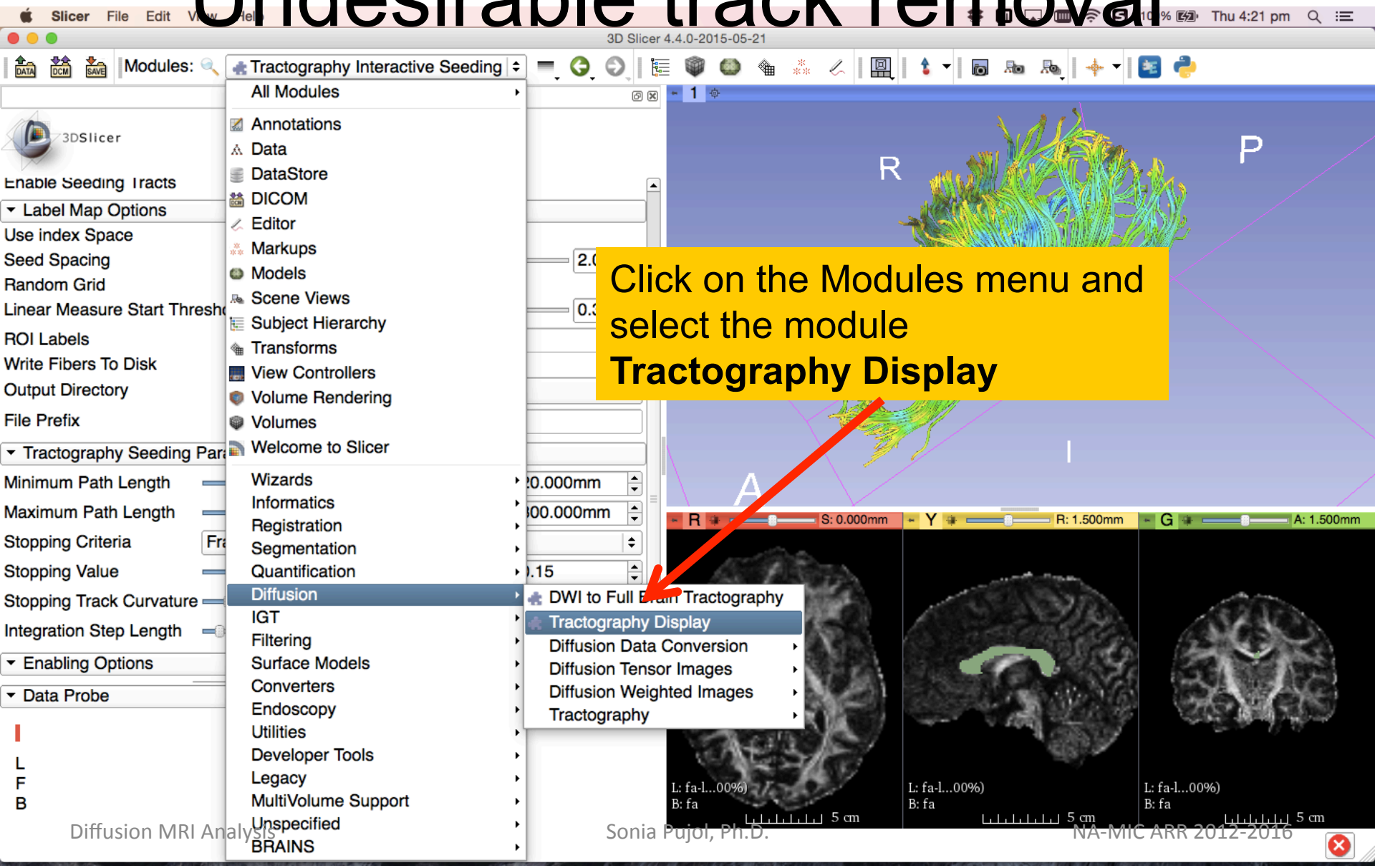
LabelMap Seeding: Step 3: Generate Tracts



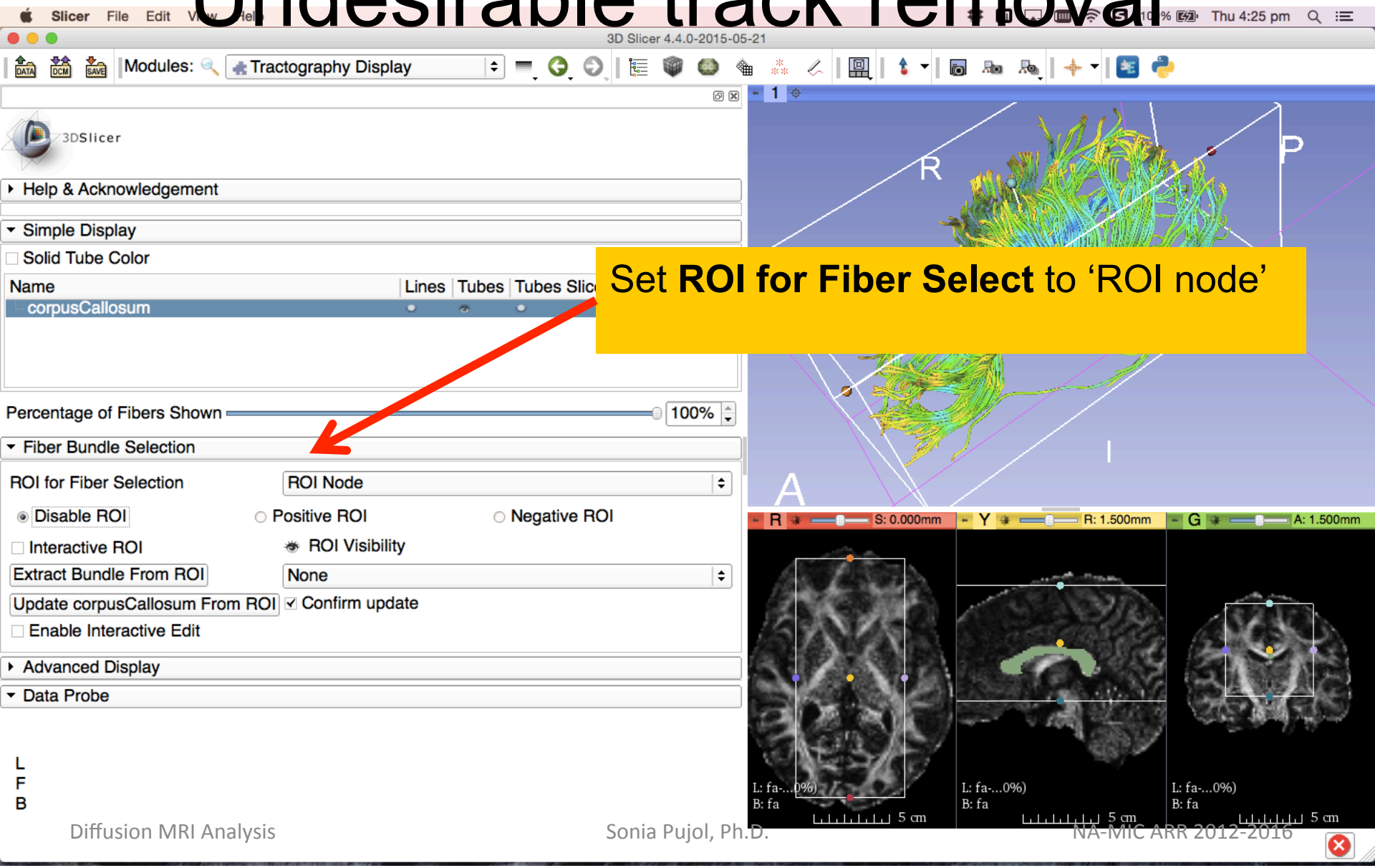
Check **Enable Seeding Tracks**

The tracts generated in the corpus callosum area appear in the 3D viewer.

