Diffusion MRI Analysis

Sonia Pujol, Ph.D.

Surgical Planning Laboratory,

Harvard Medical School

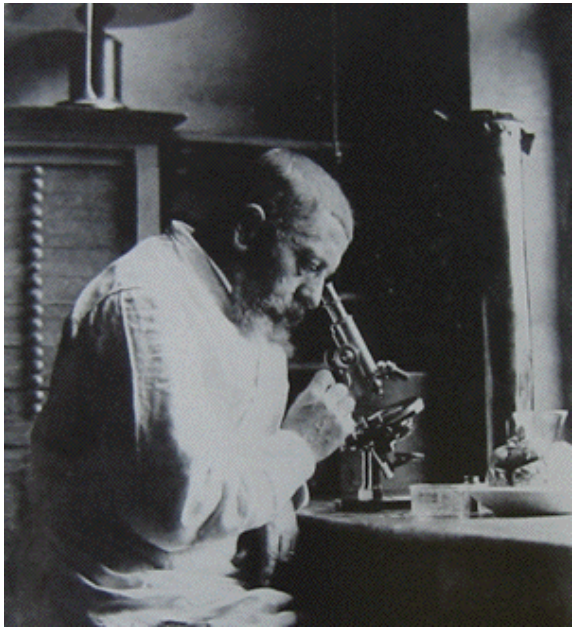
spujol@bwh.harvard.edu

Brain Anatomy

- White matter ~45% of the brain
- Myelinated nerve fibers

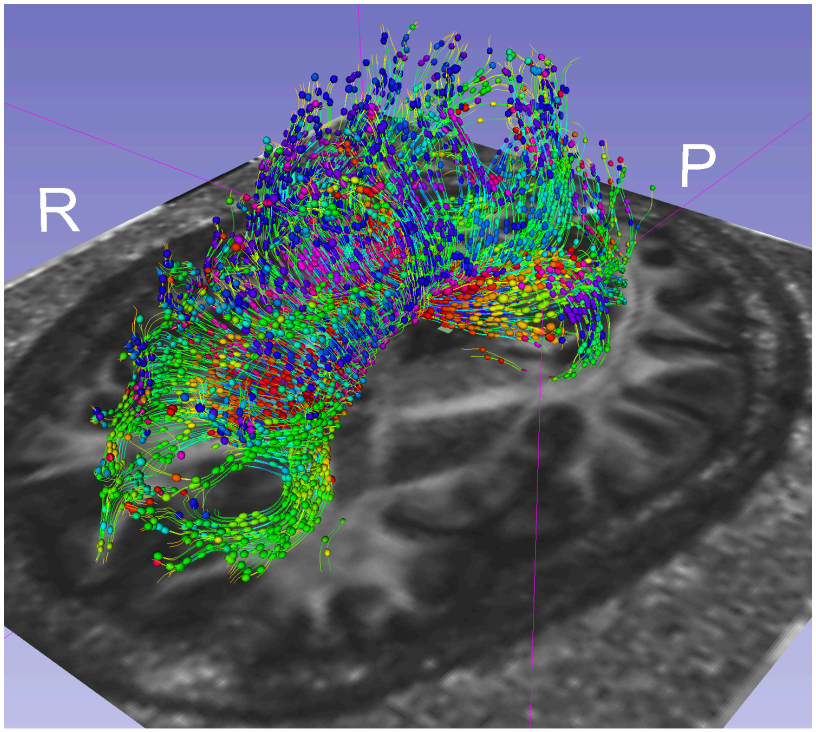
(~ 10 µm axon diameter)

White Matter Exploration



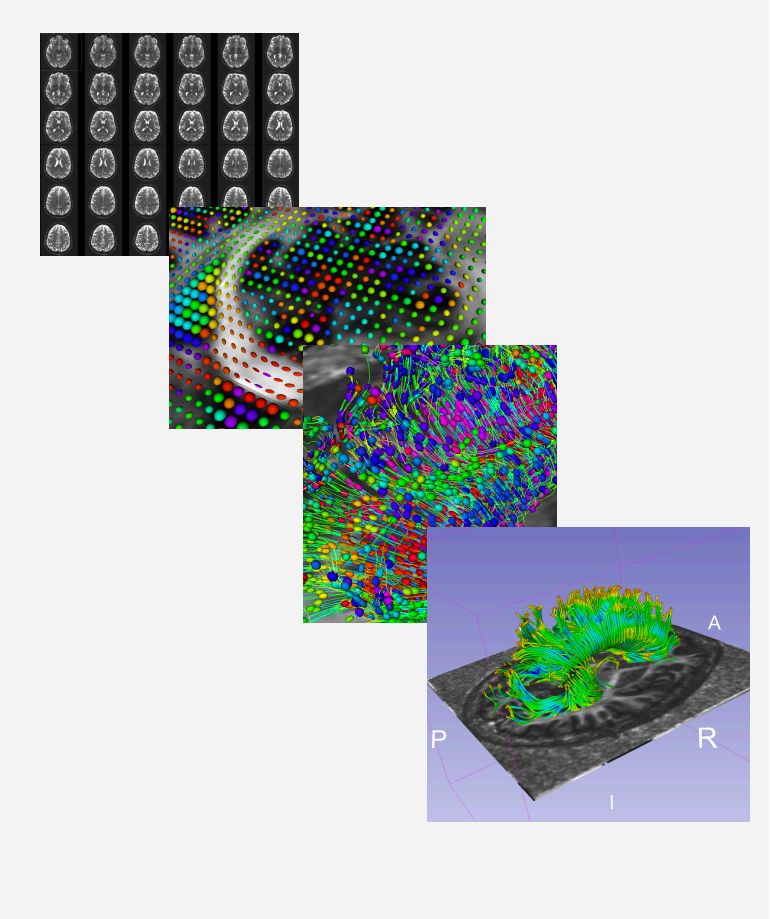
Jules Joseph Dejerine (*Anatomie des centres nerveux* (Paris, 1890-1901): Atlas of Neuroanatomy based on myelin stained preparation

White Matter Exploration



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

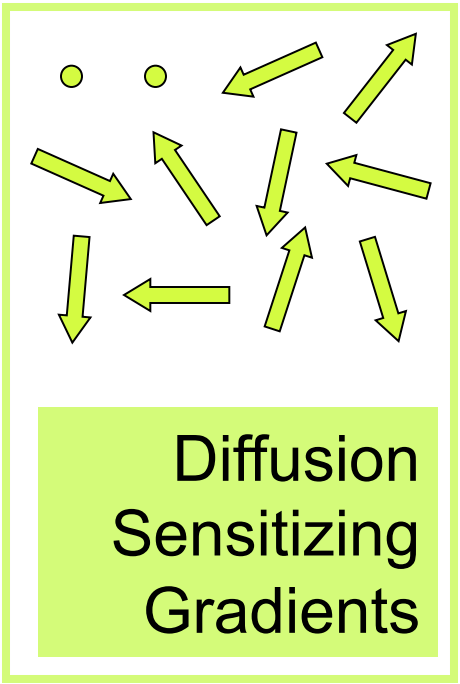
Tutorial Outline

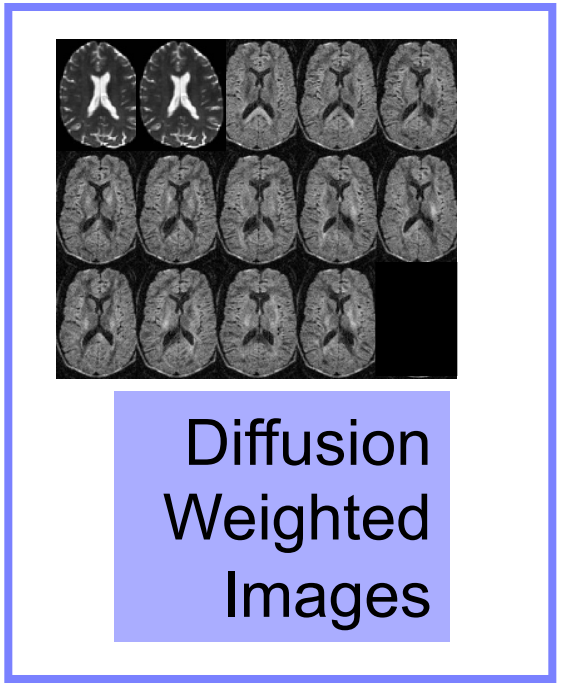


This tutorial is an introduction to the fundamentals of Diffusion MRI analysis, from the estimation of diffusion tensors to the interactive 3D visualization of fiber tracts in Slicer4.2

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)

Tutorial software

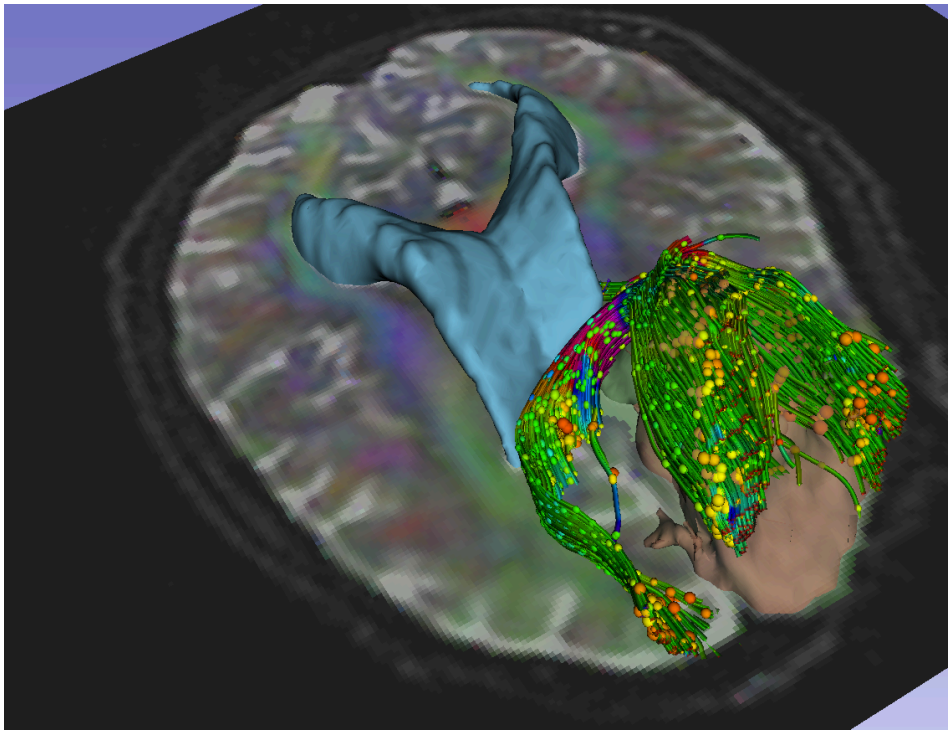
The tutorial uses the 3DSlicer version 4.2

software available at 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

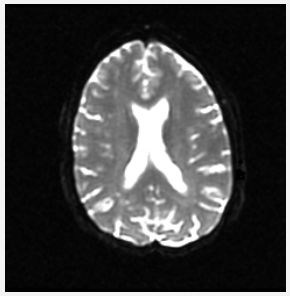
1) Estimate a tensor volume from a set of Diffusion Weighted Images

2) Understand the shape and size of the diffusion ellipsoid

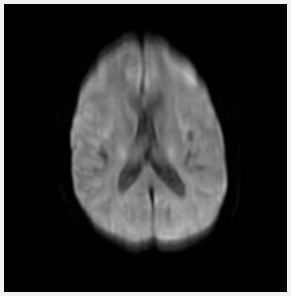
3) Reconstruct DTI tracts from a pre-defined region of interest

4) Interactively visualize DTI tracts seeded from a fiducial

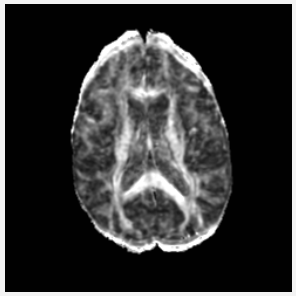
MR Diffusion Analysis Pipeline



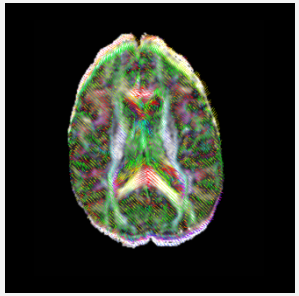
DWI
Acquisition



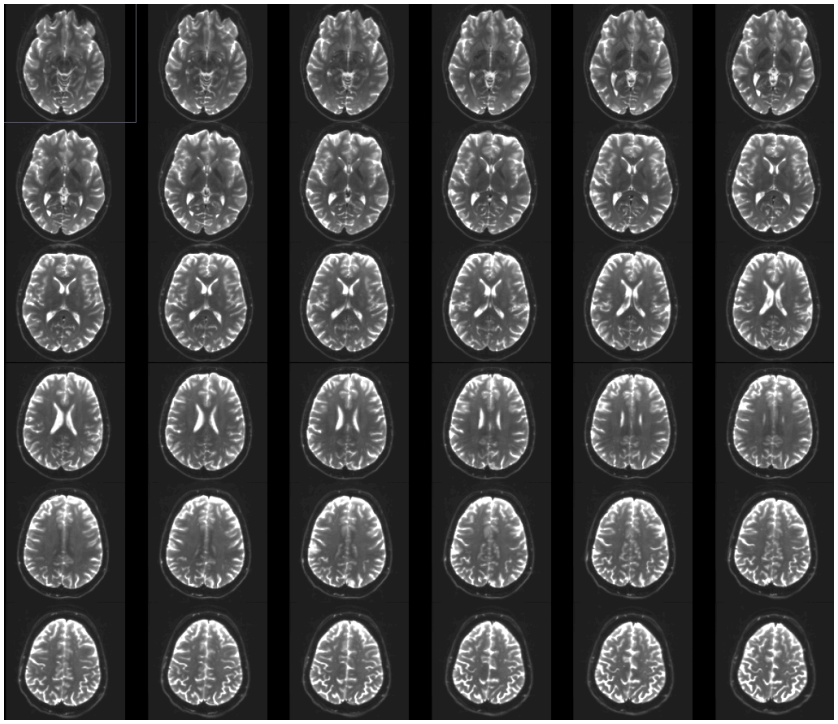
Tensor
Calculation



Scalar
Maps

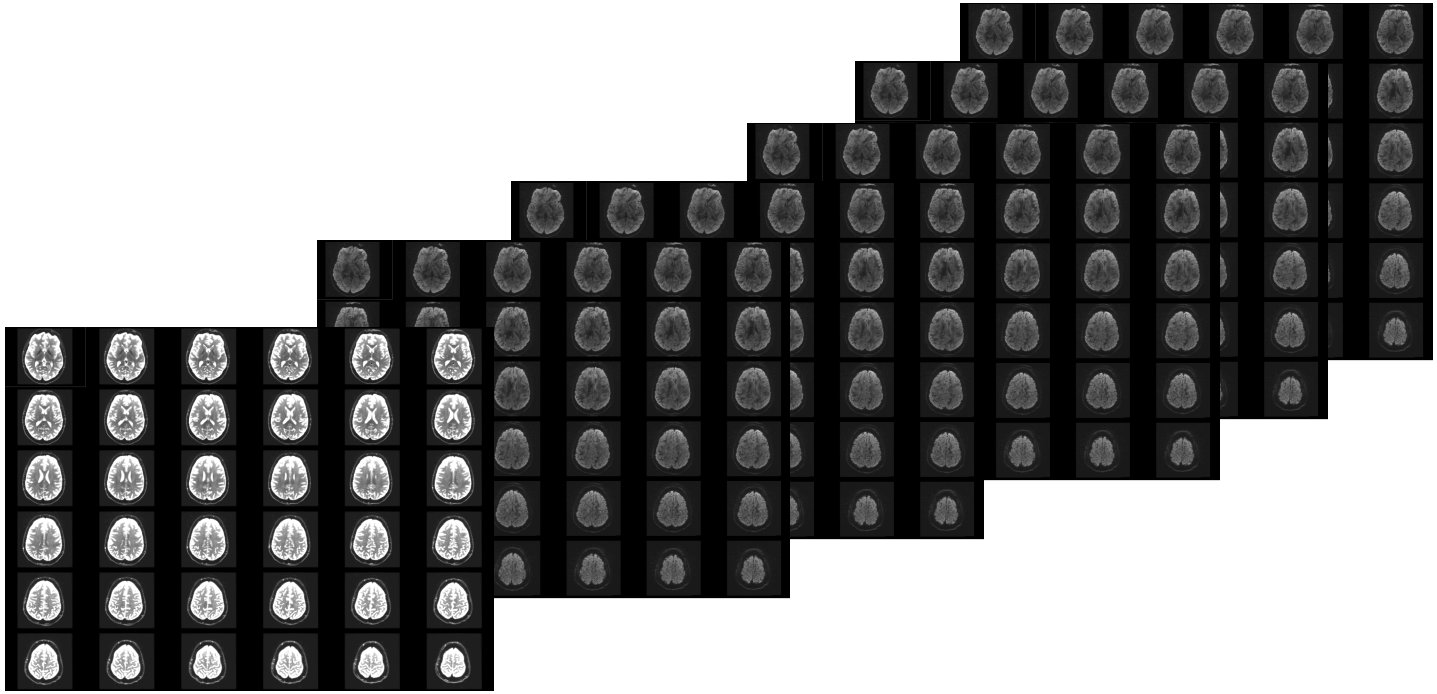


3D
Visualization



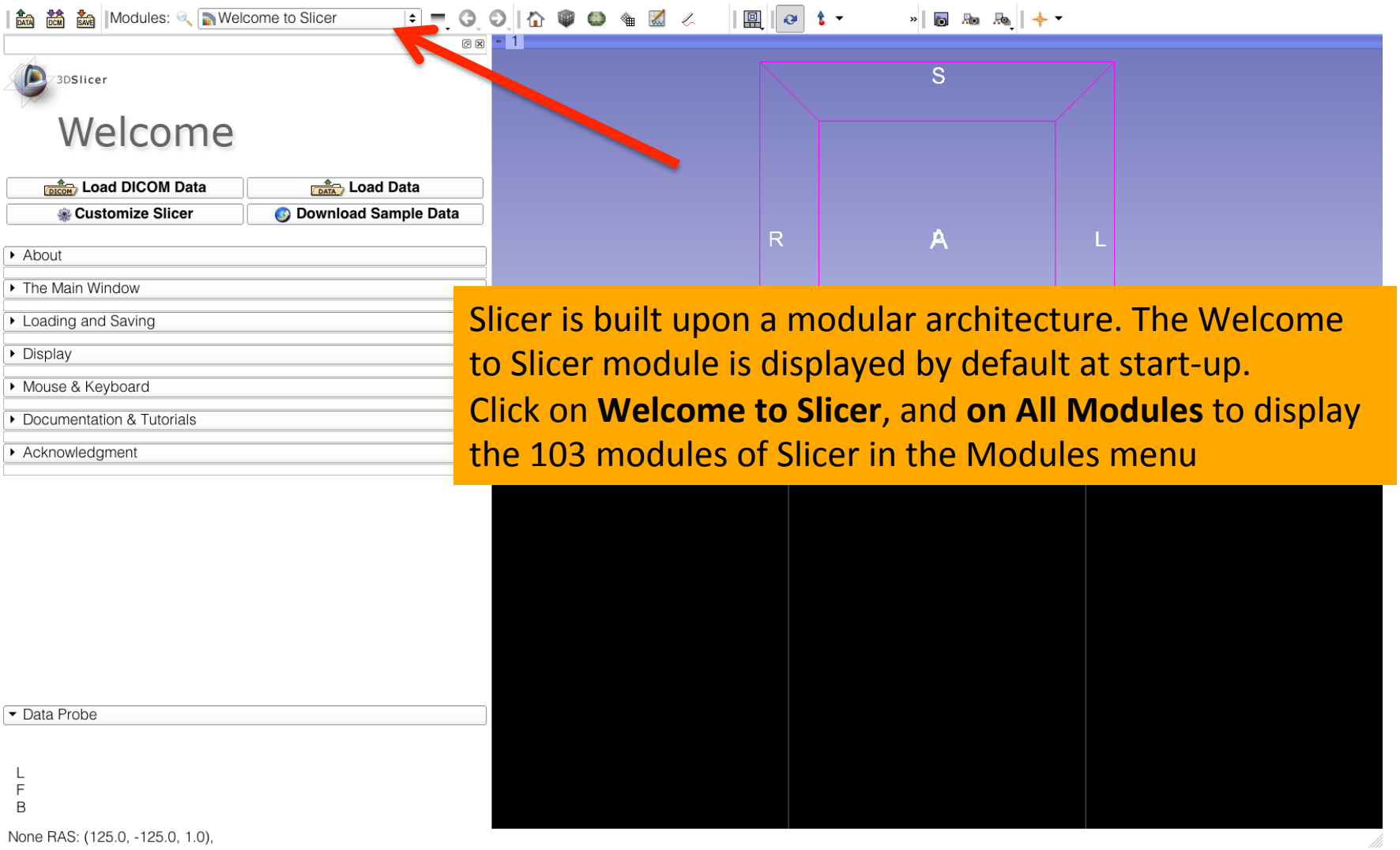
Part 1:
From DWI images to Tensors

Understanding the DWI dataset



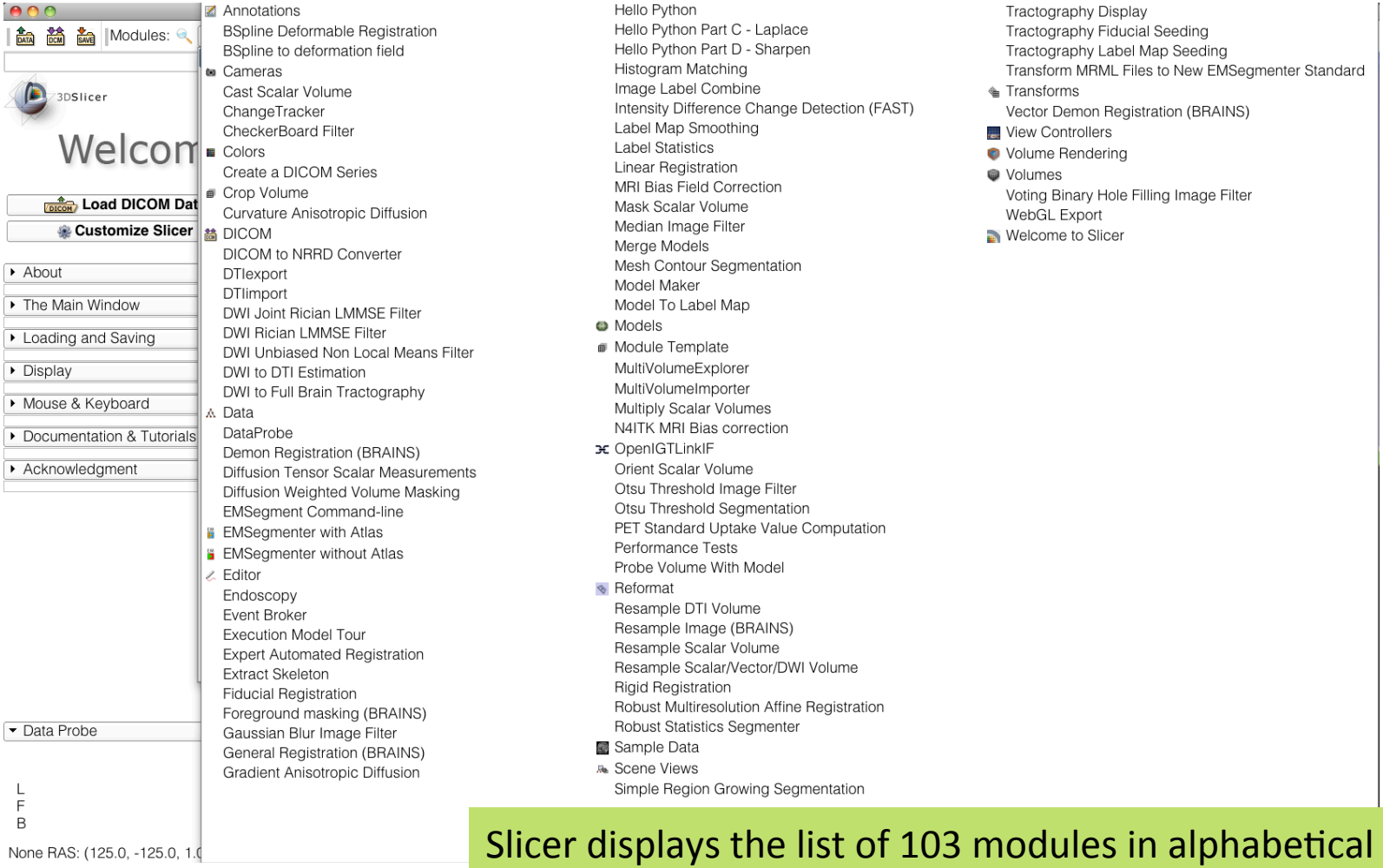
The Diffusion Weighted Imaging (DWI) dataset is composed of 1 volume acquired without diffusion-sensitizing gradient, and 41 volumes acquired with 41 different diffusion-sensitizing gradient directions.

Start the Slicer Software



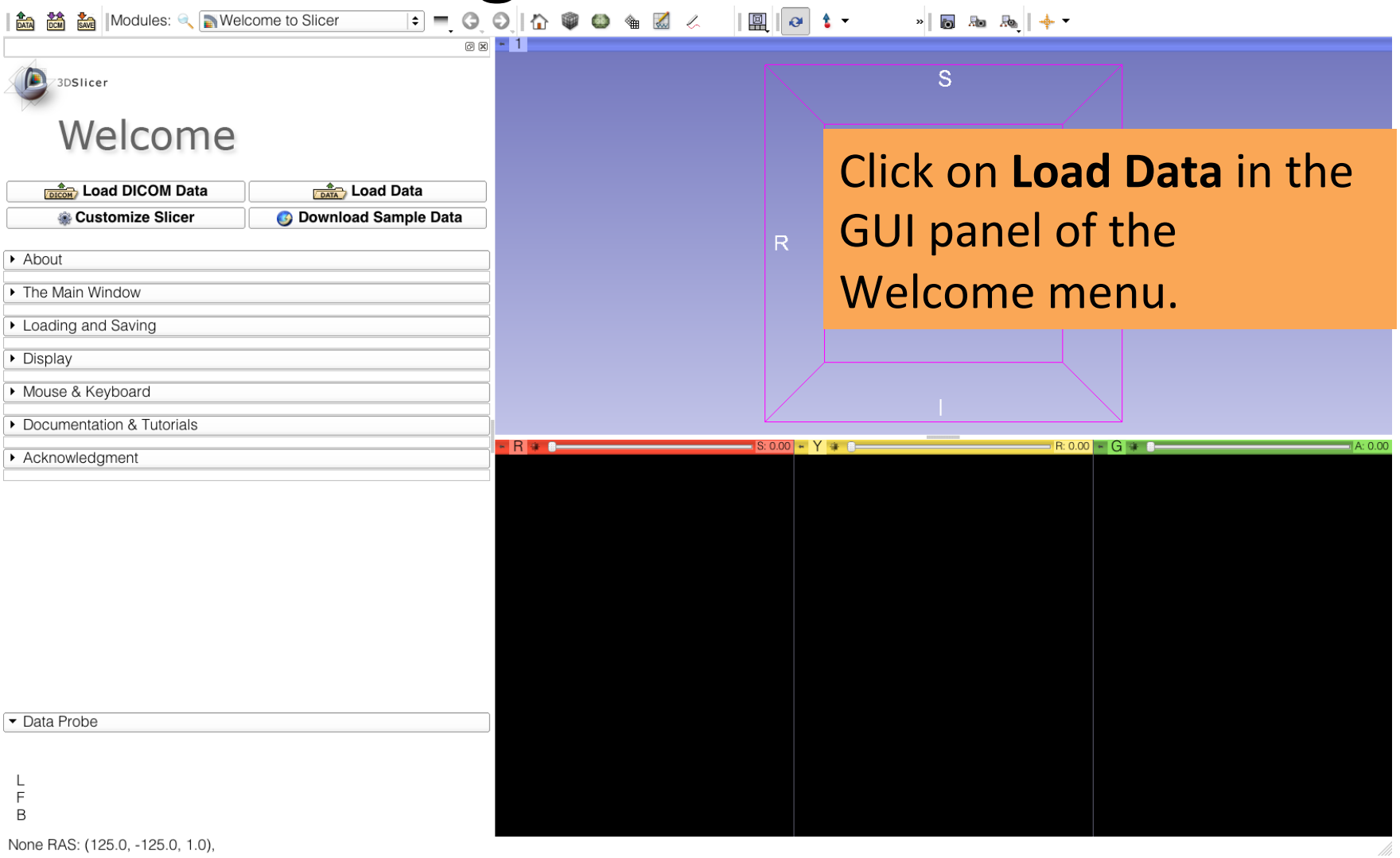
Slicer is built upon a modular architecture. The Welcome to Slicer module is displayed by default at start-up.
Click on **Welcome to Slicer**, and **on All Modules** to display the 103 modules of Slicer in the Modules menu

Start the Slicer software

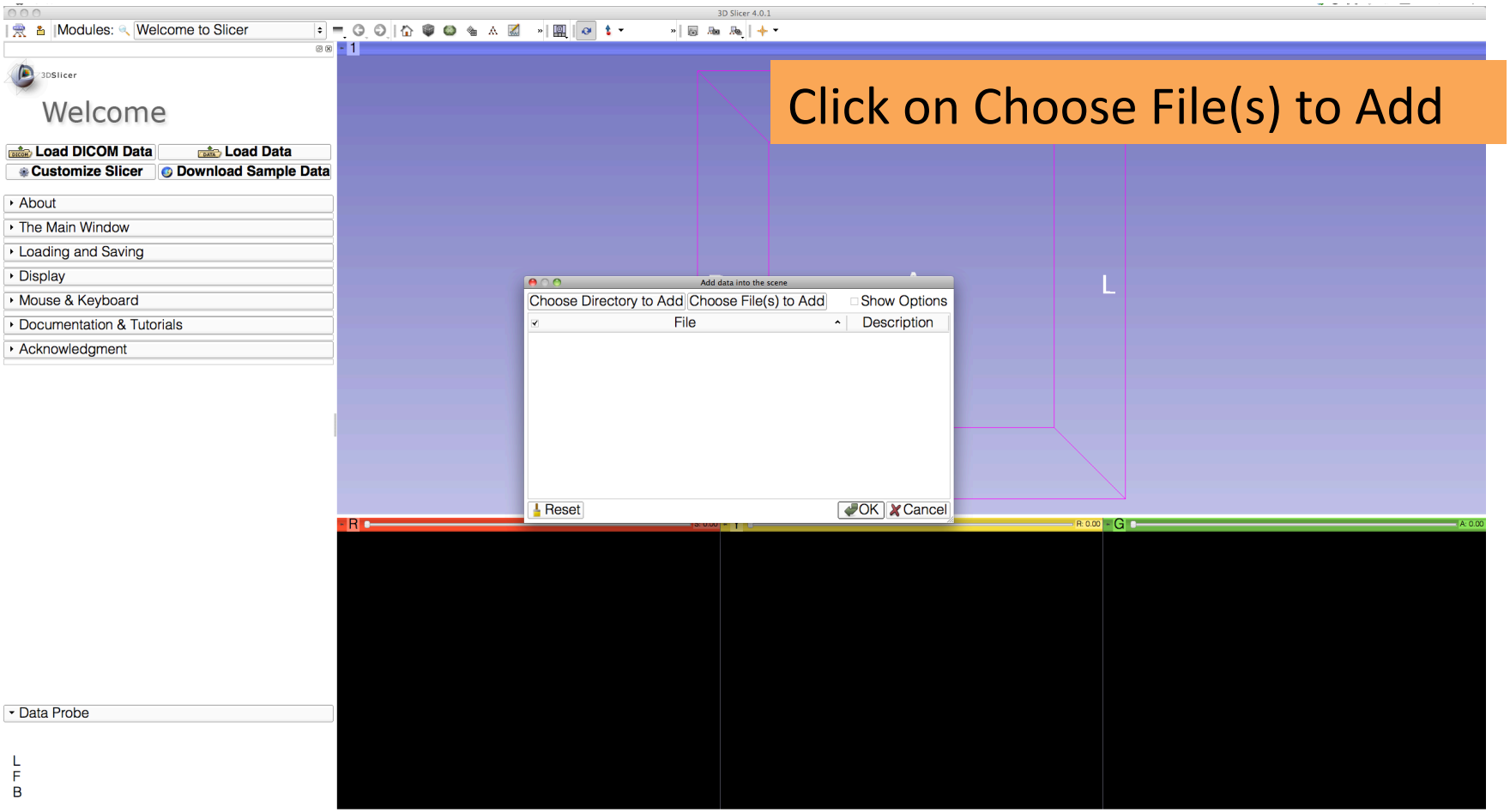


Slicer displays the list of 103 modules in alphabetical order.

