Diffusion MRI Analysis

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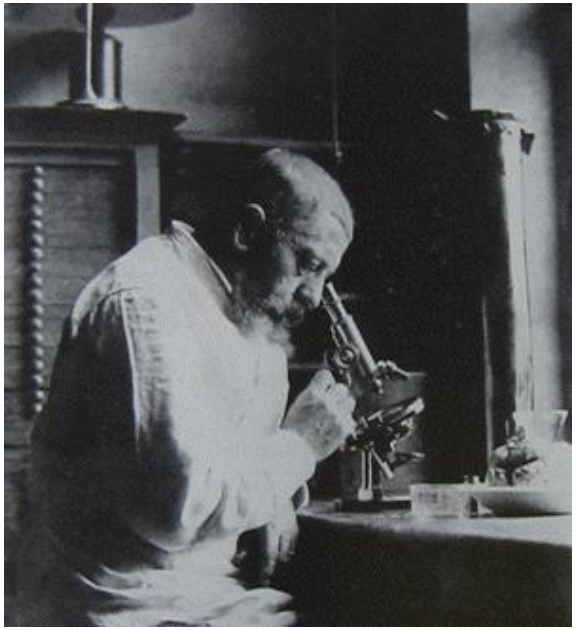
Brain Anatomy

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

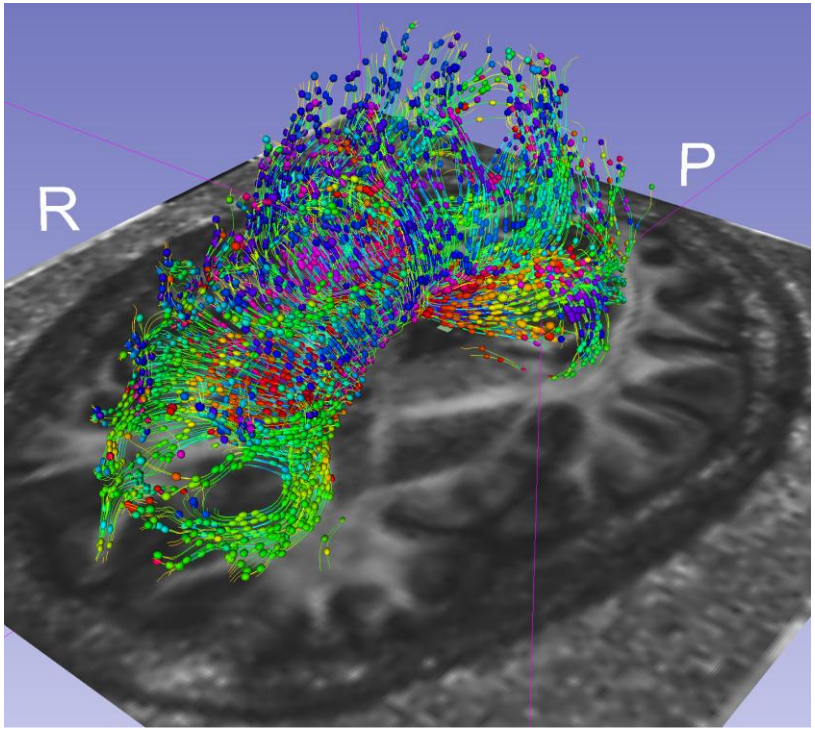
(~ 10 µm axon diameter)

White Matter Exploration



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

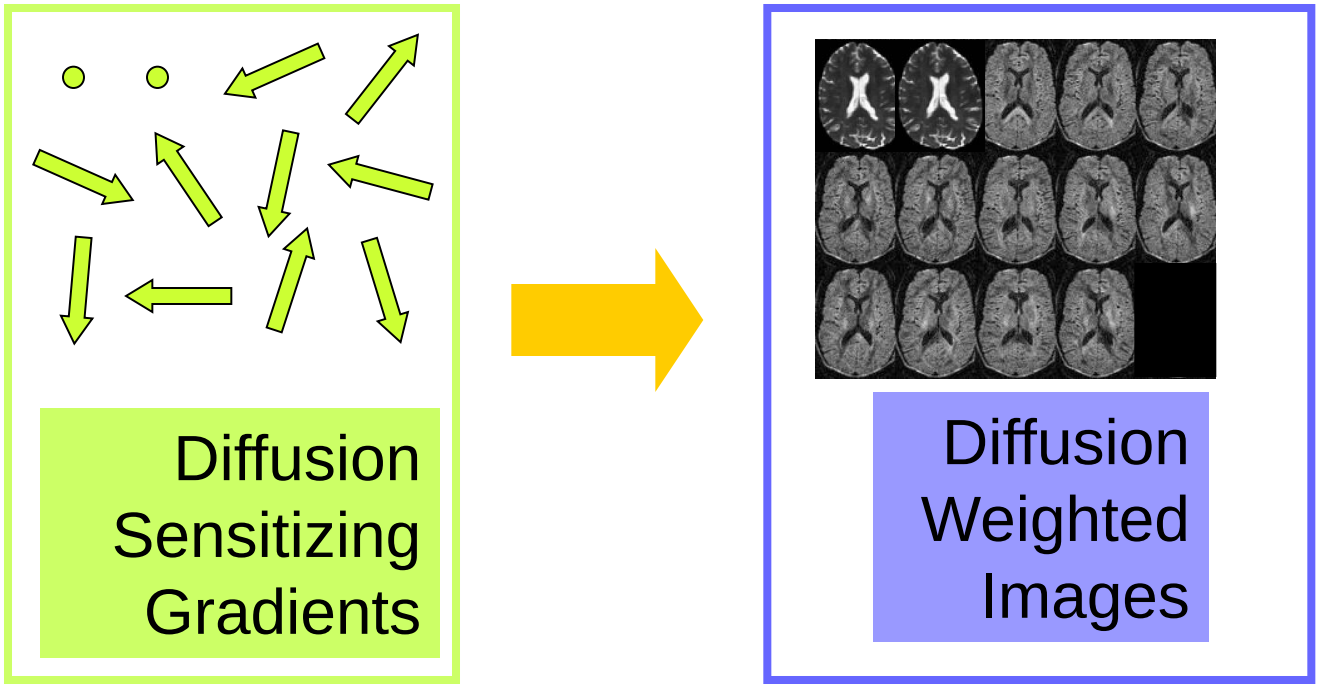
Tutorial Outline



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 is a Diffusion Weighted MR scan of the brain acquired with 42 gradient directions and one baseline.



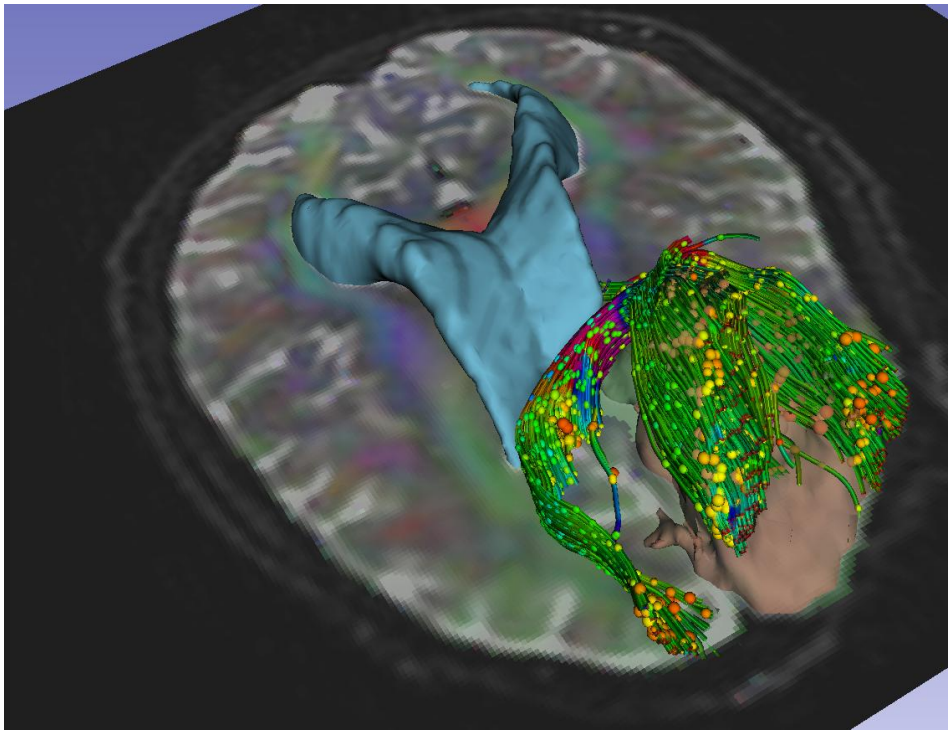
Tutorial software

The tutorial uses the 3DSlicer version 4.0.1 (Slicer-4.0.1) 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

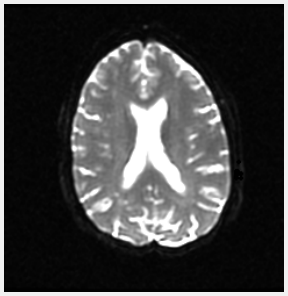
1) Estimate a tensor volume from a set of Diffusion Weighted Images

2) Understand the shape and size of the diffusion ellipsoid

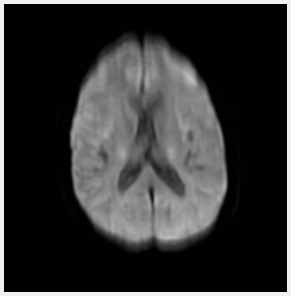
3) Reconstruct DTI tracts from a pre-defined region of interest

4) Interactively visualize DTI tracts seeded from a fiducial

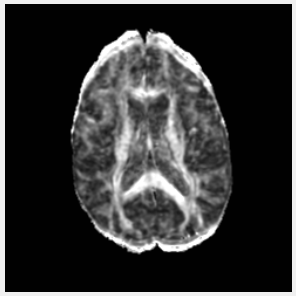
MR Diffusion Analysis Pipeline



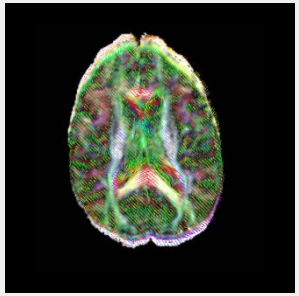
DWI
Acquisition



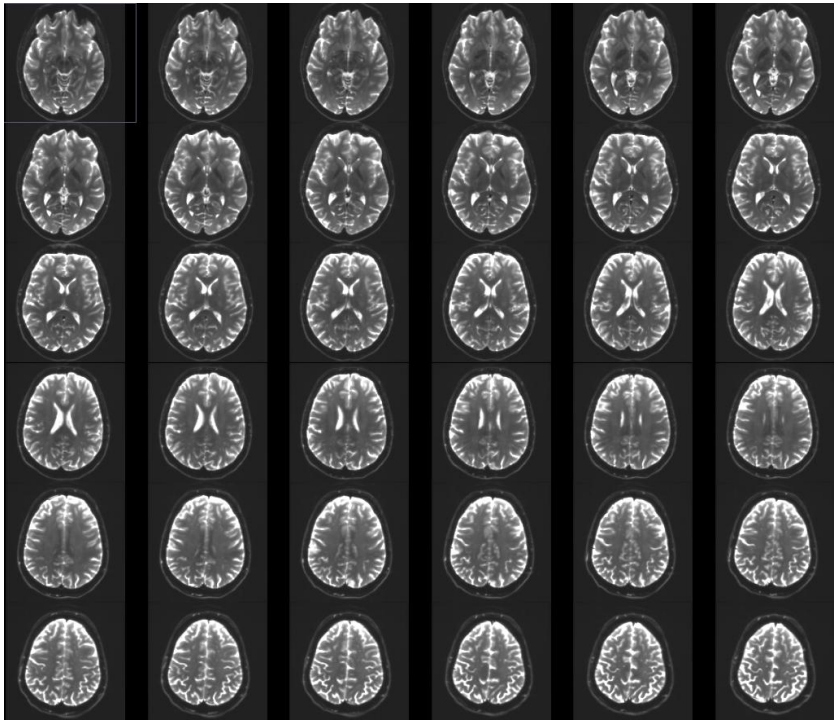
Tensor
Calculation



Scalar
Maps

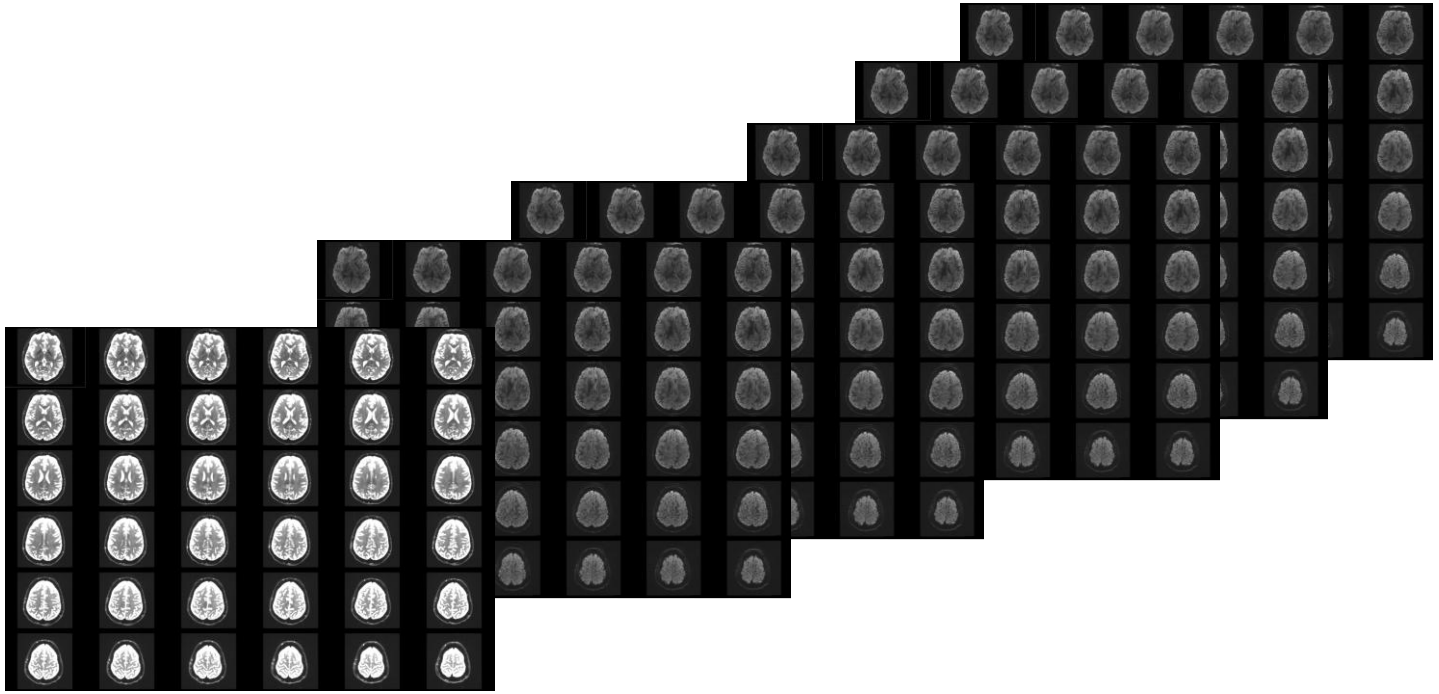


3D
Visualization



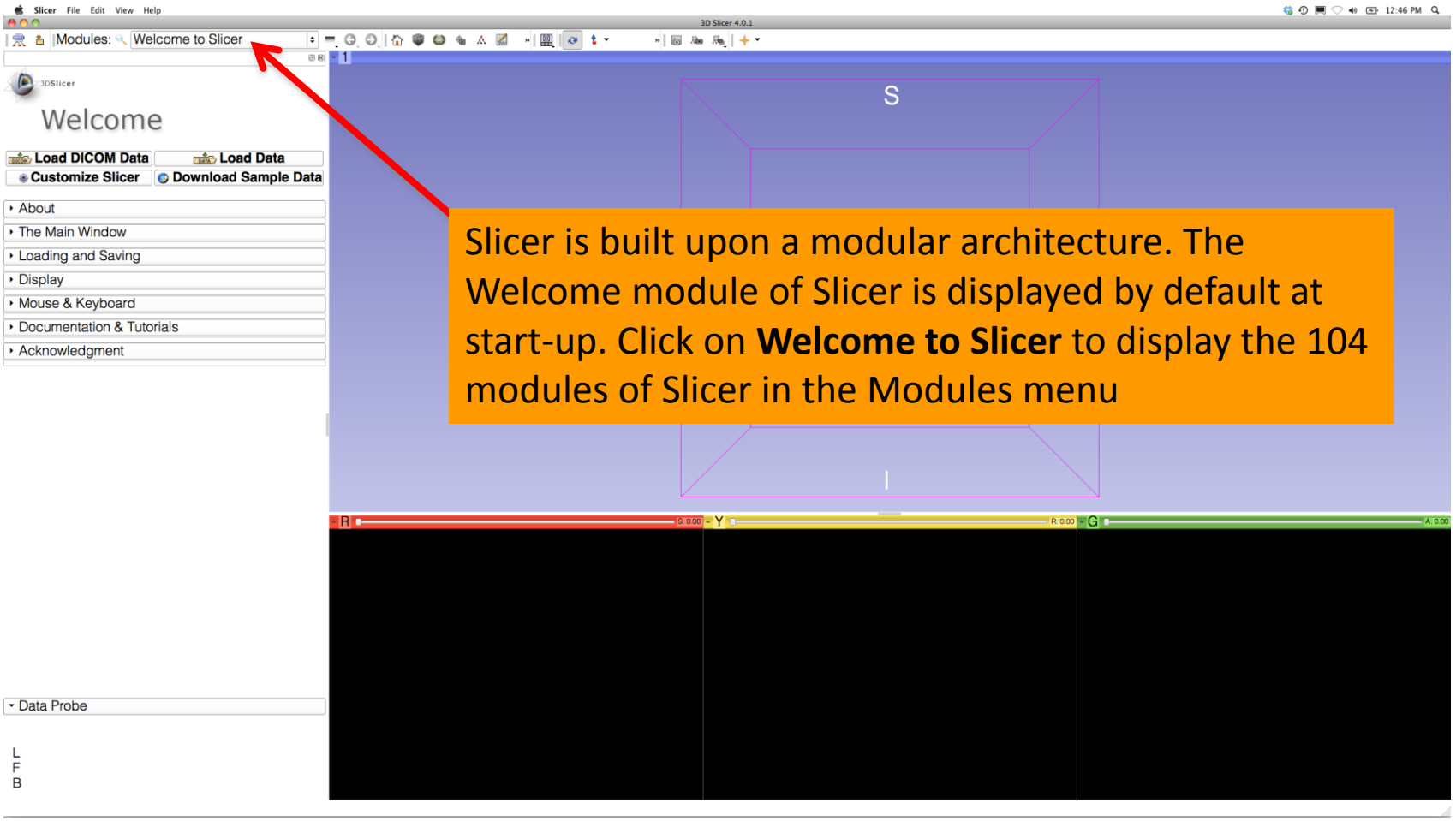
Part 1:
From DWI images to Tensors

Understanding the DWI dataset

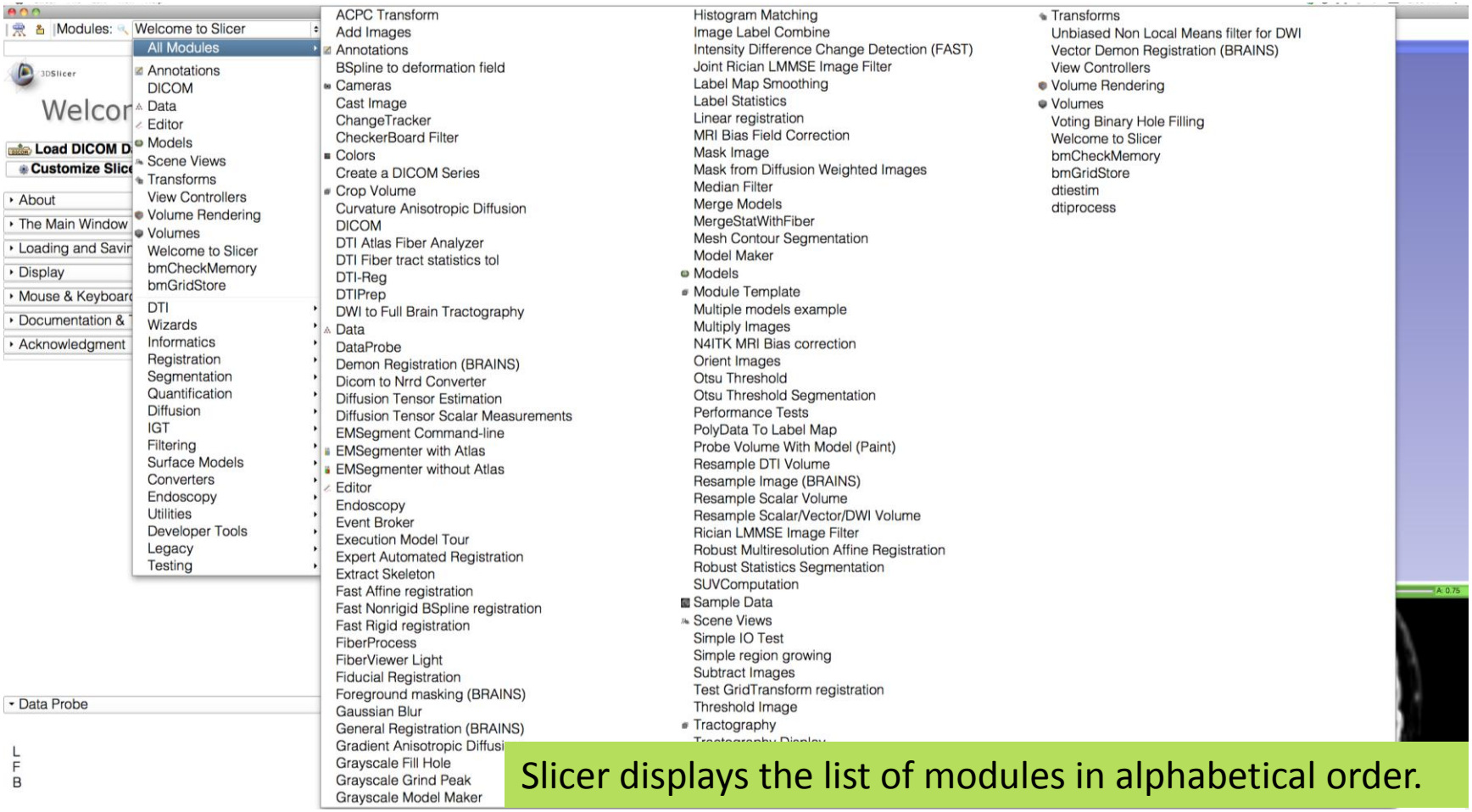


The DWI dataset is composed of 1 volume acquired without diffusion-sensitizing gradient, and 41 volumes acquired with 41 different diffusion-sensitizing gradients.

Loading the DWI dataset

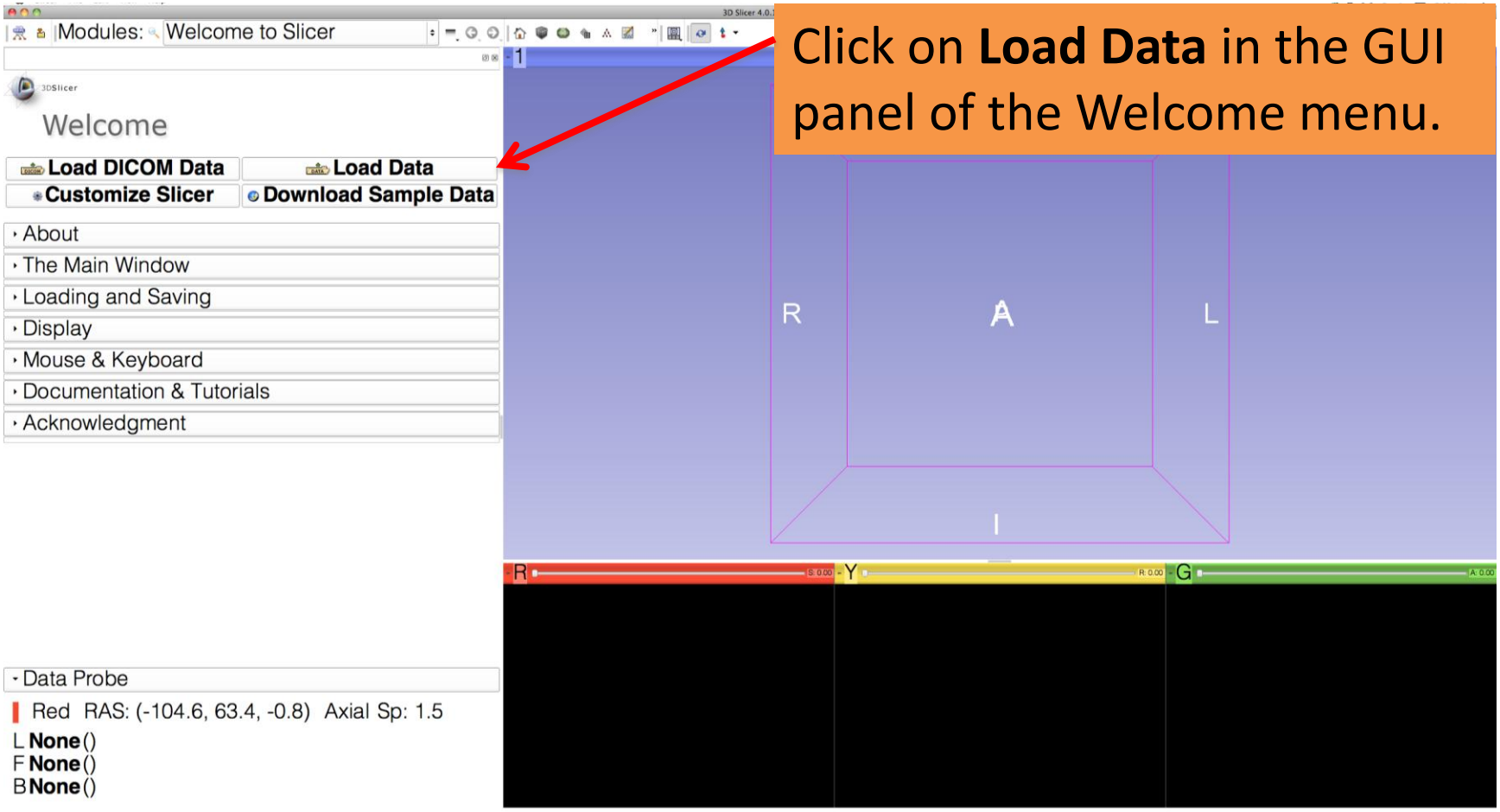


Start the Slicer software

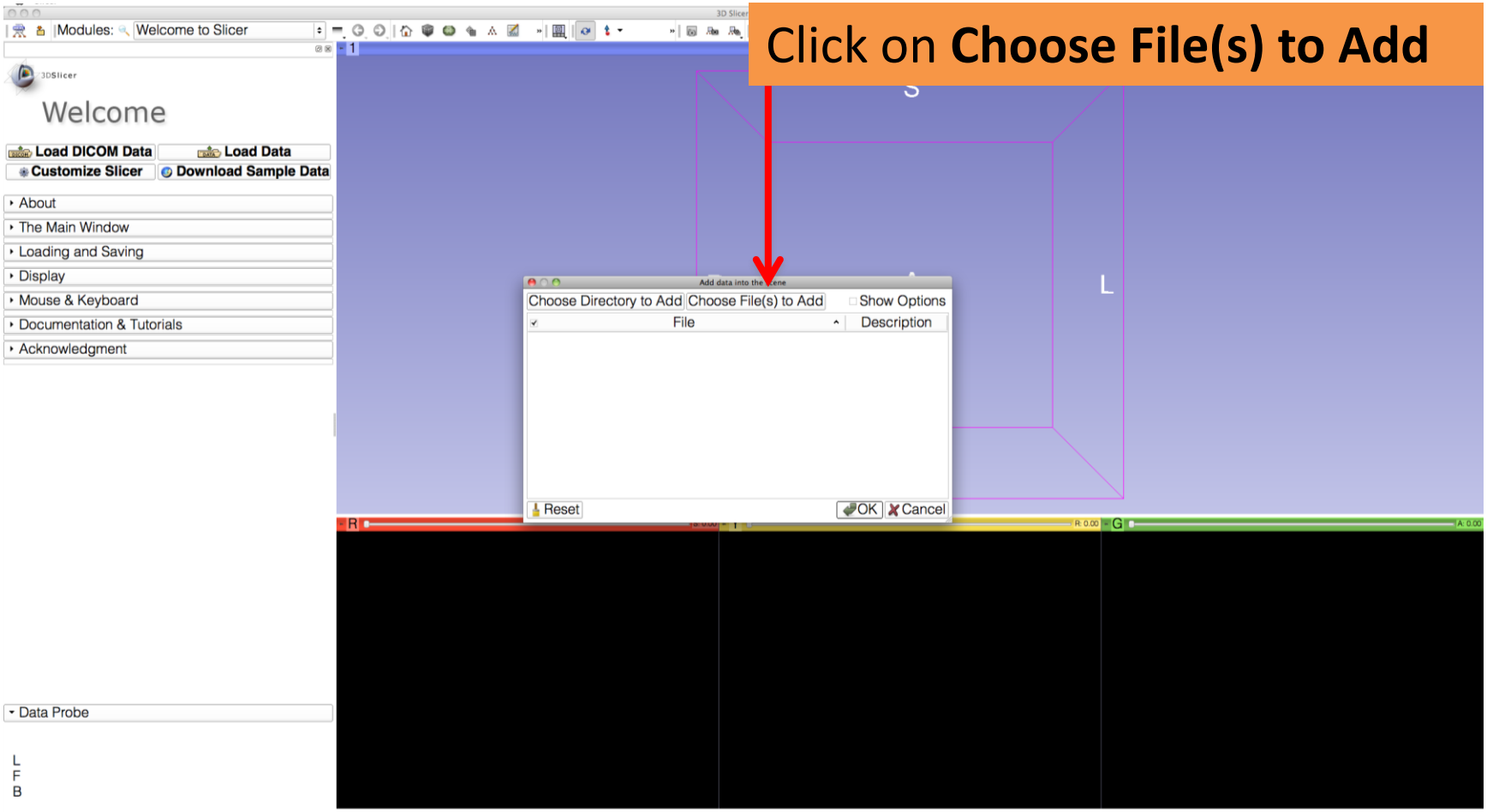


Slicer displays the list of modules in alphabetical order.

