



# Diffusion MRI Analysis

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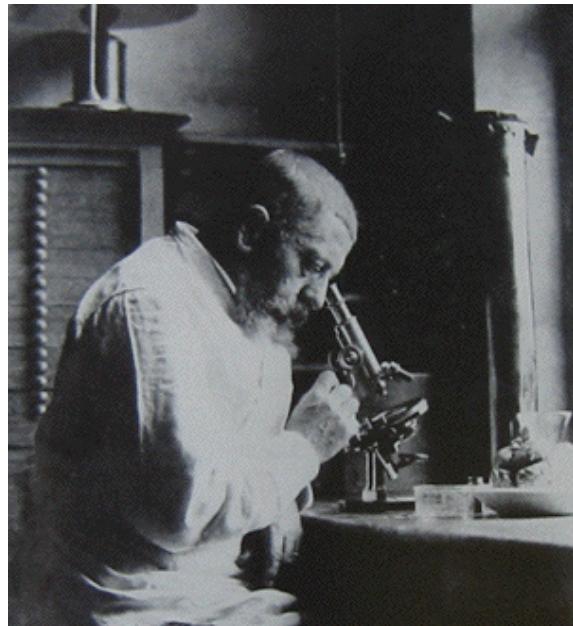
[spujol@bwh.harvard.edu](mailto:spujol@bwh.harvard.edu)

# Brain Anatomy



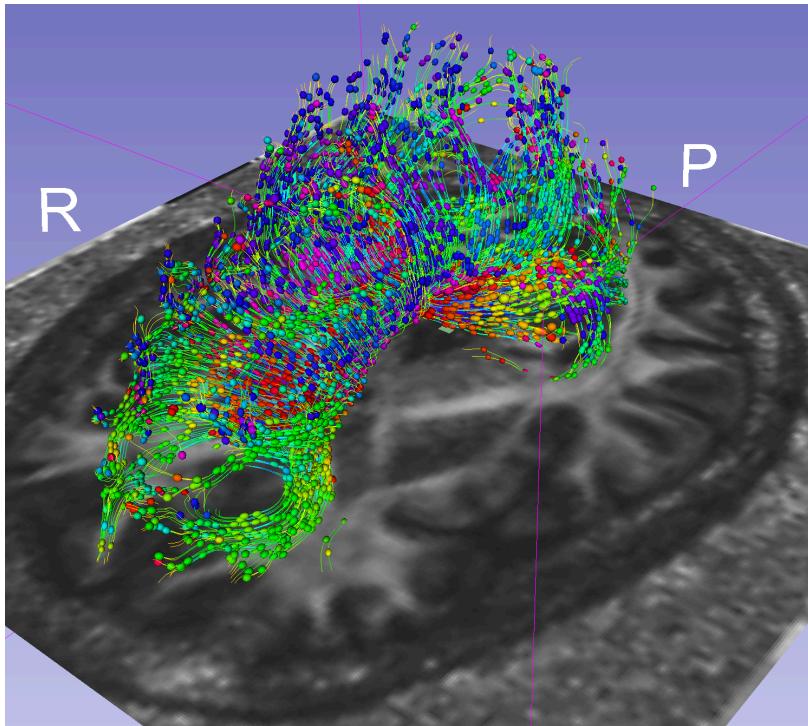
- White matter ~45% of the brain
- Myelinated nerve fibers (~ 10  $\mu\text{m}$  axon diameter)

# White Matter Exploration



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

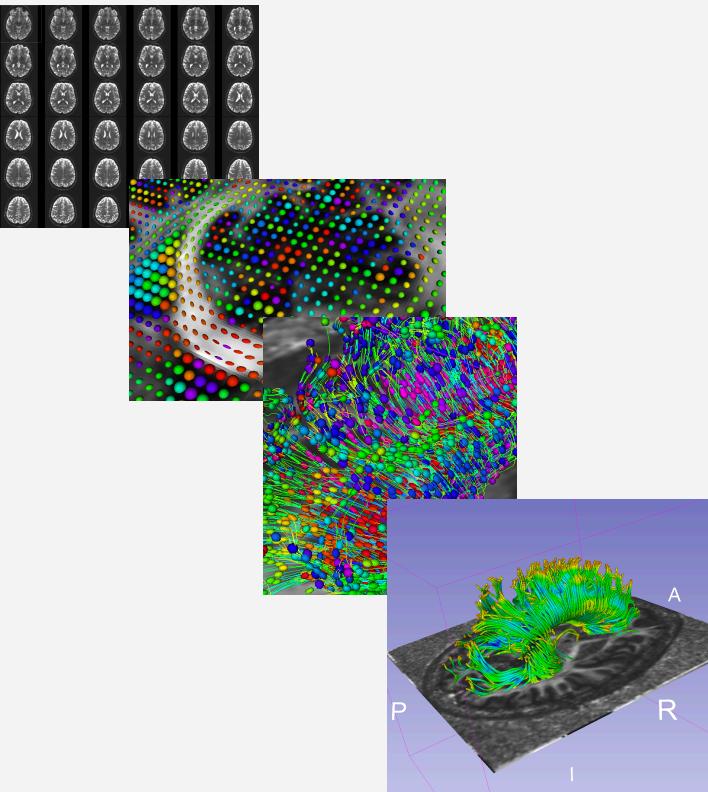
# White Matter Exploration



First non-invasive  
window on the  
organization of brain  
white matter  
pathways *in-vivo*

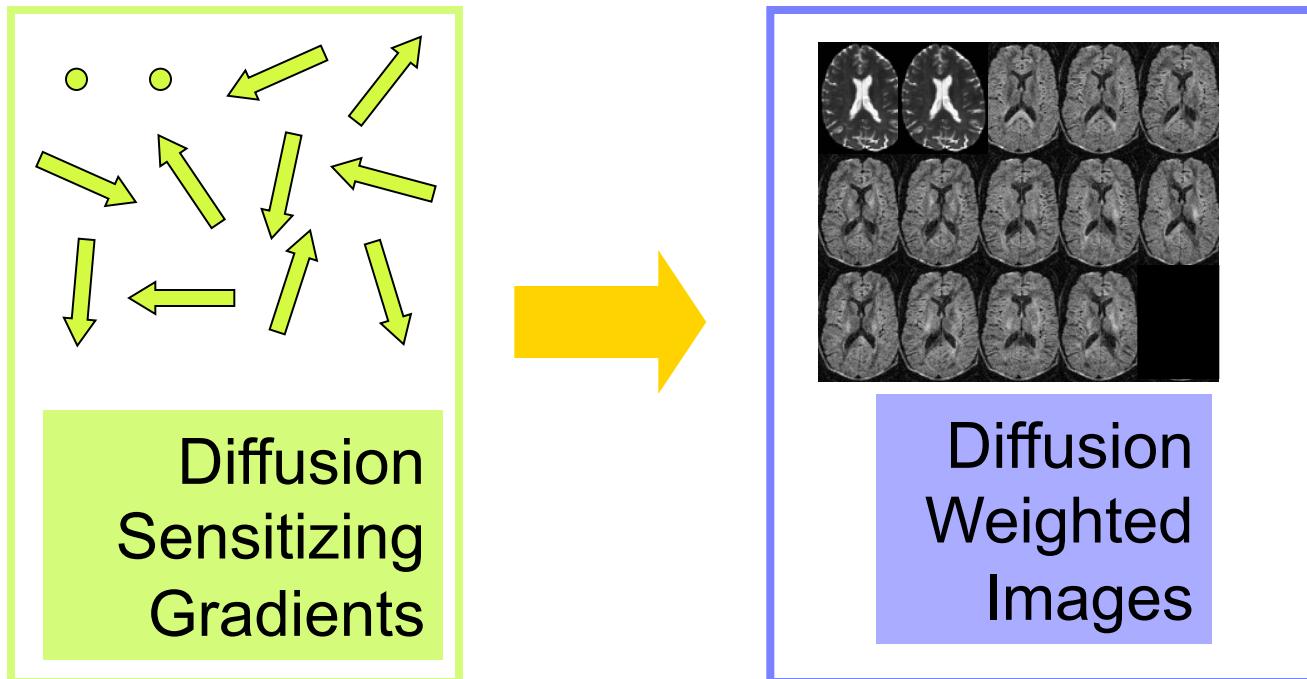
# Tutorial Outline

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



# Tutorial dataset

The tutorial dataset DiffusionMRI\_tutorialData is a Diffusion Weighted MR scan of the brain acquired with 41 gradient directions and one baseline.



The dataset is available on the Slicer Training Compendium ([www.slicer.org](http://www.slicer.org))

# Tutorial software

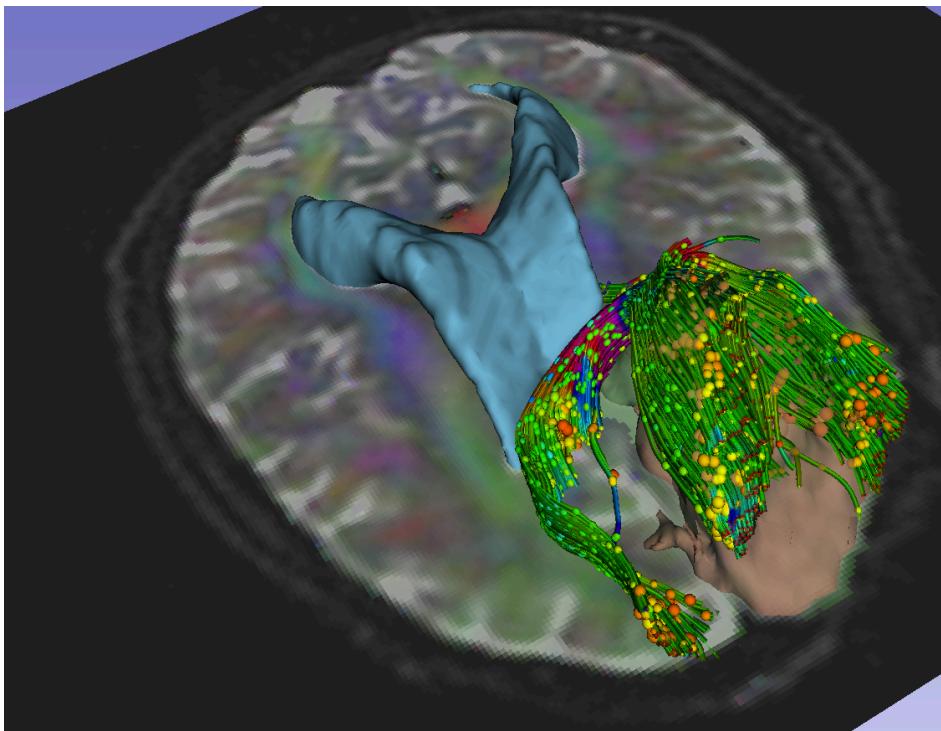


The tutorial uses the 3DSlicer version 4.1 software available at [www.slicer.org](http://www.slicer.org)

## Disclaimer

It is the responsibility of the user of 3DSlicer to comply with both the terms of the license and with the applicable laws, regulations and rules. Slicer is a tool for research, and is not FDA approved.

# 3DSlicer



3D Slicer is a multi-institution effort supported by the National Institutes of Health.

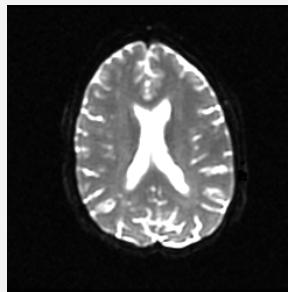
- An **end-user application** for image analysis
- An **open-source environment** for software development
- A software platform that is both **easy to use** for clinical researchers and **easy to extend** for programmers

# Learning Objectives

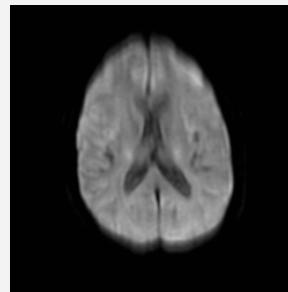
Following this tutorial, you'll be able to

- 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

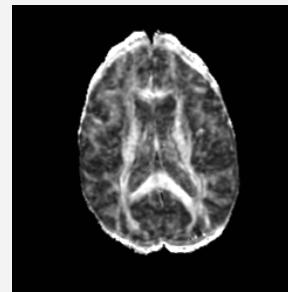
# MR Diffusion Analysis Pipeline



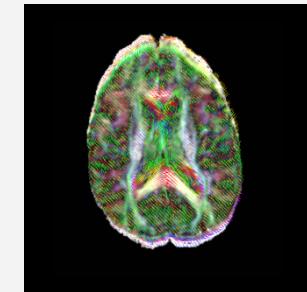
DWI  
Acquisition



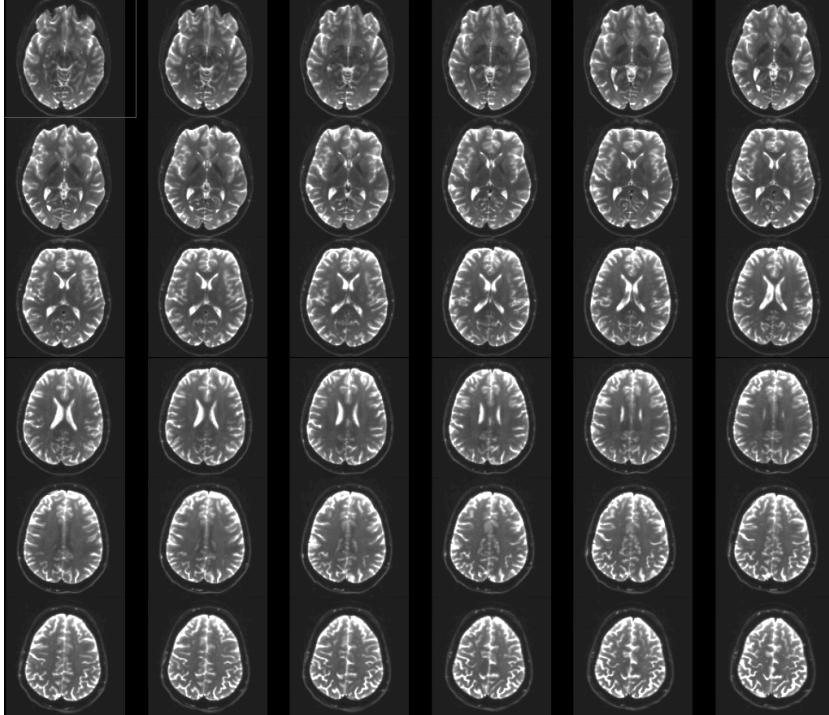
Tensor  
Calculation



Scalar  
Maps

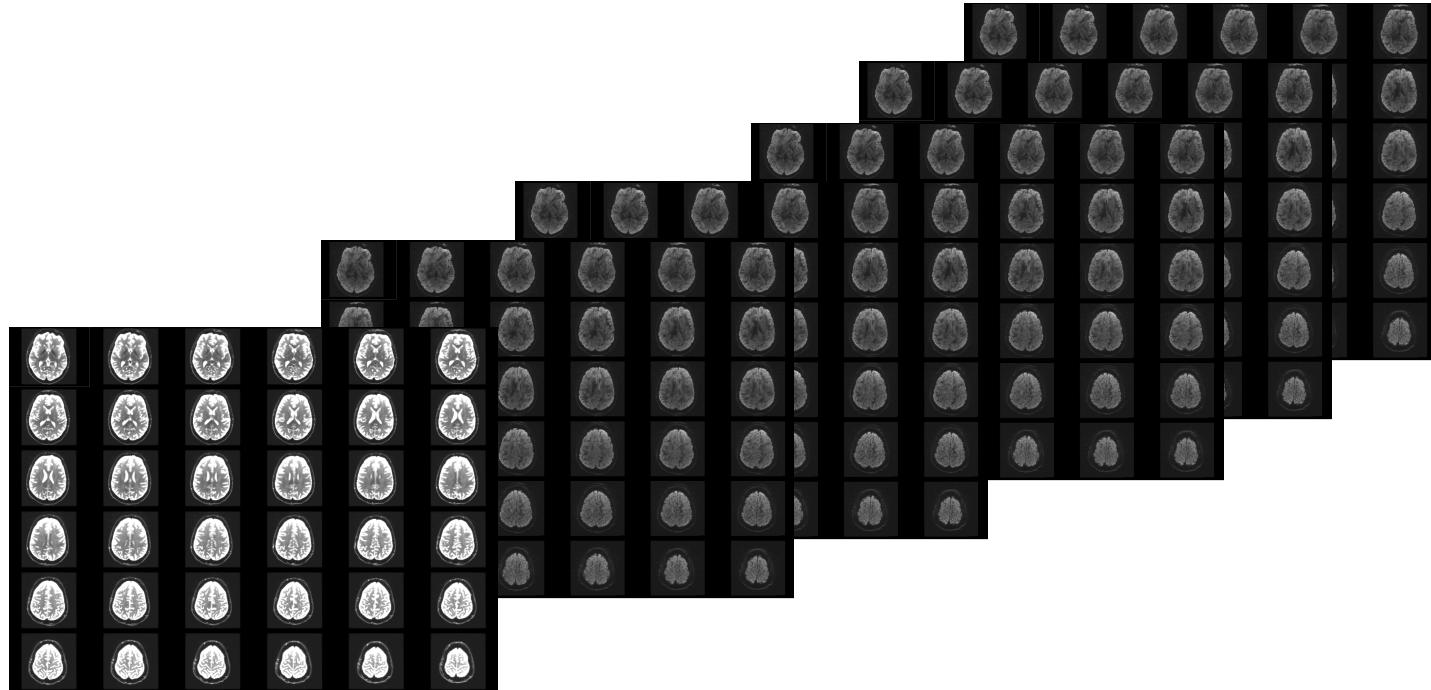


3D  
Visualization



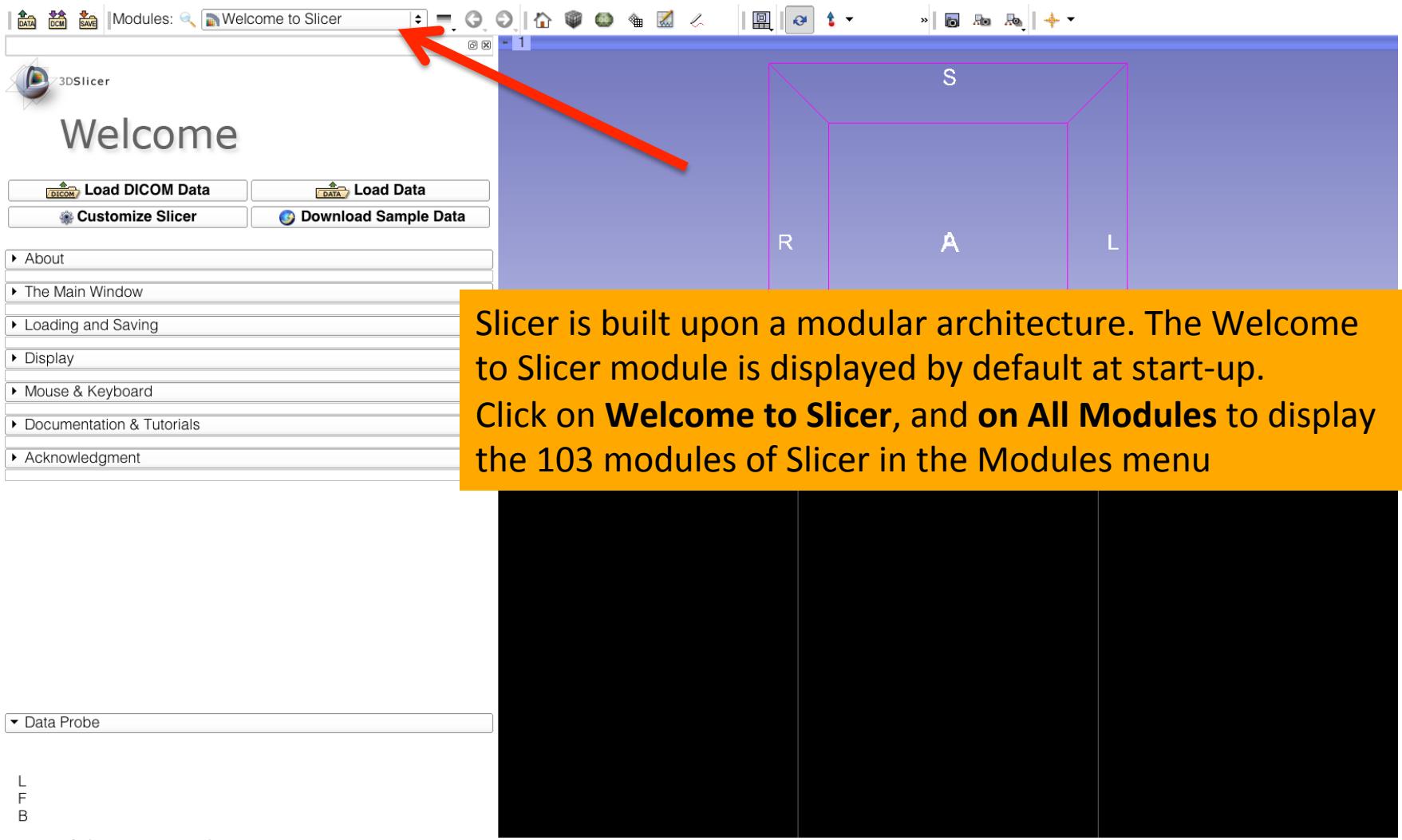
# Part 1: From DWI images to Tensors

# Understanding the DWI dataset

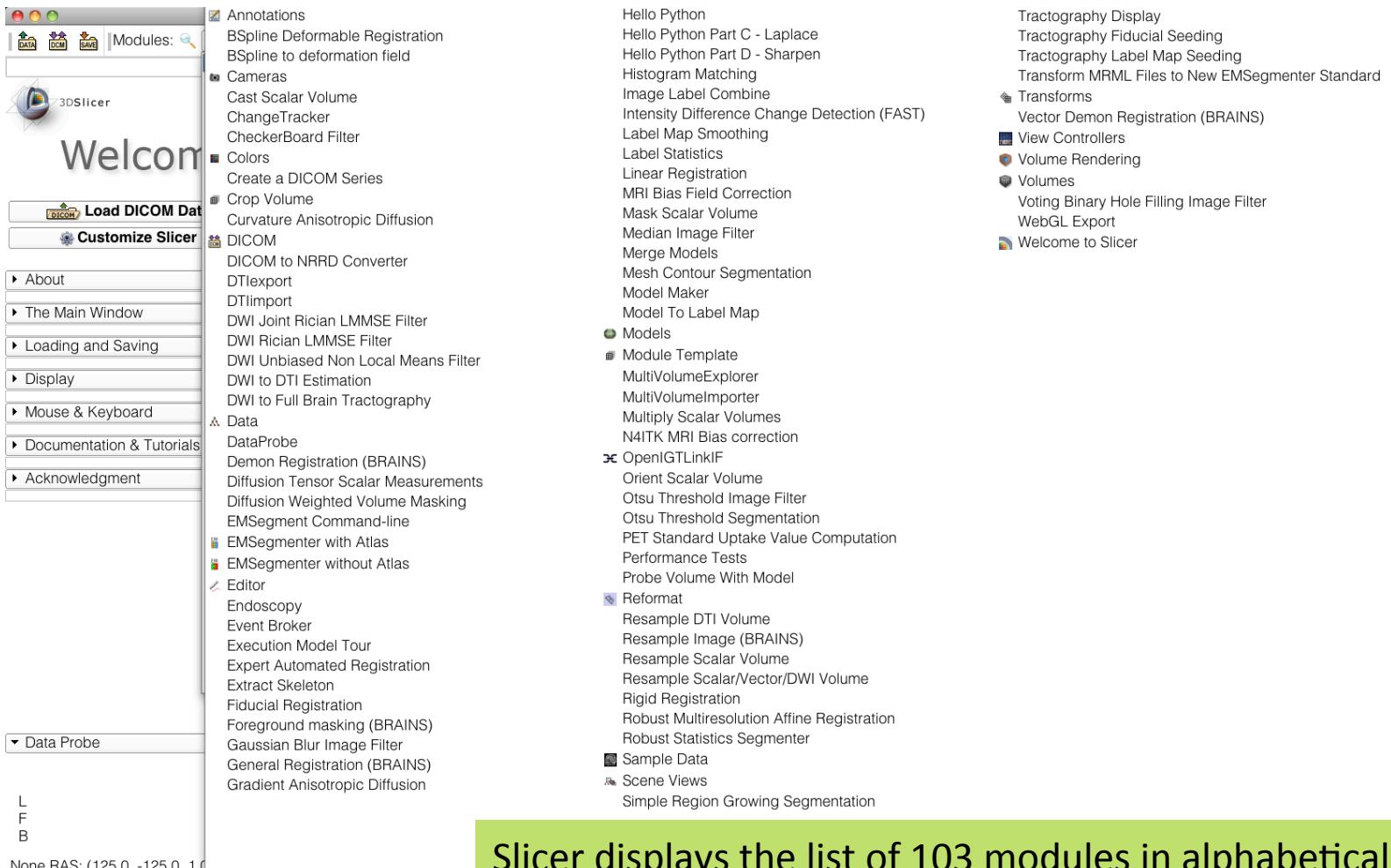


The Diffusion Weighted Imaging (DWI) dataset is composed of 1 volume acquired without diffusion-sensitizing gradient, and 41 volumes acquired with 41 different diffusion-sensitizing gradient directions.

# Start the Slicer Software

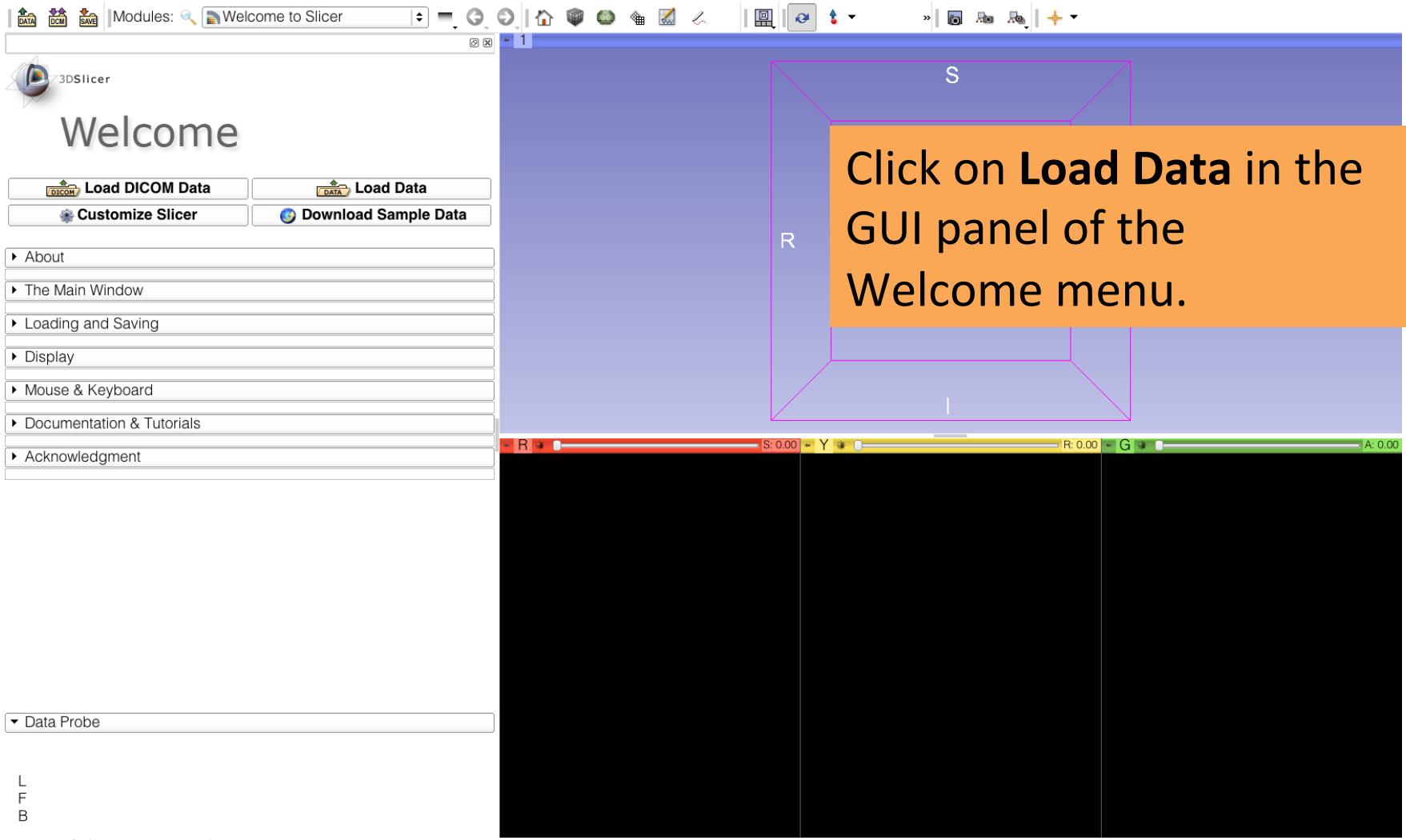


# Start the Slicer software

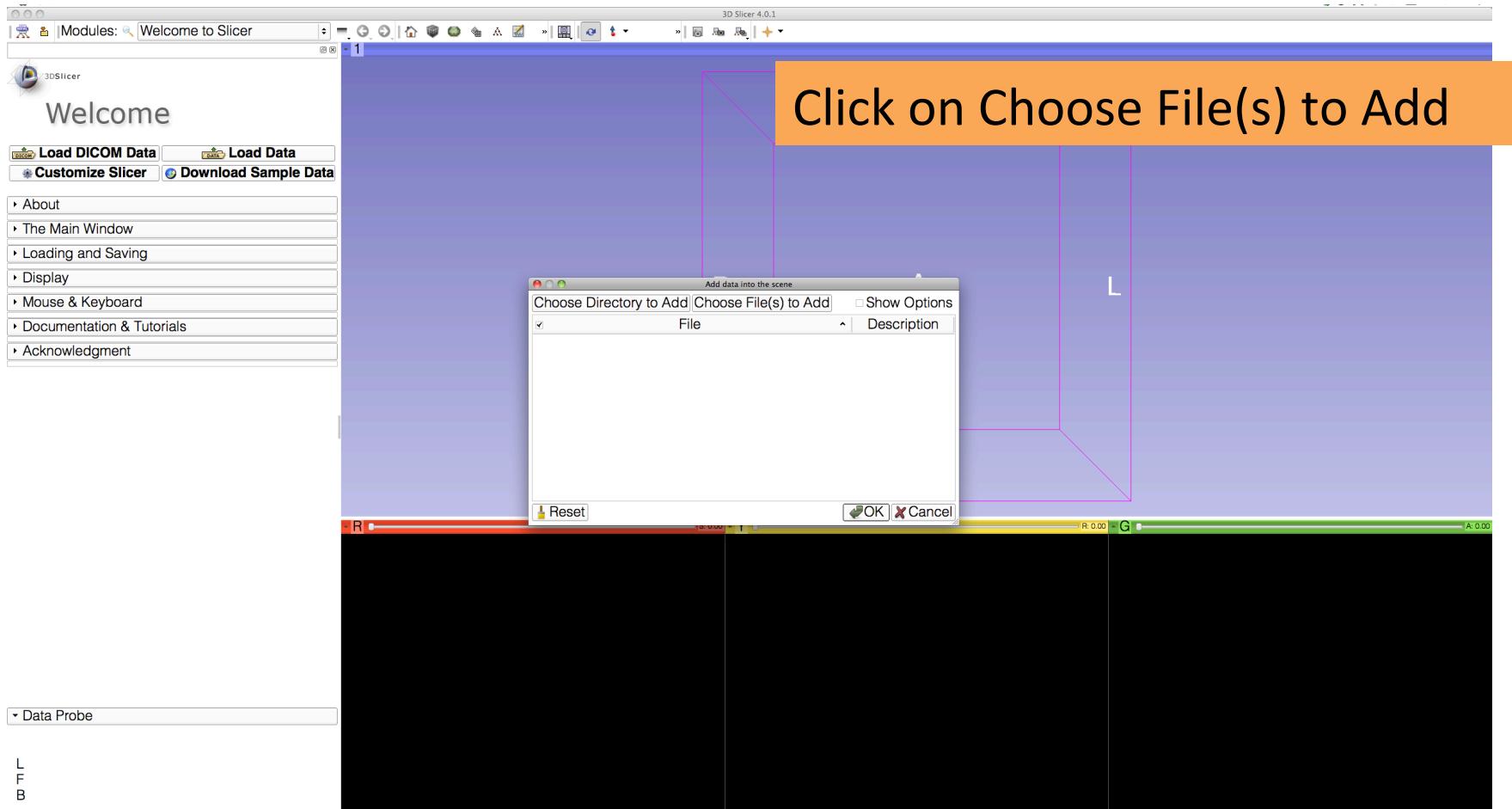


Slicer displays the list of 103 modules in alphabetical order.