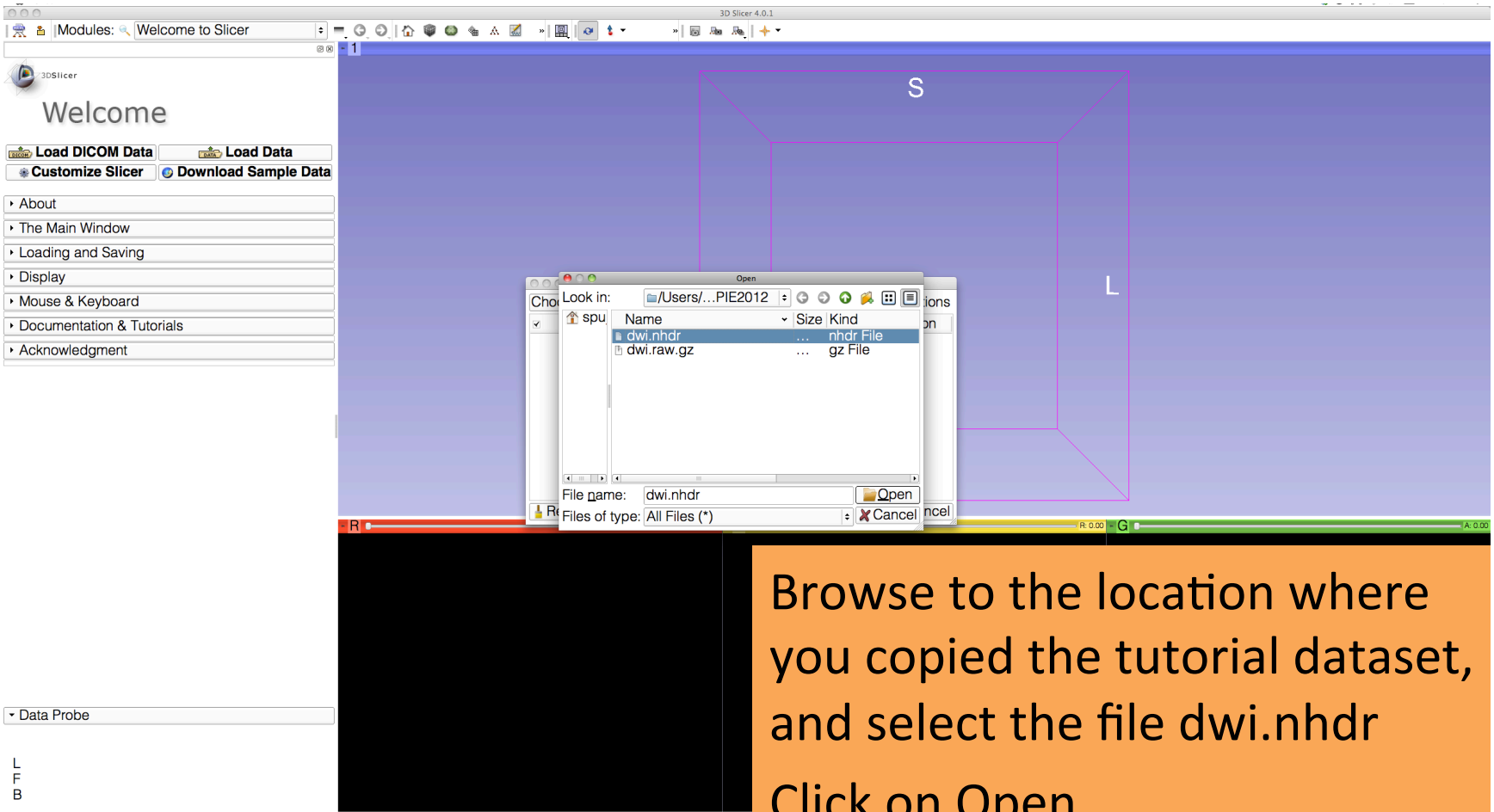
Loading the DWI dataset



Loading the DWI dataset



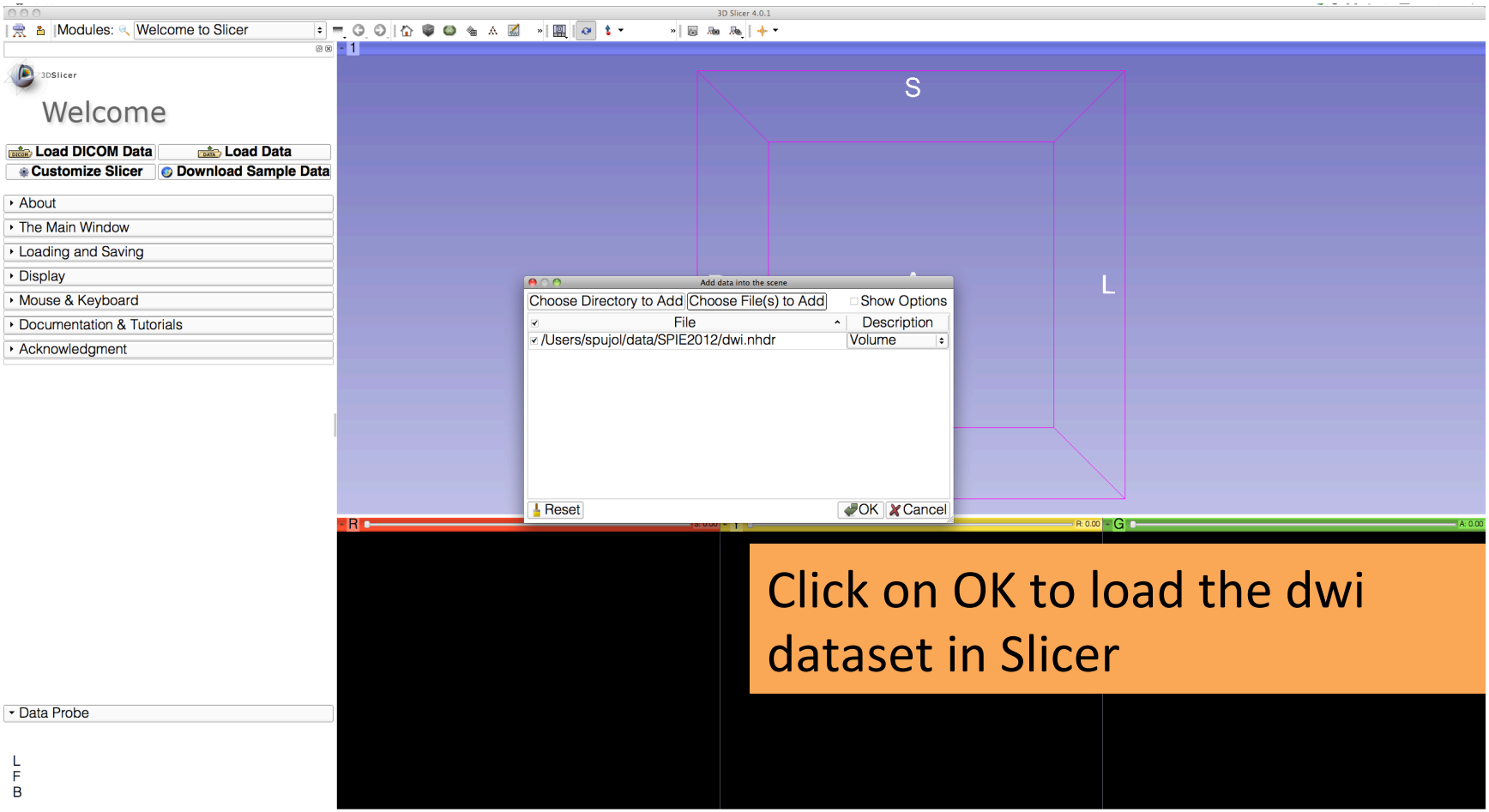
Loading the DWI dataset



Browse to the location where you copied the tutorial dataset, and select the file dwi.nhdr

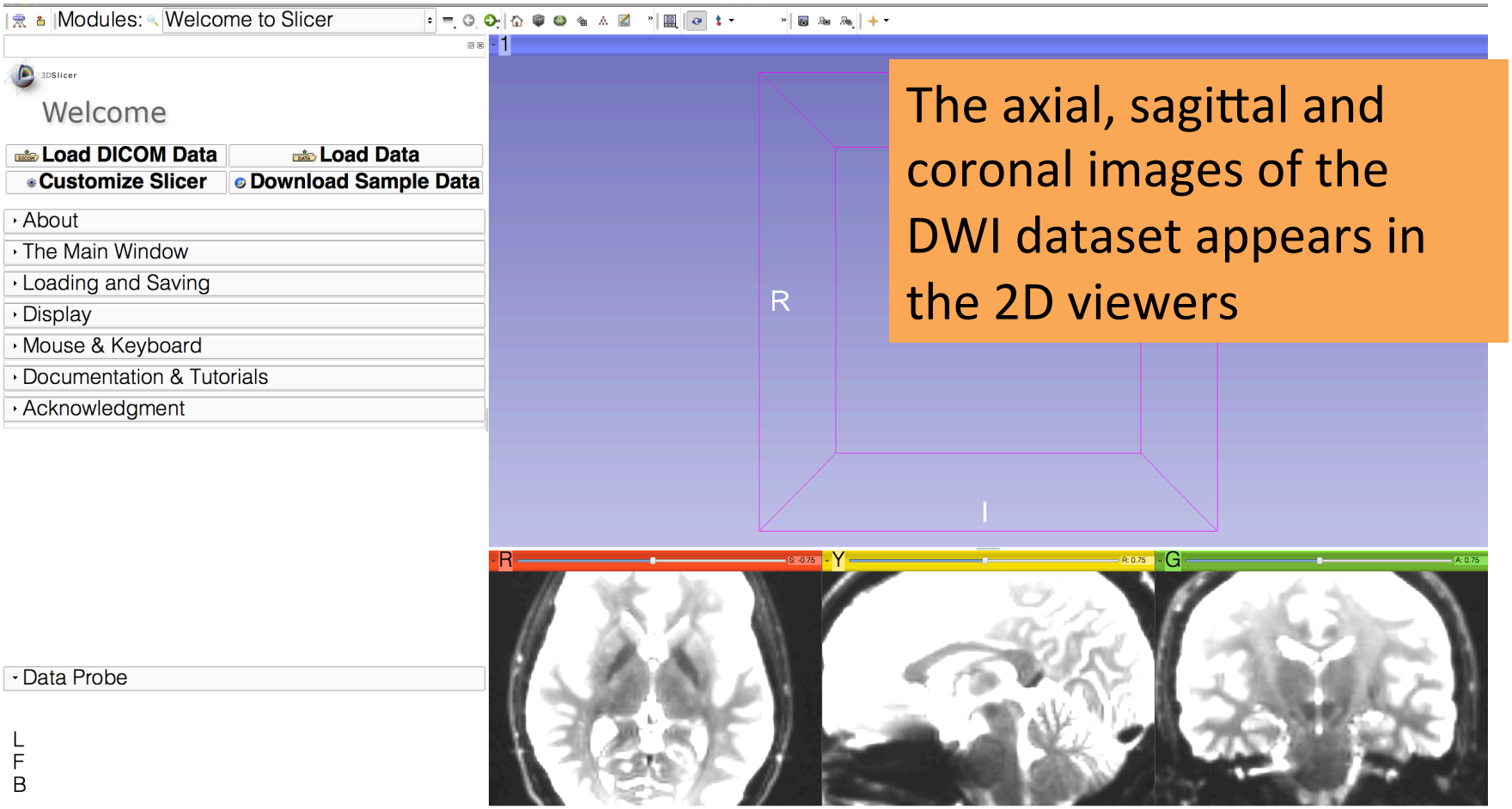
Click on Open

Loading the DWI dataset



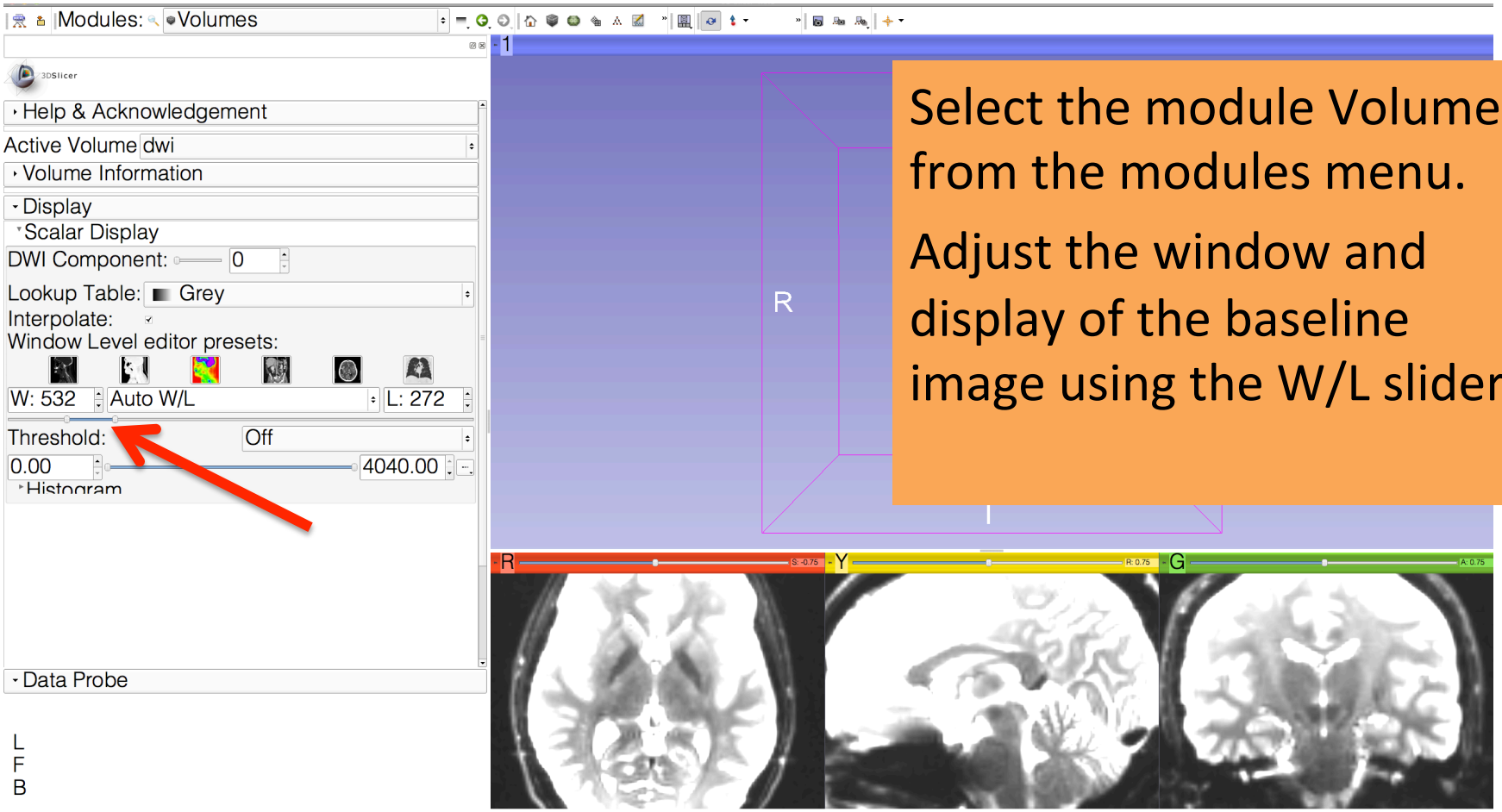
Click on OK to load the dwi dataset in Slicer

Loading the DWI dataset



The axial, sagittal and coronal images of the DWI dataset appears in the 2D viewers

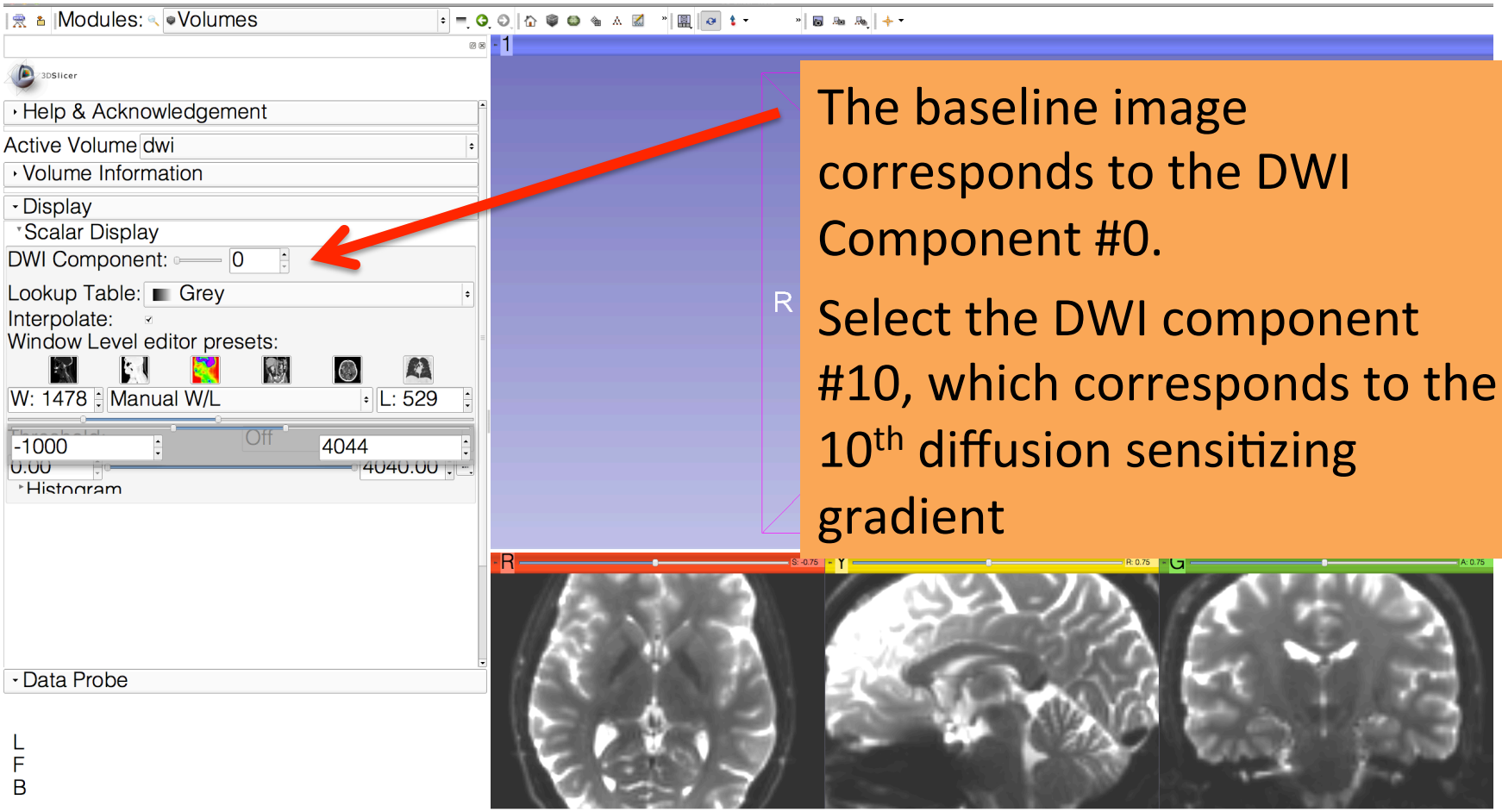
Adjusting Window and Level



Select the module Volumes from the modules menu.

Adjust the window and display of the baseline image using the W/L slider

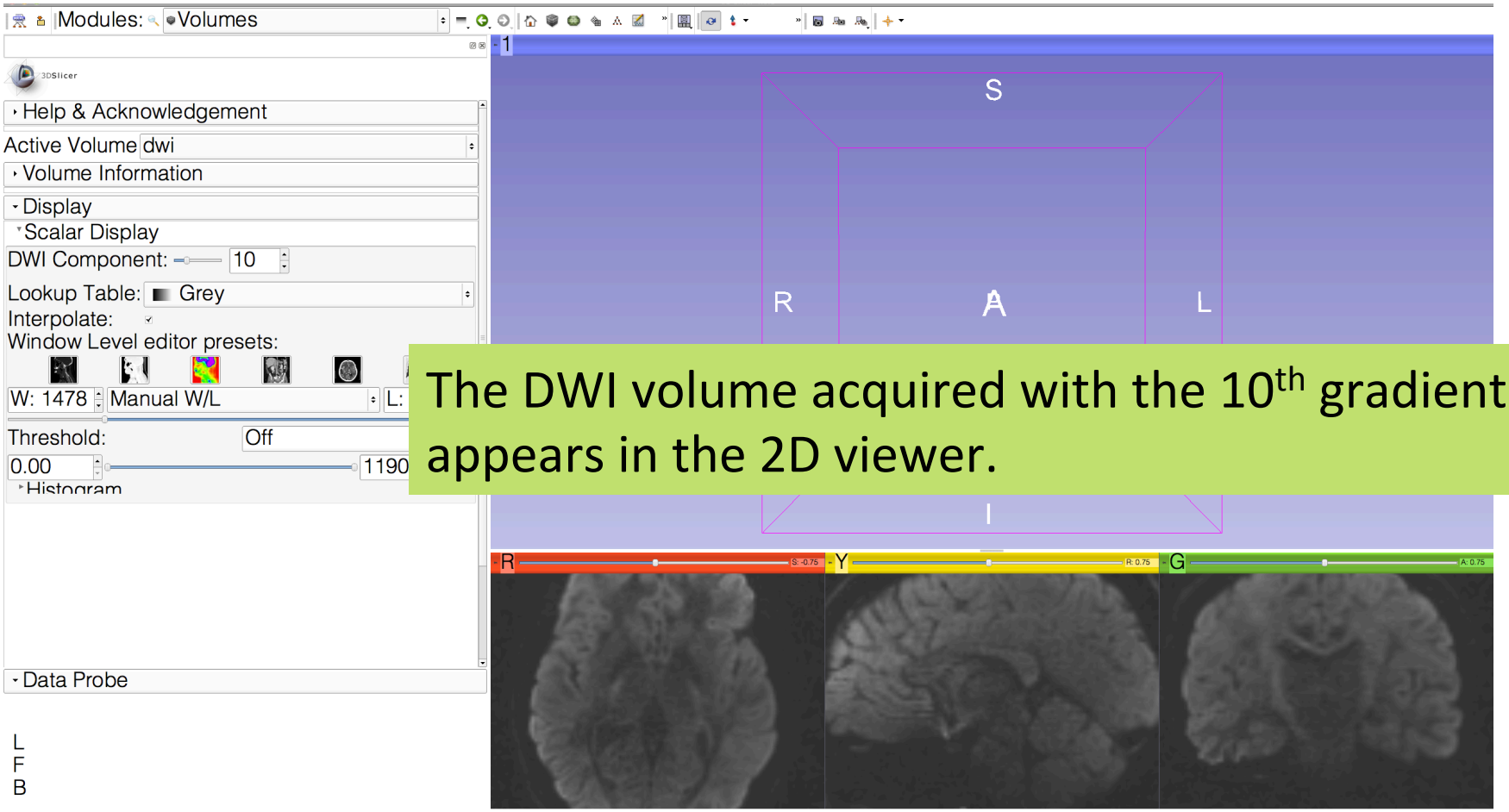
Exploring the DWI dataset



The baseline image corresponds to the DWI Component #0.

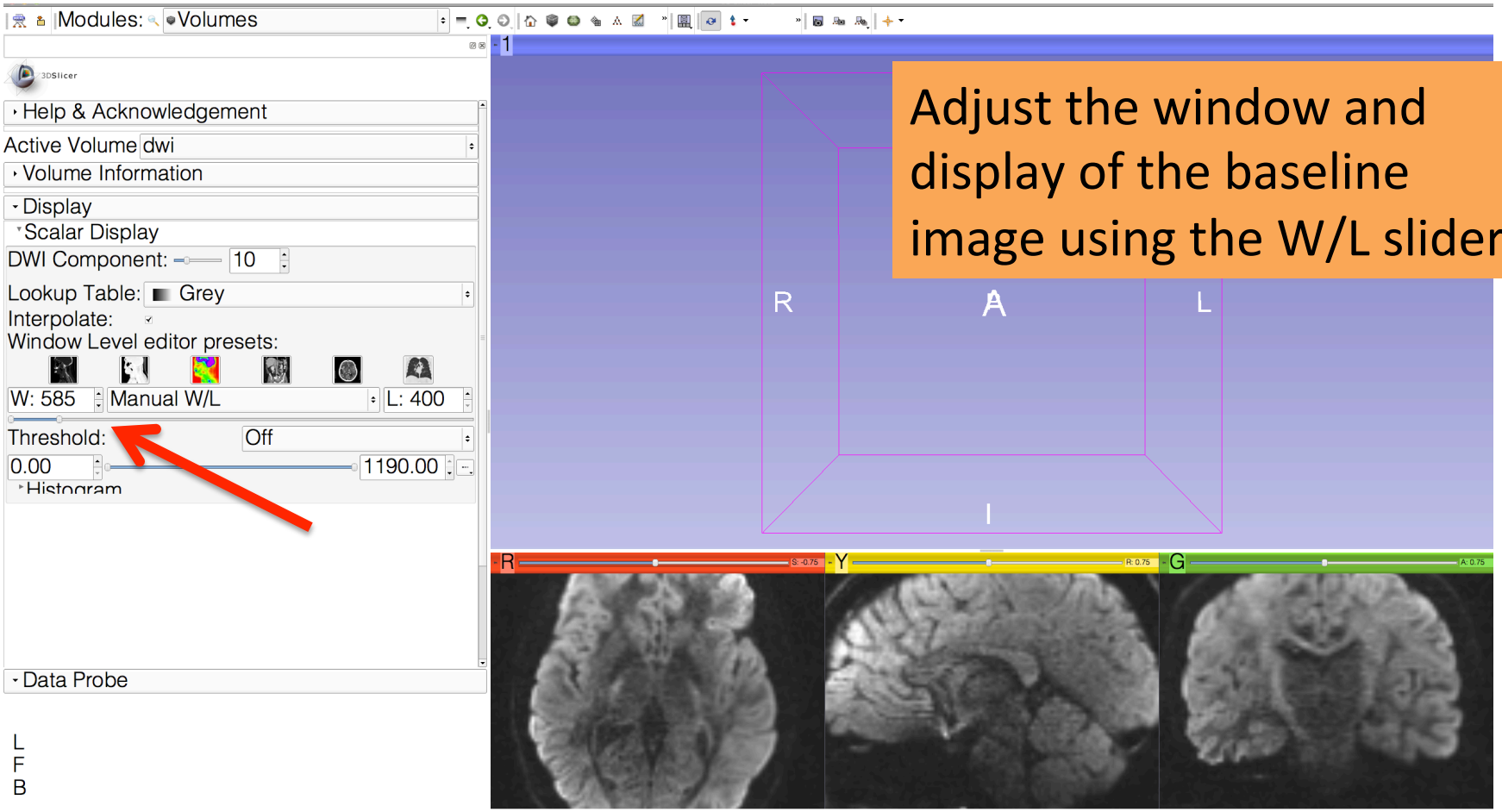
Select the DWI component #10, which corresponds to the 10th diffusion sensitizing gradient

Exploring the DWI dataset



The DWI volume acquired with the 10th gradient appears in the 2D viewer.

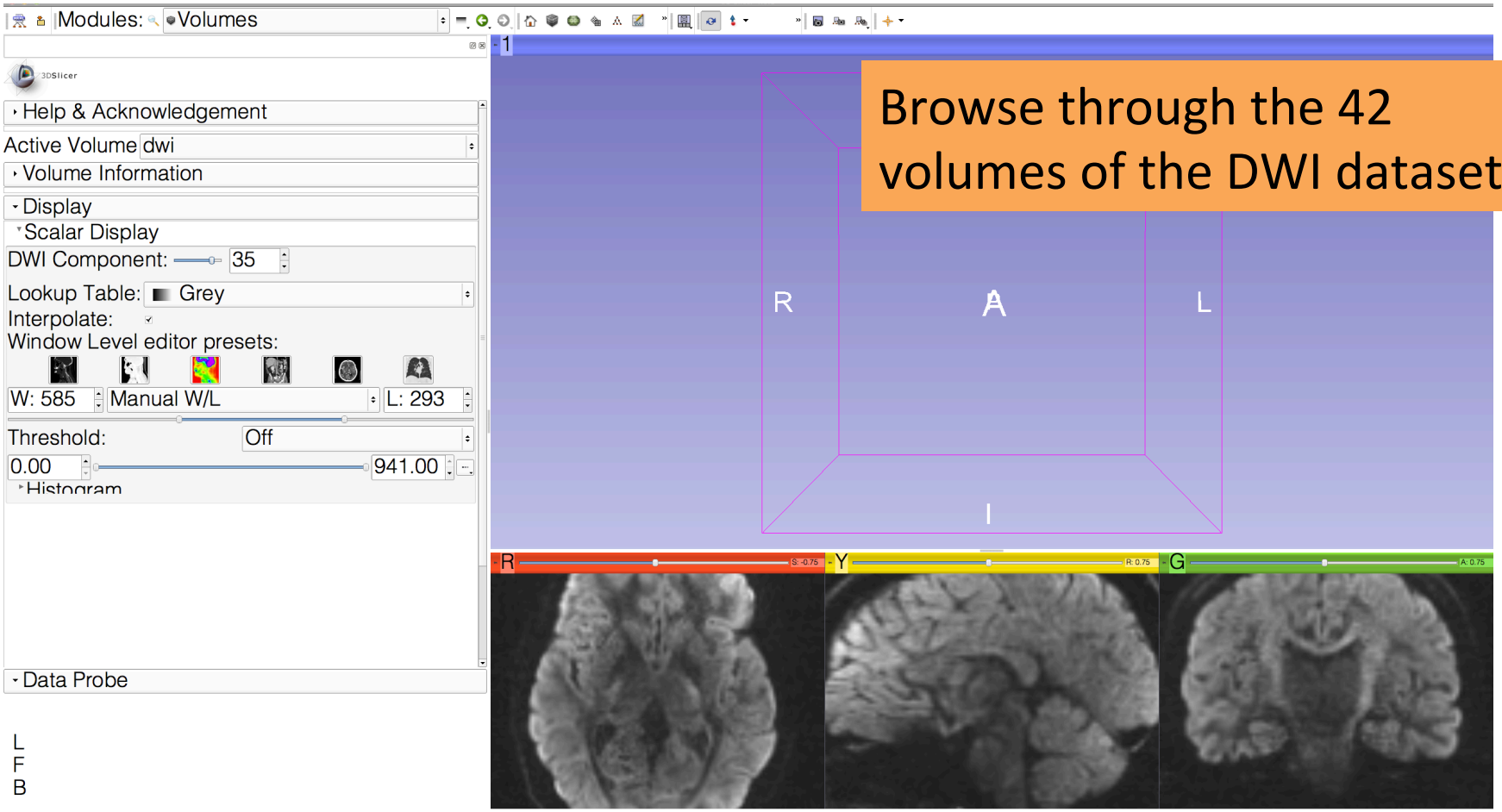
Exploring the DWI dataset



Adjust the window and display of the baseline image using the W/L slider

L
F
B

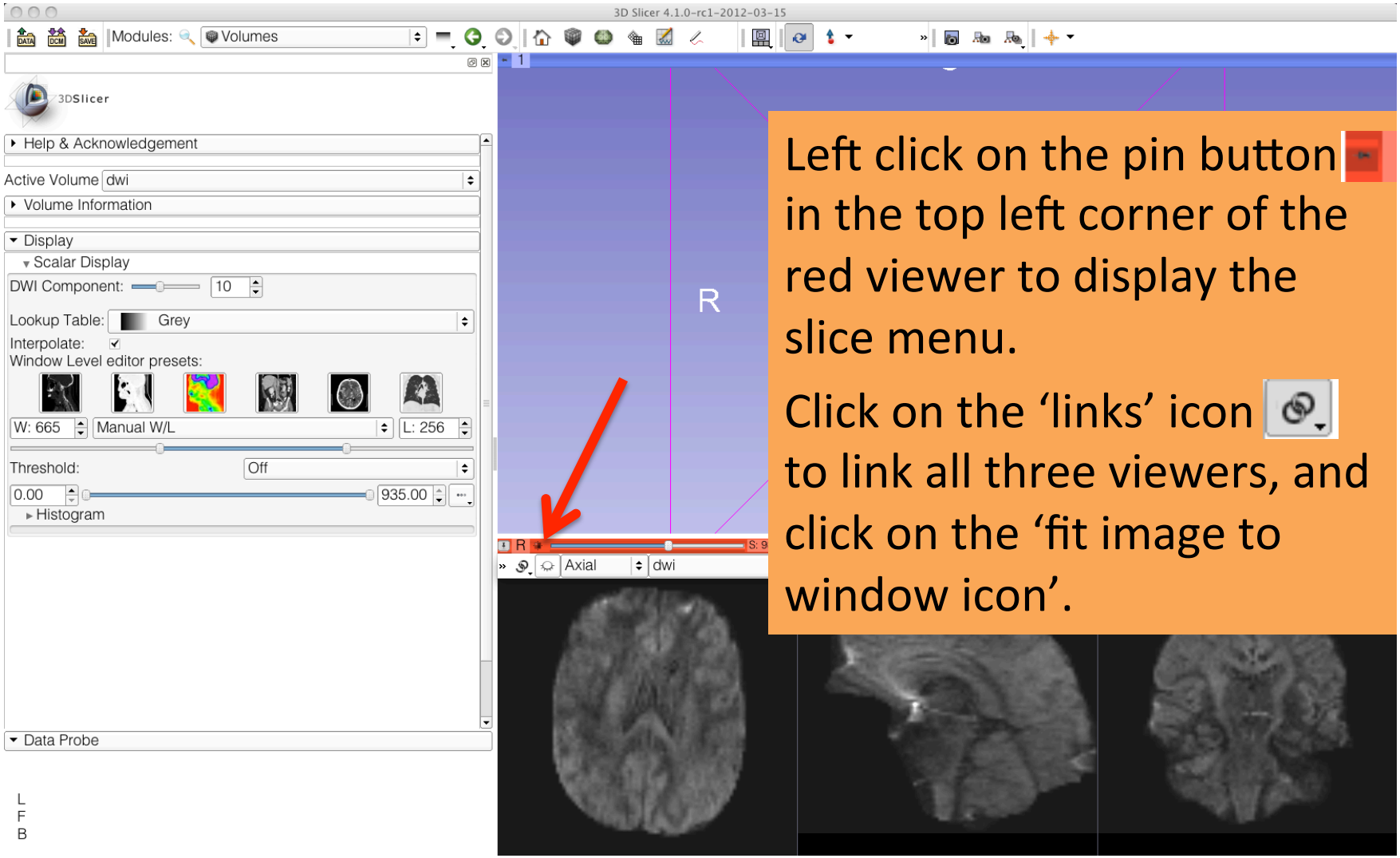
Exploring the DWI dataset



Browse through the 42 volumes of the DWI dataset

L
F
B

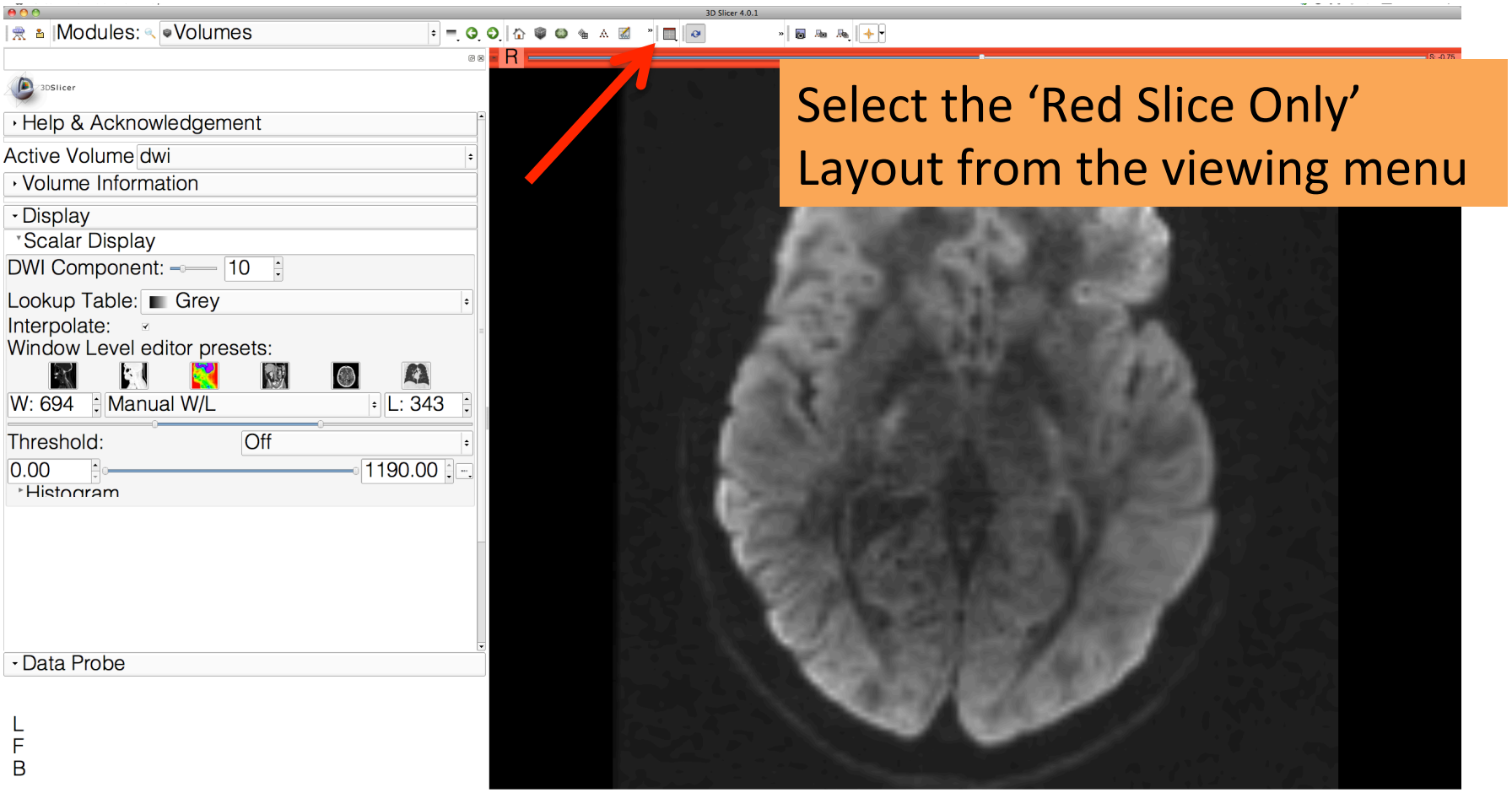
Exploring the DWI dataset



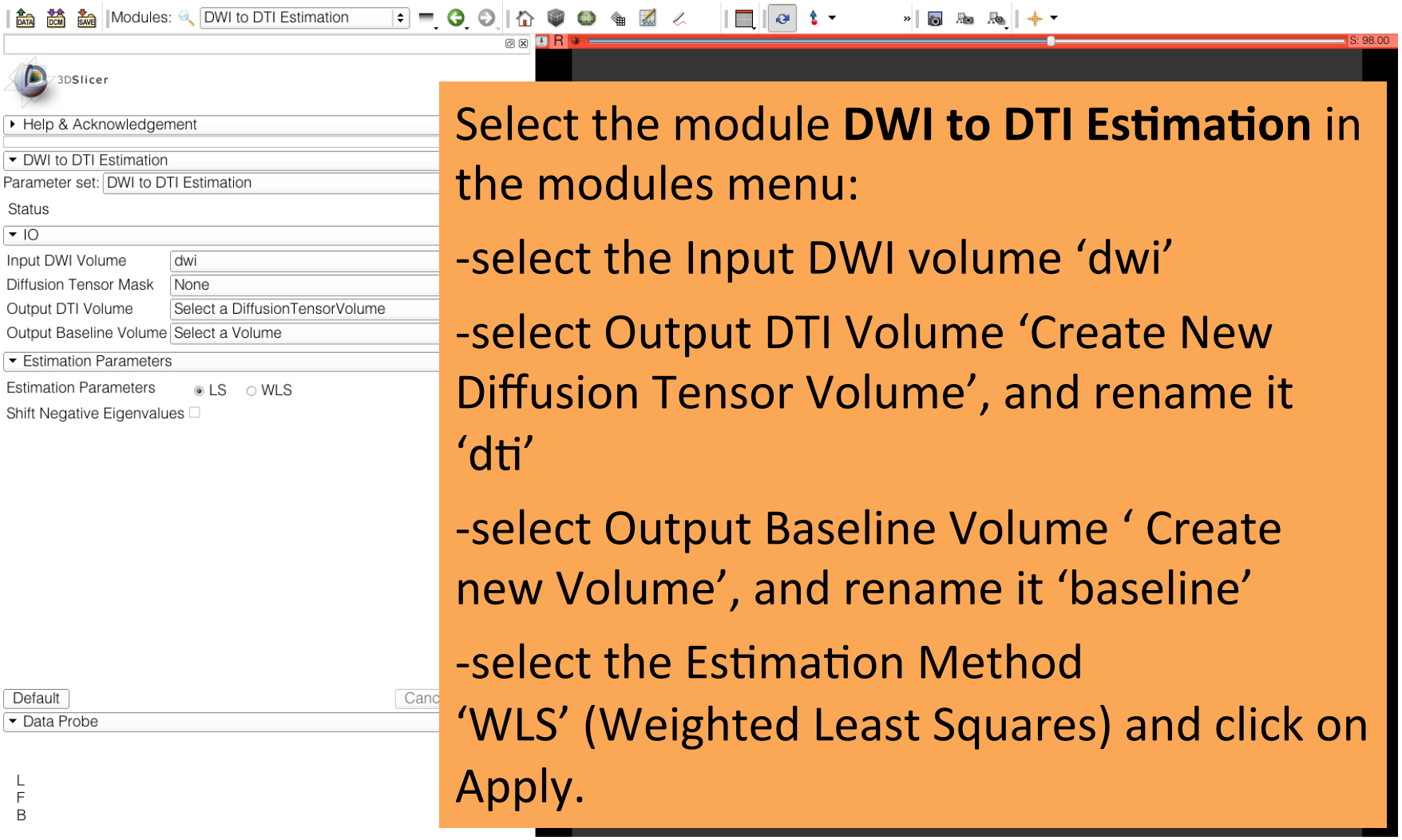
Left click on the pin button in the top left corner of the red viewer to display the slice menu.