LabelMap Seeding: Step 4: Undesirable track removal

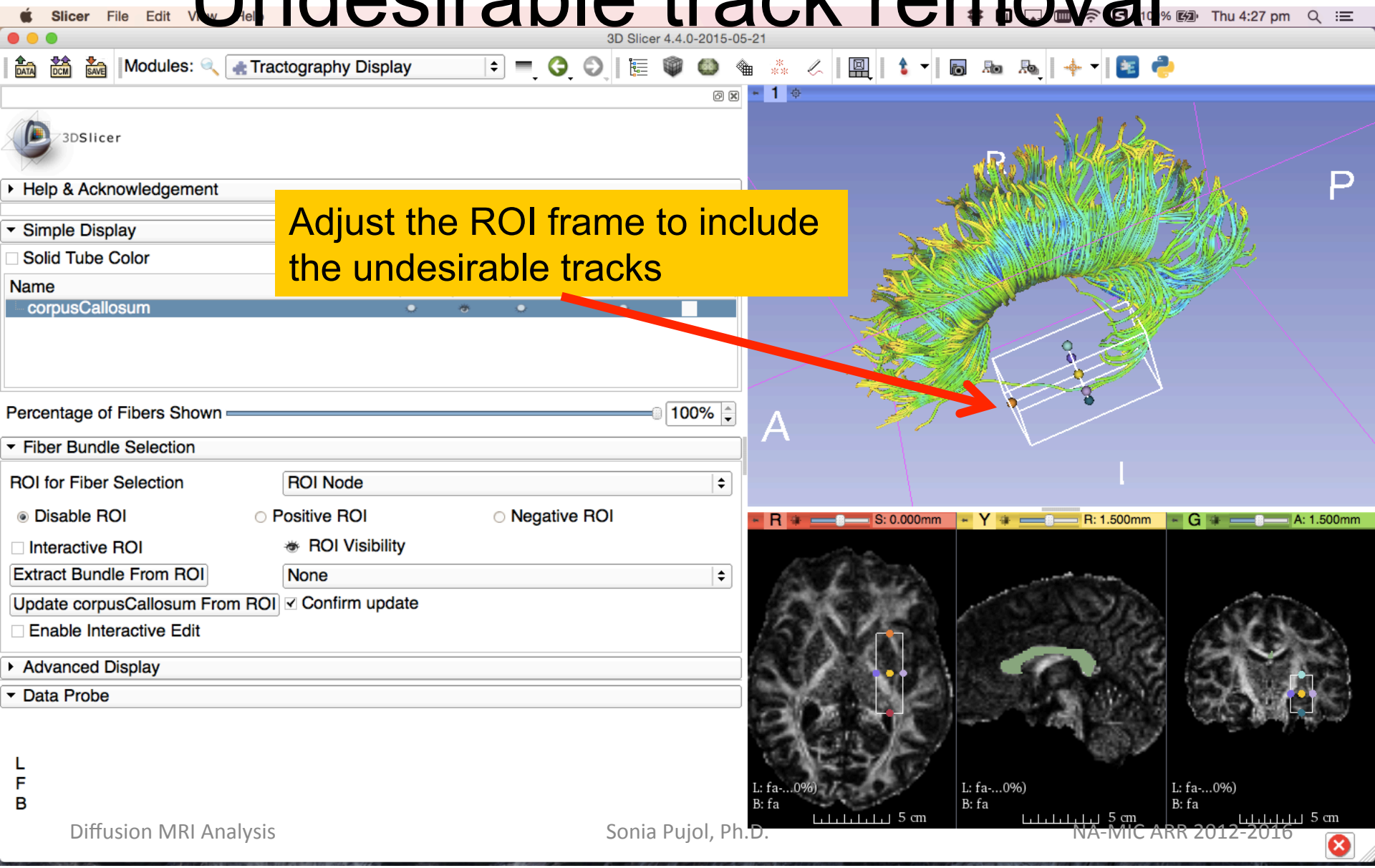


LabelMap Seeding: Step 4: Undesirable track removal



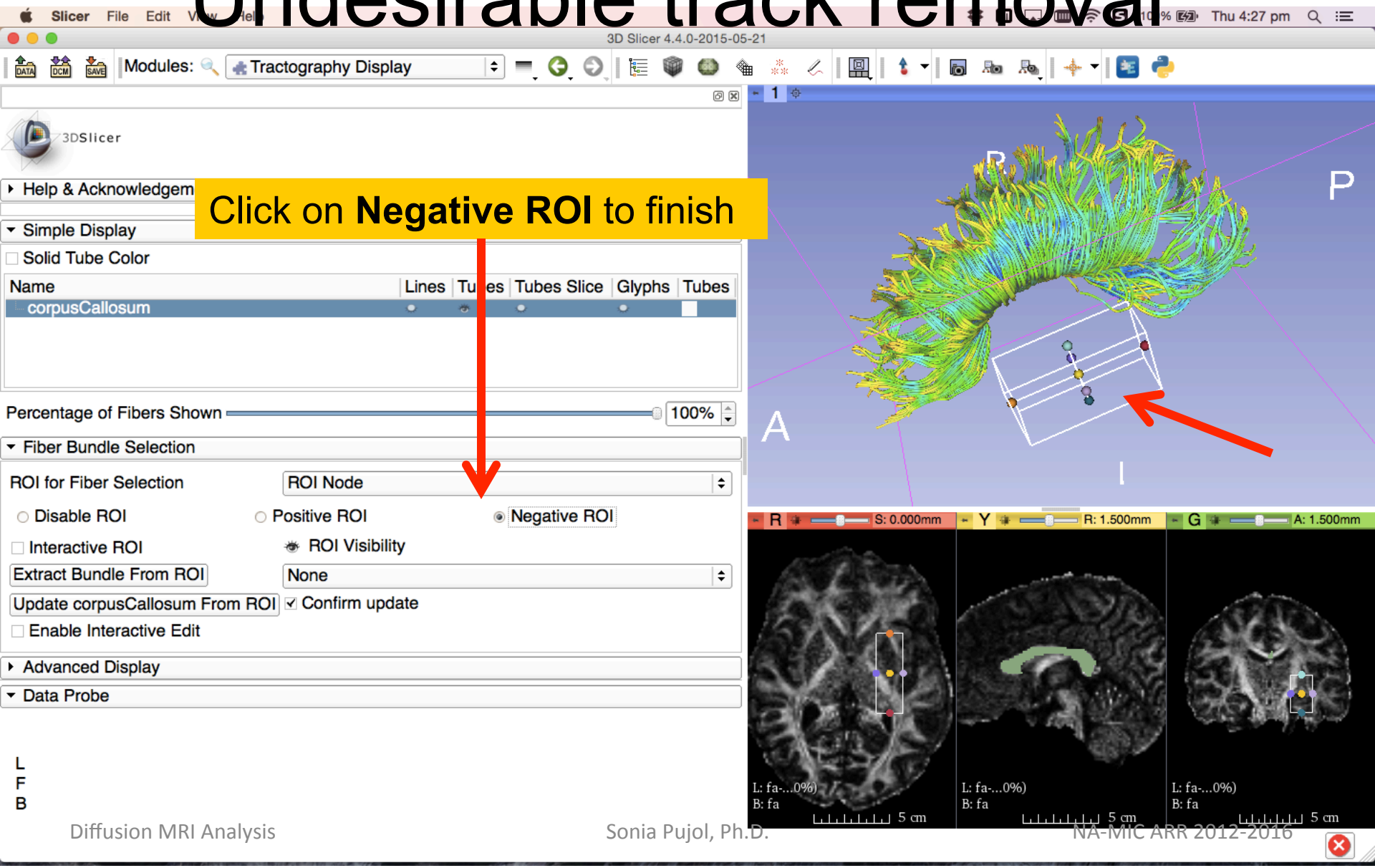
Set **ROI for Fiber Select** to 'ROI node'