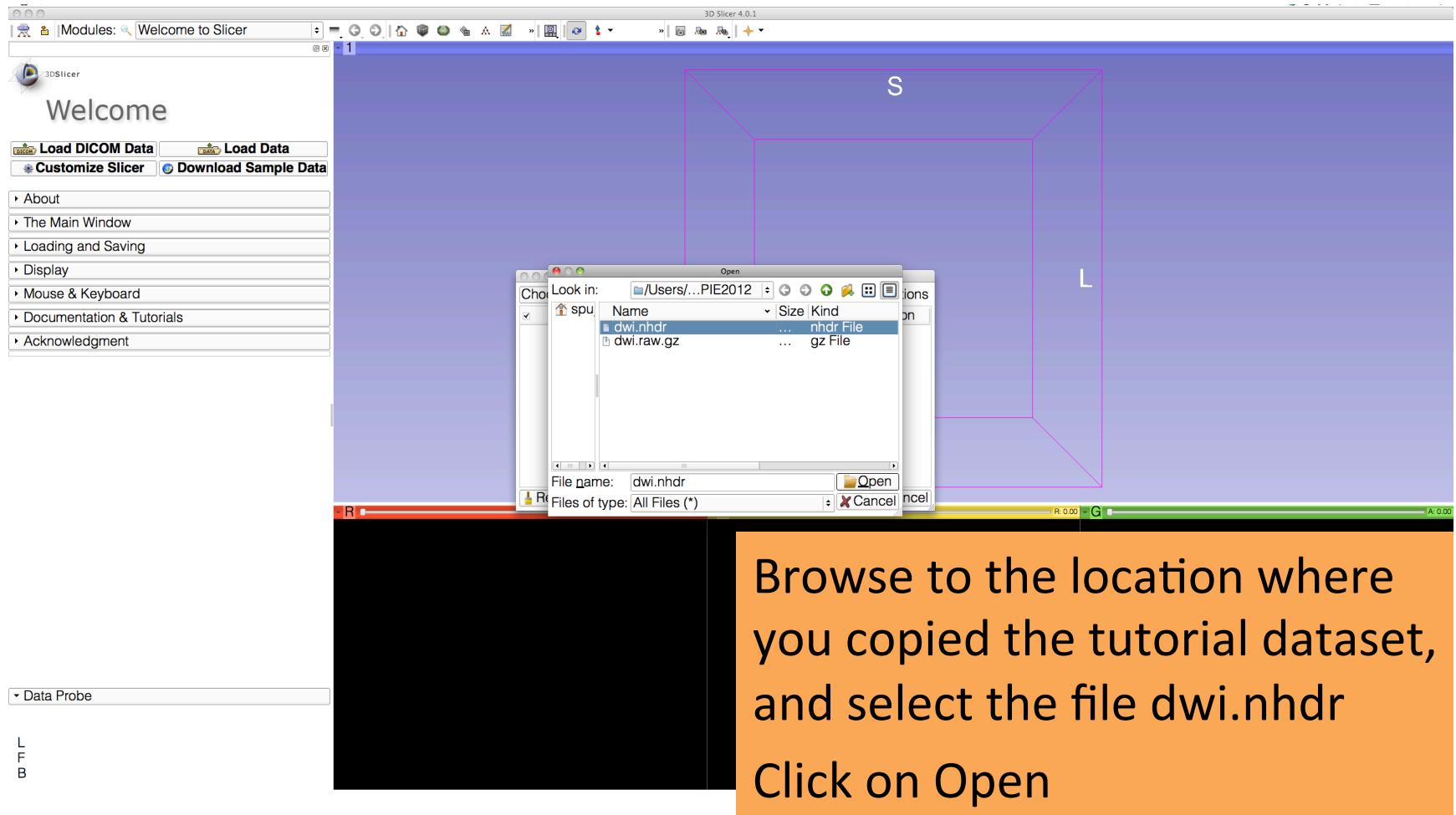
# Loading the DWI dataset



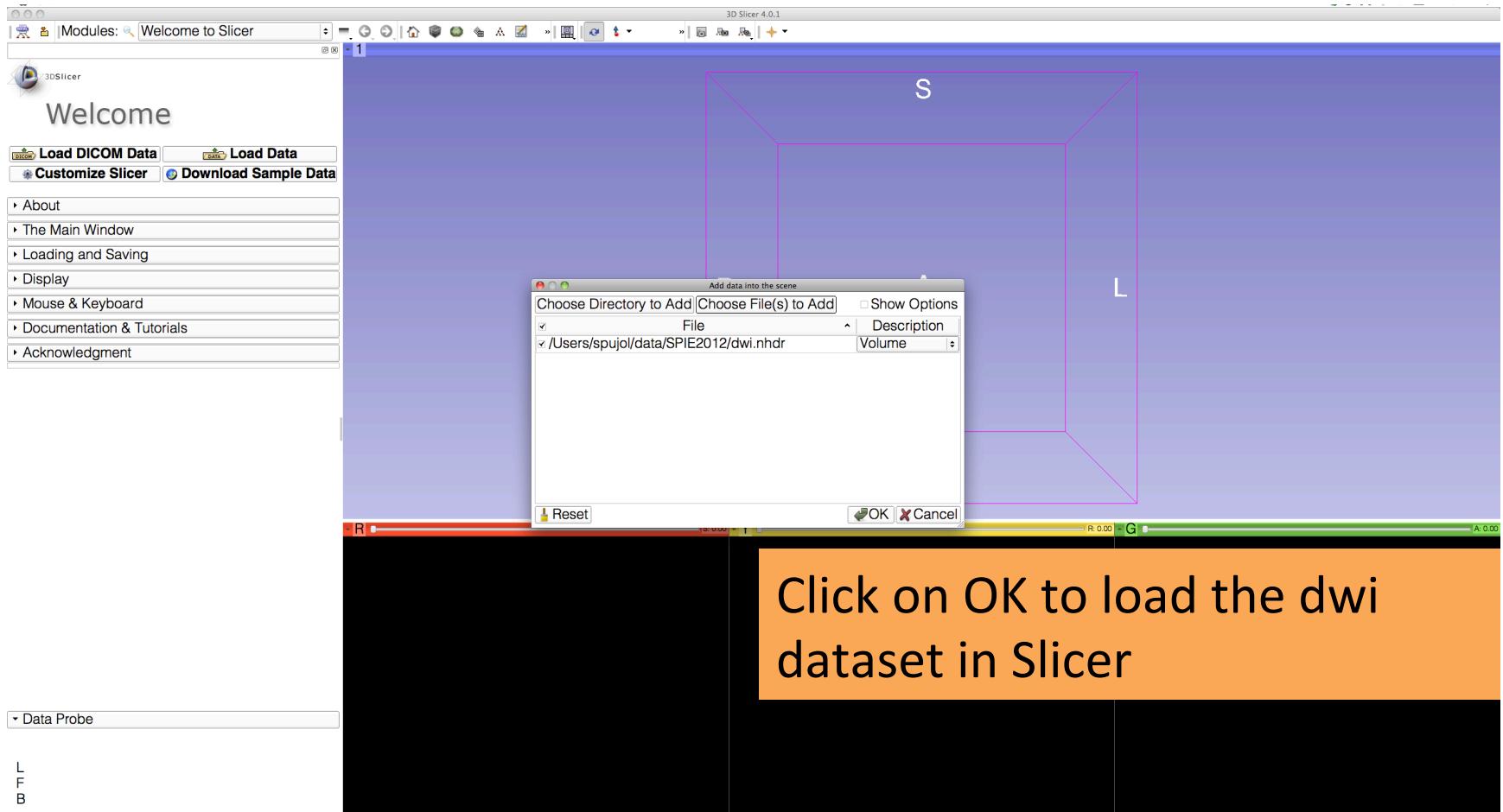
# Loading the DWI dataset



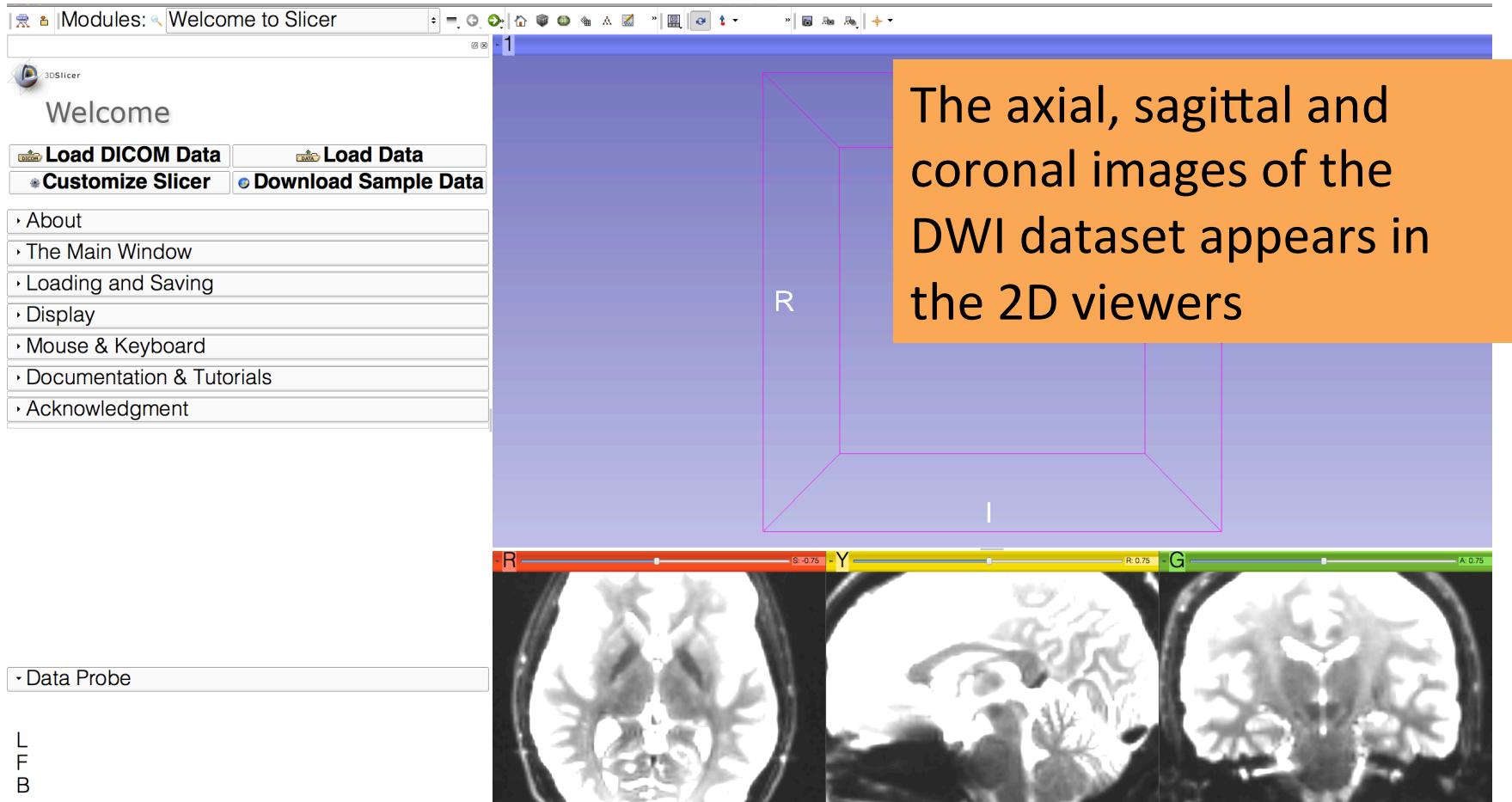
# Loading the DWI dataset



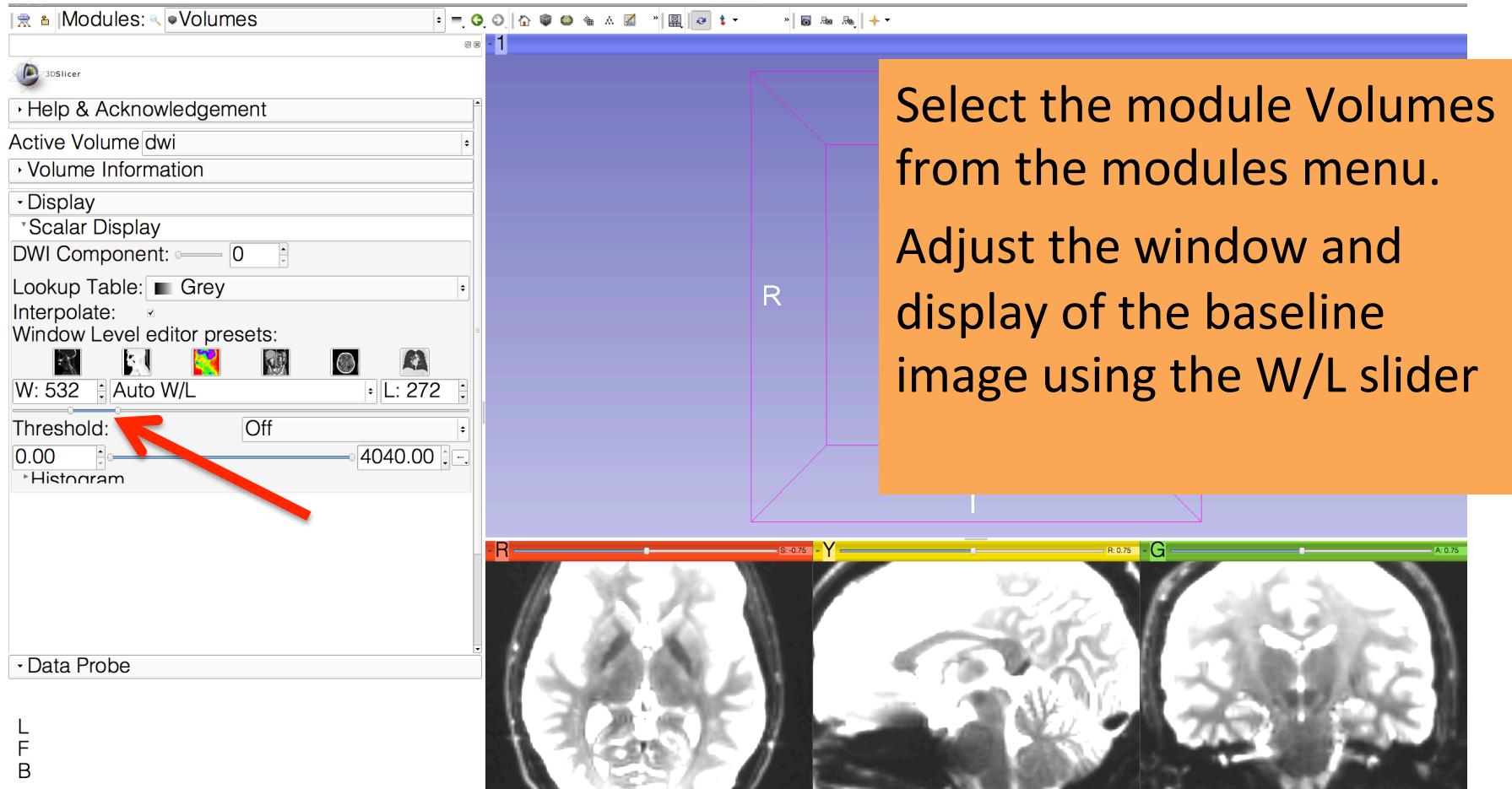
# Loading the DWI dataset



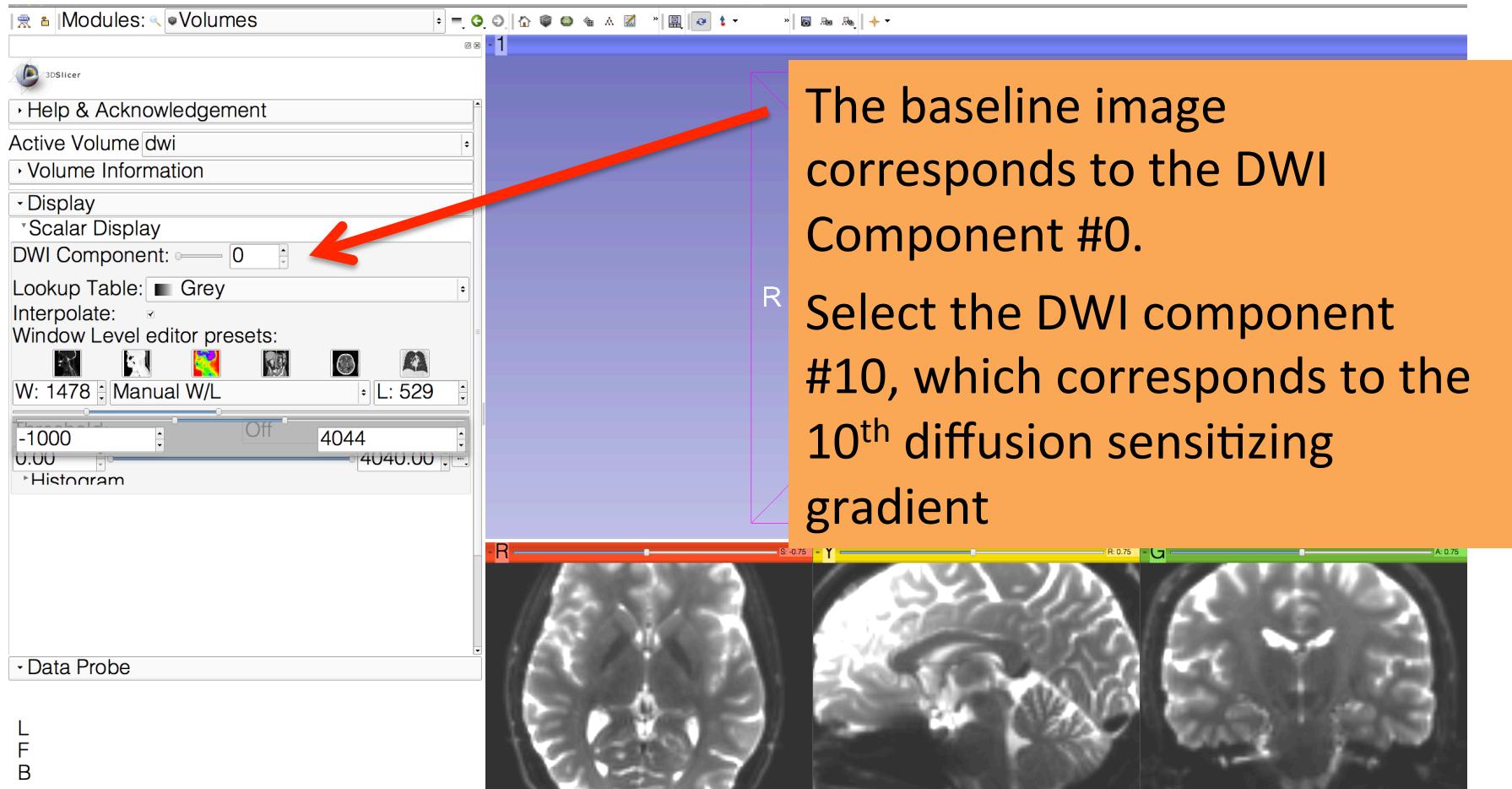
# Loading the DWI dataset



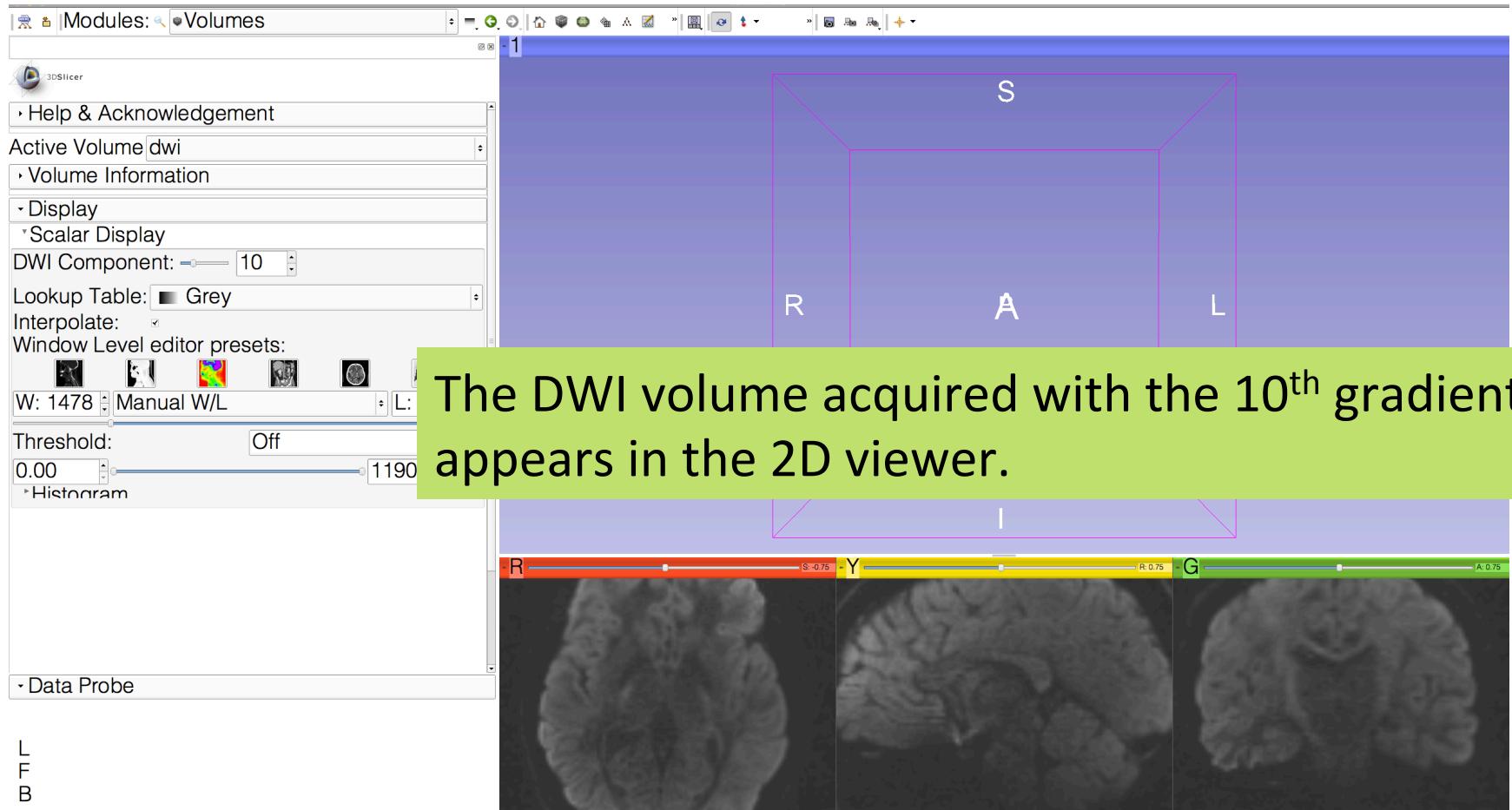
# Adjusting Window and Level



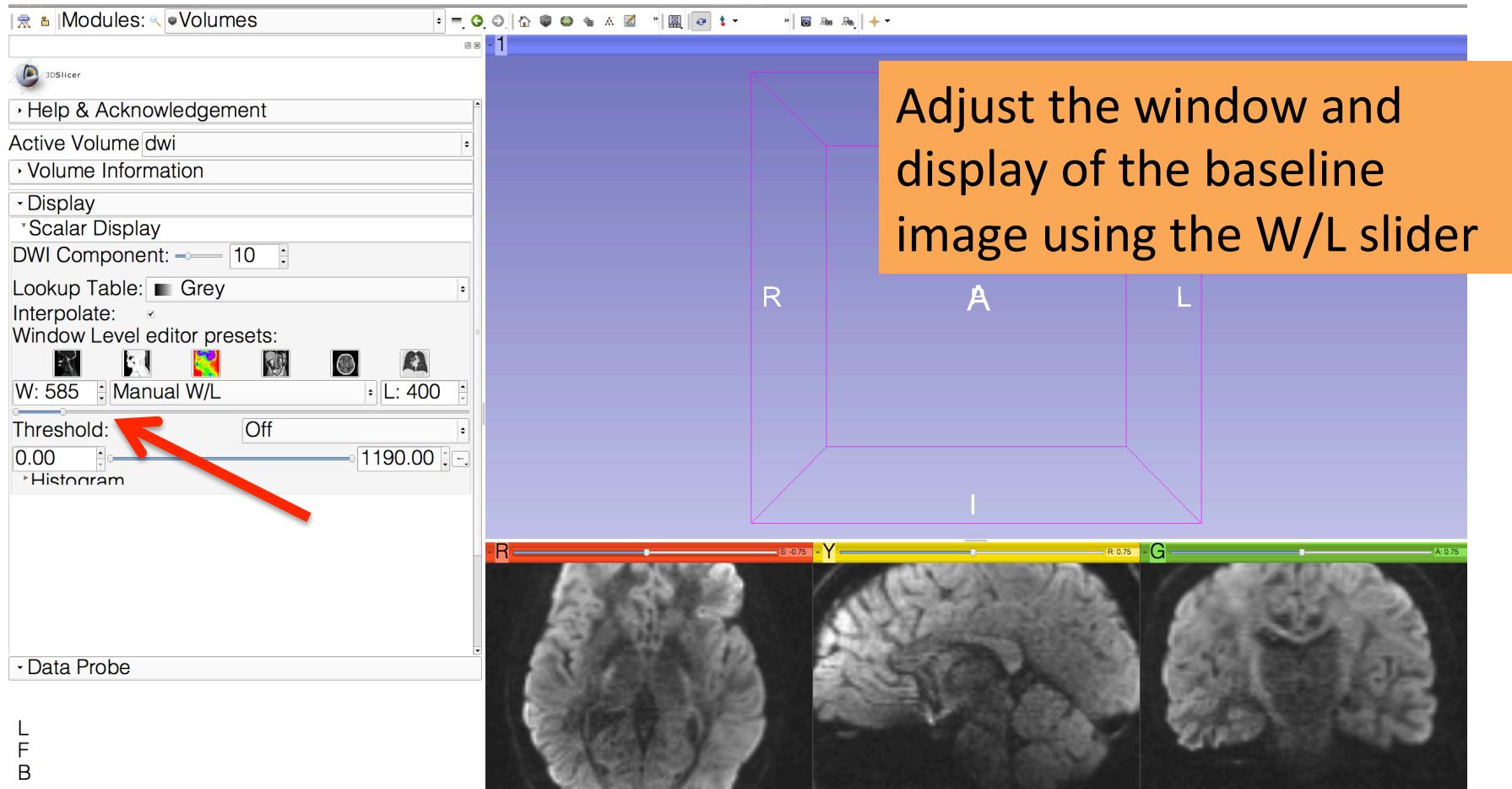
# Exploring the DWI dataset



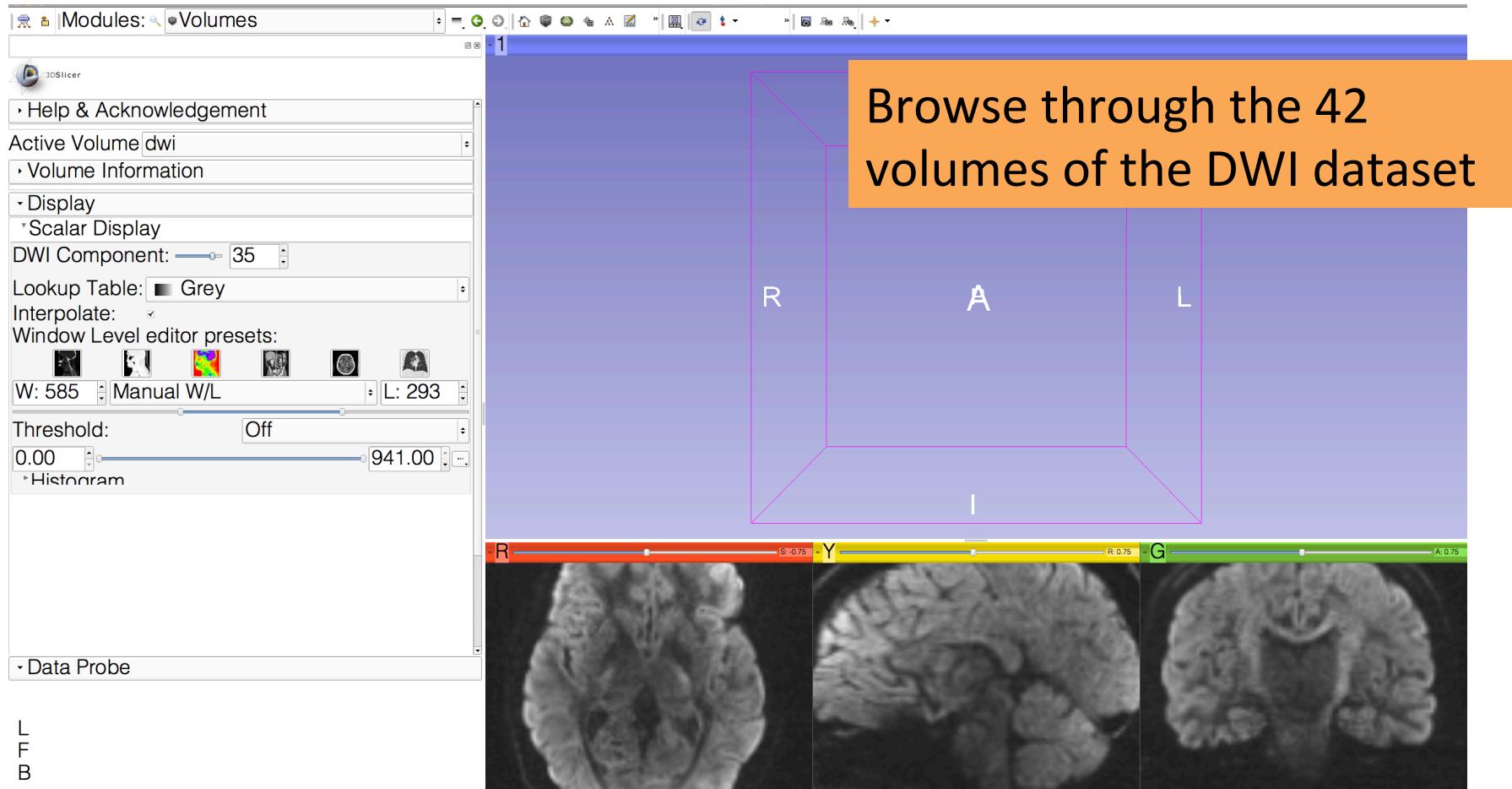
# Exploring the DWI dataset



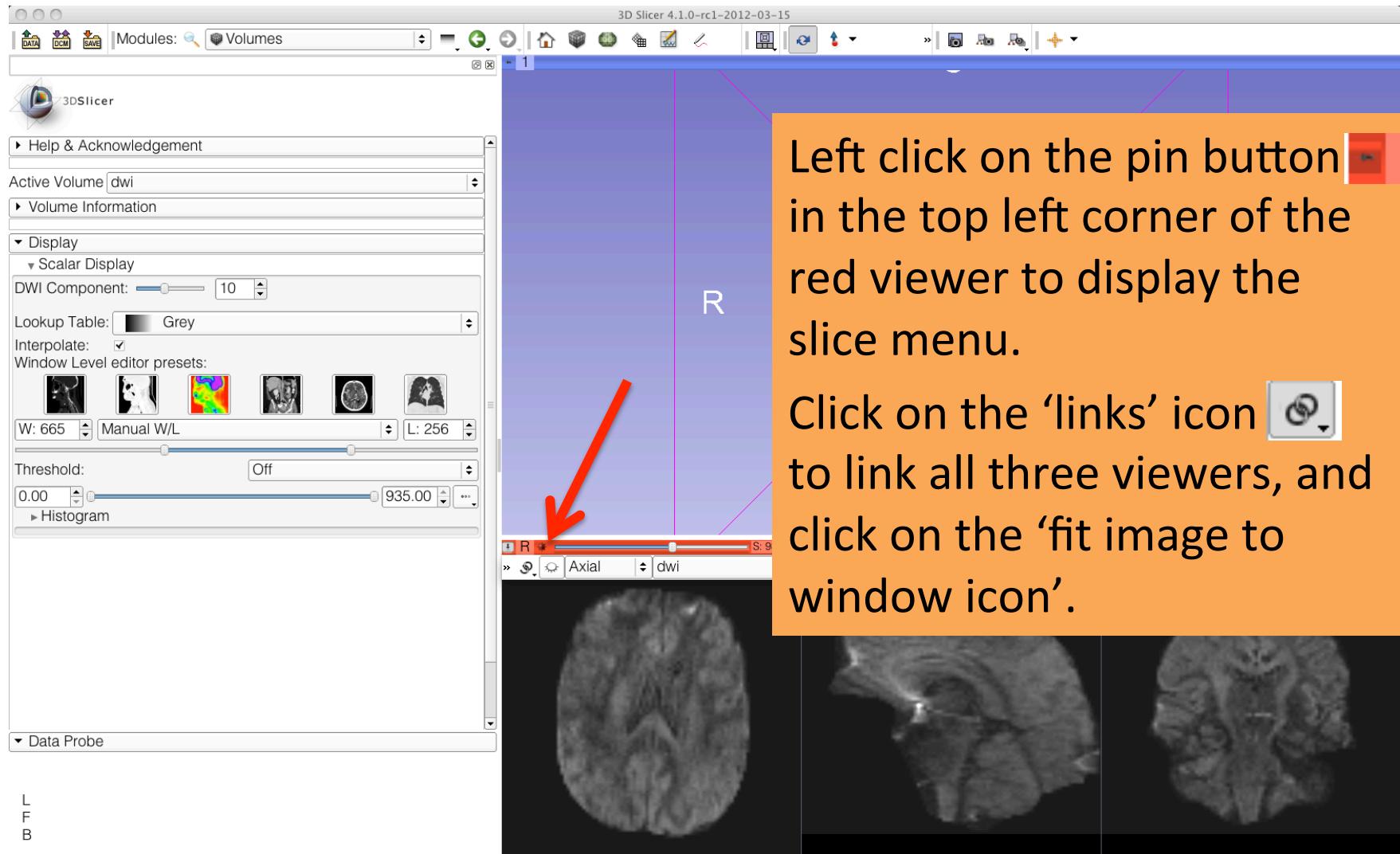
# Exploring the DWI dataset



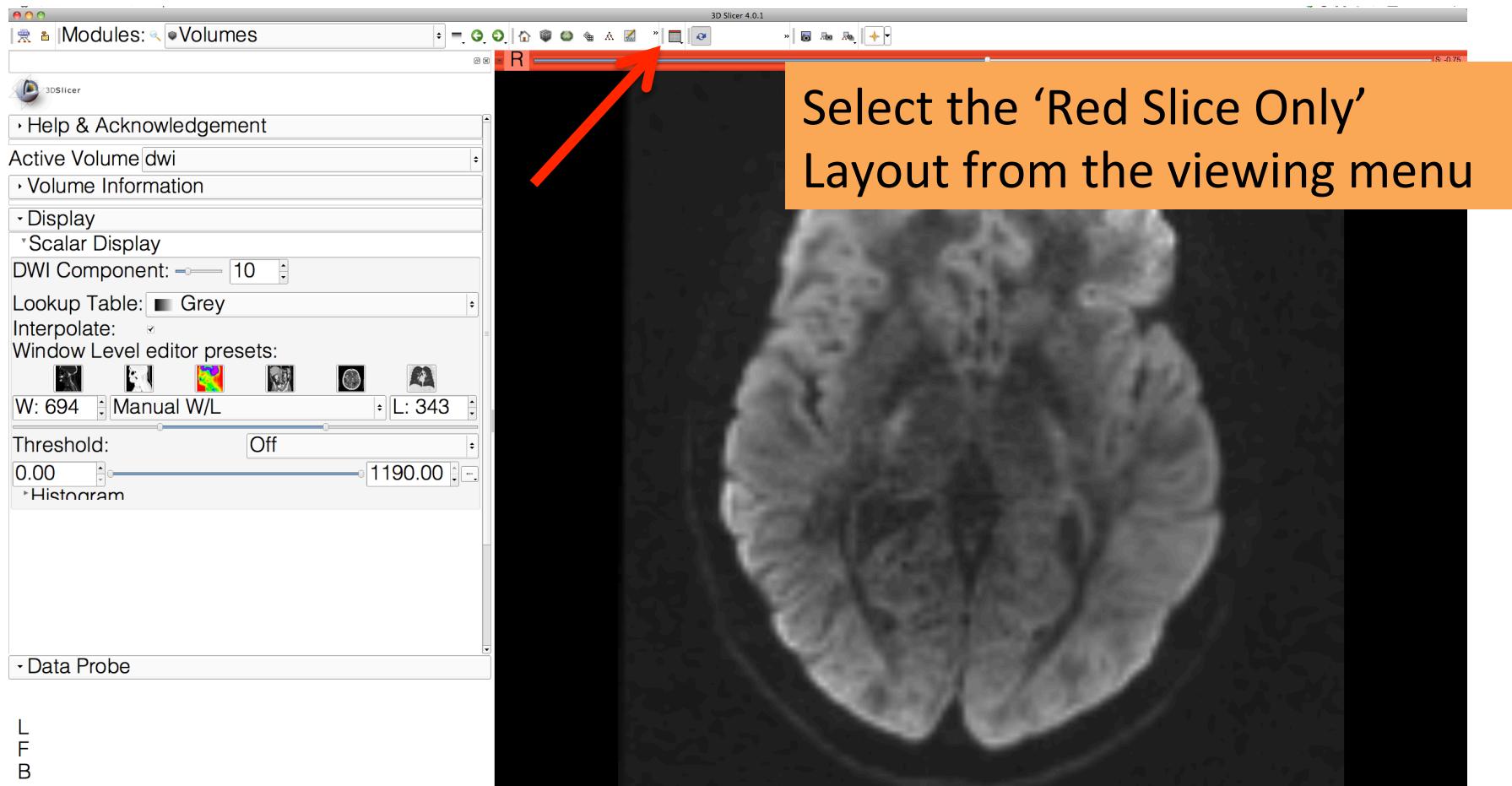
# Exploring the DWI dataset



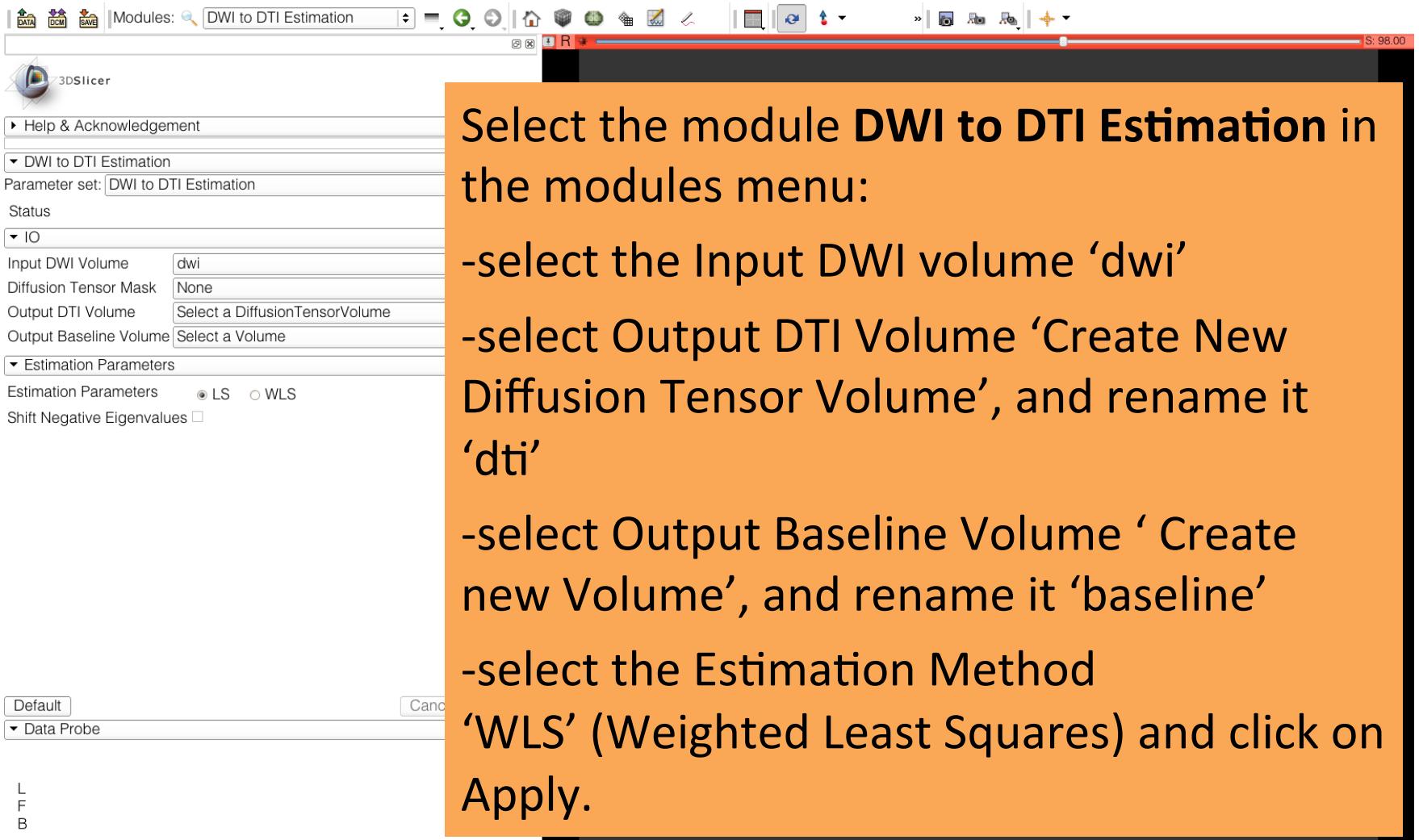
# Exploring the DWI dataset



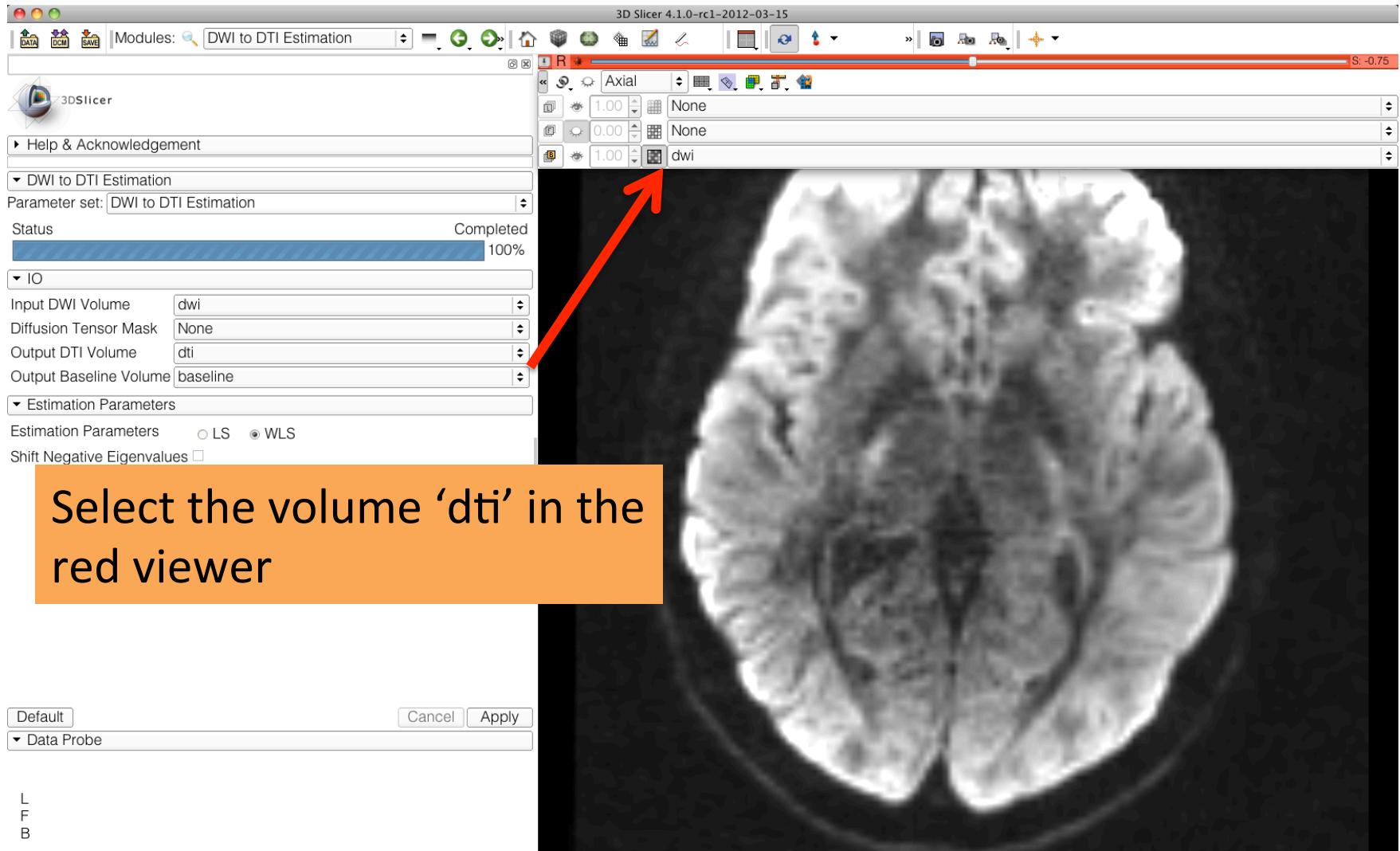
# Exploring the DWI dataset



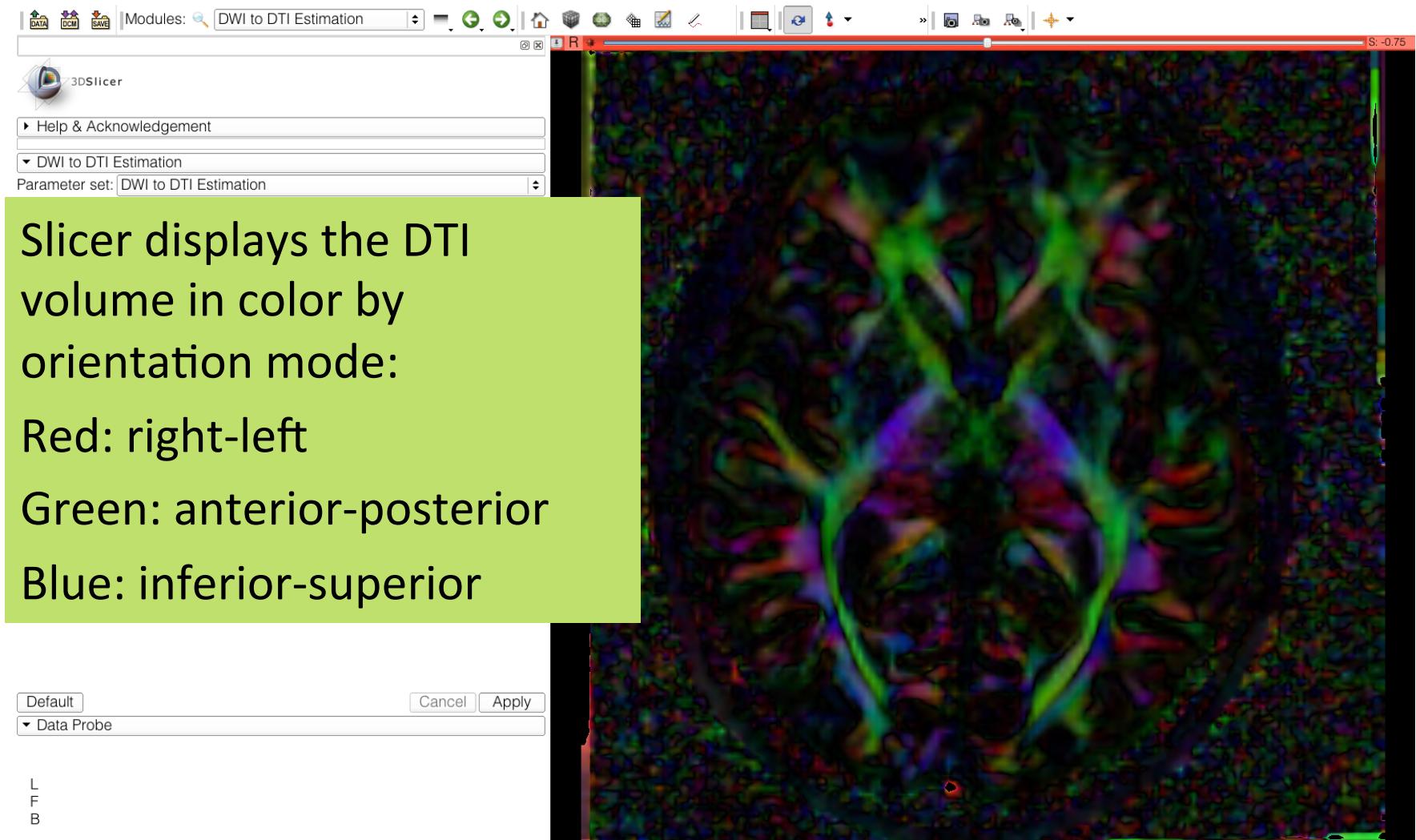
# Diffusion Tensor Estimation



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# Diffusion Tensor Estimation



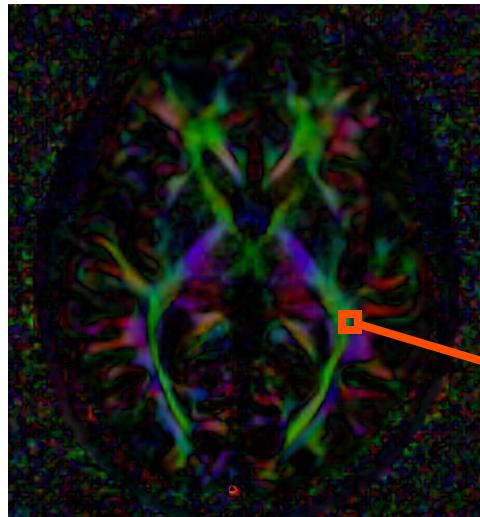
Slicer displays the DTI  
volume in color by  
orientation mode:

Red: right-left

Green: anterior-posterior

Blue: inferior-superior

# Diffusion Tensor Data



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

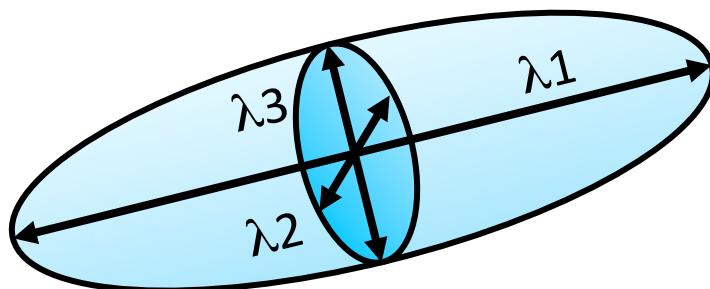
Stejskal-Tanner equation (1965)

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