Click on the 'links' icon to link all three viewers, and click on the 'fit image to window icon'.

Exploring the DWI dataset



Diffusion Tensor Estimation



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

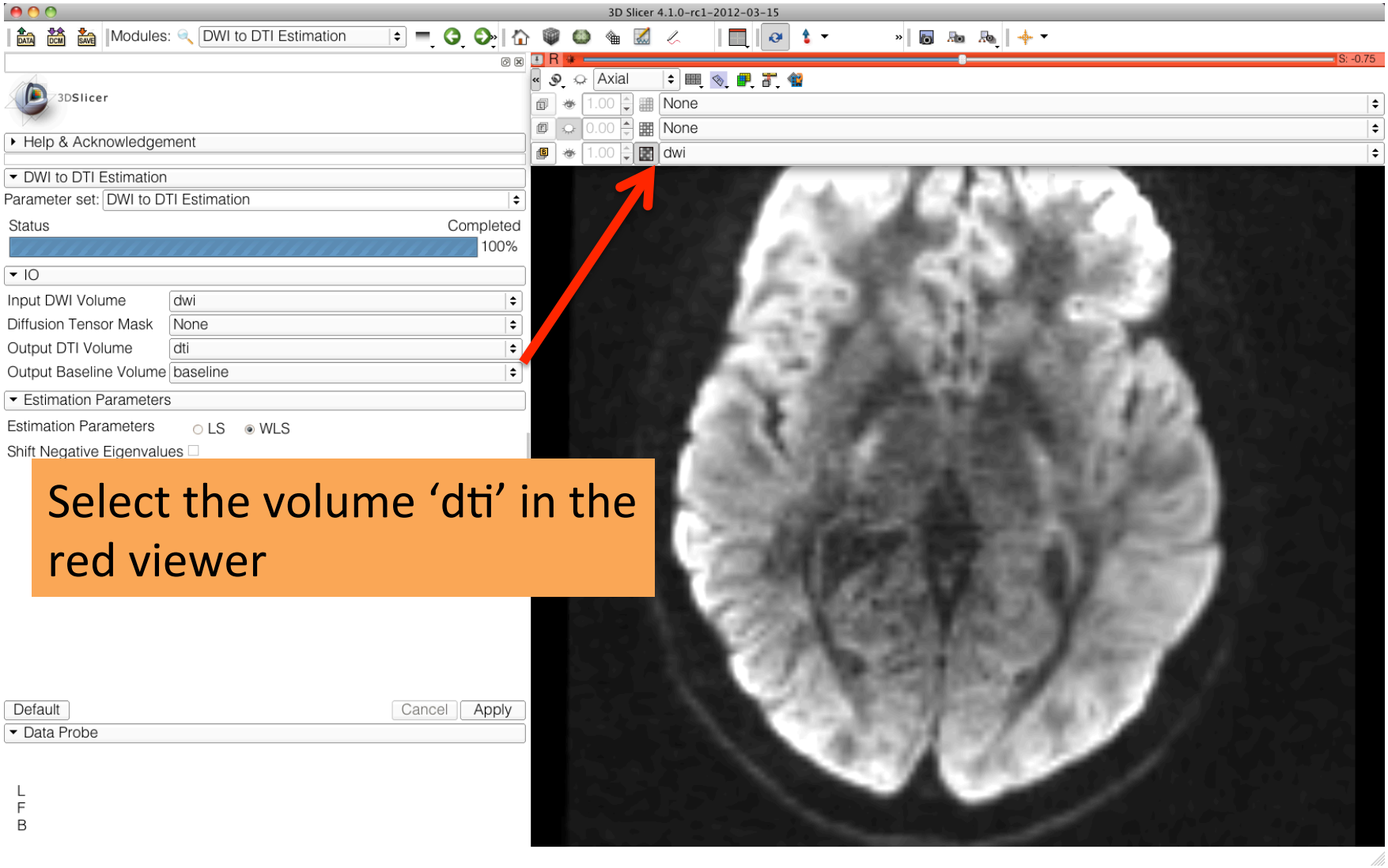
-select the Input DWI volume ‘dwi’

-select Output DTI Volume ‘Create New Diffusion Tensor Volume’, and rename it ‘dti’

-select Output Baseline Volume ‘ Create new Volume’, and rename it ‘baseline’

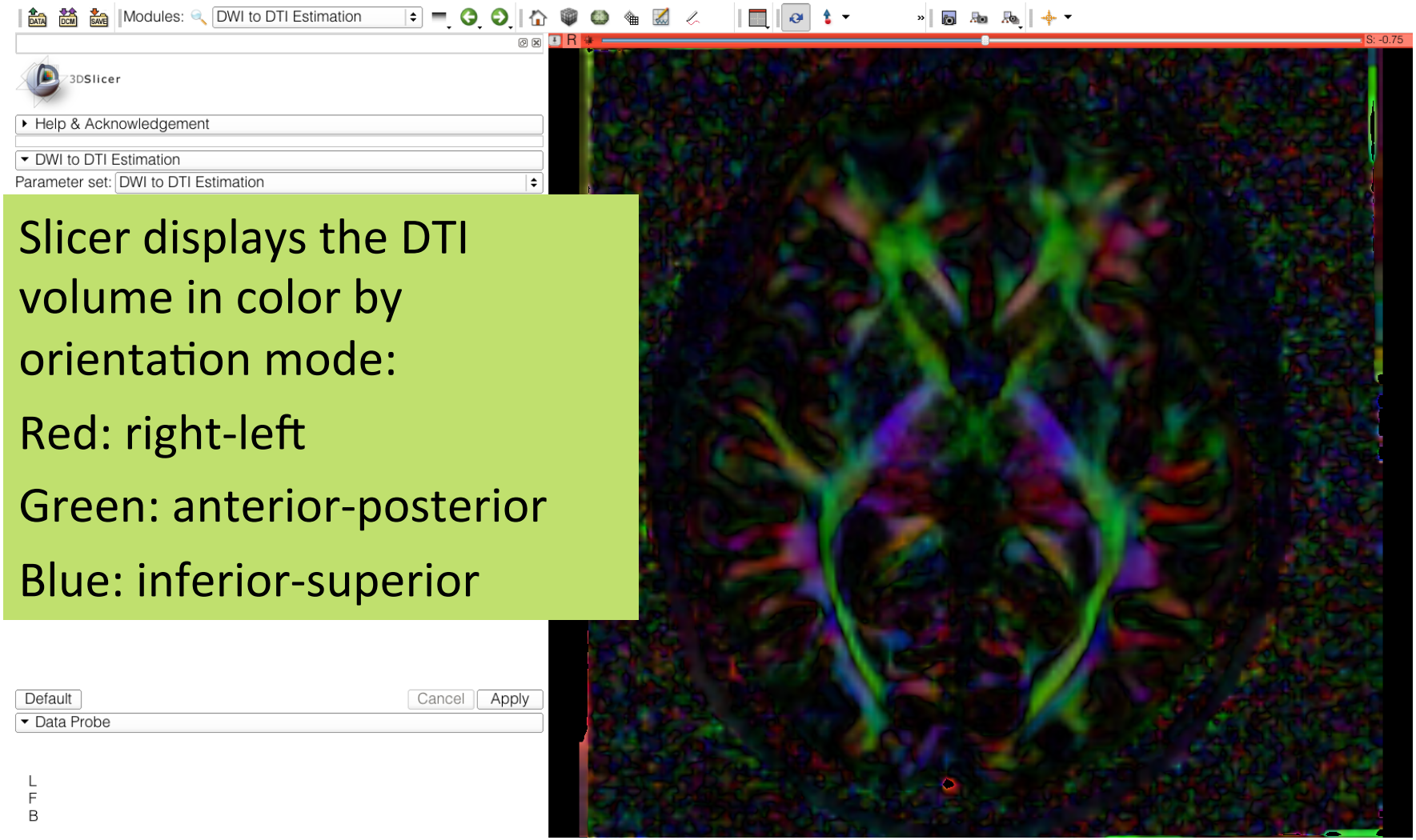
-select the Estimation Method ‘WLS’ (Weighted Least Squares) and click on Apply.

Diffusion Tensor Estimation



Select the volume 'dti' in the red viewer

Diffusion Tensor Estimation



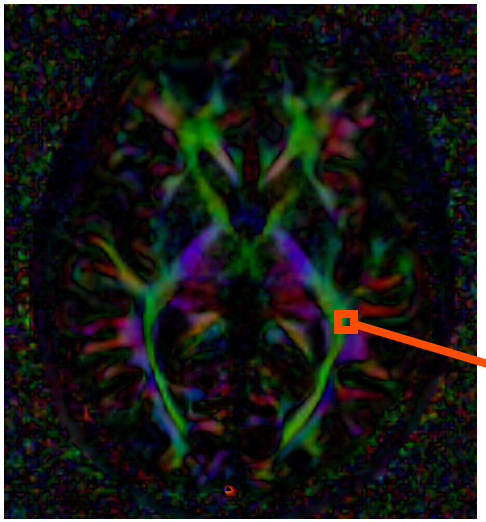
Slicer displays the DTI volume in color by orientation mode:

Red: right-left

Green: anterior-posterior

Blue: inferior-superior

Diffusion Tensor Data



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

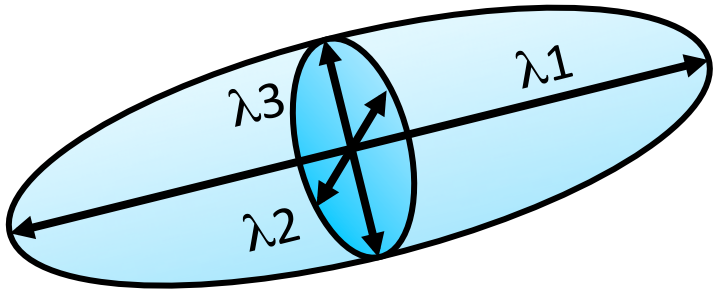
Stejskal-Tanner equation (1965)

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

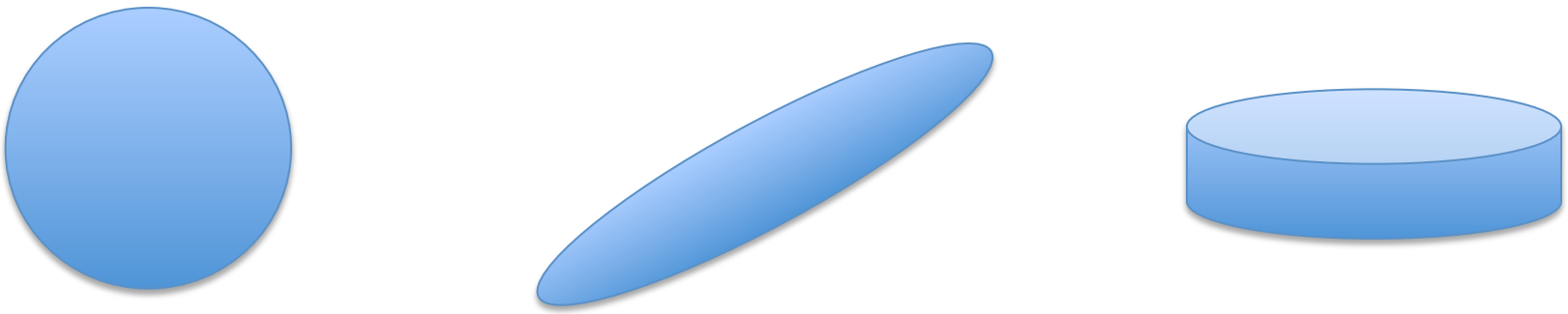
The diffusion tensor <u>D</u> in the voxel (I,J,K) is a 3x3 symmetric matrix.

Diffusion Tensor

- The diffusion tensor D in 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 λ1, λ2, λ3 to characterize the size and shape of the diffusion tensor.



Diffusion Tensor Shape



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

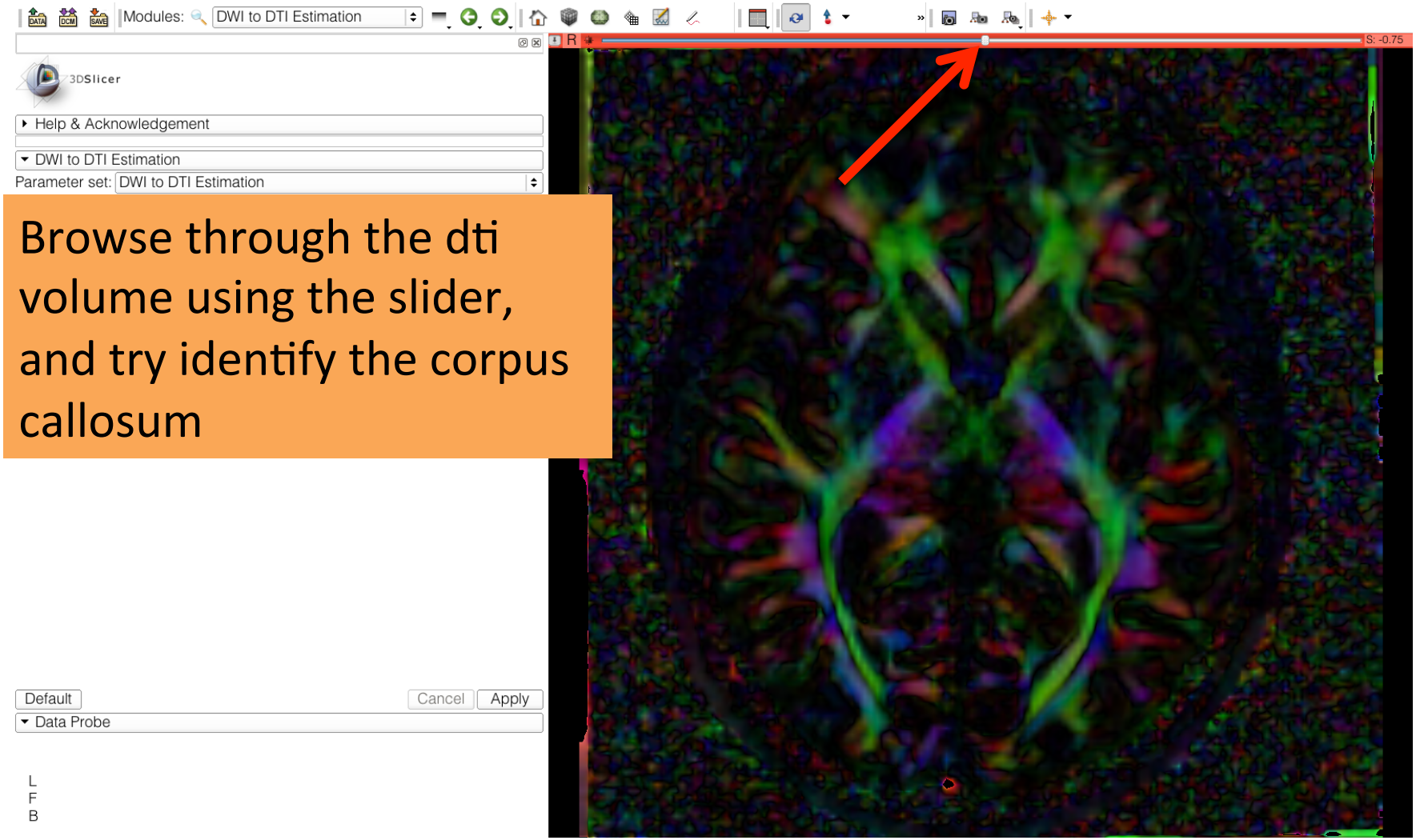
$\lambda 1 >> \lambda 2, \lambda 3$

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

Isotropic media
(CSF, gray matter)

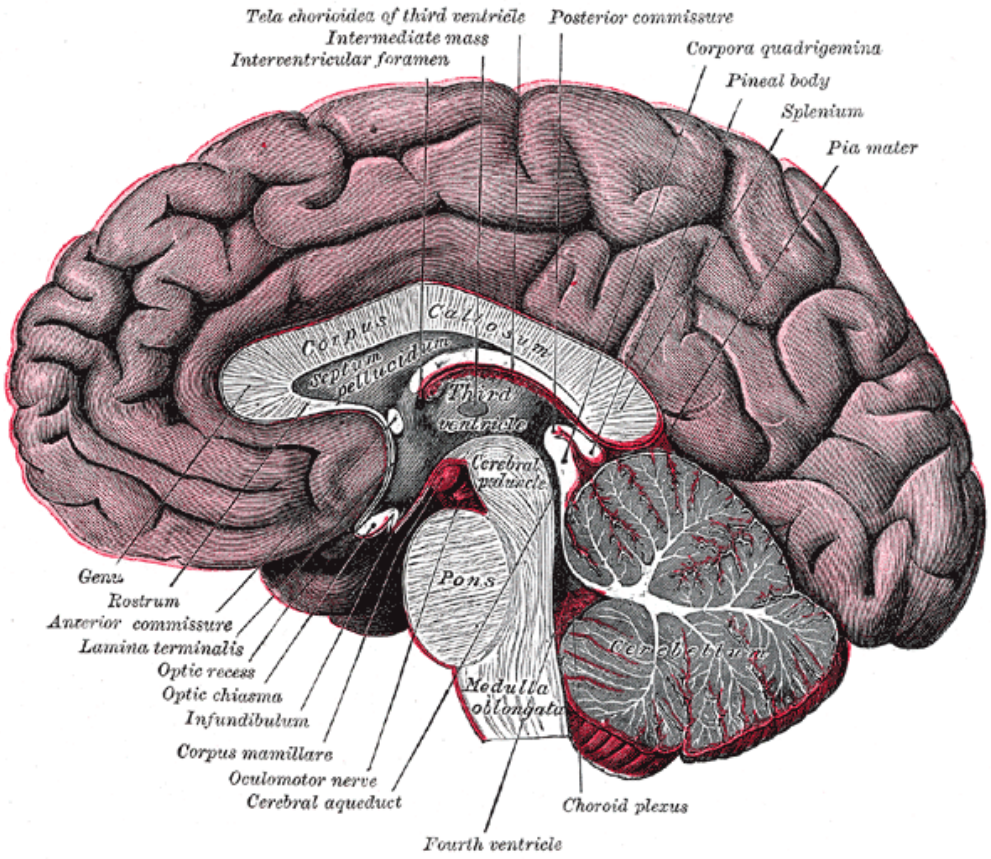
Anisotropic media
(white matter)

Exploring the Diffusion Tensor Data



Browse through the dti volume using the slider, and try identify the corpus callosum

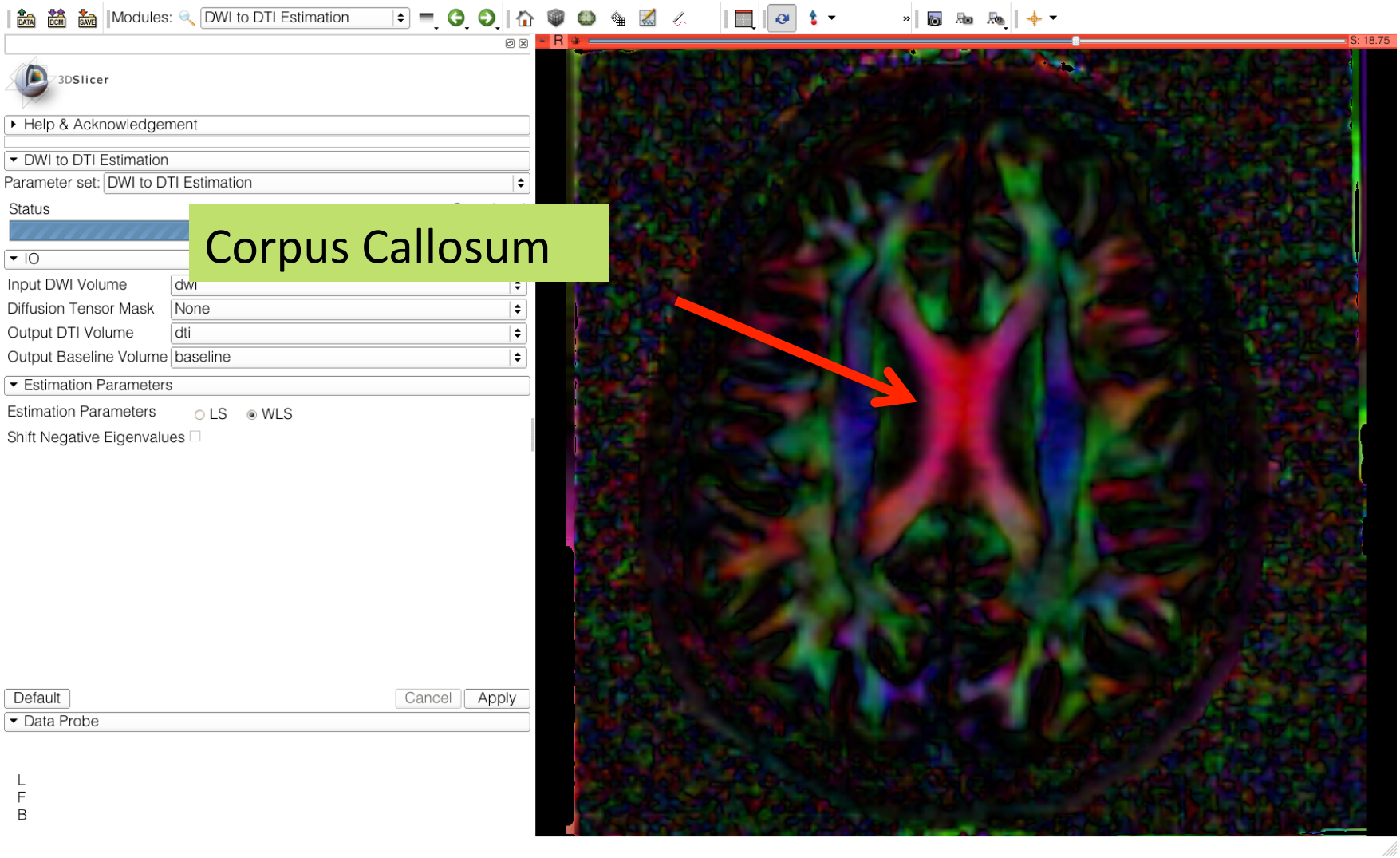
Corpus Callosum



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

Image from Gray's Anatomy

Exploring the Diffusion Tensor Data

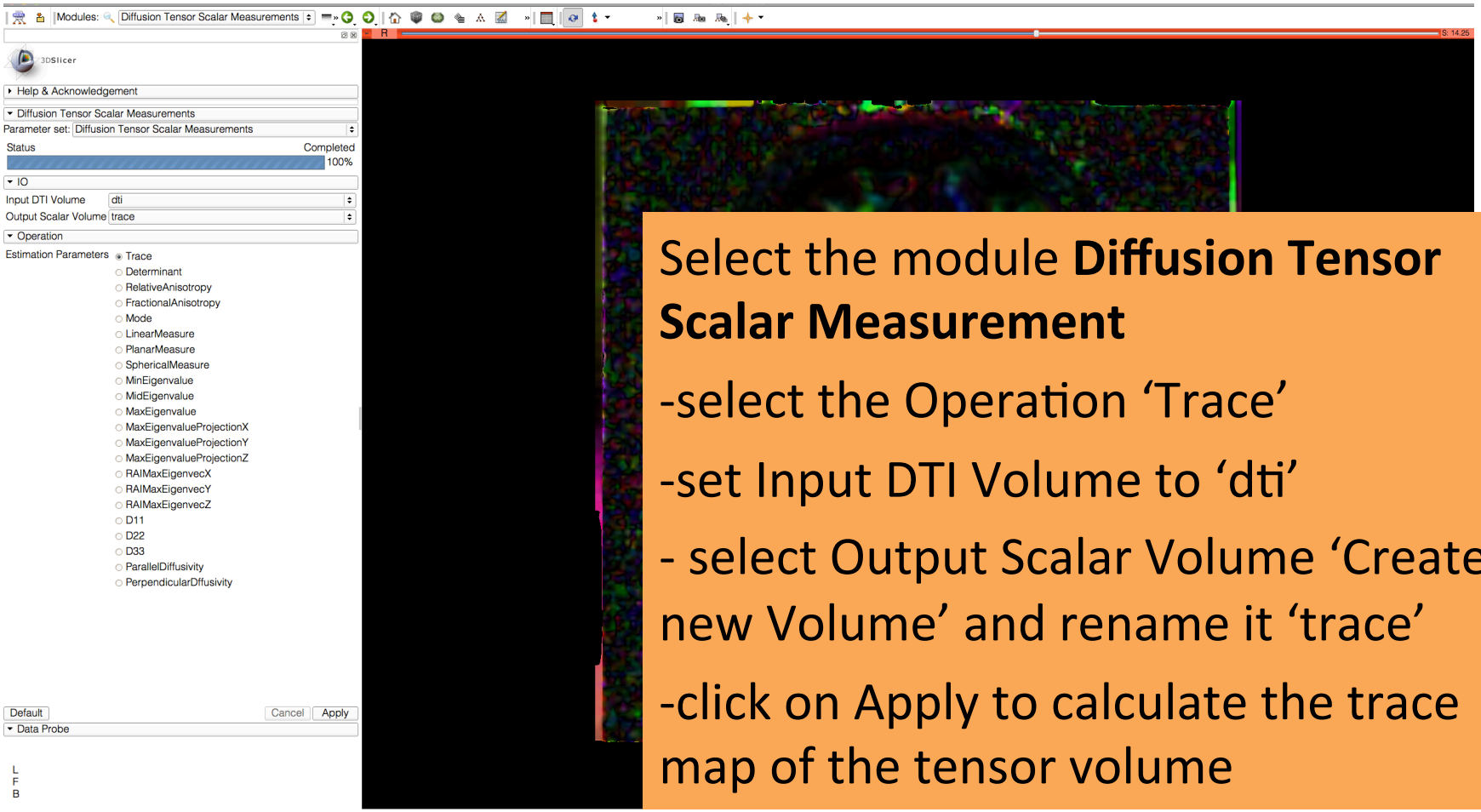


Characterizing the Size of the tensor: Trace

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

- 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

Characterizing the Size of the tensor: Trace



Select the module **Diffusion Tensor Scalar Measurement**

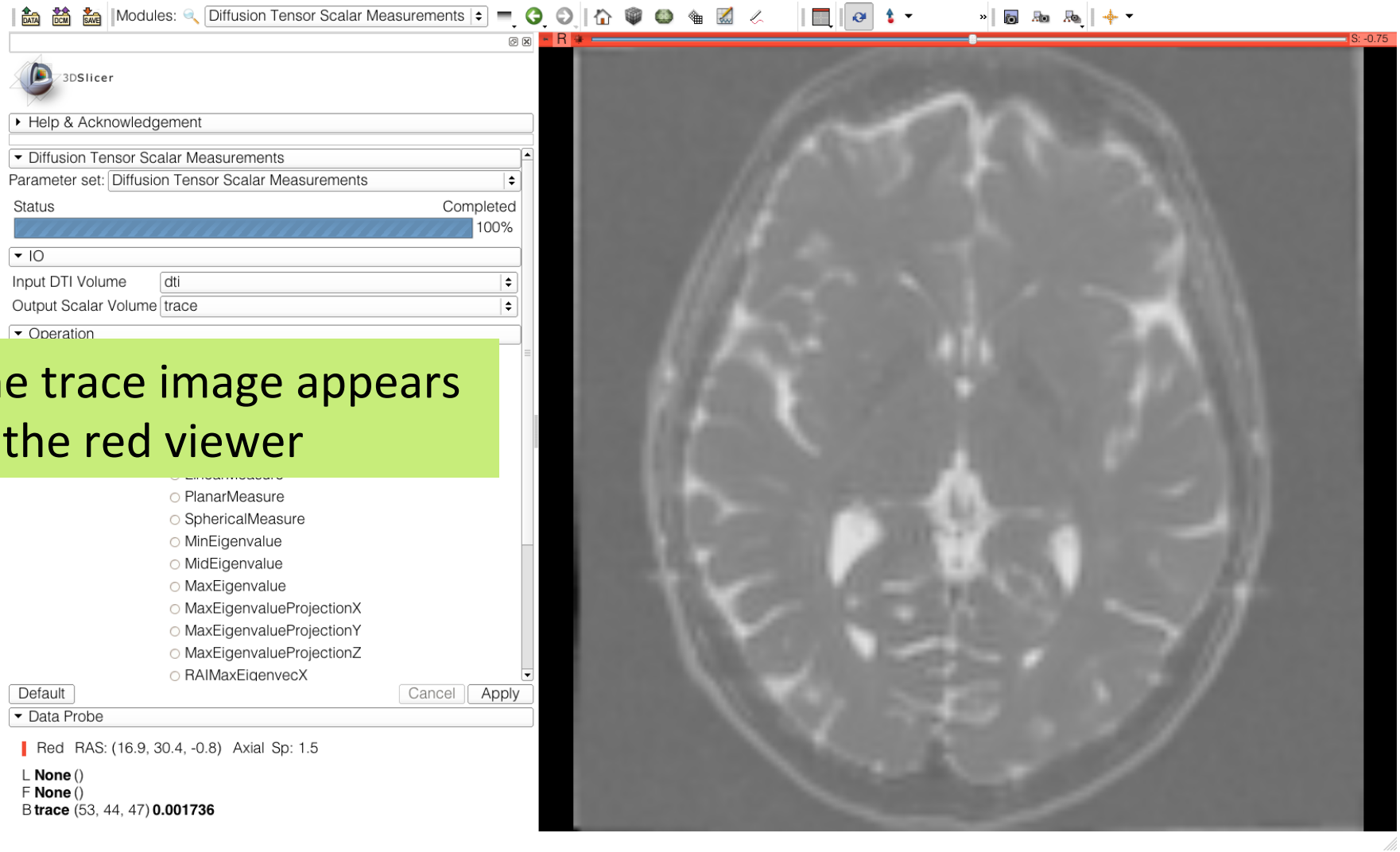
-select the Operation 'Trace'

-set Input DTI Volume to 'dti'