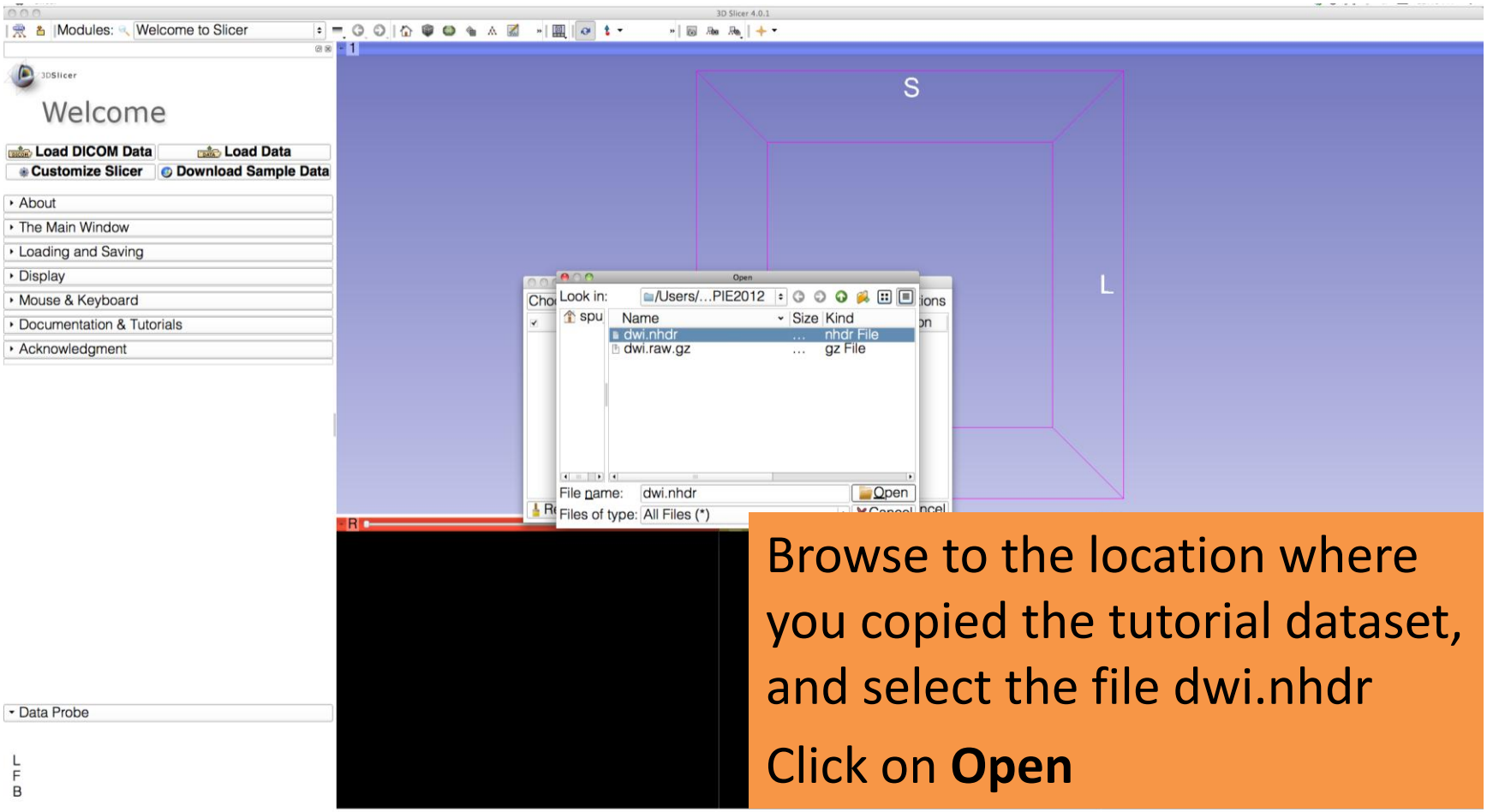
Loading the DWI dataset



Loading the DWI dataset



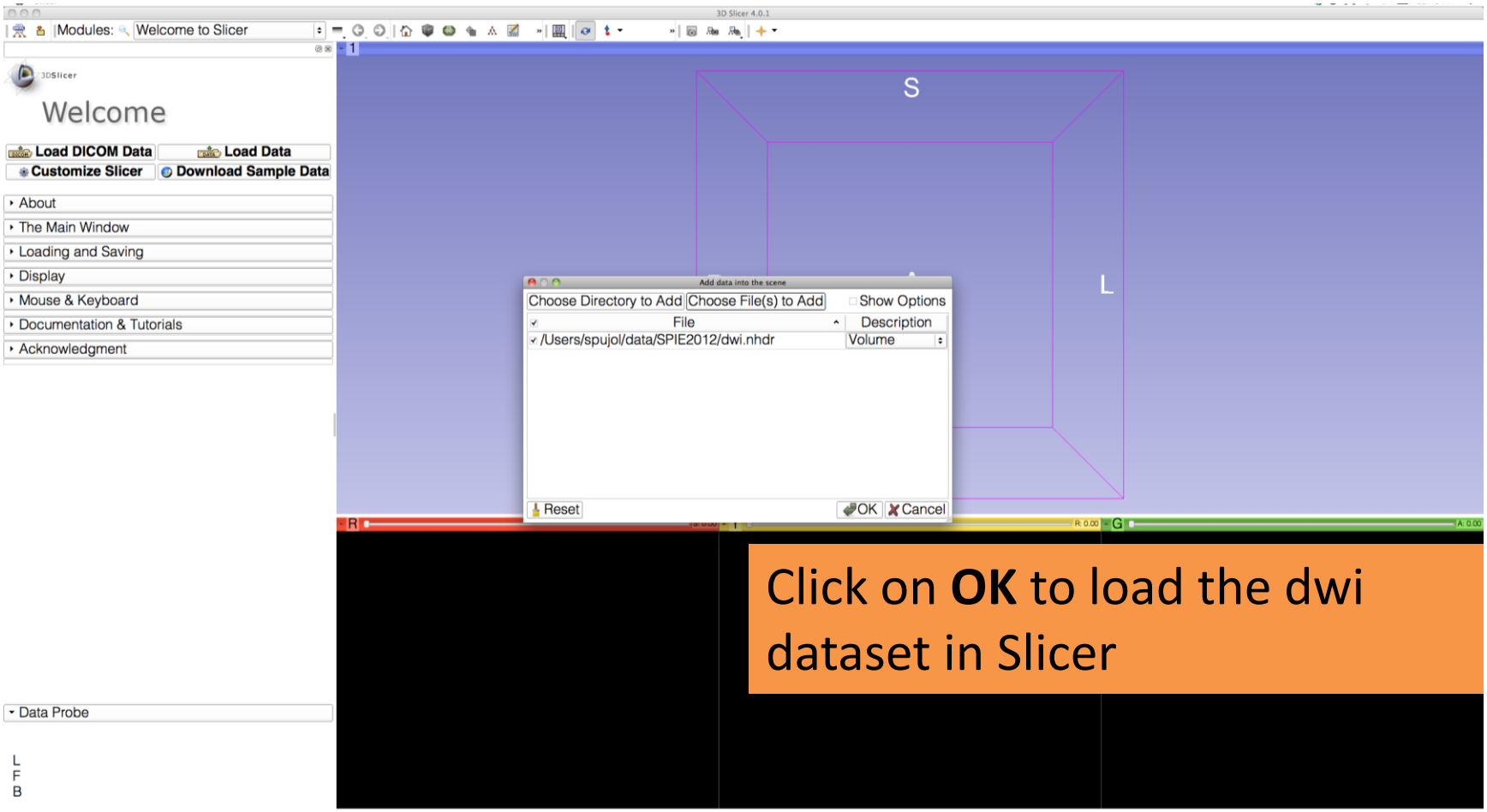
Loading the DWI dataset



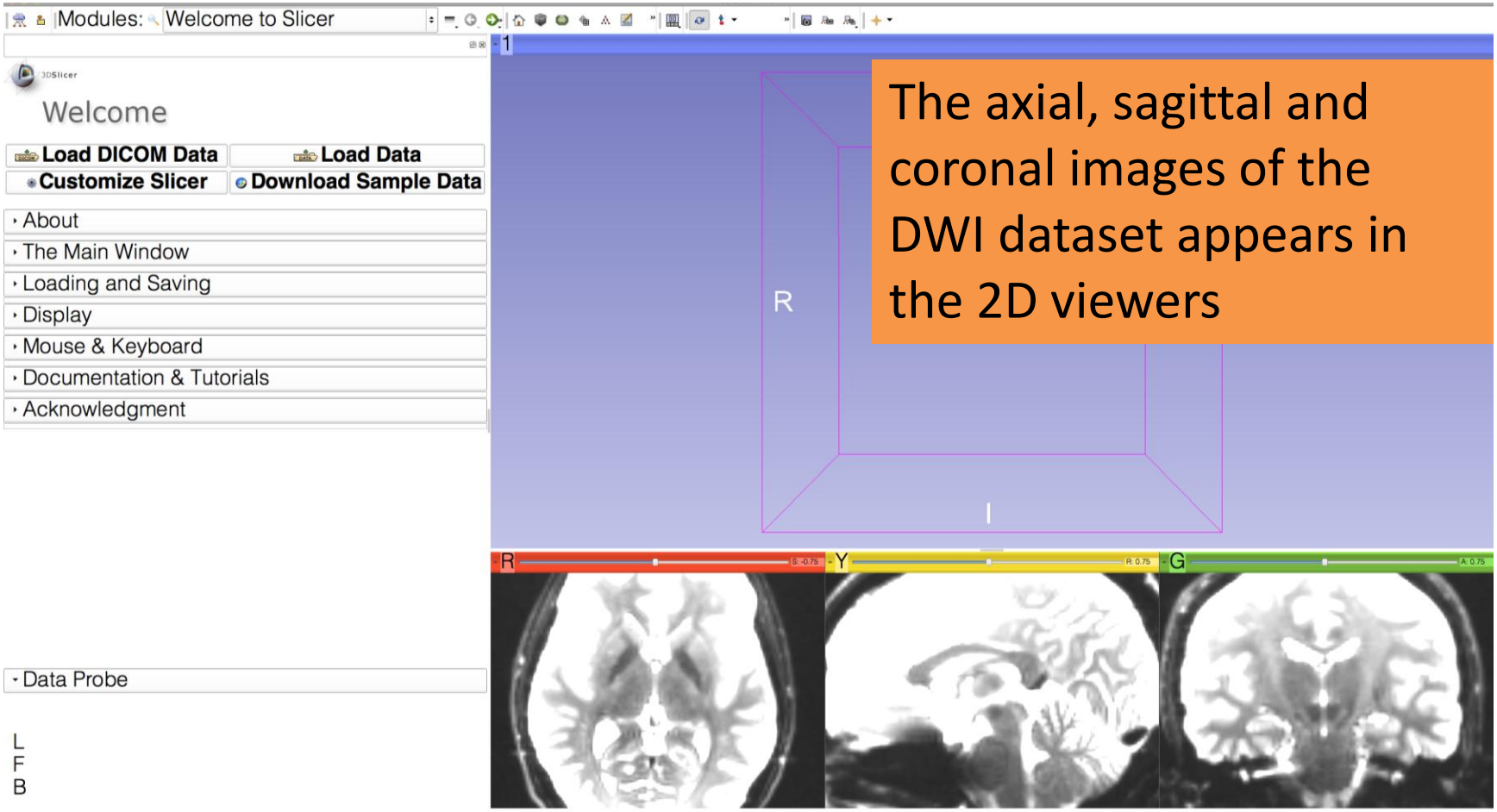
Browse to the location where you copied the tutorial dataset, and select the file dwi.nhdr

Click on **Open**

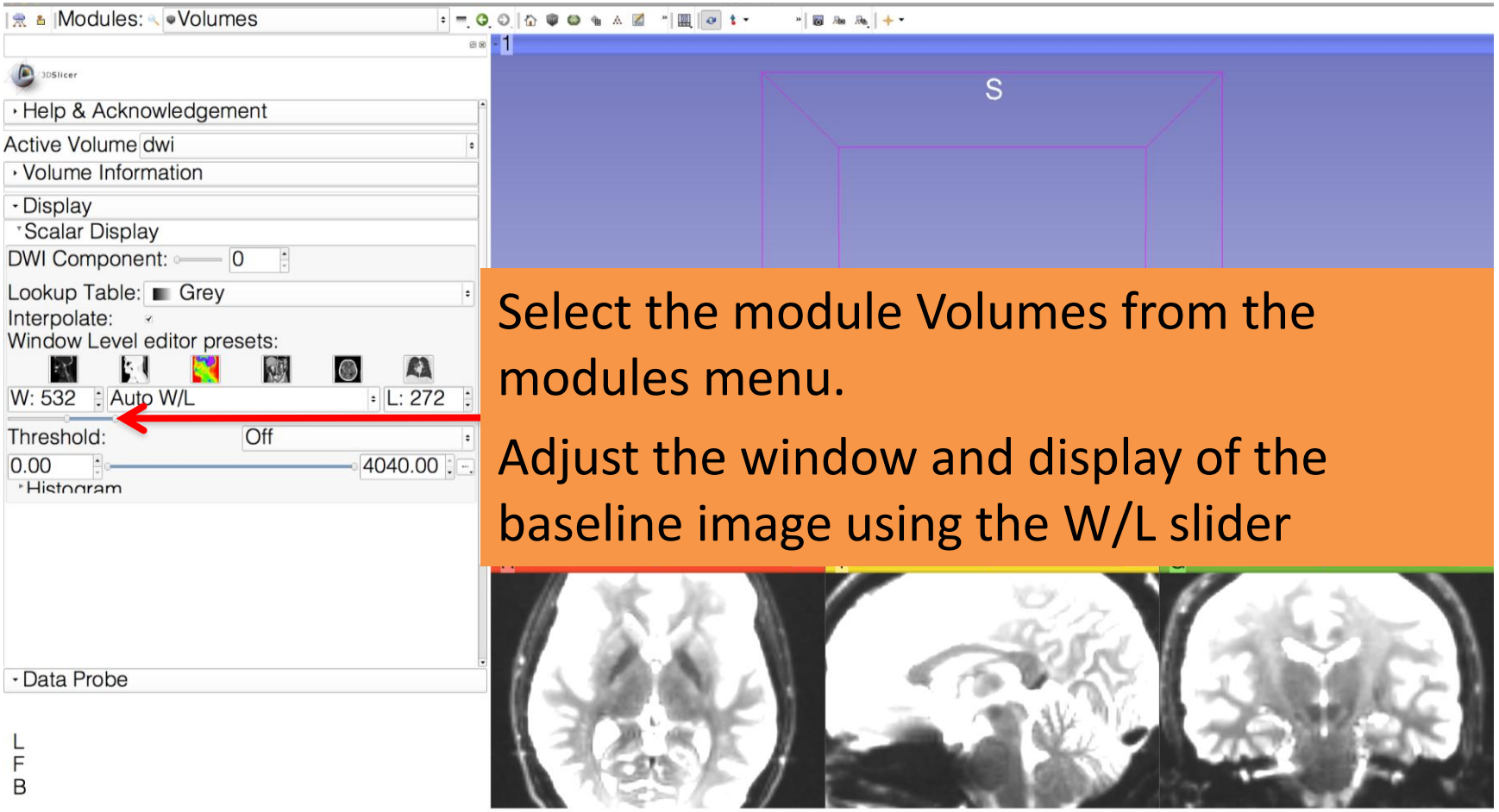
Loading the DWI dataset



Loading the DWI dataset



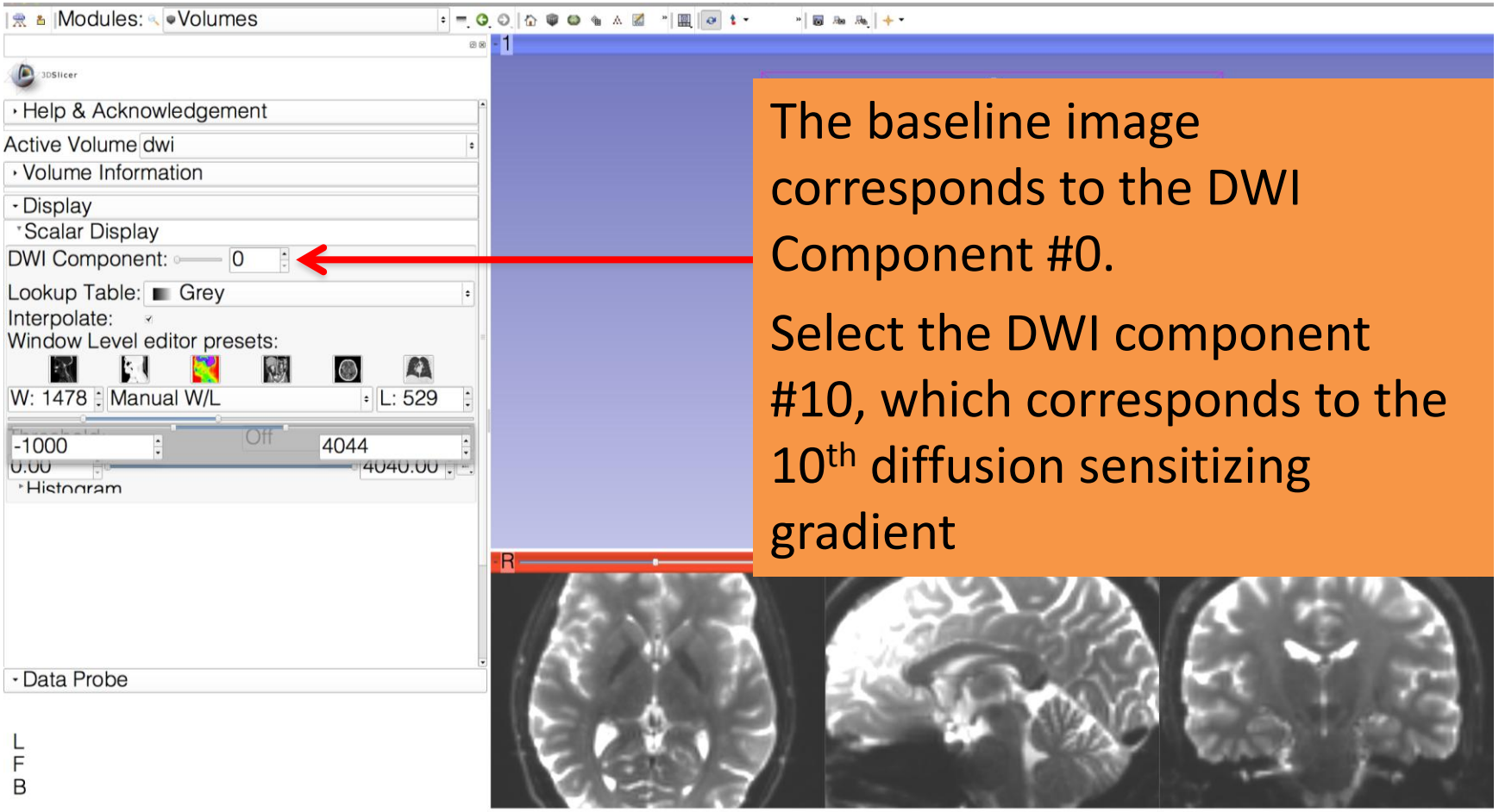
Adjusting Window and Level



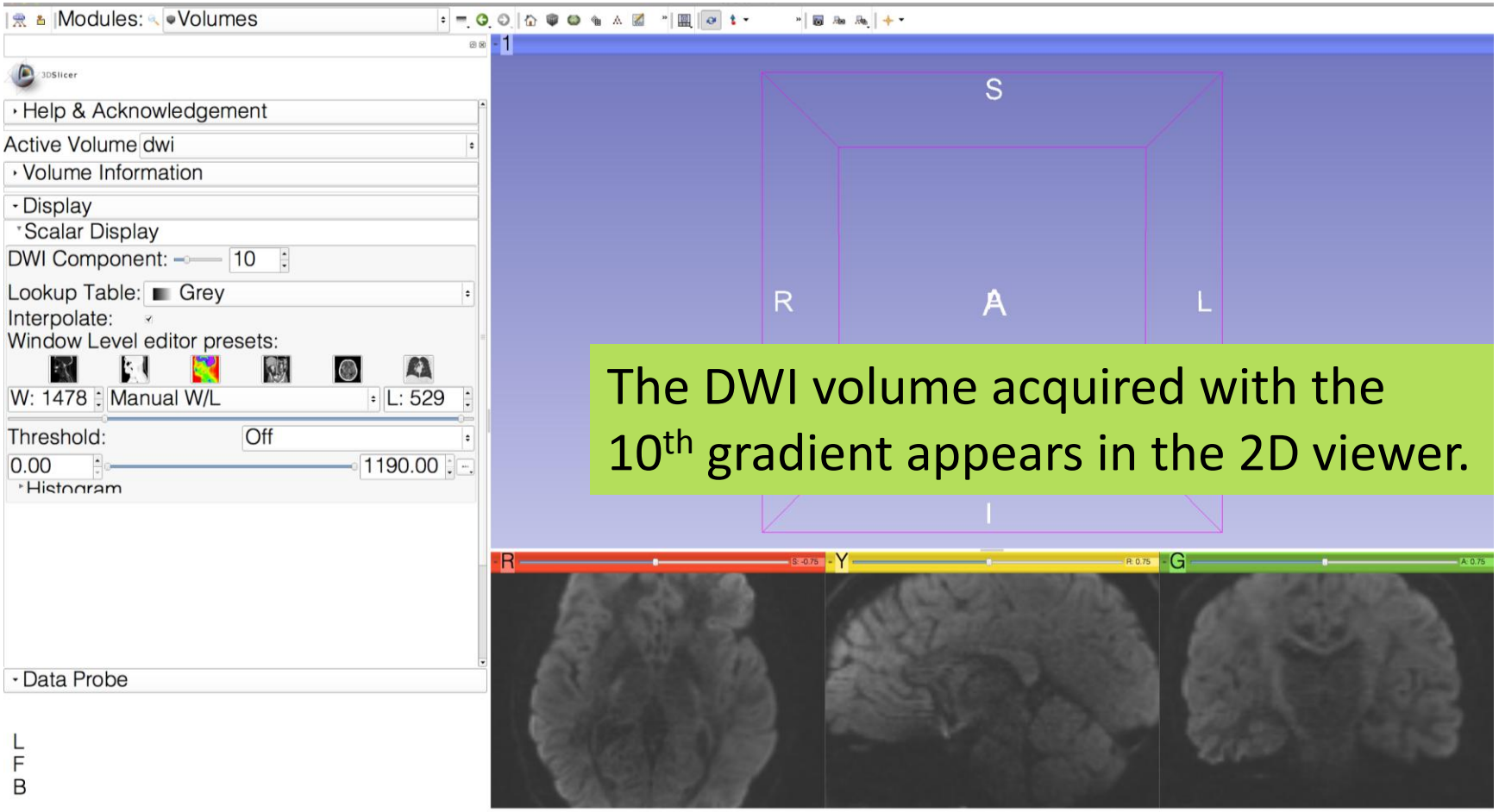
Select the module Volumes from the modules menu.