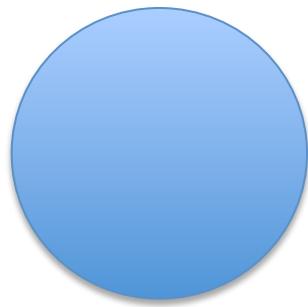
The diffusion tensor  $\underline{\mathbf{D}}$  in the voxel (I,J,K) is a 3x3 symmetric matrix.

# Diffusion Tensor

- The diffusion tensor  $D$  in the voxel (I,J,K) can be visualized as an ellipsoid, with the eigenvectors indicating the directions of the principal axes, and the square root of the eigenvalues defining the ellipsoidal radii.
- Scalar maps can be derived from the rotationally invariant eigenvalues  $\lambda_1$ ,  $\lambda_2$ ,  $\lambda_3$  to characterize the size and shape of the diffusion tensor.

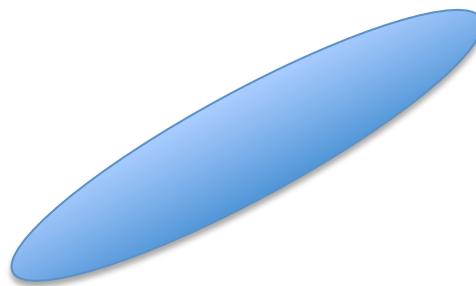


# Diffusion Tensor Shape



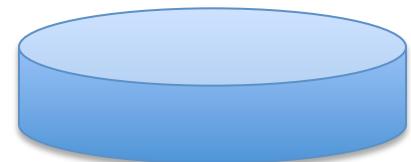
$$\lambda_1 = \lambda_2 = \lambda_3$$

Isotropic media  
(CSF, gray matter)



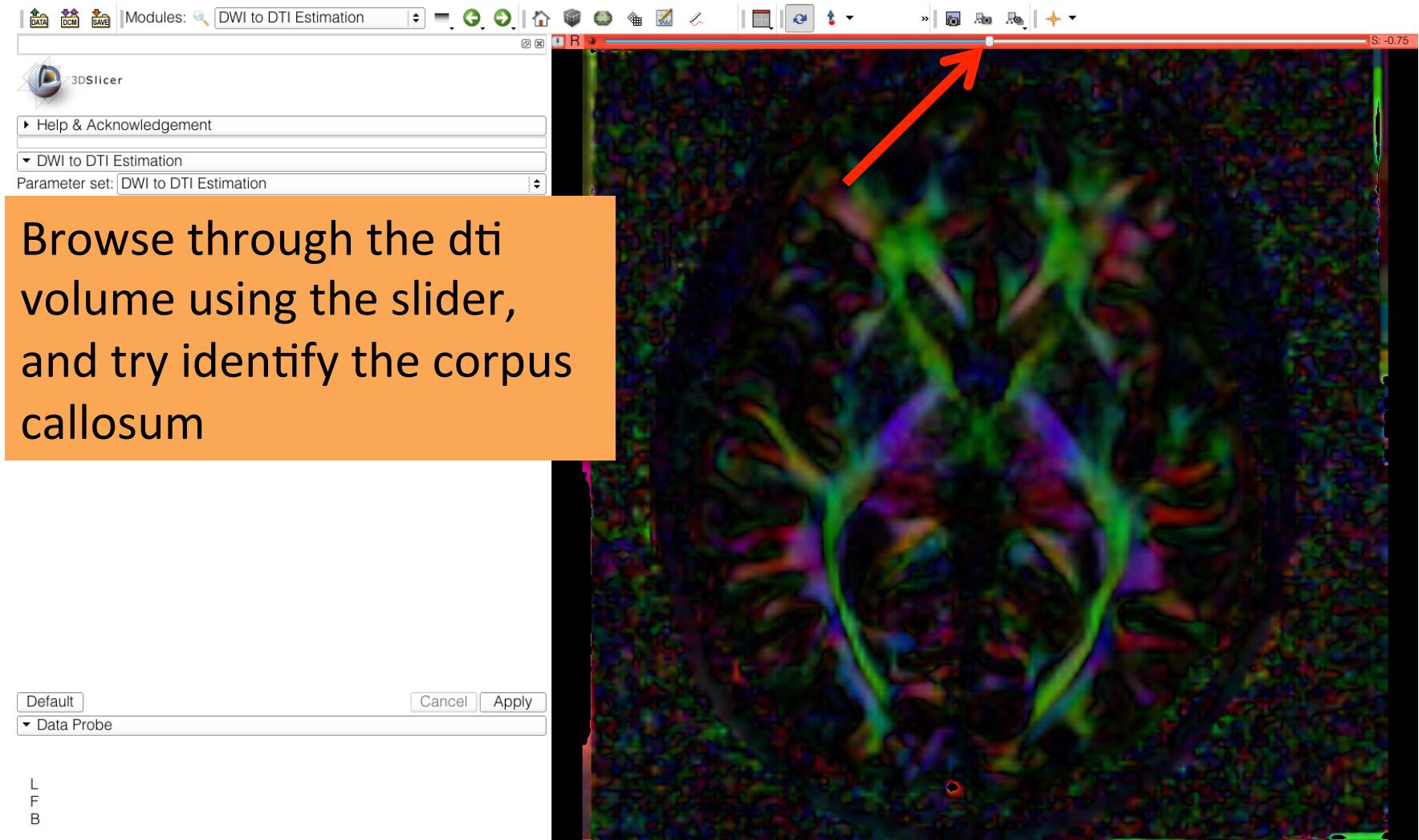
$$\lambda_1 >> \lambda_2, \lambda_3$$

Anisotropic media  
(white matter)



$$\lambda_1 \sim \lambda_2 >> \lambda_3$$

# Exploring the Diffusion Tensor Data



# Corpus Callosum

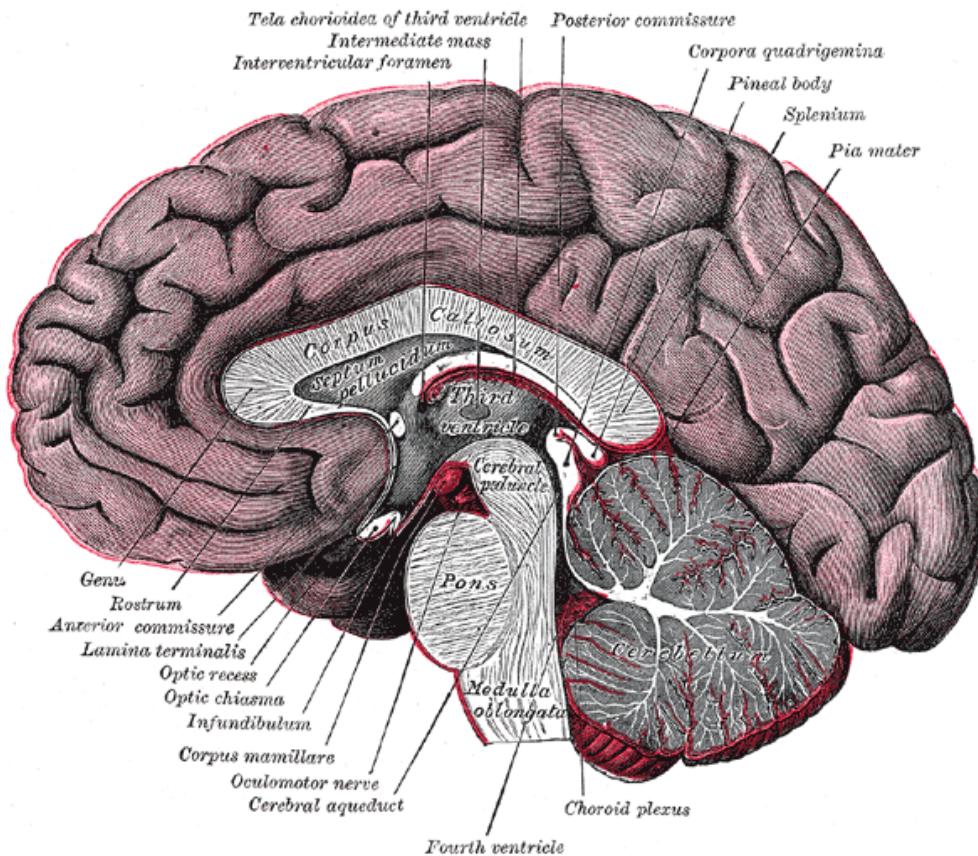
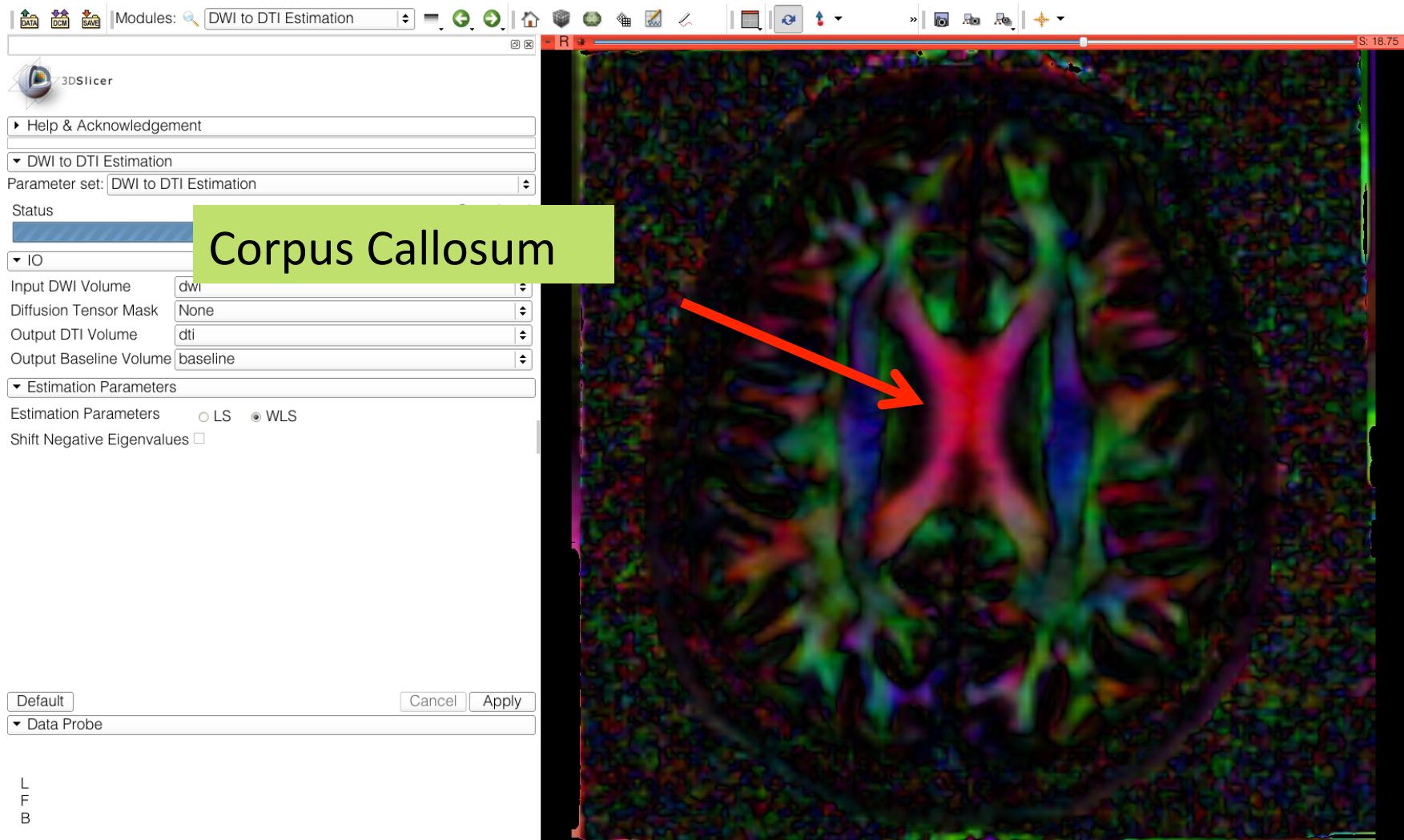


Image from Gray's Anatomy

Diffusion MRI Analysis – Sonia Pujol, Ph.D.  
NA-MIC ARR 2012

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

# Exploring the Diffusion Tensor Data

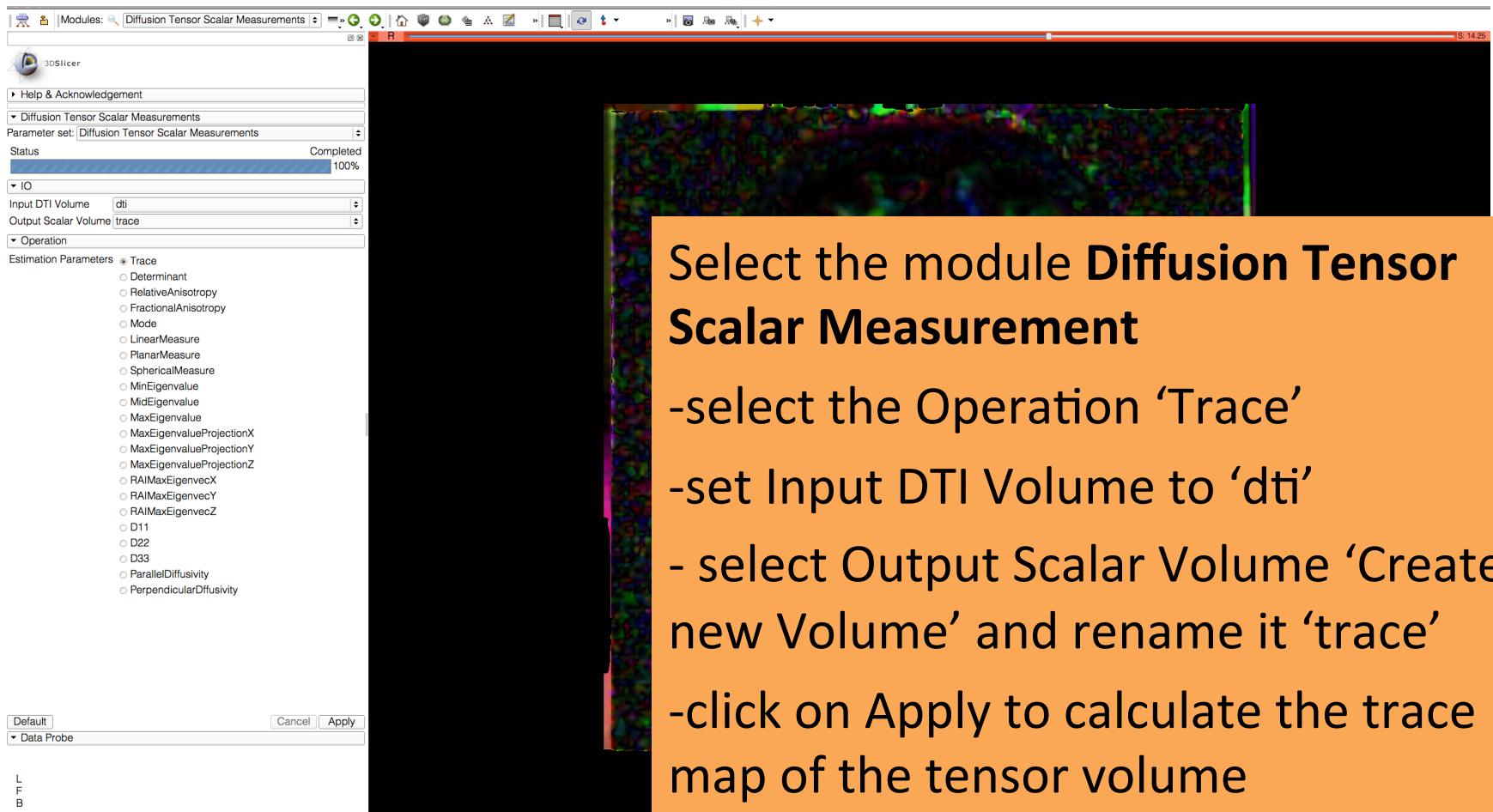


# Characterizing the Size of the tensor: Trace

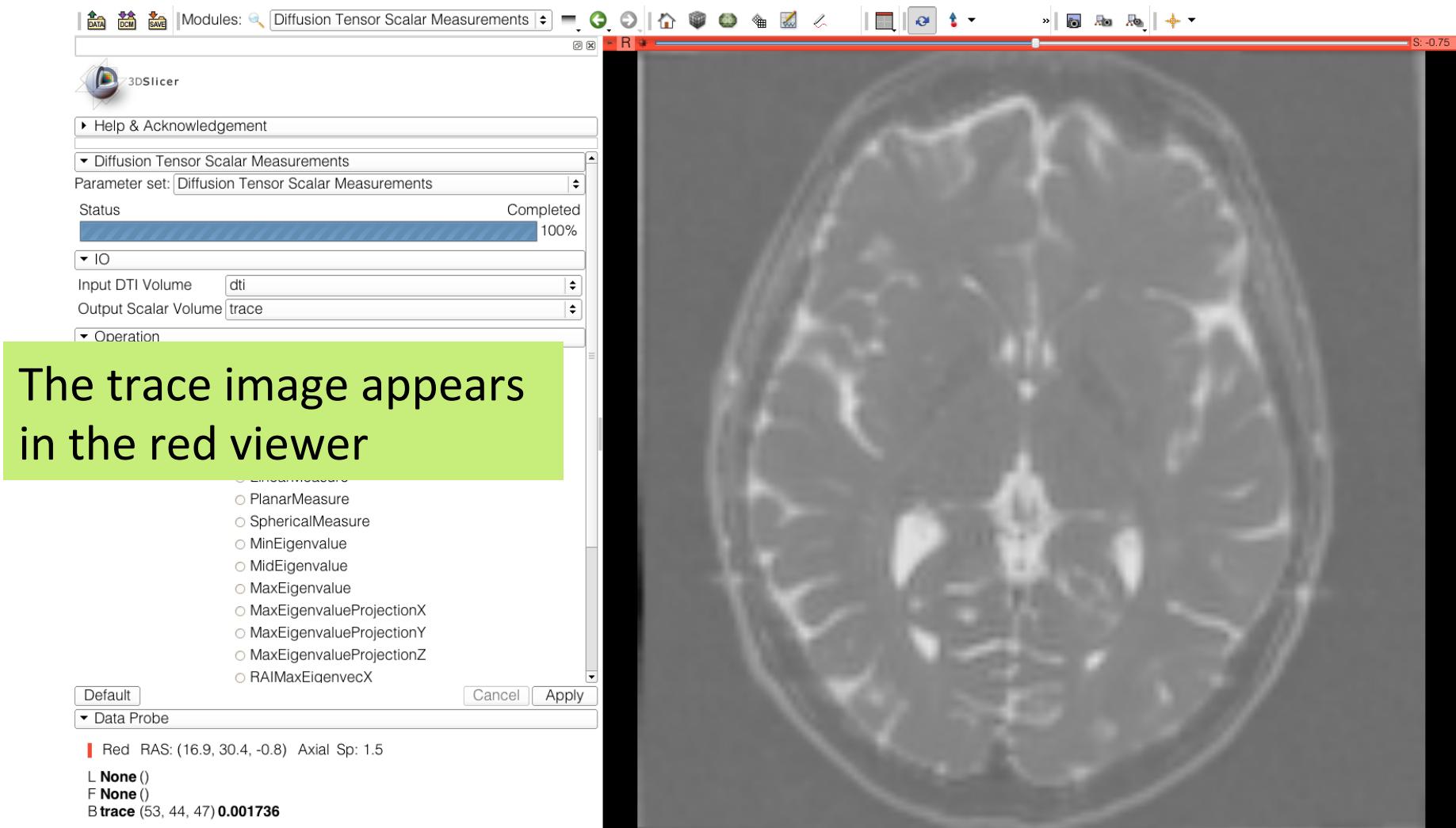
$$\text{Trace}(D) = \lambda_1 + \lambda_2 + \lambda_3$$