LabelMap Seeding: Step 4: Undesirable track removal

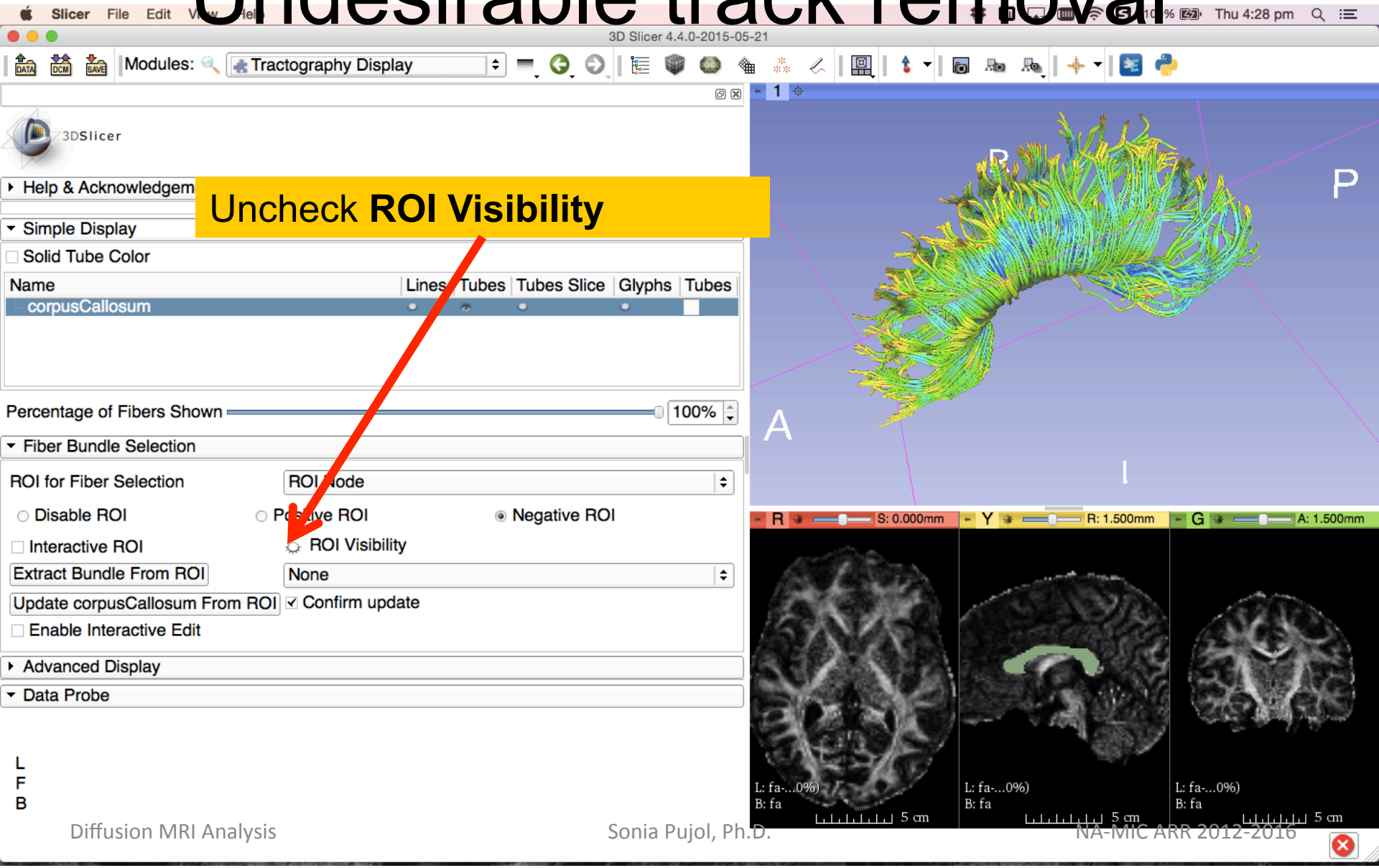


Adjust the ROI frame to include the undesirable tracks

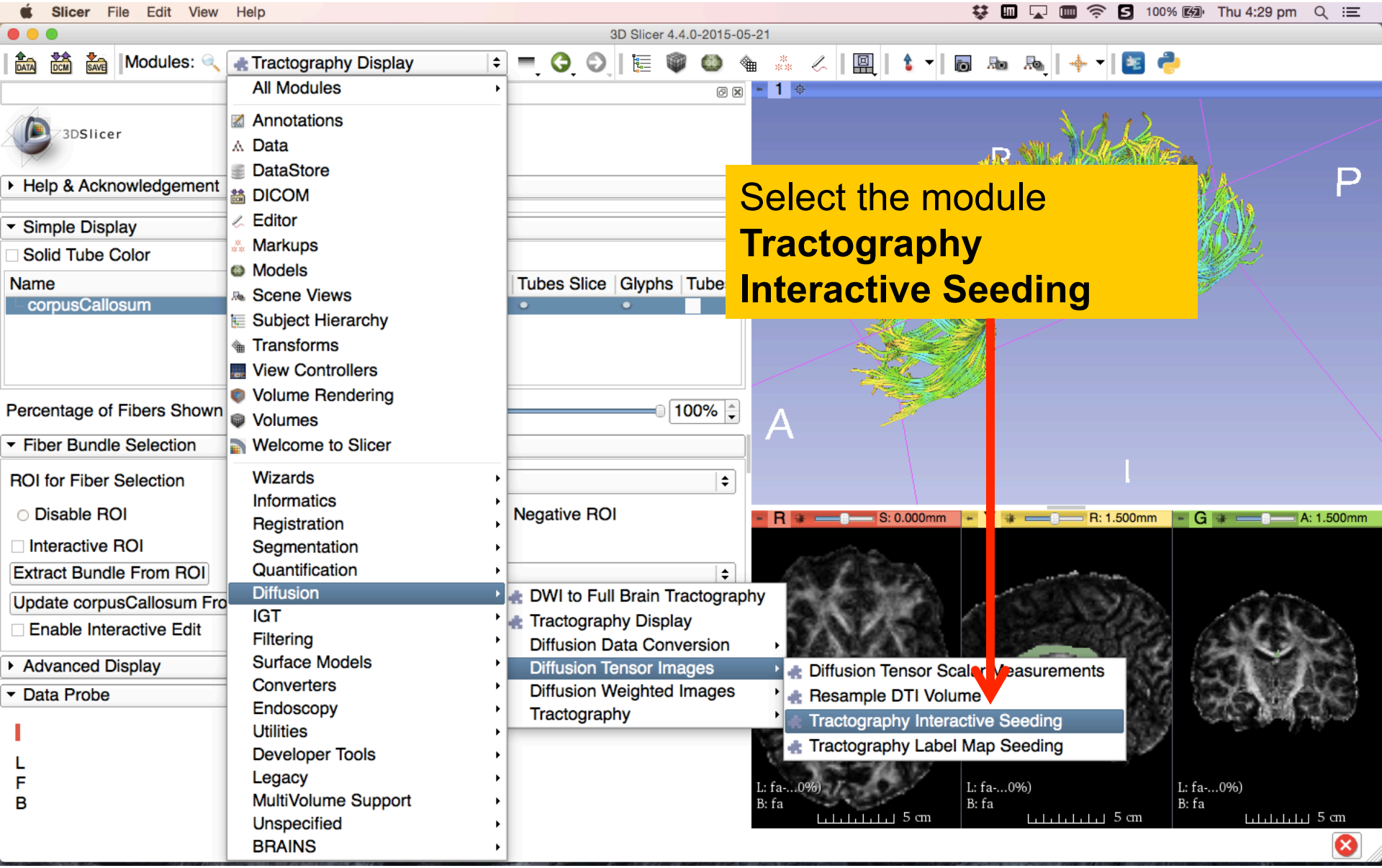
LabelMap Seeding: Step 4: Undesirable track removal