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

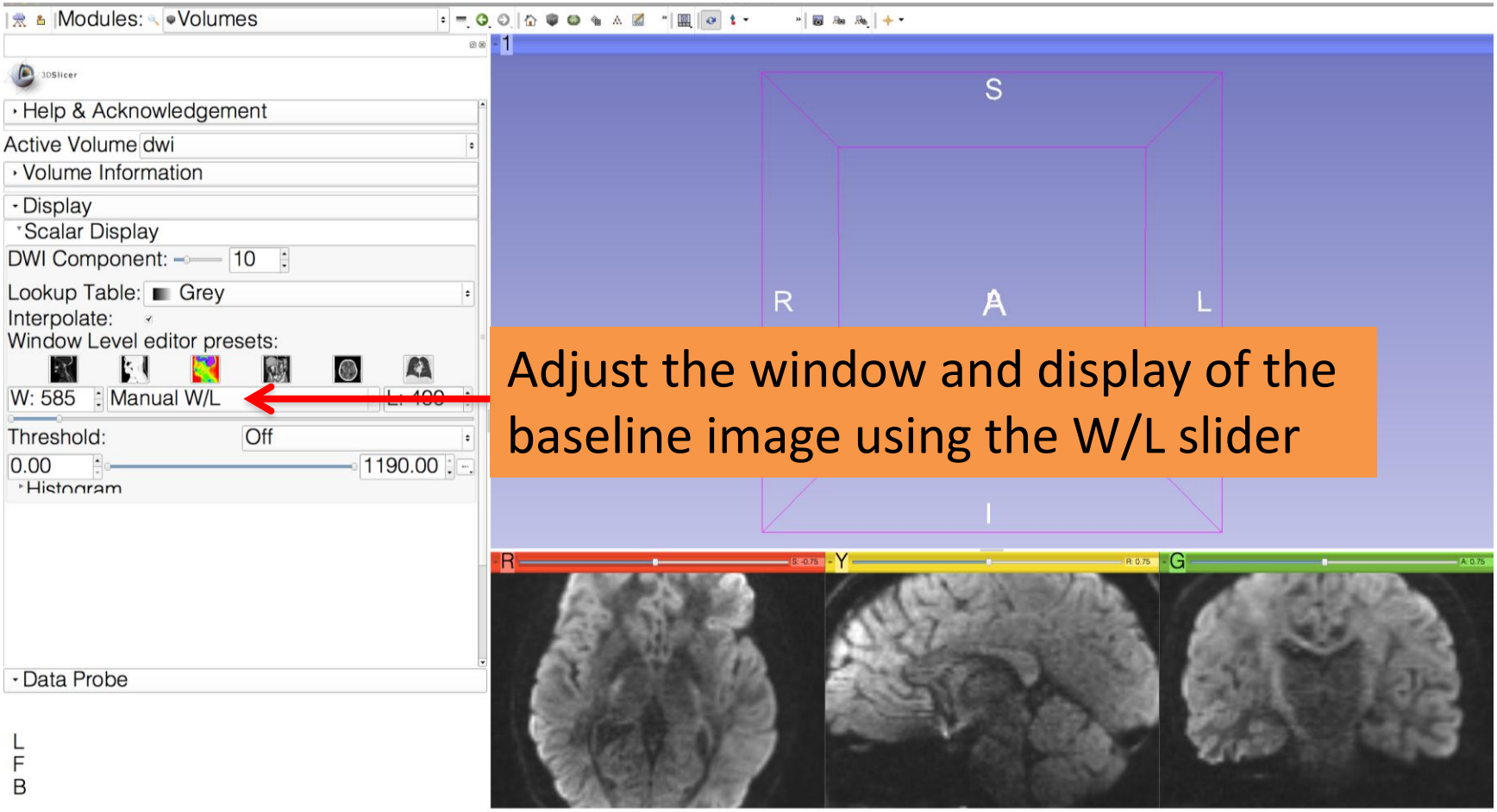
Exploring the DWI dataset



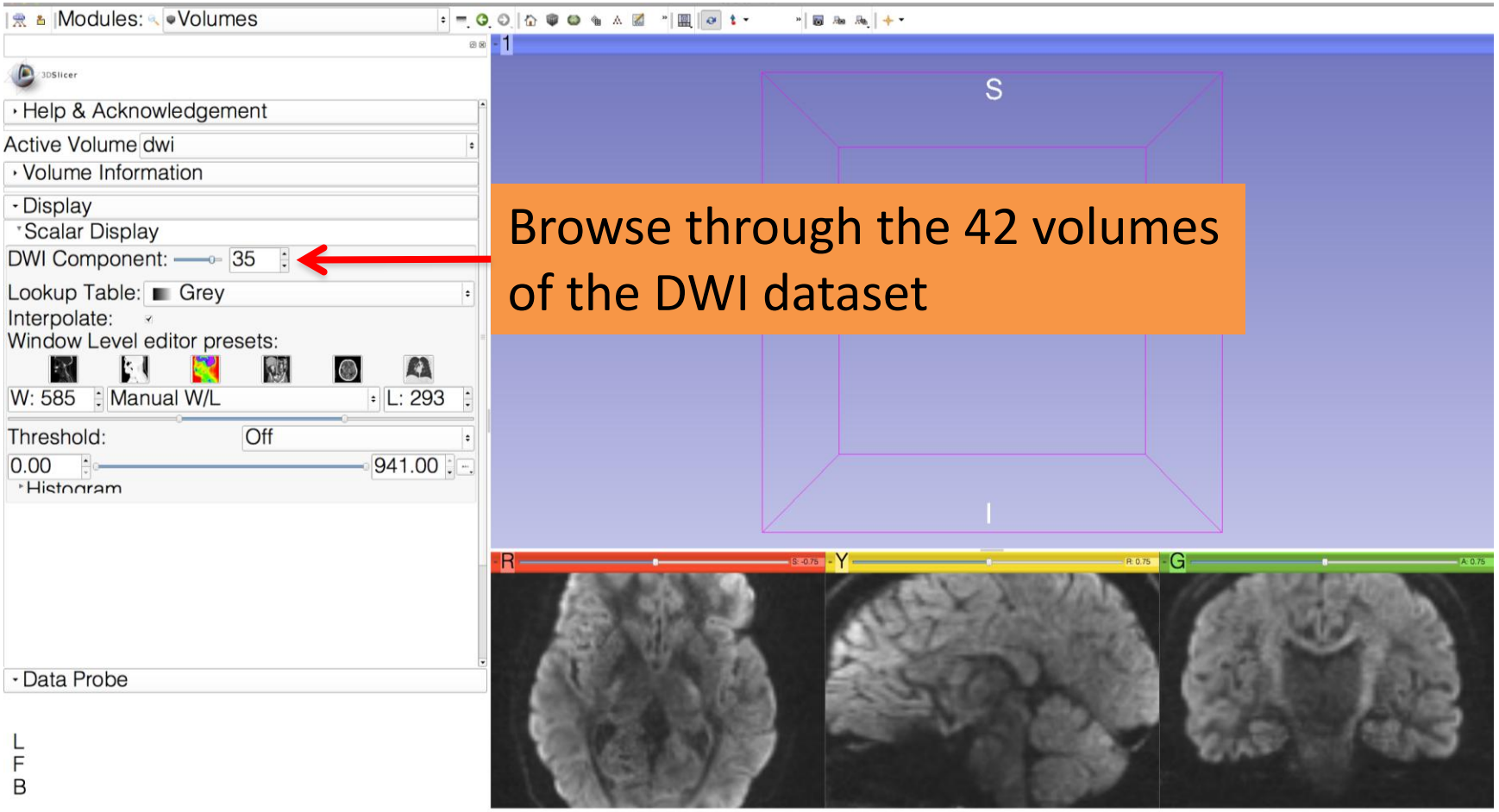
Exploring the DWI dataset



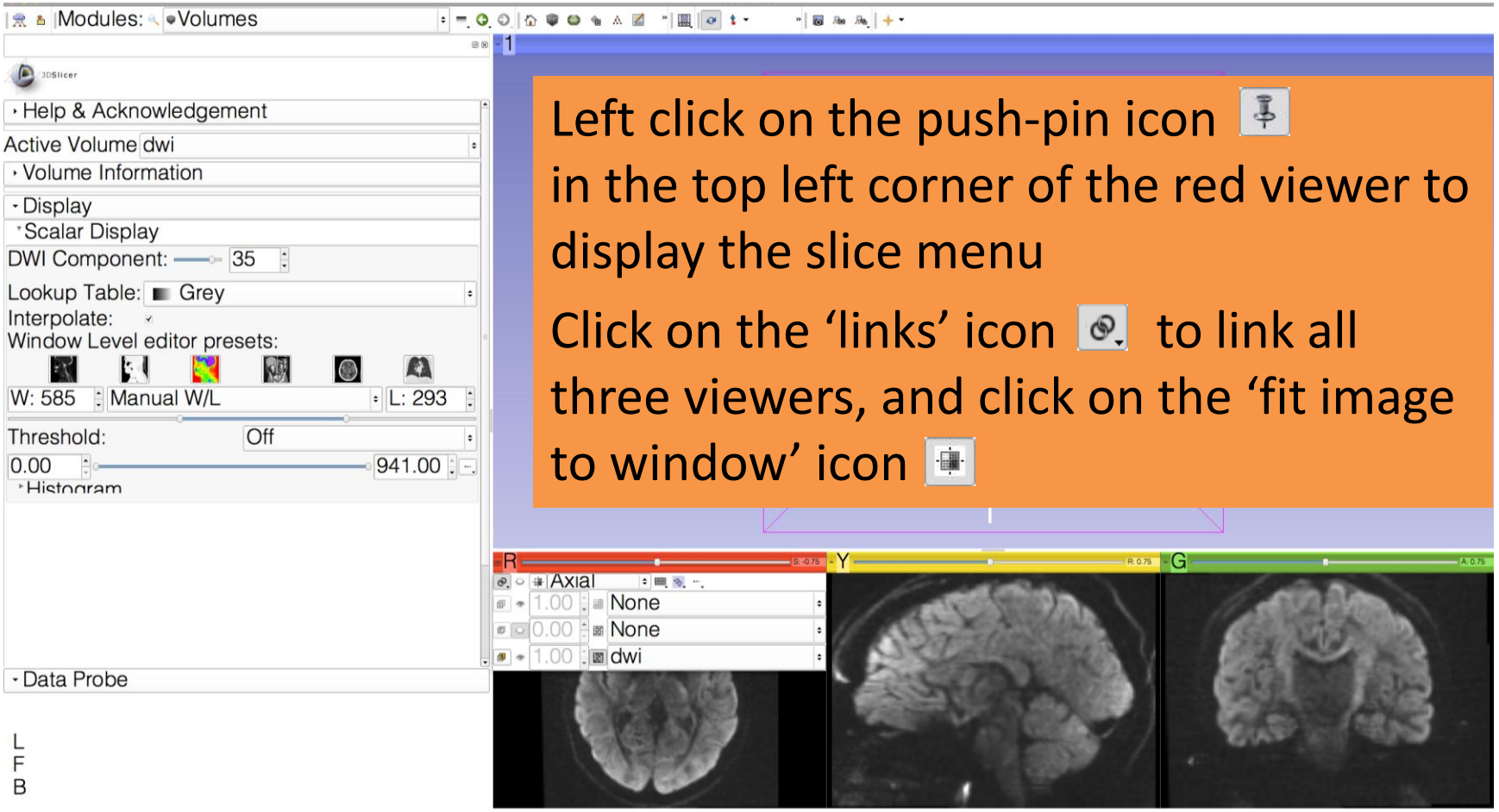
Exploring the DWI dataset



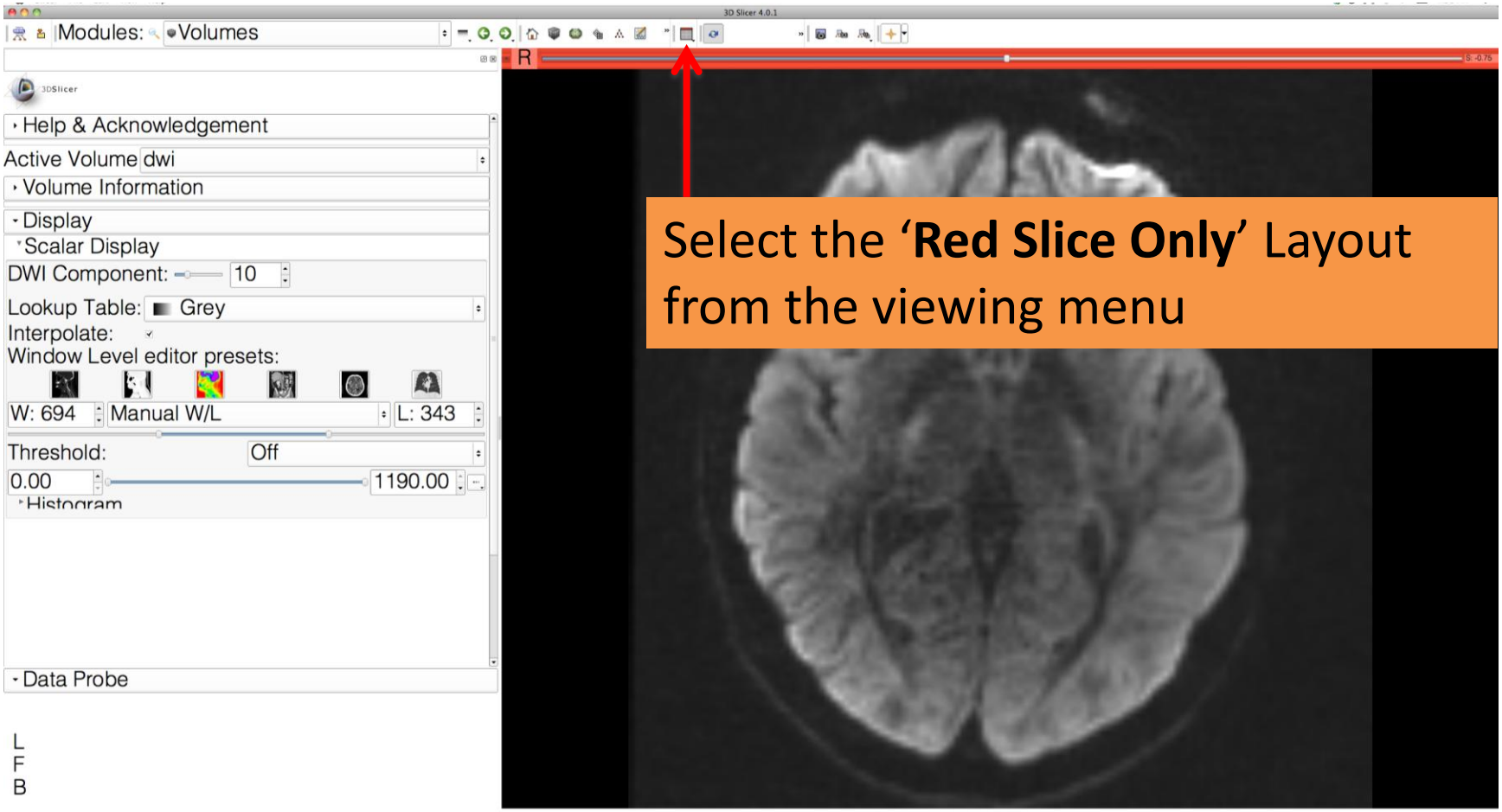
Exploring the DWI dataset



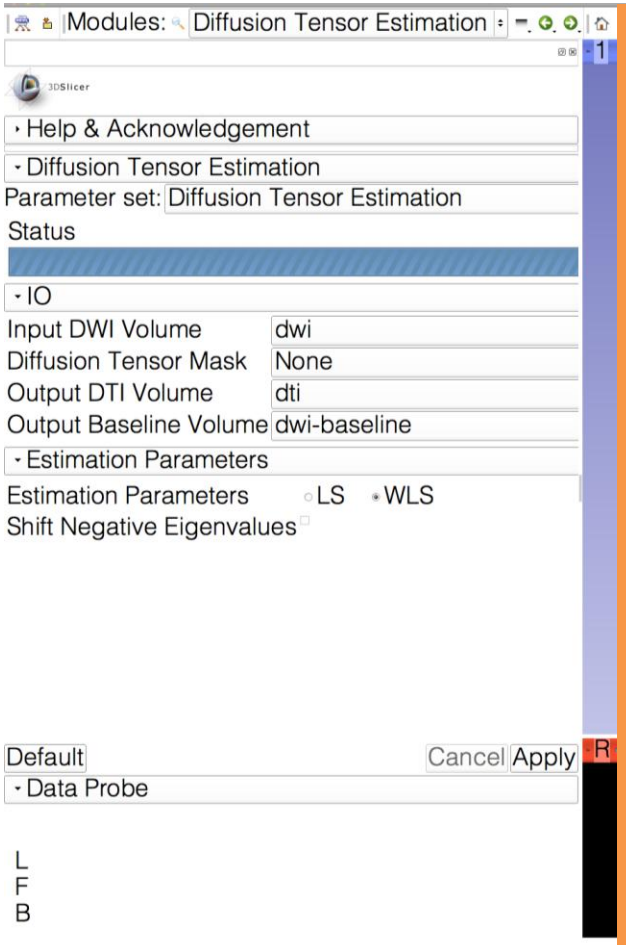
Exploring the DWI dataset



Exploring the DWI dataset



Diffusion Tensor Estimation



Select the module **Diffusion Tensor Estimation** in the modules menu:

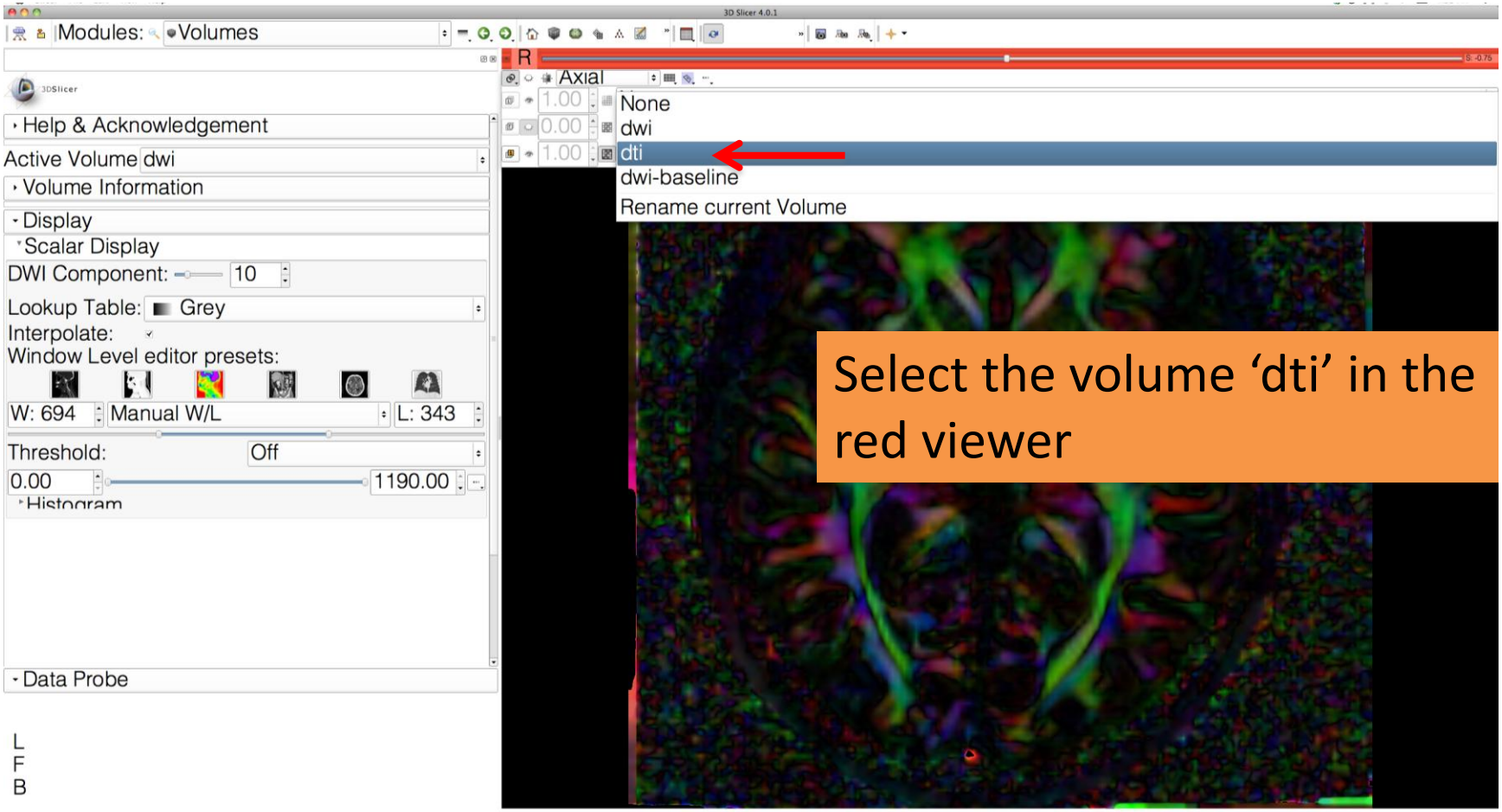
-set the **Input DWI volume** to 'dwi'

-select **Output DTI Volume** 'Create New Diffusion Tensor Volume', and rename it 'dti'

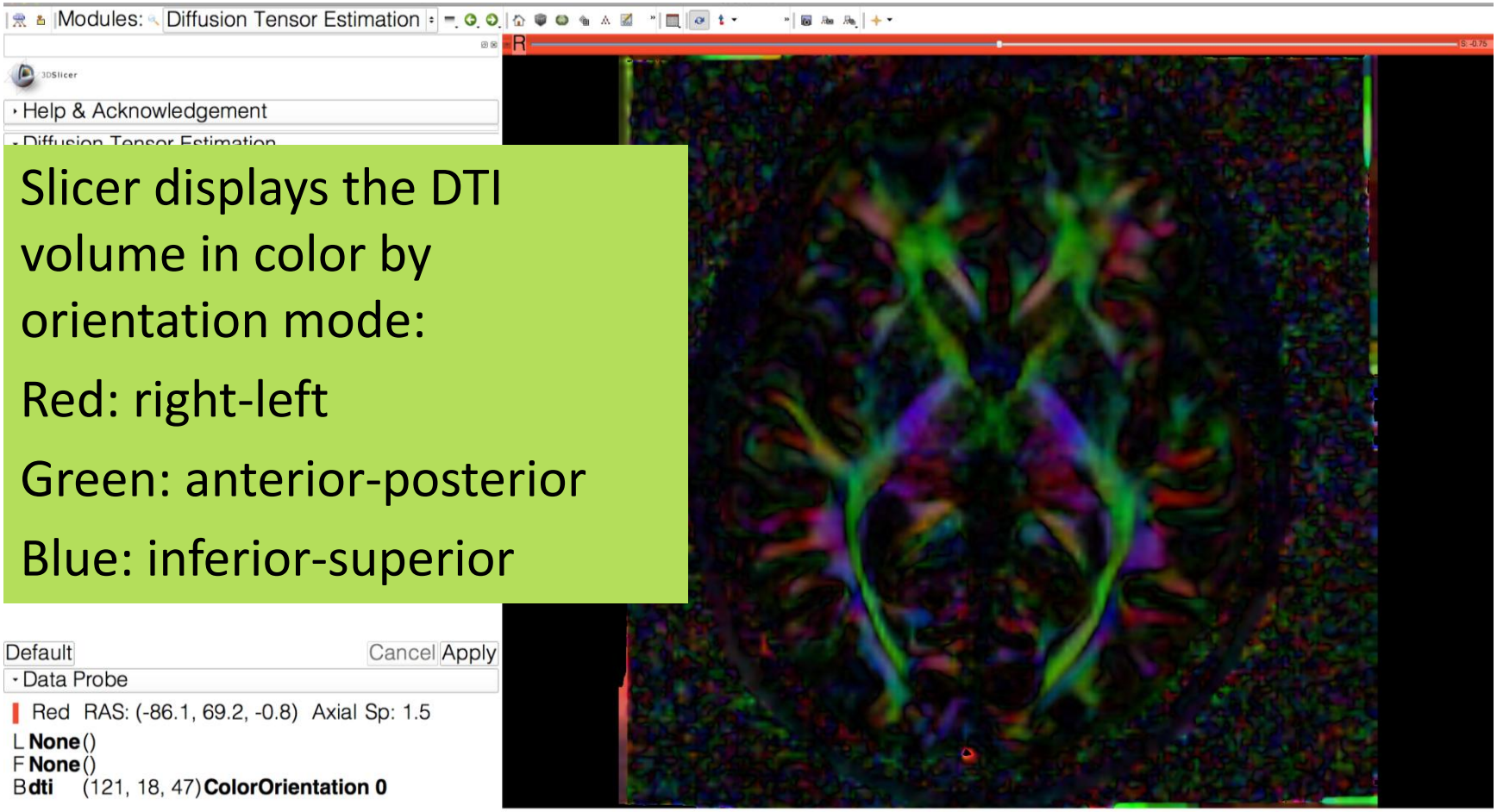
-select **Output Baseline Volume** ' Create new Volume', and rename it 'dwi-baseline'

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

Diffusion Tensor Estimation



Diffusion Tensor Estimation



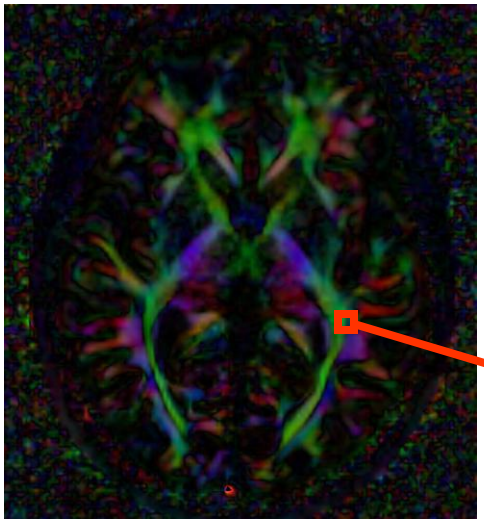
Slicer displays the DTI volume in color by orientation mode:

Red: right-left

Green: anterior-posterior

Blue: inferior-superior

Diffusion Tensor Data



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

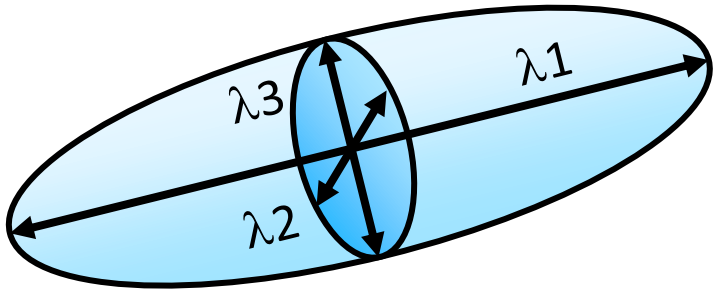
Stejskal-Tanner equation (1965)

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

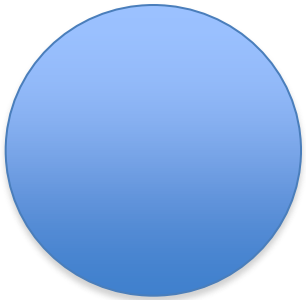
The diffusion tensor $\underline{D}$ in the voxel (I,J,K) is a 3x3 symmetric matrix.

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 λ1, λ2, λ3 to characterize the size and shape of the diffusion tensor.

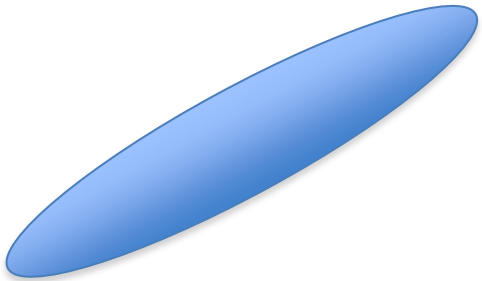


Diffusion Tensor Shape

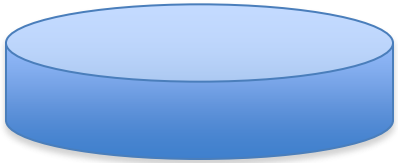


$\lambda 1 = \lambda 2 = \lambda 3$

Isotropic media
(CSF, gray matter)



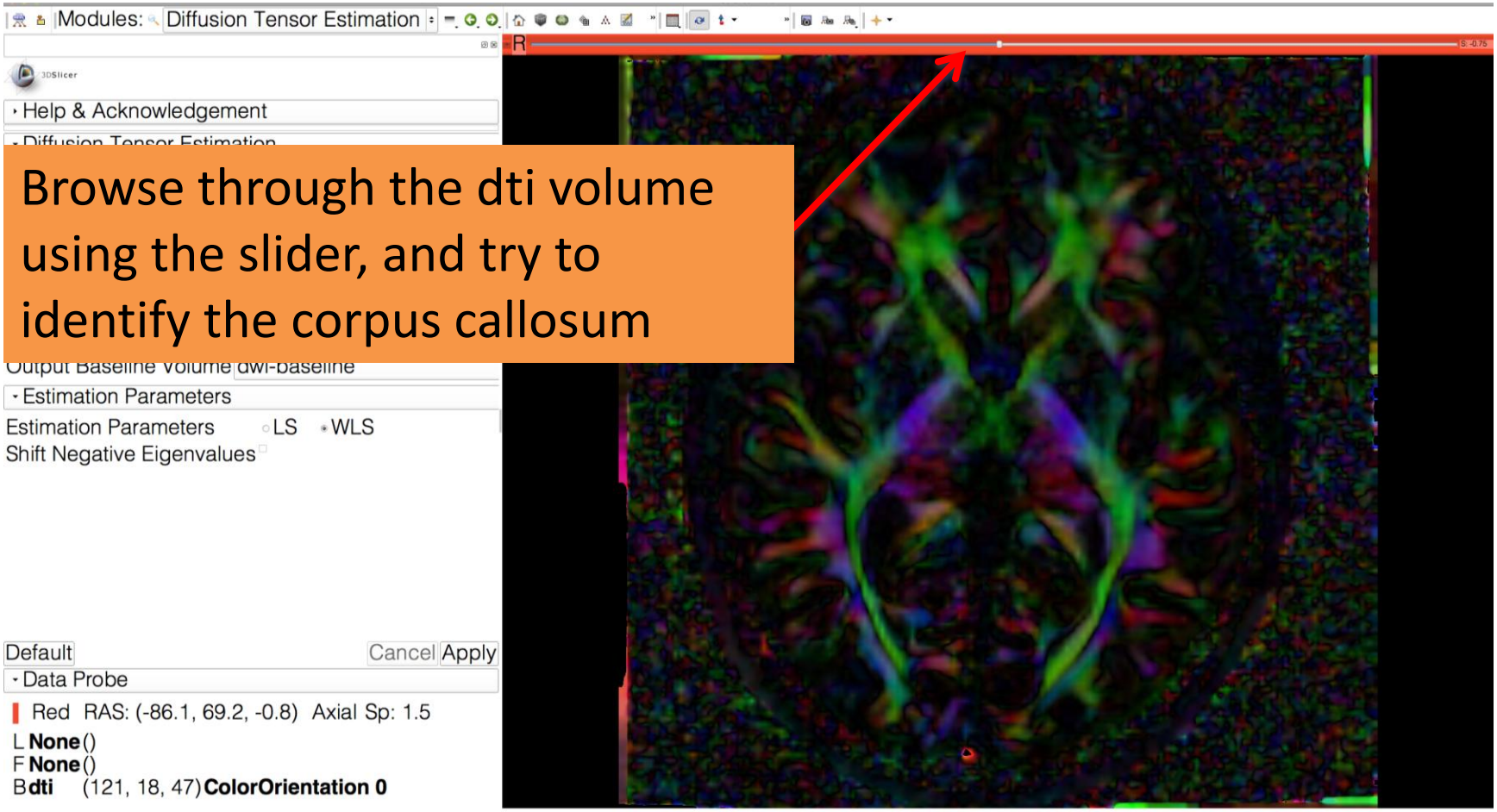
$\lambda 1 >> \lambda 2, \lambda 3$



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

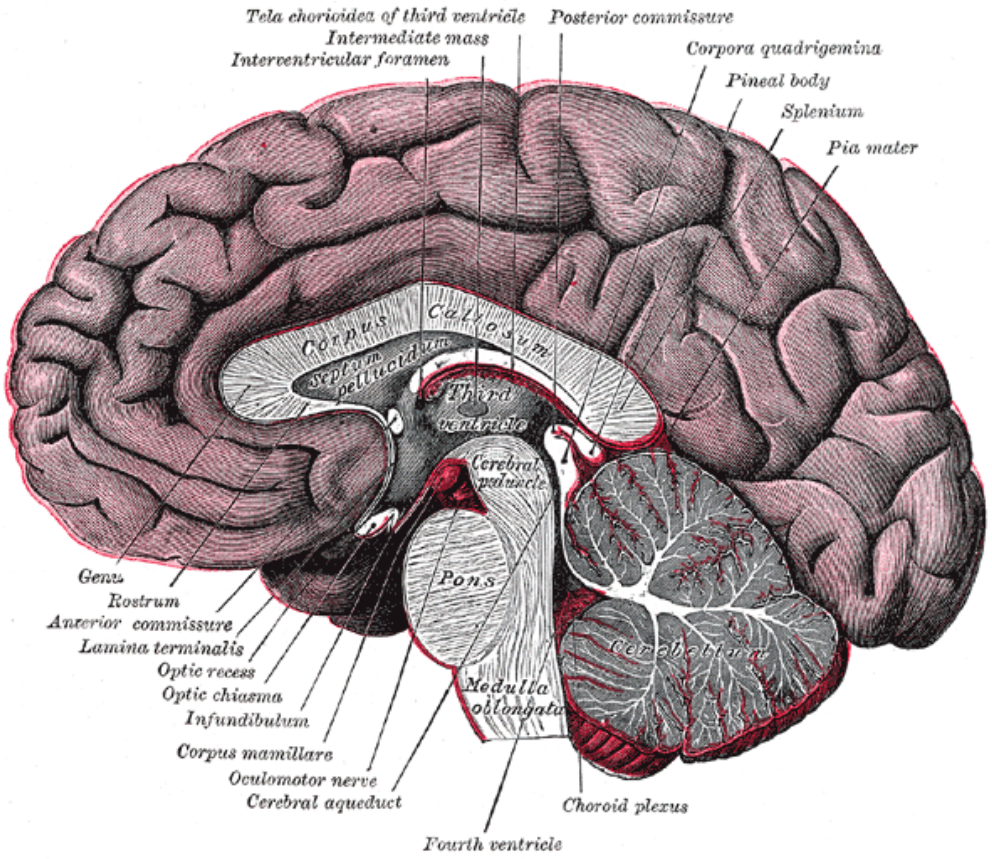
Anisotropic media
(white matter)

Exploring the Diffusion Tensor Data



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

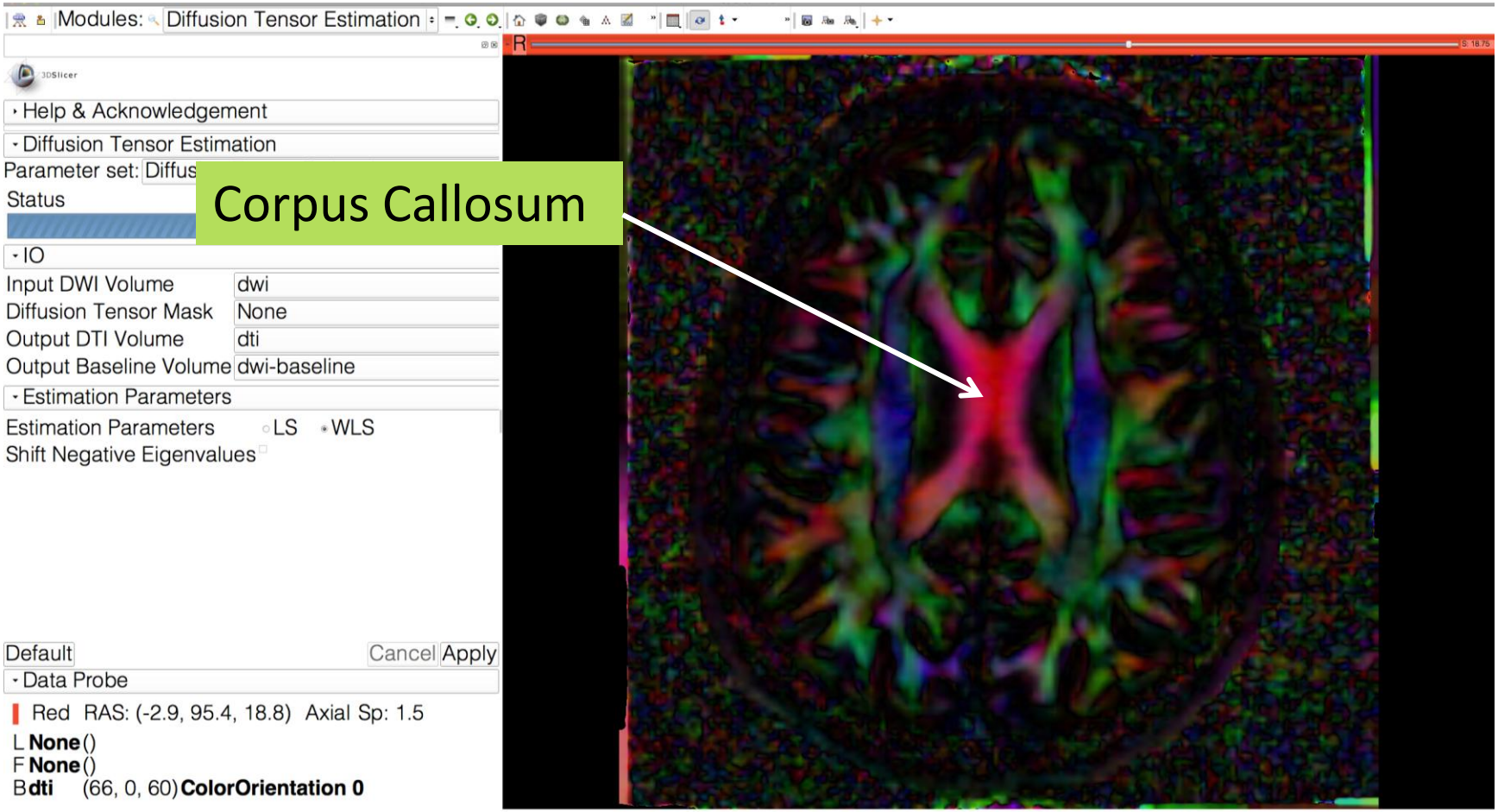
Corpus Callosum



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

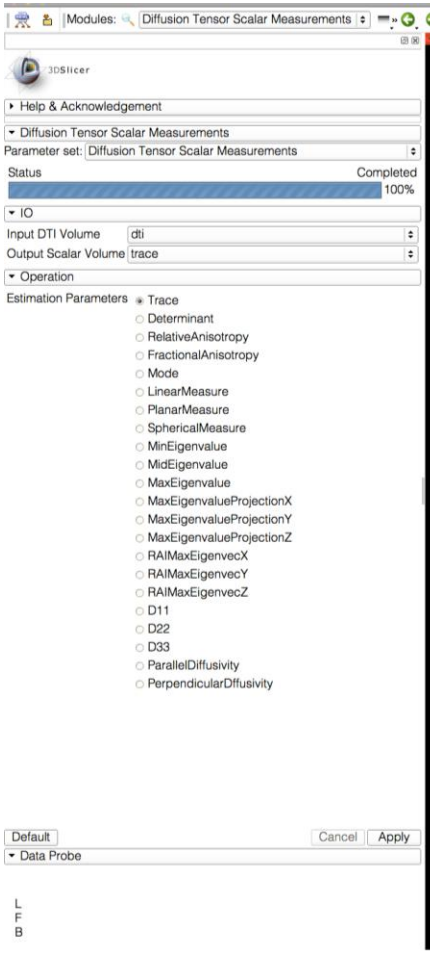


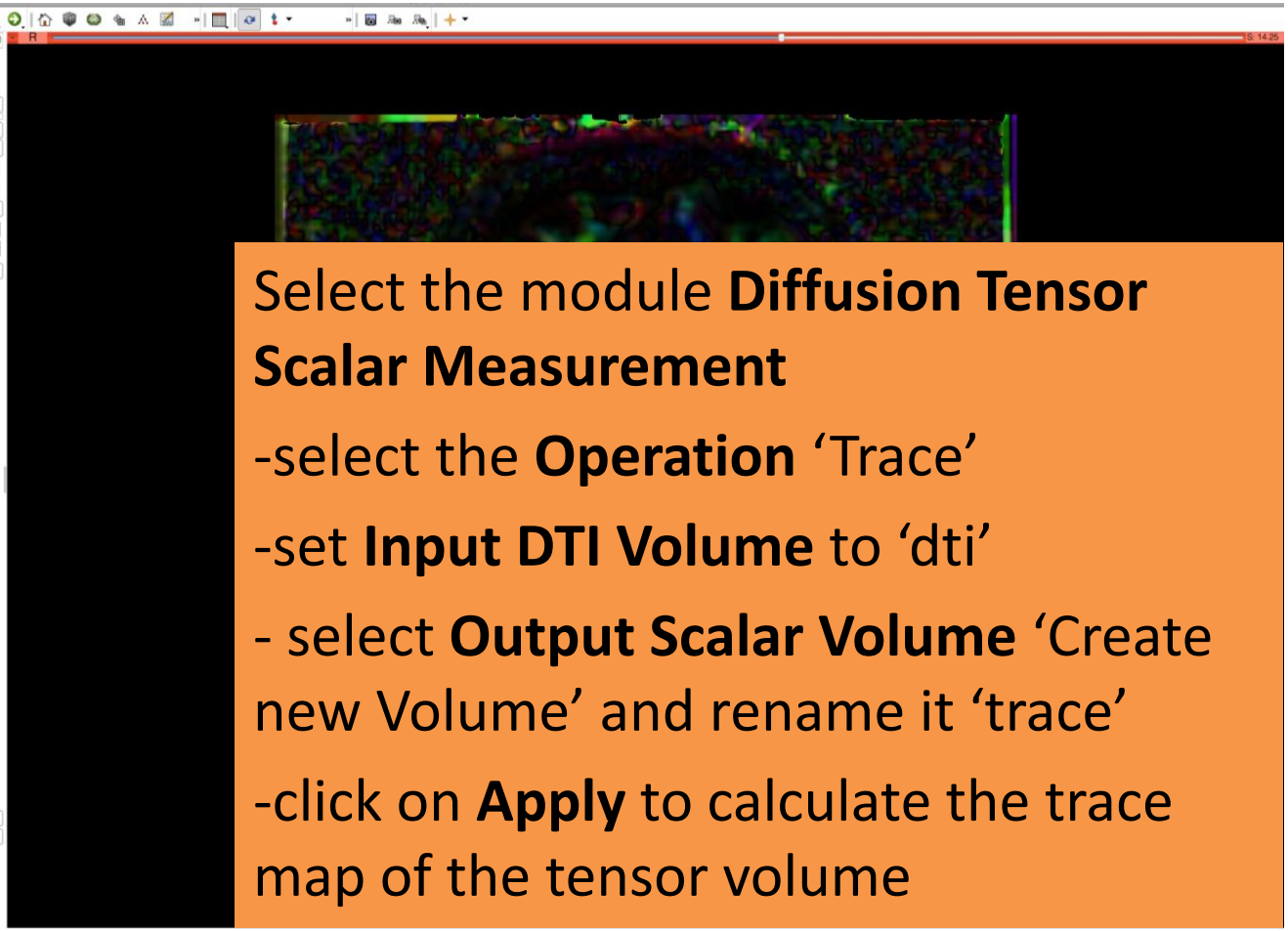
Characterizing the Shape of the tensor: Trace