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

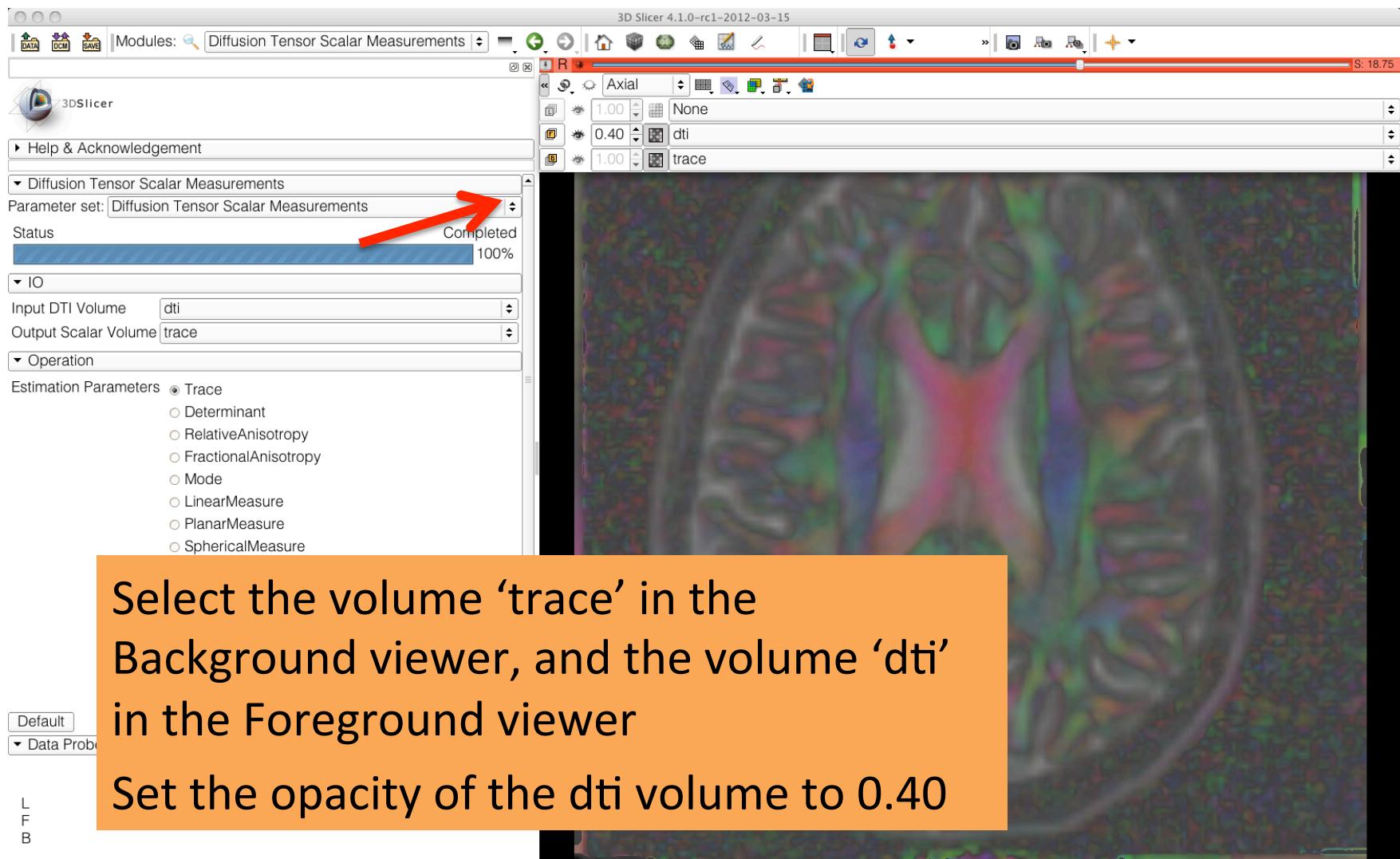
# Characterizing the Size of the tensor: Trace



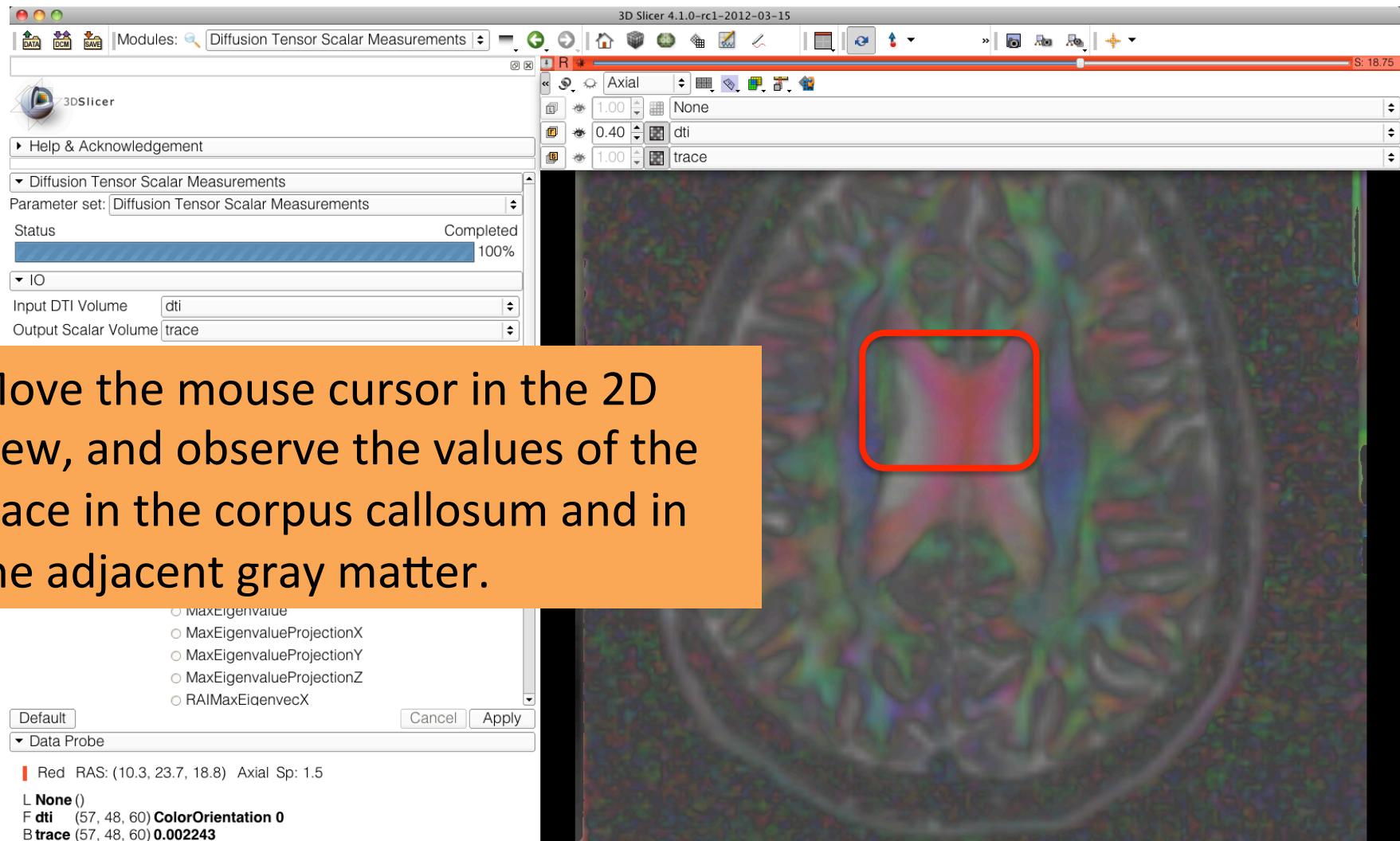
# Trace



# Trace

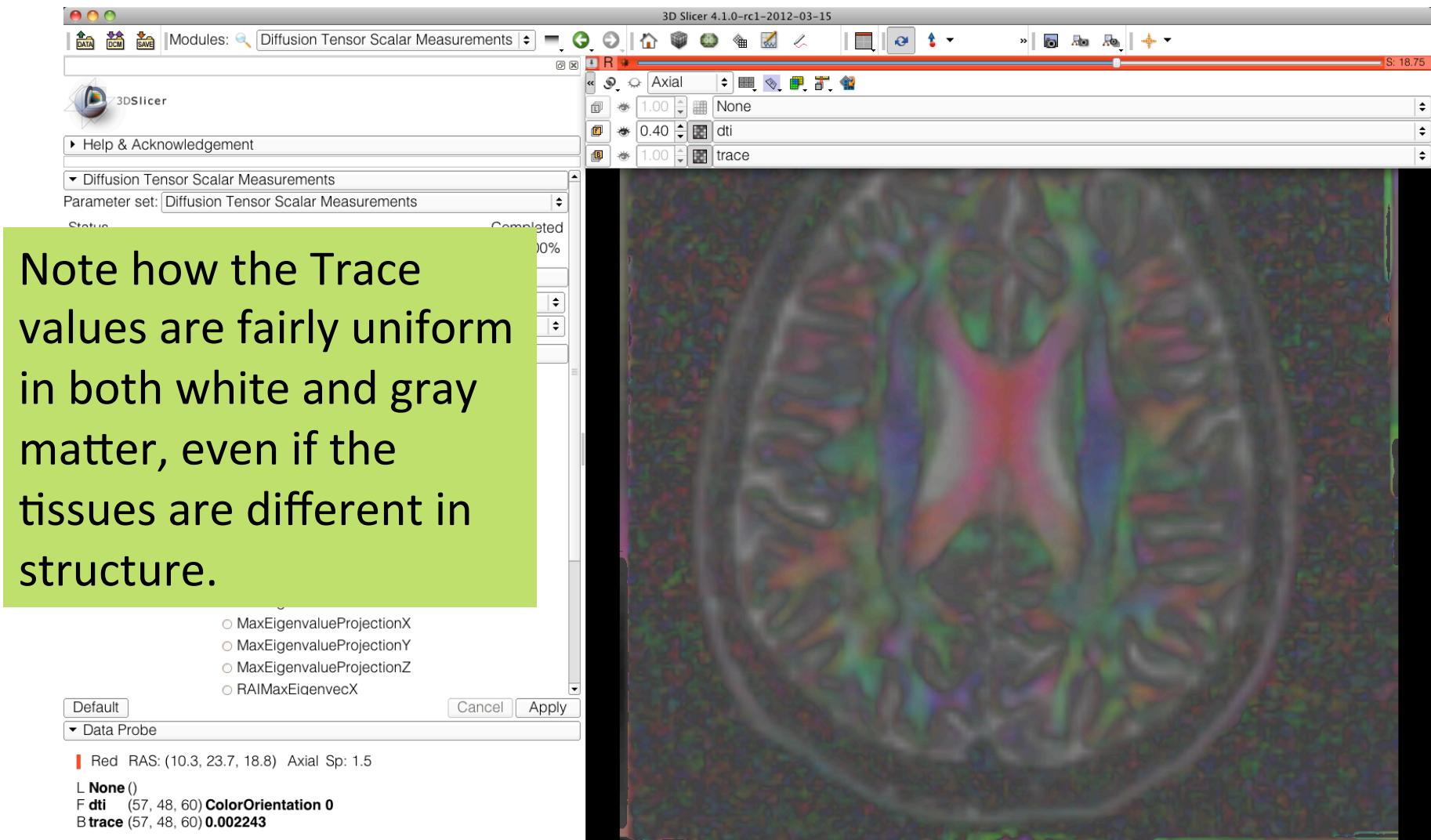


# Trace



Move the mouse cursor in the 2D view, and observe the values of the trace in the corpus callosum and in the adjacent gray matter.

# Trace

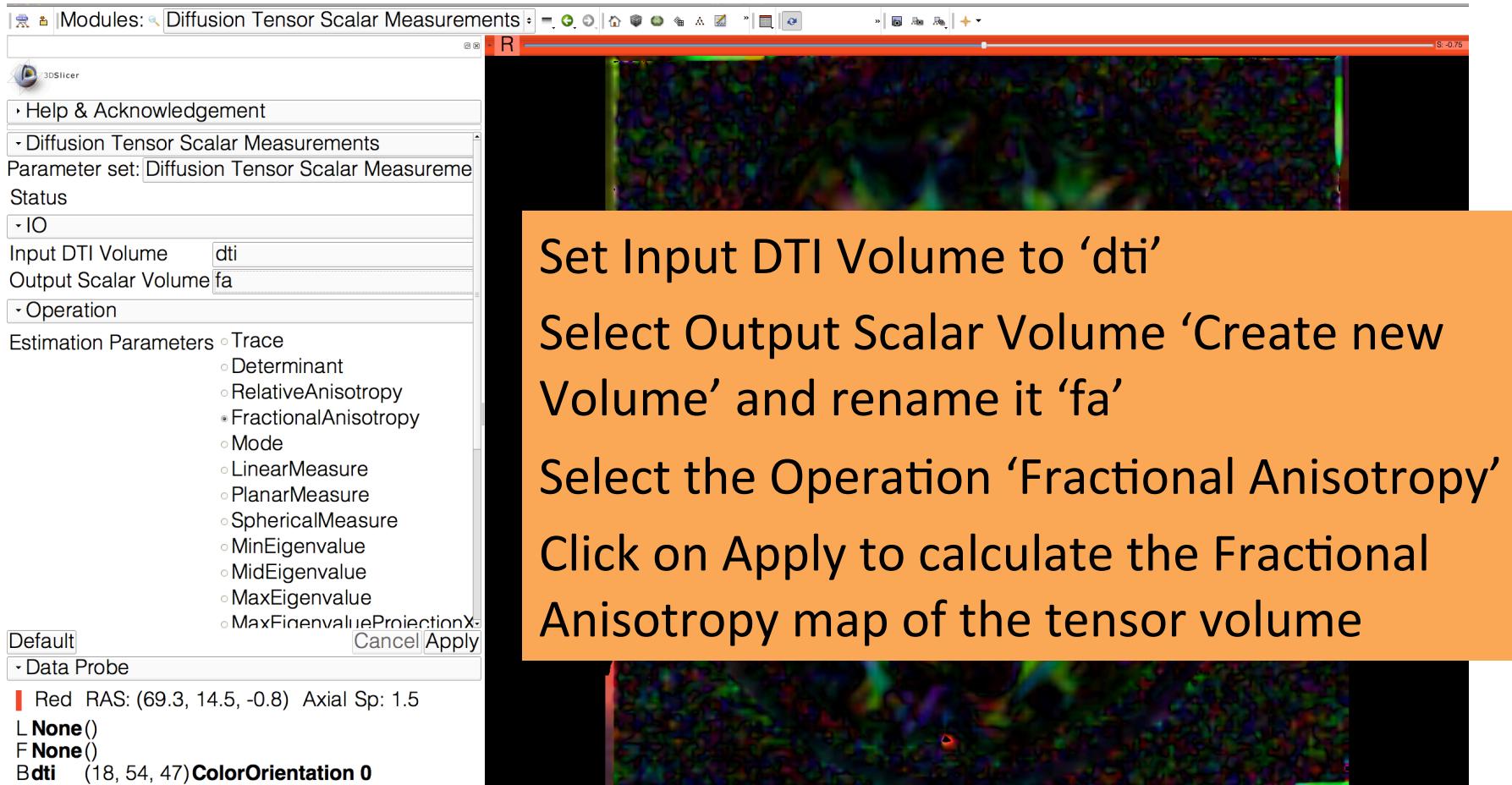


# Scalar Maps: Fractional Anisotropy

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

- 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: 

# Characterizing the Shape of the tensor: Fractional Anisotropy



Set Input DTI Volume to 'dti'

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

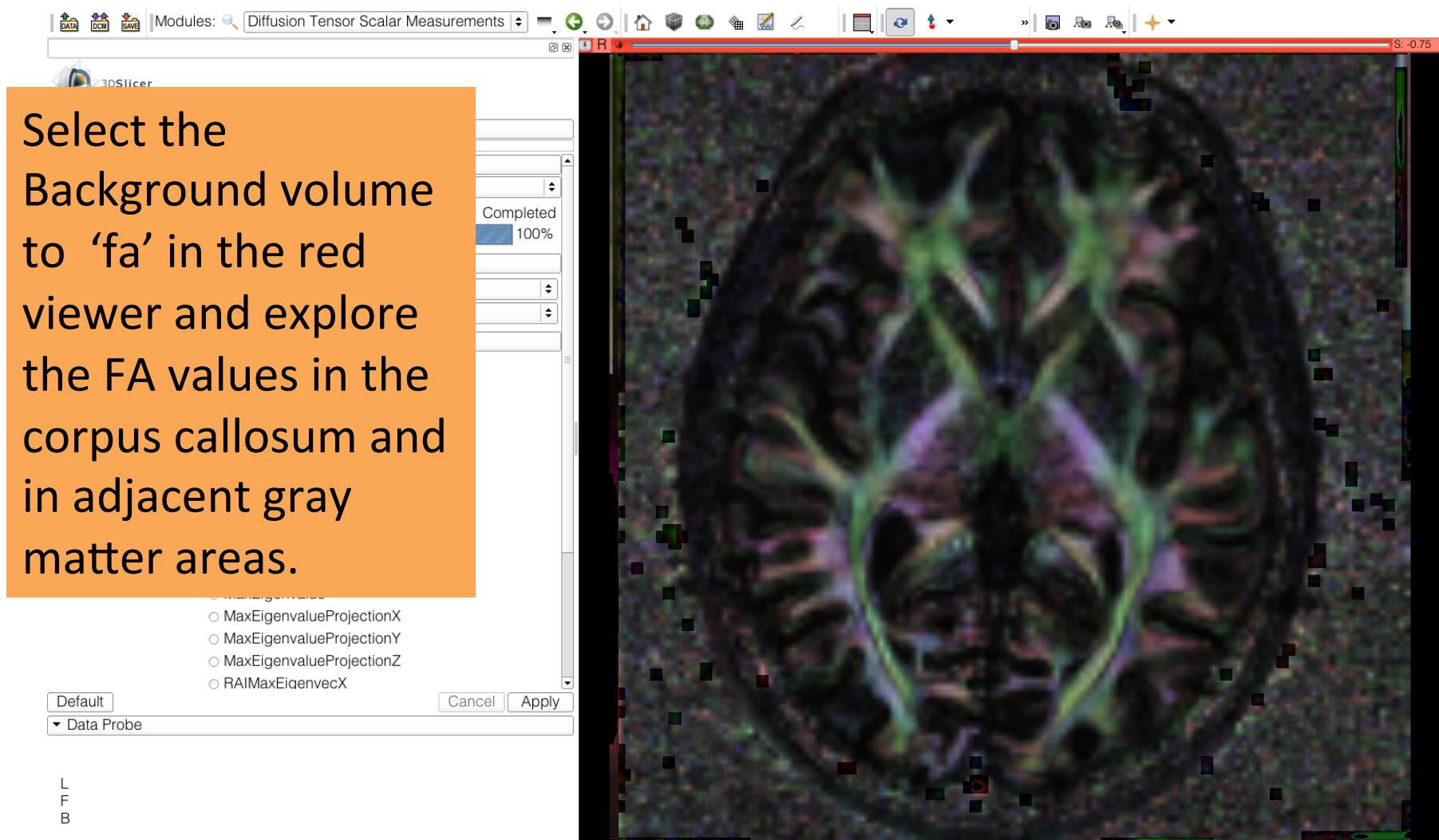
Select the Operation 'Fractional Anisotropy'

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

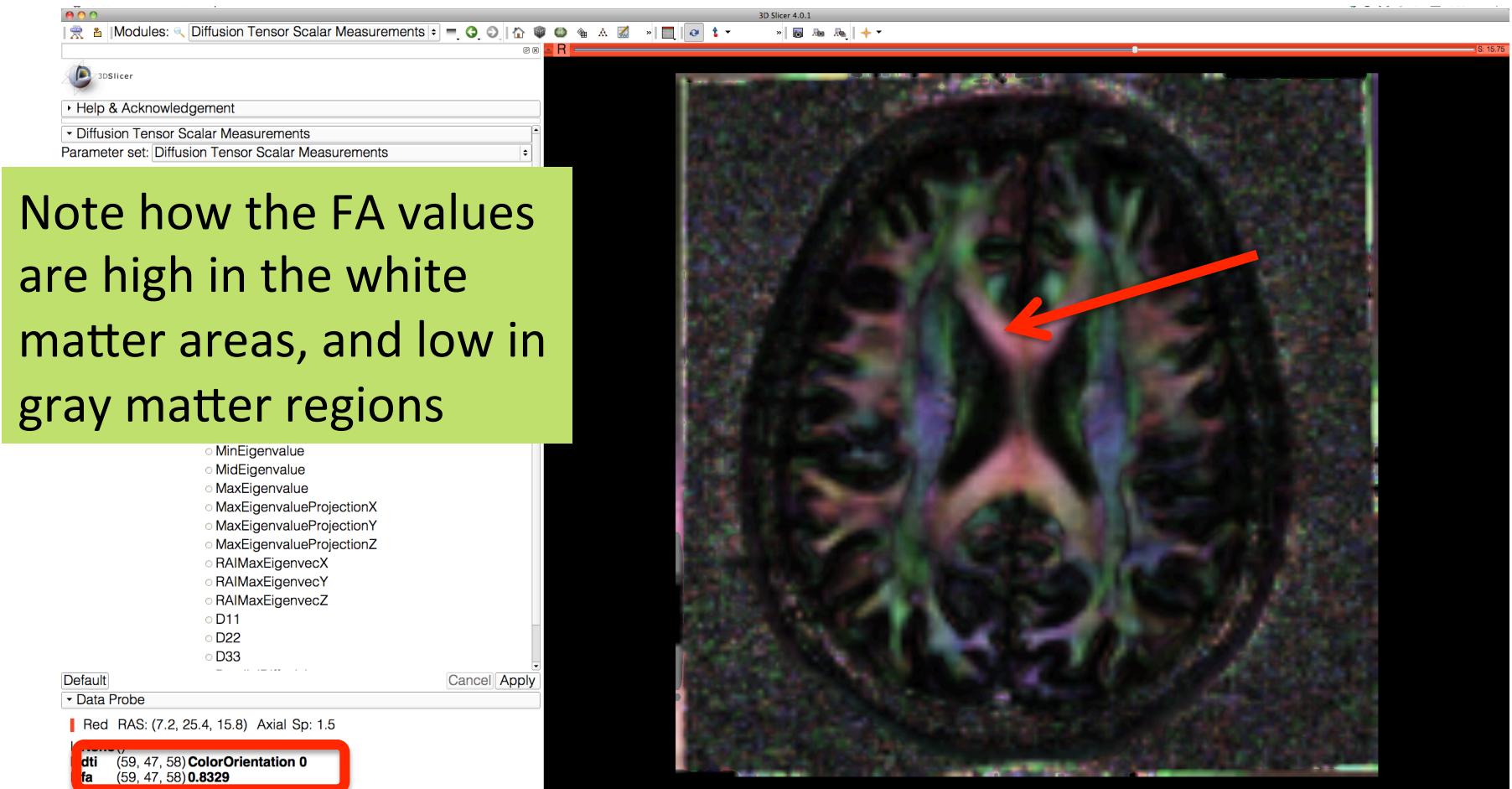
Red RAS: (69.3, 14.5, -0.8) Axial Sp: 1.5