LabelMap Seeding: Step 4: Undesirable track removal



Labelmap Seeding: Tracts

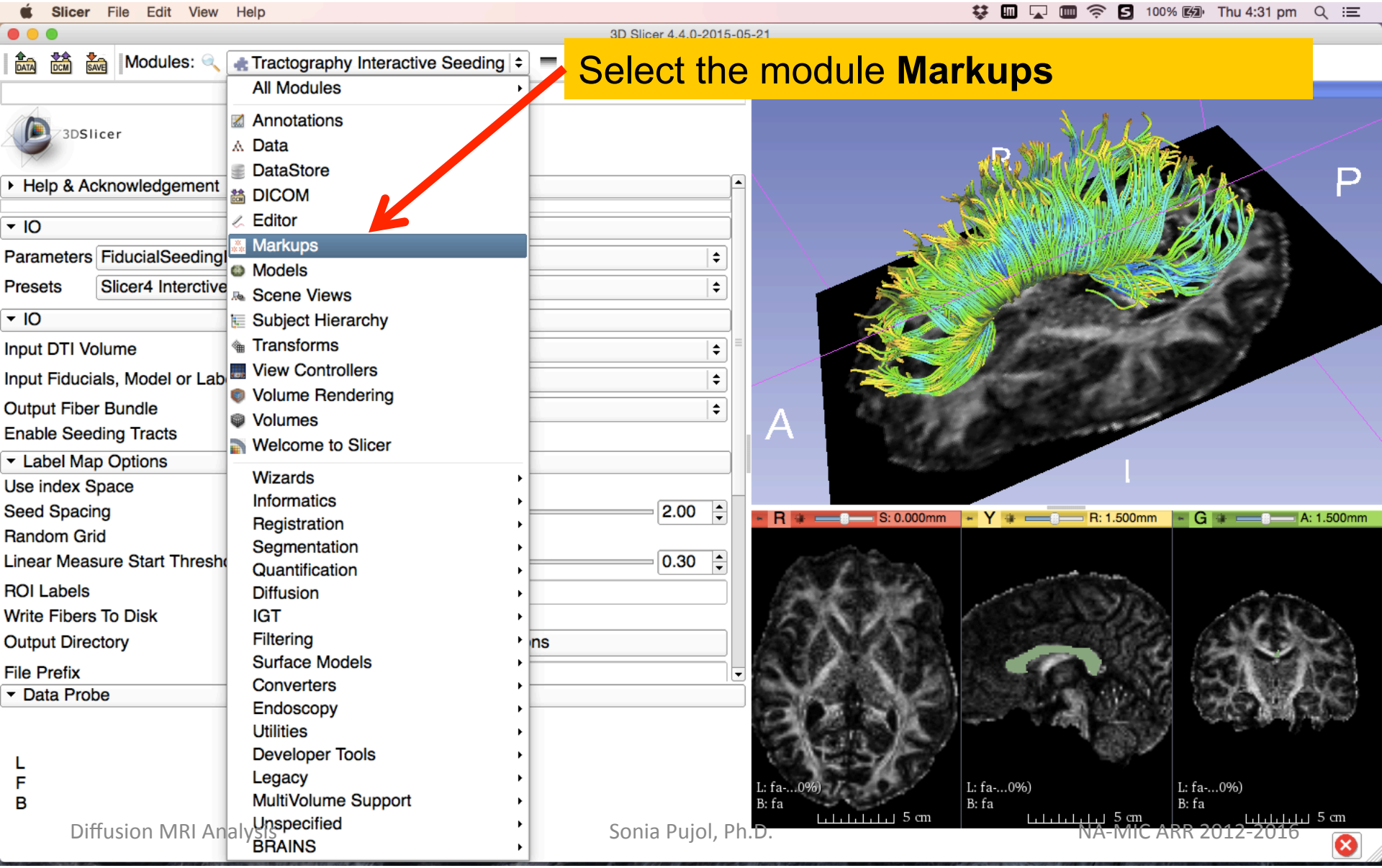


Tractography Results

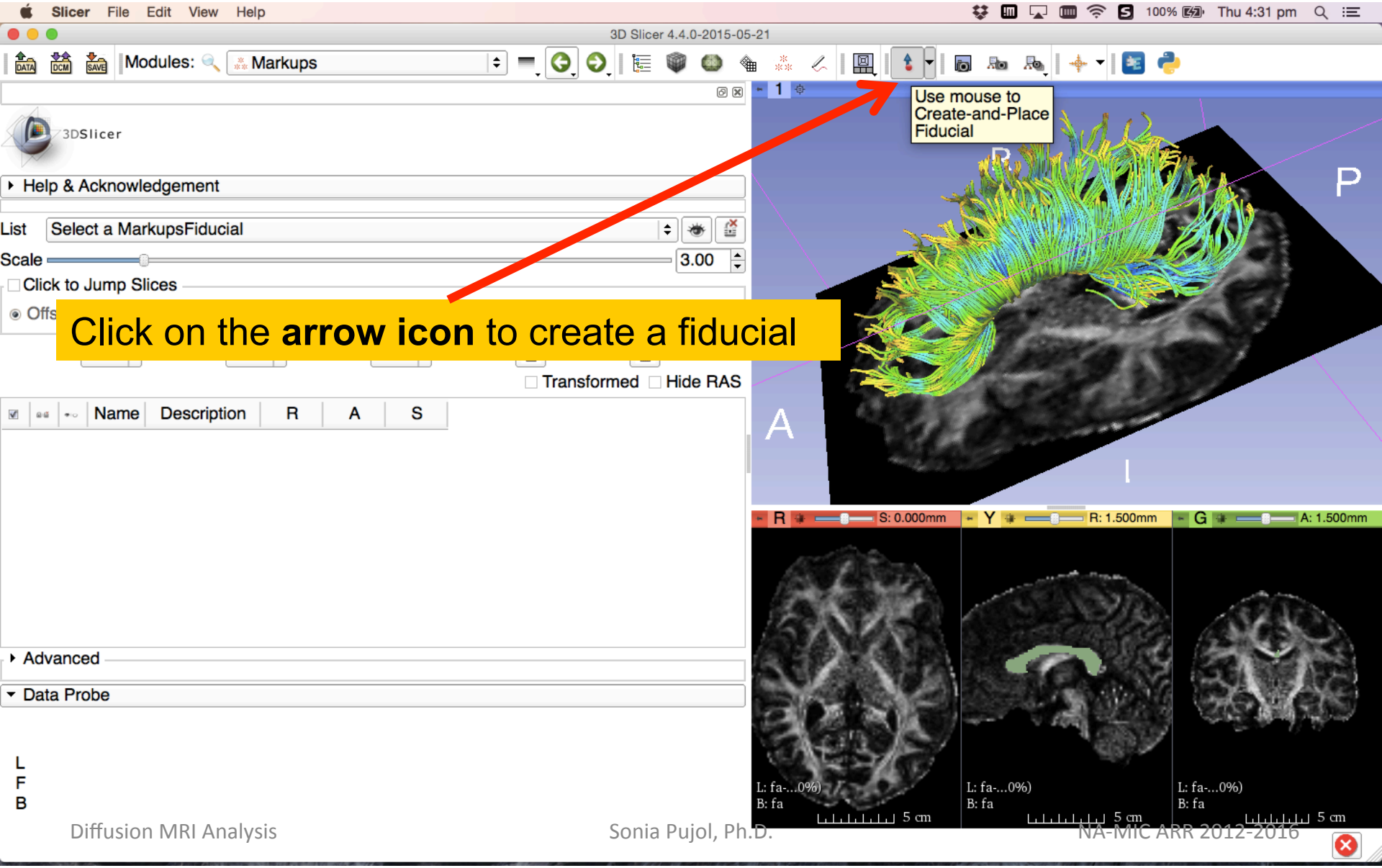
Position the mouse over the **pin icon** and click on the **eye icon** to display the axial slice in the 3D viewer