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

- 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
- Trace(D) is useful to characterize the size of the diffusion ellipsoid

Characterizing the Shape of the tensor: Trace





Select the module **Diffusion Tensor Scalar Measurement**

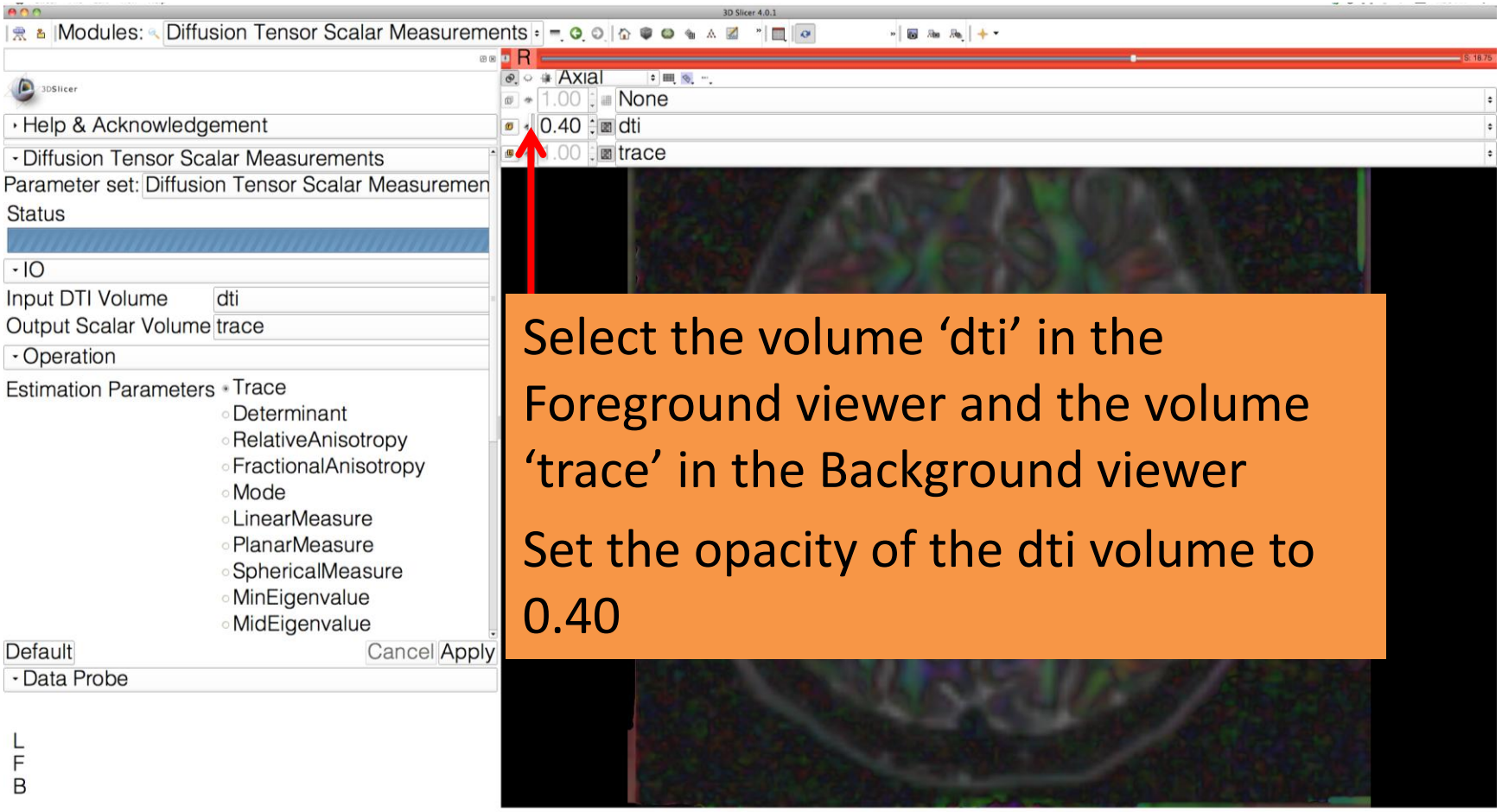
-select the **Operation** ‘Trace’

-set **Input DTI Volume** to ‘dti’

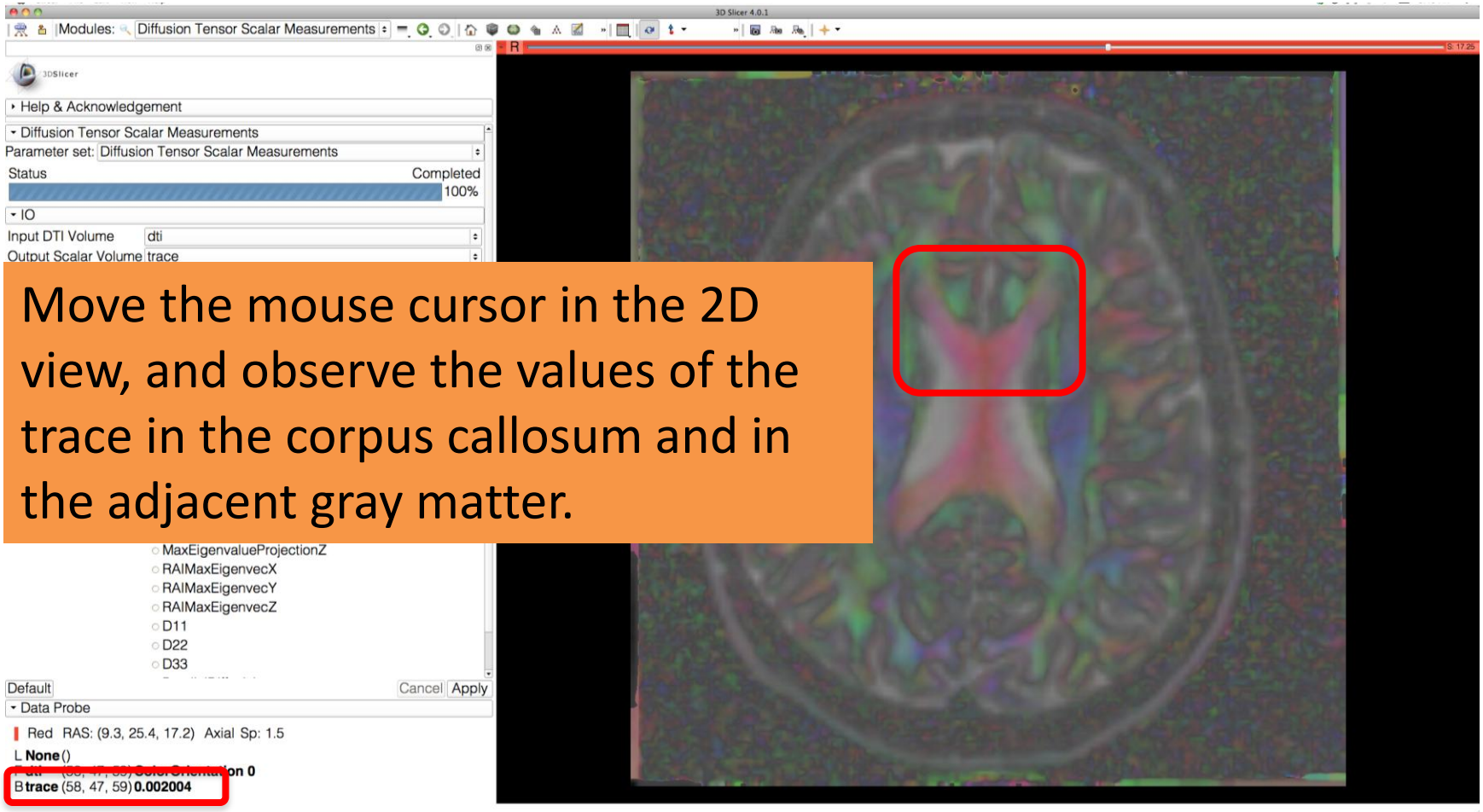
- select **Output Scalar Volume** ‘Create new Volume’ and rename it ‘trace’

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

Exploring the Diffusion Tensor Data

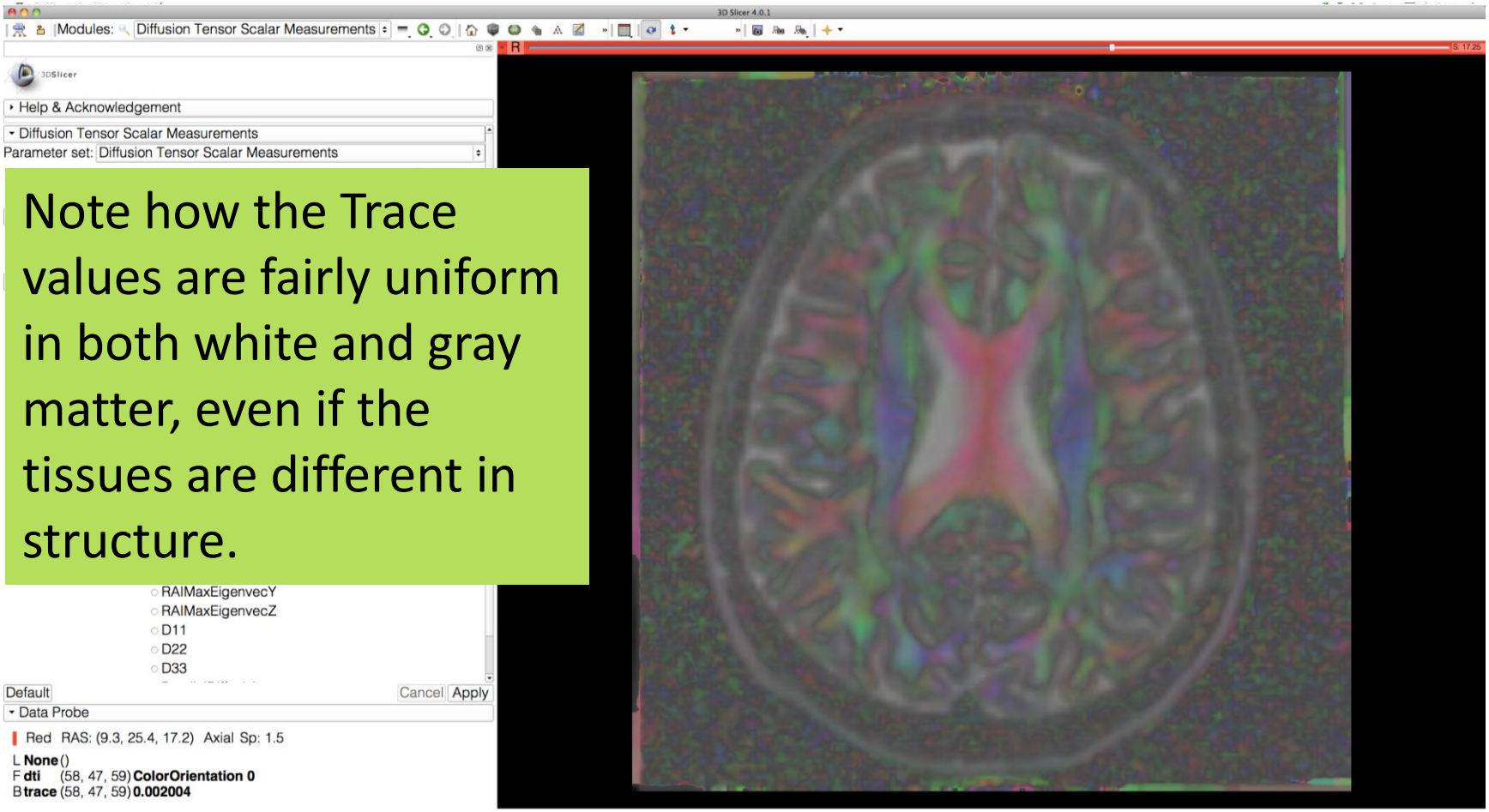


Exploring the Diffusion Tensor Data



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.

Characterizing the Shape of the tensor: Trace



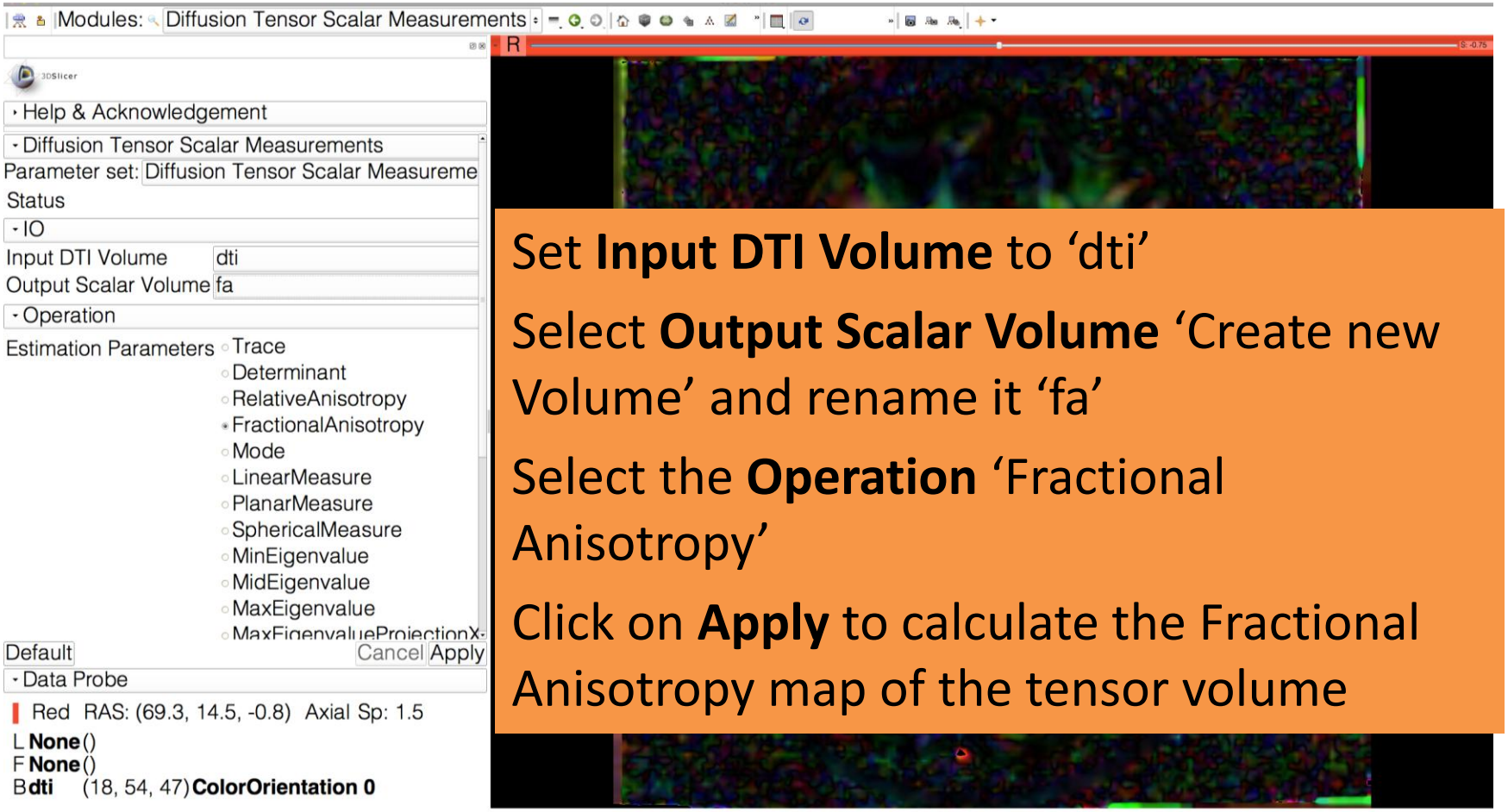
Note how the Trace values are fairly uniform in both white and gray matter, even if the tissues are different in structure.

Scalar Maps: Fractional Anisotropy

$$FA(D) = \frac{\sqrt{(I_1 - I_2)^2 + (I_1 - I_3)^2 + (I_2 - I_3)^2}}{\sqrt{2}\sqrt{I_1^2 + I_2^2 + I_3^2}}$$

- 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



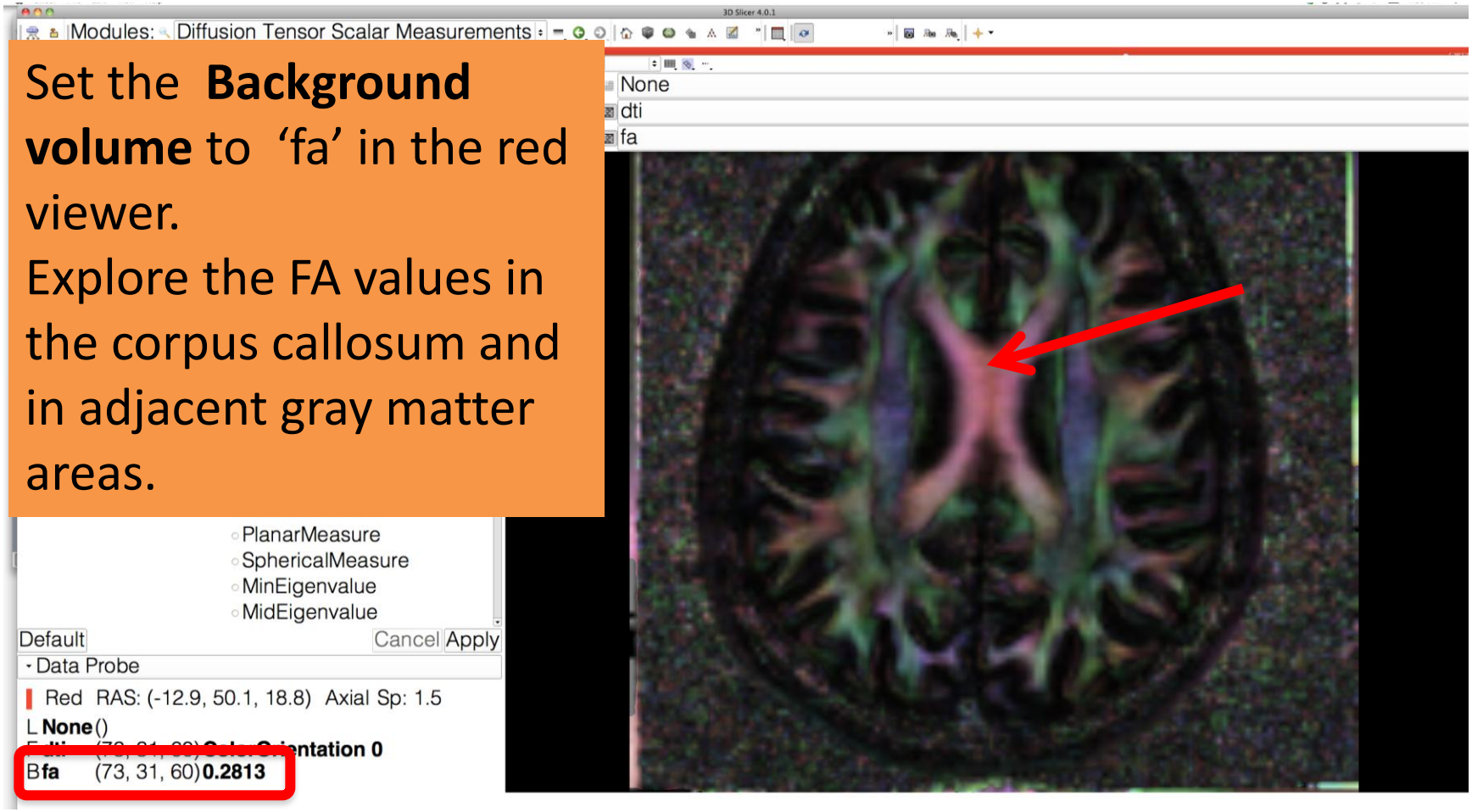
Set **Input DTI Volume** to ‘dti’

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

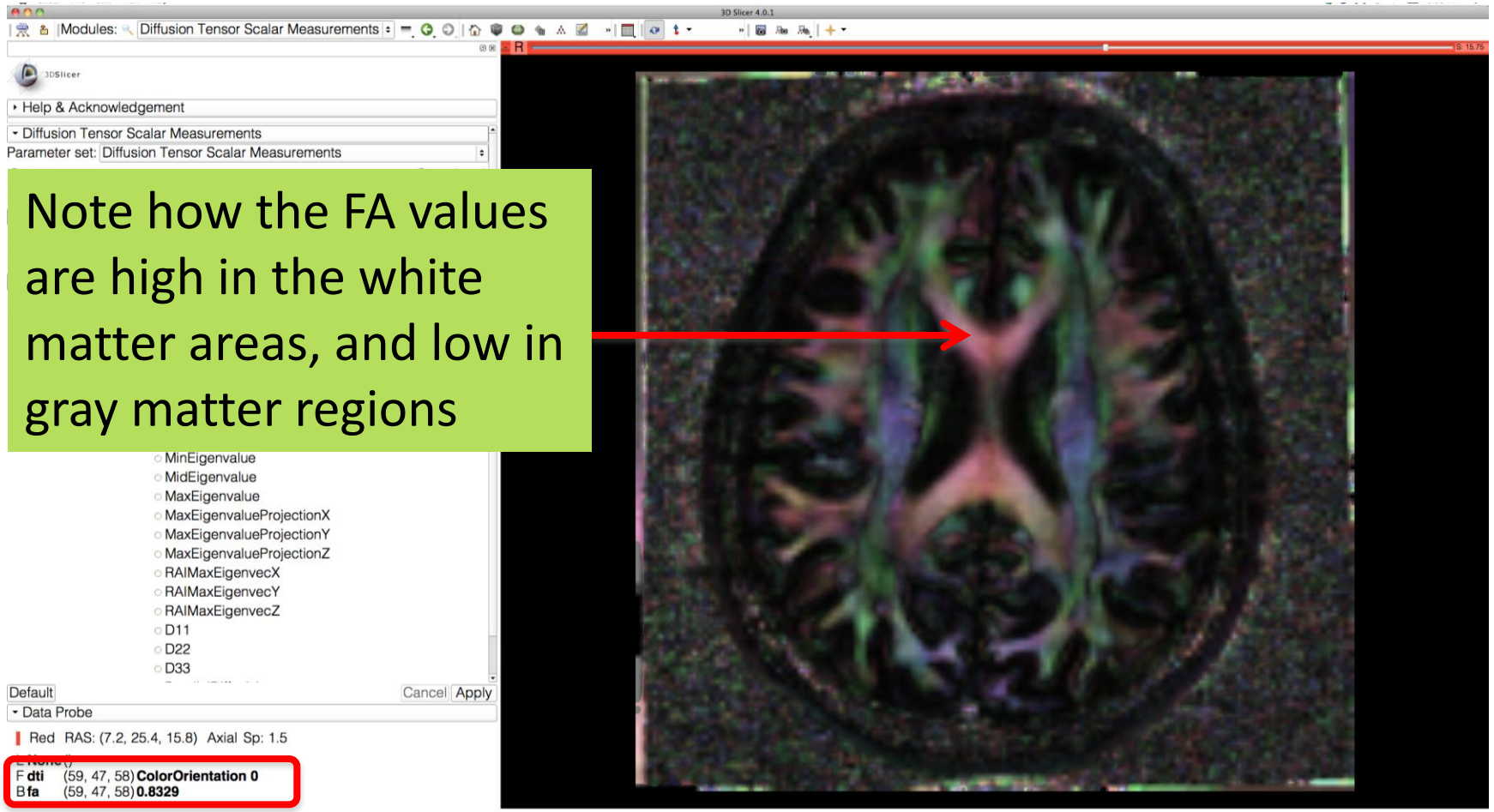
Fractional Anisotropy



Set the **Background volume** to 'fa' in the red viewer.

Explore the FA values in the corpus callosum and in adjacent gray matter areas.

Fractional Anisotropy

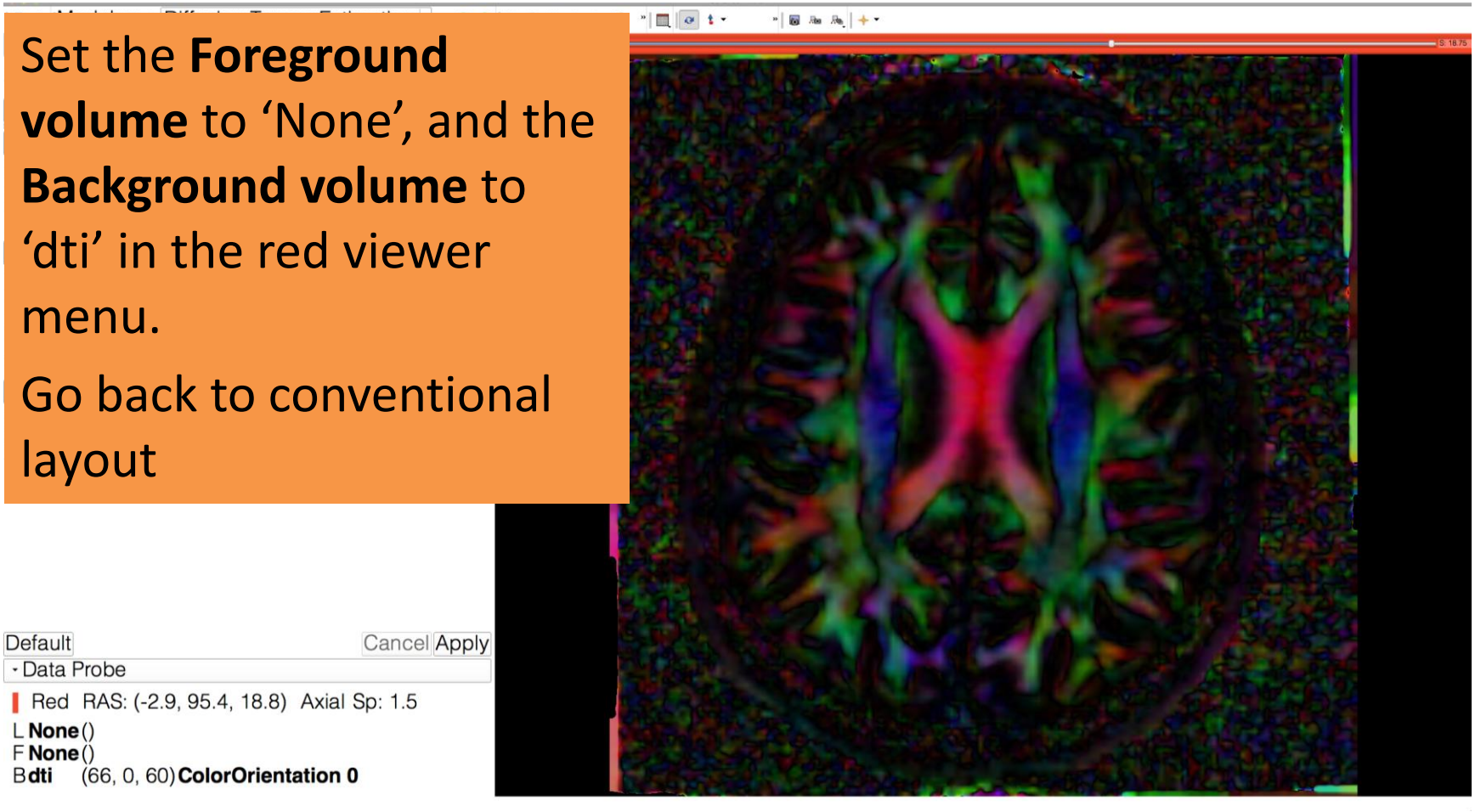


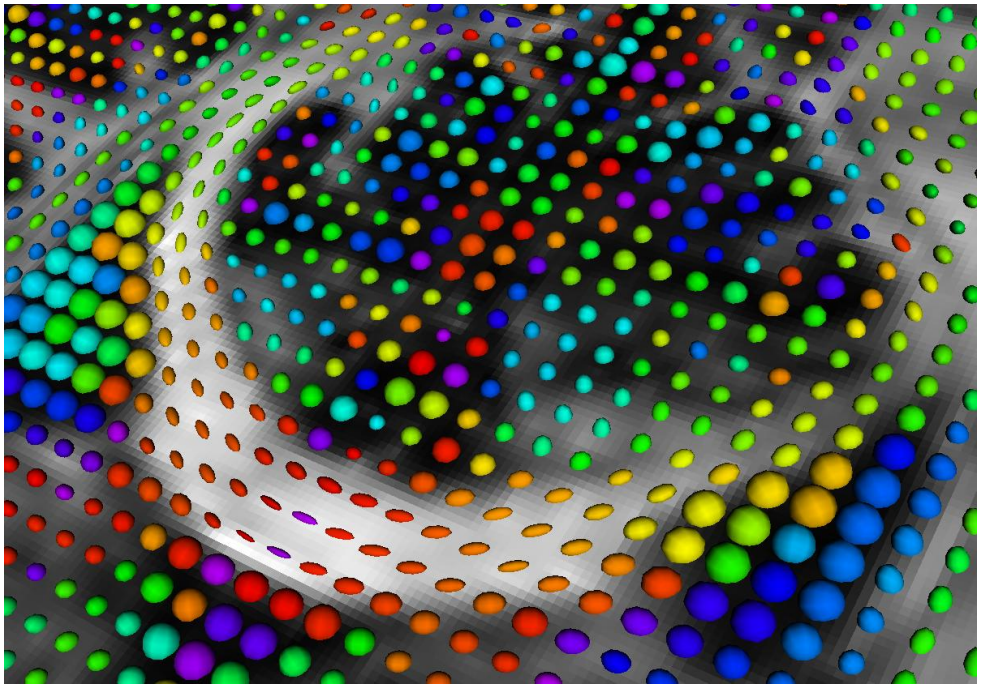
Note how the FA values are high in the white matter areas, and low in gray matter regions

Fractional Anisotropy

Set the **Foreground volume** to ‘None’, and the **Background volume** to ‘dti’ in the red viewer menu.