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

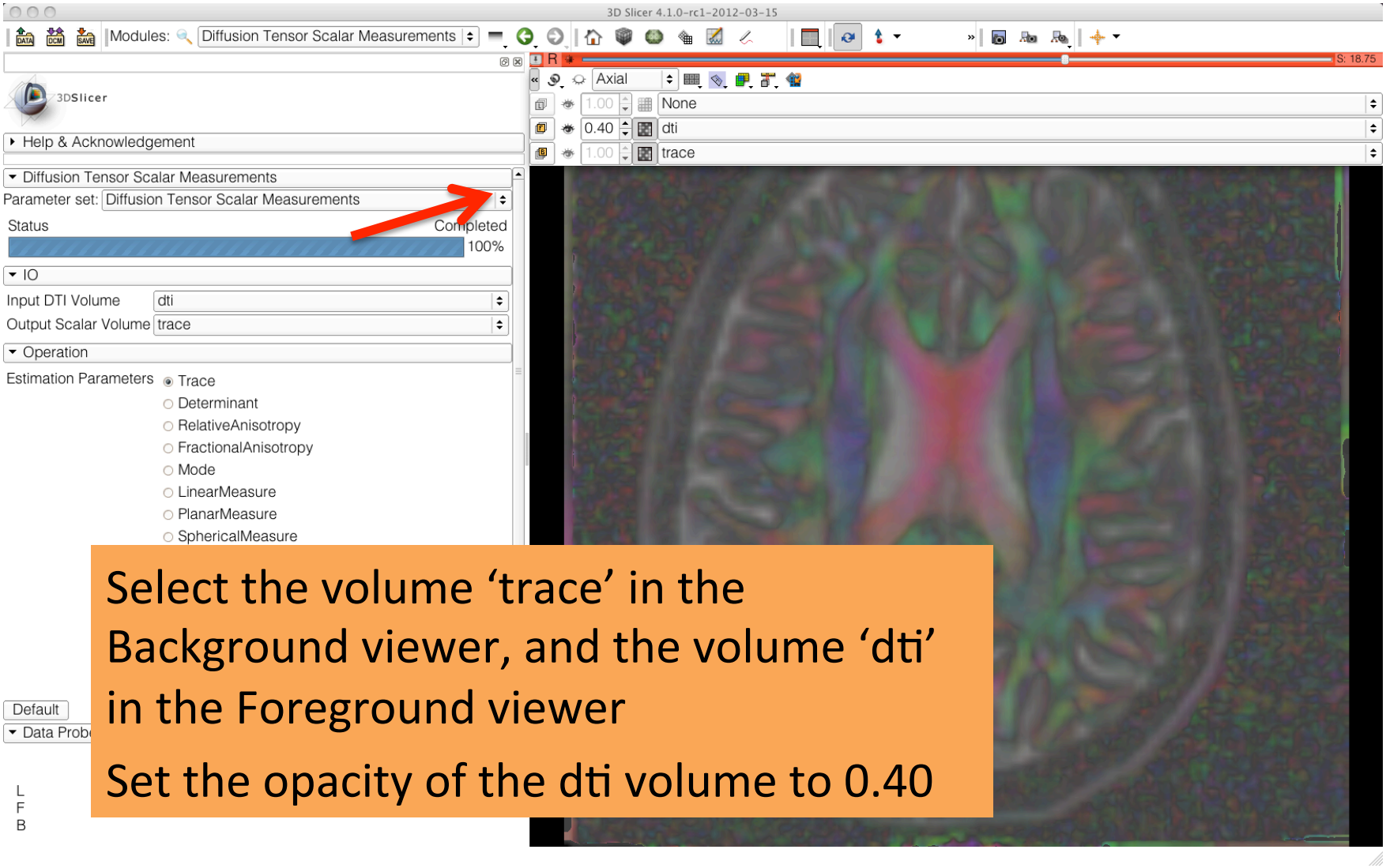
-click on Apply to calculate the trace map of the tensor volume

Trace



The trace image appears in the red viewer

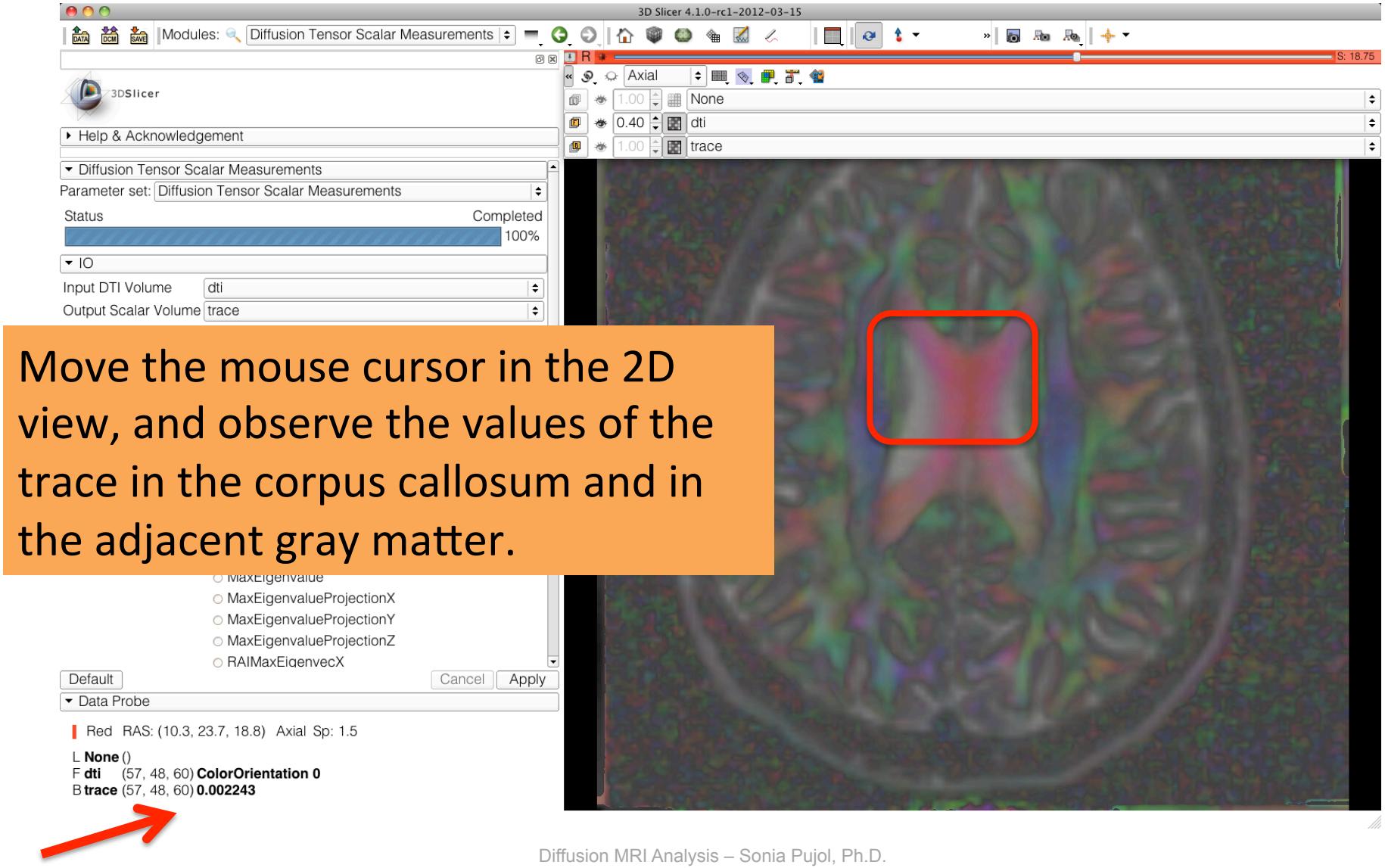
Trace



Select the volume 'trace' in the Background viewer, and the volume 'dti' in the Foreground viewer

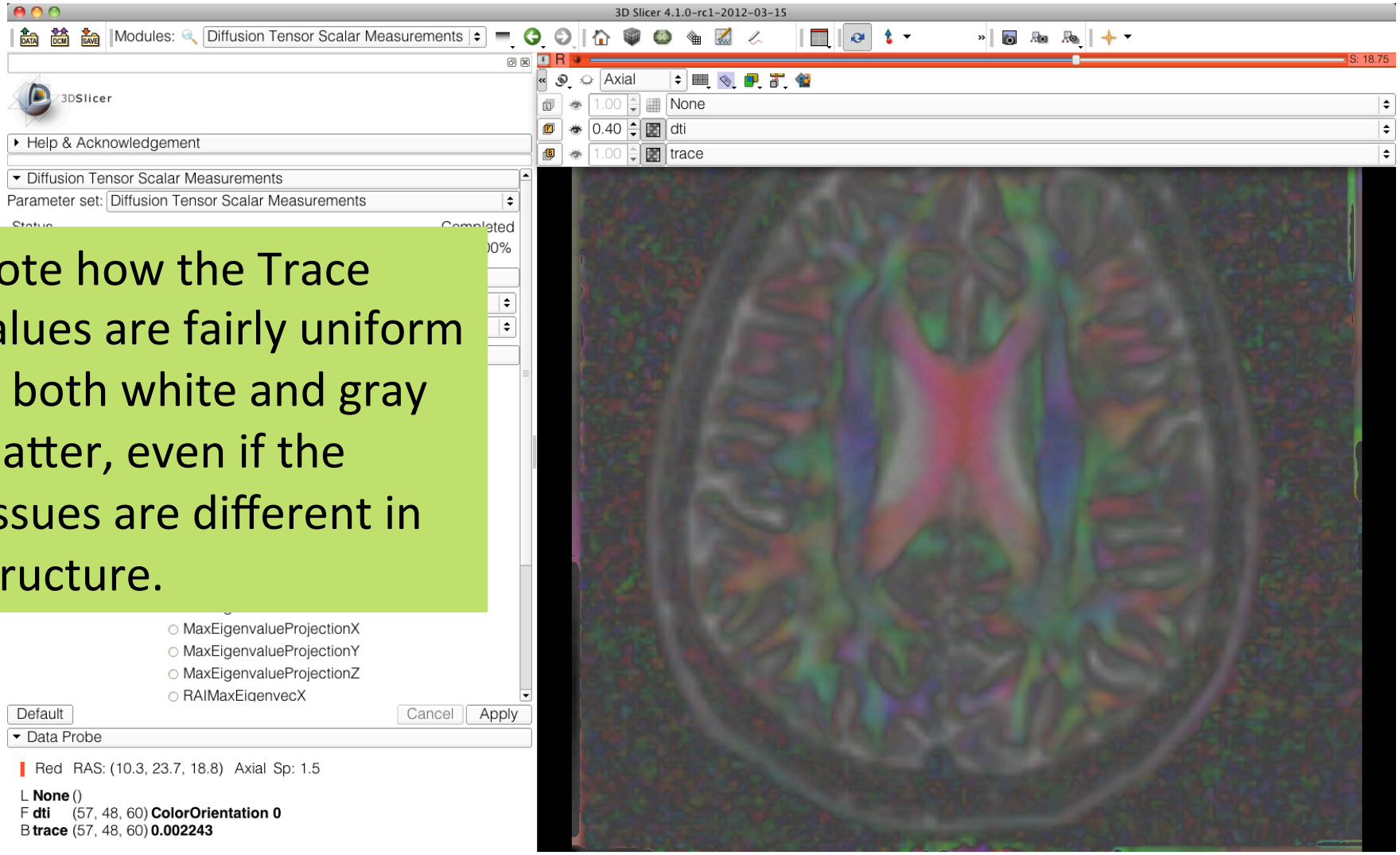
Set the opacity of the dti volume to 0.40

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



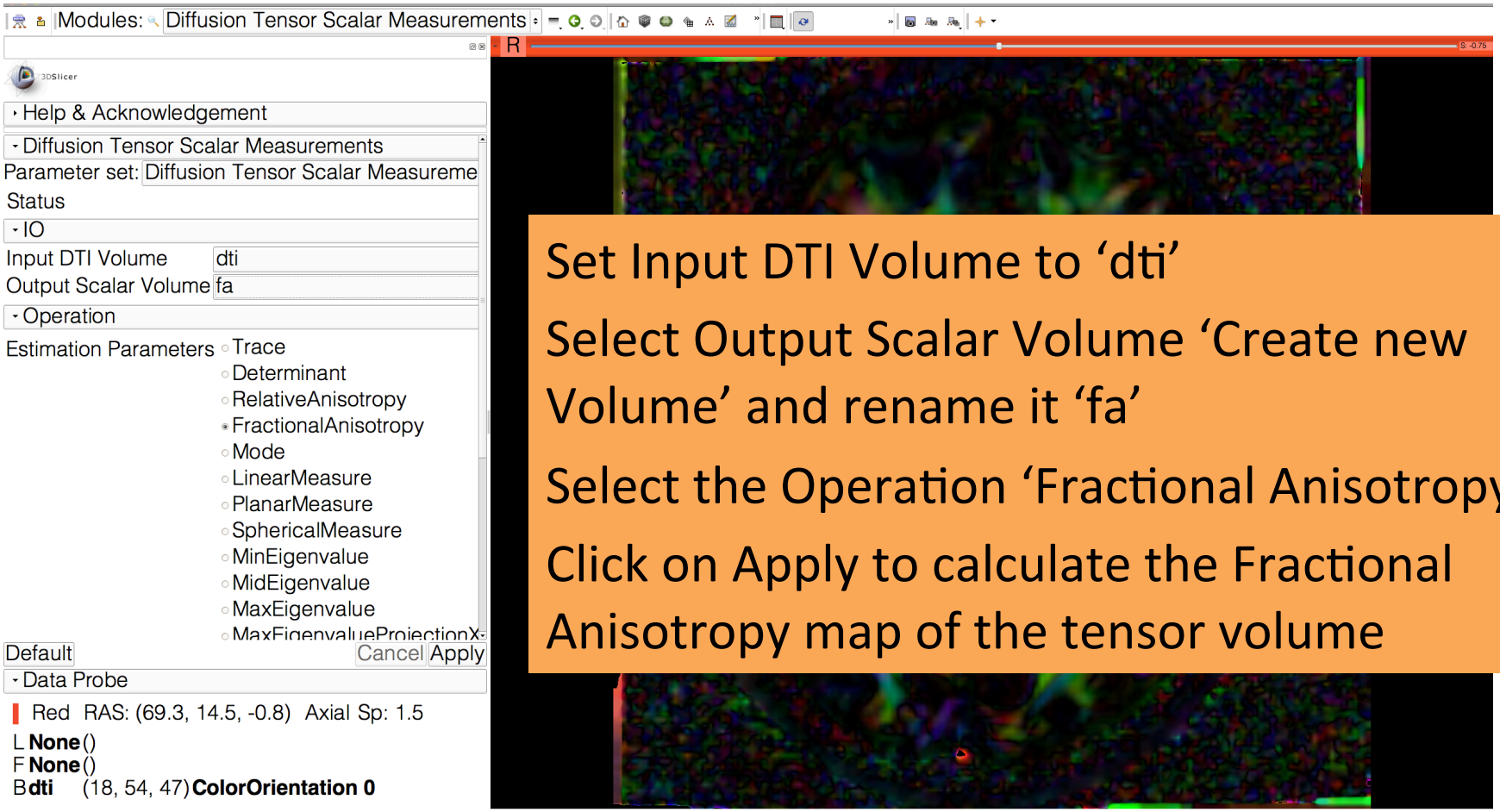
Note how the Trace values are fairly uniform in both white and gray matter, even if the tissues are different in structure.

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



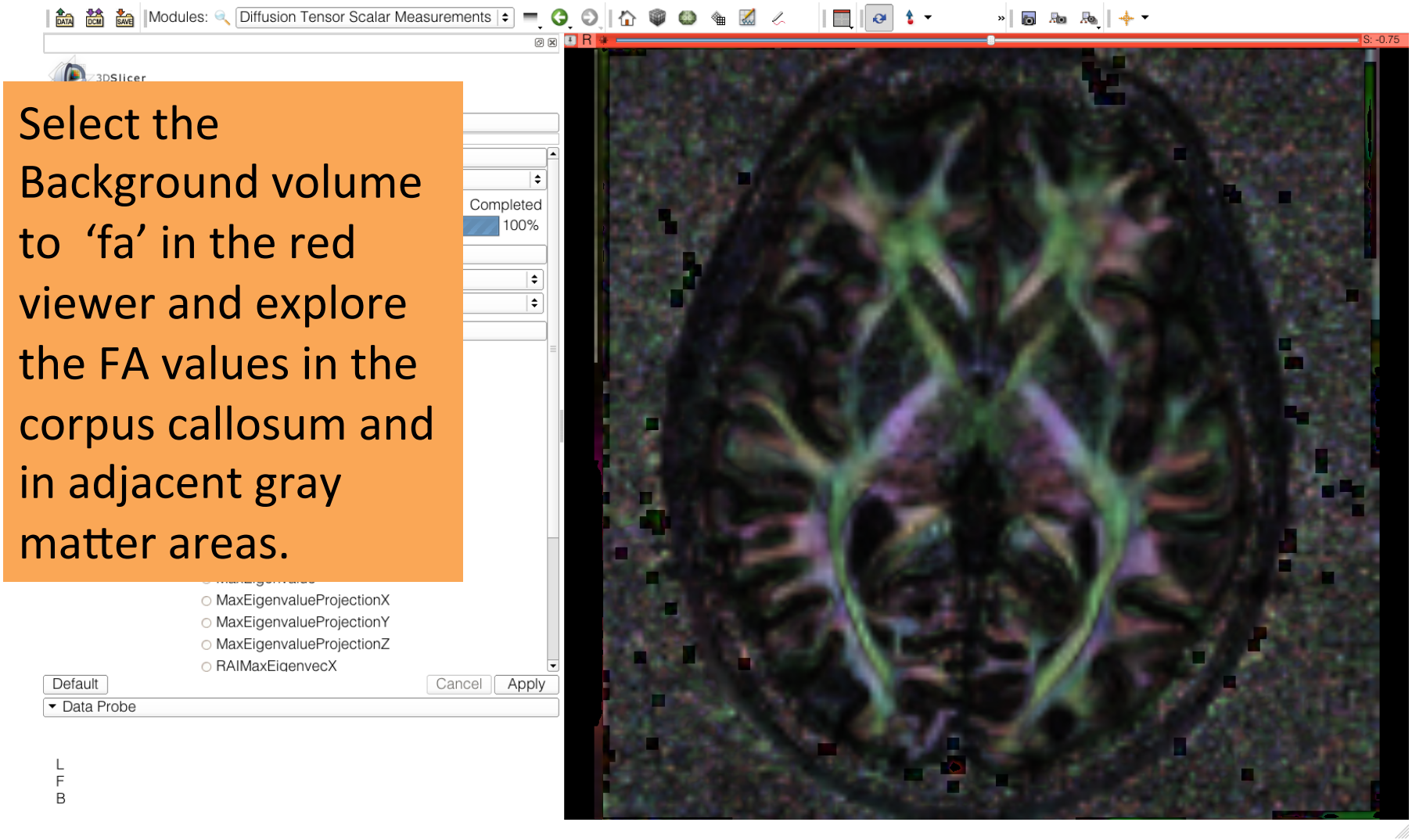
Set Input DTI Volume to ‘dti’

Select Output Scalar Volume ‘Create new Volume’ and rename it ‘fa’

Select the Operation ‘Fractional Anisotropy’

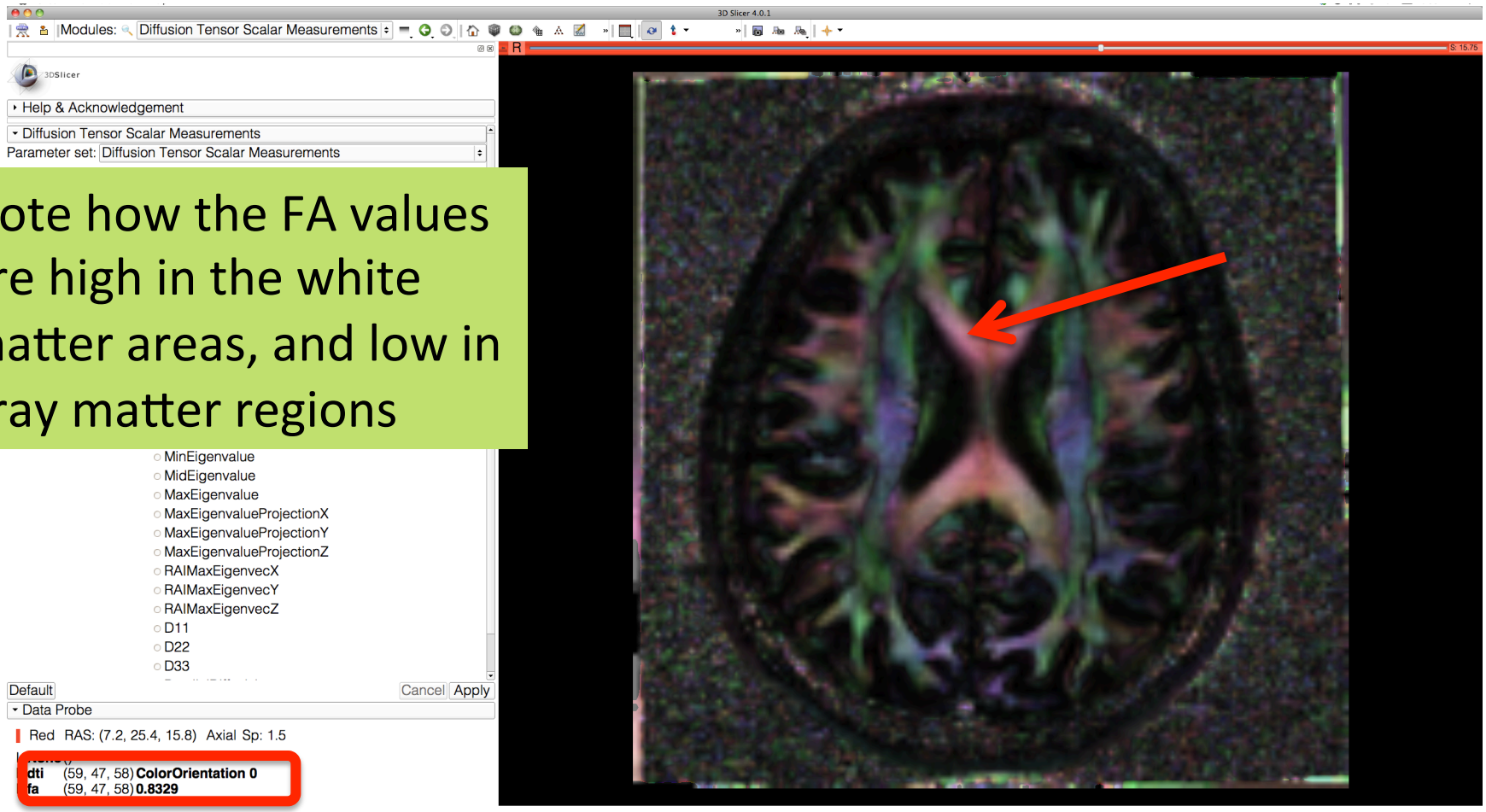
Click on Apply to calculate the Fractional Anisotropy map of the tensor volume

Fractional Anisotropy



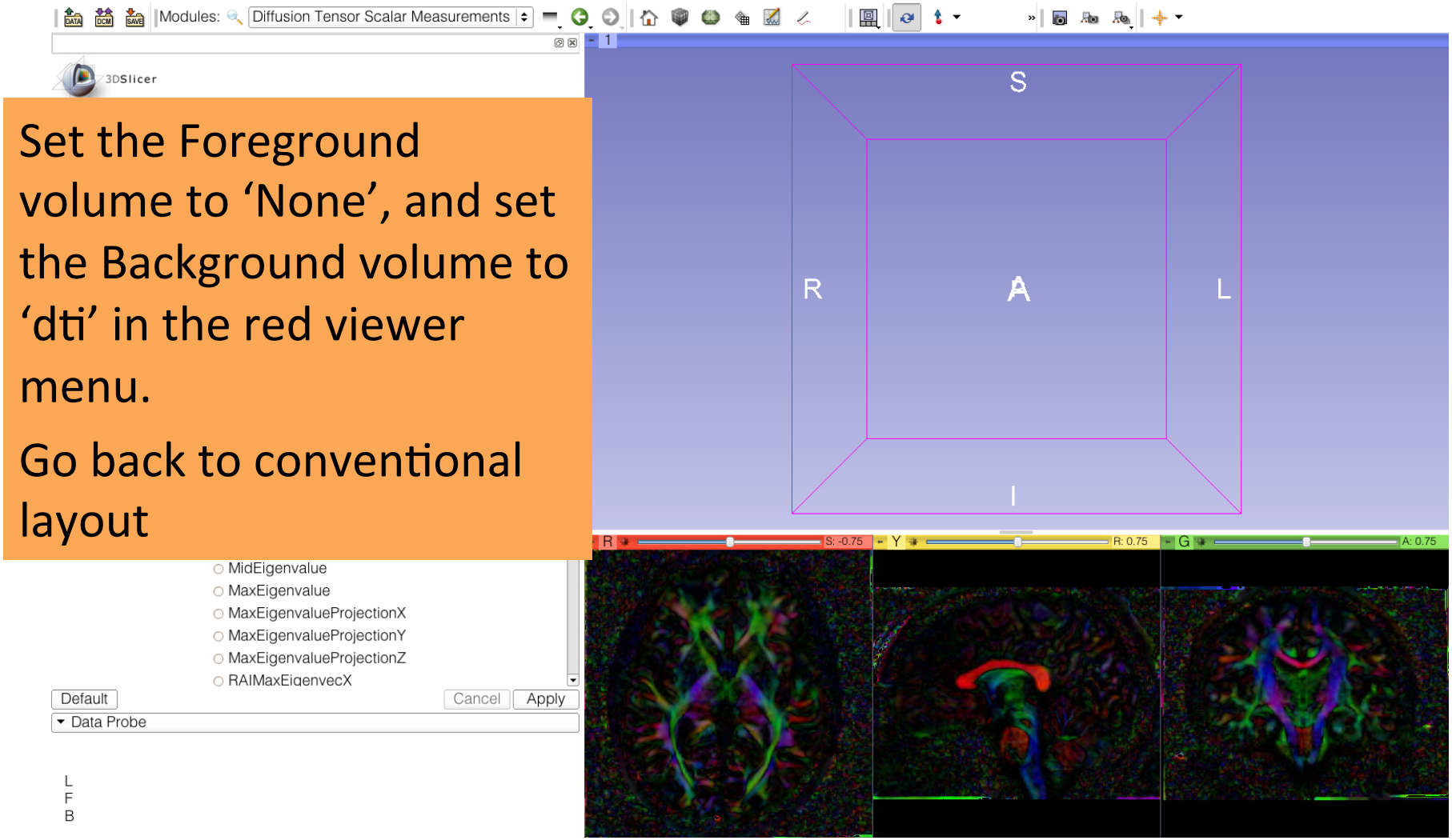
Select the Background volume to 'fa' in the red viewer and explore the FA values in the corpus callosum and in adjacent gray matter areas.

Fractional Anisotropy



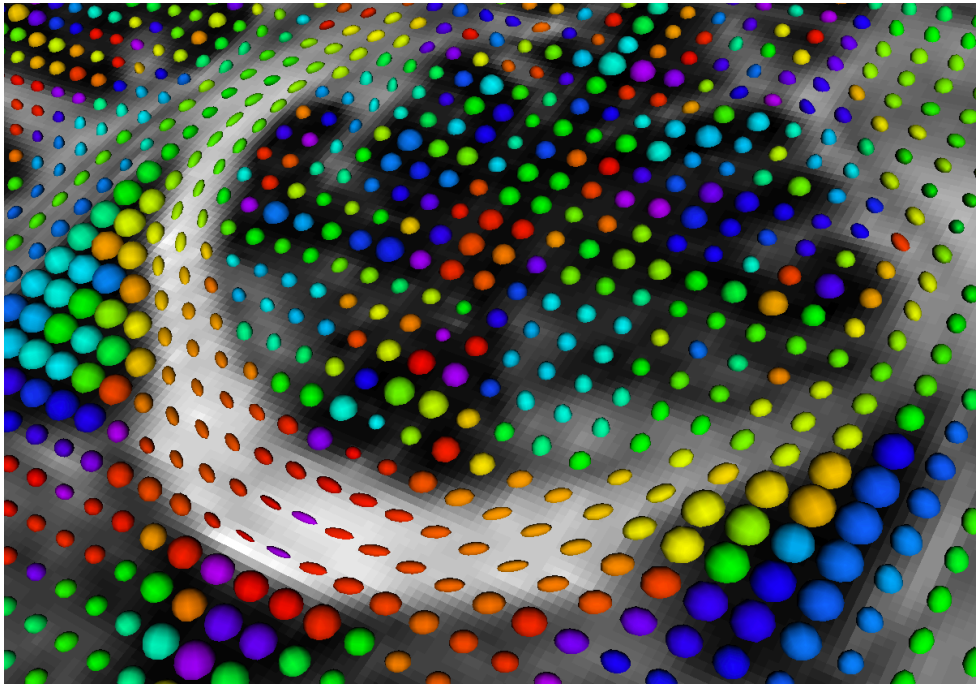
Note how the FA values are high in the white matter areas, and low in gray matter regions

Fractional Anisotropy



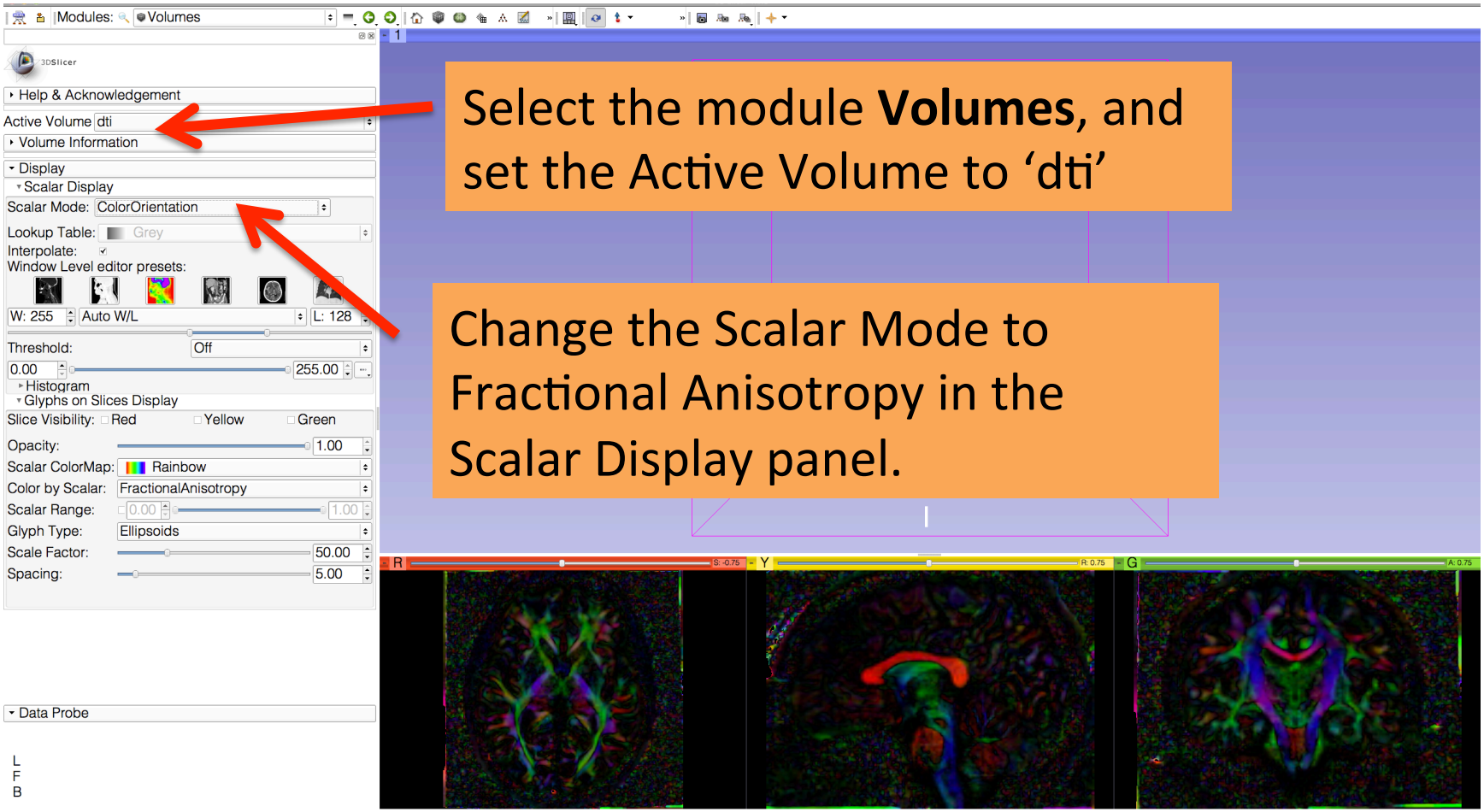
Set the Foreground volume to 'None', and set the Background volume to 'dti' in the red viewer menu.