L **None()**  
F **None()**  
**dti** (18, 54, 47) **ColorOrientation 0**

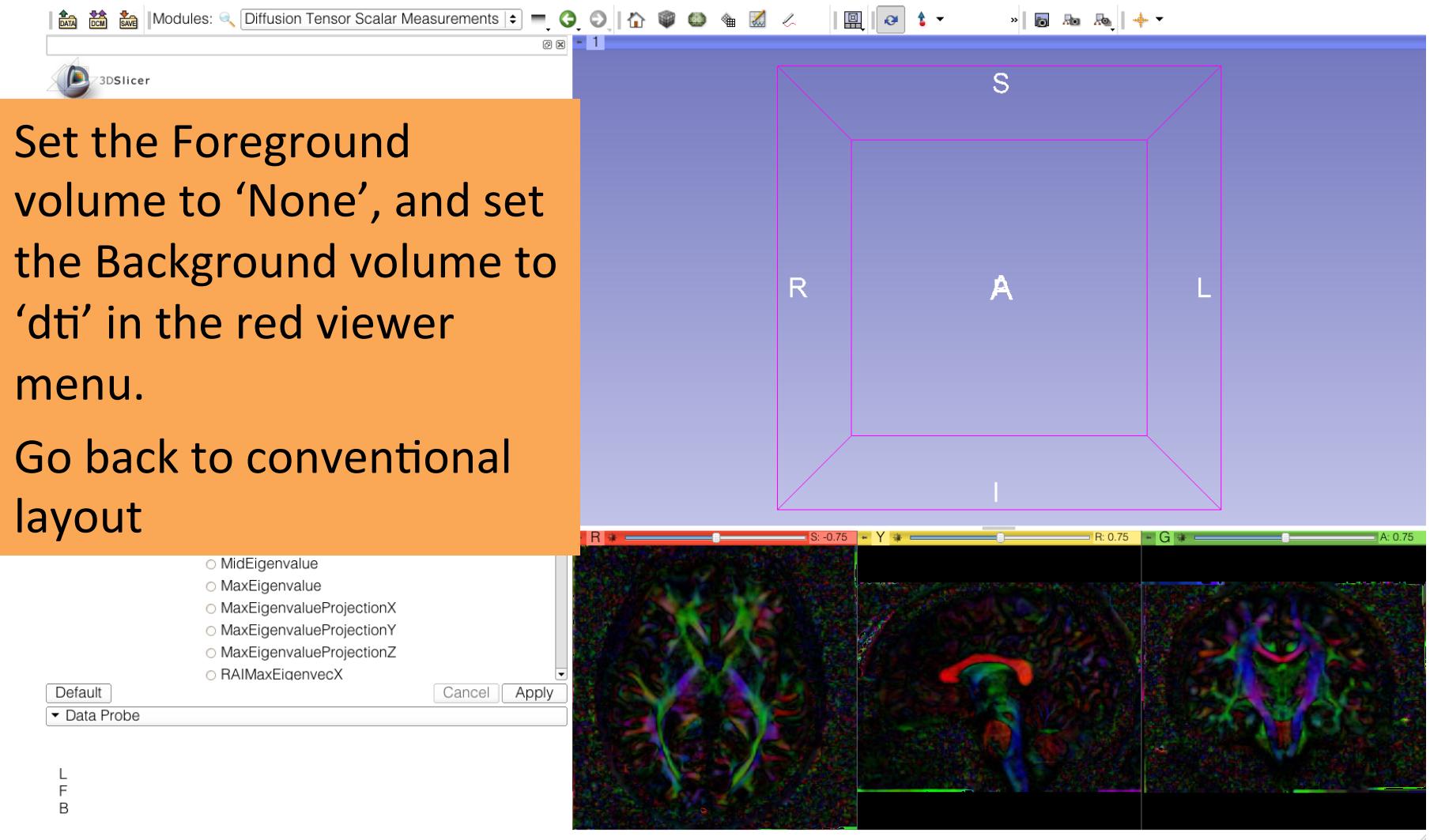
# Fractional Anisotropy

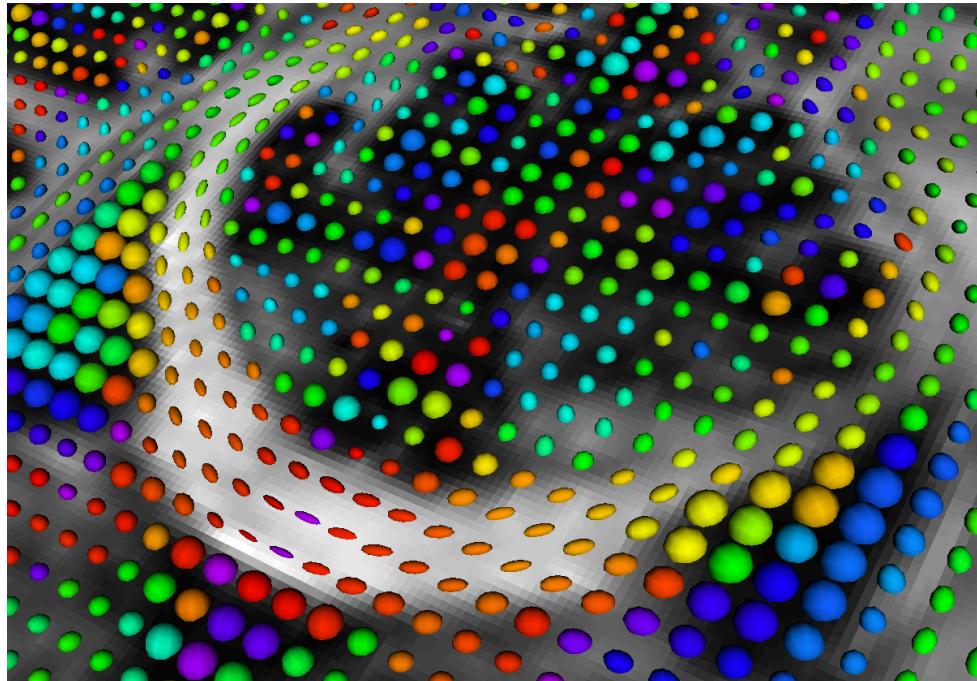


# Fractional Anisotropy



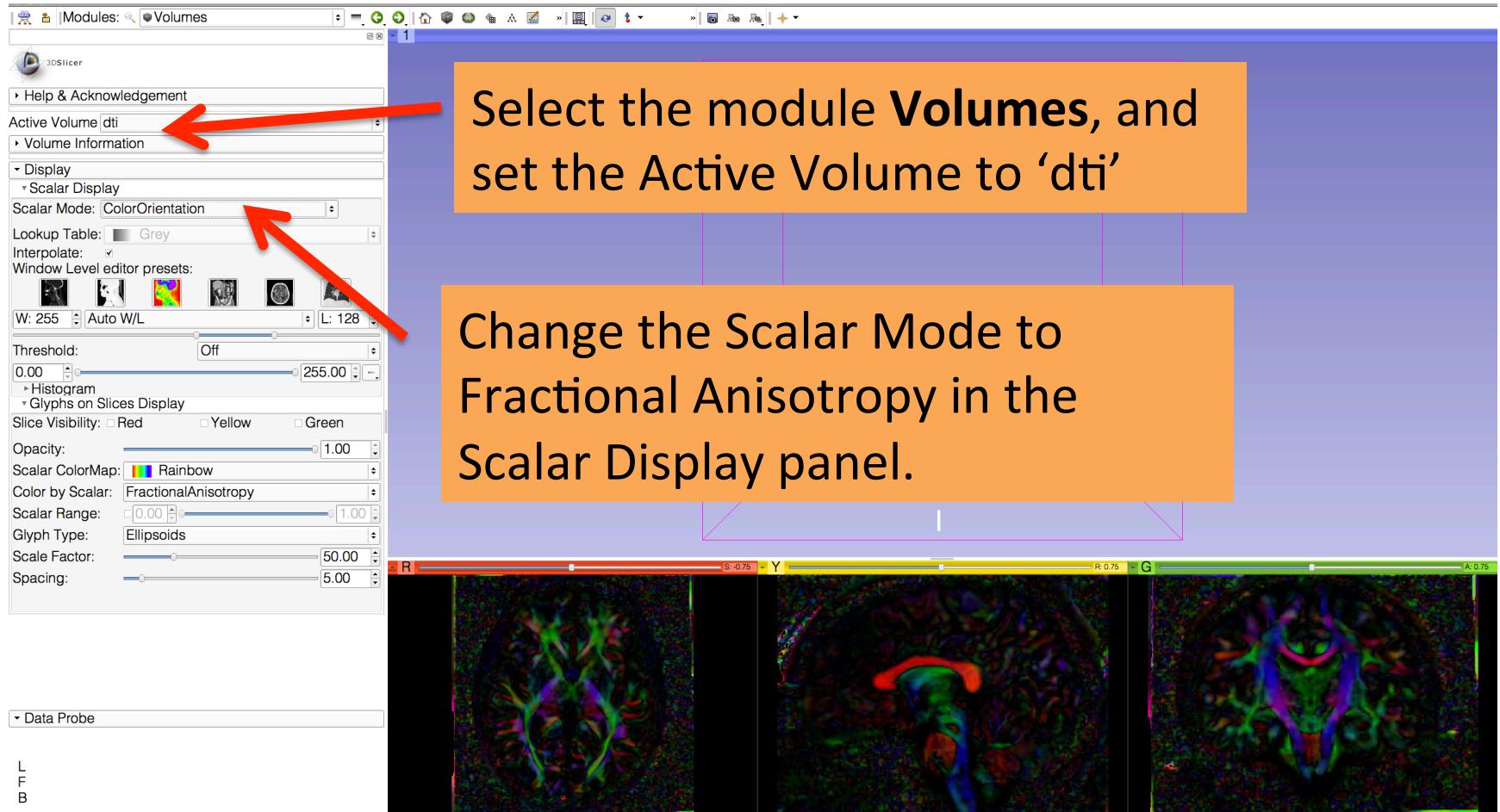
# Fractional Anisotropy



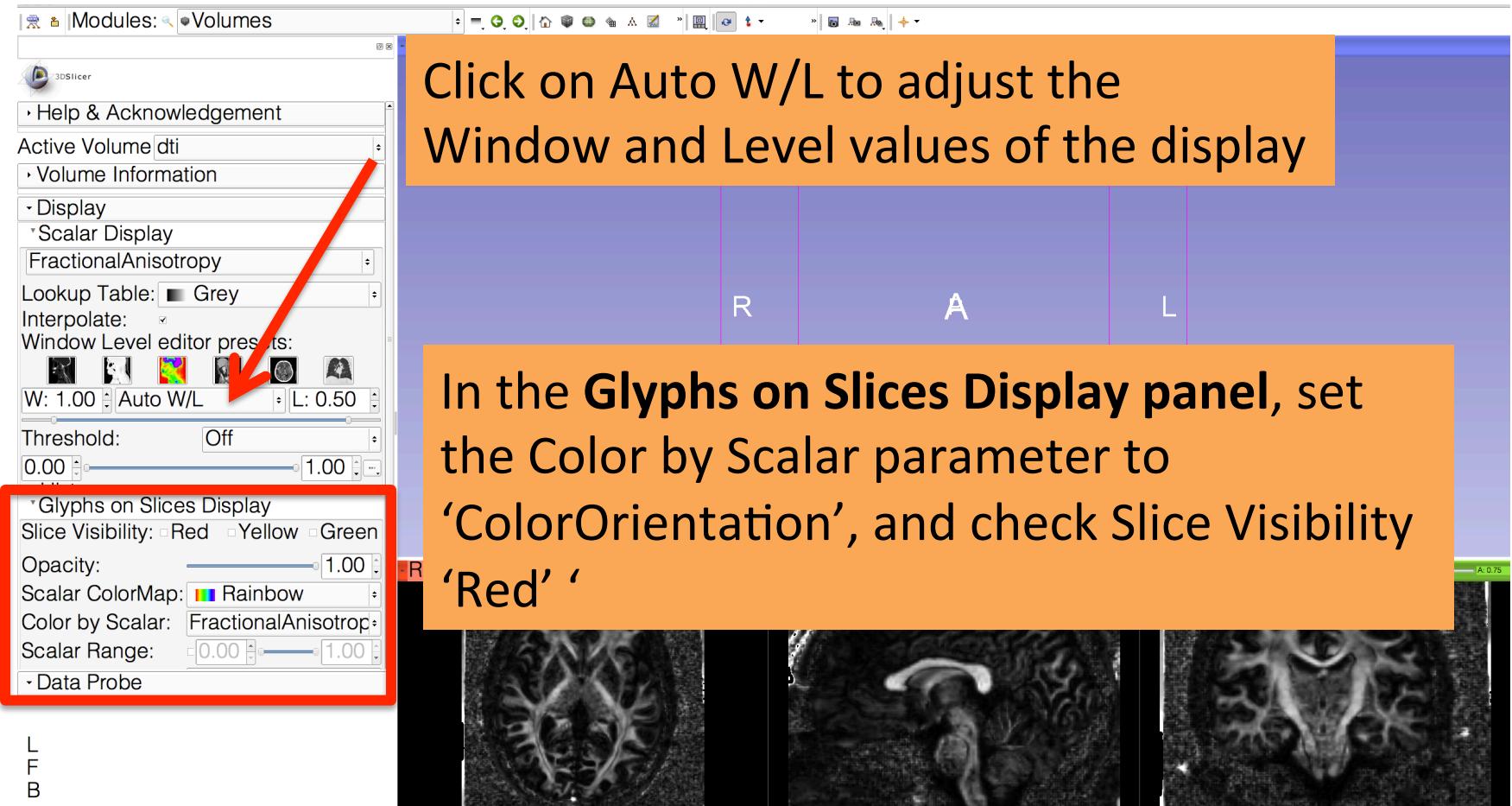


## Part 2: Visualizing the tensor data

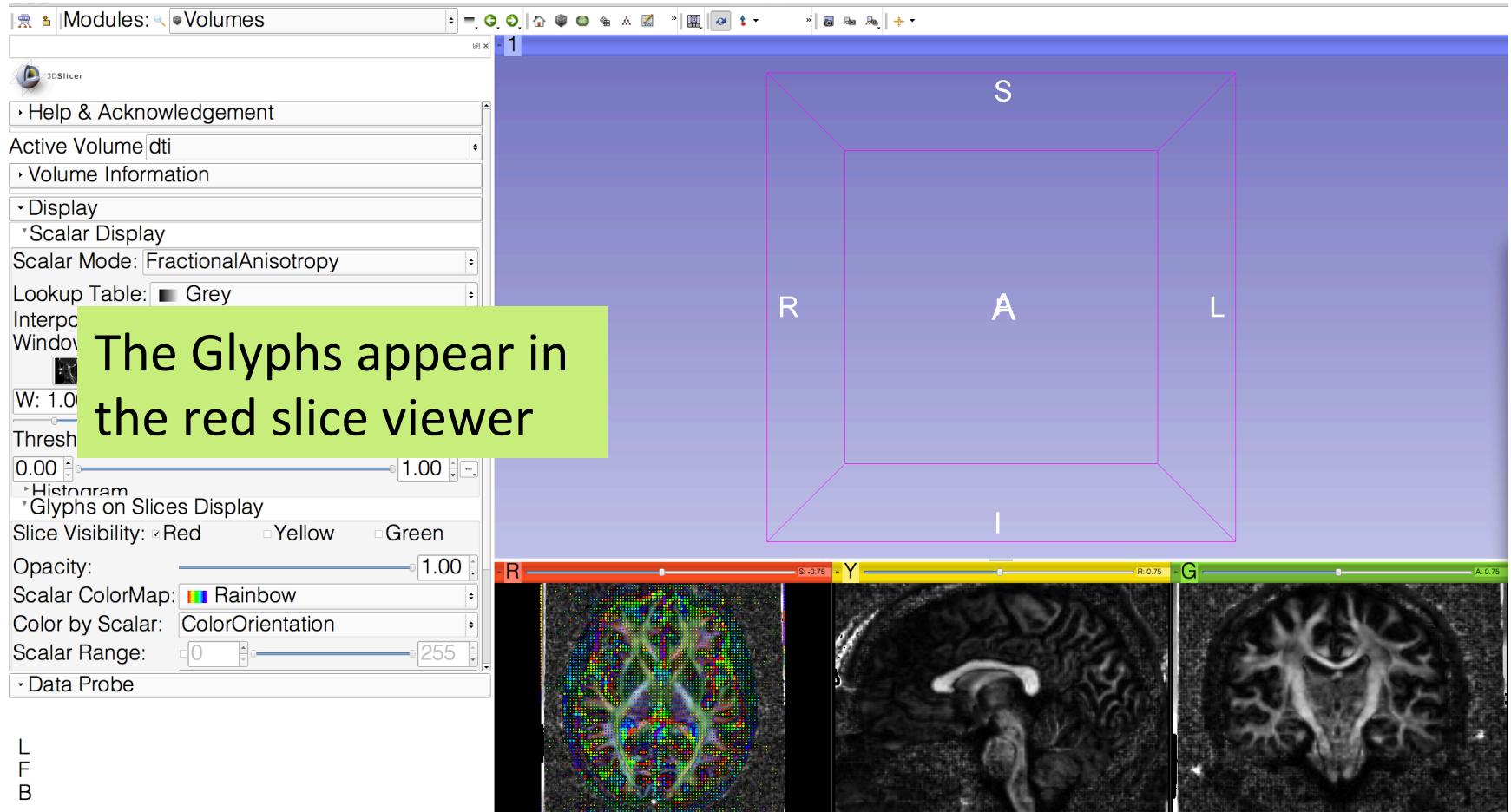
# 3D Visualization: Glyphs



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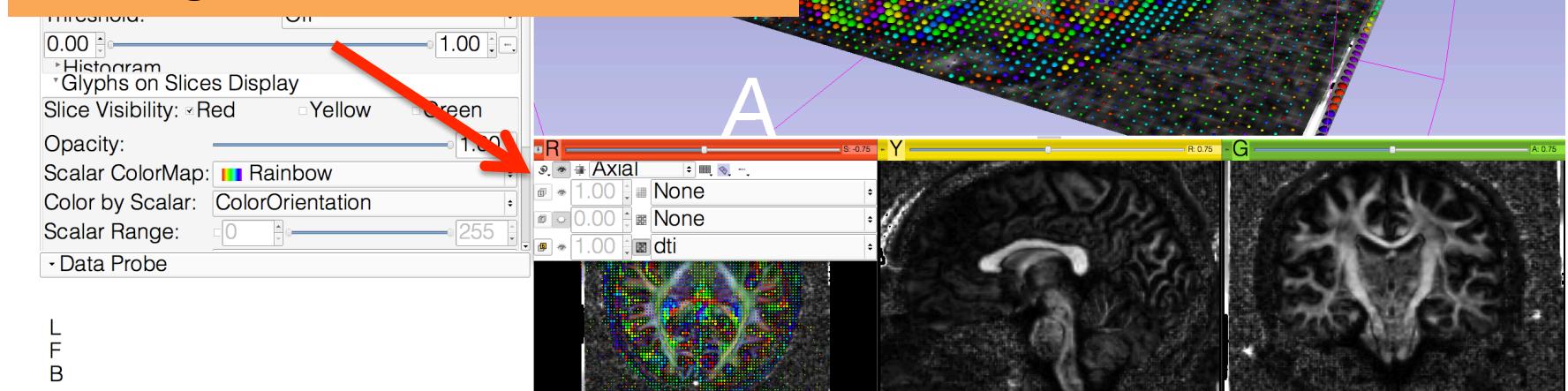
# 3D Visualization: Glyphs



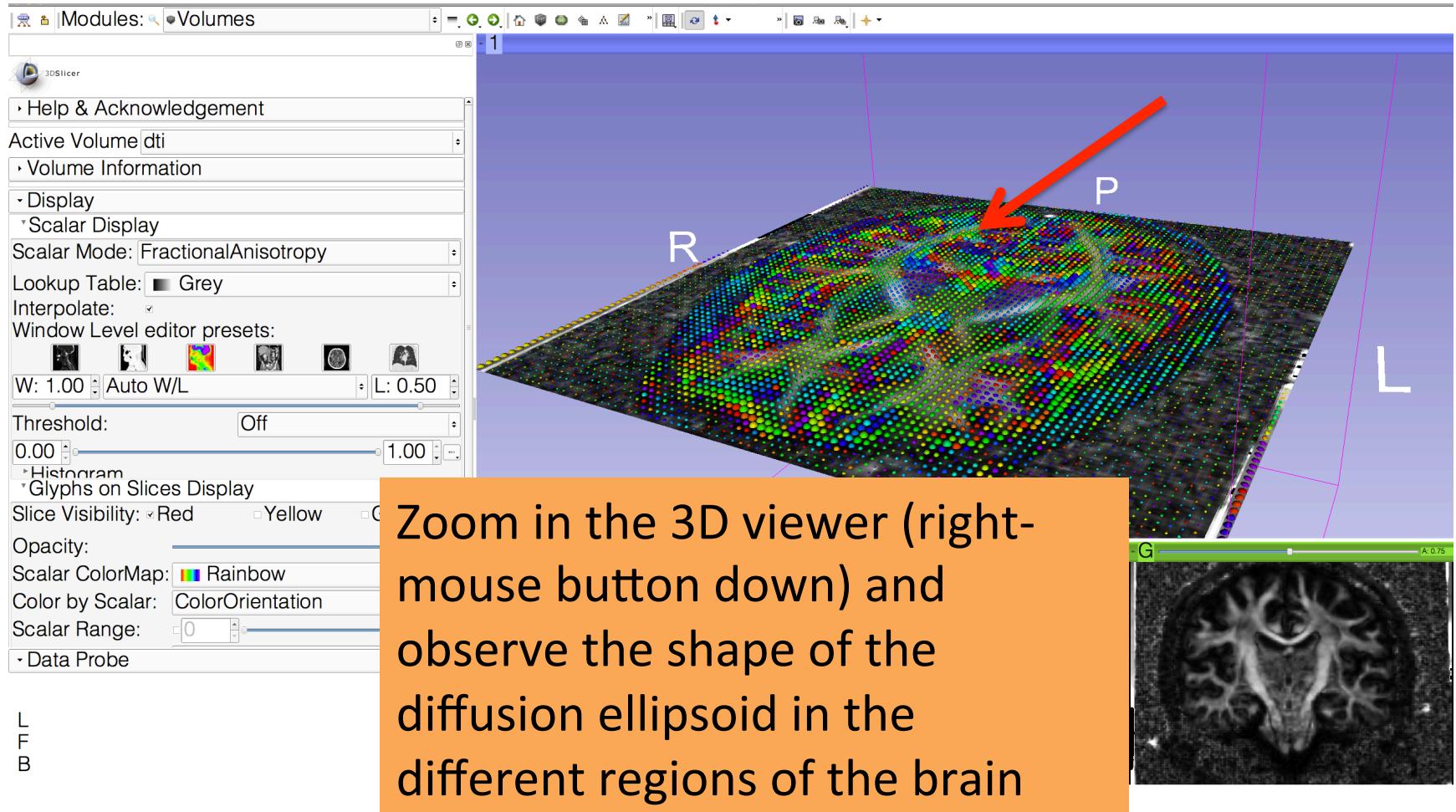
# 3D Visualization: Glyphs

Click on the link icon in the red slice viewer to unlink the three viewers.

Click on the eye icon to display the glyphs superimposed on the FA image in the 3D Viewer

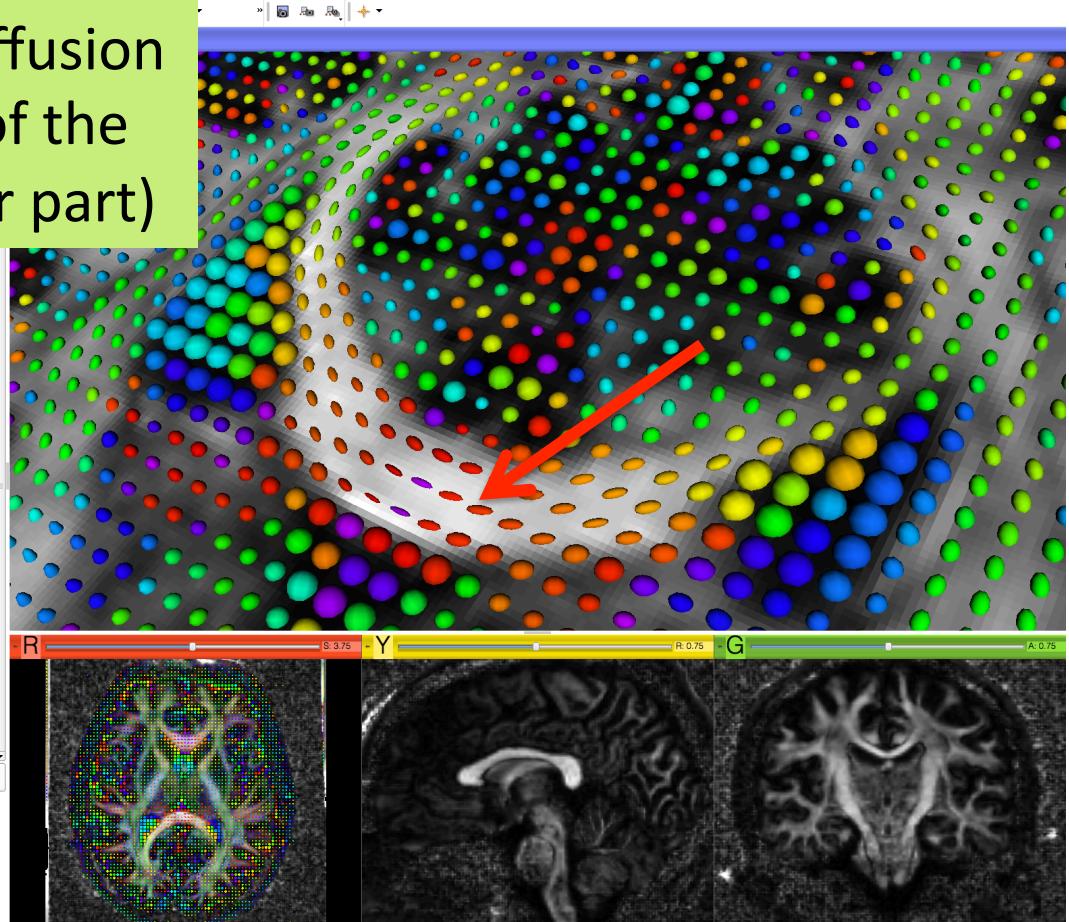
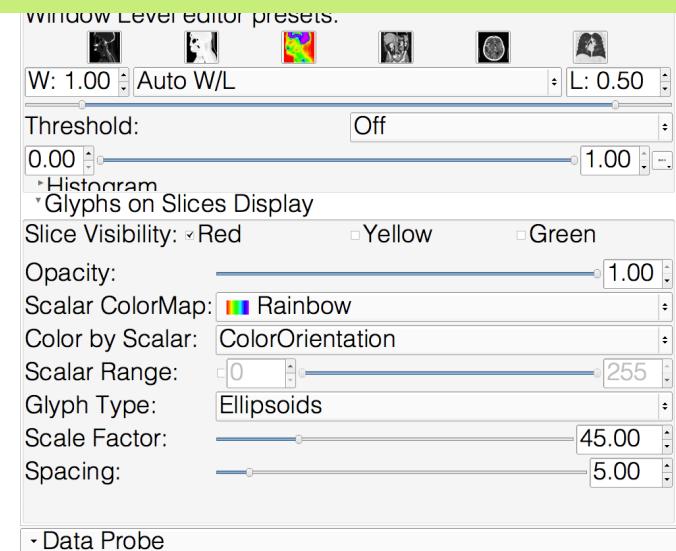


# 3D Visualization: Glyphs



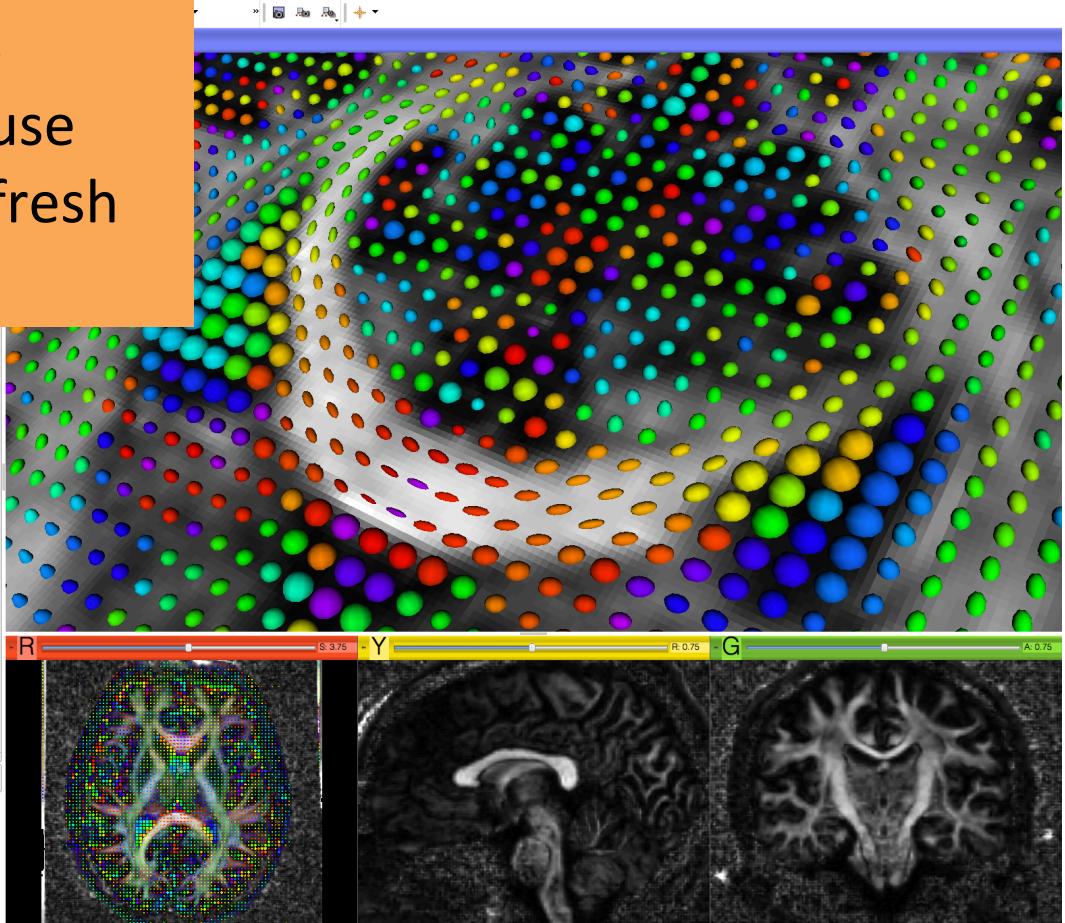
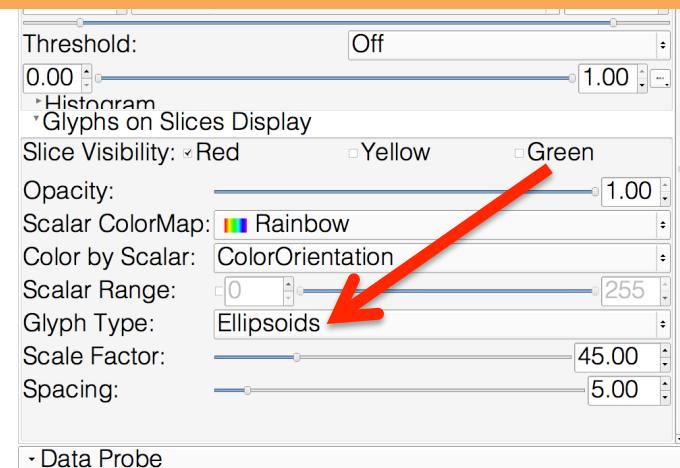
# 3D Visualization: Glyphs

Note the orientation of diffusion ellipsoid of the splenium of the corpus callosum (posterior part)



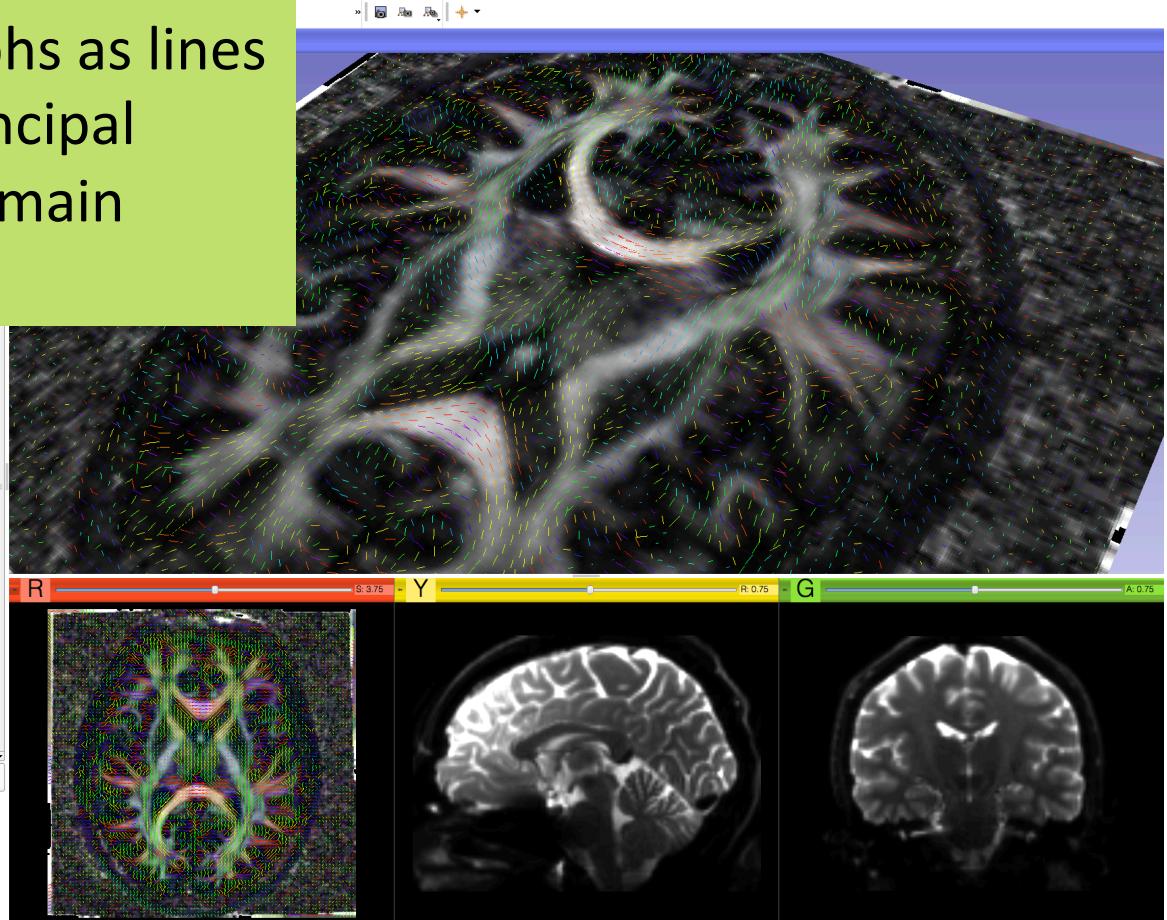
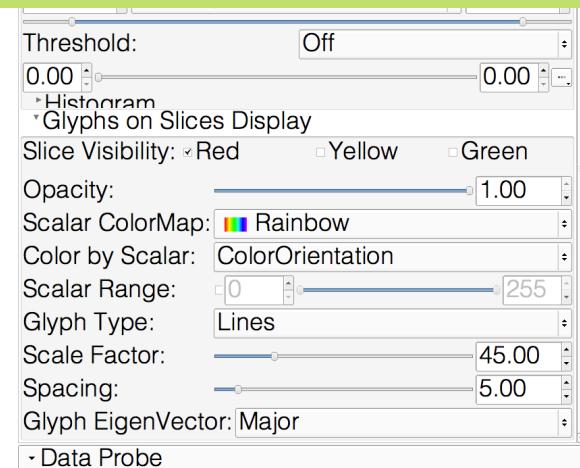
# 3D Visualization: Glyphs

Change the Glyph Type to 'Lines', and move the mouse inside the 3D viewer to refresh the display.



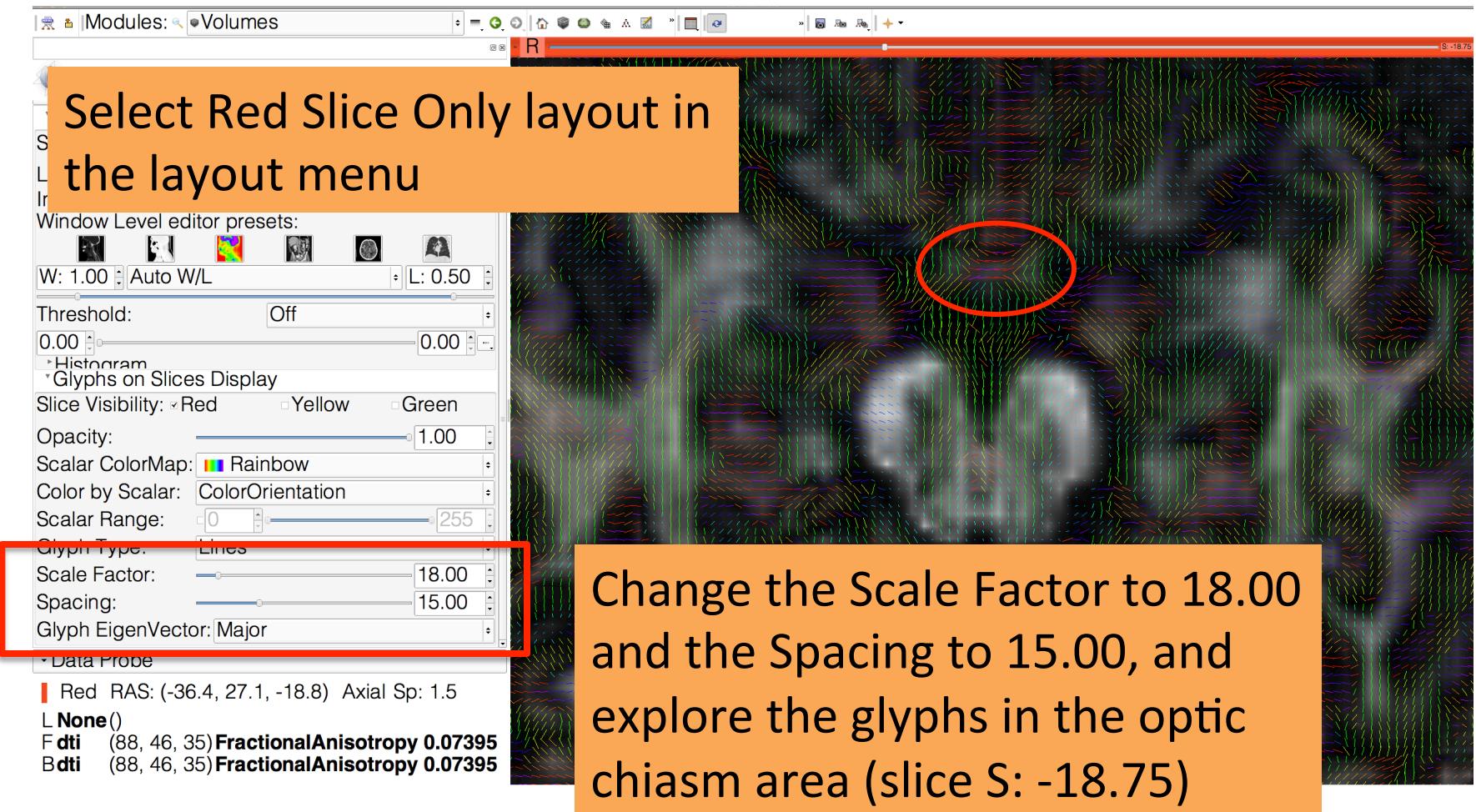
# 3D Visualization: Glyphs

Slicer displays the glyphs as lines that represent the principal direction of diffusion (main eigenvector)

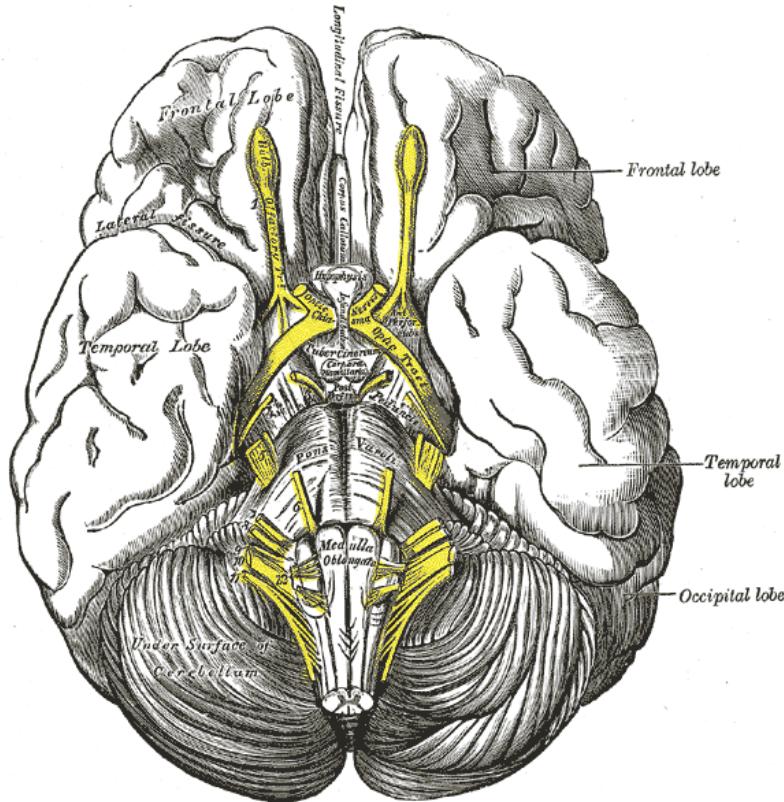


L  
F  
B

# 3D Visualization: Glyphs



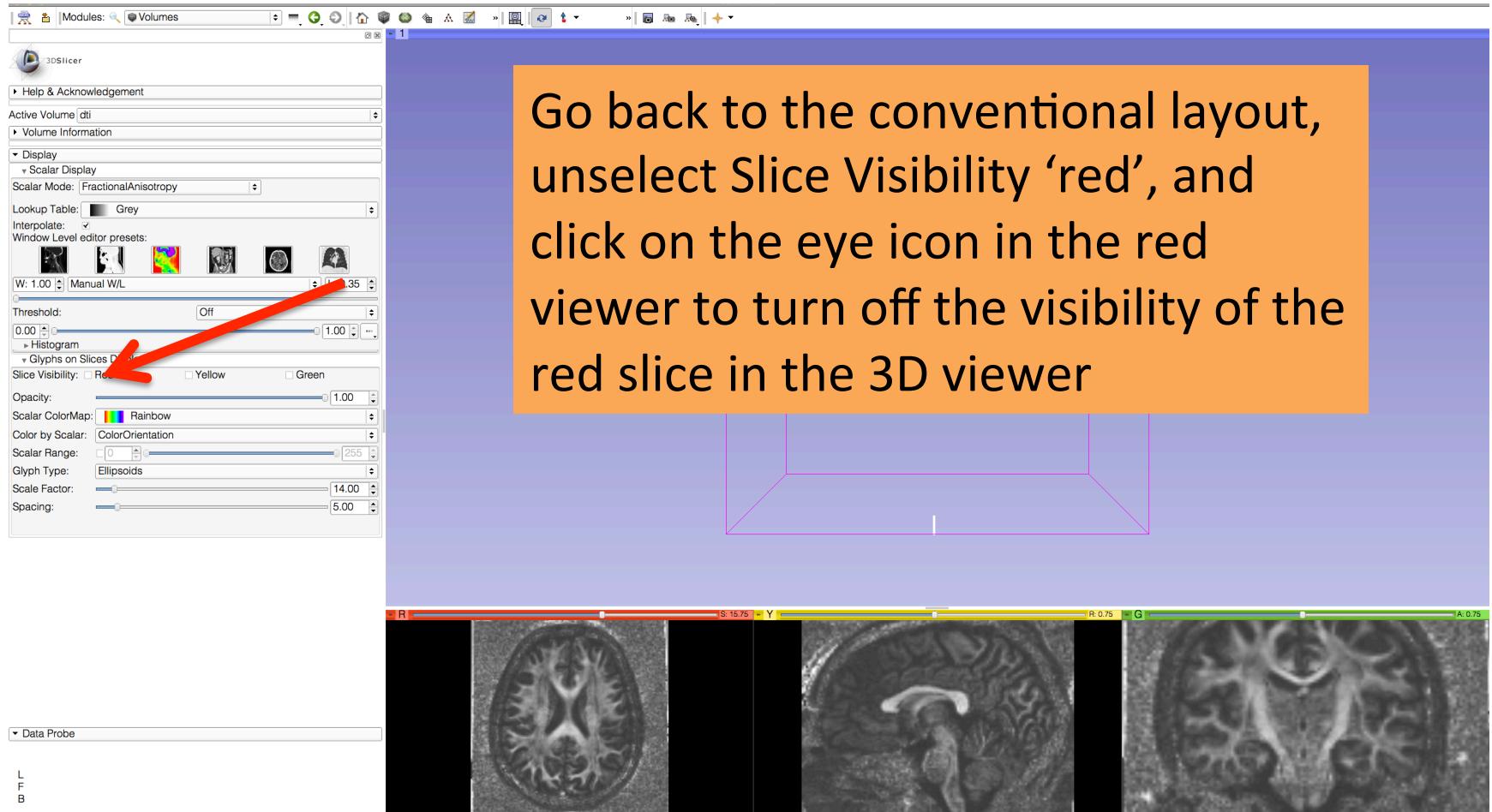
# Optic Chiasm

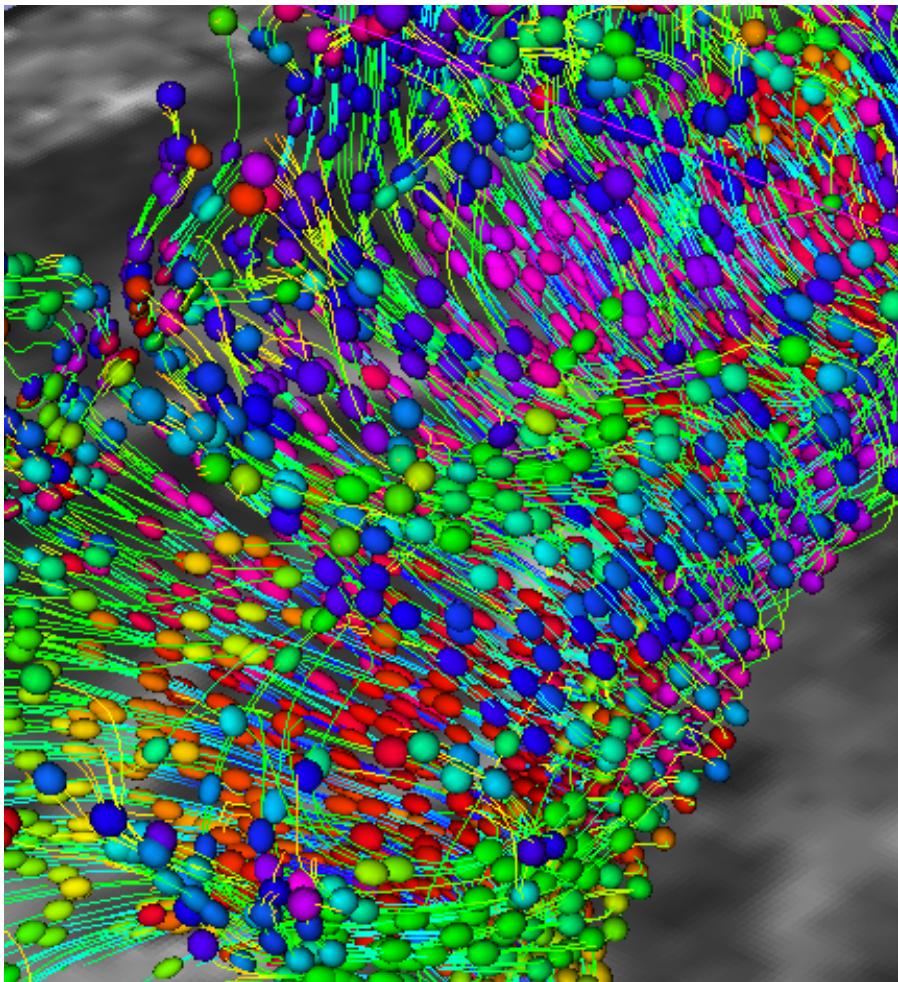


The optic chiasm corresponds to the part of the brain where the optic nerves cross.