Uncheck **Enable Seeing Tracks**

Fiducial Seeding

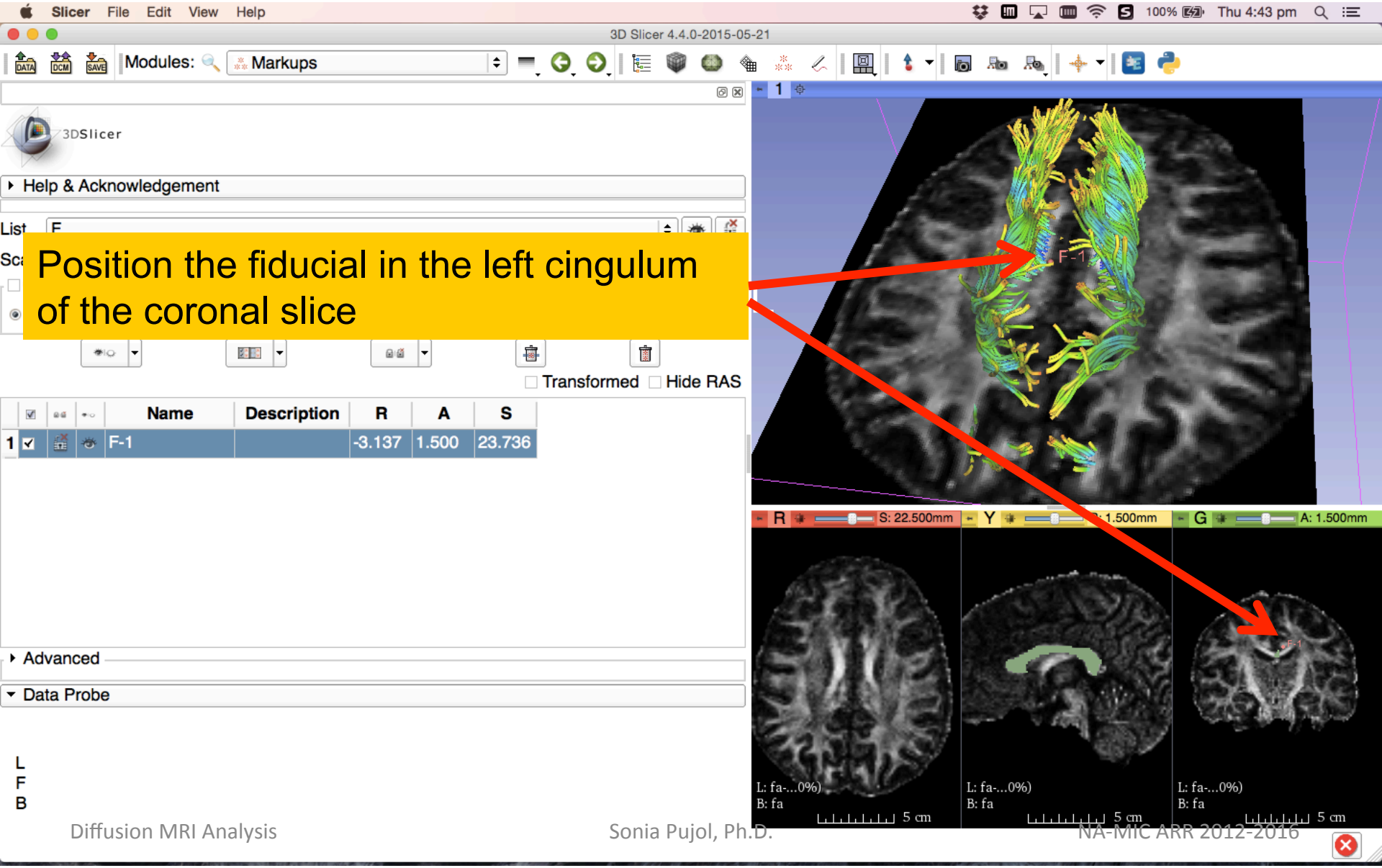


Fiducial Seeding

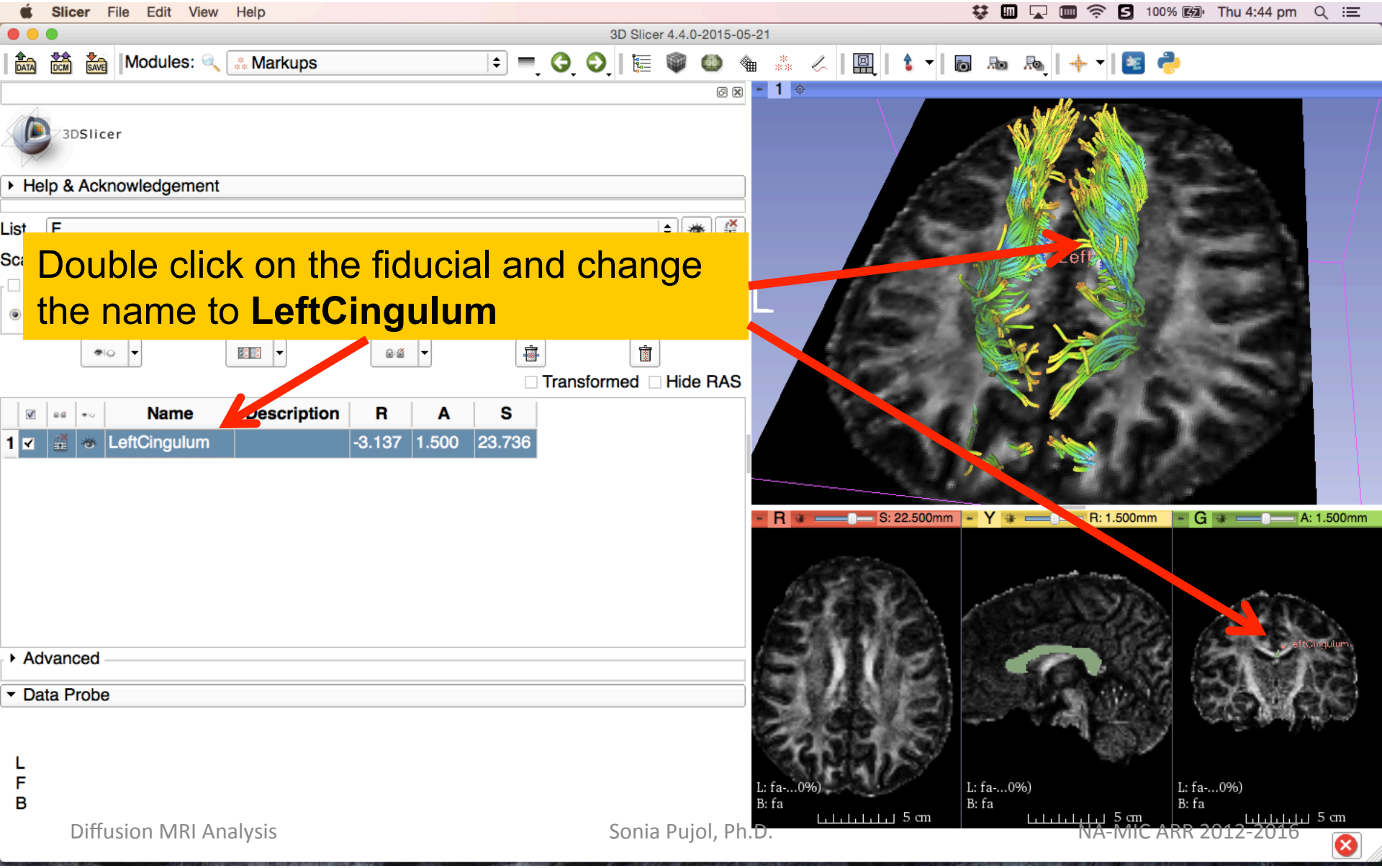


Click on the **arrow icon** to create a fiducial

Fiducial Seeding



Fiducial Seeding



Double click on the fiducial and change the name to **LeftCingulum**

Fiducial Seeding

Select the module **Tractography Interactive Seeding**

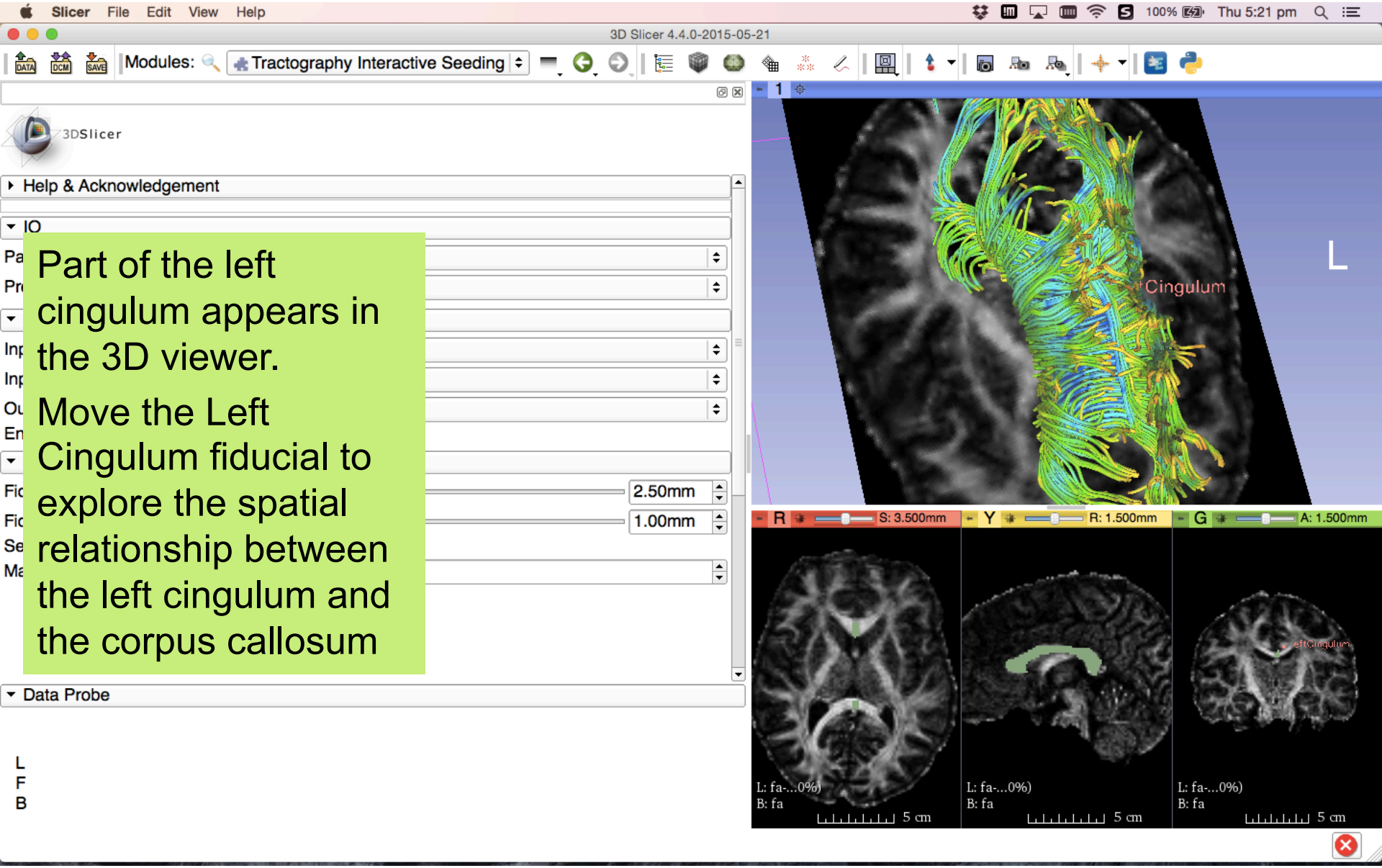
Set the Input DTI volume to ‘**dti**’

Set the Input **Fiducials, Model or Label Map** to ‘**F**’

Select the Output Fiber Bundle ‘Create New Fiber Bundle’ and rename it ‘**Cingulum**’