Go back to conventional layout

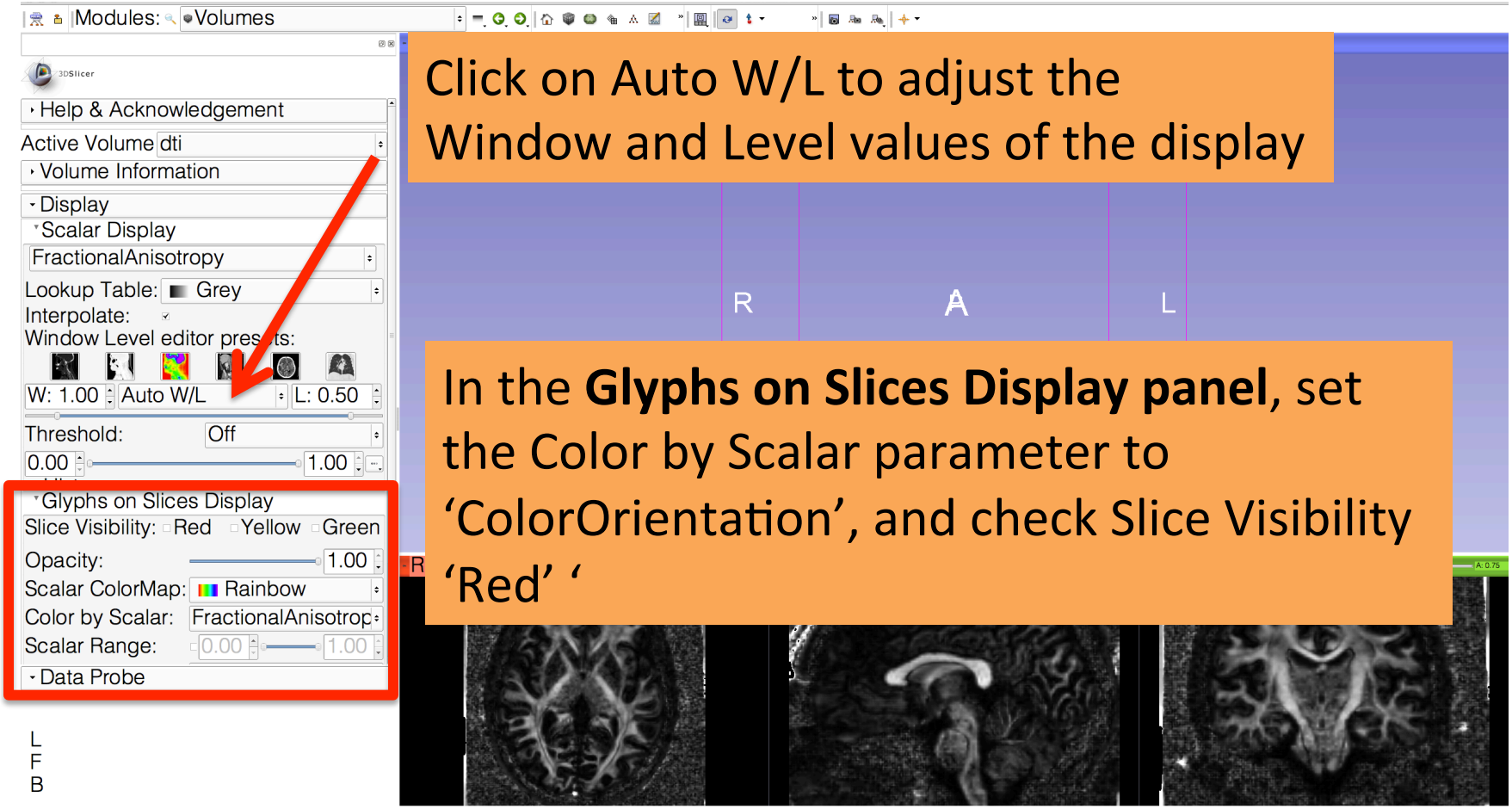


Part 2: Visualizing the tensor data

3D Visualization: Glyphs



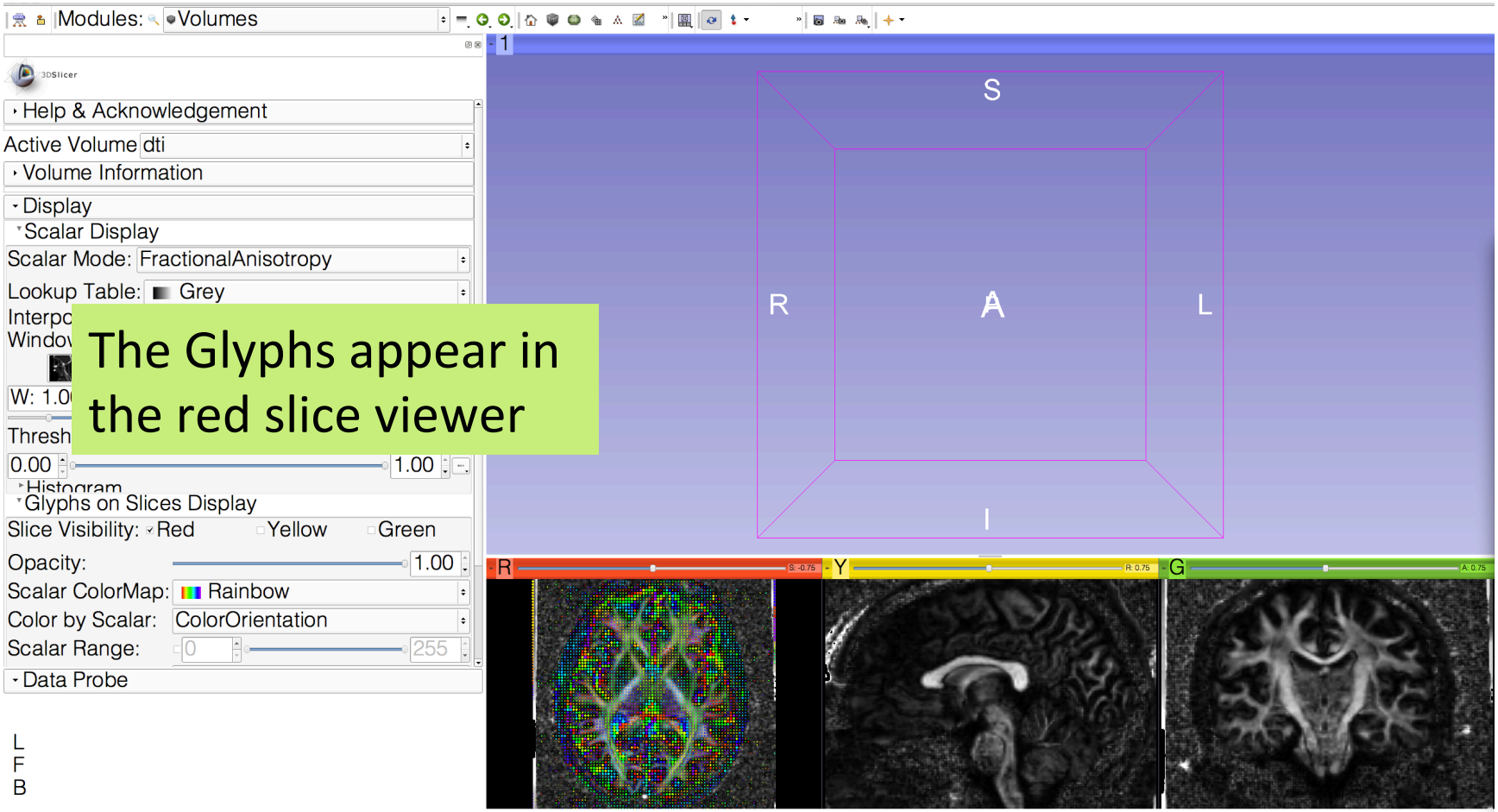
3D Visualization: Glyphs



Click on Auto W/L to adjust the Window and Level values of the display

In the **Glyphs on Slices Display panel**, set the Color by Scalar parameter to 'ColorOrientation', and check Slice Visibility 'Red' '

3D Visualization: Glyphs



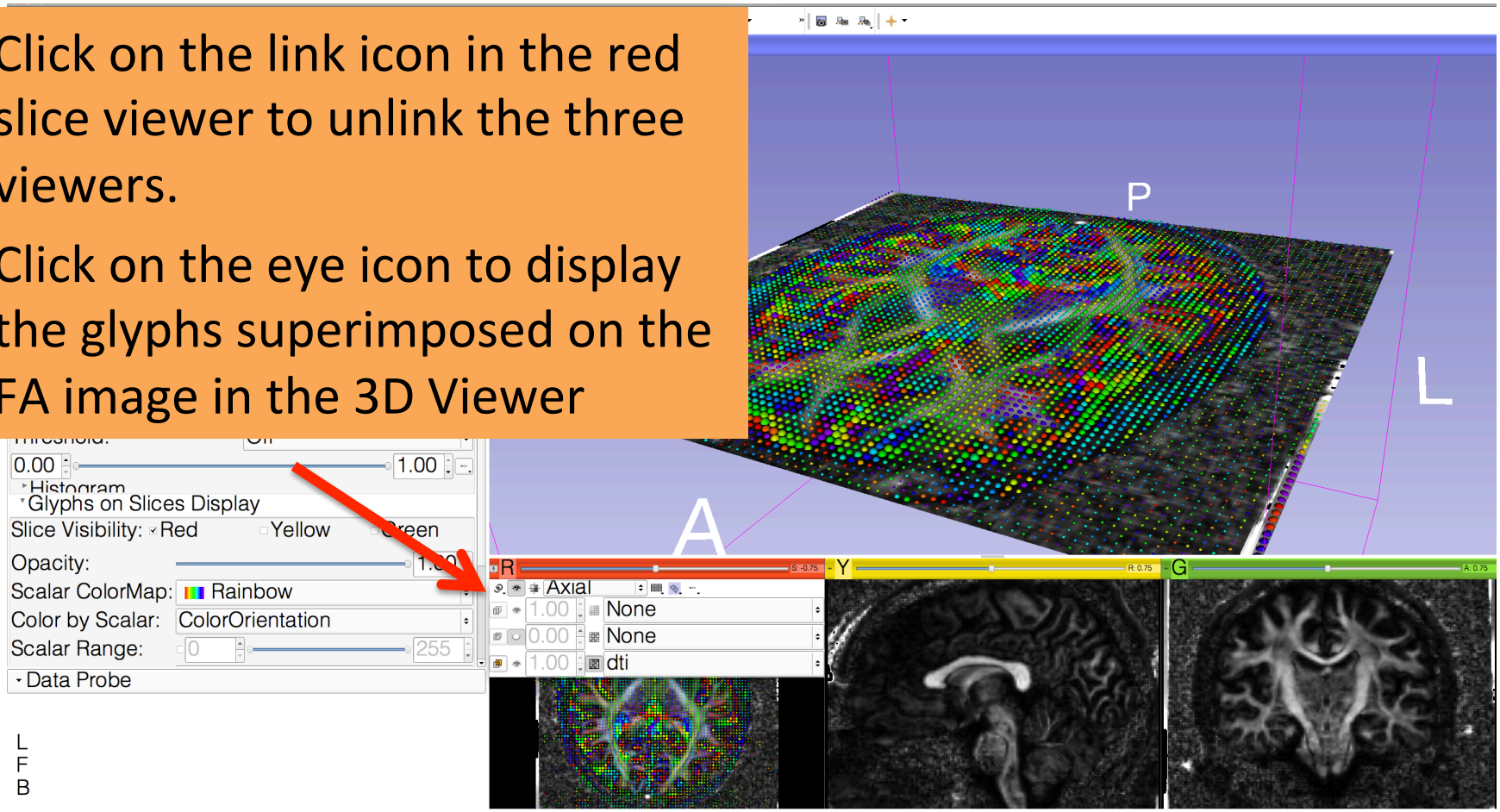
The Glyphs appear in the red slice viewer

L
F
B

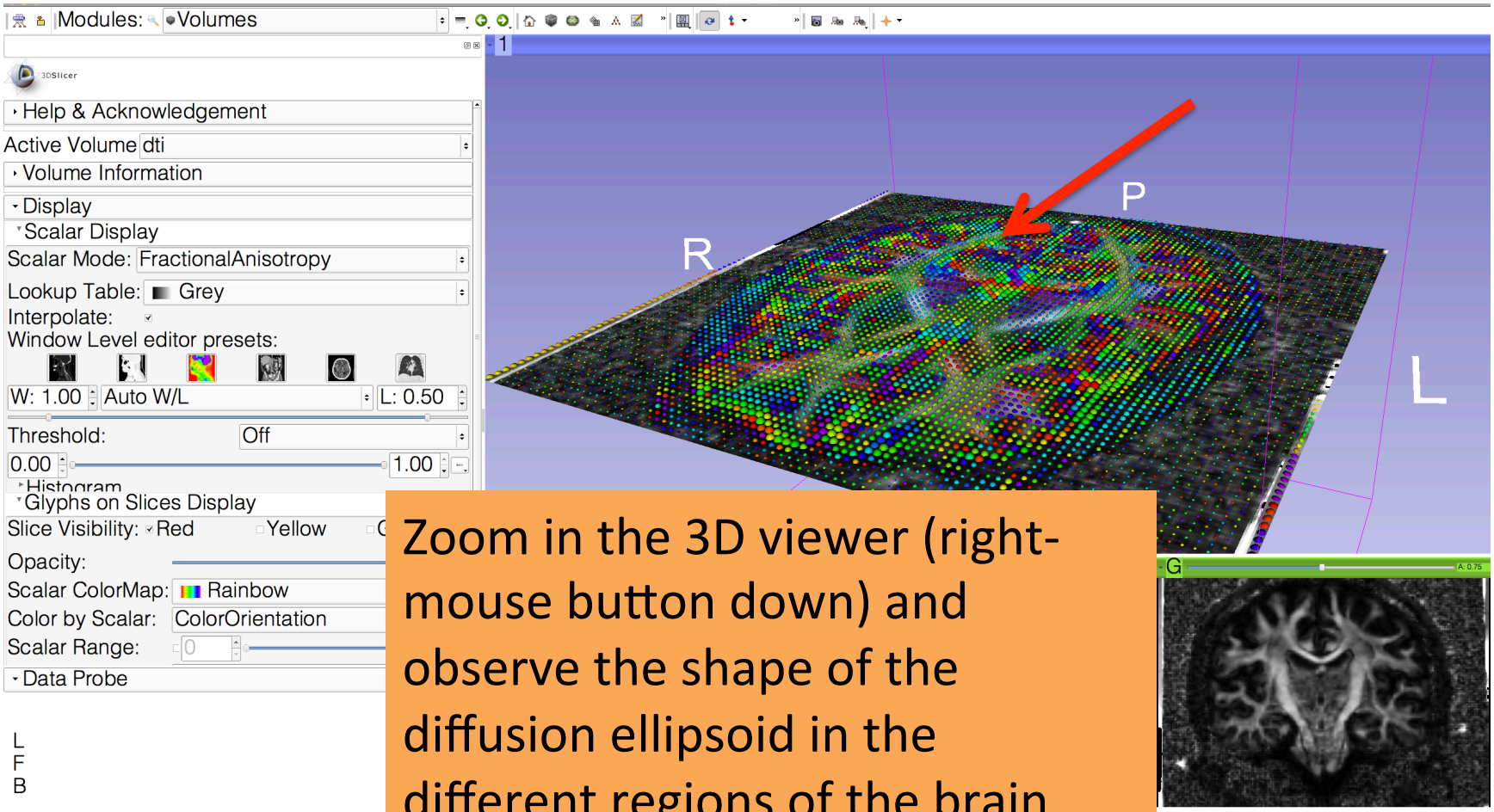
3D Visualization: Glyphs

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



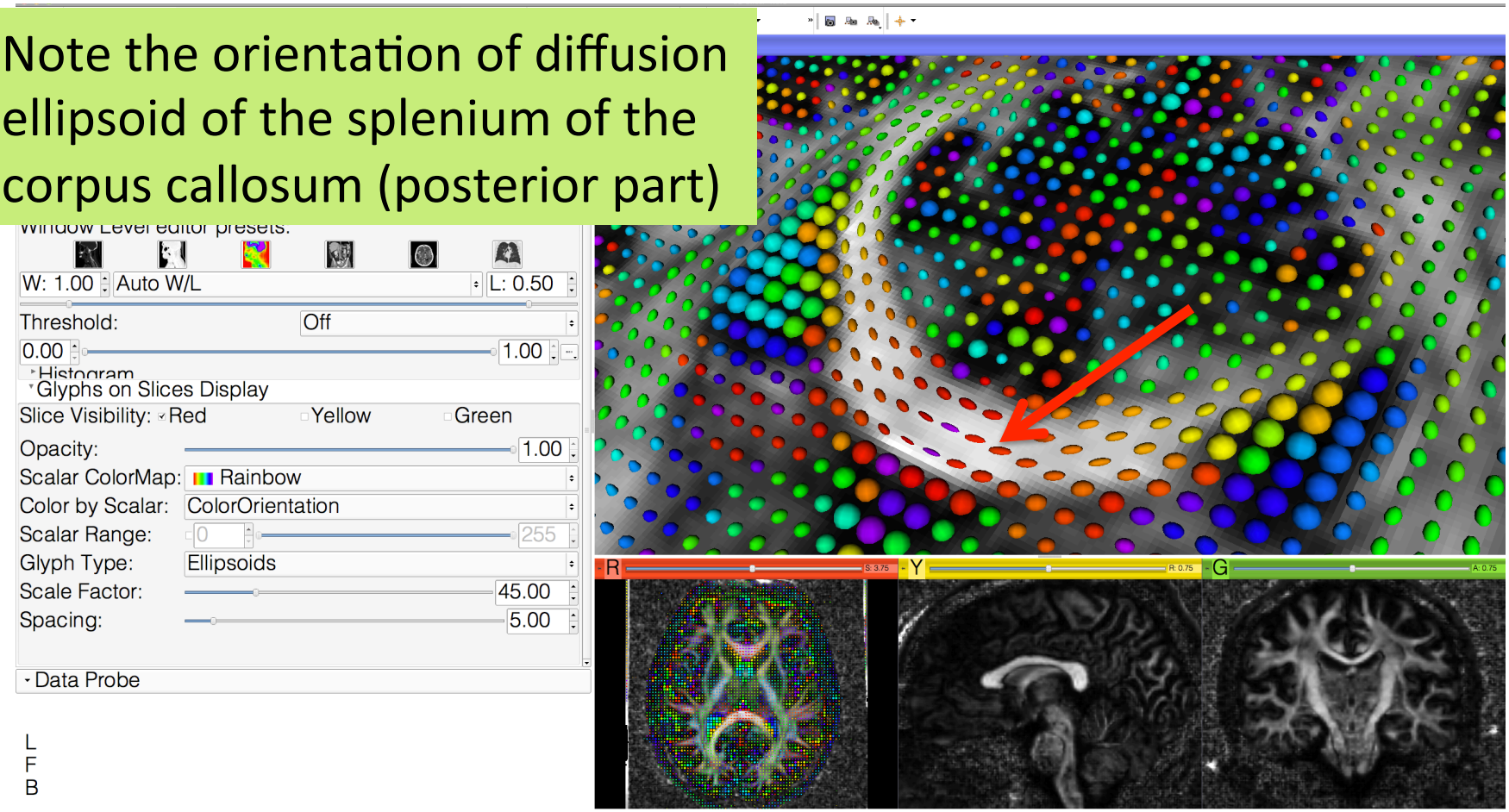
3D Visualization: Glyphs



Zoom in the 3D viewer (right-mouse button down) and observe the shape of the diffusion ellipsoid in the different regions of the brain

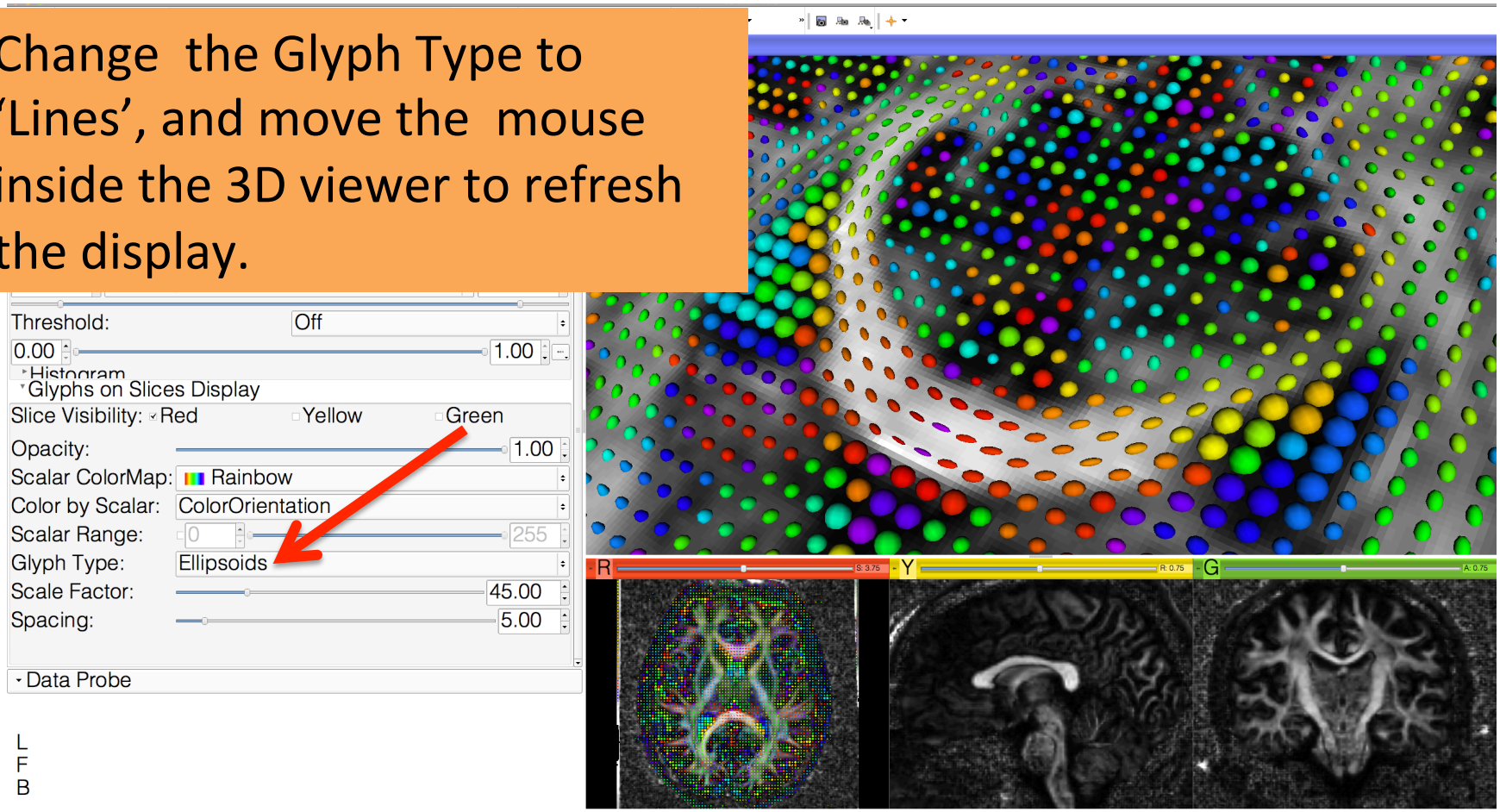
3D Visualization: Glyphs

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



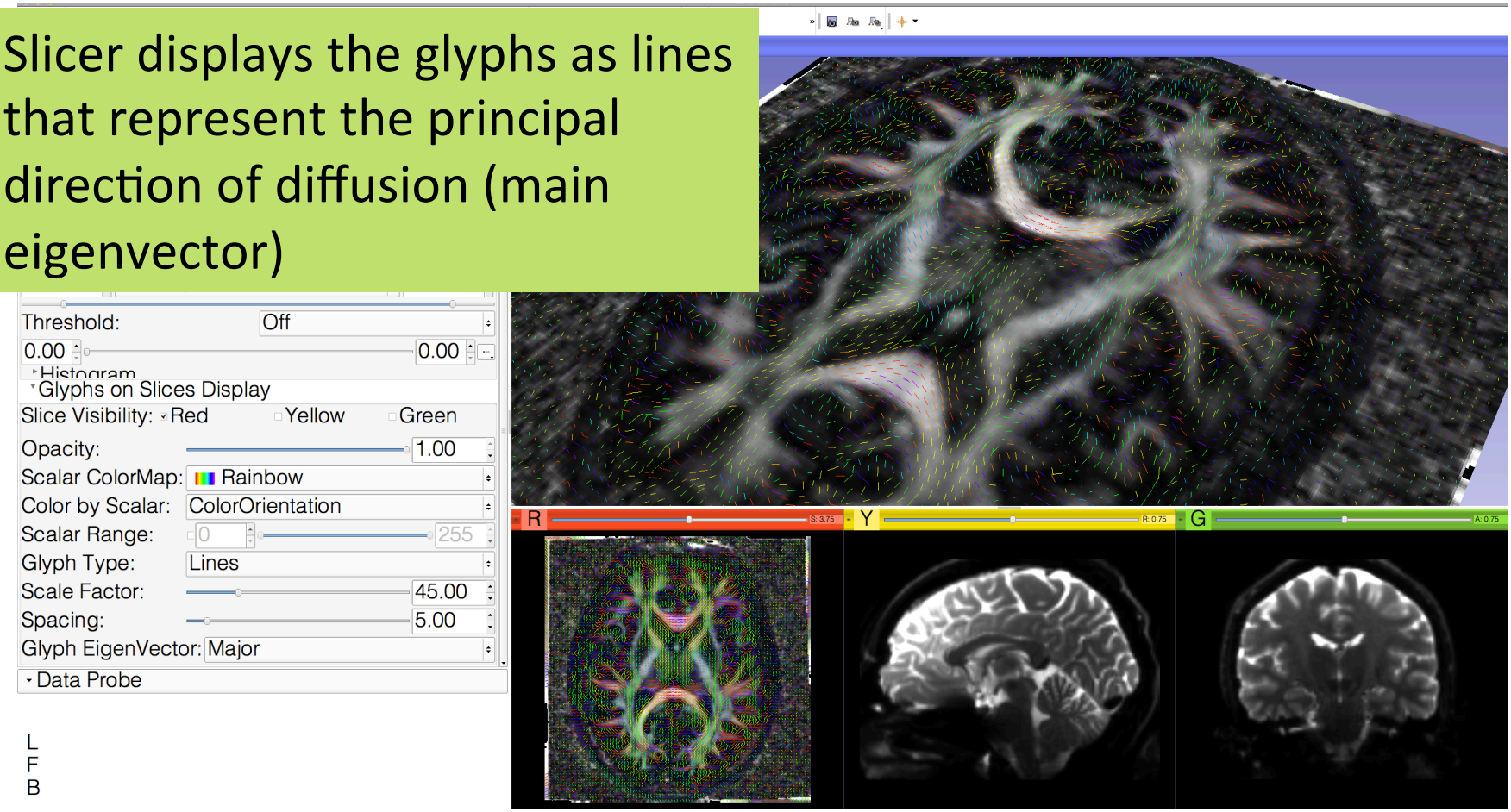
3D Visualization: Glyphs

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

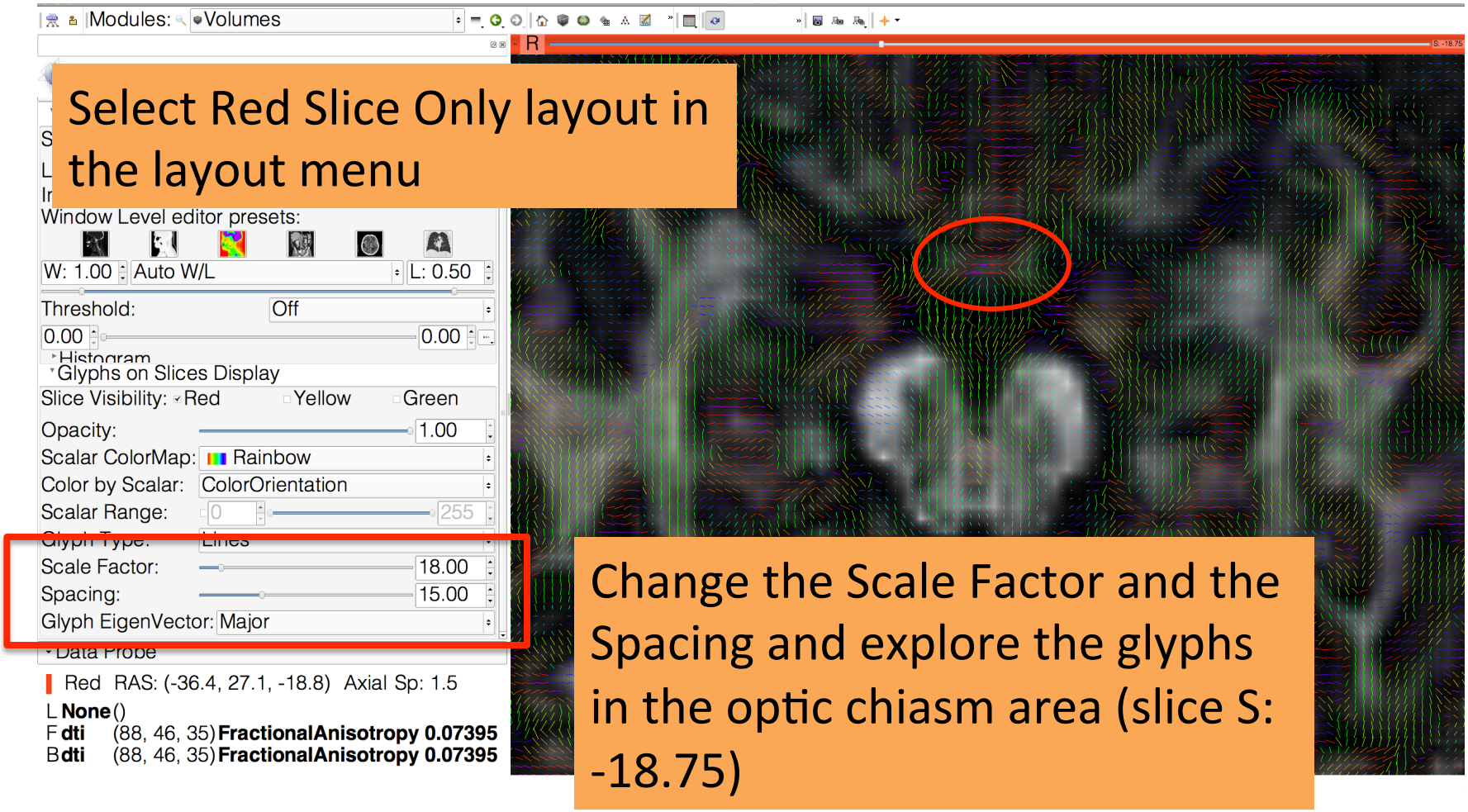


3D Visualization: Glyphs

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



3D Visualization: Glyphs



Select Red Slice Only layout in the layout menu

Change the Scale Factor and the Spacing and explore the glyphs in the optic chiasm area (slice S: -18.75)

Optic Chiasm

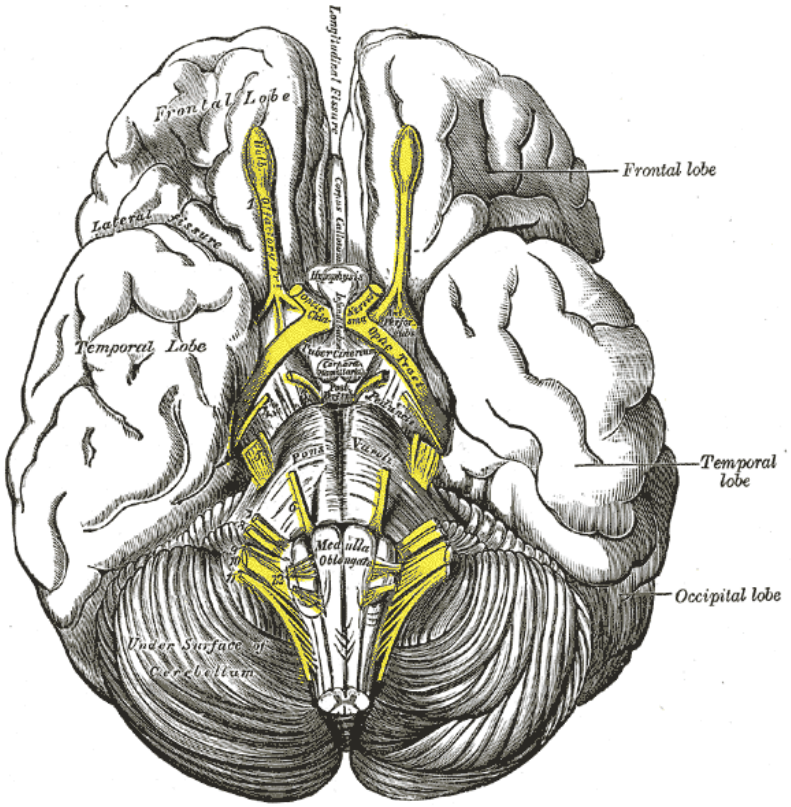
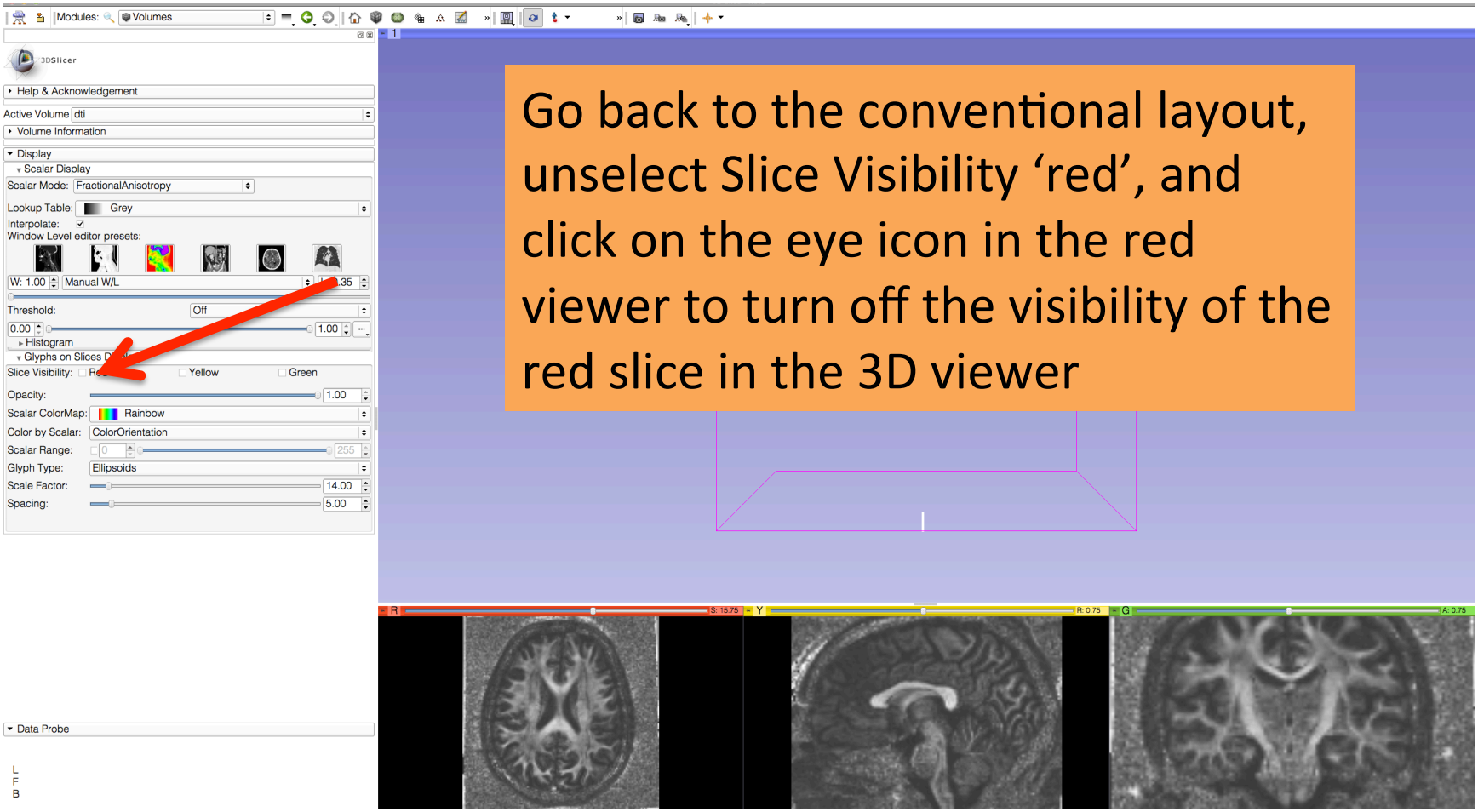
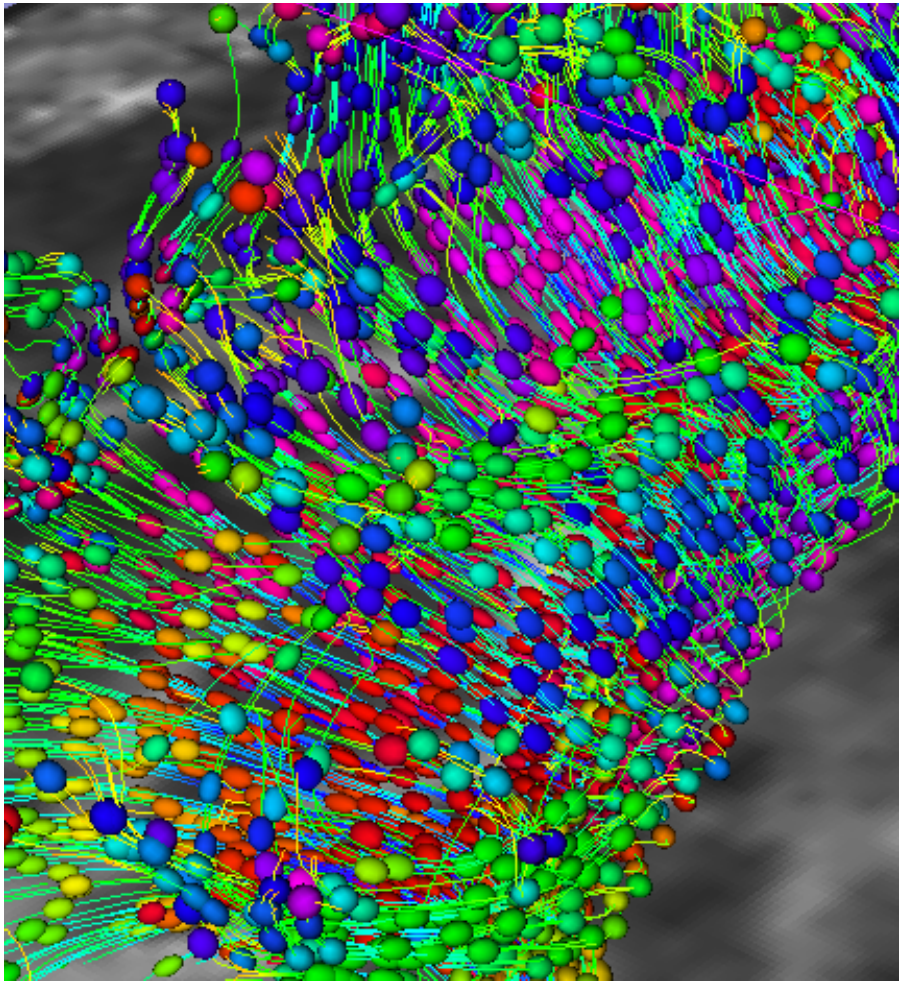