Image from Gray's Anatomy

# 3D Visualization: Glyphs



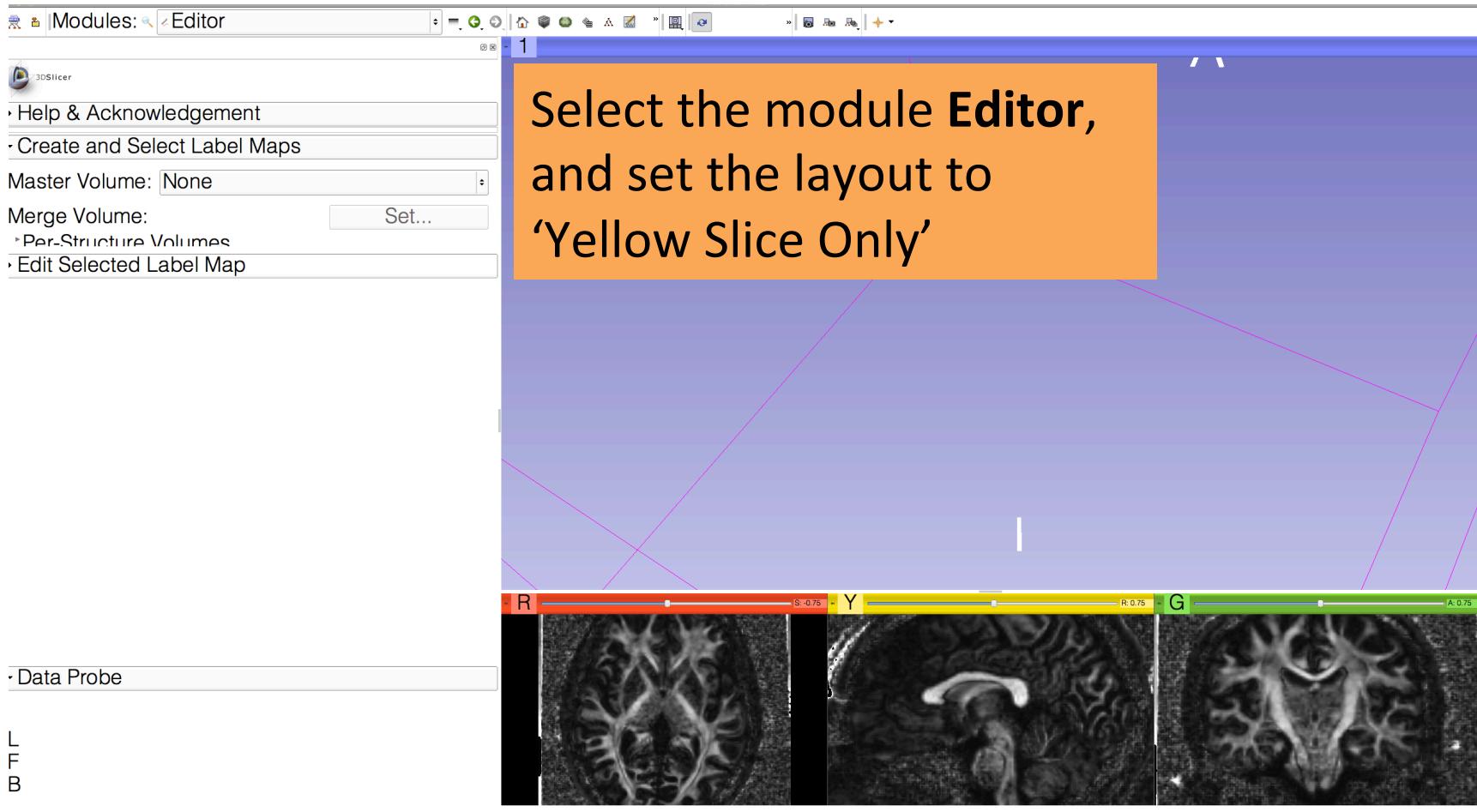


## Part 3: From tensors to tracts

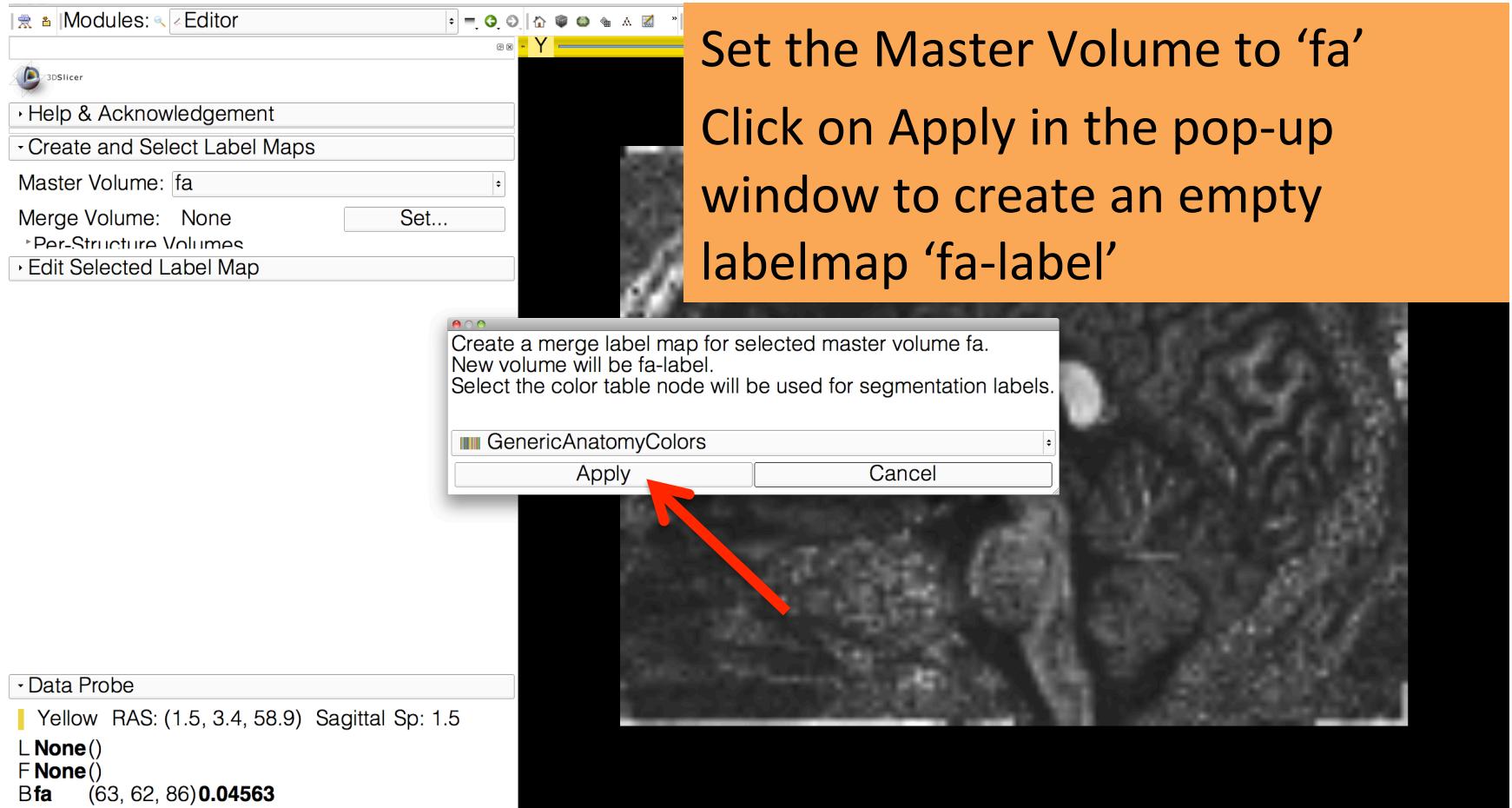
# Diffusion MRI tractography

- Tractography can be defined as the virtual reconstruction of the trajectory of water molecules along white matter bundles.
  - DTI tracts provide a mathematical representation of the underlying white matter anatomy.
  - Each voxel contains hundreds of thousands of axon fibers: size of a voxel  $\sim 1\text{-}5 \text{ mm}$  is very different from the diameter of an axon  $\sim 0.1\text{-}10 \mu\text{m}$
- A DTI tract is not equivalent to a real fiber.

# Tractography Seeding: ROI definition

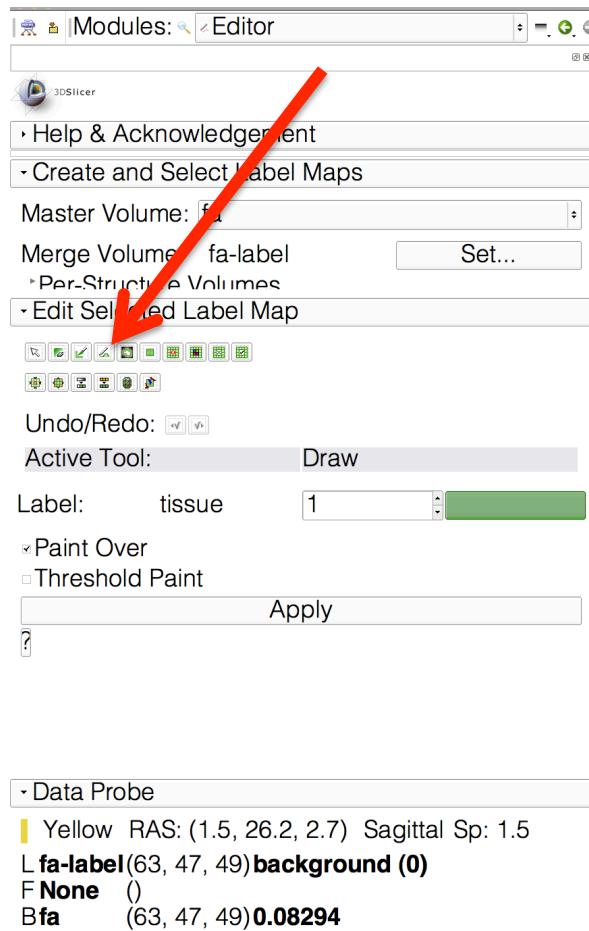


# ROI Definition



Set the Master Volume to 'fa'  
Click on Apply in the pop-up window to create an empty labelmap 'fa-label'

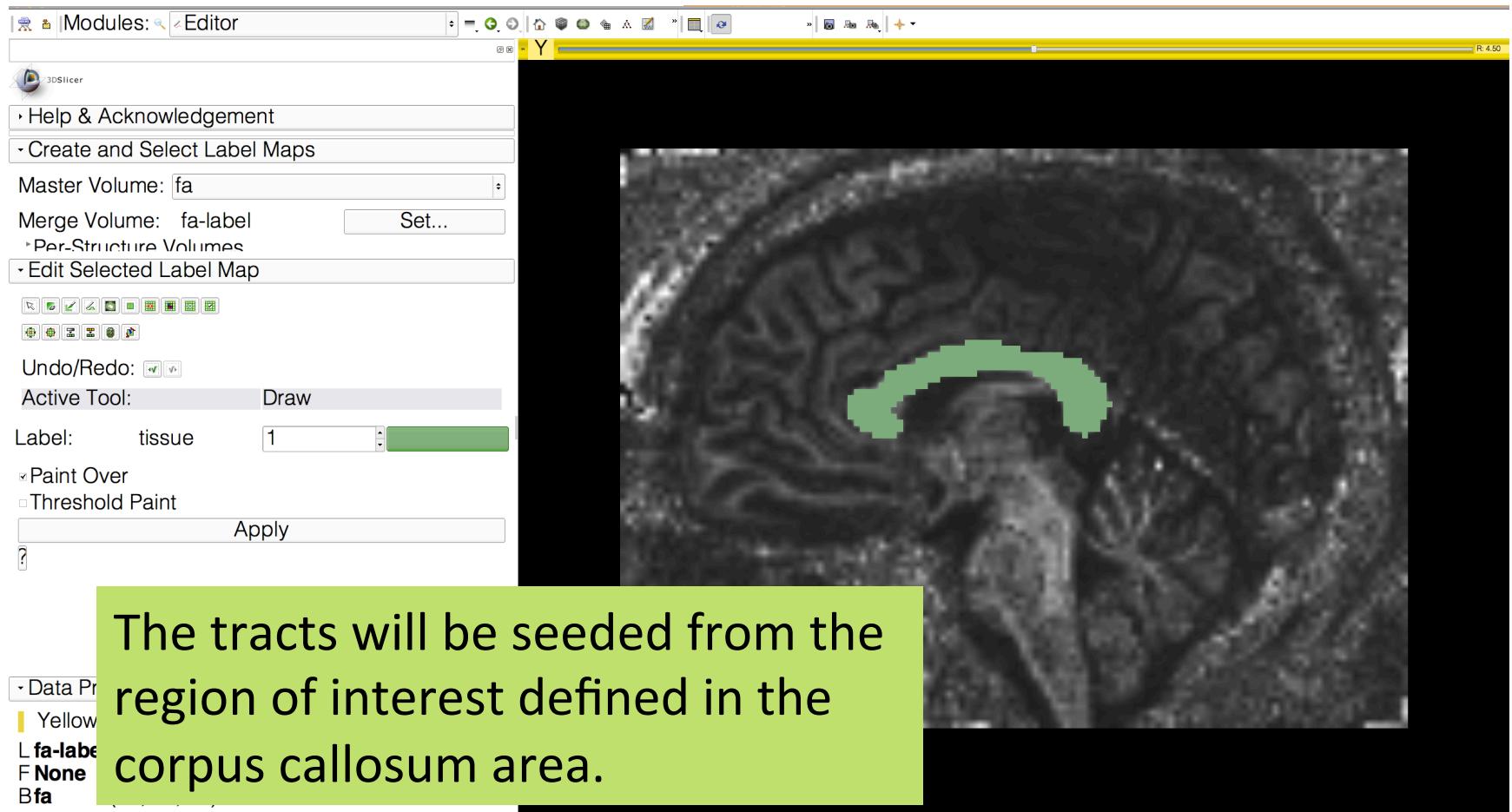
# ROI Drawing



Use the draw tool to outline the contour of the corpus callosum in the sagittal slice, and press Enter.  
Repeat the same operation on 3 adjacent sagittal slices.

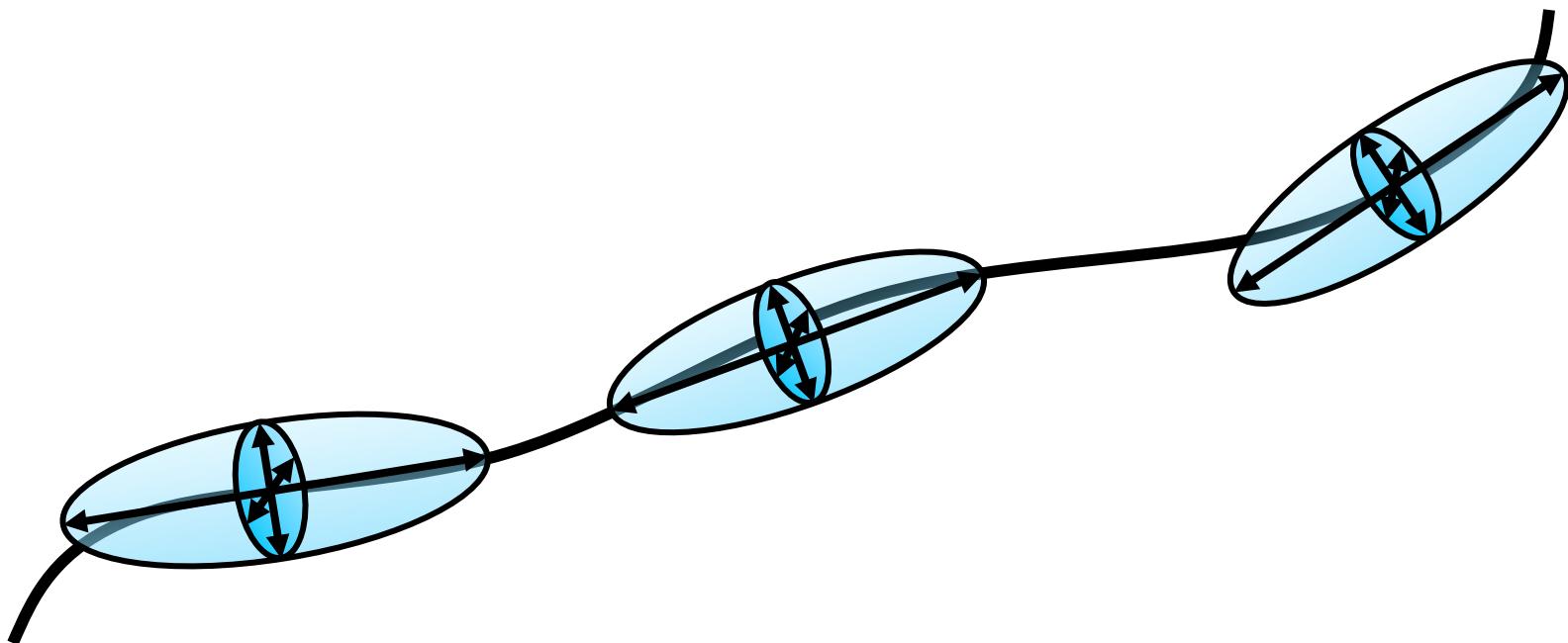


# ROI Drawing

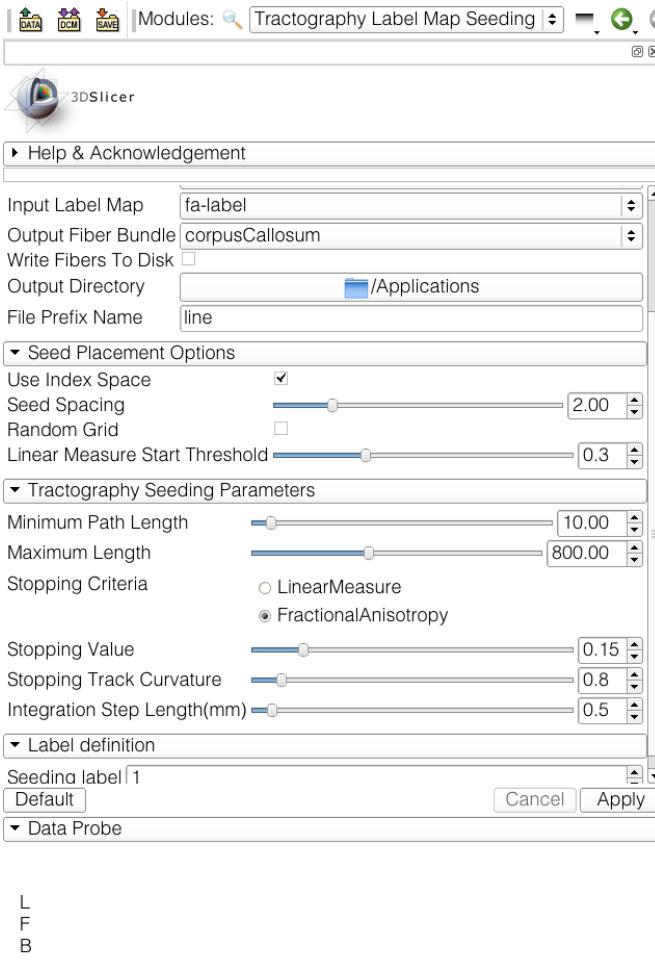


# Streamline tractography

Underlying Assumption: the orientation of the fibers is collinear with the direction of the principal eigenvector



# Labelmap Seeding: I/O



The screenshot shows the 3DSlicer interface with the 'Tractography Label Map Seeding' module selected. The left panel displays various parameters:

- Input Label Map: fa-label
- Output Fiber Bundle: corpusCallosum
- Write Fibers To Disk:
- Output Directory: /Applications
- File Prefix Name: line
- Seed Placement Options:
  - Use Index Space:
  - Seed Spacing: 2.00
  - Random Grid:
  - Linear Measure Start Threshold: 0.3
- Tractography Seeding Parameters:
  - Minimum Path Length: 10.00
  - Maximum Length: 800.00
  - Stopping Criteria:
    - LinearMeasure
    - FractionalAnisotropy
  - Stopping Value: 0.15
  - Stopping Track Curvature: 0.8
  - Integration Step Length(mm): 0.5
- Label definition:
  - Seeding label 1: Default
- Data Probe

The right panel shows a grayscale diffusion MRI volume with a prominent white matter fiber tract highlighted in red.

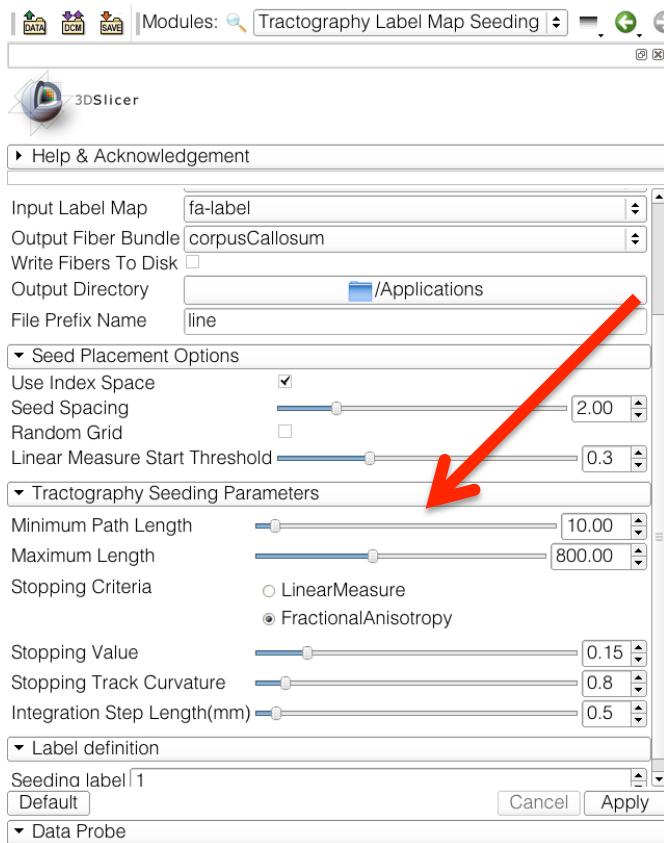
Select the module **Tractography Label Map Seeding**

Set the Input DTI Volume to 'dti'

Set the Input Label Map to 'fa-label'

Set Output Fiber Bundle to 'Create New Fiber Bundle' and rename it 'corpusCallosum'

# Labelmap Seeding: parameters



Select the Seed Placement Options to 'Use Index Space'.

Select Stopping Mode 'Fractional Anisotropy'

Select the default tractography Seeding parameters:

-Minimum length: 10 mm

-Maximum length: 800 mm

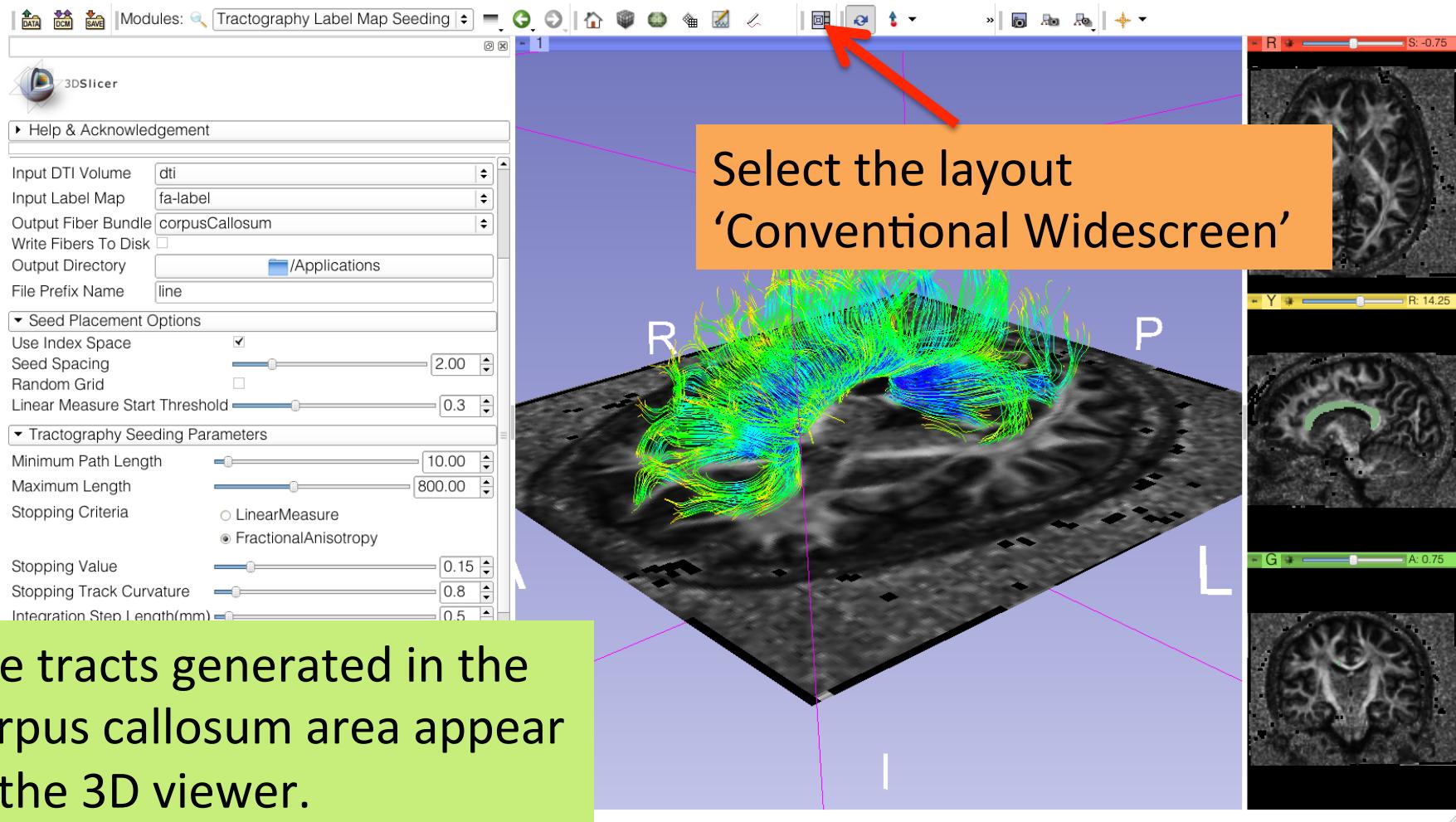
-Stopping value: 0.15

-Stopping track curvature: 0.8

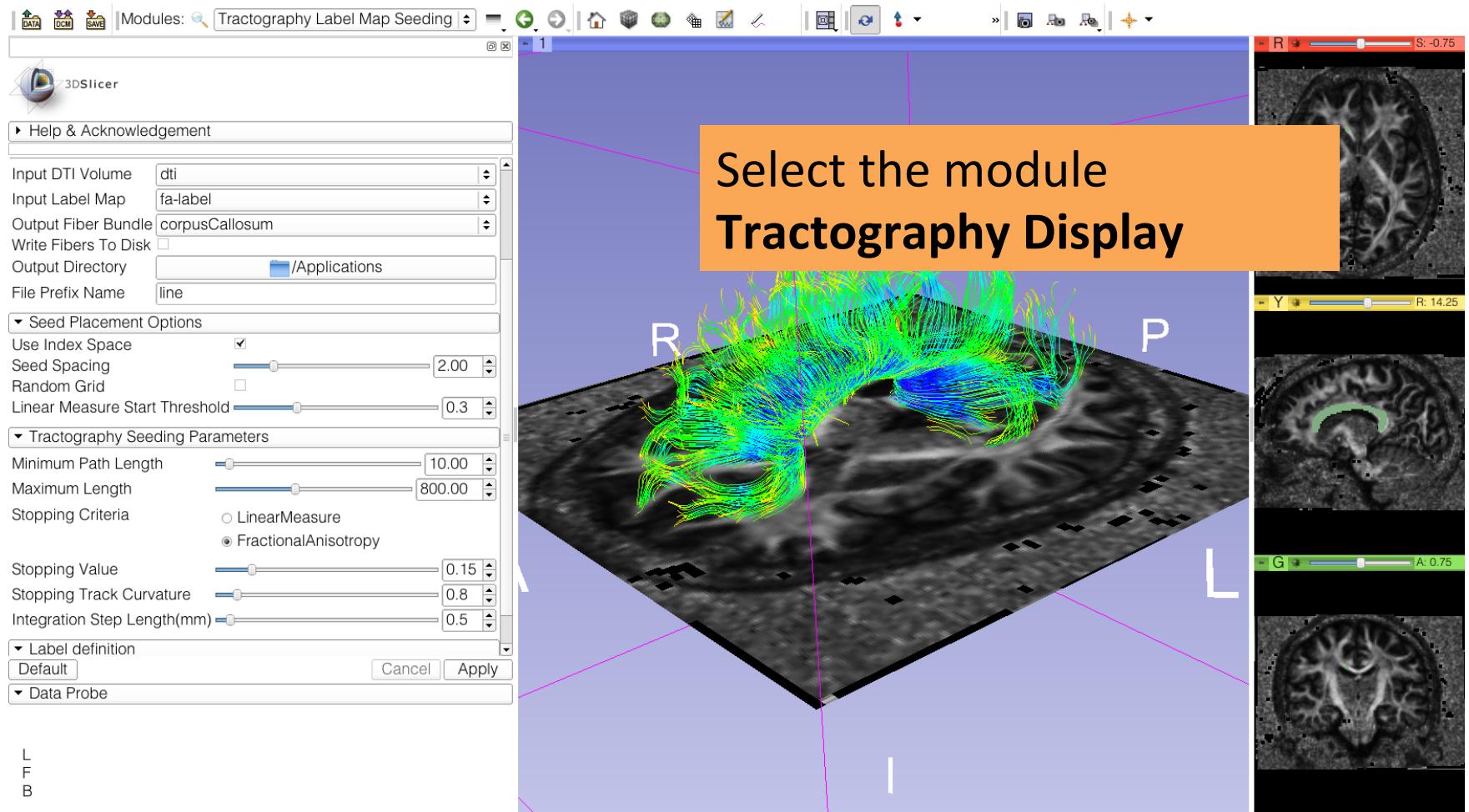
-Integration step length: 0.5 mm

Click on Apply

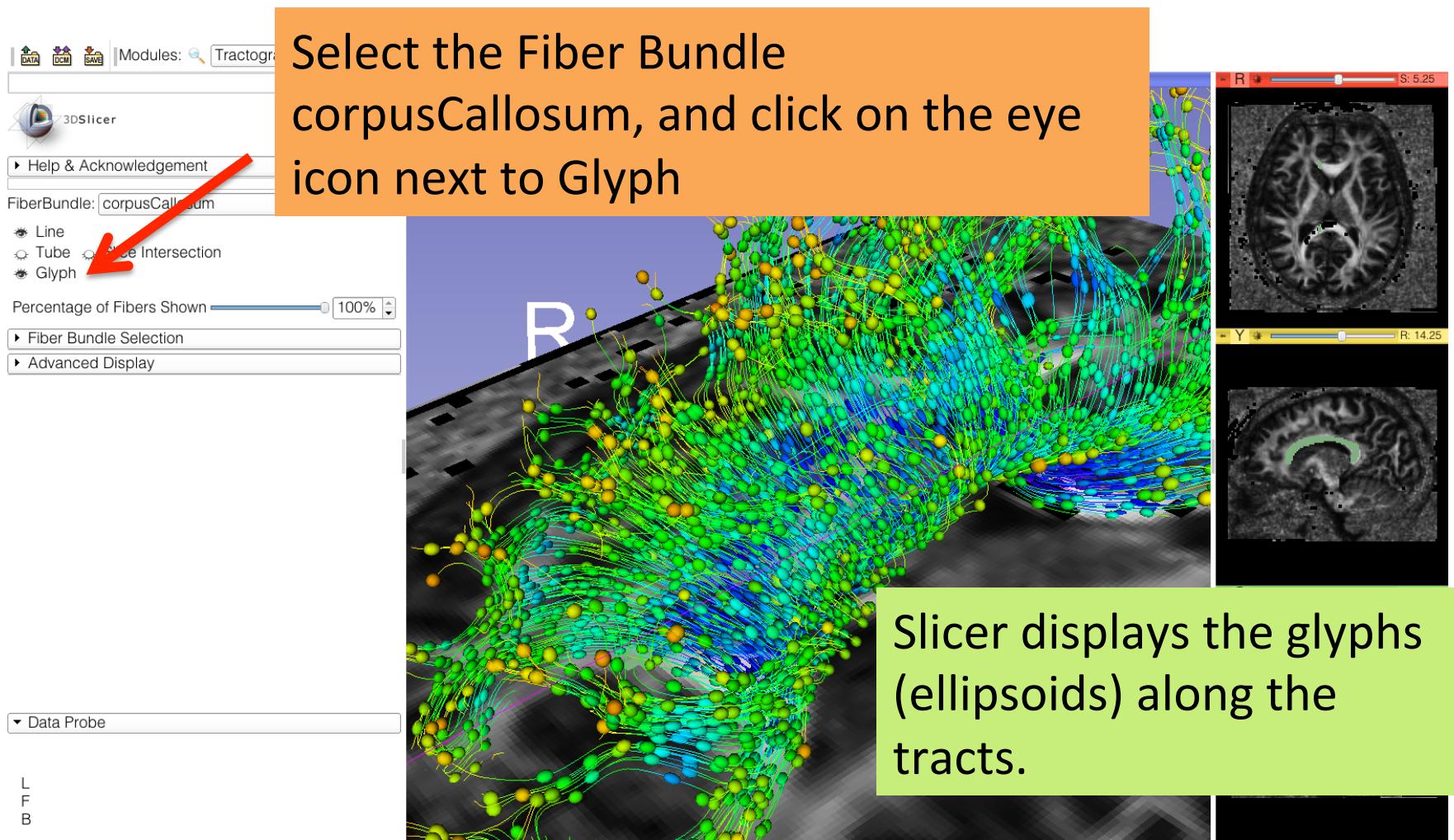
# Labelmap Seeding: Tracts



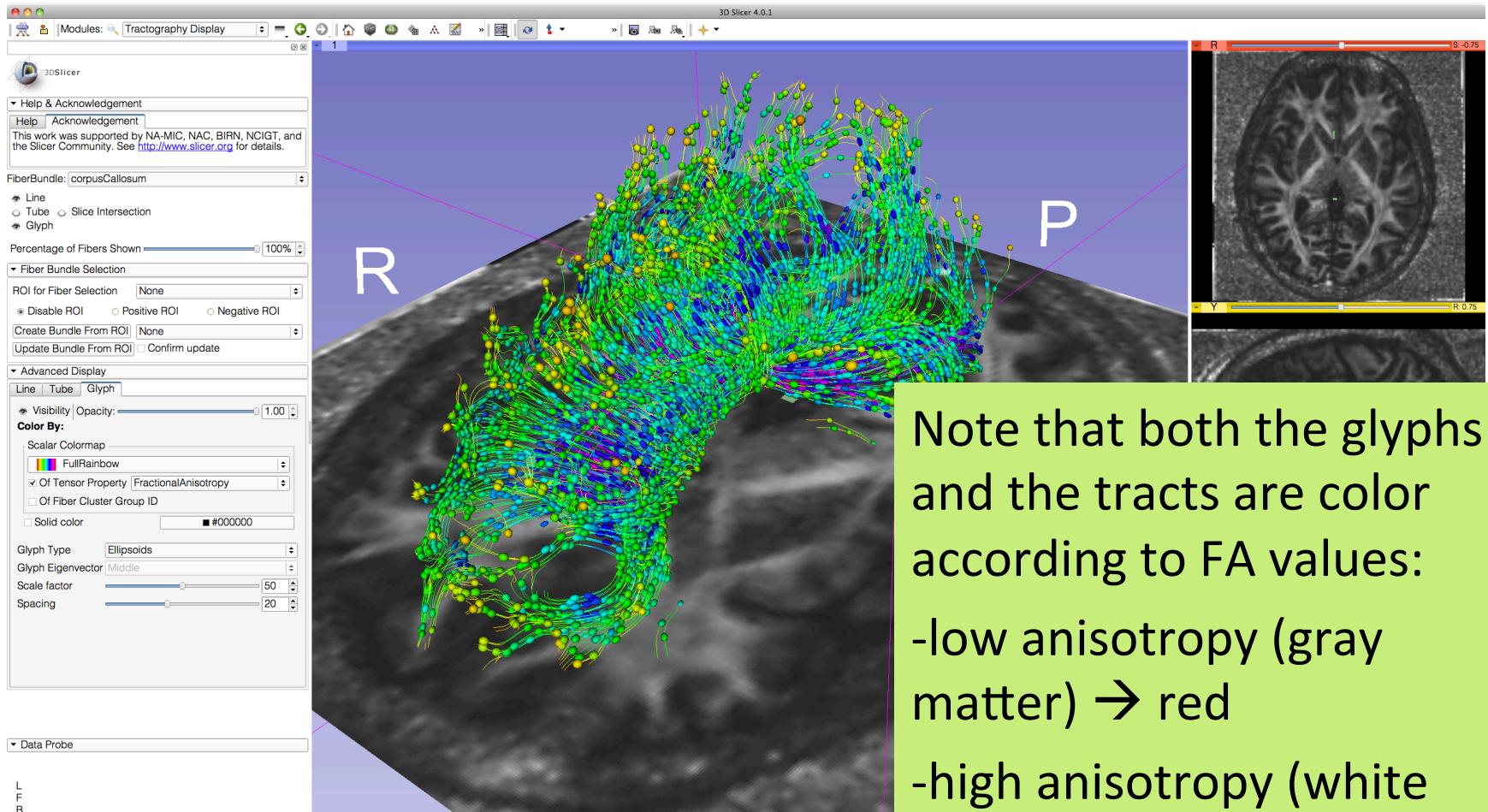
# Labelmap Seeding: Tracts



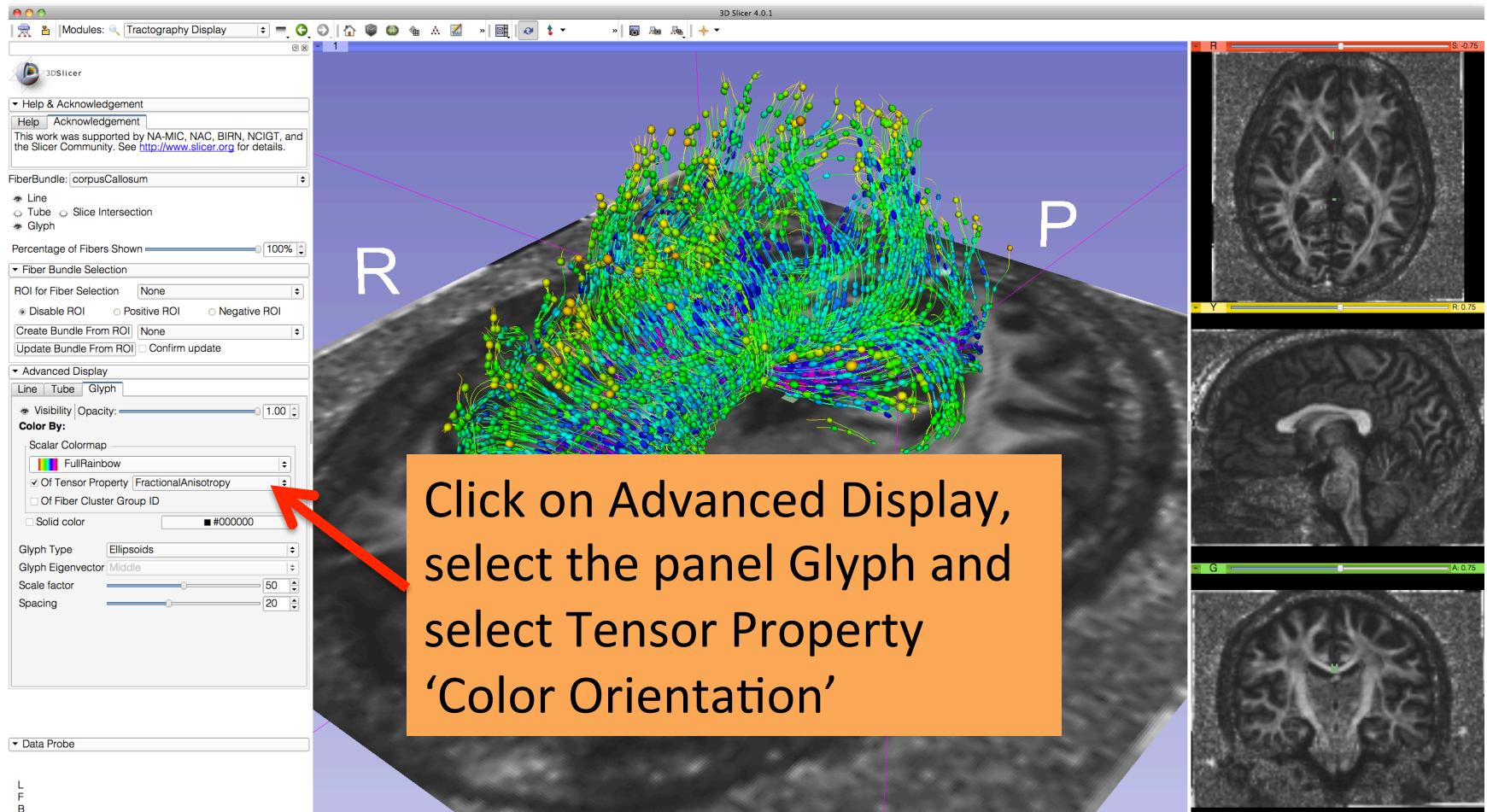
# Tractography Results



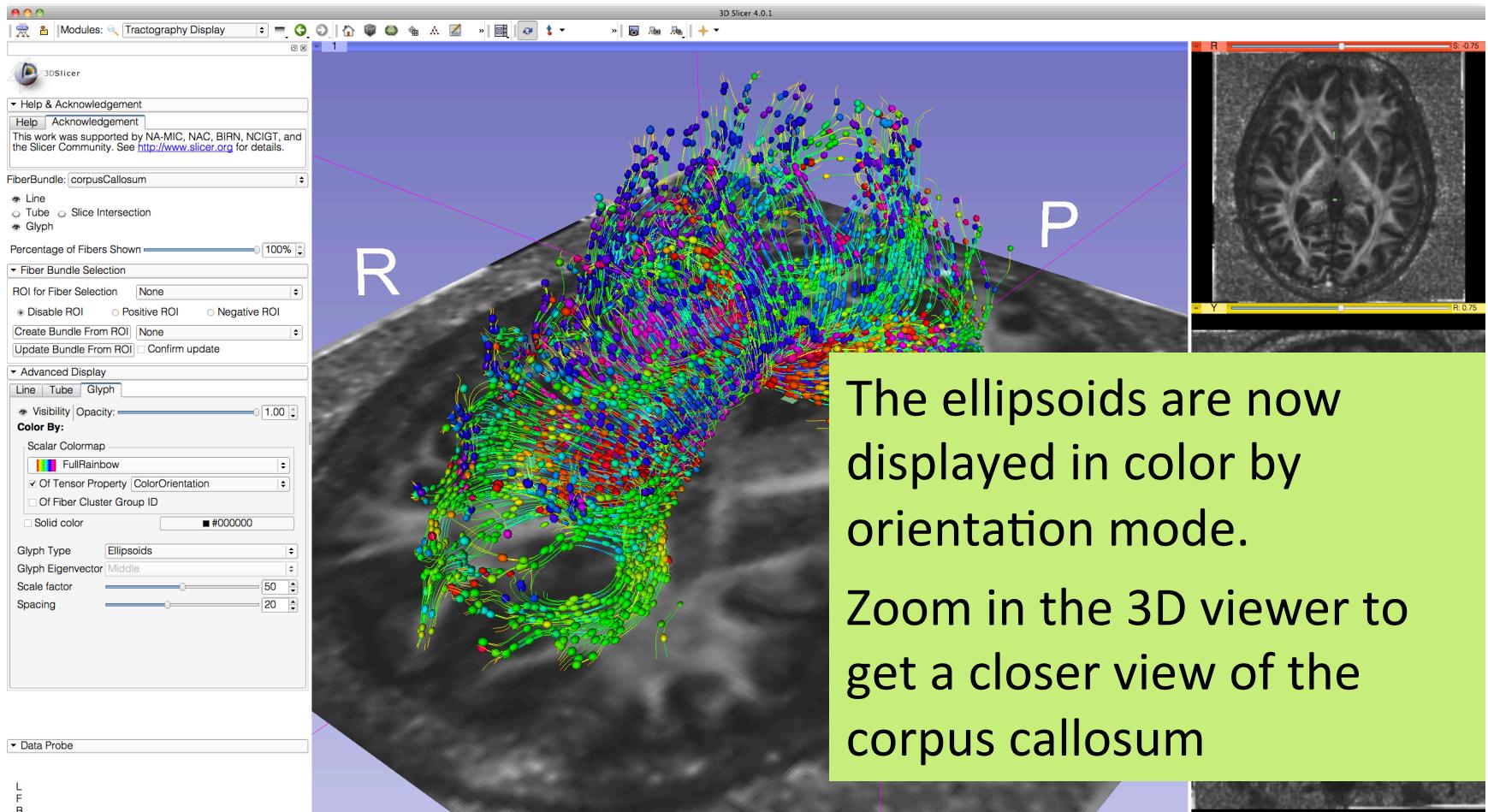
# Tractography Results



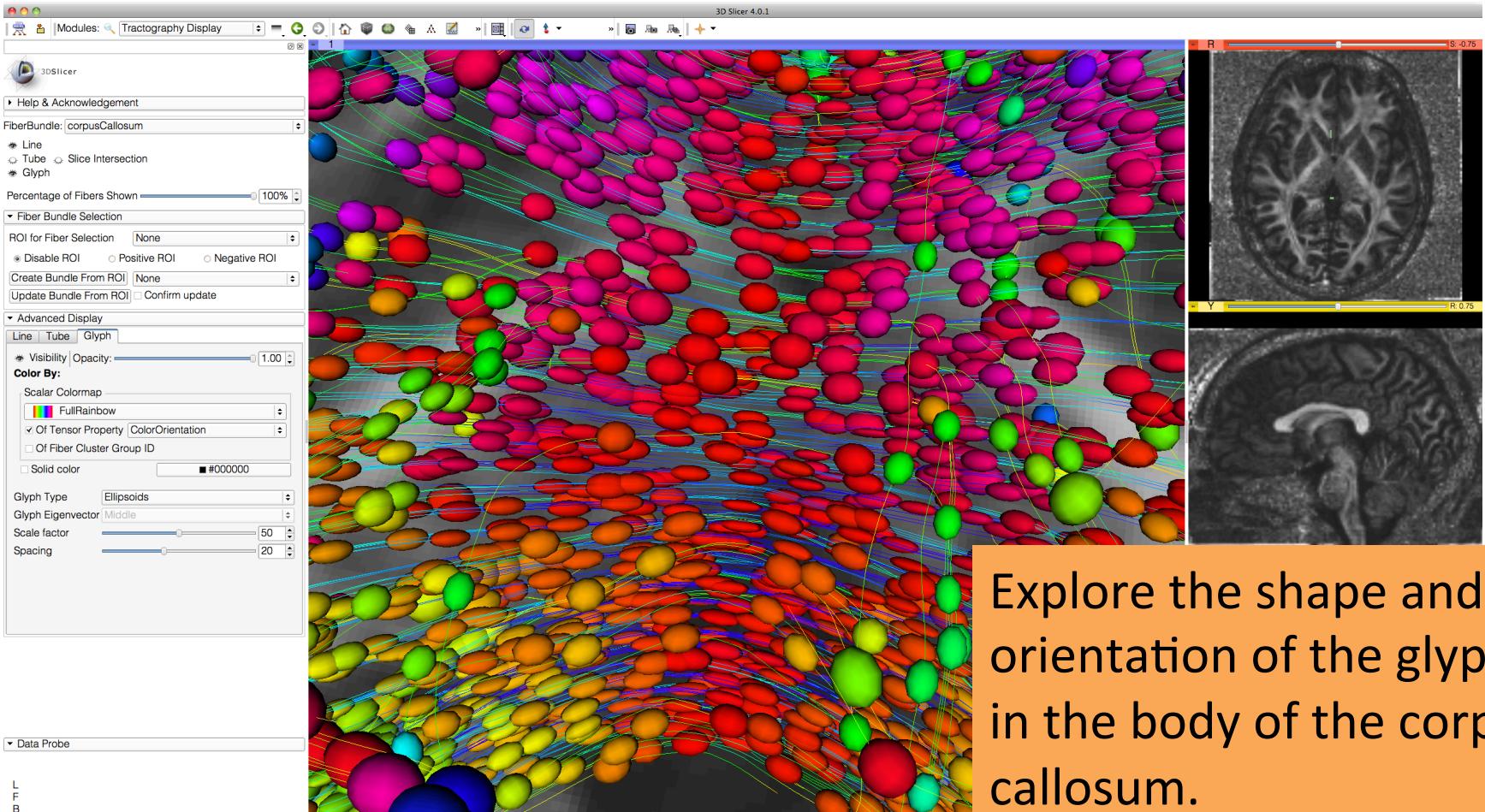
# Tractography Results



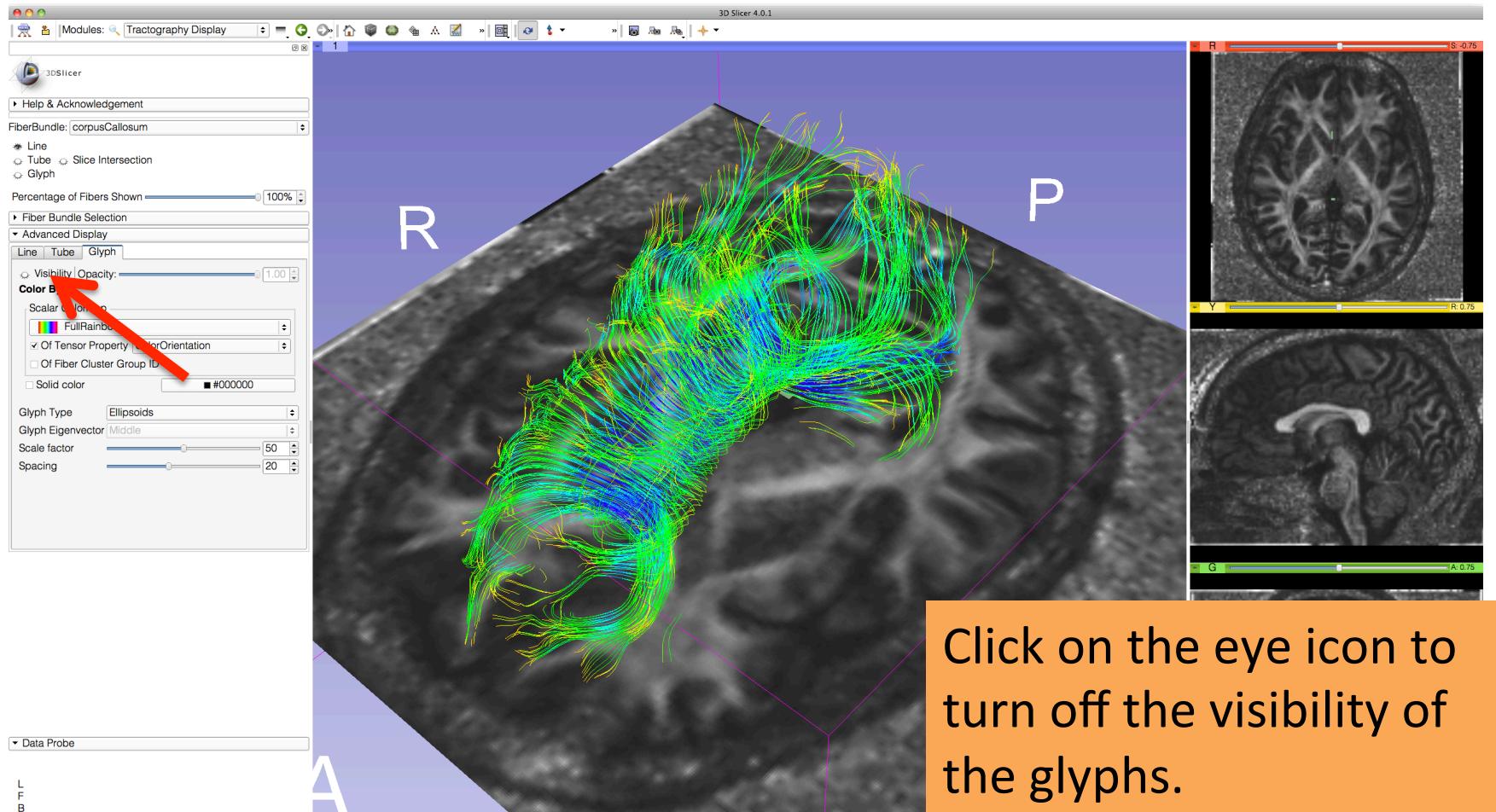
# Tractography Results



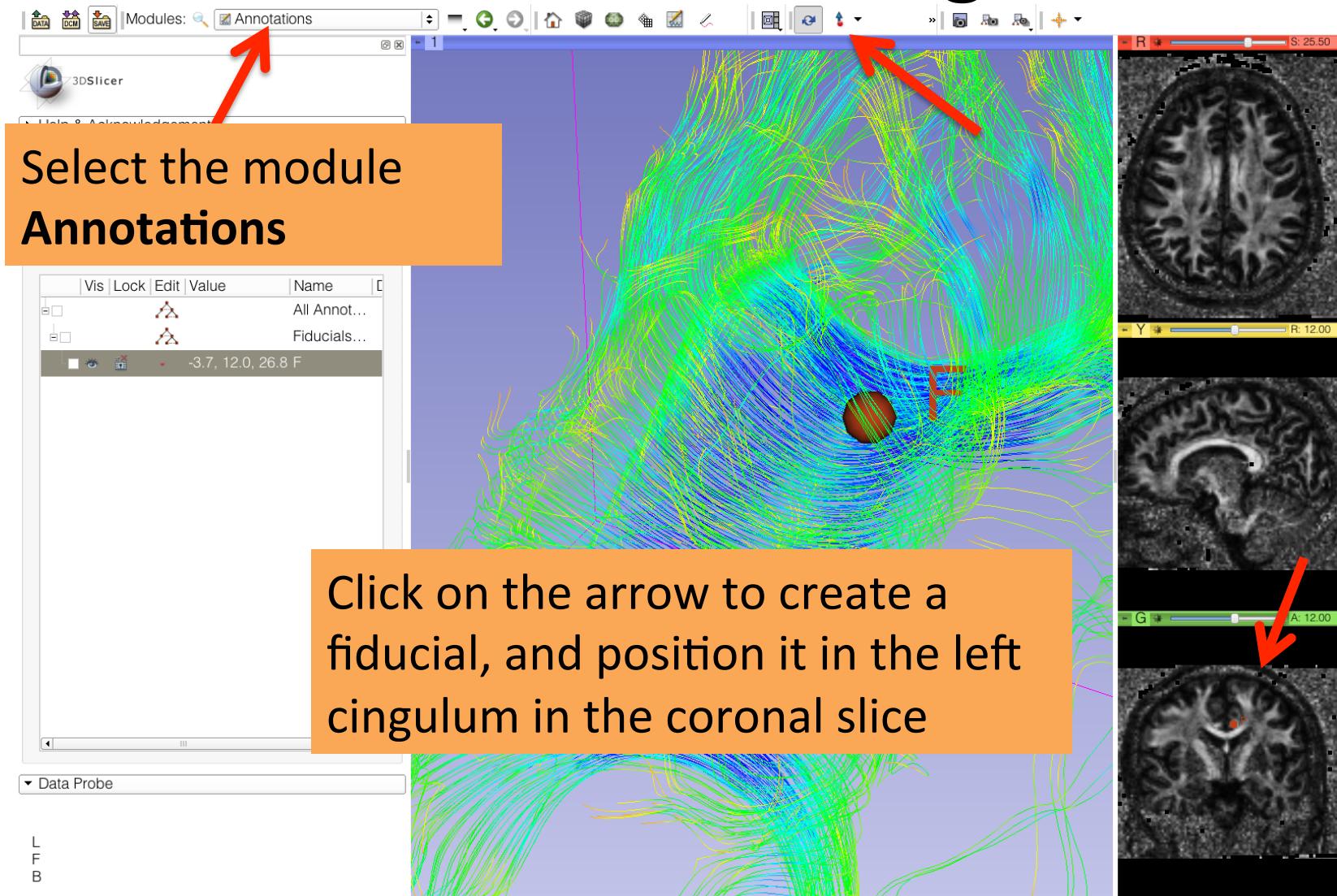
# Tractography Results



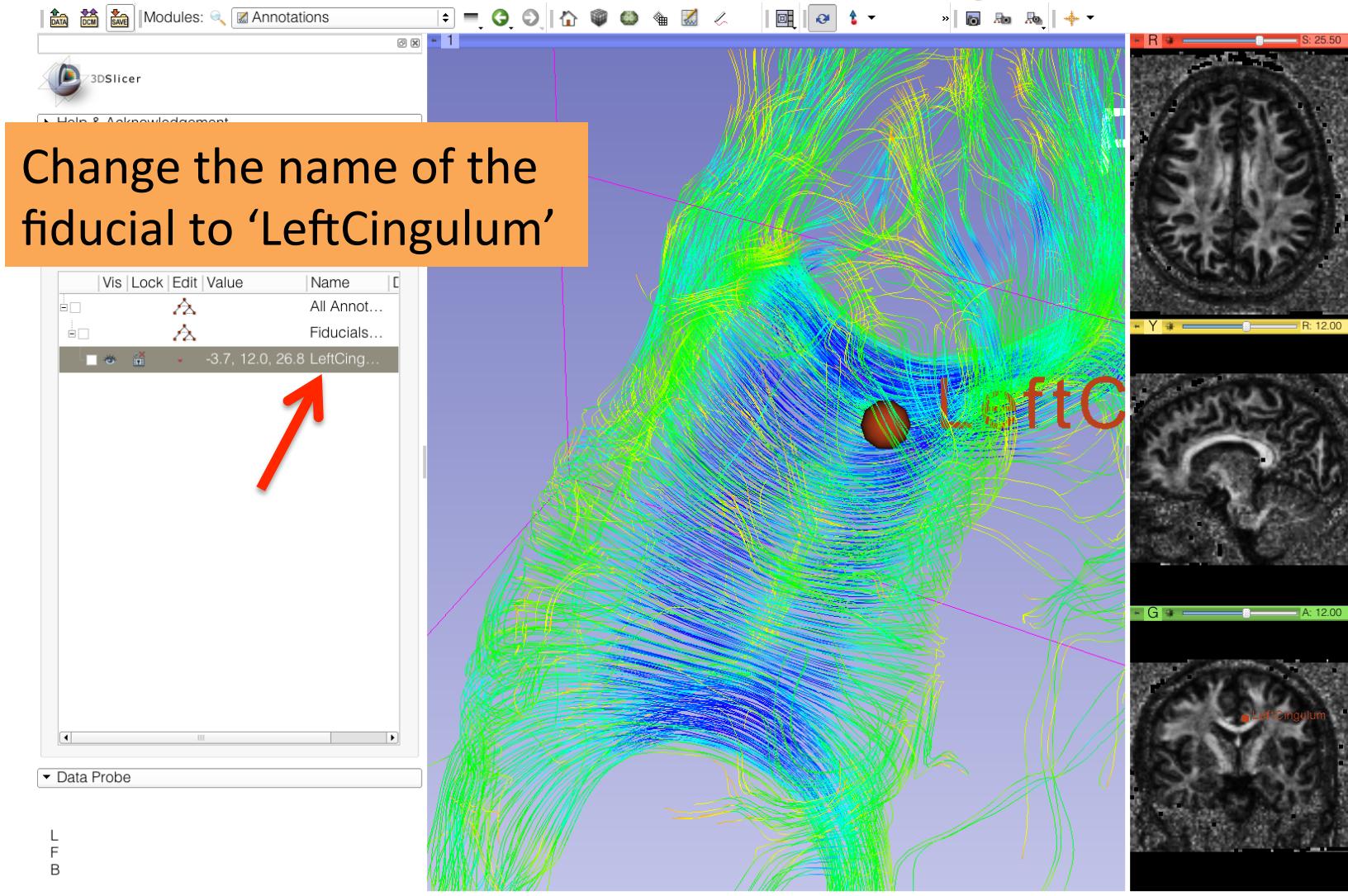
# Tractography Results



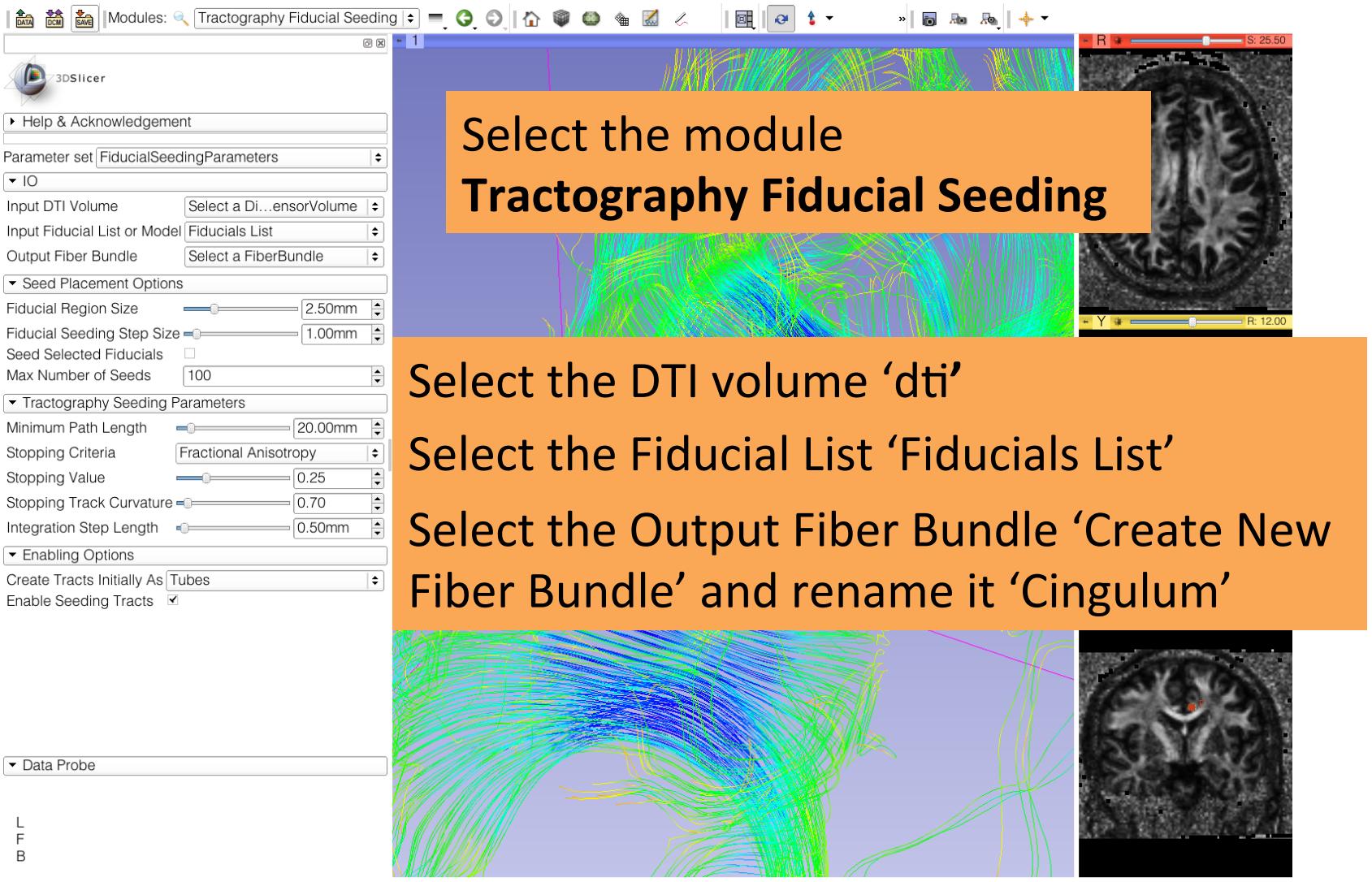
# Fiducial Seeding



# Fiducial Seeding



# Fiducial Seeding

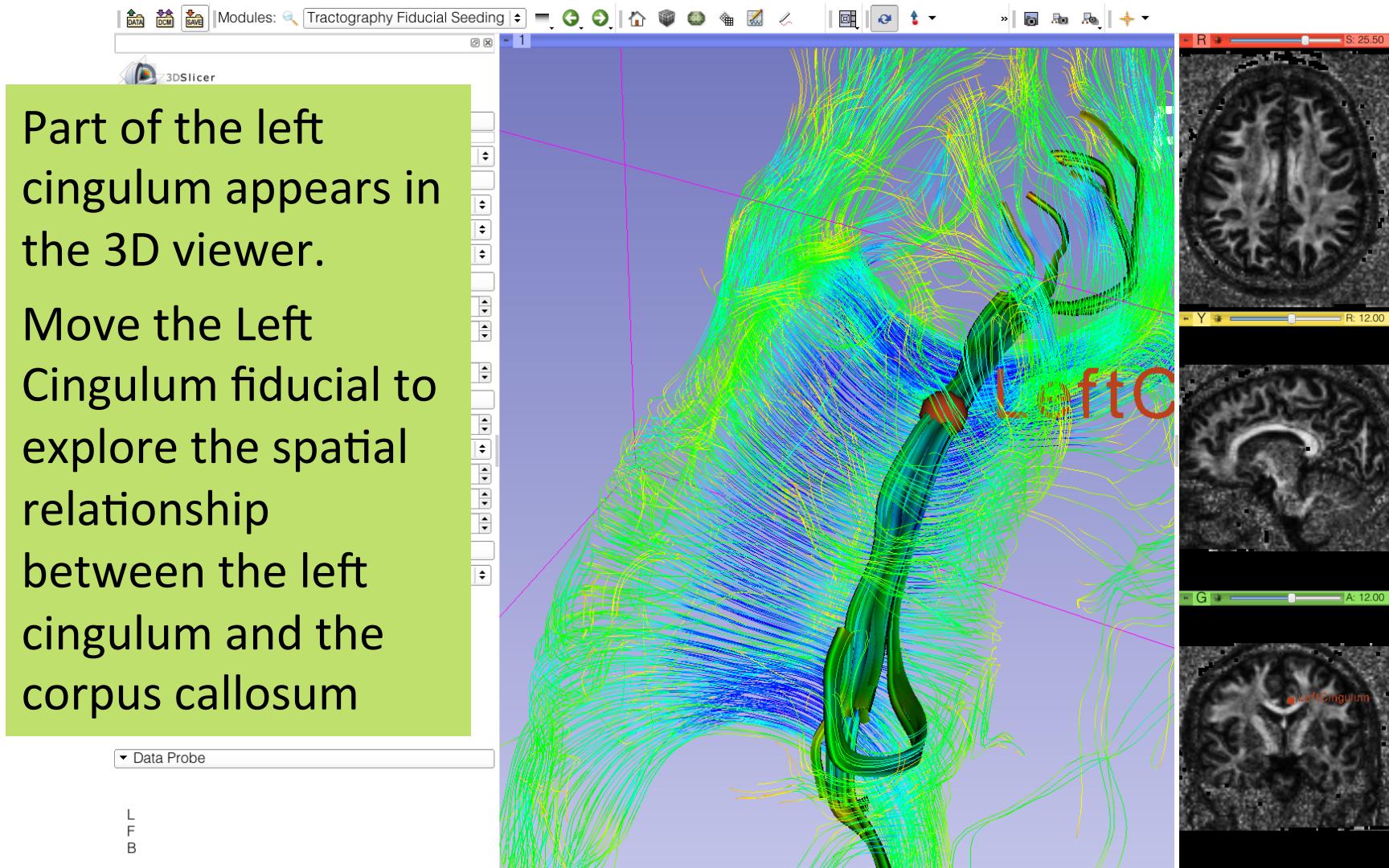


# Fiducial Seeding

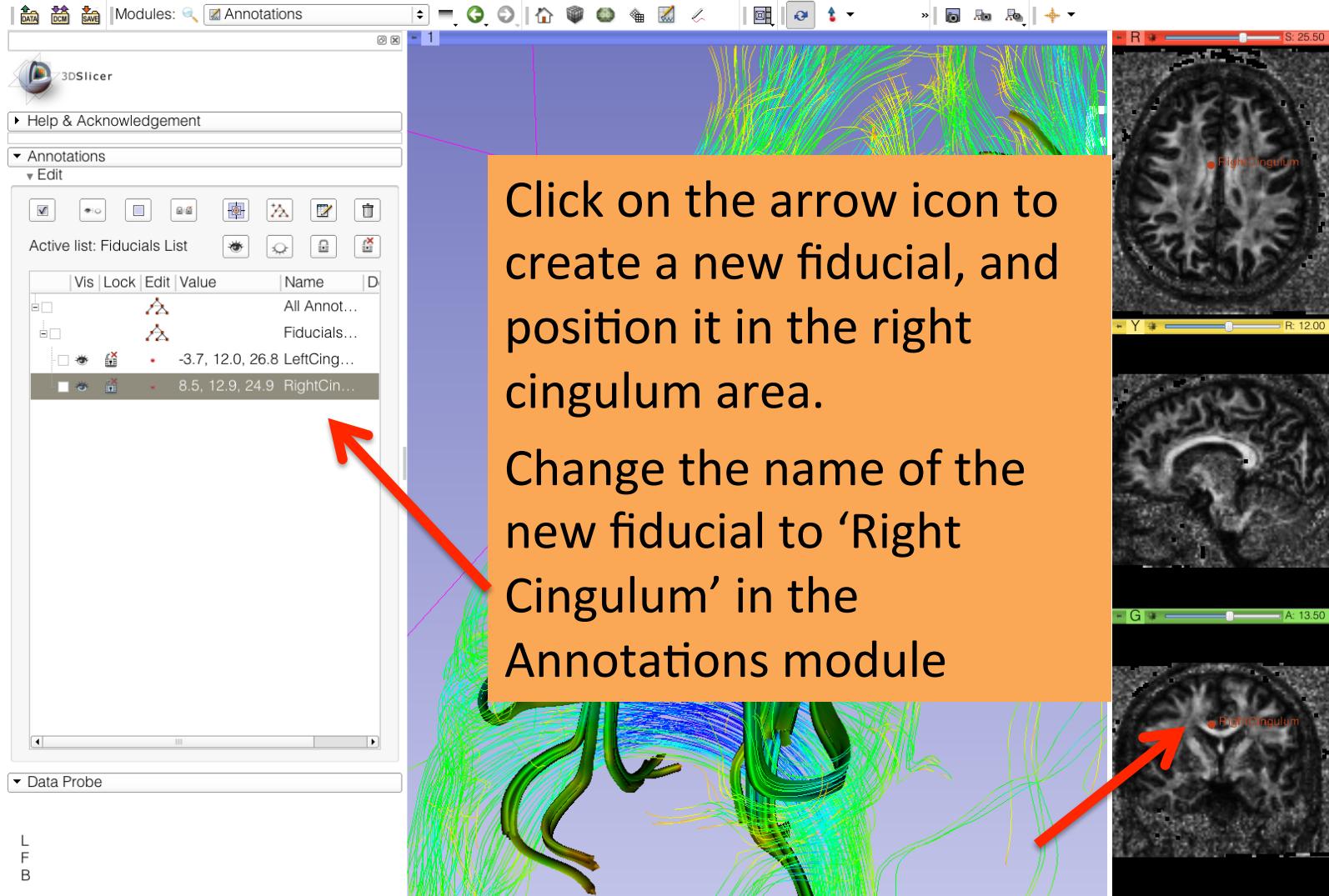
Set the tractography parameters as follows:

- Fiducial region size: 2.5 mm