Check **Enable Seeing Tracks**

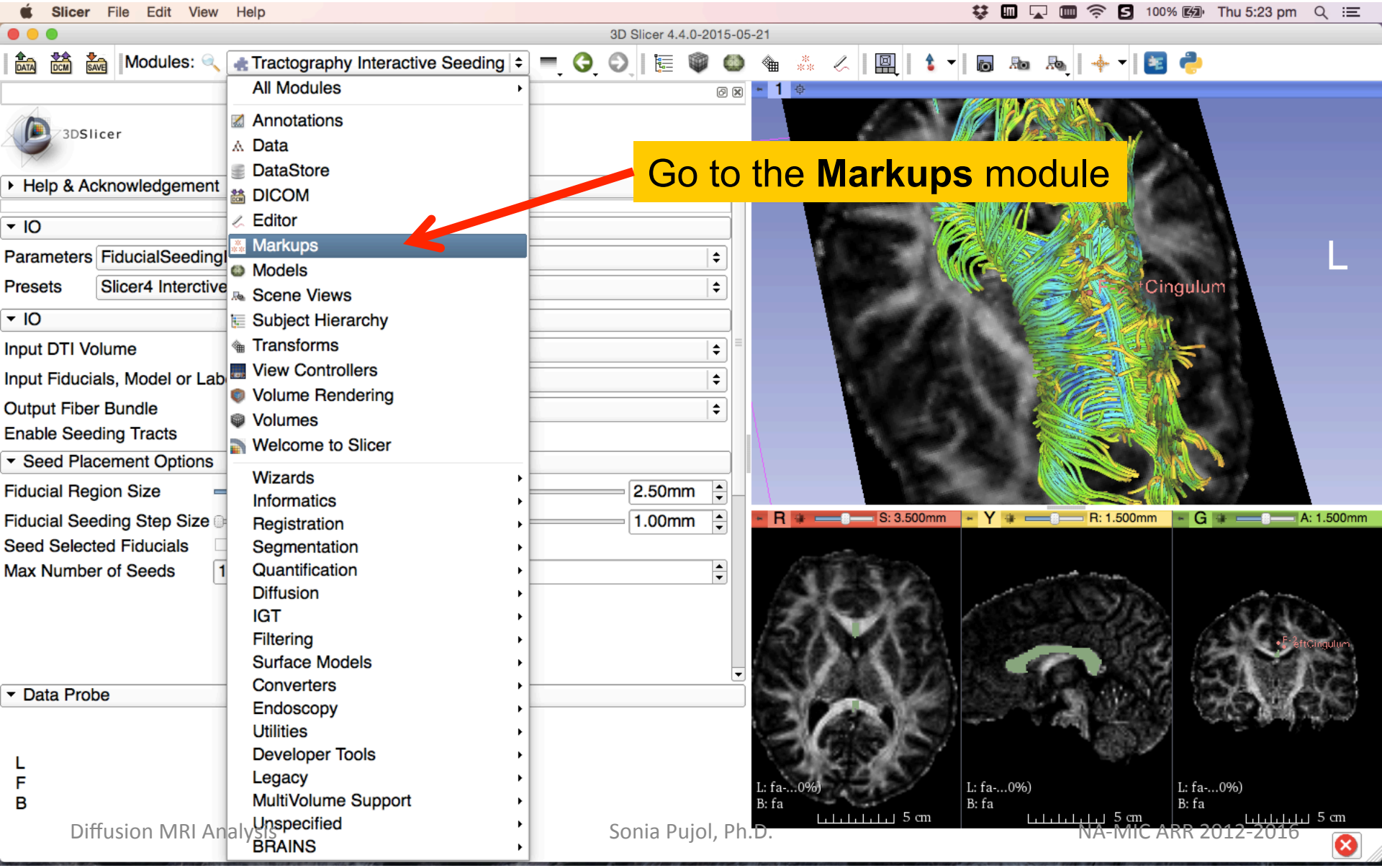
Fiducial Seeding



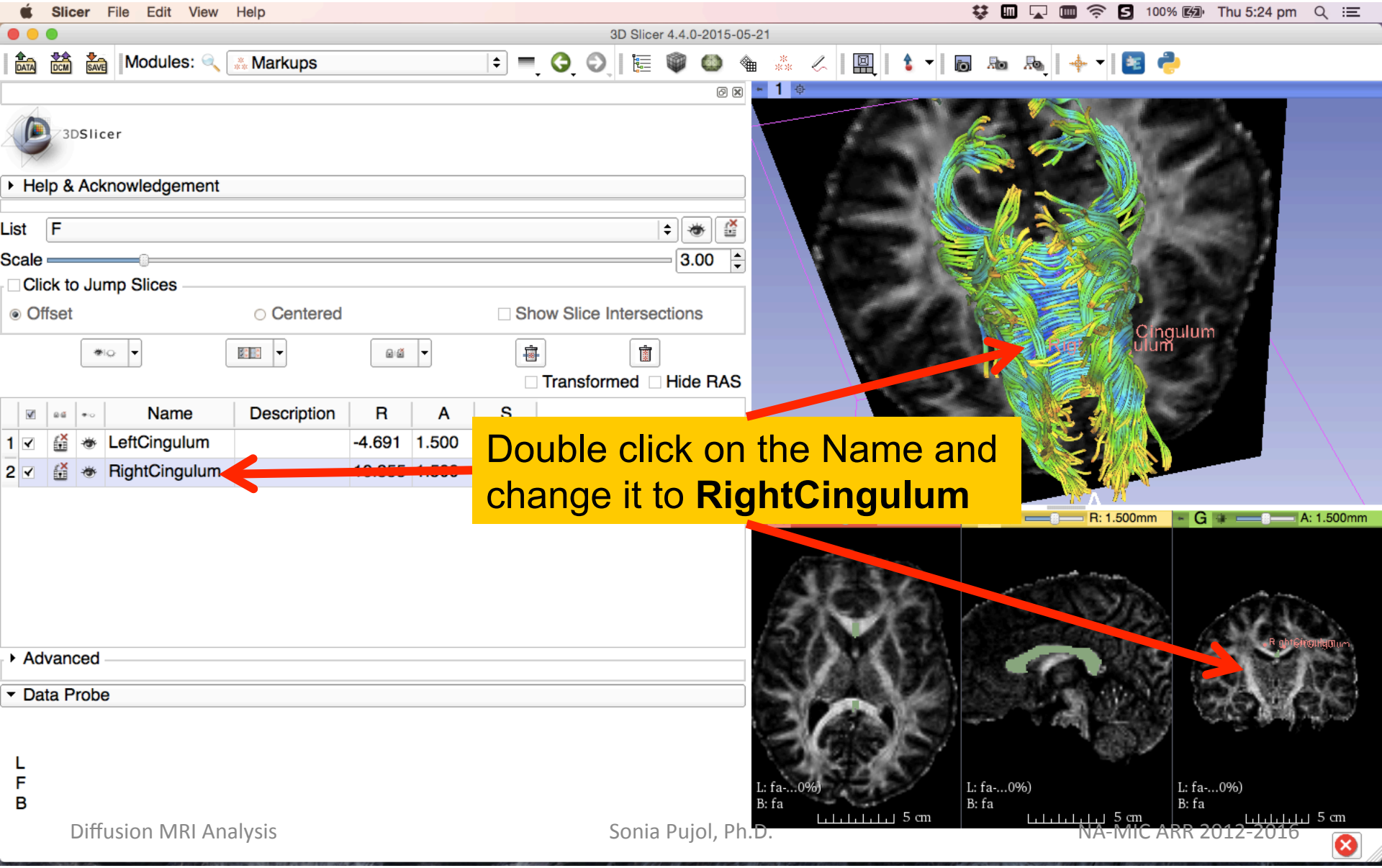
Part of the left cingulum appears in the 3D viewer.

Move the Left Cingulum fiducial to explore the spatial relationship between the left cingulum and the corpus callosum