Image from Gray's Anatomy

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

3D Visualization: Glyphs





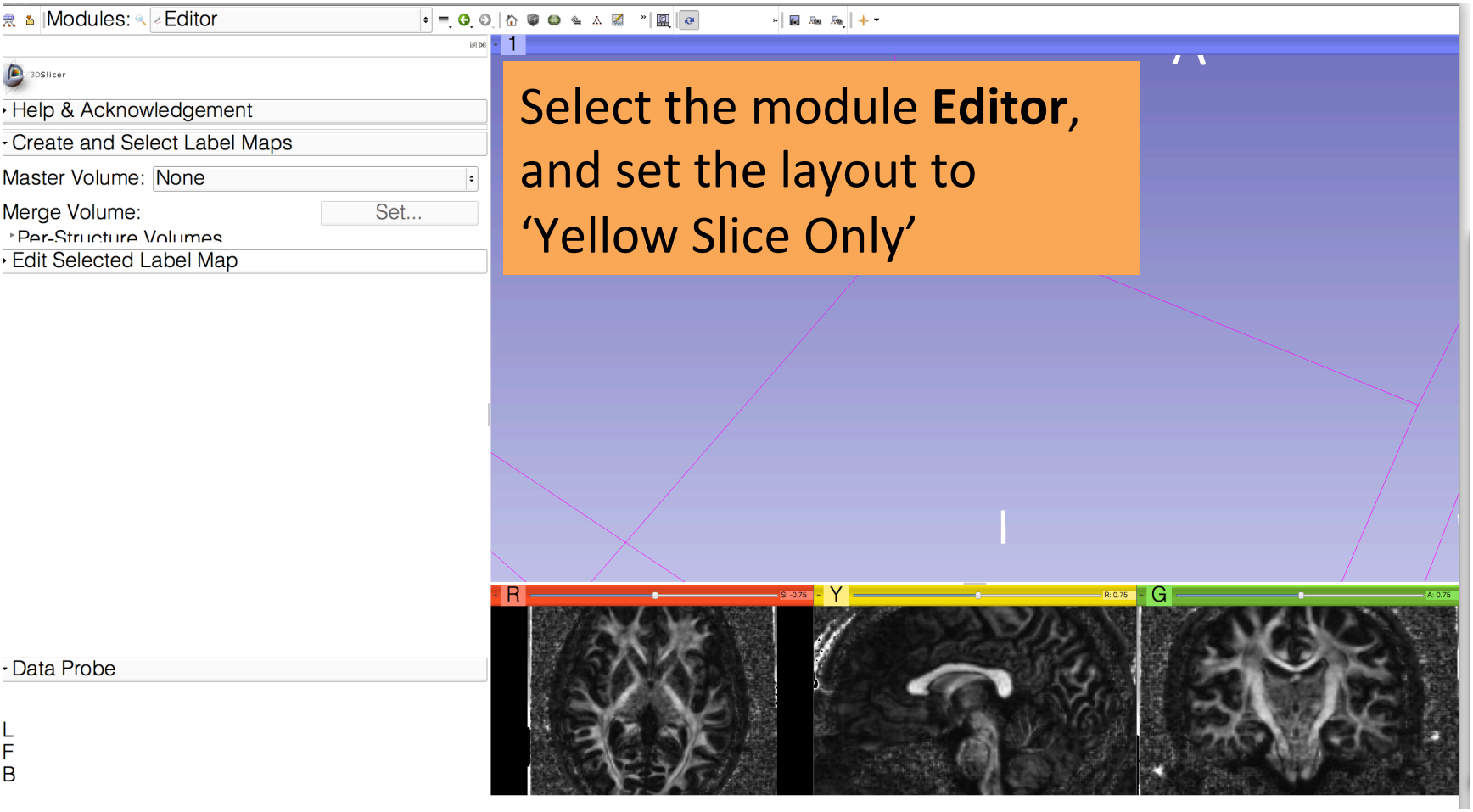
Part 3: From tensors to tracts

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 ~ 1-5 mm is <u>very different</u> from the diameter of an axon~0.1-10 µm

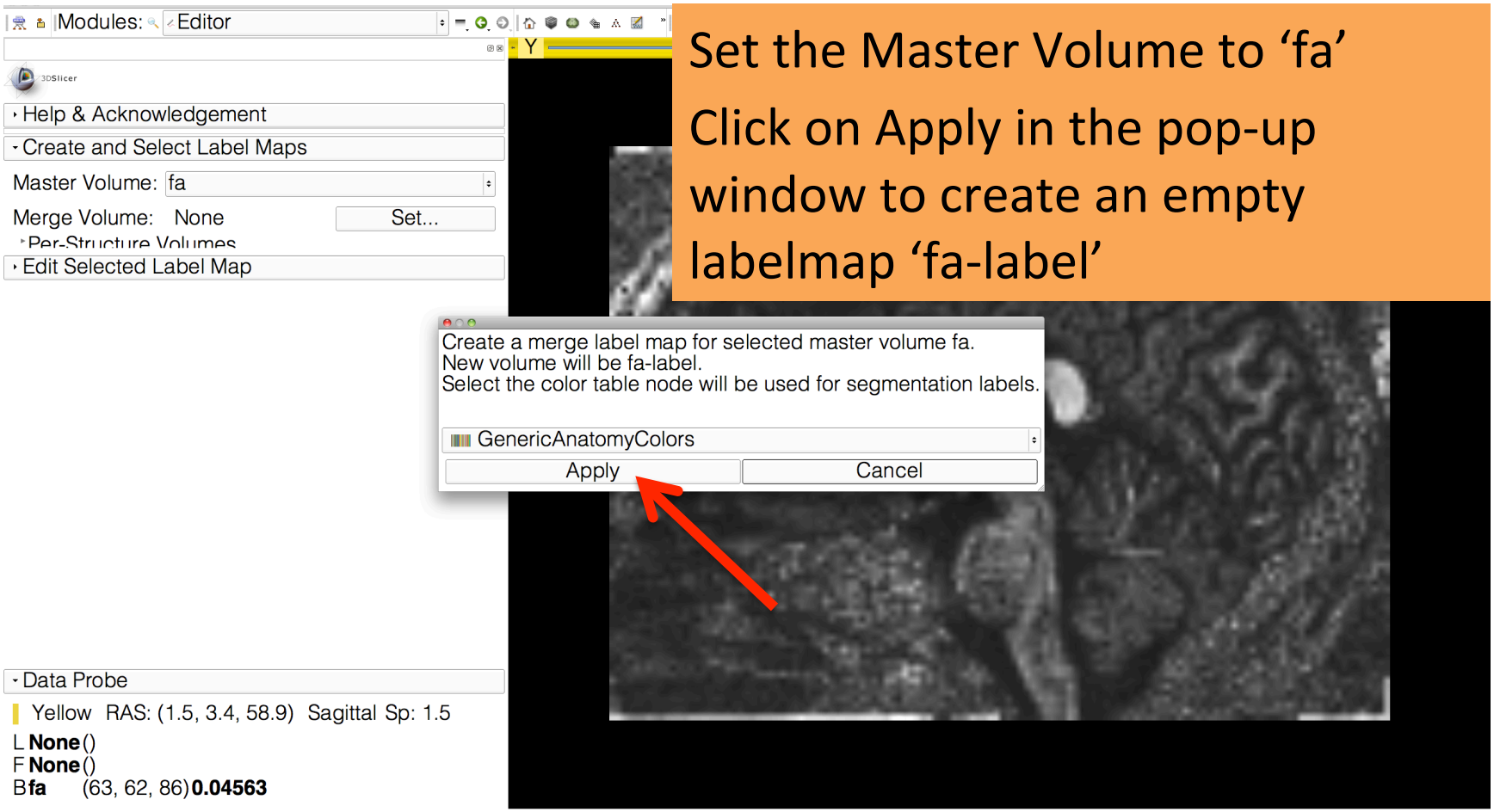
→ A DTI tract is not equivalent to a real fiber.

Tractography Seeding: ROI definition



Select the module **Editor**, and set the layout to 'Yellow Slice Only'

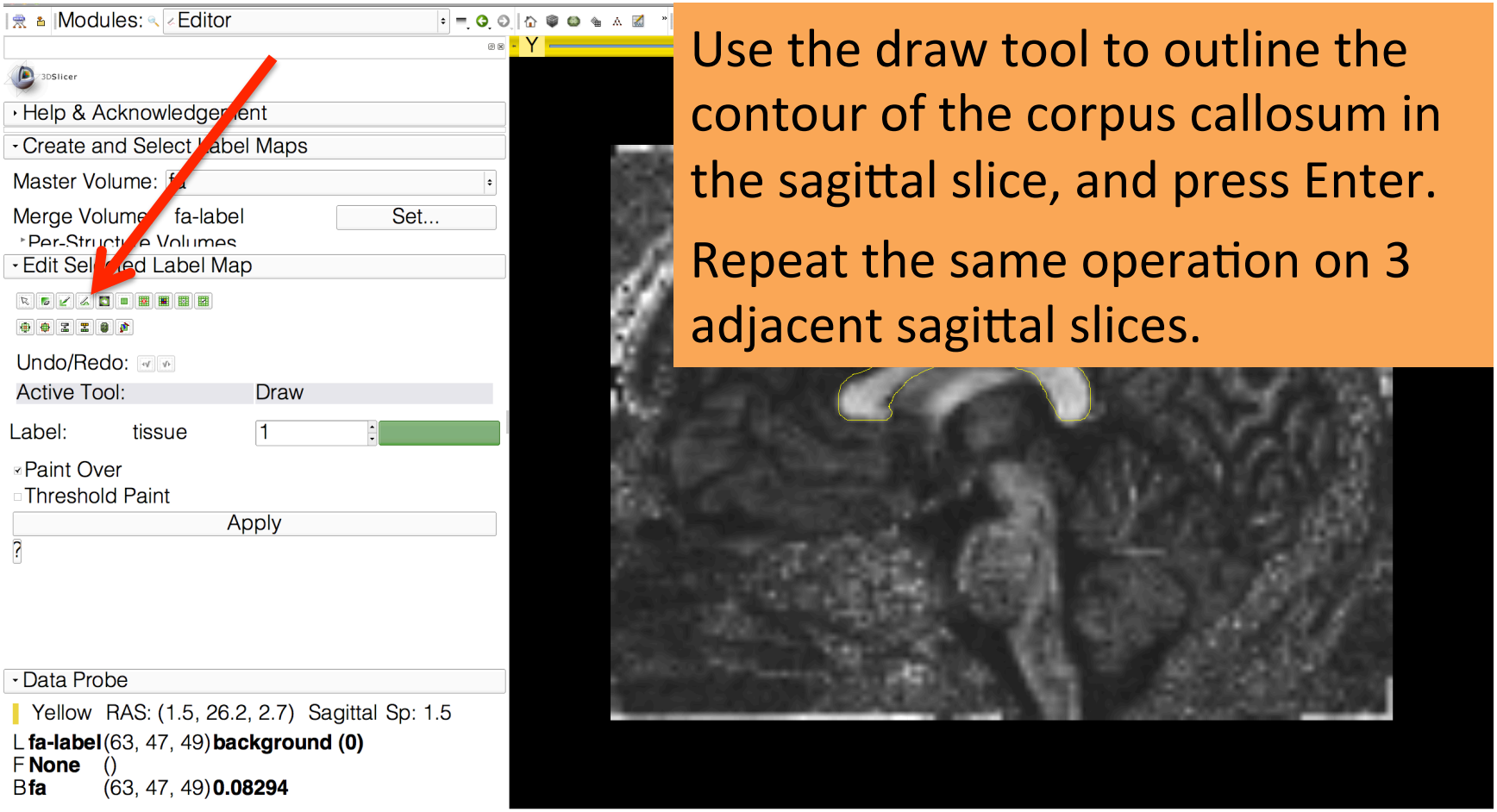
ROI Definition



Set the Master Volume to 'fa'

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

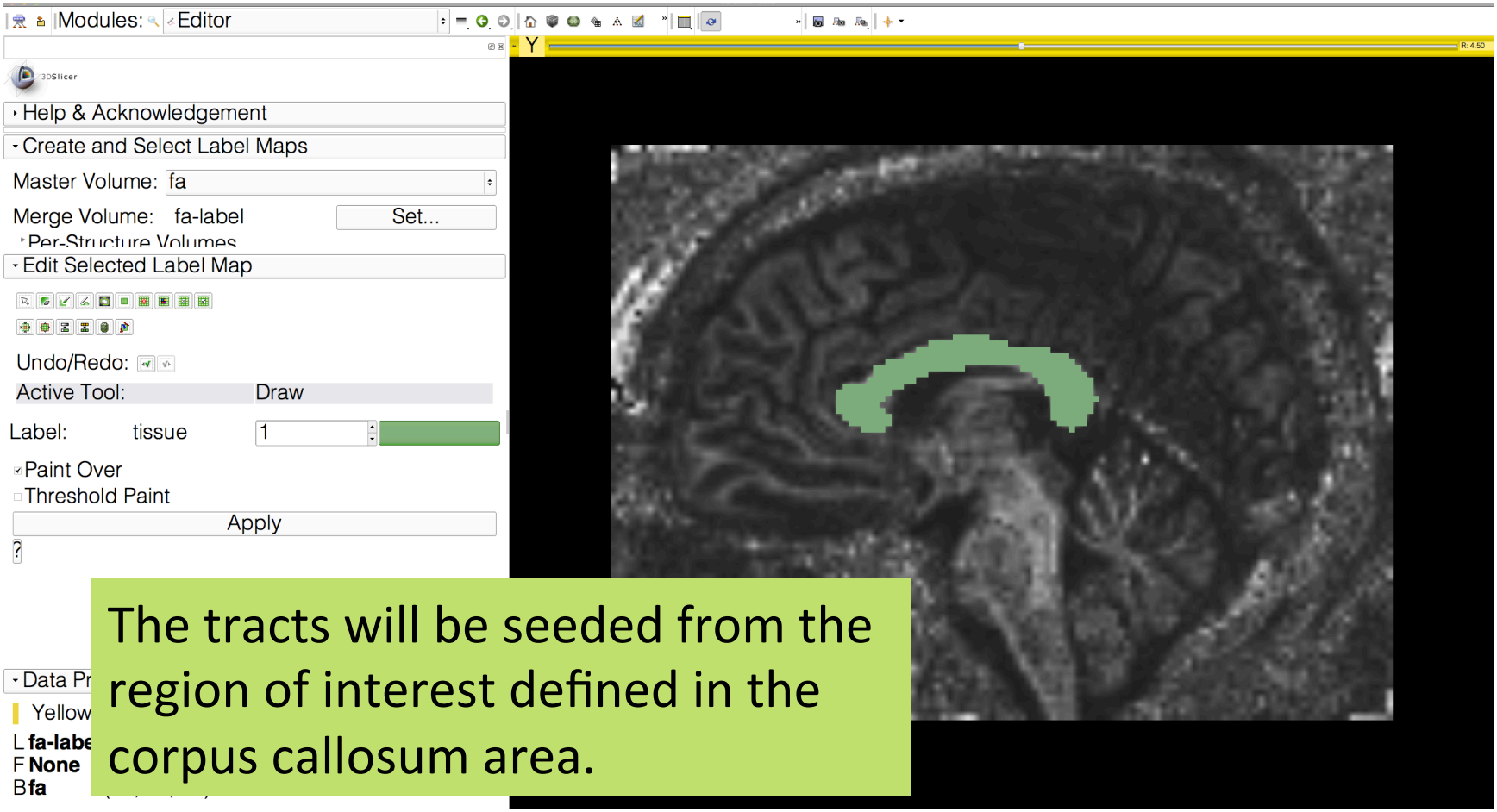
ROI Drawing



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.

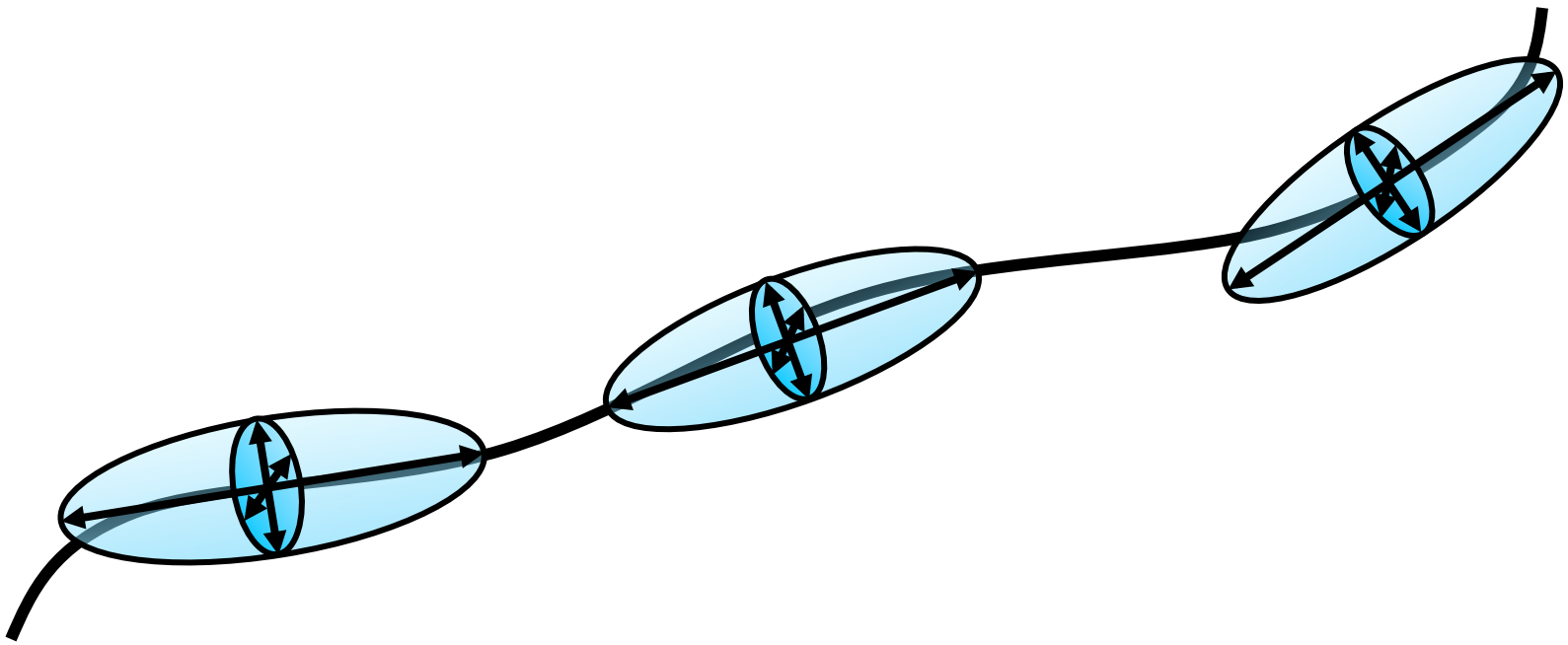
ROI Drawing



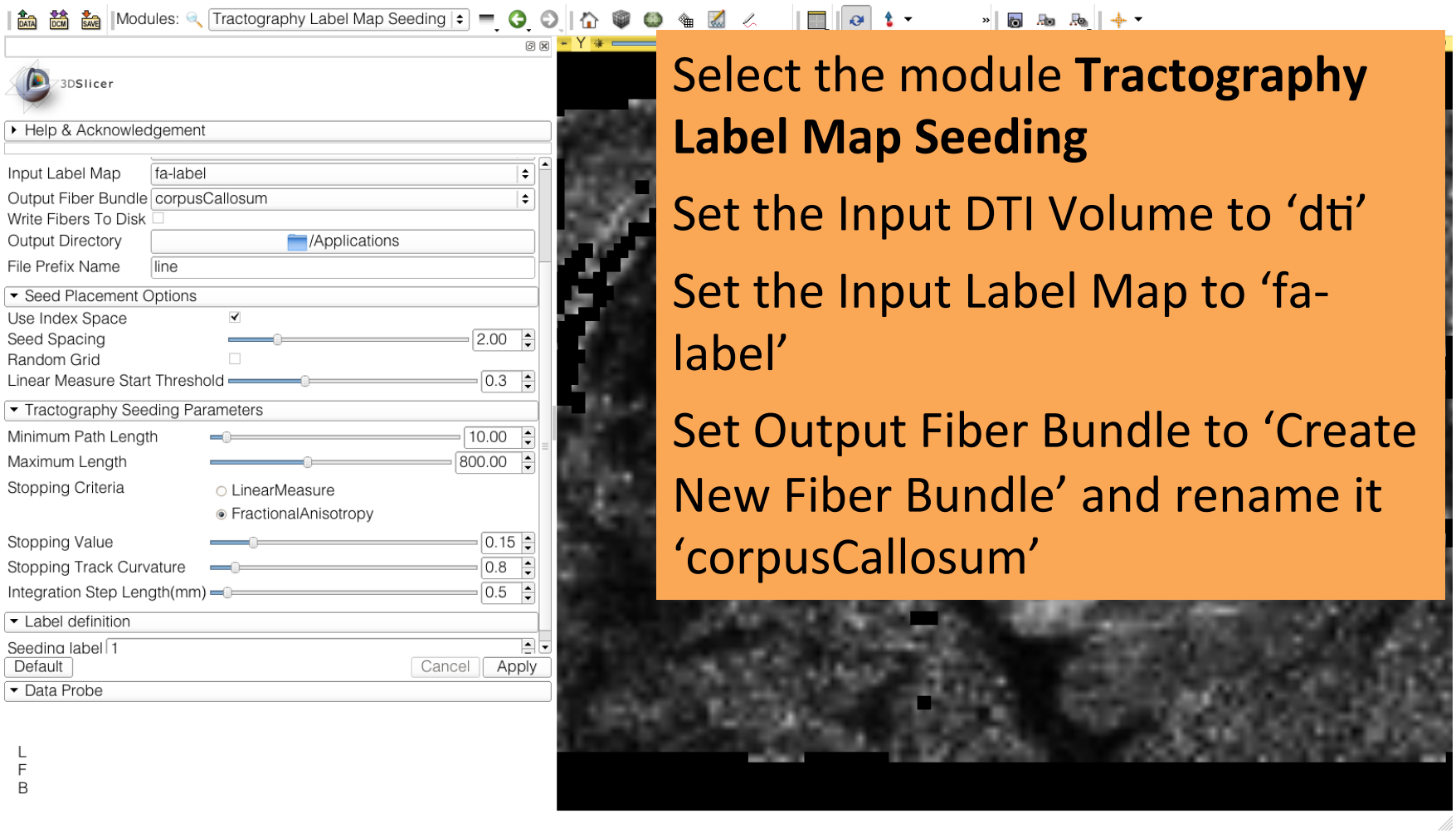
The tracts will be seeded from the region of interest defined in the corpus callosum area.

Streamline tractography

<u>Underlying Assumption</u>: the orientation of the fibers is collinear with the direction of the principal eigenvector



Labelmap Seeding: I/O



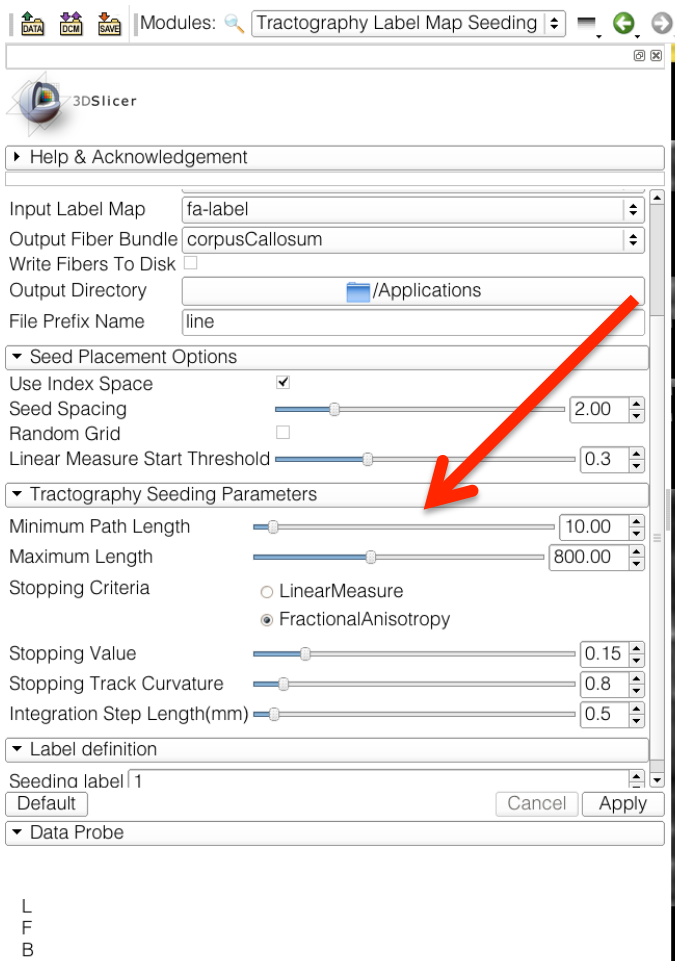
Select the module **Tractography Label Map Seeding**