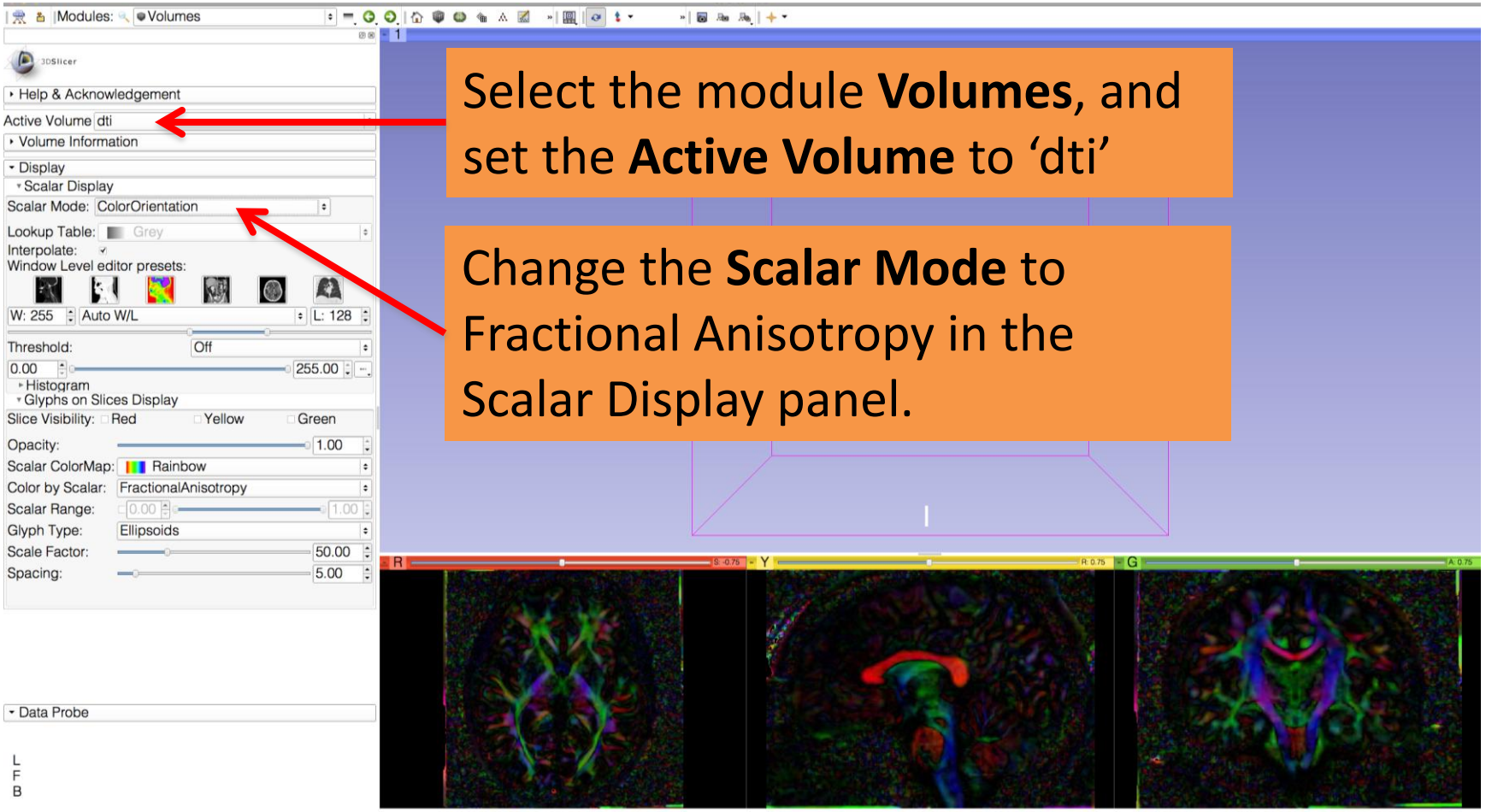
Go back to conventional layout



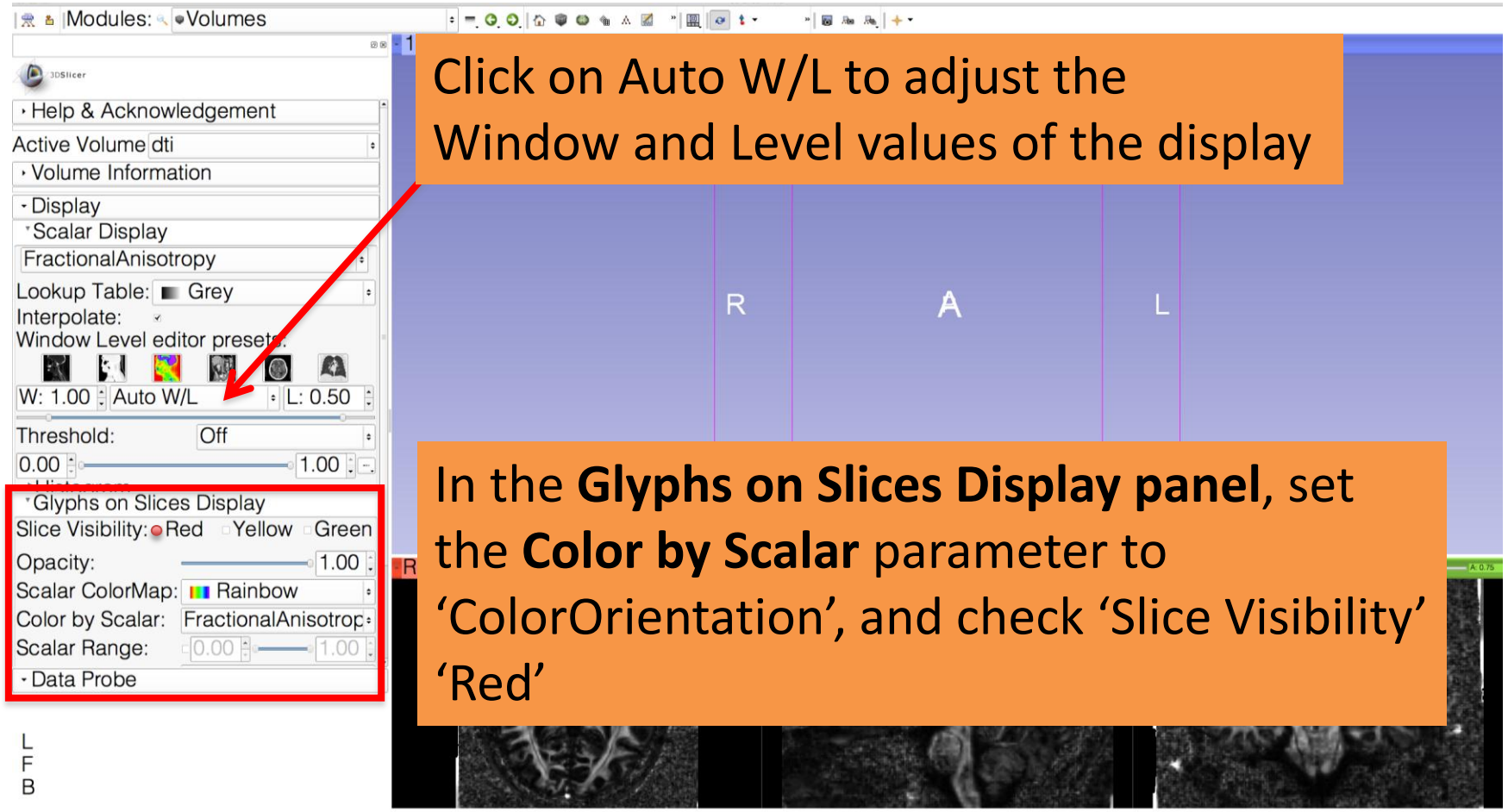


Part 2: Visualizing the tensor data

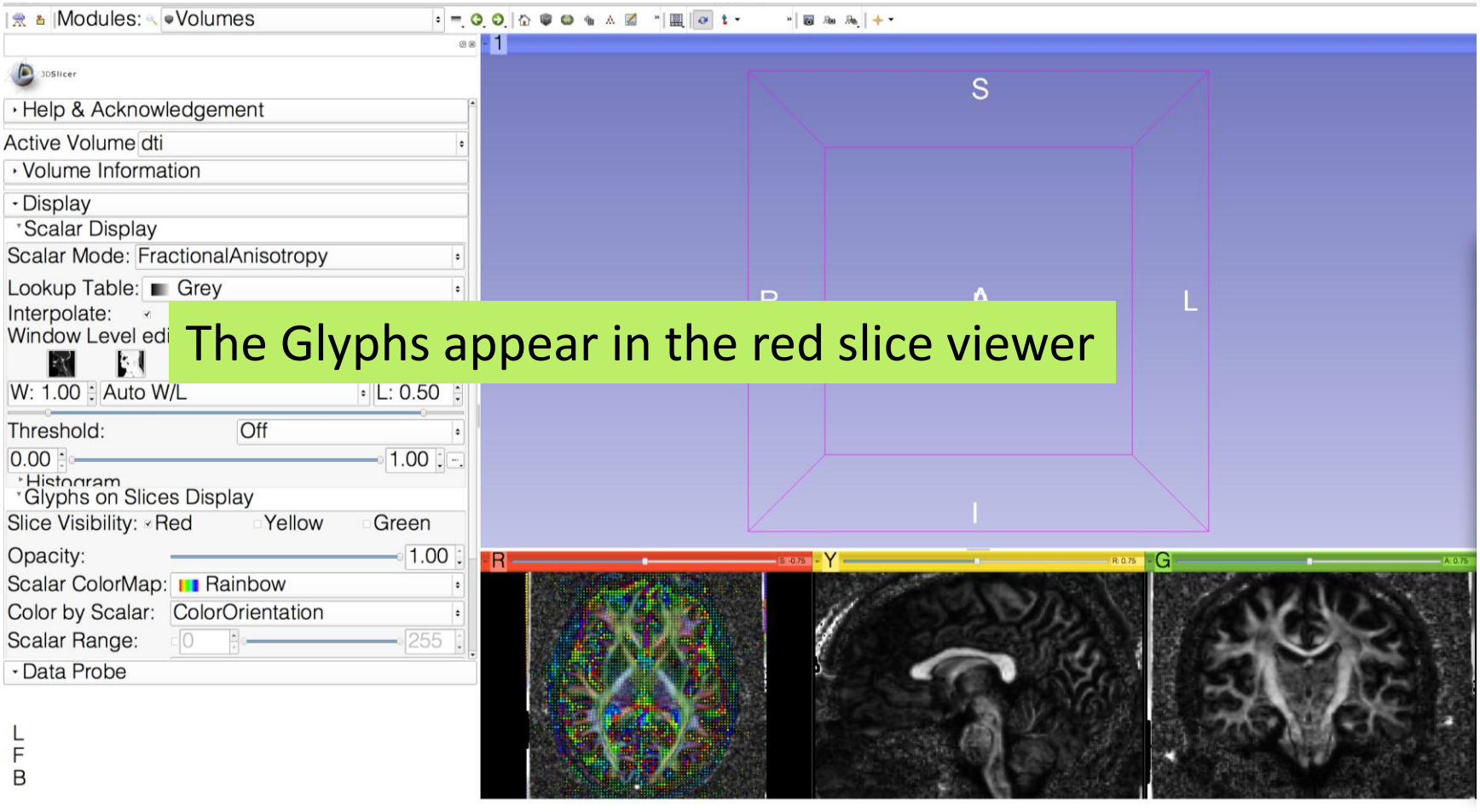
3D Visualization: Glyphs



3D Visualization: Glyphs



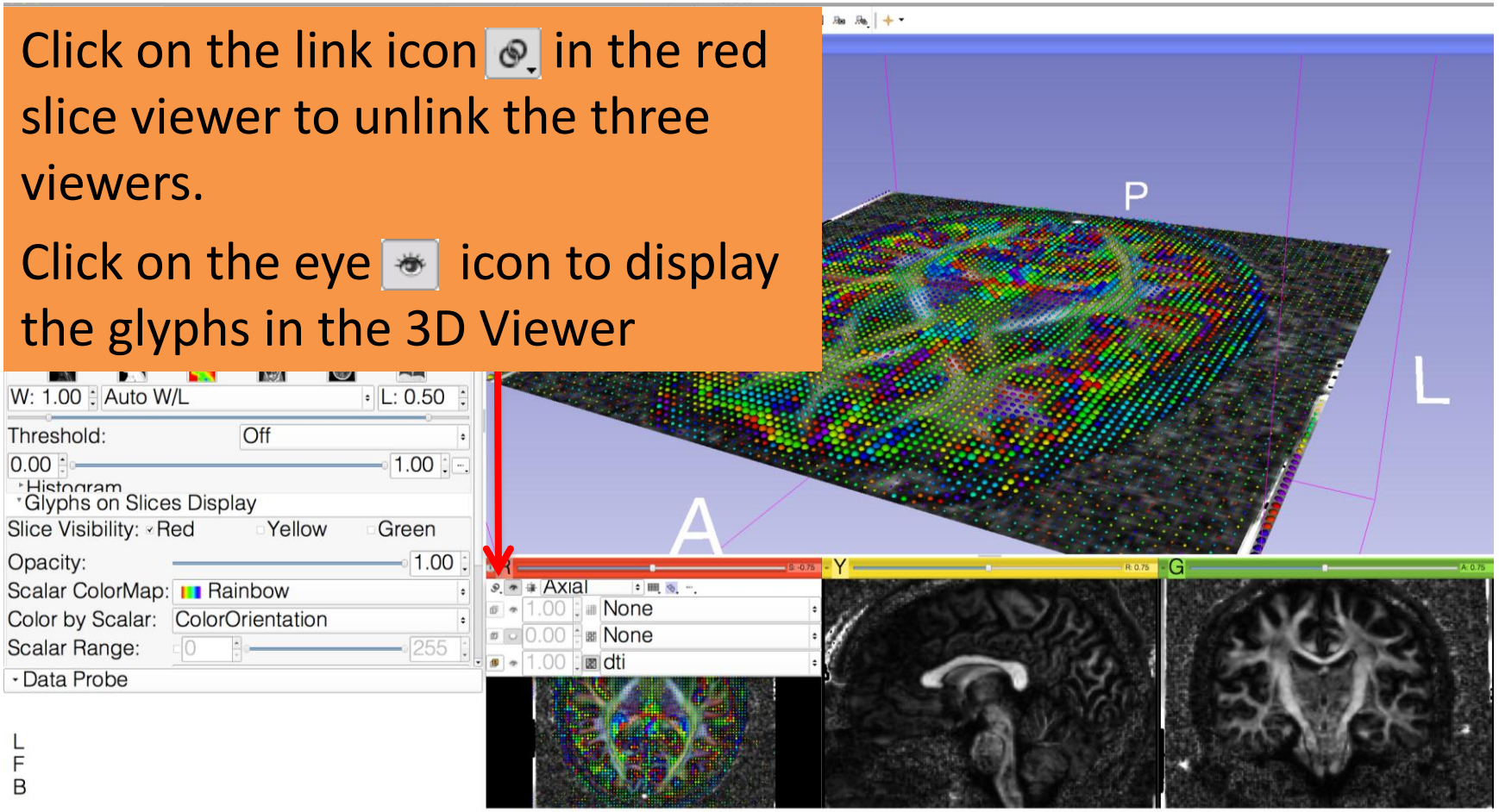
3D Visualization: Glyphs



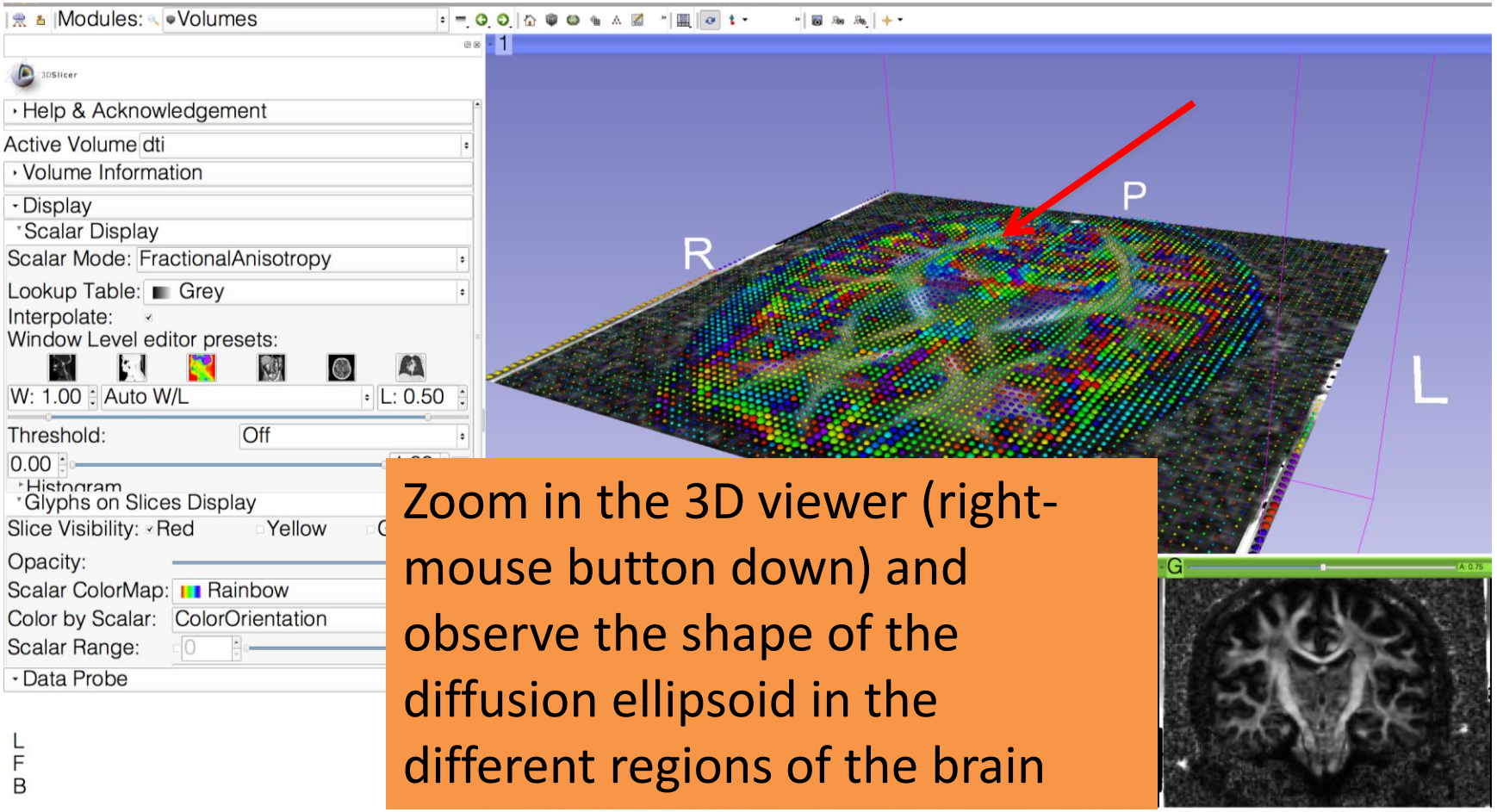
3D Visualization: Glyphs

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

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



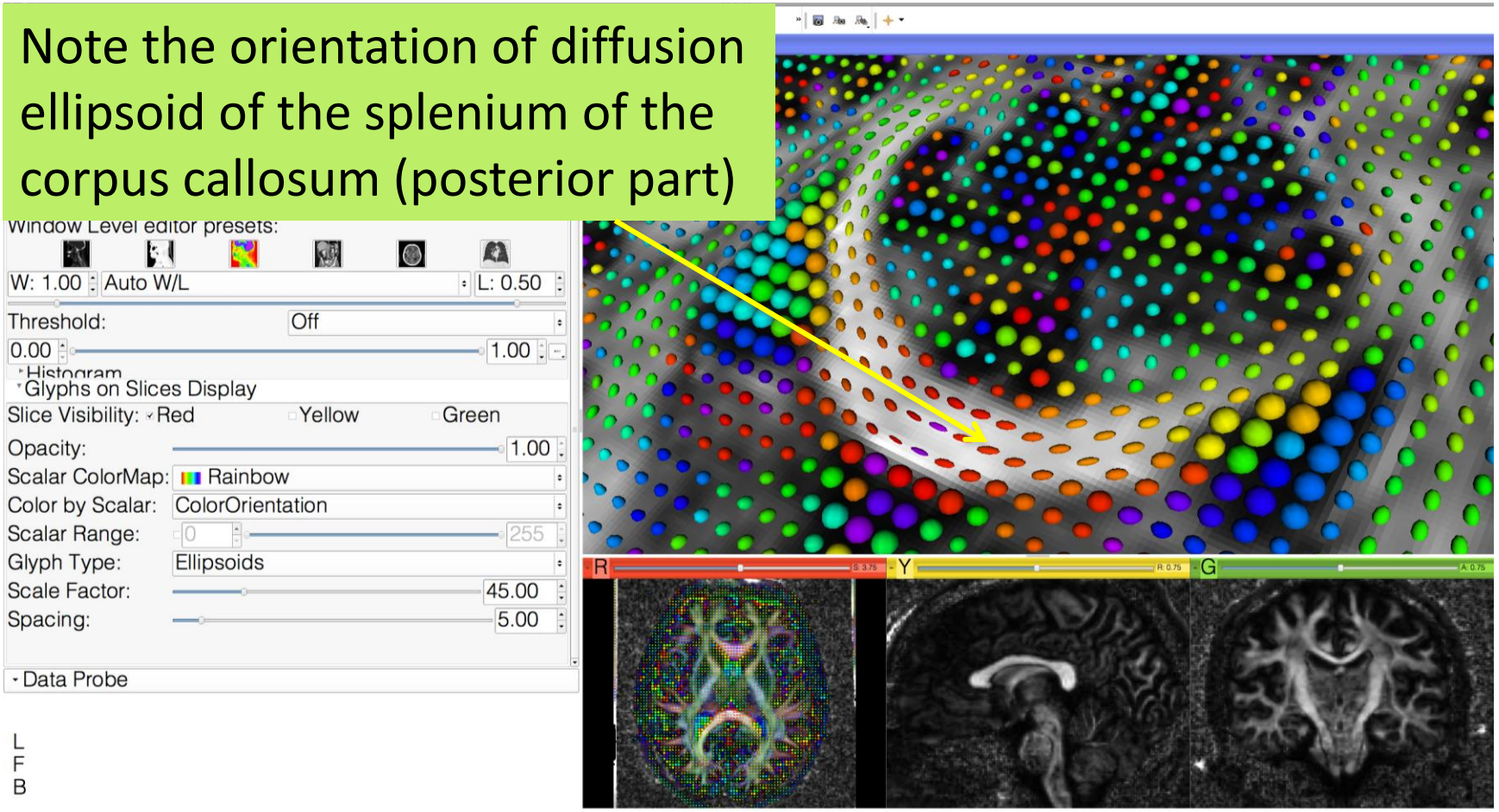
3D Visualization: Glyphs



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

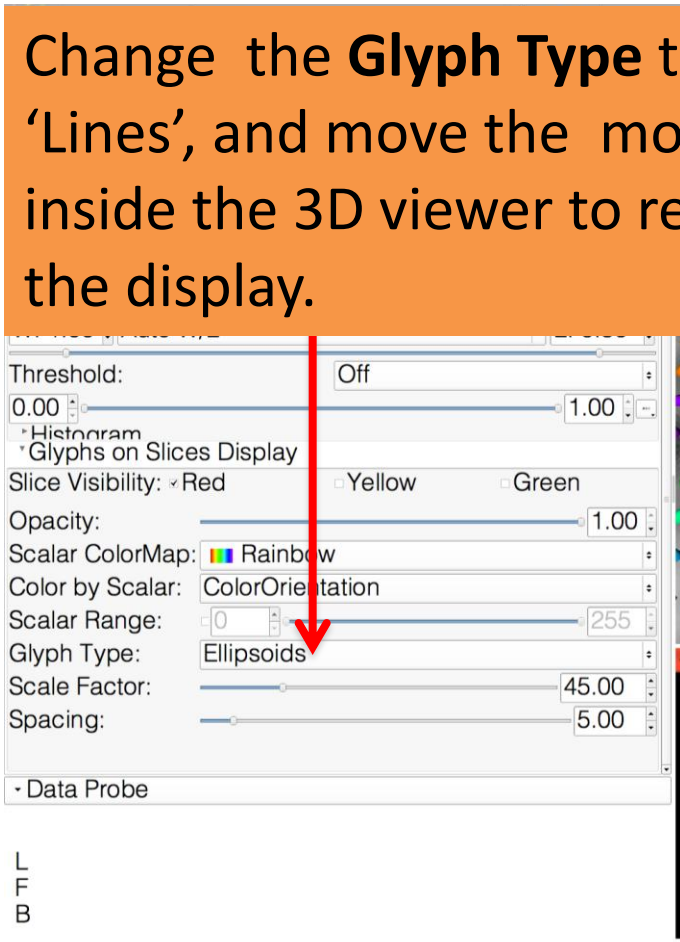
3D Visualization: Glyphs

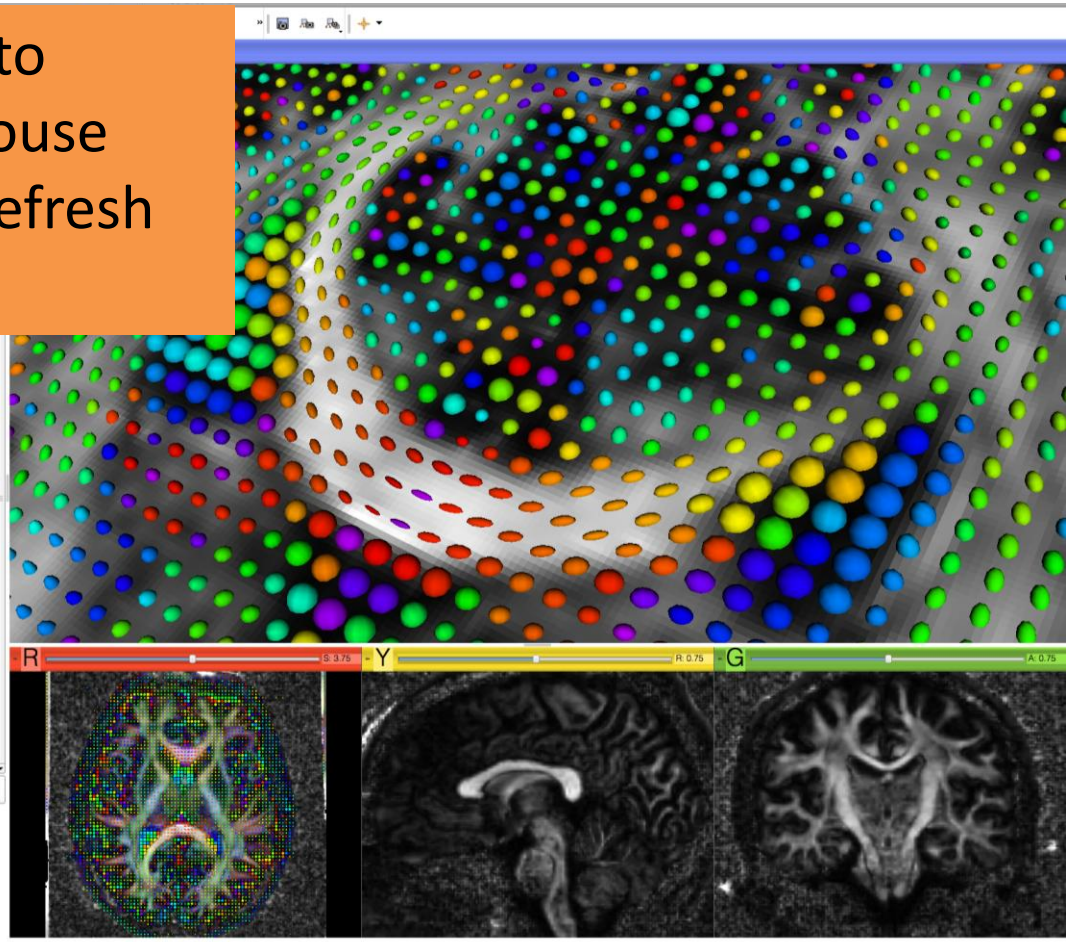
Note the orientation of diffusion ellipsoid of the splenium of the corpus callosum (posterior part)



3D Visualization: Glyphs

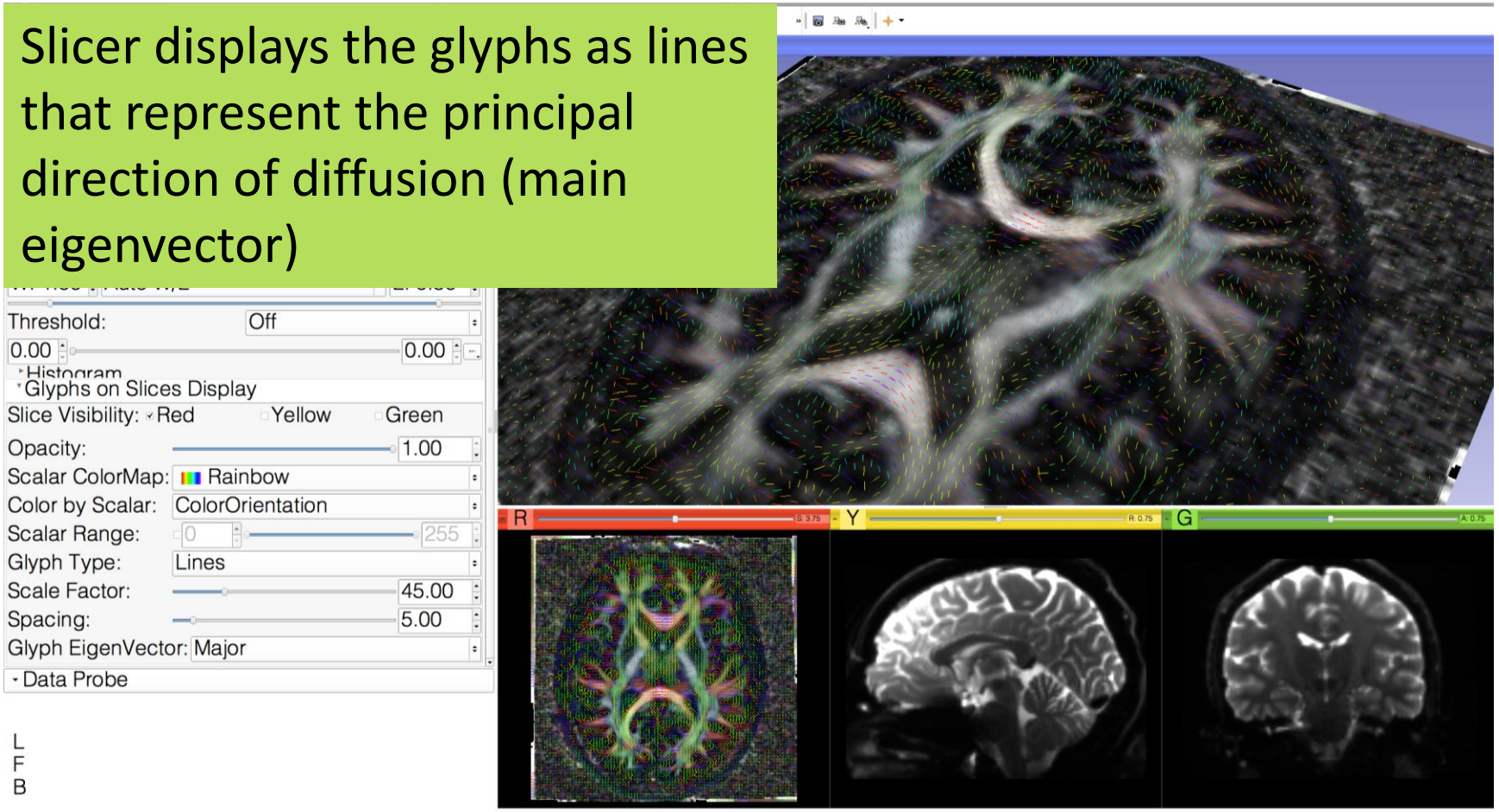
Change the **Glyph Type** to ‘Lines’, and move the mouse inside the 3D viewer to refresh the display.