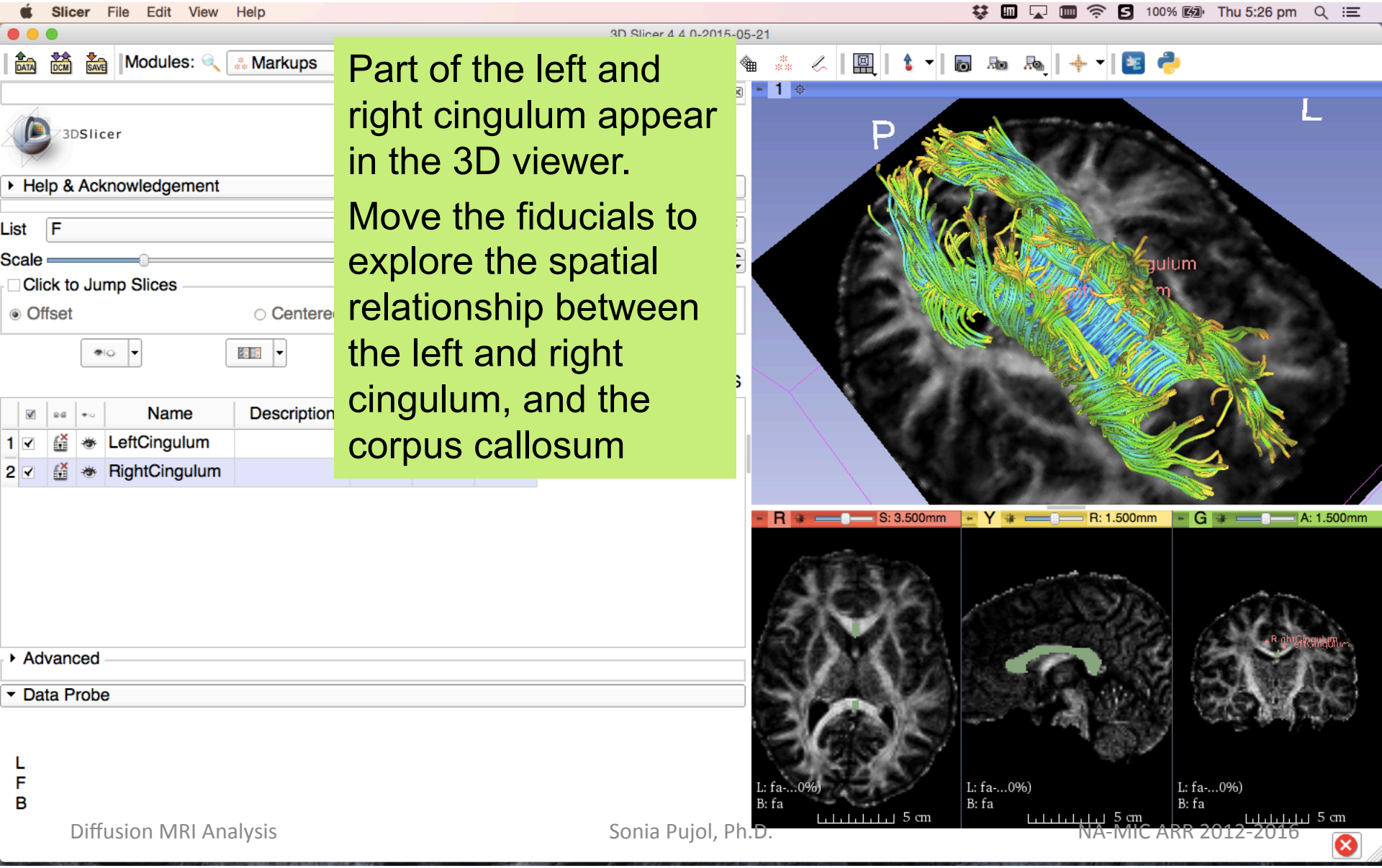
Fiducial Seeding



Fiducial Seeding



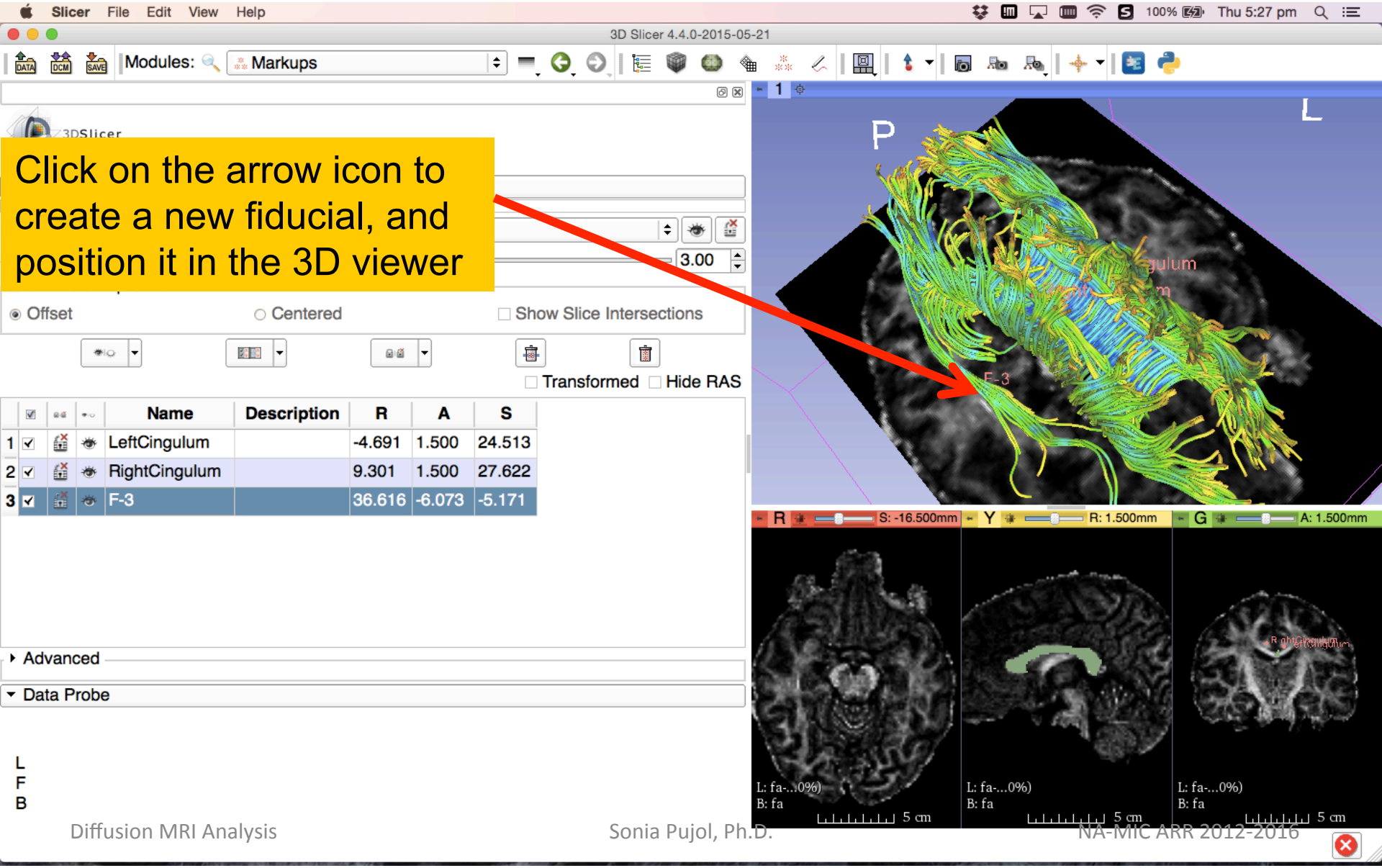
Fiducial Seeding



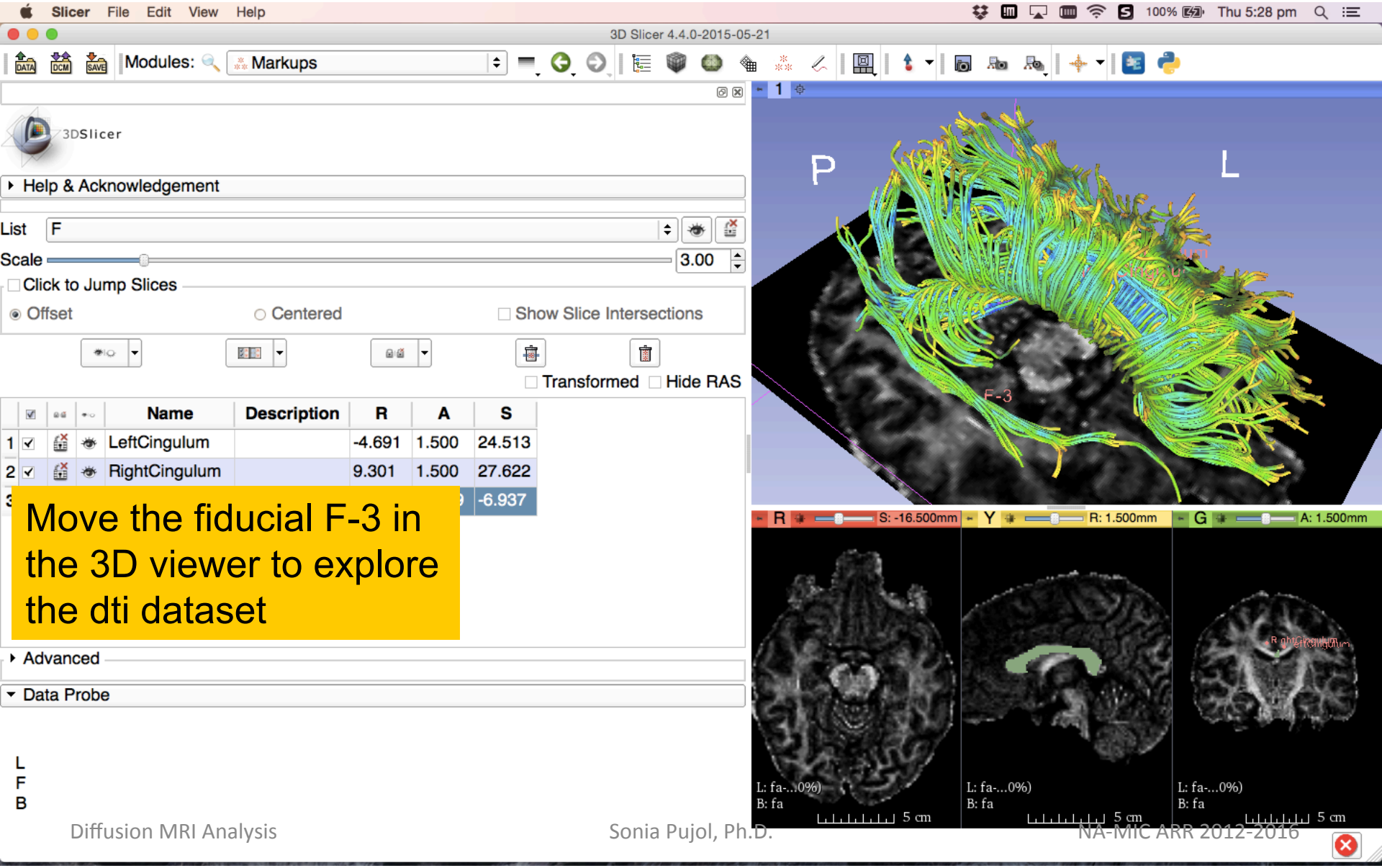
Part of the left and right cingulum appear in the 3D viewer.