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

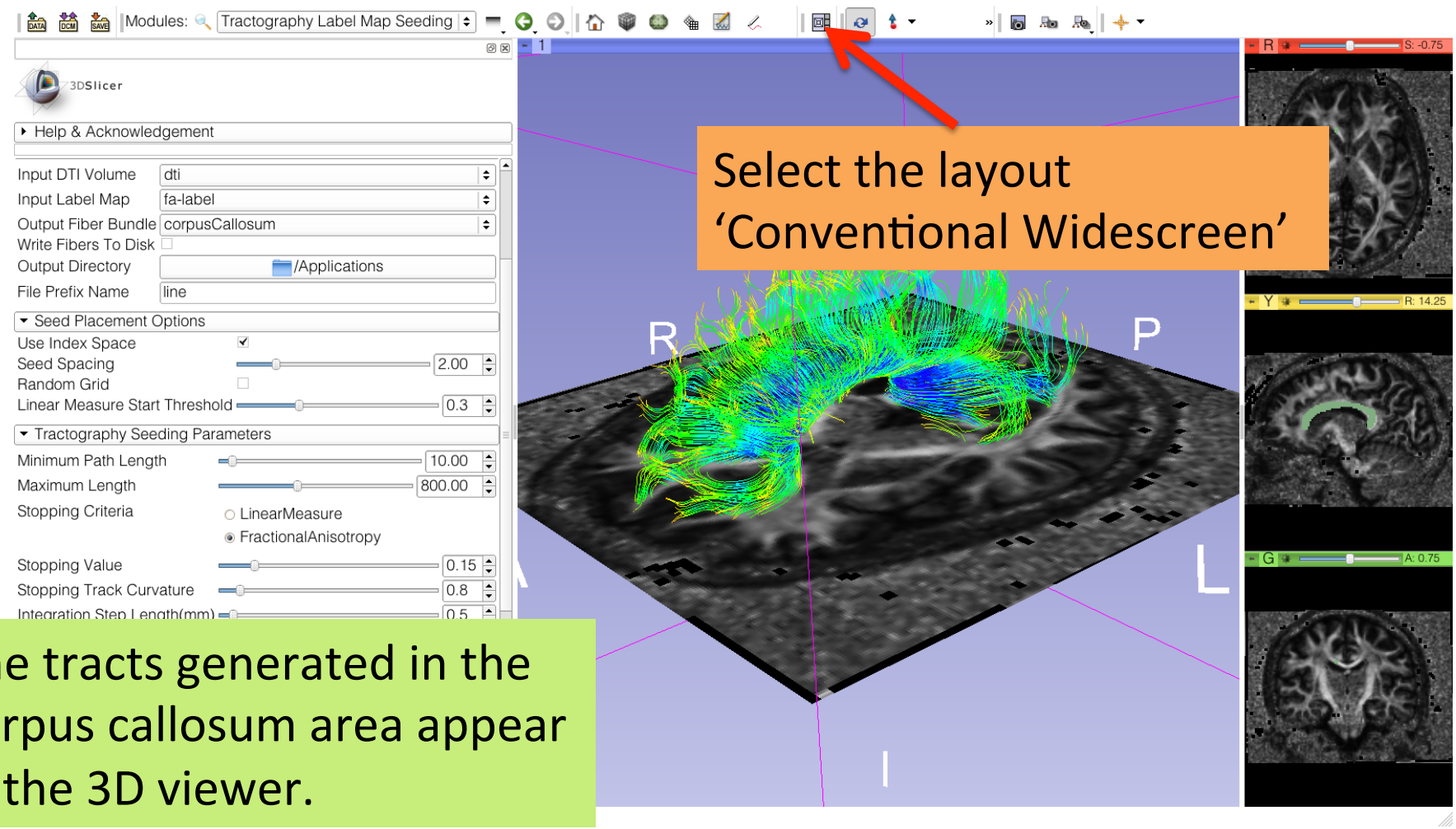
-Stopping value: 0.15

-Stopping track curvature: 0.8

-Integration step length: 0.5 mm

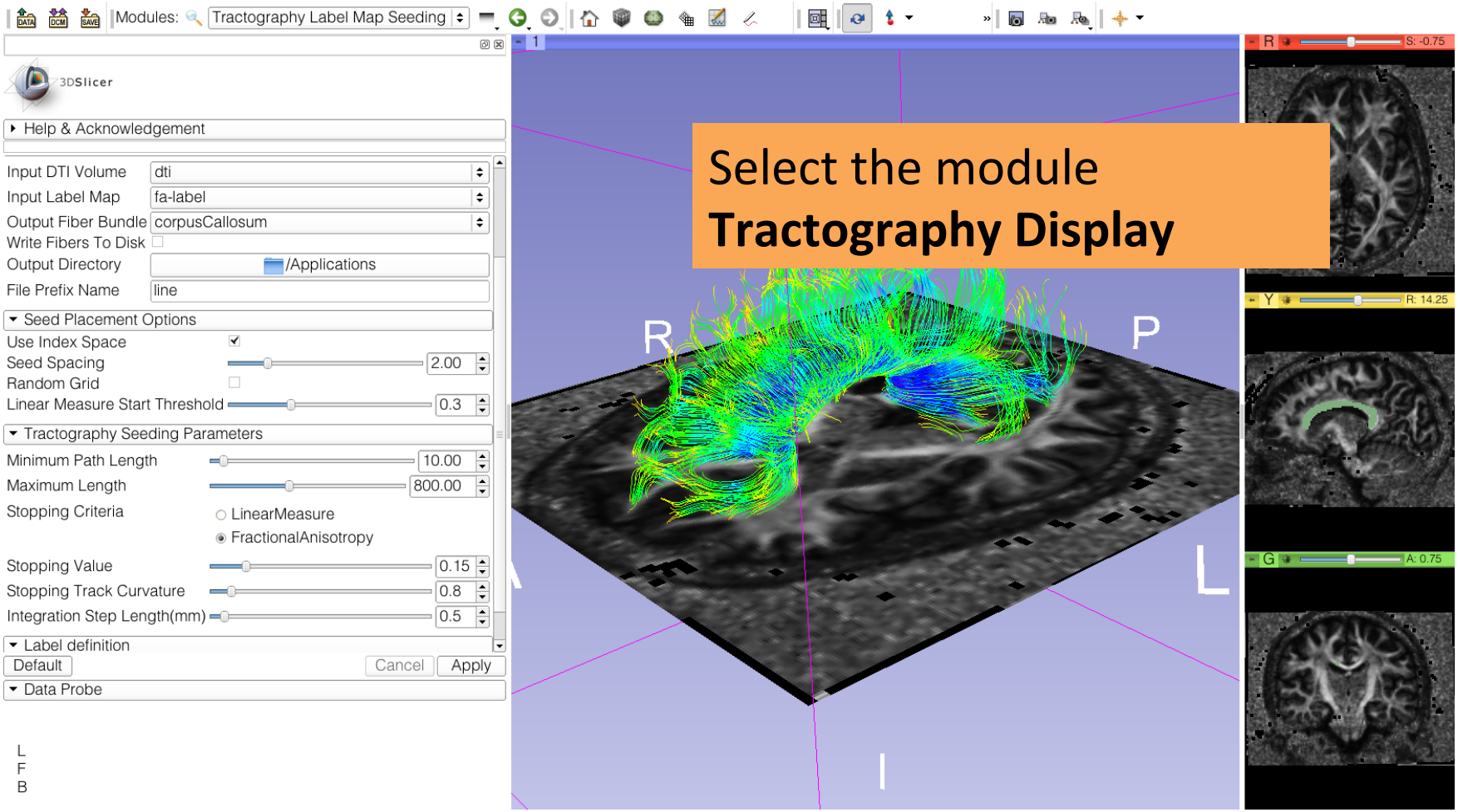
Click on **Apply**

Labelmap Seeding: Tracts



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

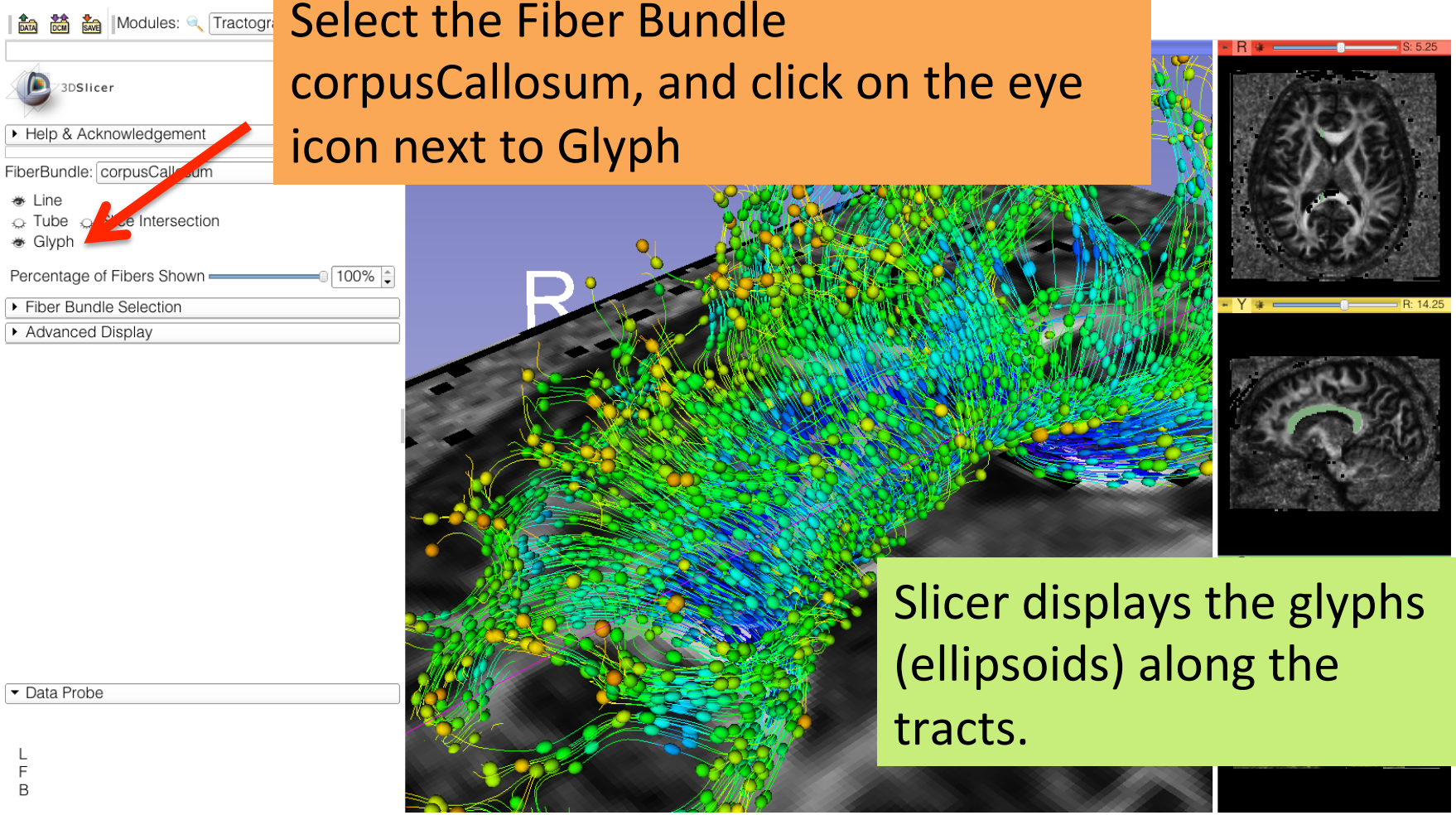
Labelmap Seeding: Tracts



Select the module
Tractography Display

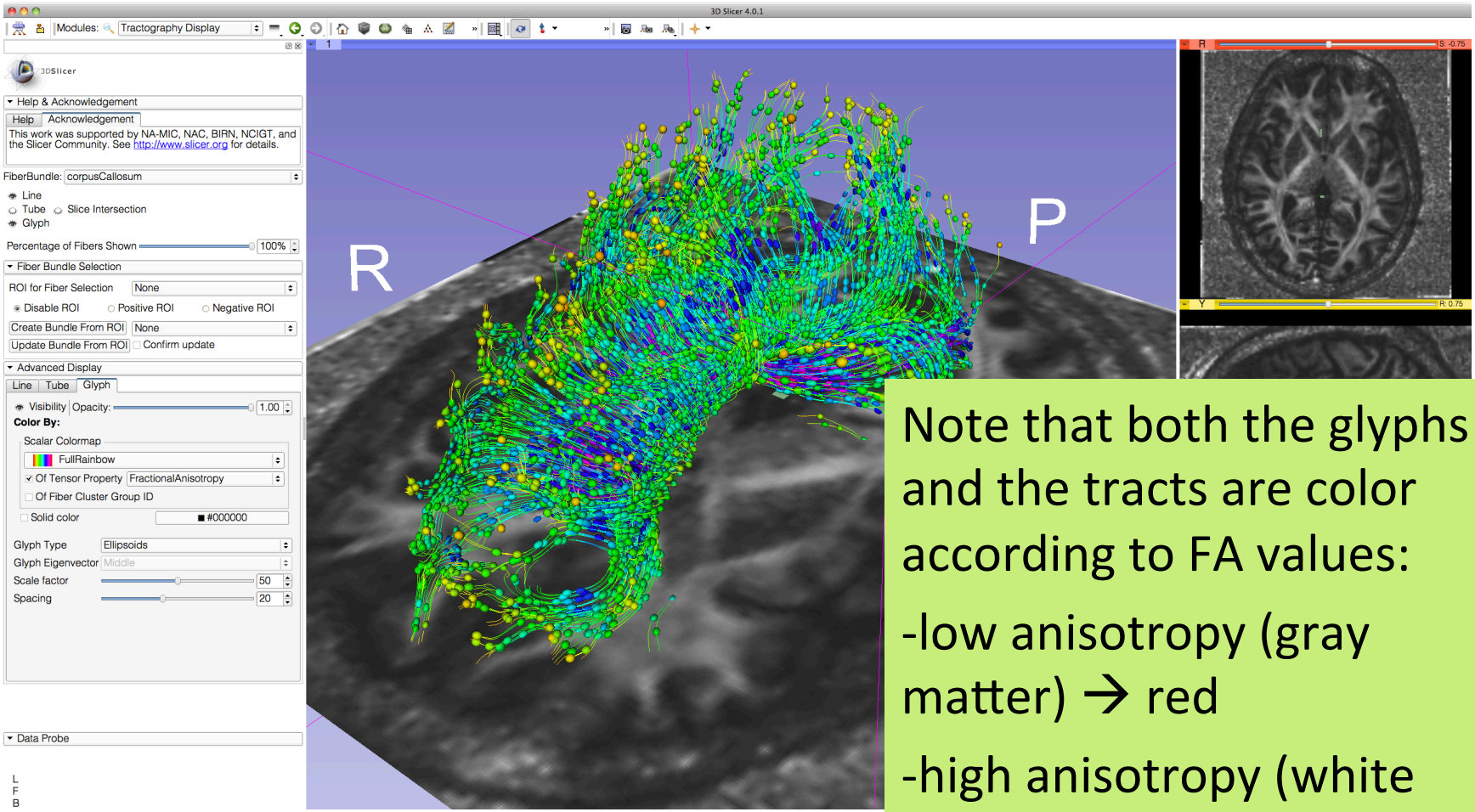
Tractography Results

Select the Fiber Bundle corpusCallosum, and click on the eye icon next to Glyph



Slicer displays the glyphs (ellipsoids) along the tracts.

Tractography Results

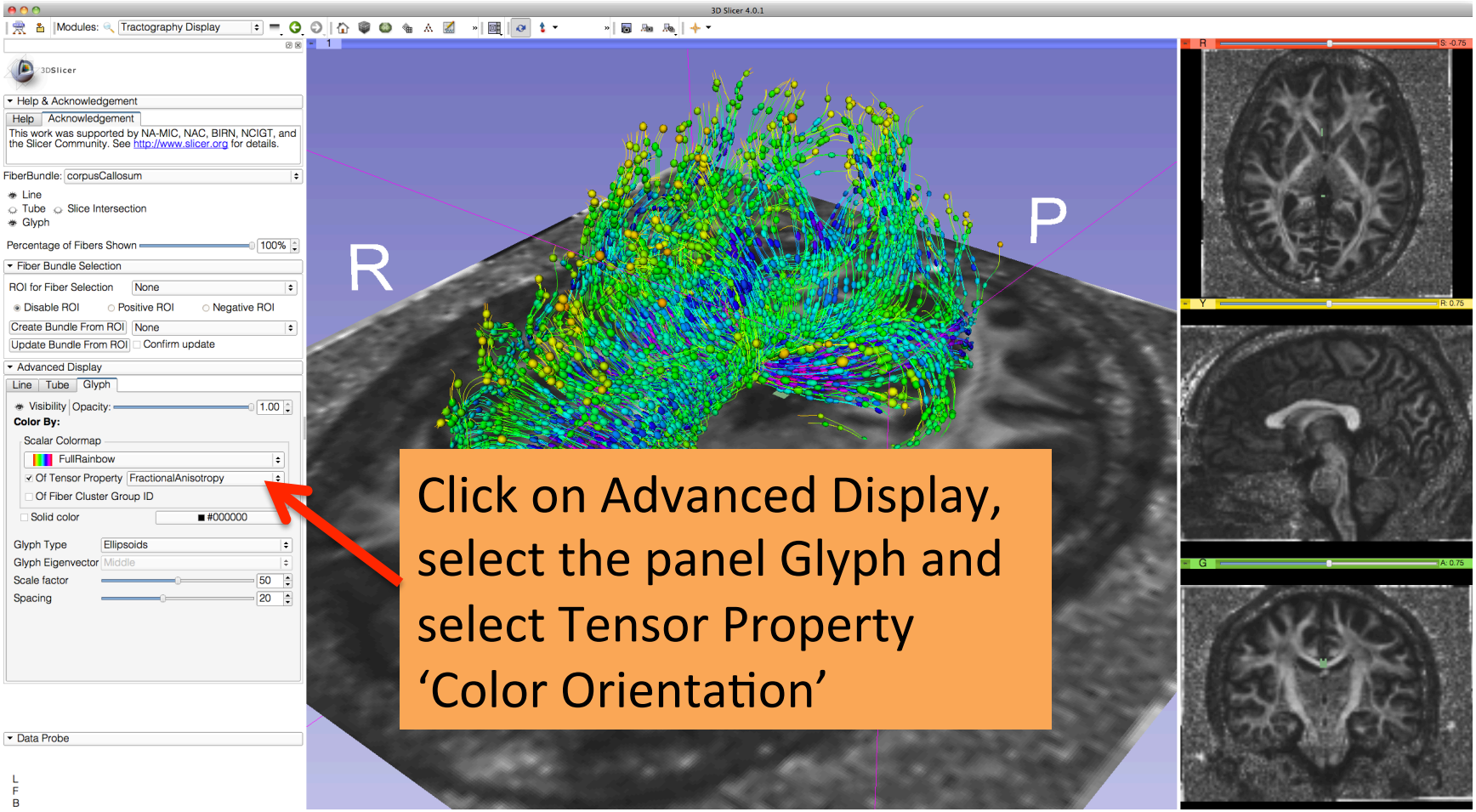


Note that both the glyphs and the tracts are color according to FA values:

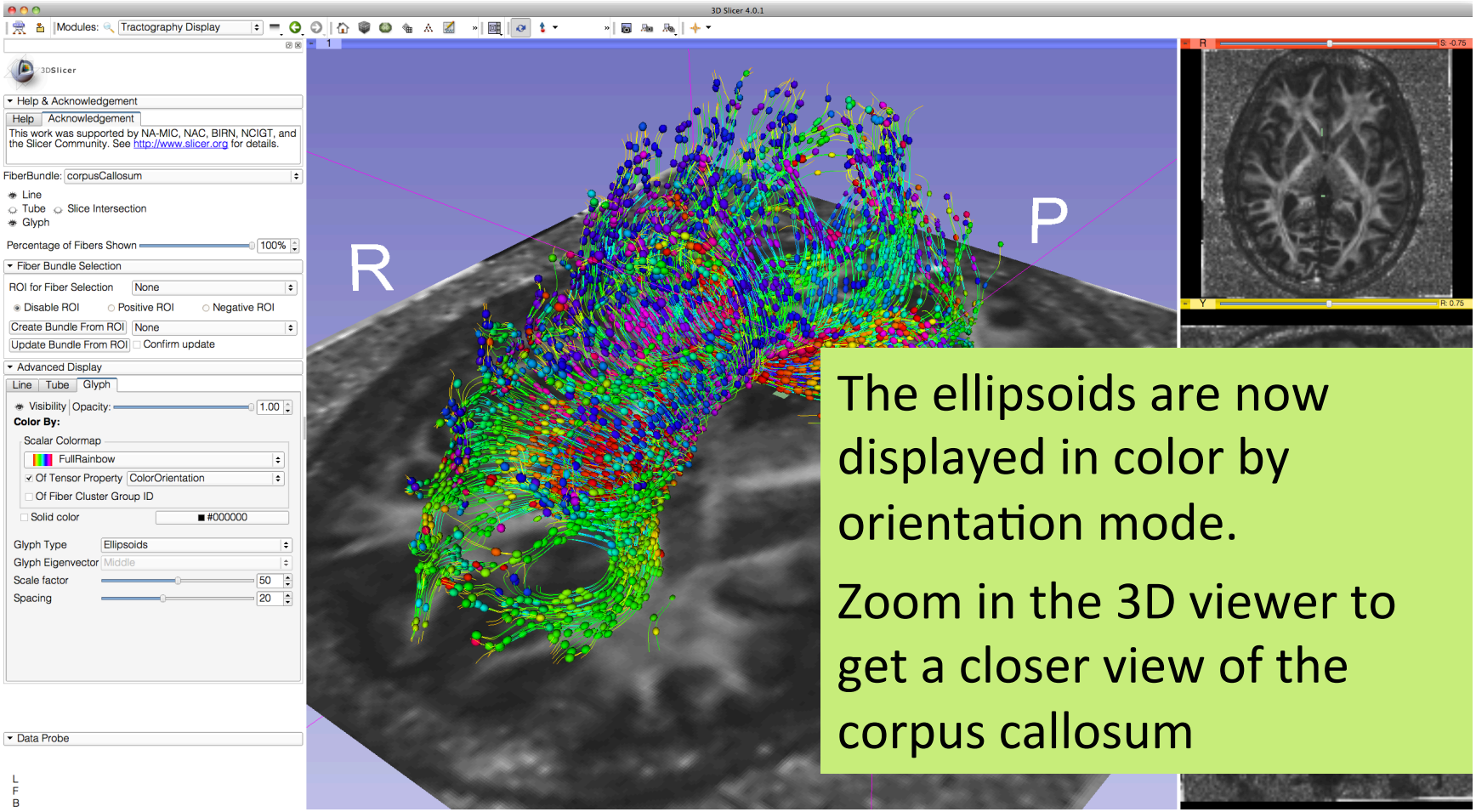
-low anisotropy (gray matter) → red

-high anisotropy (white matter) → blue

Tractography Results



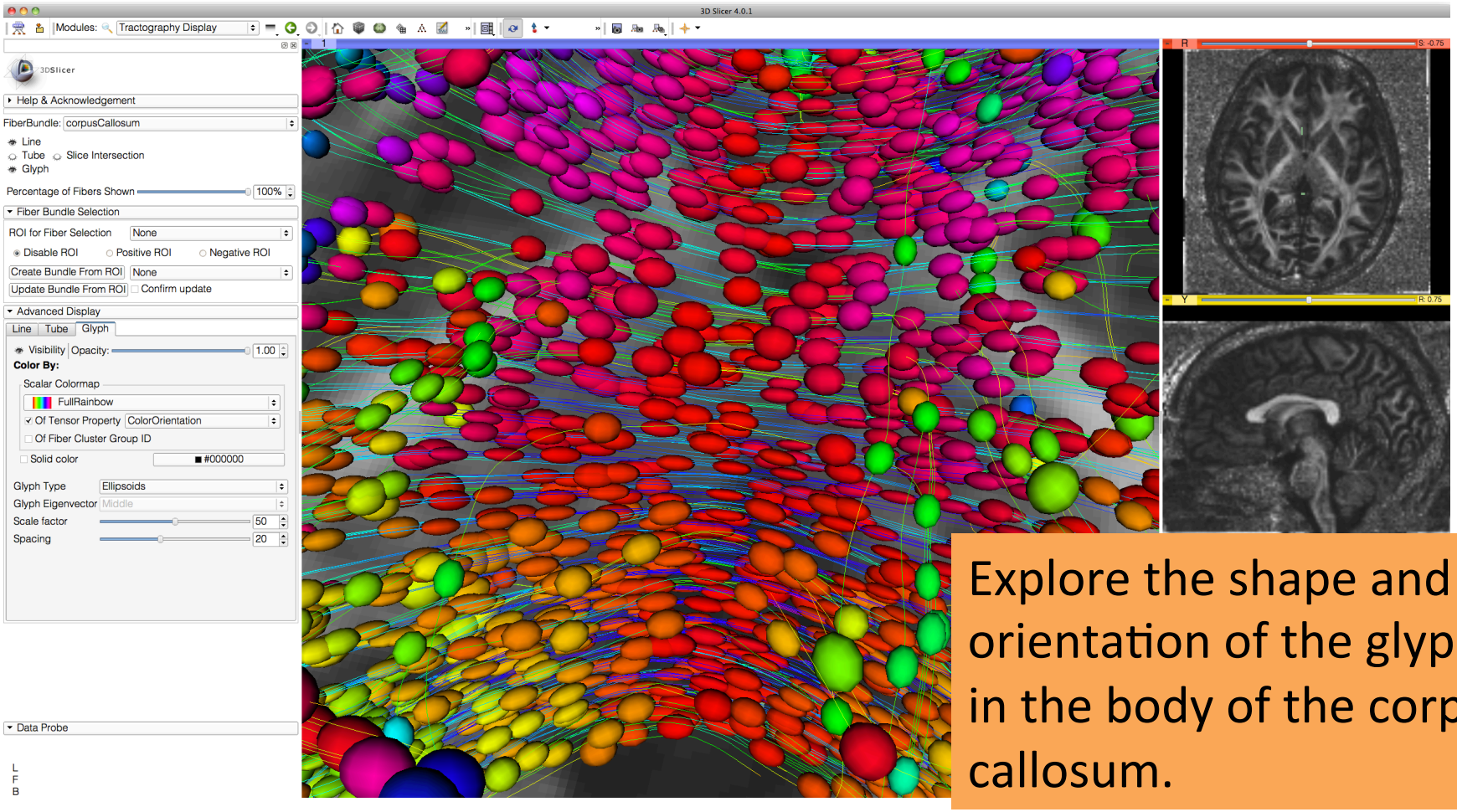
Tractography Results



The ellipsoids are now displayed in color by orientation mode.

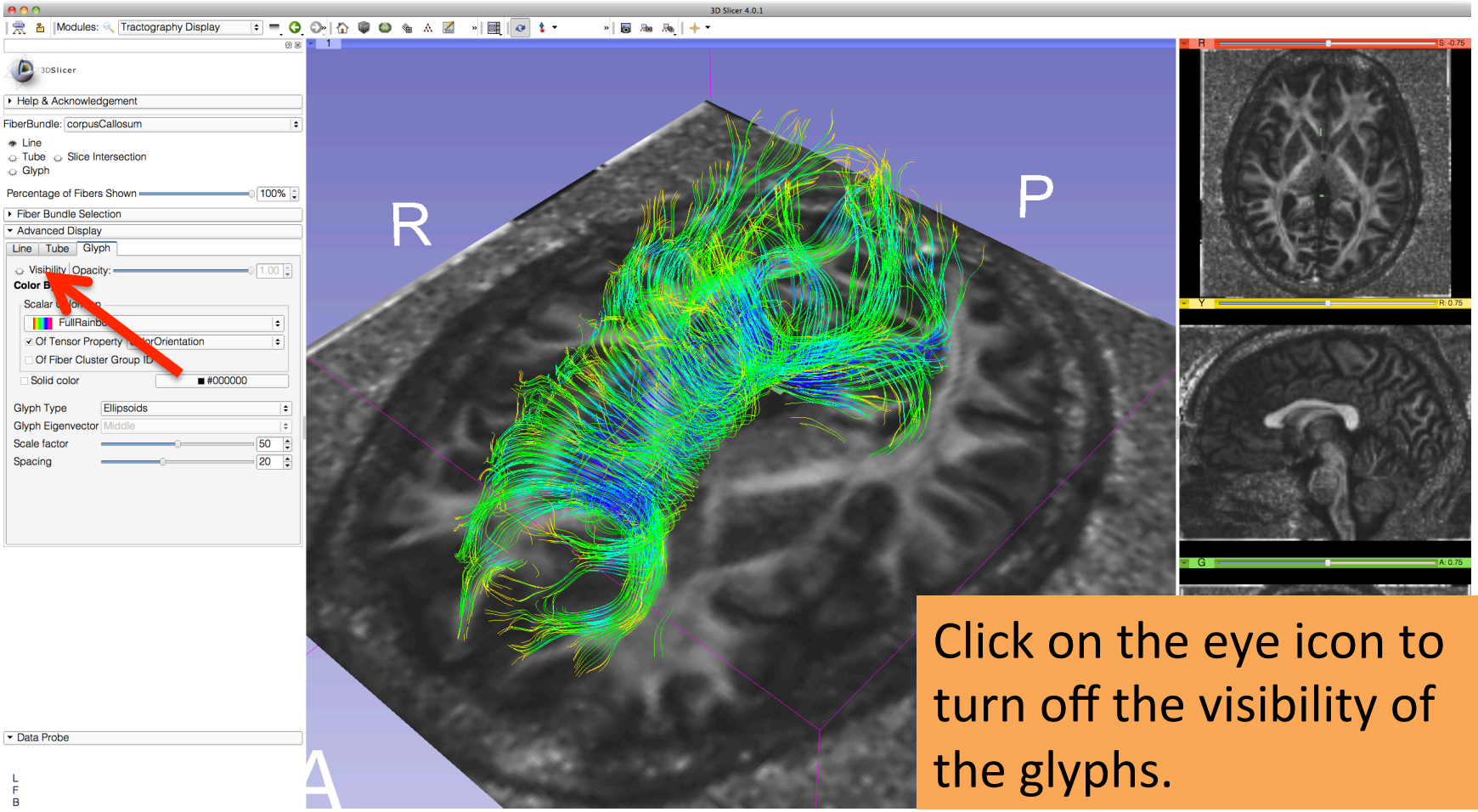
Zoom in the 3D viewer to get a closer view of the corpus callosum

Tractography Results



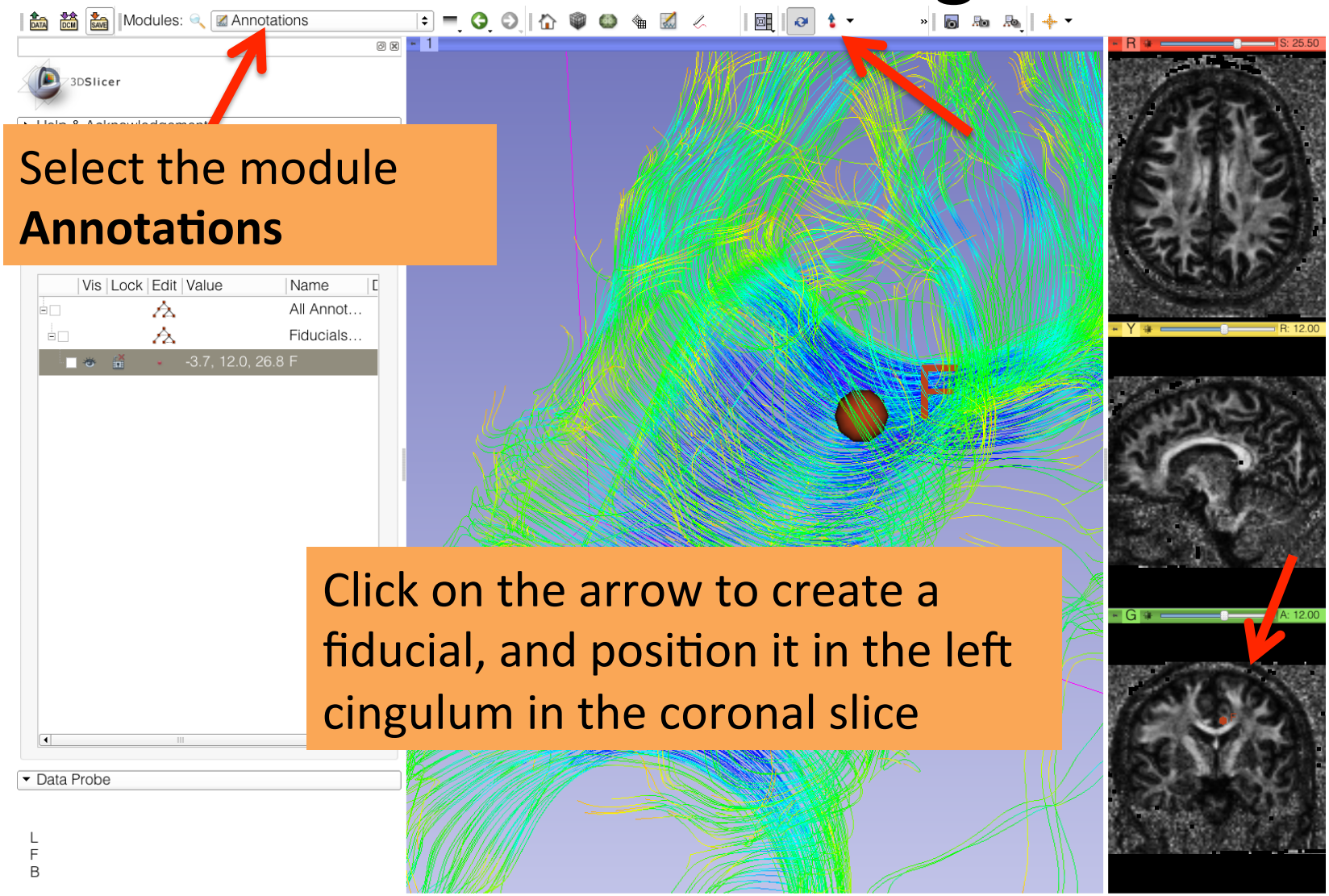
Explore the shape and orientation of the glyphs in the body of the corpus callosum.

Tractography Results



Click on the eye icon to turn off the visibility of the glyphs.

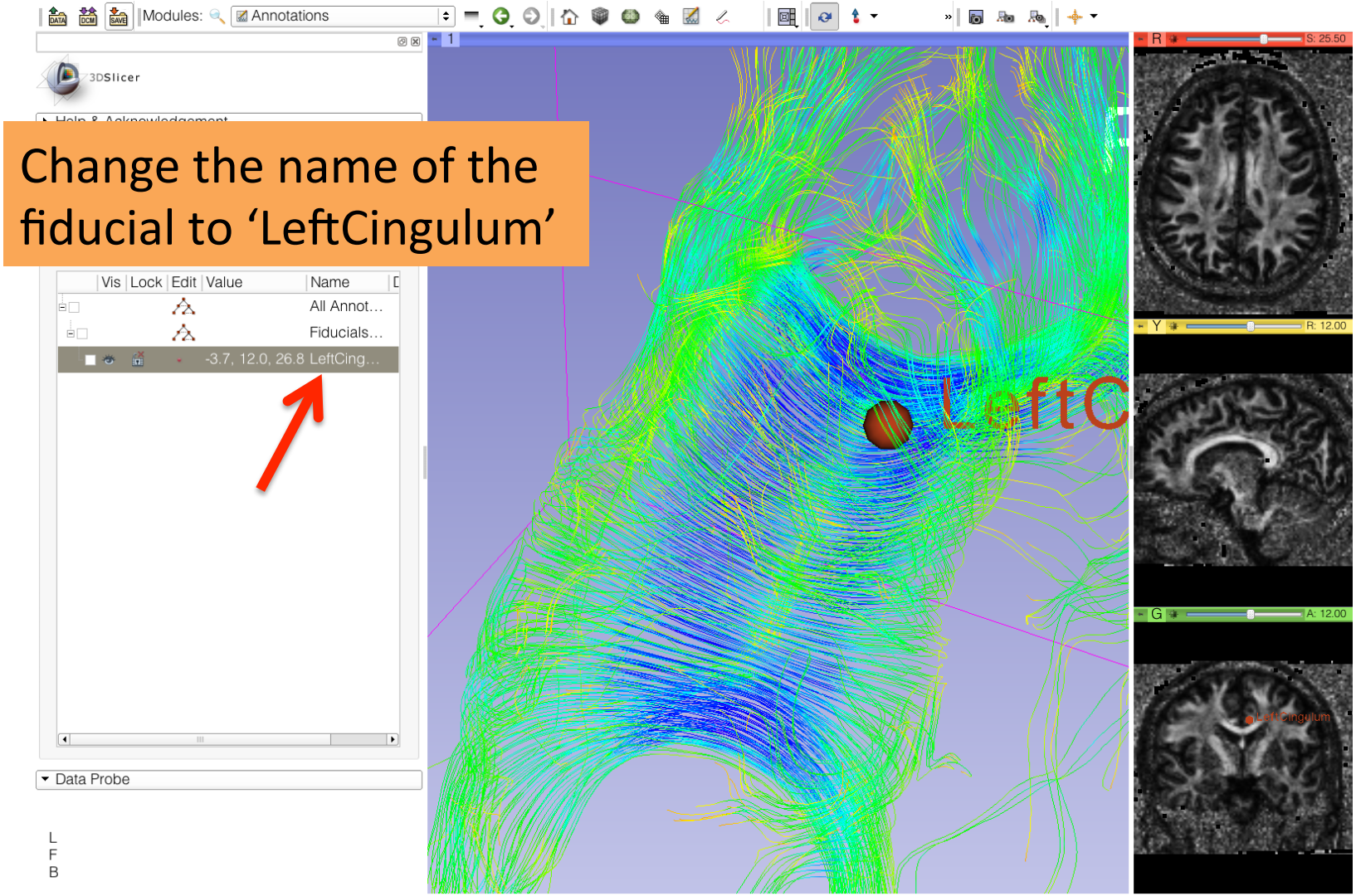
Fiducial Seeding



Select the module **Annotations**

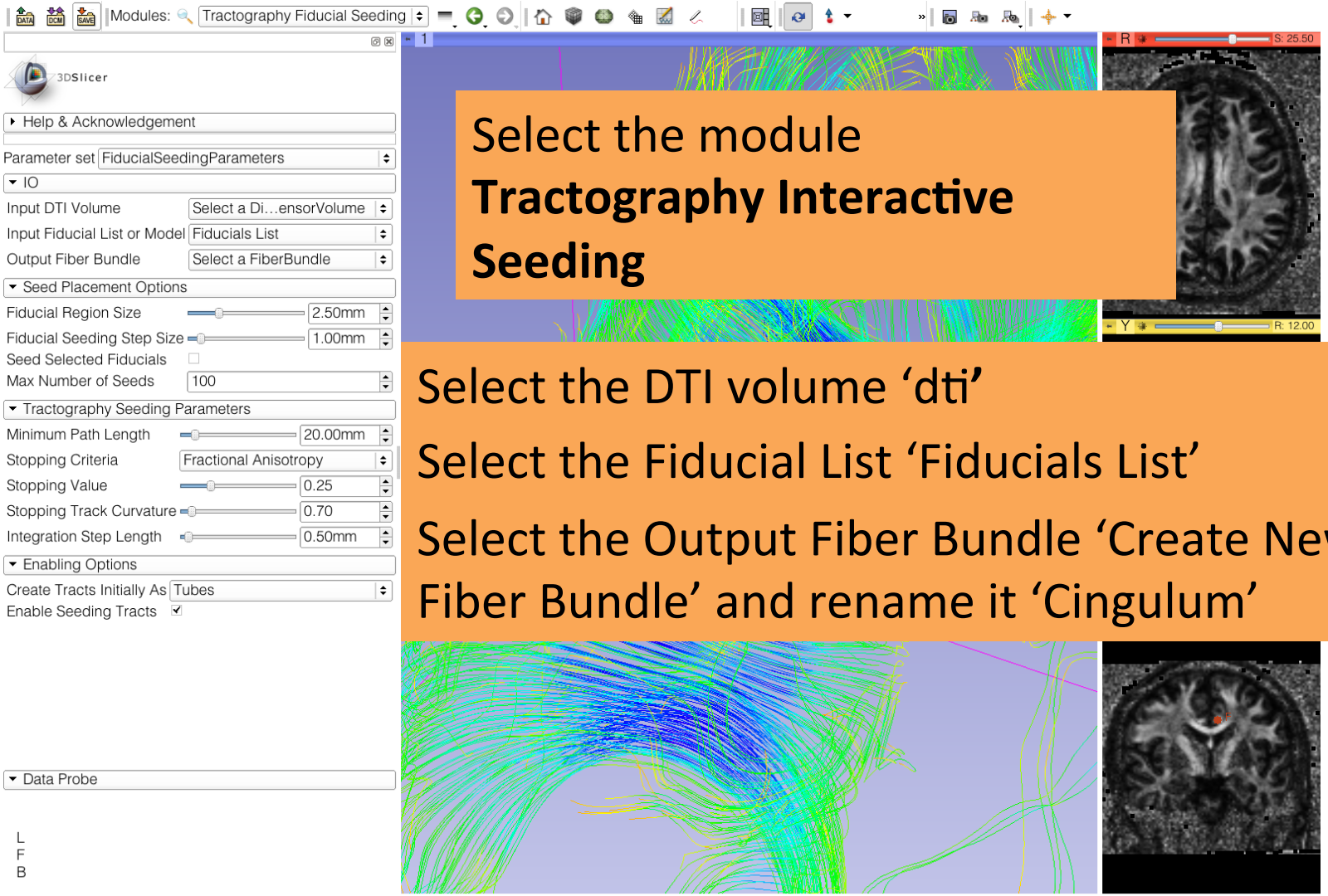
Click on the arrow to create a fiducial, and position it in the left cingulum in the coronal slice

Fiducial Seeding



Change the name of the fiducial to 'LeftCingulum'

Fiducial Seeding



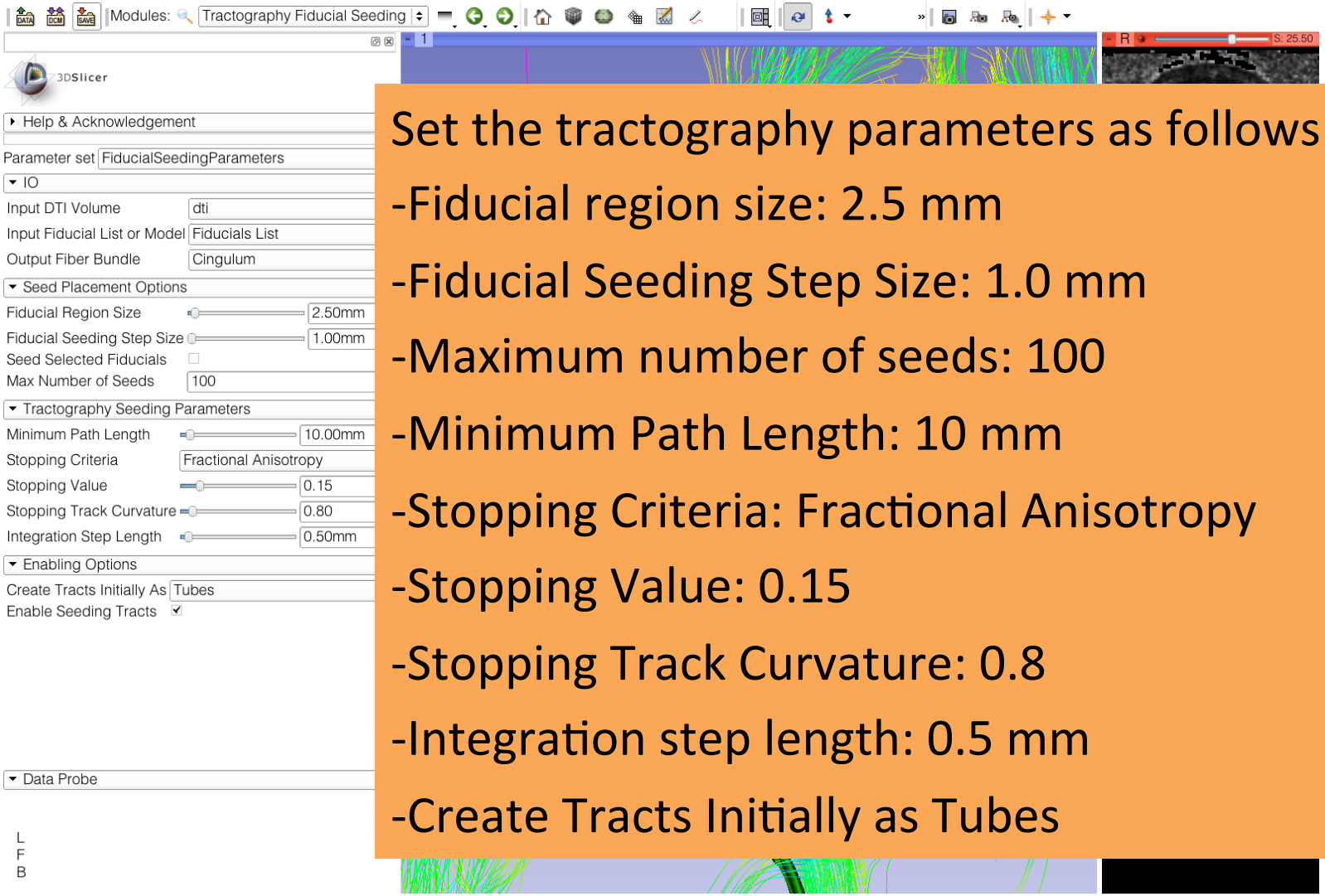
Select the module **Tractography Interactive Seeding**