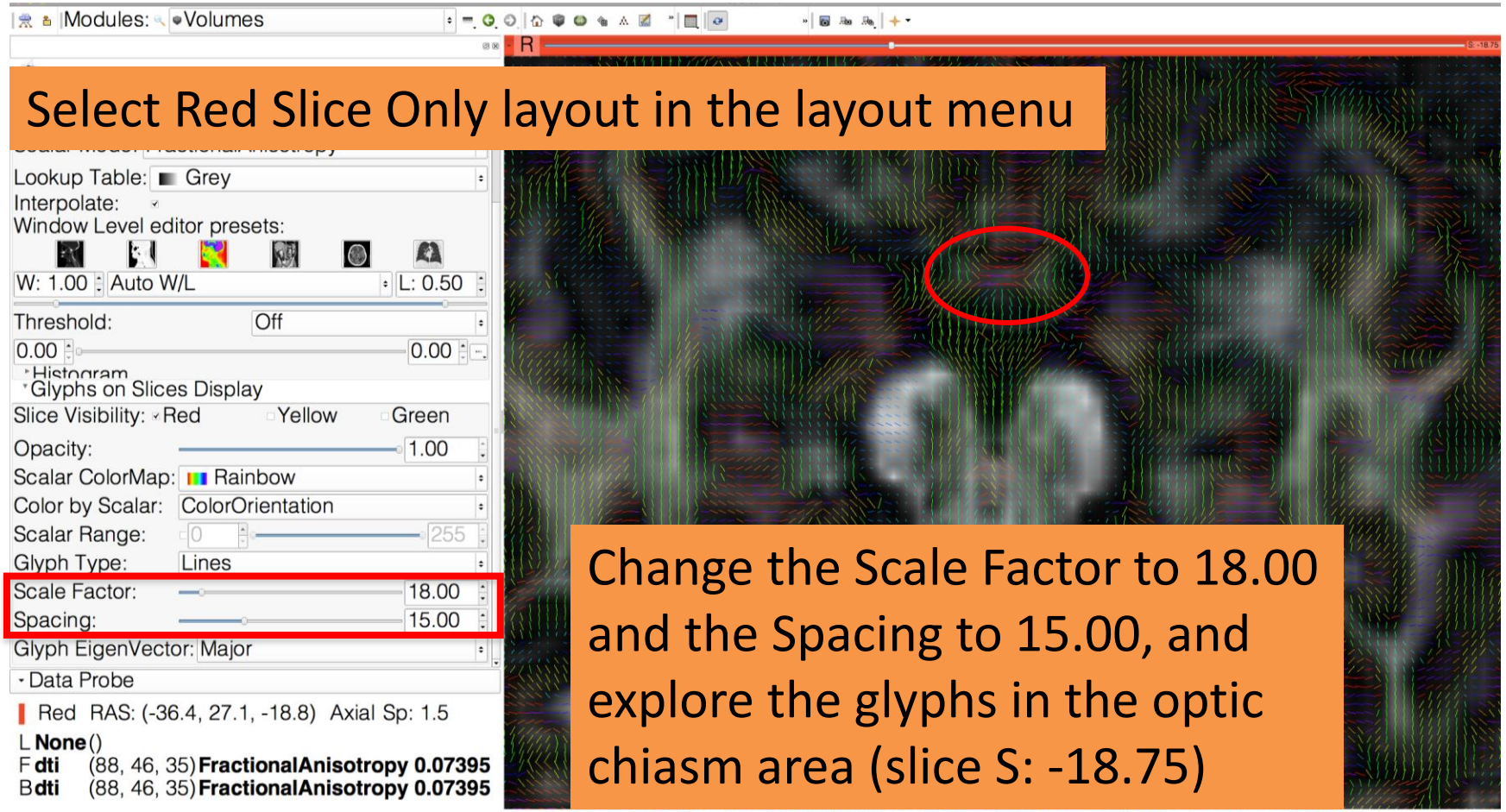


3D Visualization: Glyphs

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



3D Visualization: Glyphs



Optic Chiasm

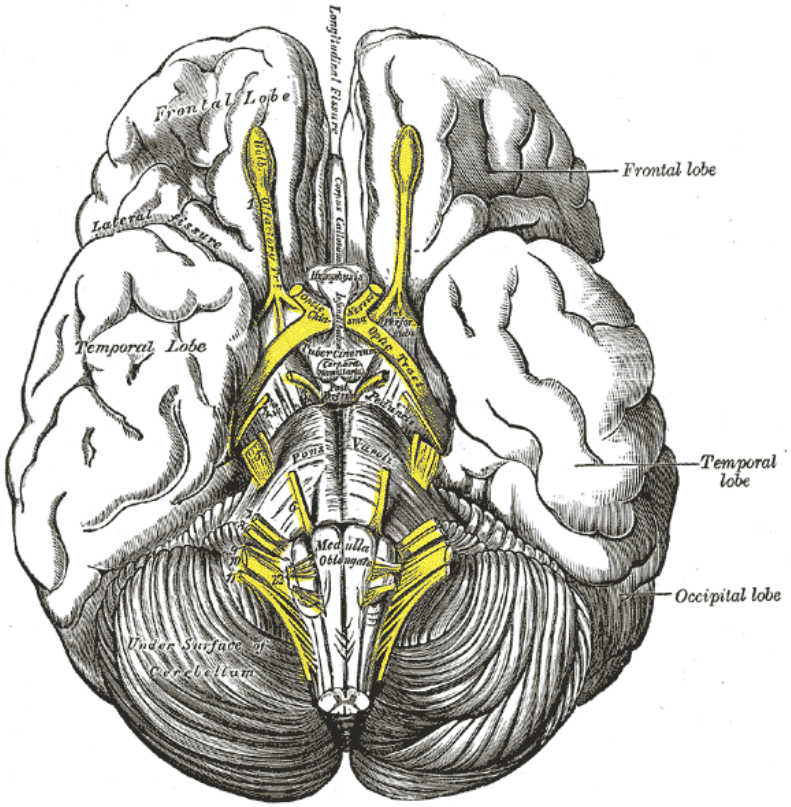
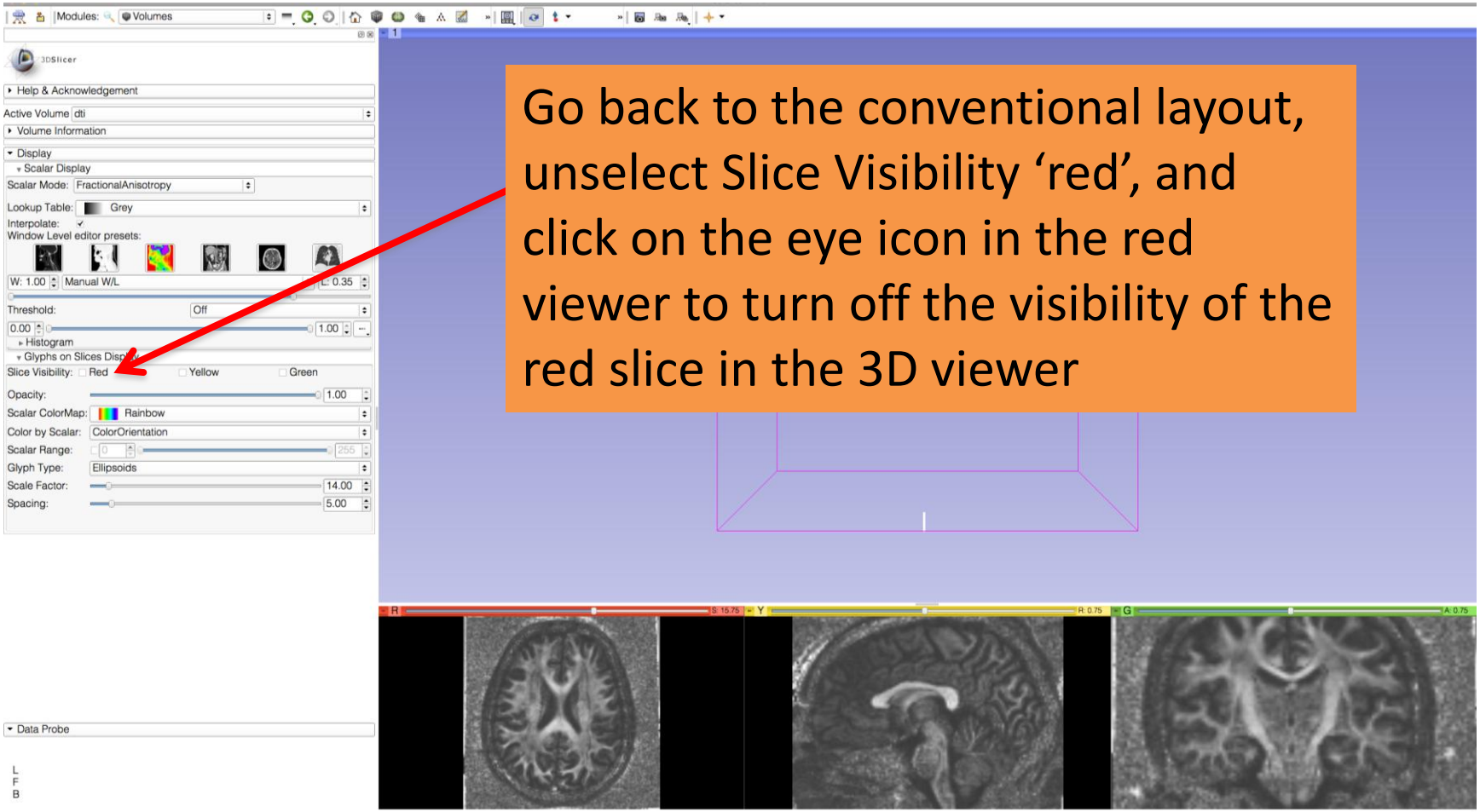
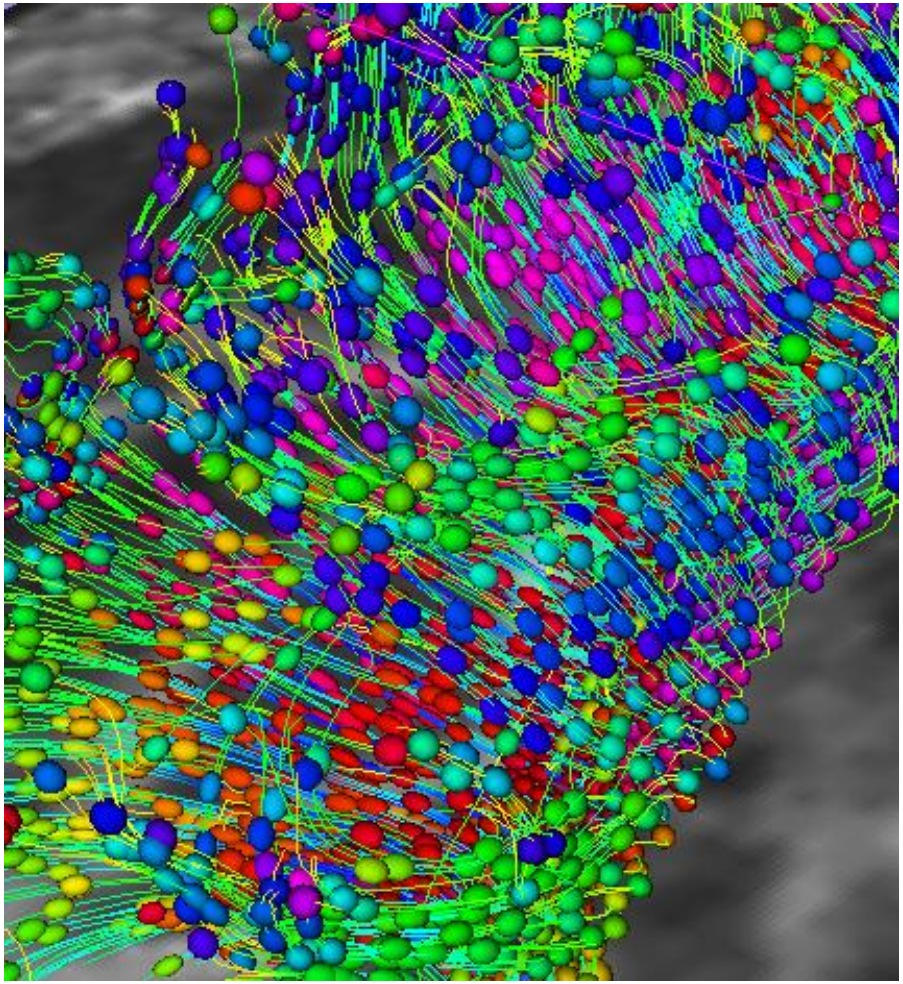


Image from Gray's Anatomy

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

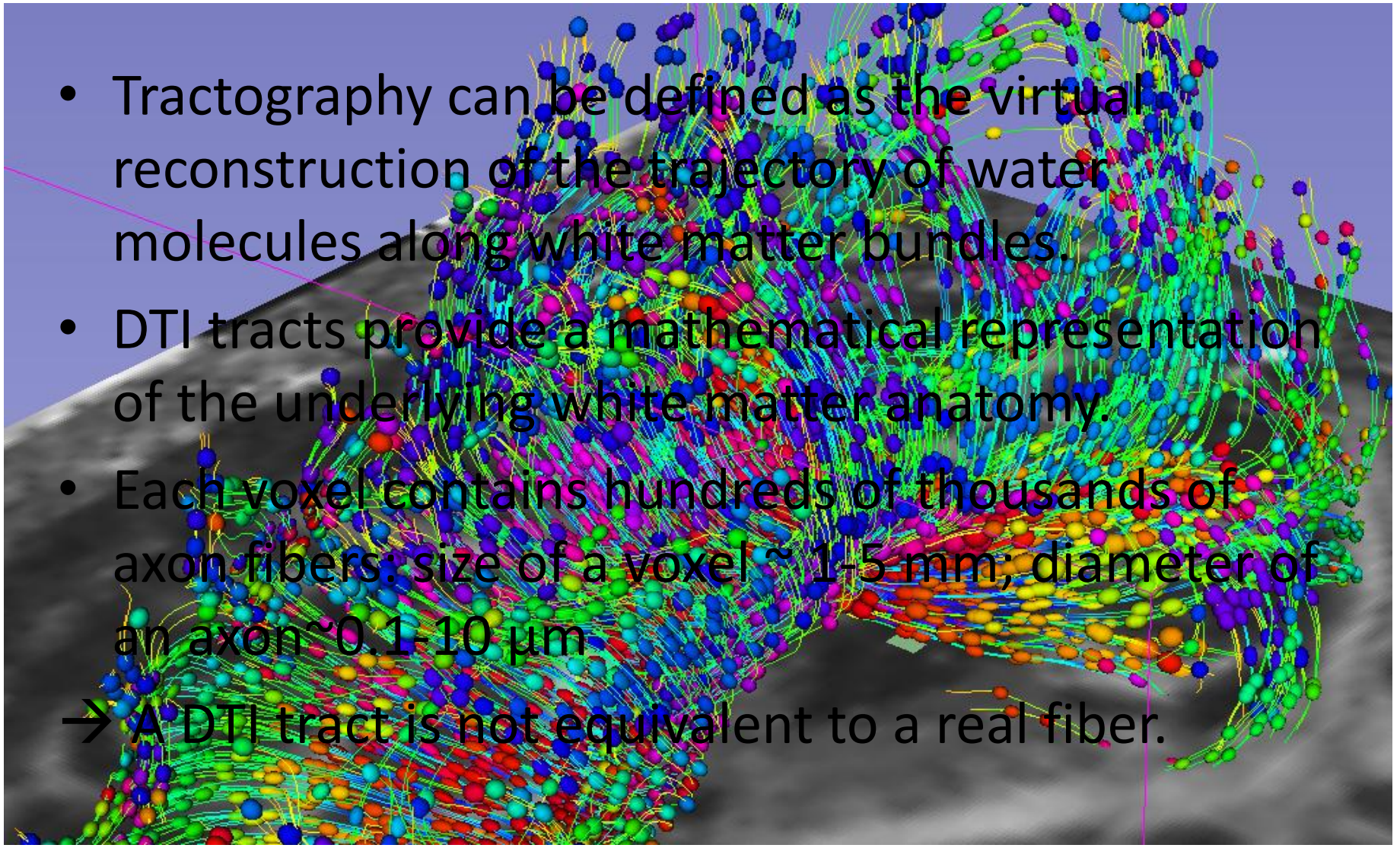
3D Visualization: Glyphs





Part 3:
From tensors to tracts

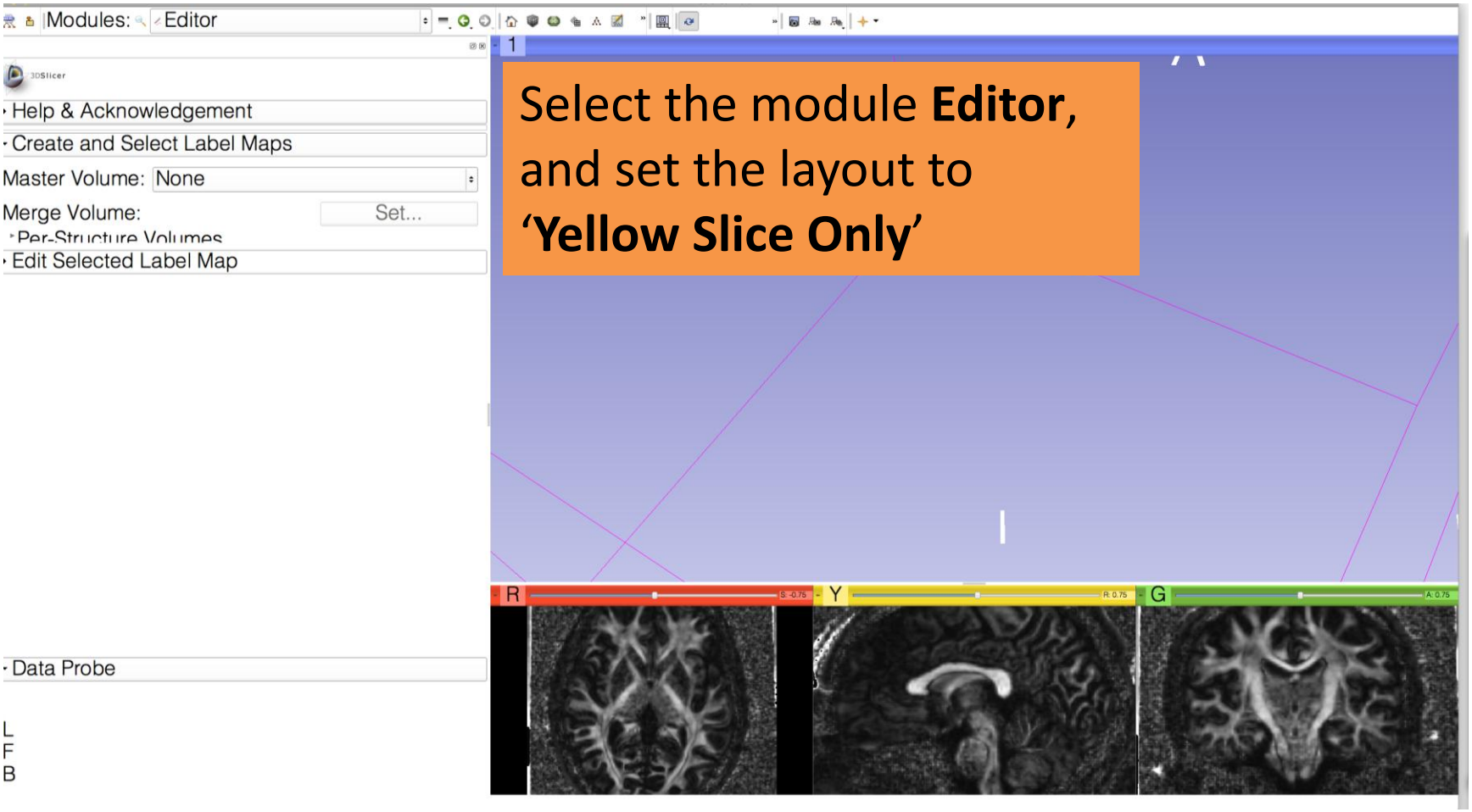
Diffusion MRI tractography



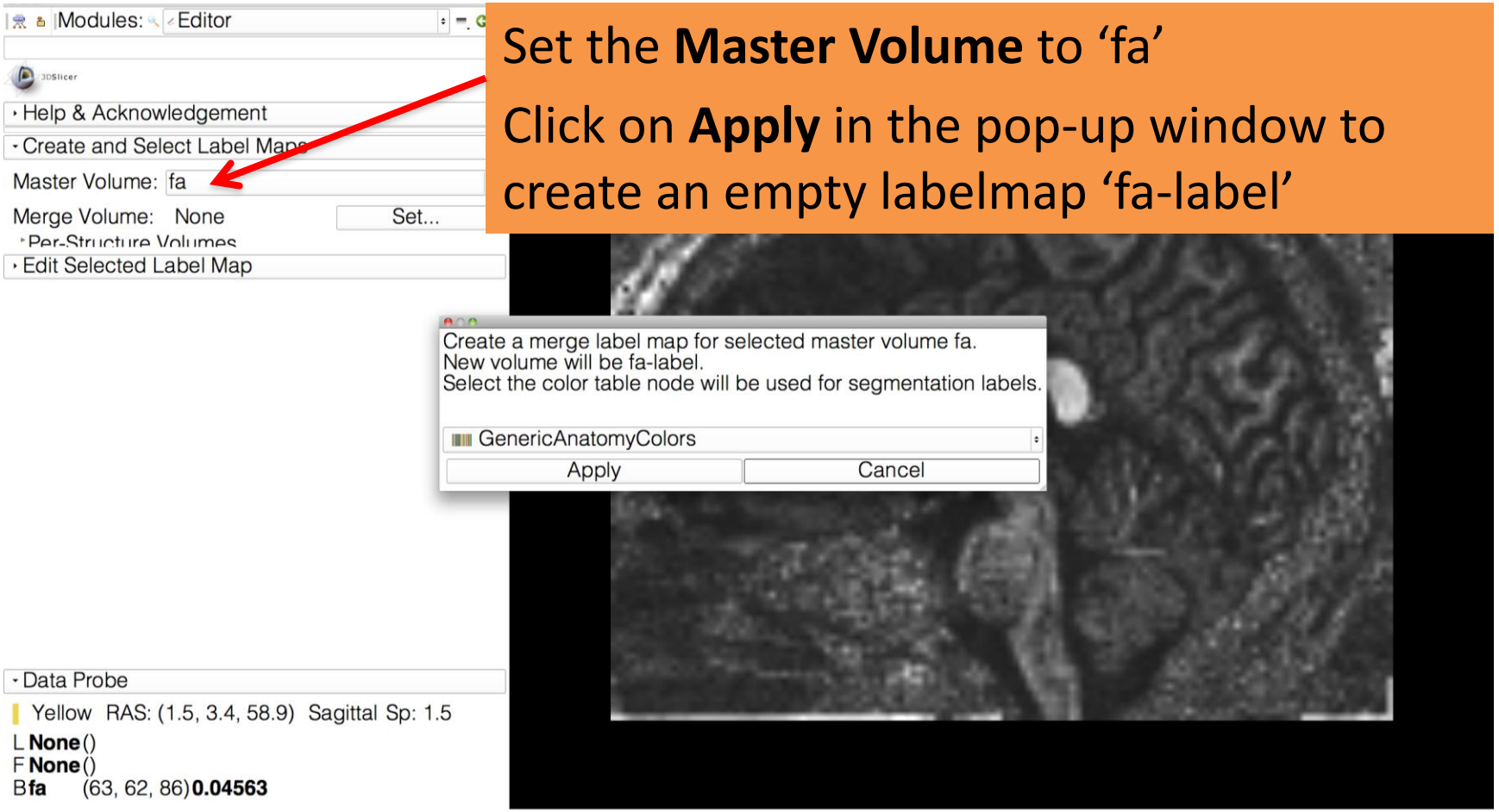
- Tractography can be defined as the virtual reconstruction of the trajectory of water molecules along white matter bundles.
- DTI tracts provide a mathematical representation of the underlying white matter anatomy.
- Each voxel contains hundreds of thousands of axon fibers: size of a voxel ~ 1-5 mm; diameter of an axon~0.1-10 µm.