Move the fiducials to explore the spatial relationship between the left and right cingulum, and the corpus callosum

Fiducial Seeding

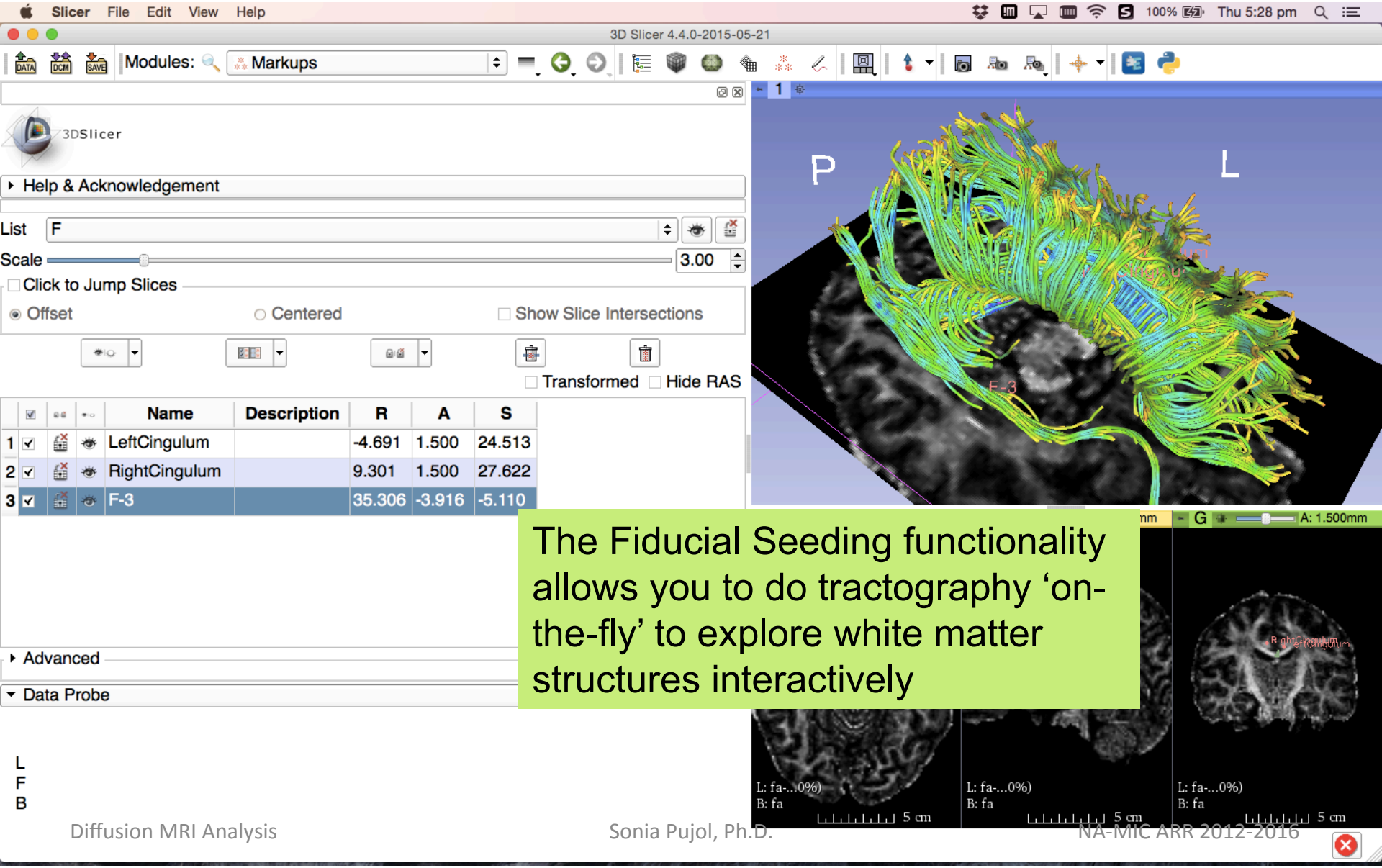


Fiducial Seeding



Move the fiducial F-3 in the 3D viewer to explore the dti dataset

Tractography ‘on-the-fly’

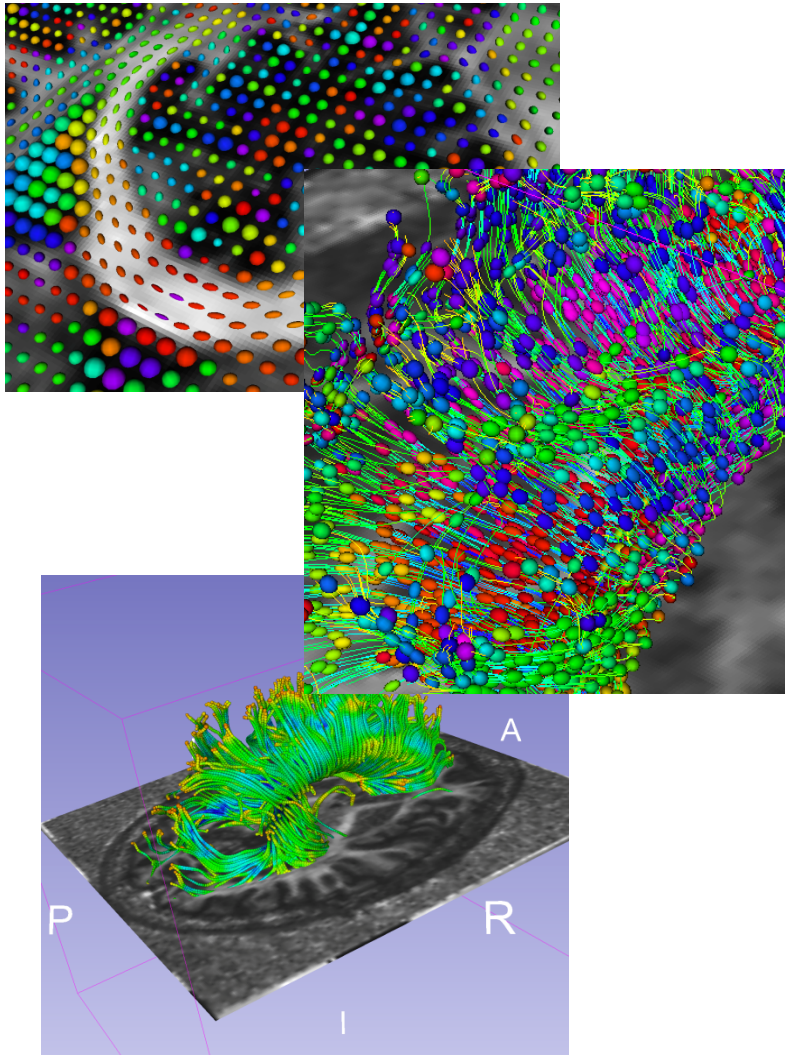


The Fiducial Seeding functionality allows you to do tractography ‘on-the-fly’ to explore white matter structures interactively

DTI Analysis

Select the module **Data** to display the list of elements that have been generated in this tutorial

Conclusion



This tutorial guided you through the different steps of a Diffusion MR analysis pipeline, from tensor estimation to 3D tracts visualization, for exploring and studying the 3D architecture of the brain white matter.

Acknowledgments

- Neuroimage Analysis Center (NAC)

  NIH P41RR013218
- National Alliance for Medical Image Computing (NA-MIC)

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- Fan Zhang, MSc., University of Sydney