- Fiducial Seeding Step Size: 1.0 mm
- Maximum number of seeds: 100
- Minimum Path Length: 10 mm
- Stopping Criteria: Fractional Anisotropy
- Stopping Value: 0.15
- Stopping Track Curvature: 0.8
- Integration step length: 0.5 mm
- Create Tracts Initially as Tubes

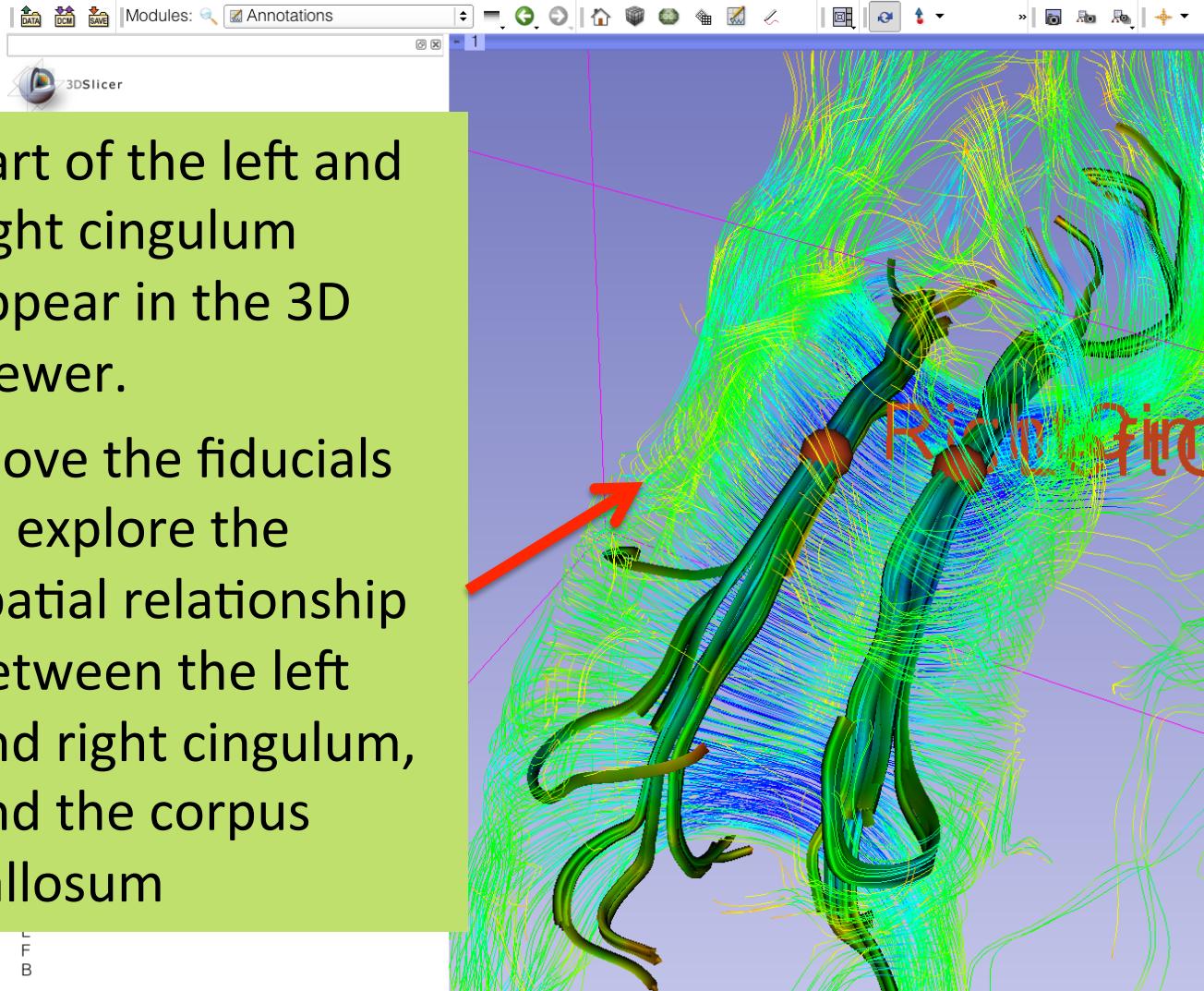
# Fiducial Seeding



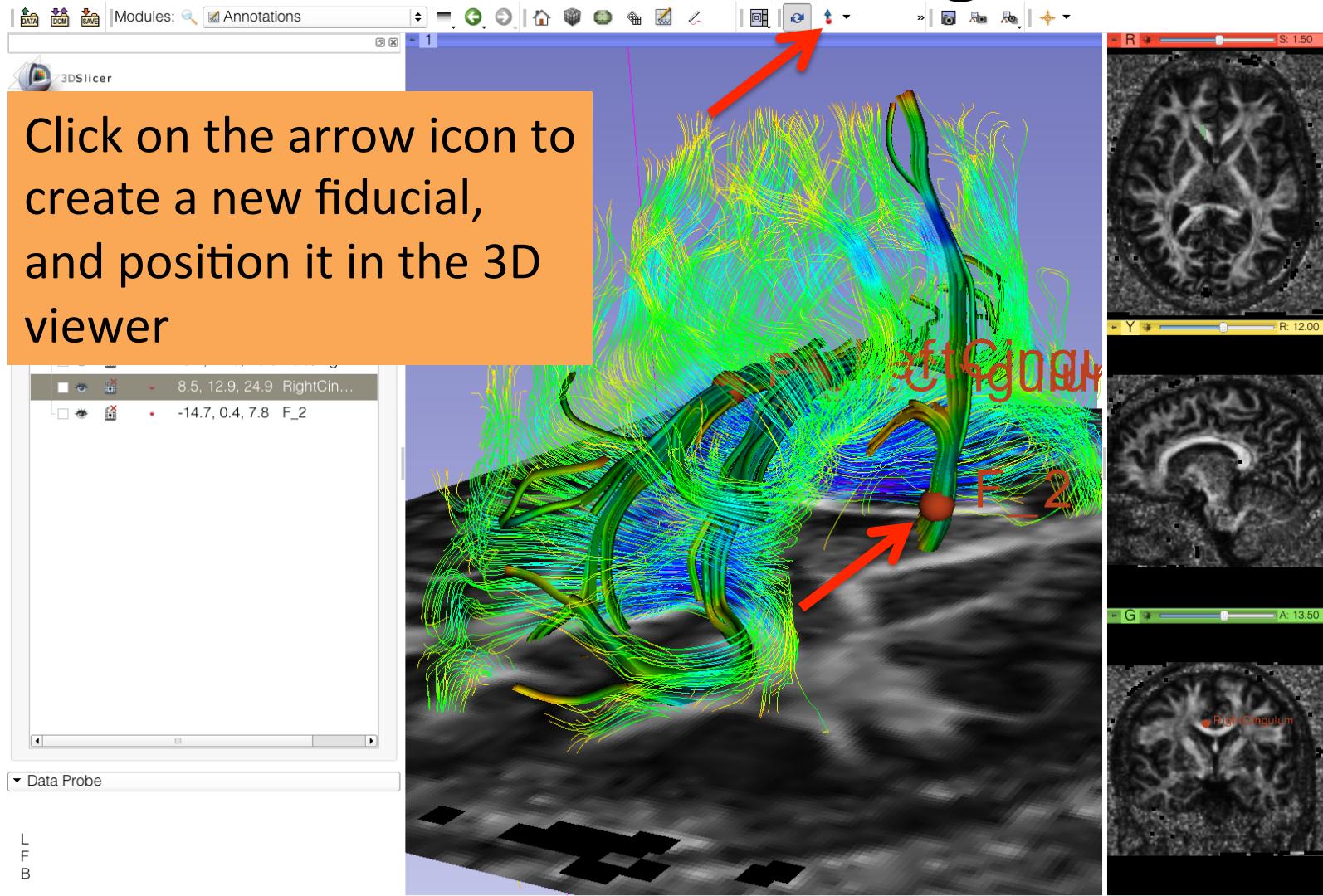
# Fiducial Seeding



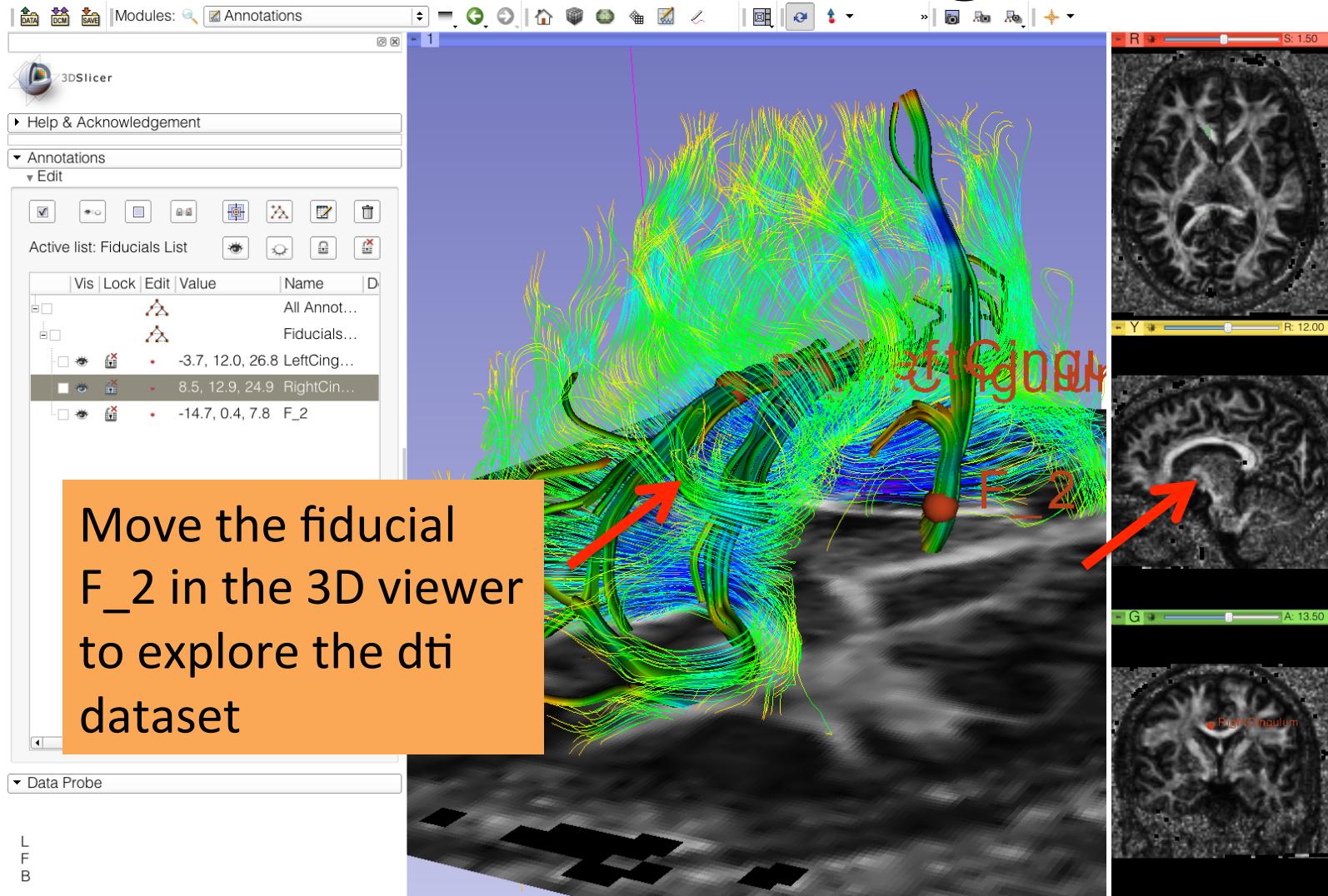
# Fiducial Seeding



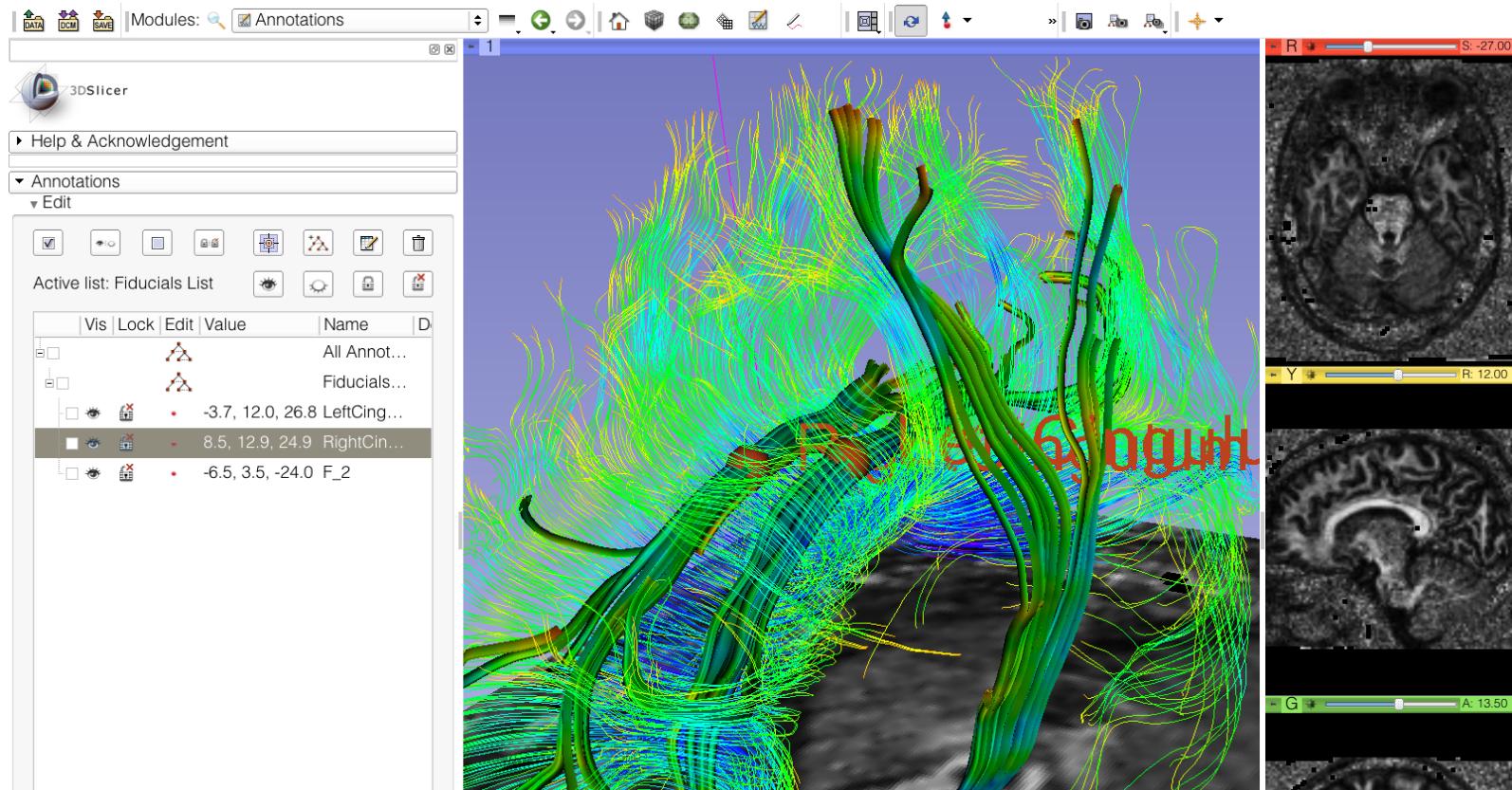
# Fiducial Seeding



# Fiducial Seeding

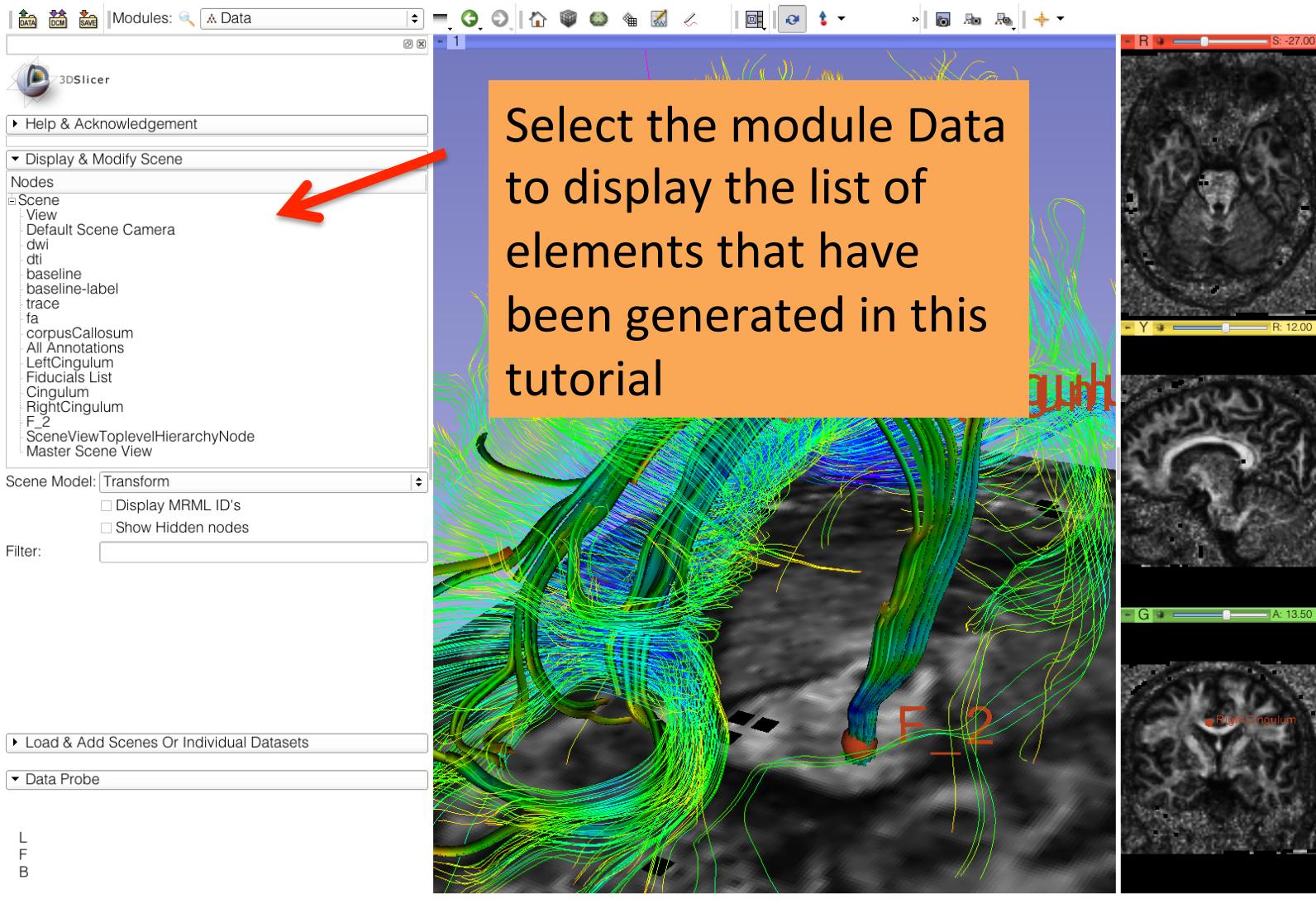


# Tractography ‘on-the-fly’

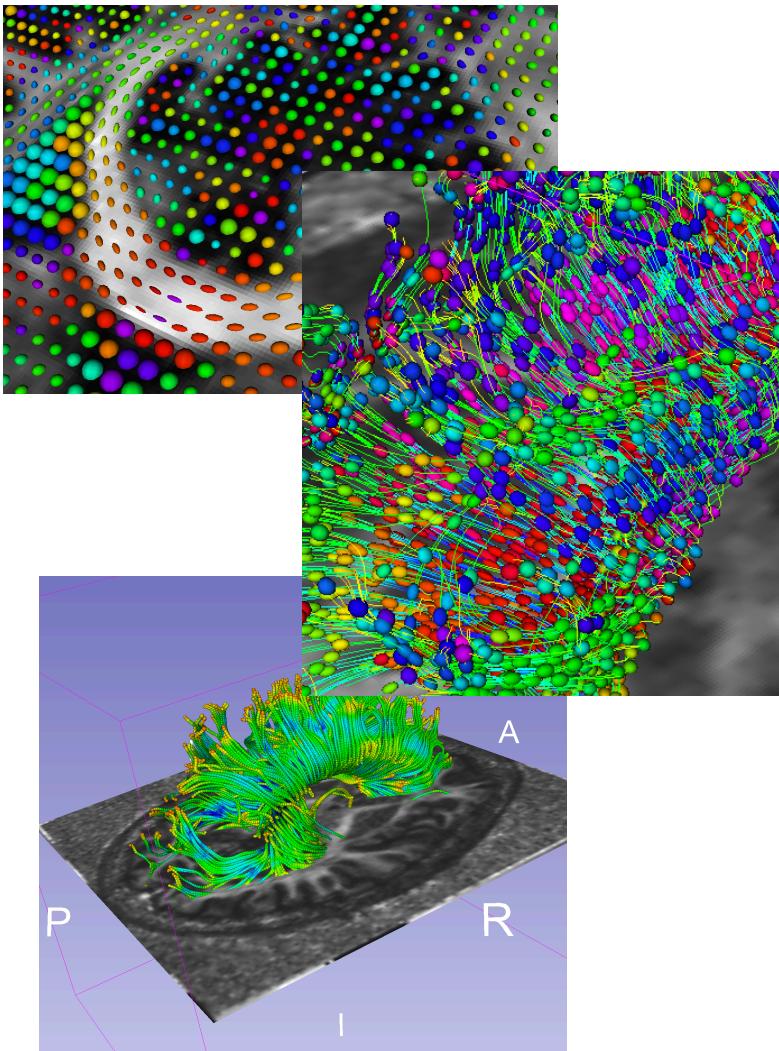


The Fiducial Seeding functionality allows you to do tractography ‘on-the-fly’ to explore white matter structures interactively

# DTI Analysis



# 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 brain white matter pathways.

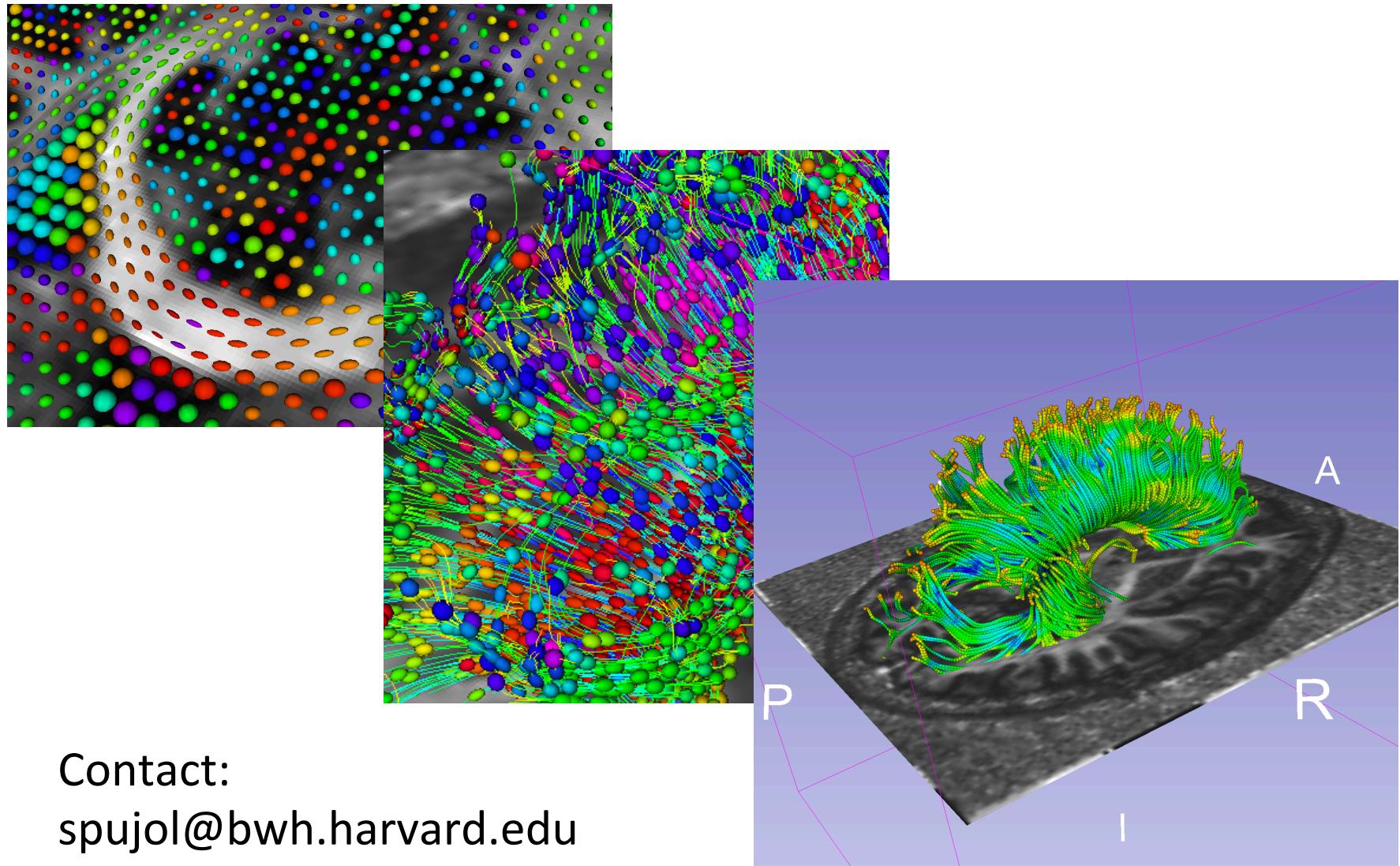
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Neuroimage Analysis Center  
NIH P41RR013218



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