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

Tractography Seeding: ROI definition



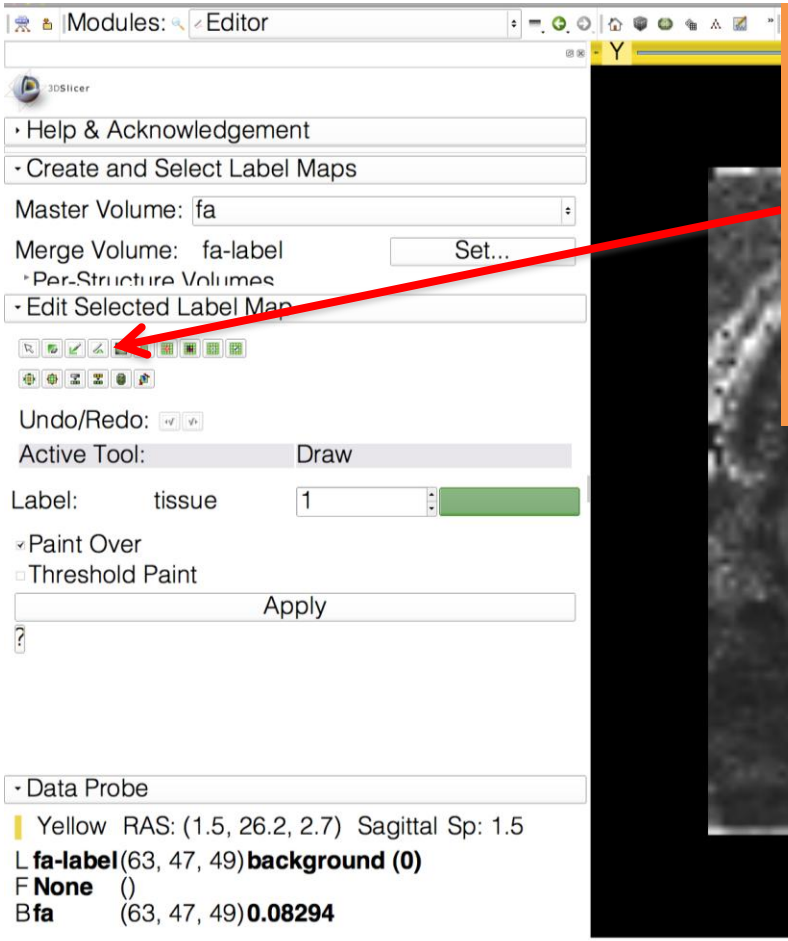
ROI Definition



Set the **Master Volume** to ‘fa’

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

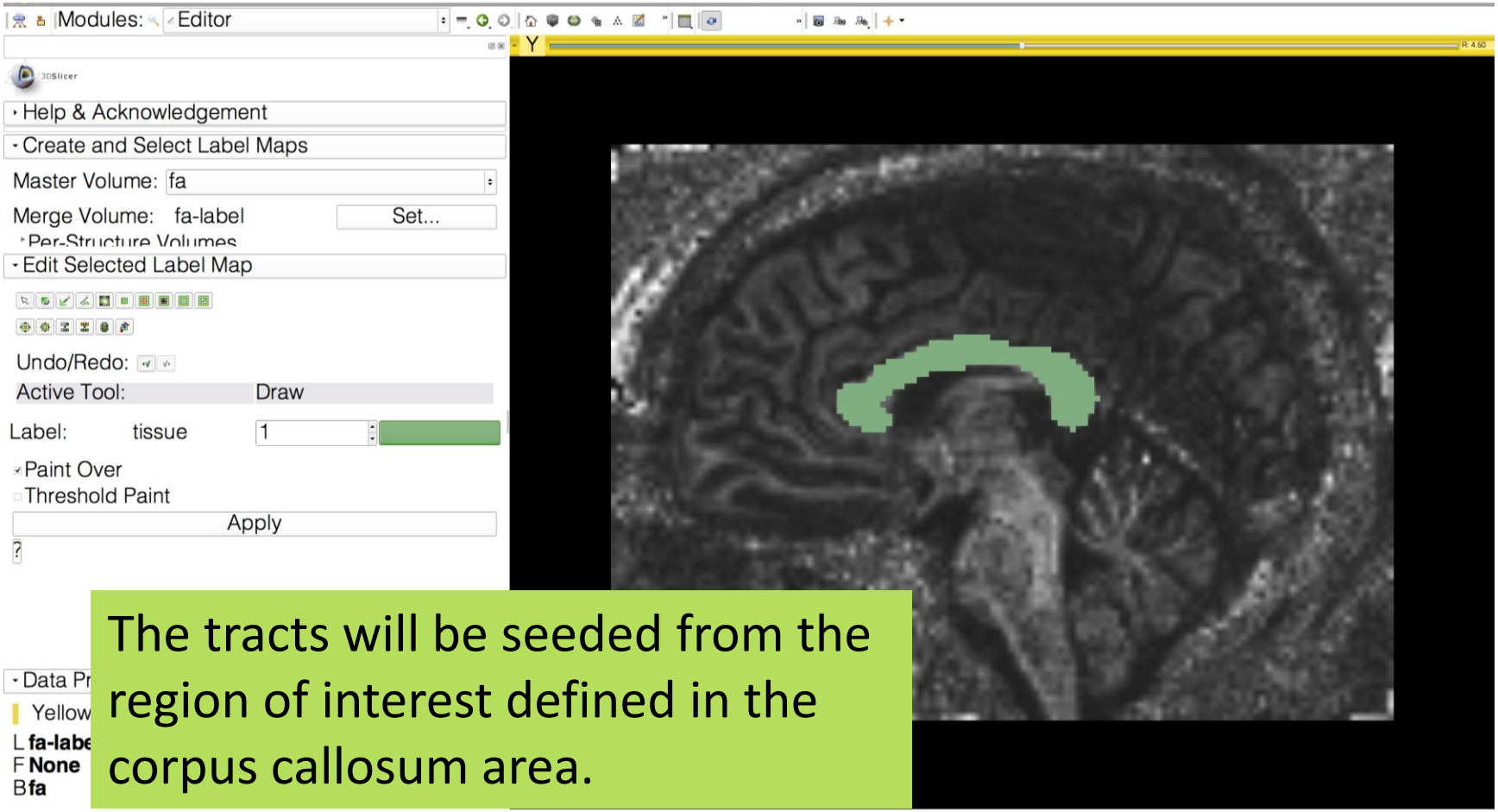
ROI Drawing



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.

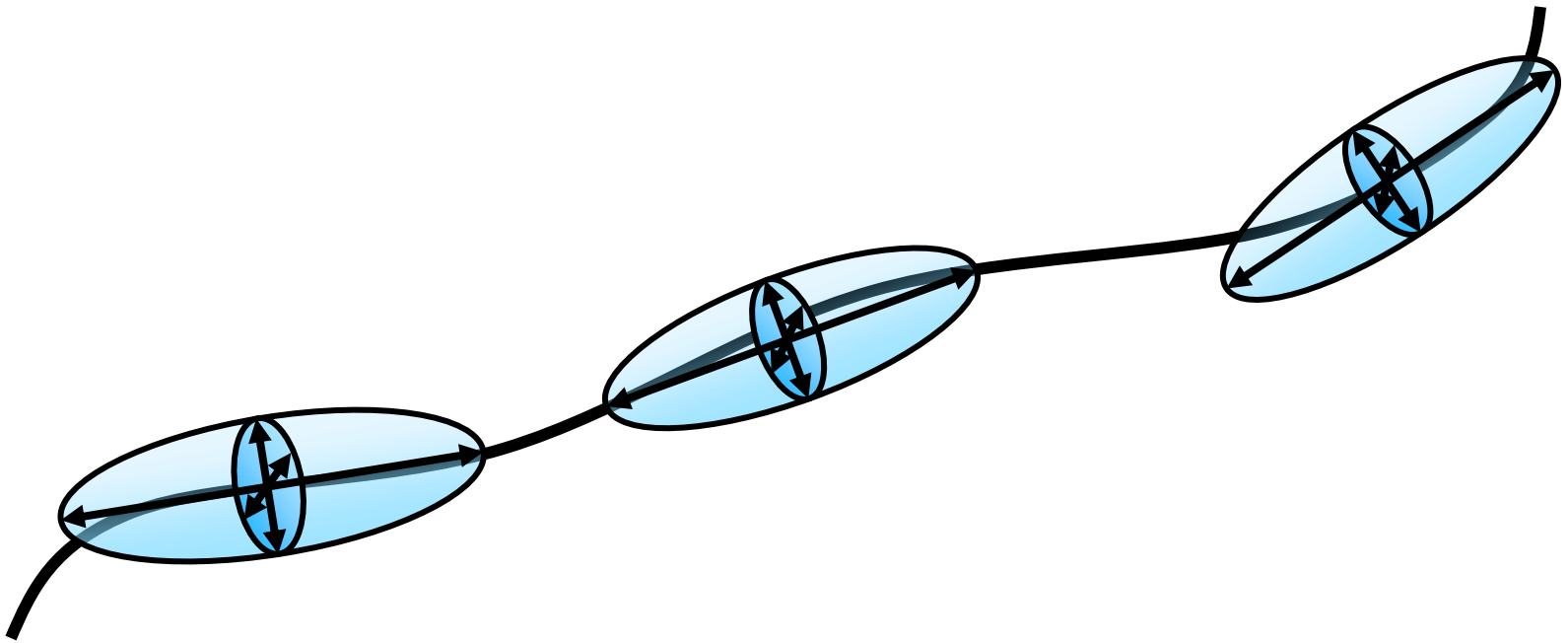
ROI Drawing



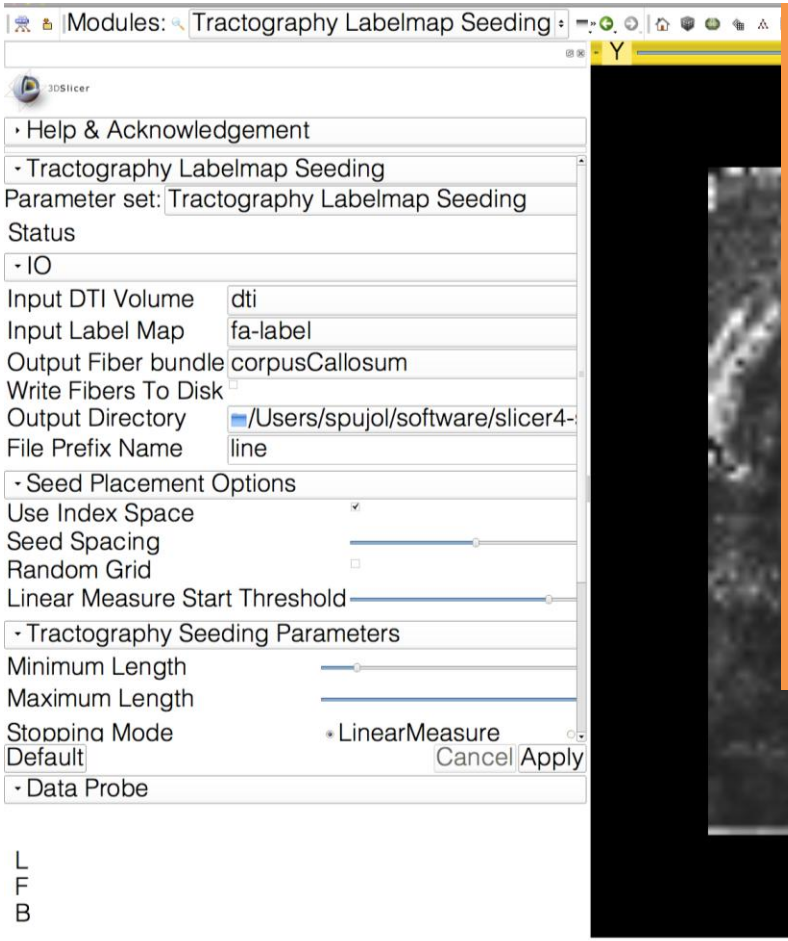
The tracts will be seeded from the region of interest defined in the corpus callosum area.

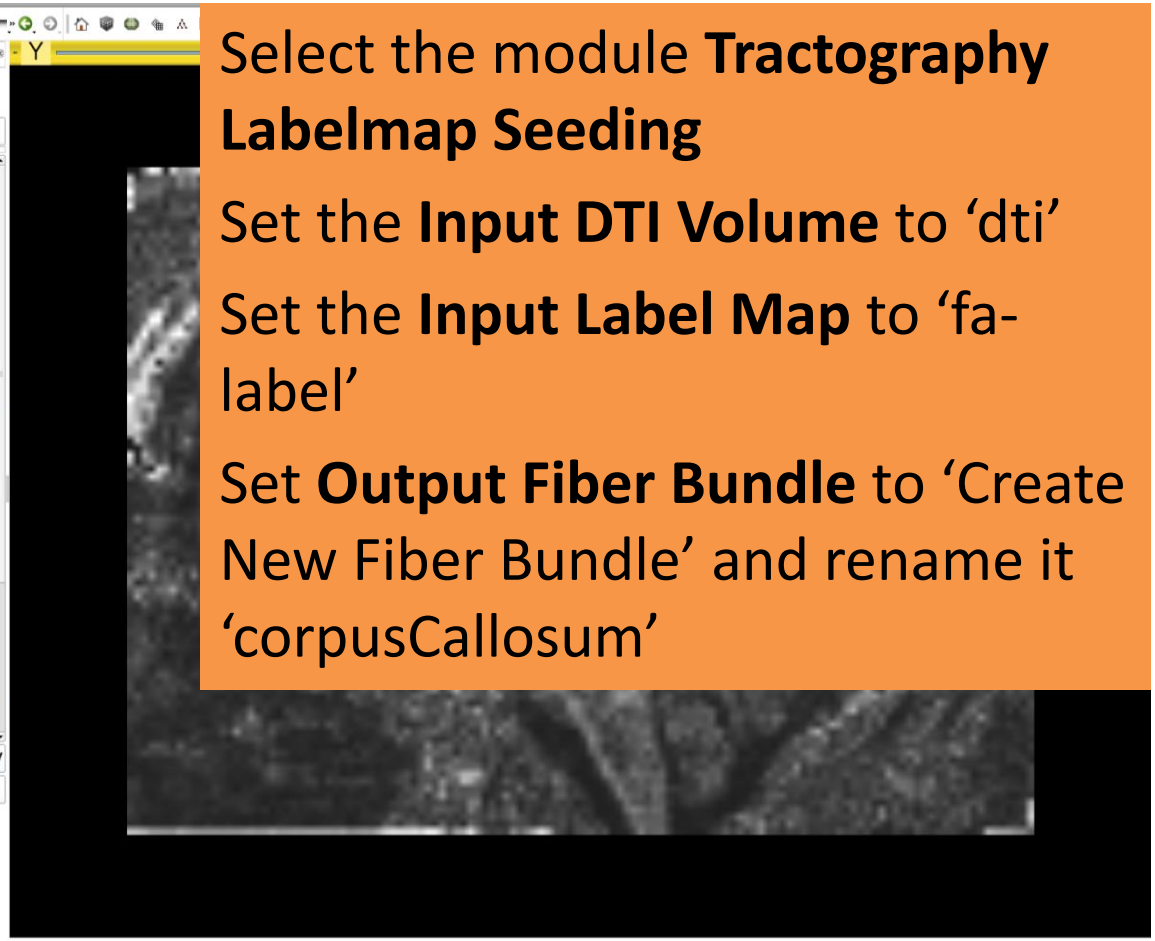
Streamline tractography

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



Labelmap Seeding: I/O





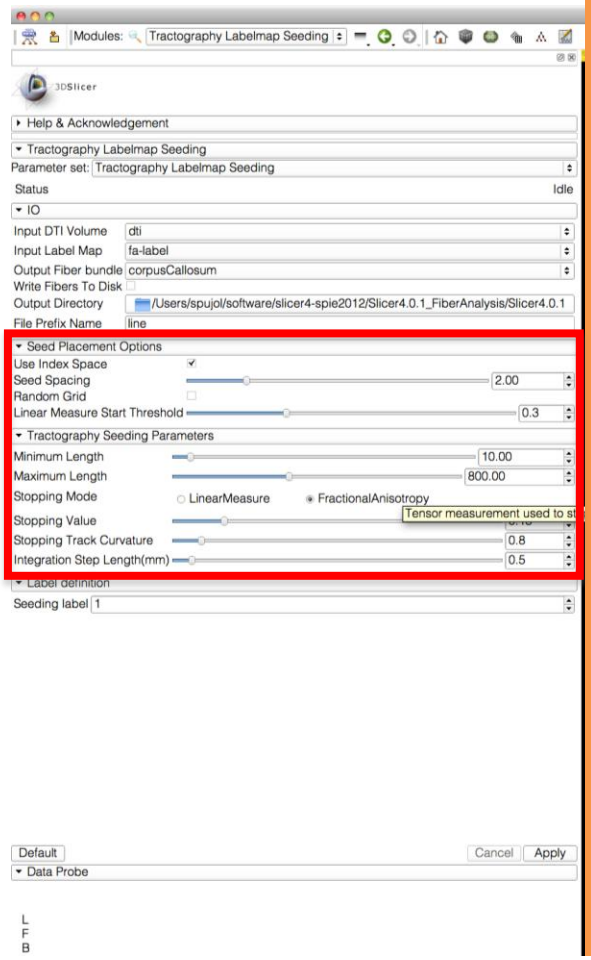
Select the module **Tractography Labelmap Seeding**

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



Set 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

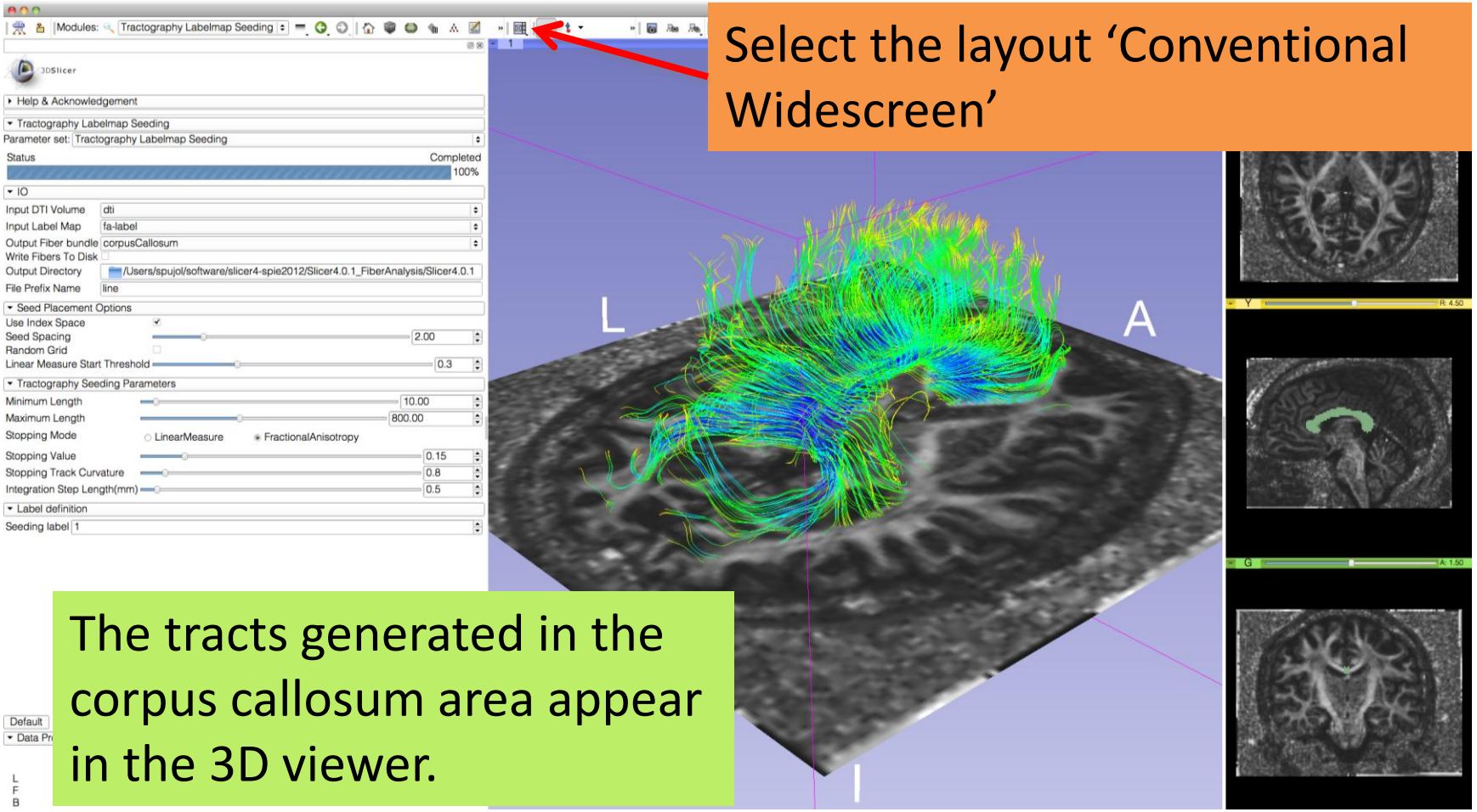
-Stopping value: 0.15

-Stopping track curvature: 0.8

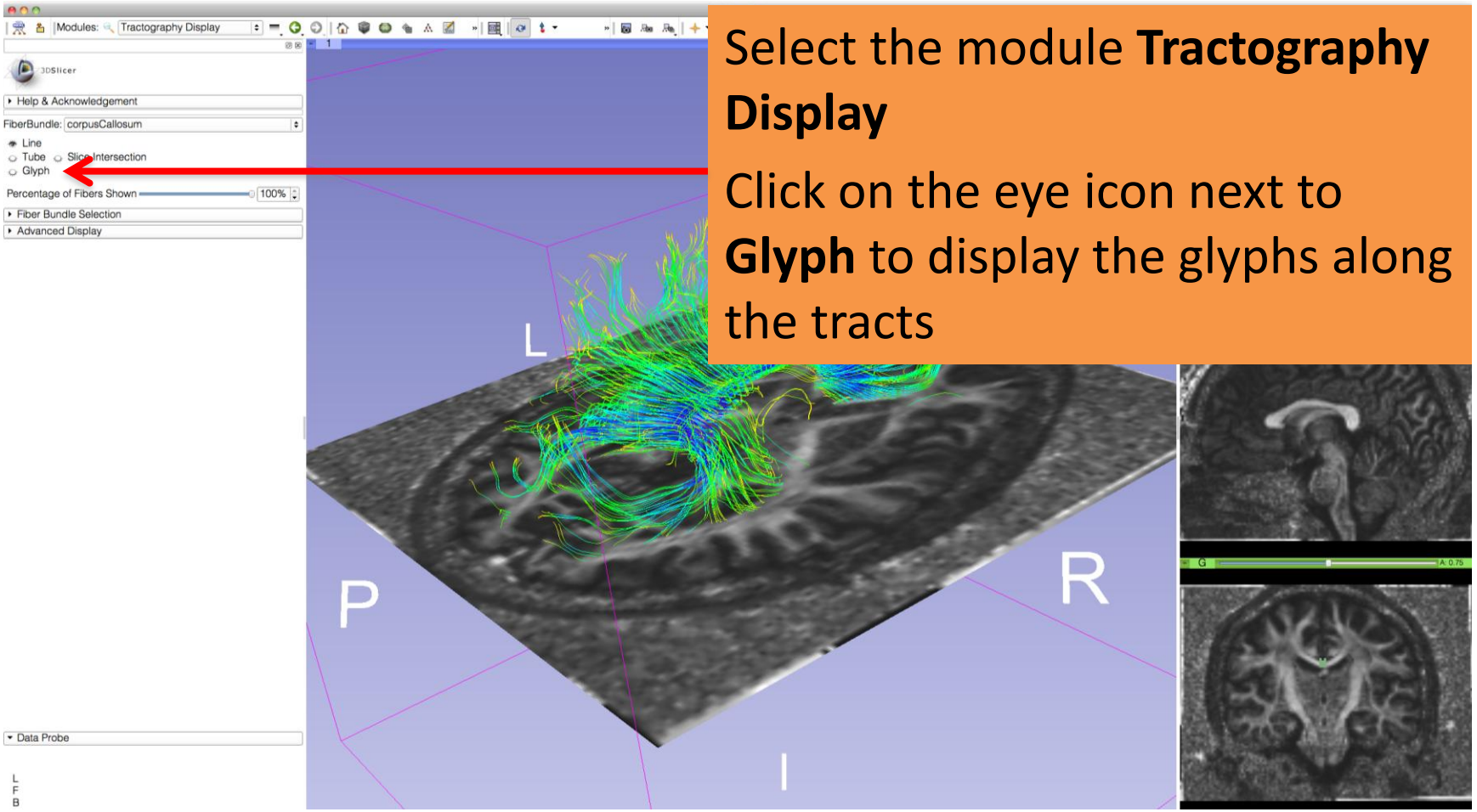
-Integration step length: 0.5 mm

Click on **Apply**

Labelmap Seeding: Tracts



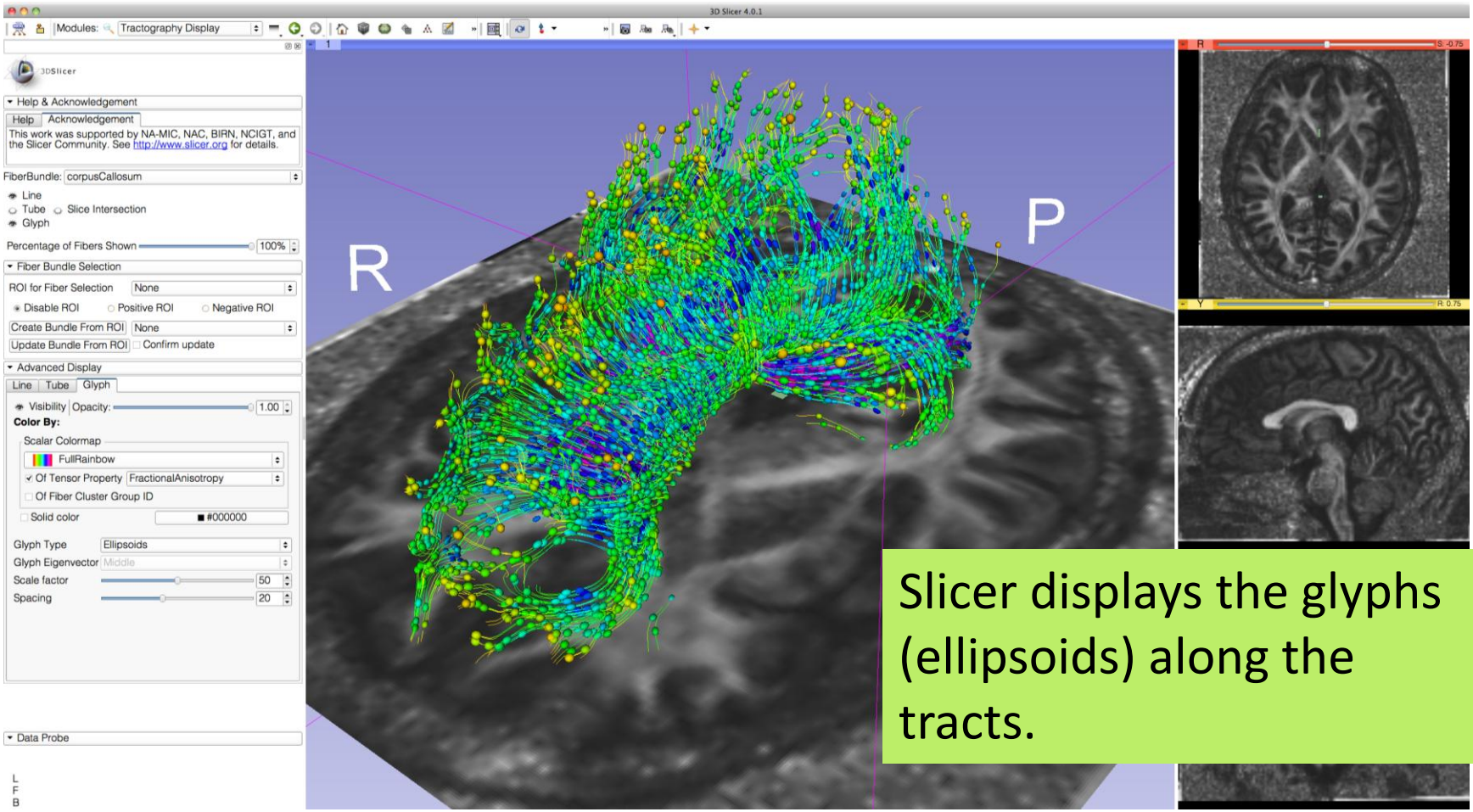
LabelMap Seeding: Tracts



Select the module **Tractography Display**

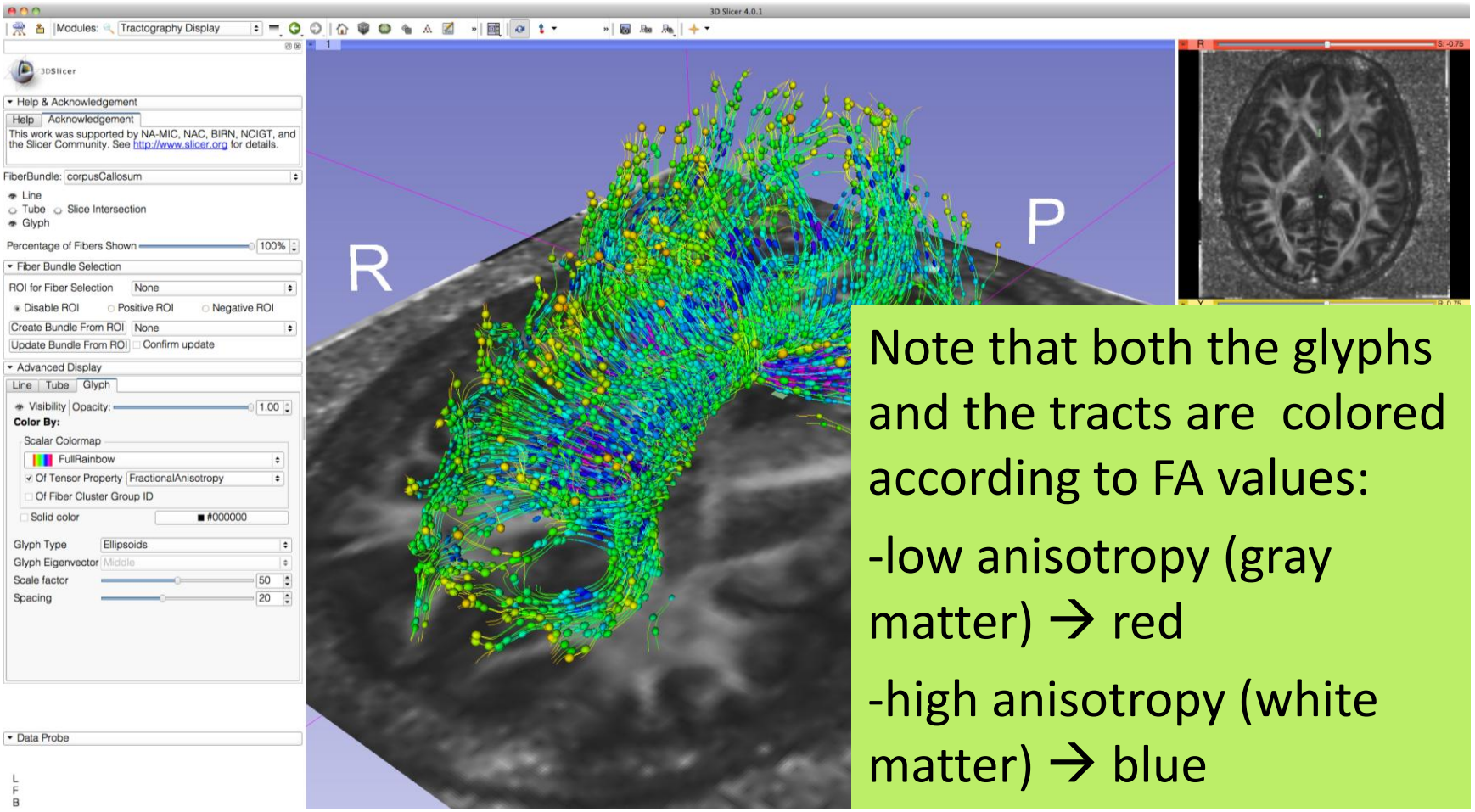
Click on the eye icon next to **Glyph** to display the glyphs along the tracts

Tractography Results



Slicer displays the glyphs (ellipsoids) along the tracts.