Select the DTI volume ‘dti’

Select the Fiducial List ‘Fiducials List’

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

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

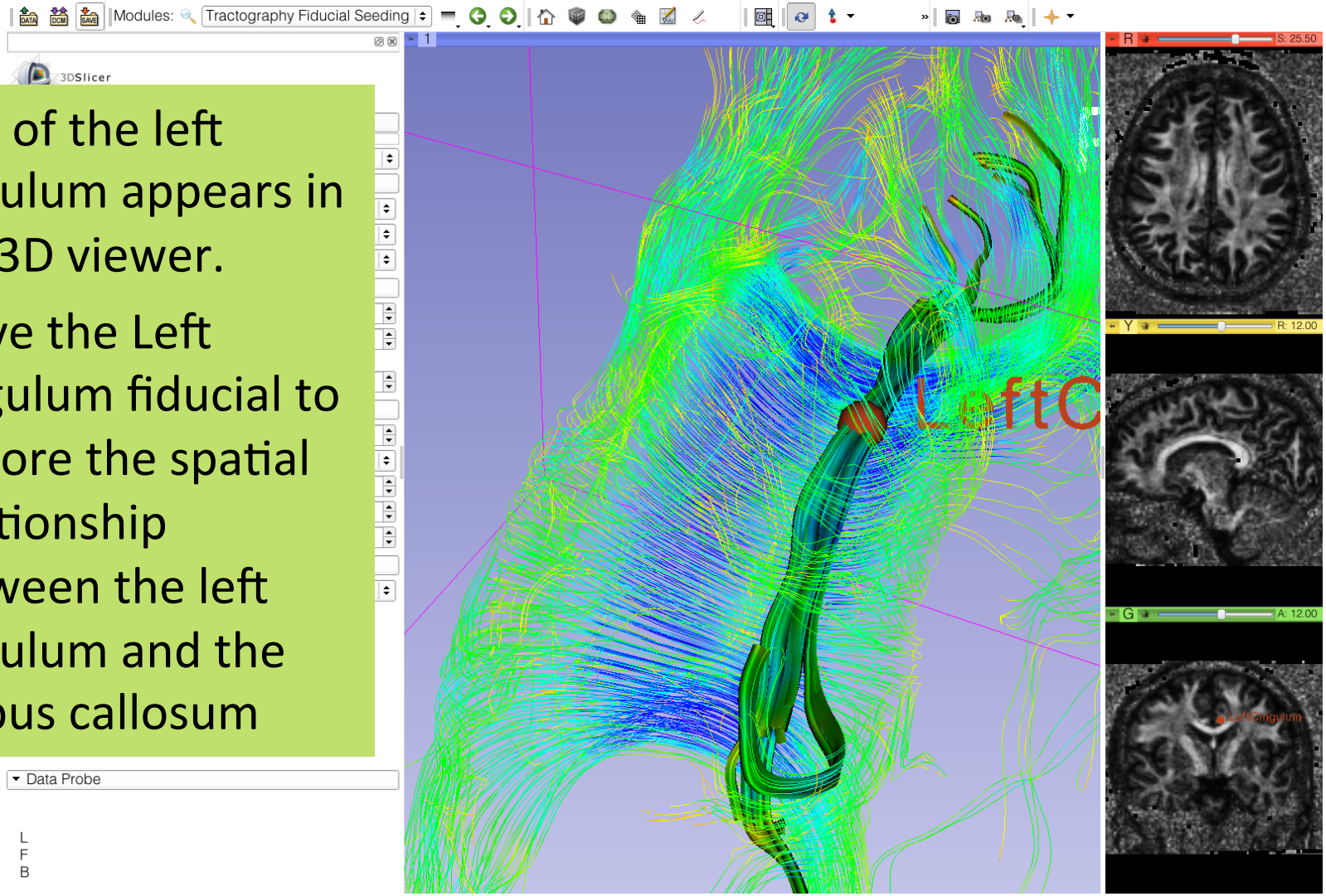
-Integration step length: 0.5 mm

-Create Tracts Initially as Tubes

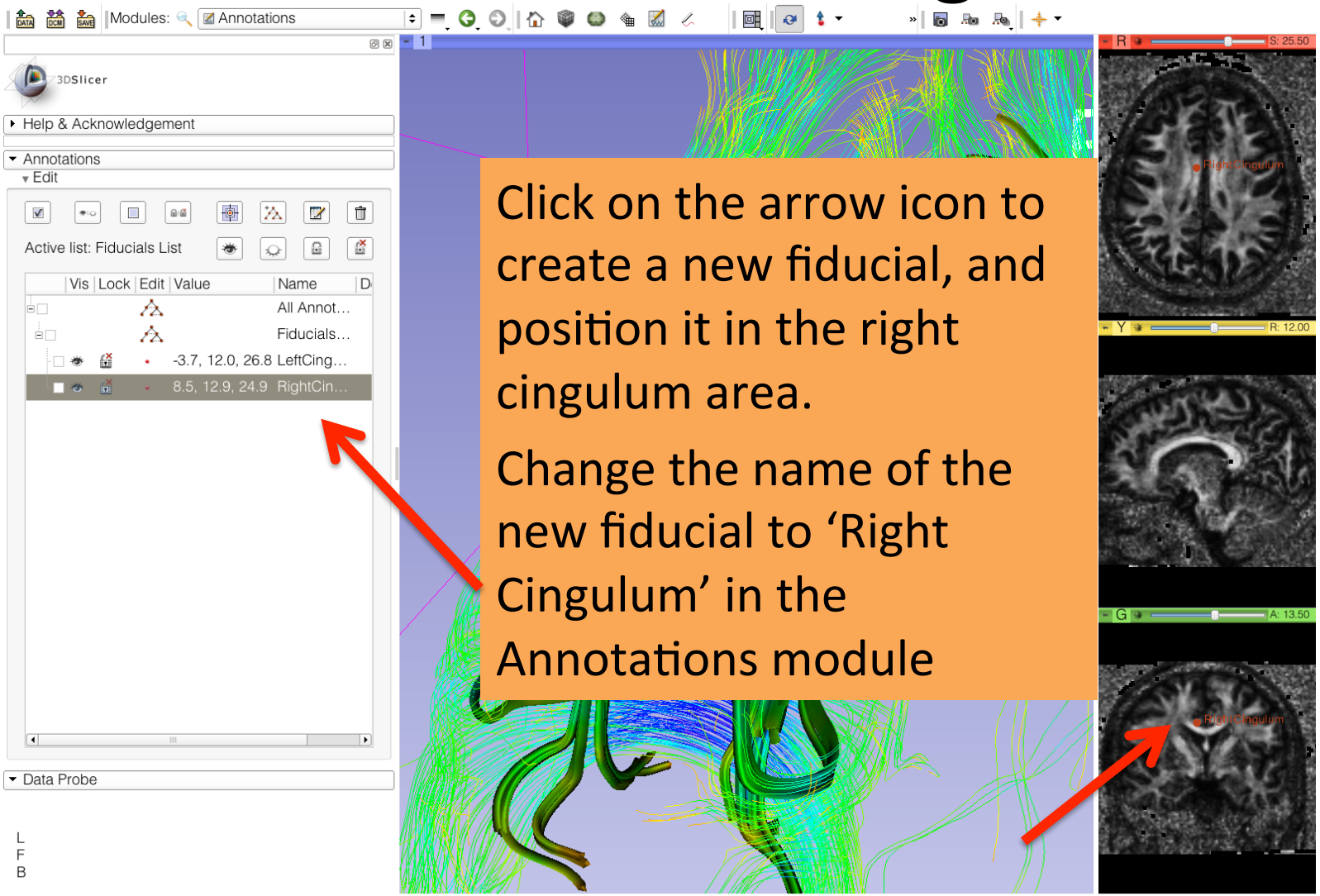
Fiducial Seeding

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



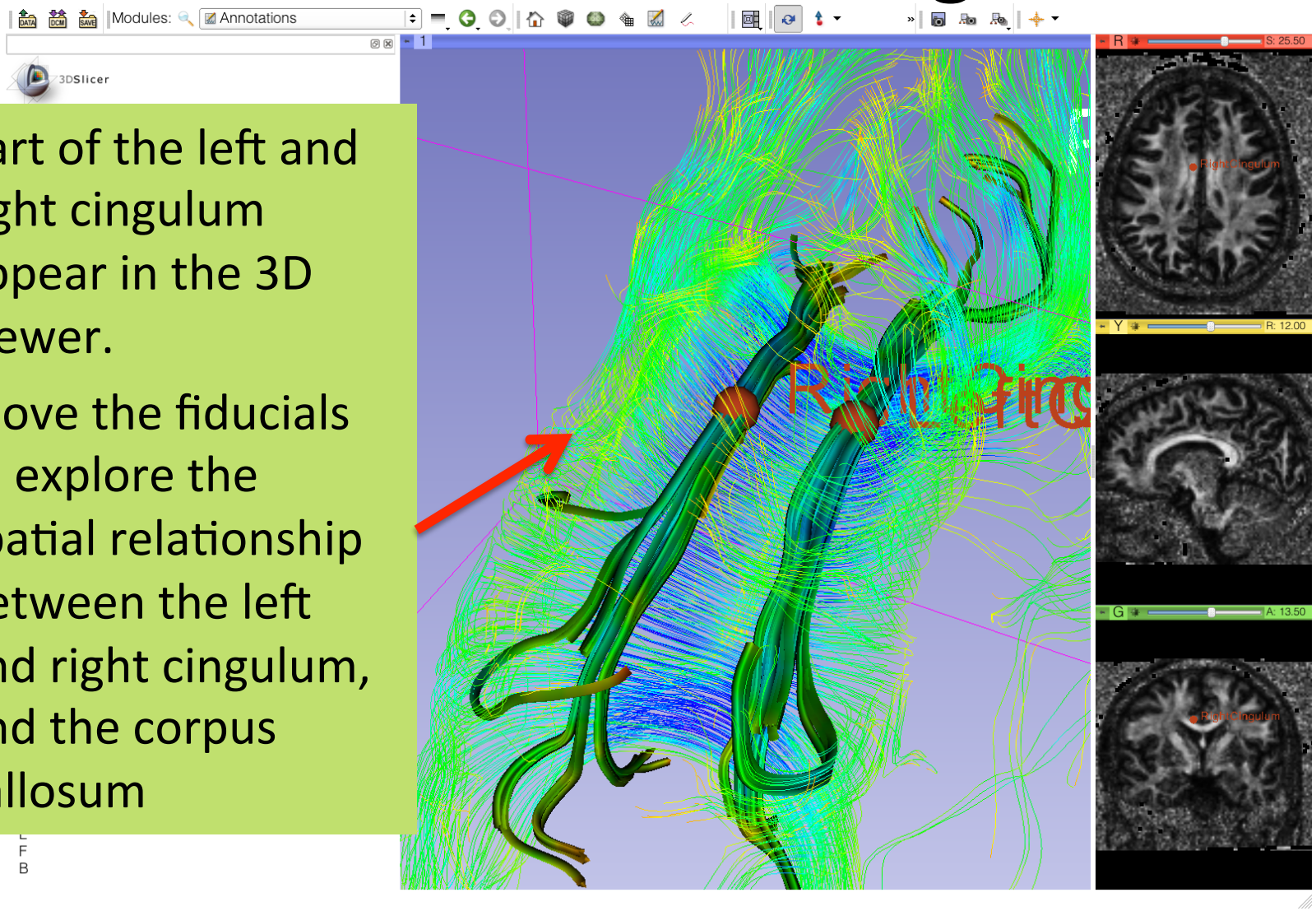
Fiducial Seeding



Click on the arrow icon to create a new fiducial, and position it in the right cingulum area.

Change the name of the new fiducial to 'Right Cingulum' in the Annotations module

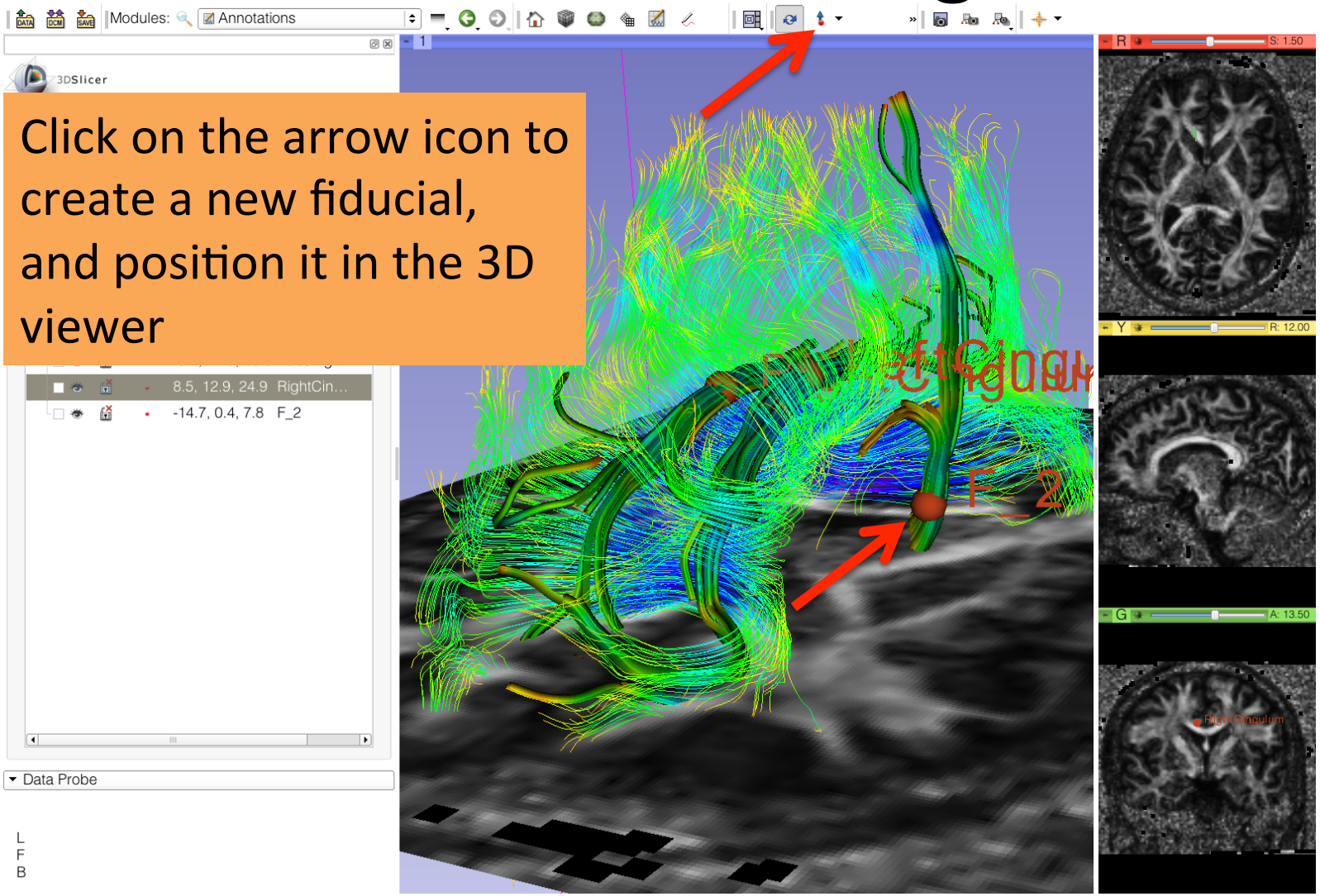
Fiducial Seeding



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

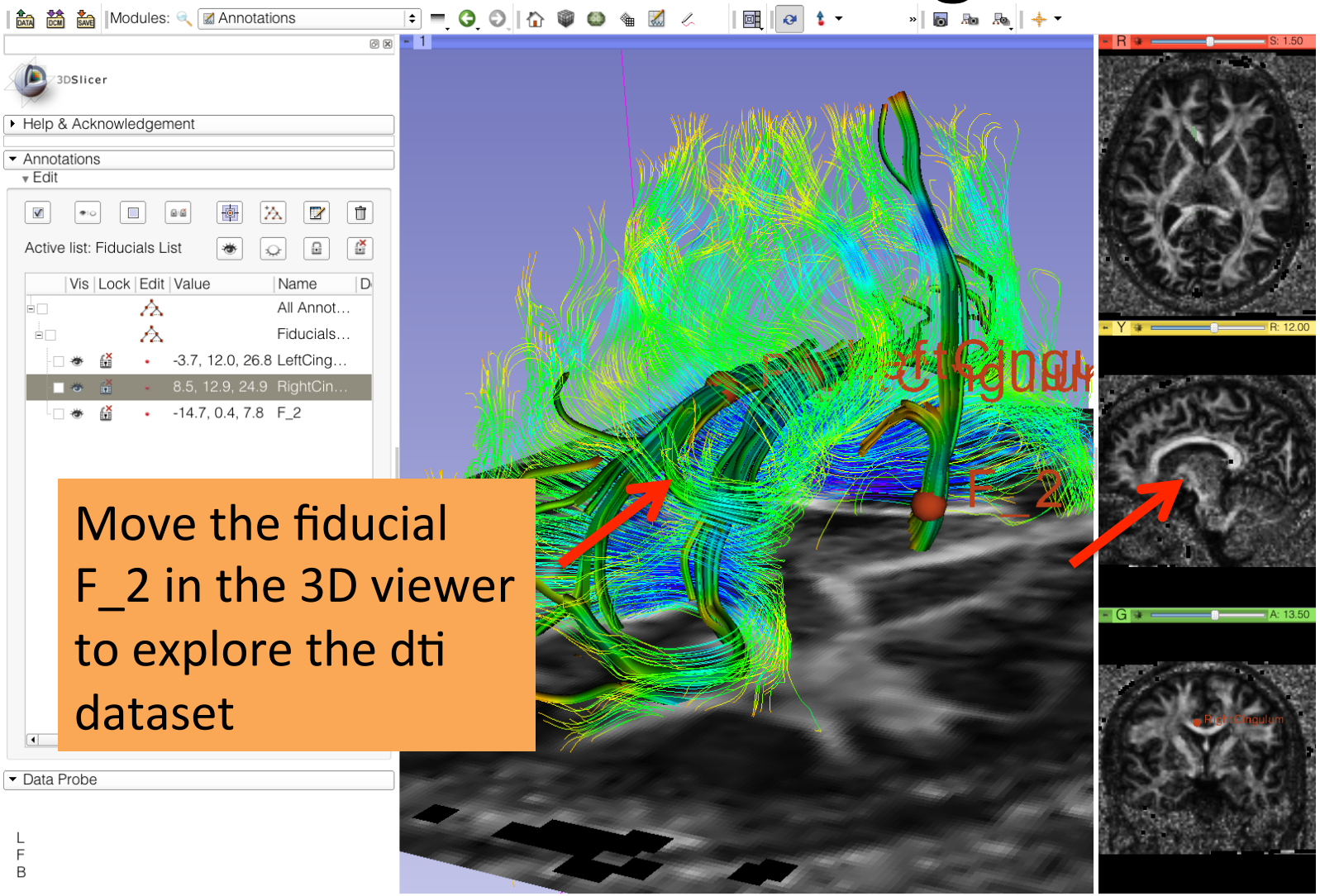
Move the fiducials to explore the spatial relationship between the left and right cingulum, and the corpus callosum

Fiducial Seeding



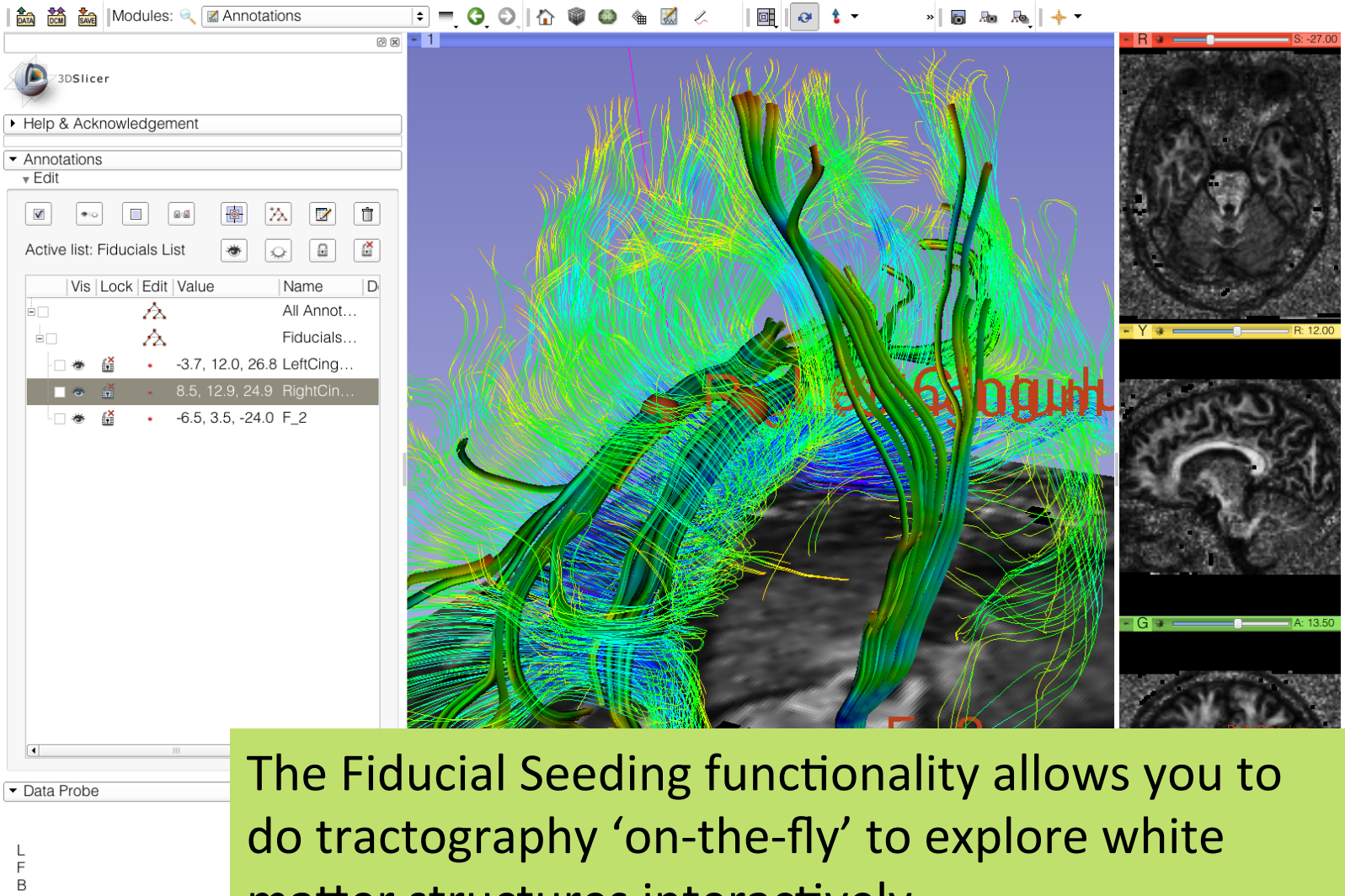
Click on the arrow icon to create a new fiducial, and position it in the 3D viewer

Fiducial Seeding



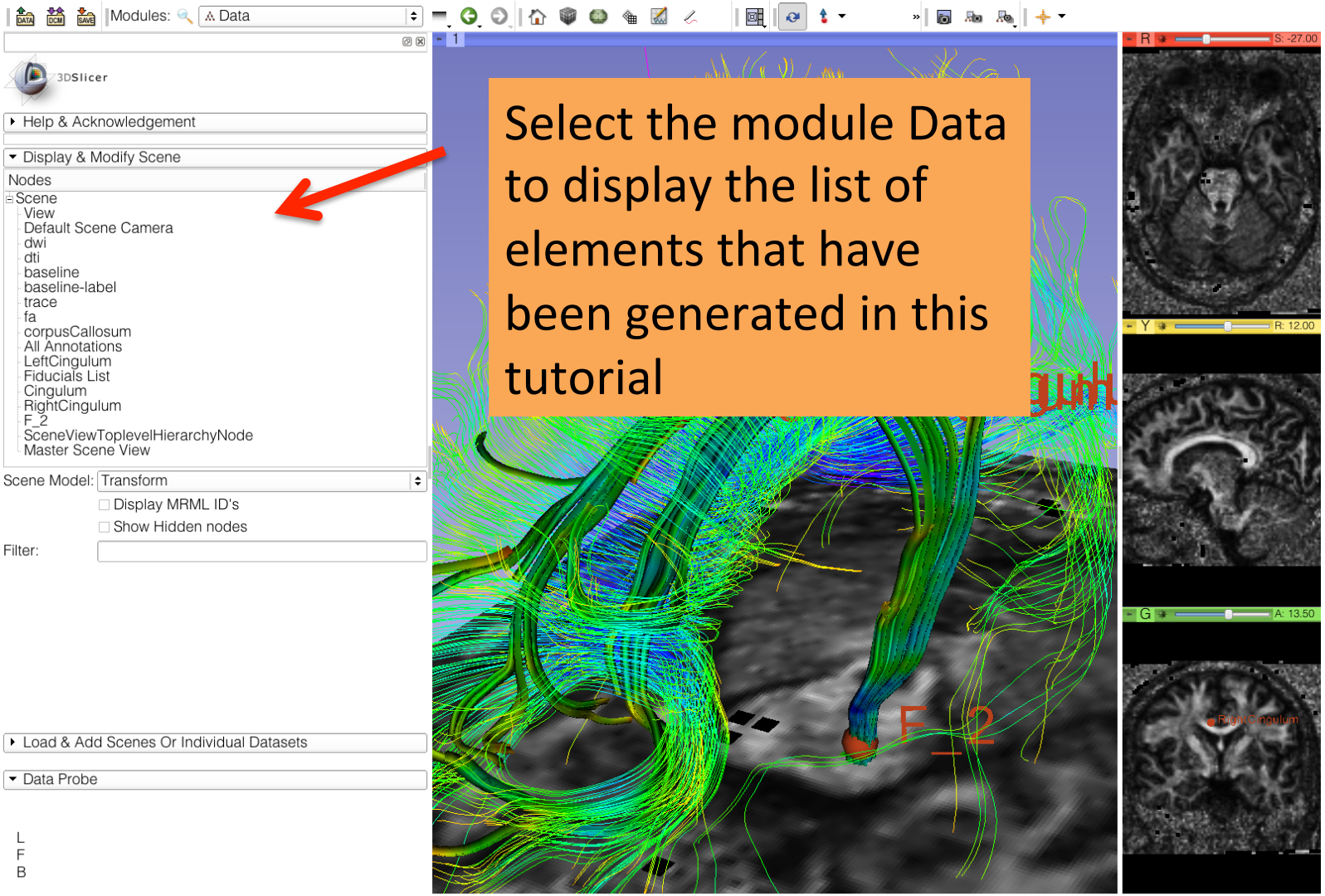
Move the fiducial F_2 in the 3D viewer to explore the dti dataset

Tractography ‘on-the-fly’



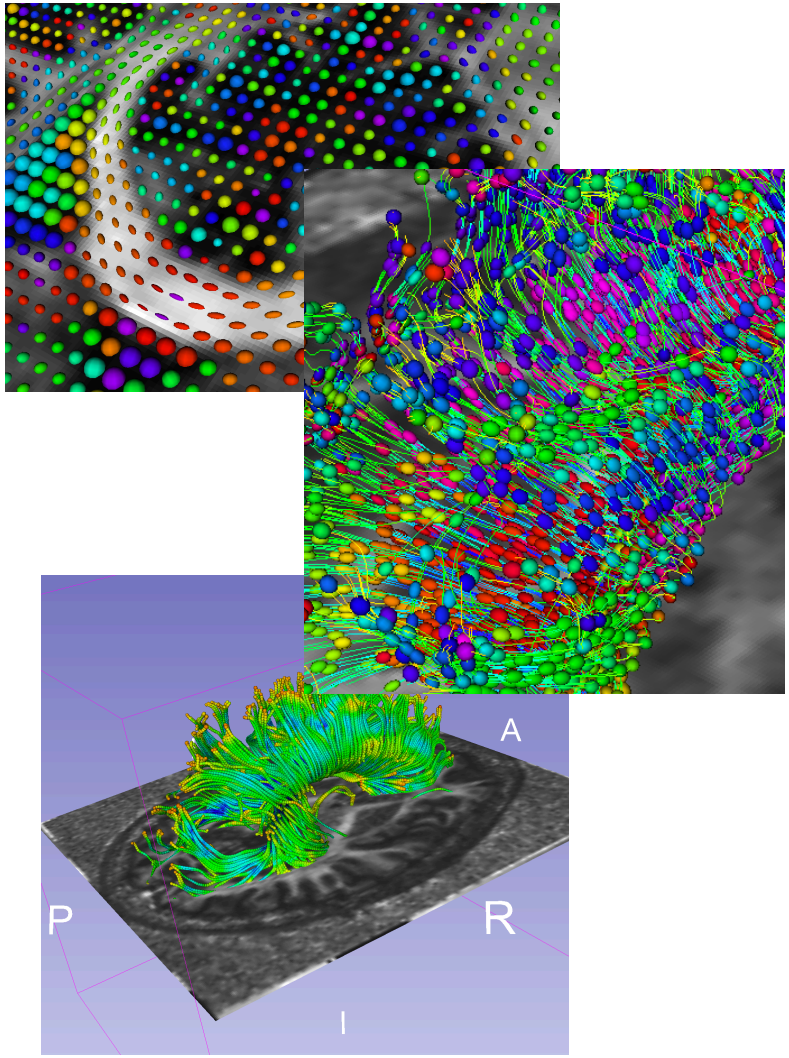
The Fiducial Seeding functionality allows you to do tractography ‘on-the-fly’ to explore white matter structures interactively

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 brain white matter pathways.

Acknowledgments

National Alliance for Medical Image Computing
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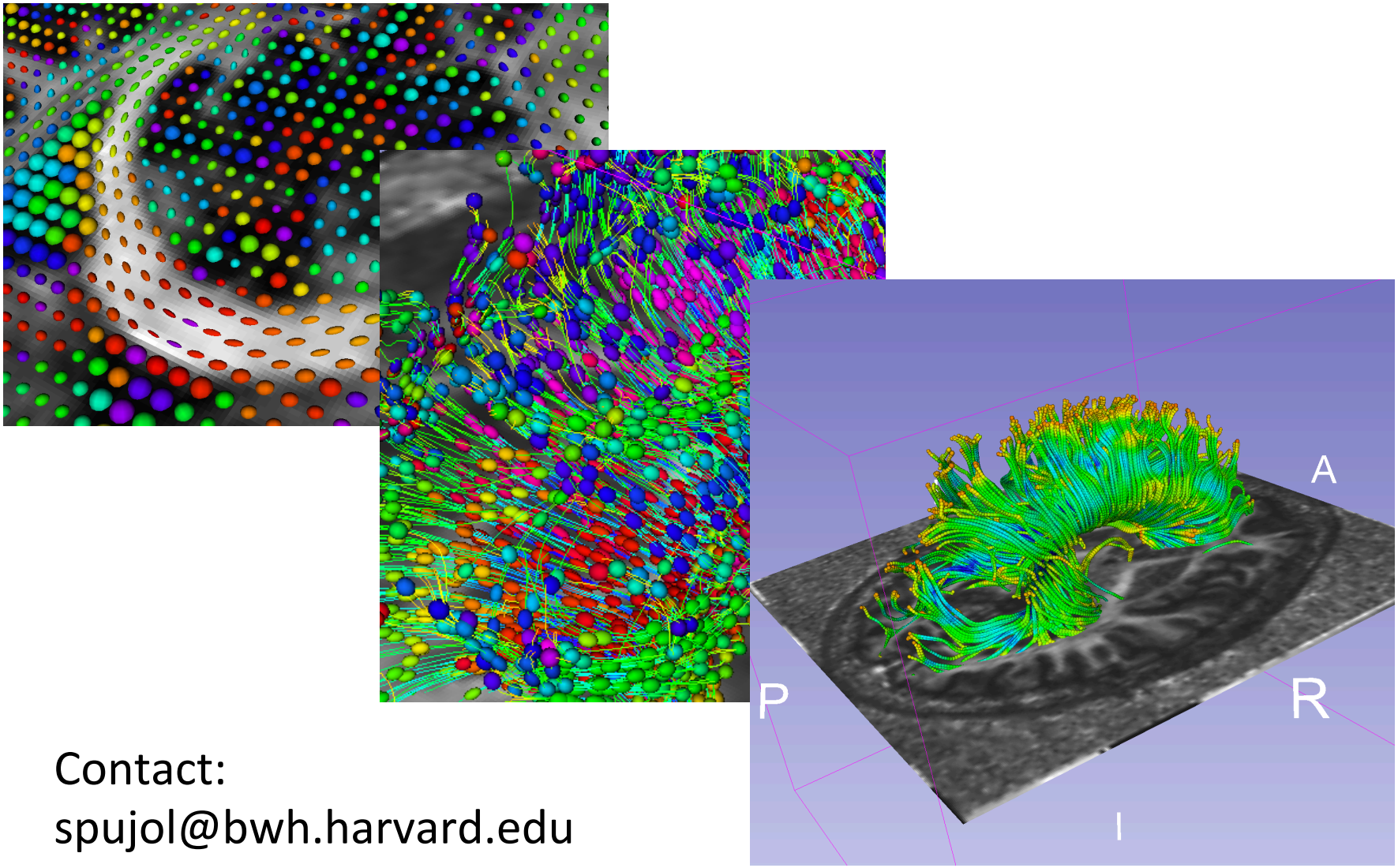
Neuroimage Analysis Center
NIH P41RR013218



Contact:
spujol@bwh.harvard.edu

Slicer Community

- www.slicer.org

- Mailing lists:

slicer-user@bwh.harvard.edu

slicer-devel@bwh.harvard.edu