Tractography Results

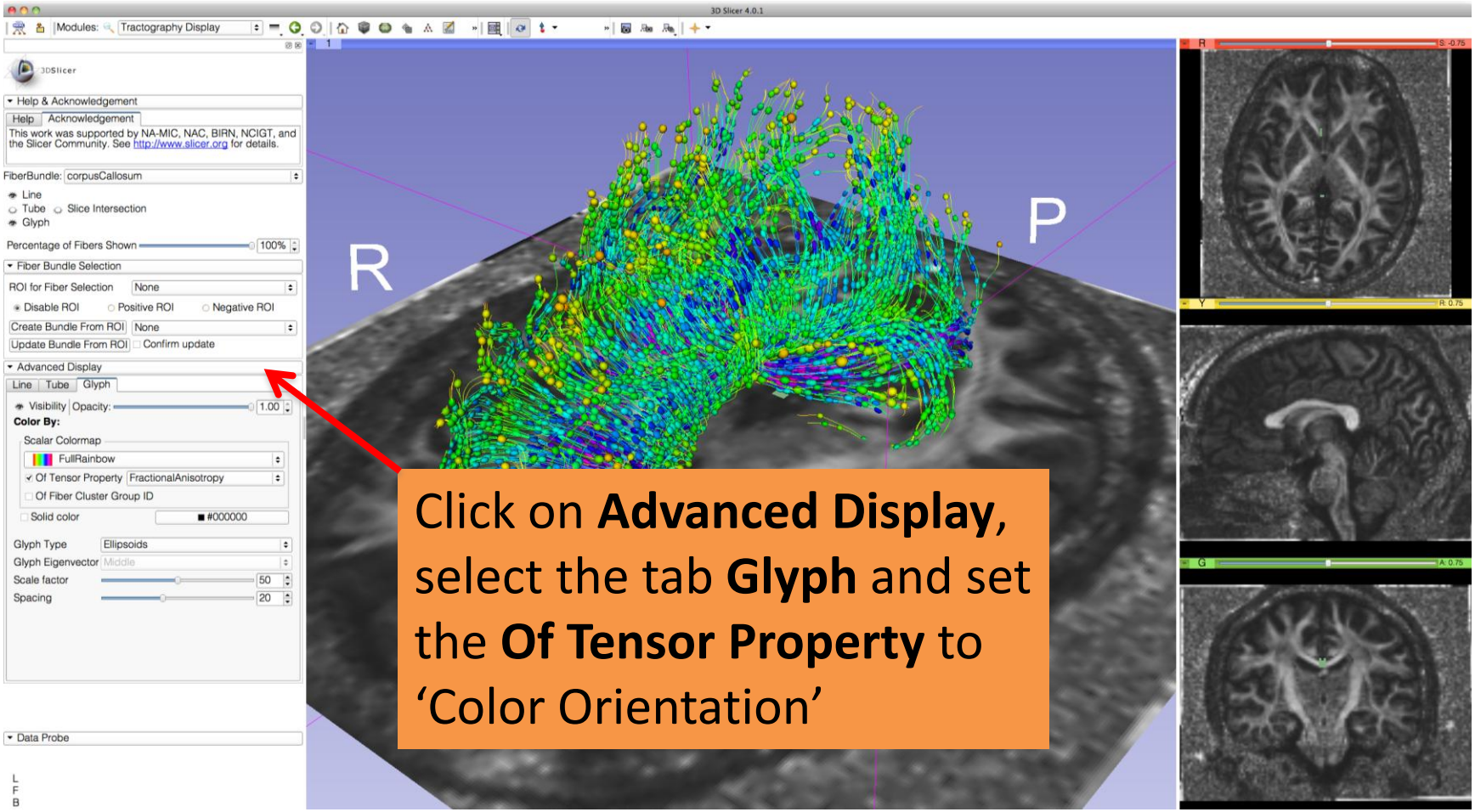


Note that both the glyphs and the tracts are colored according to FA values:

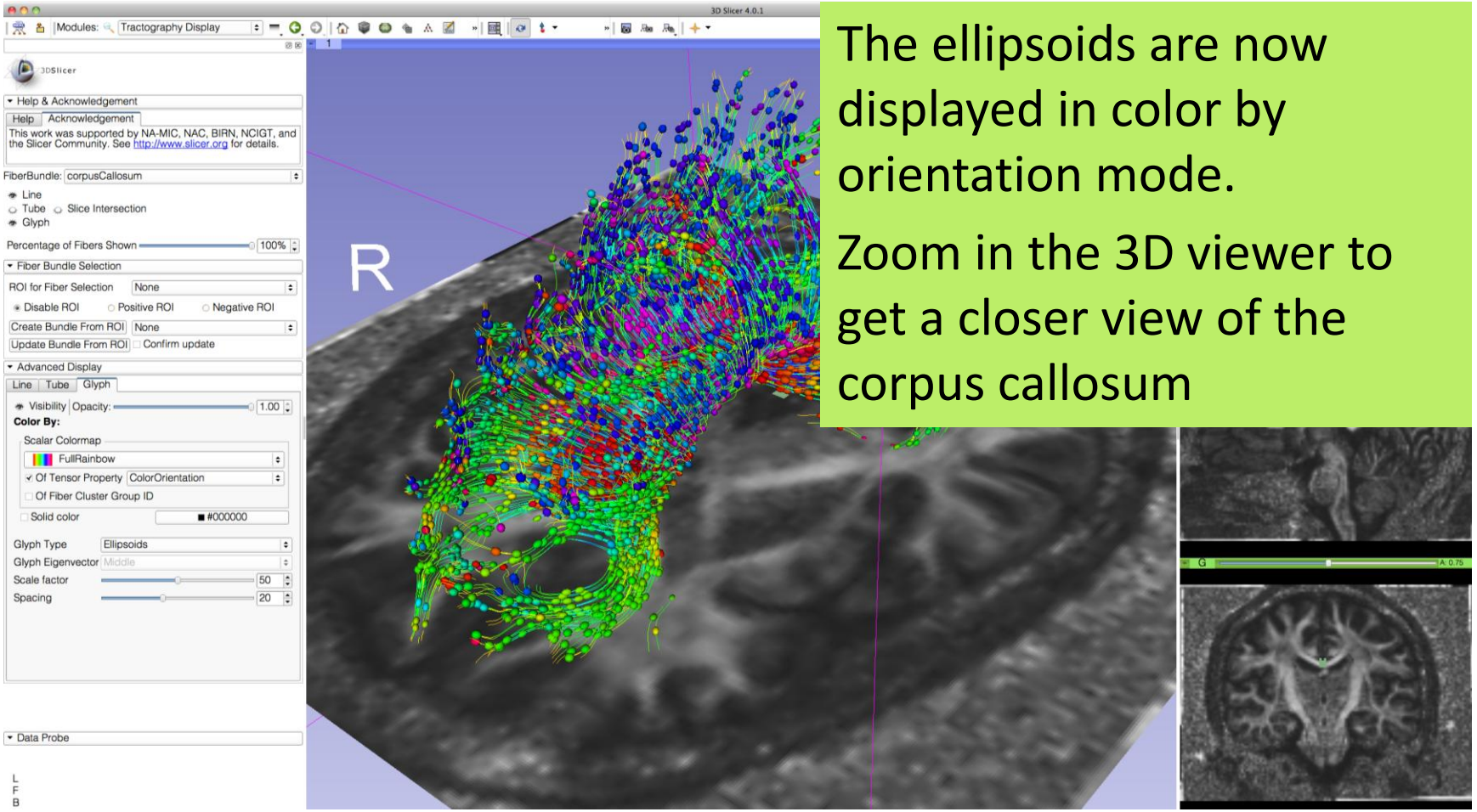
-low anisotropy (gray matter) → red

-high anisotropy (white matter) → blue

Tractography Results



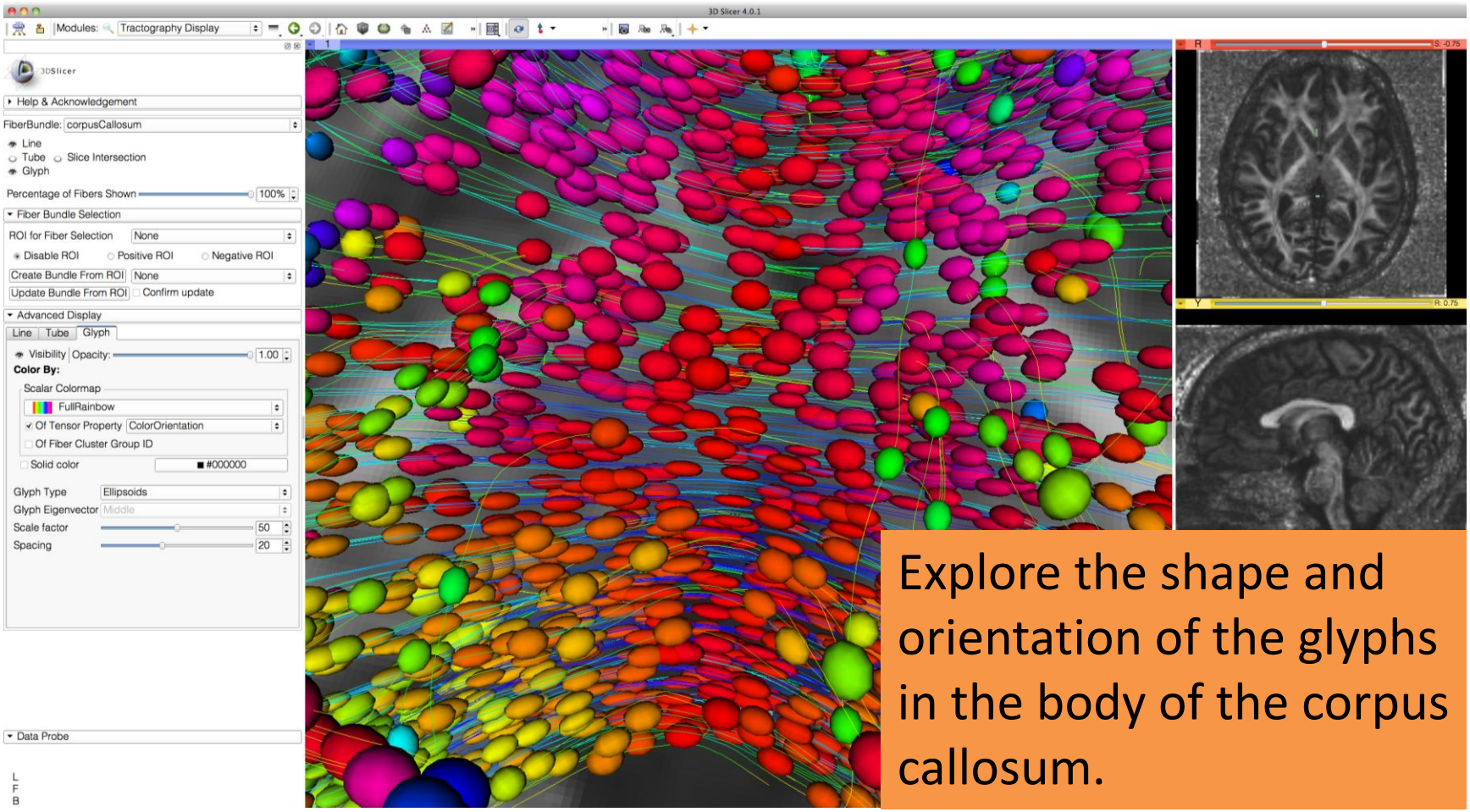
Tractography Results



The ellipsoids are now displayed in color by orientation mode.

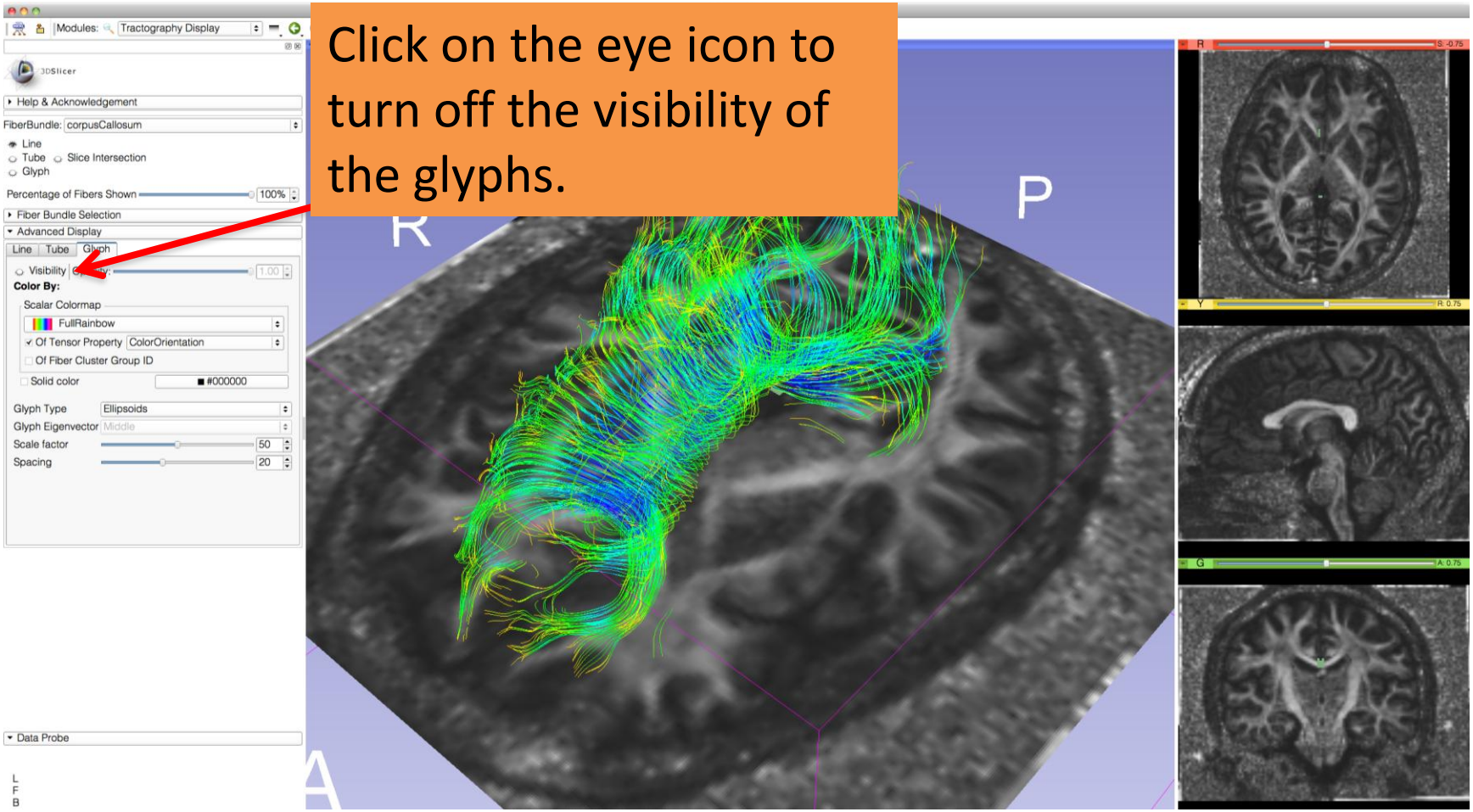
Zoom in the 3D viewer to get a closer view of the corpus callosum

Tractography Results

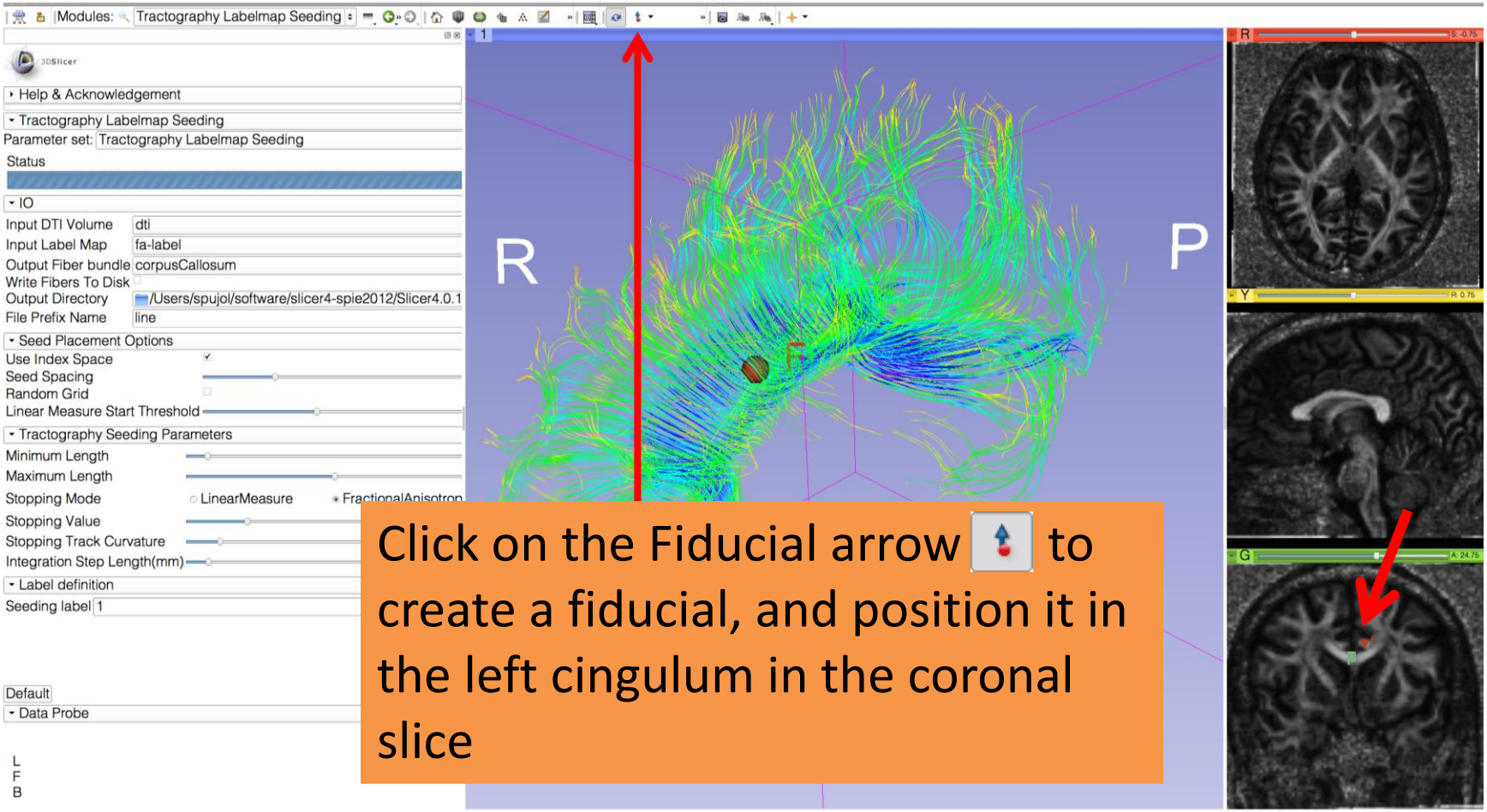


Explore the shape and orientation of the glyphs in the body of the corpus callosum.

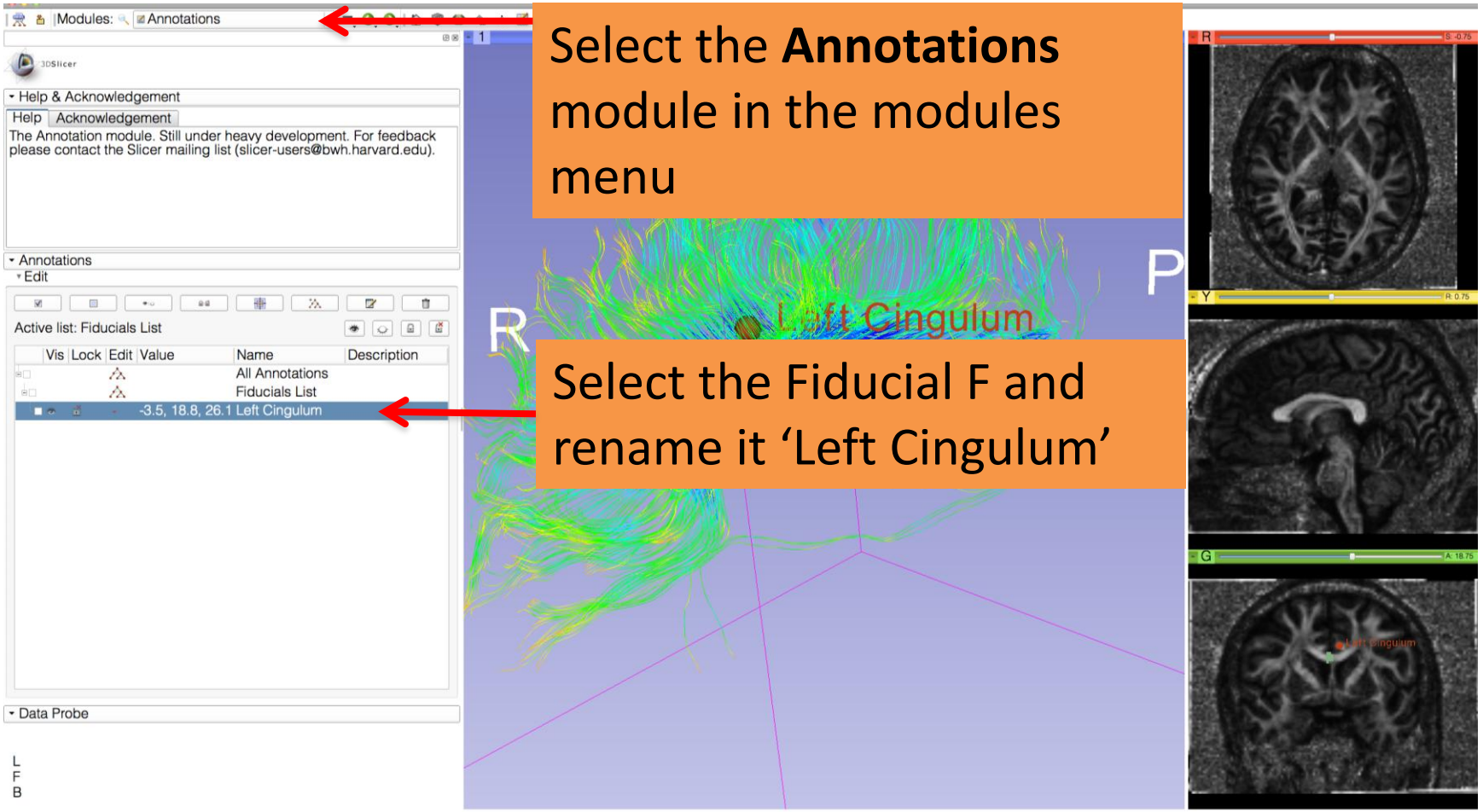
Tractography Results



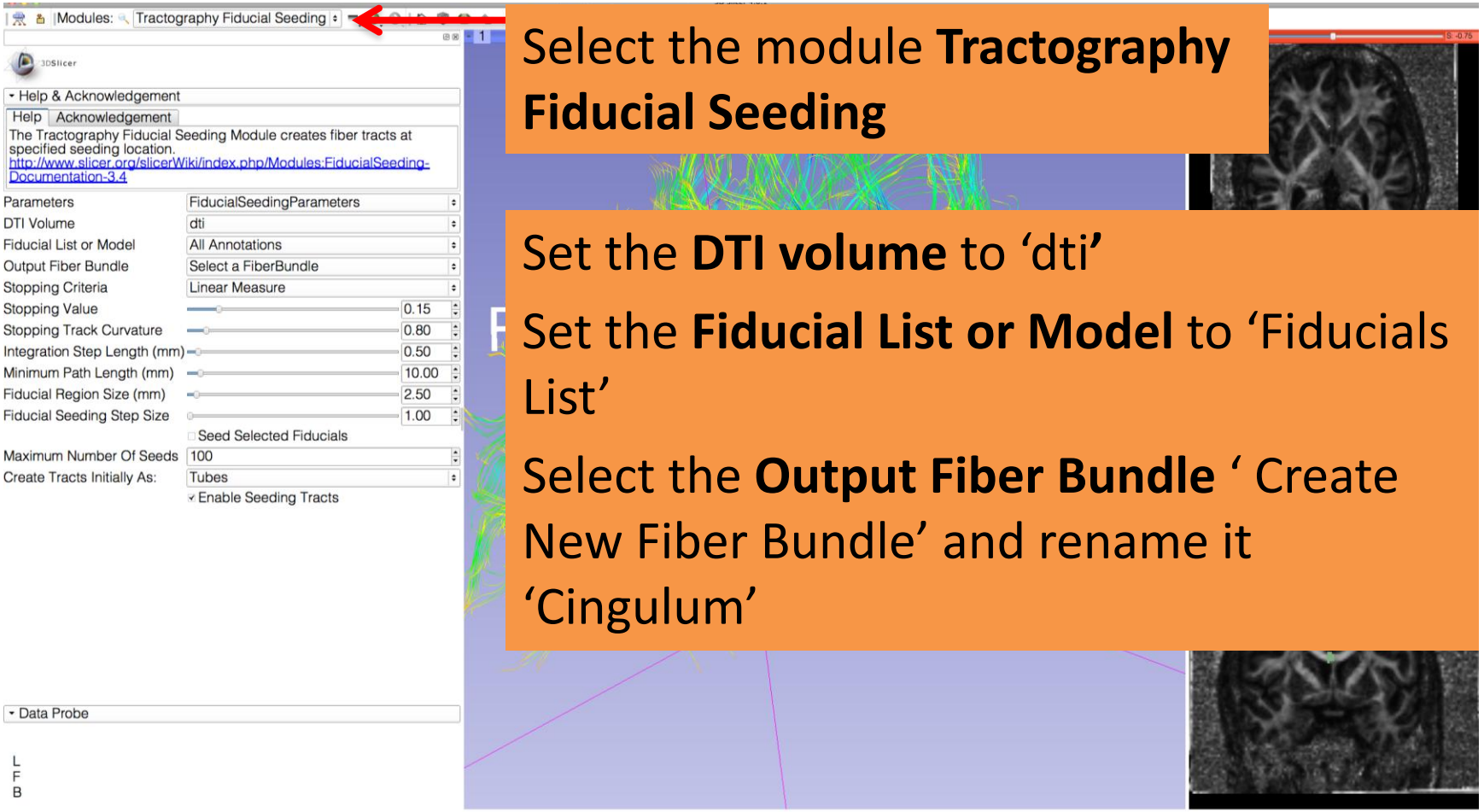
Fiducial Seeding



Fiducial Seeding



Fiducial Seeding



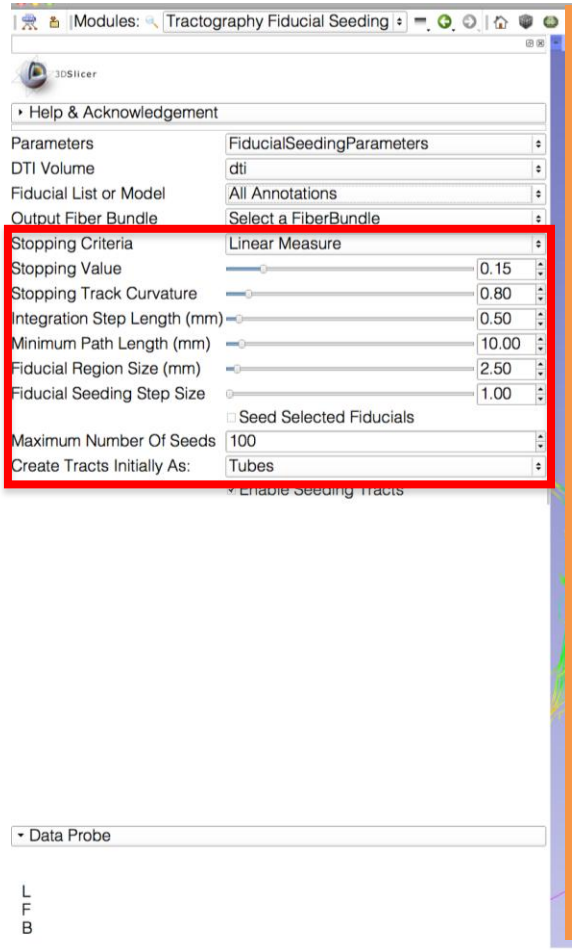
Select the module **Tractography Fiducial Seeding**

Set the **DTI volume** to ‘dti’

Set the **Fiducial List or Model** to ‘Fiducials List’

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

Fiducial Seeding



Set the tractography parameters as follows:

-Stopping Criteria: Fractional Anisotropy

-Stopping Value: 0.15

-Stopping Track Curvature: 0.8

-Integration step length: 0.5 mm

-Minimum length: 10 mm

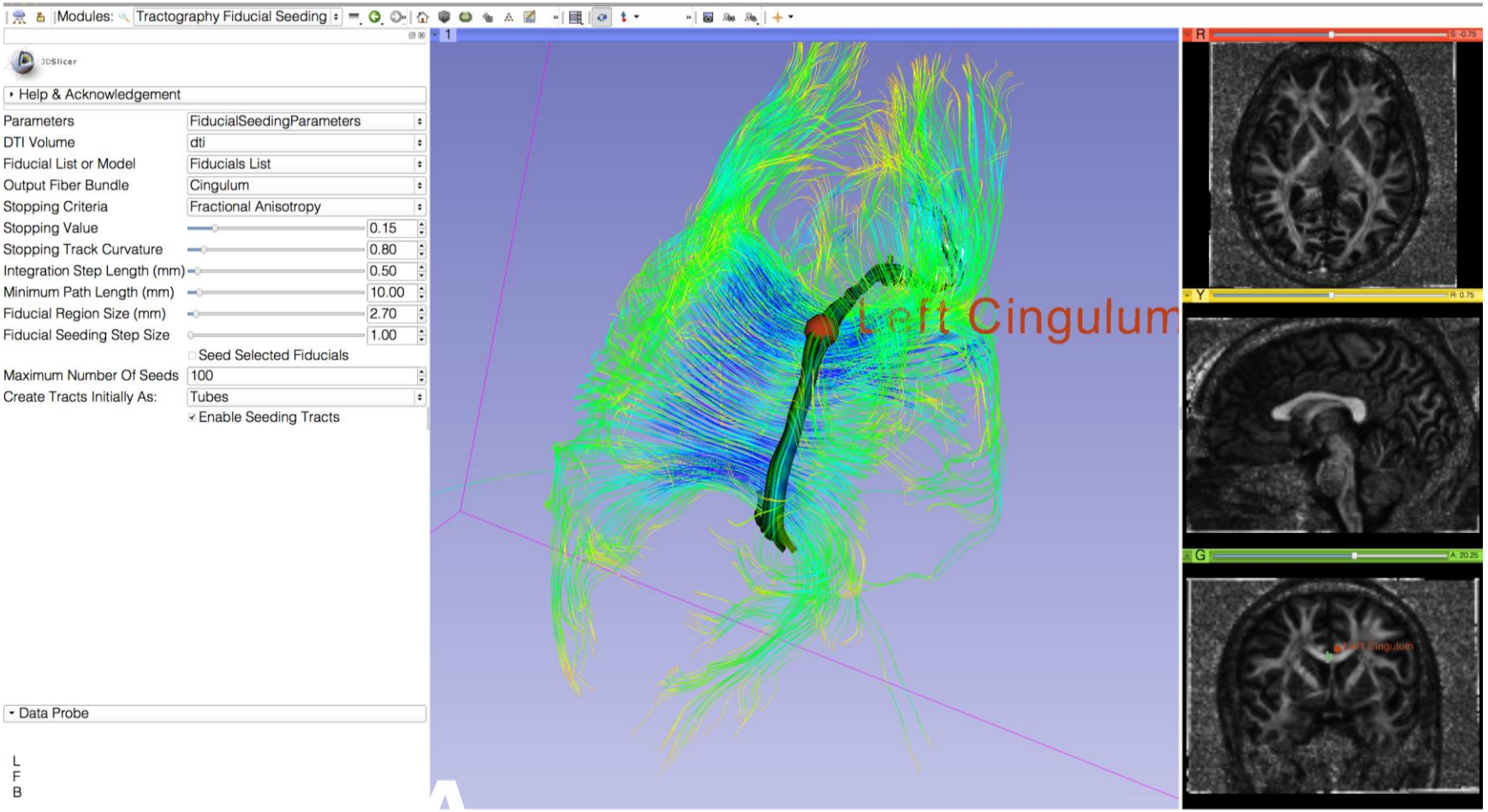
-Fiducial regions size: 2.5 mm

-Fiducial step size: 1.0

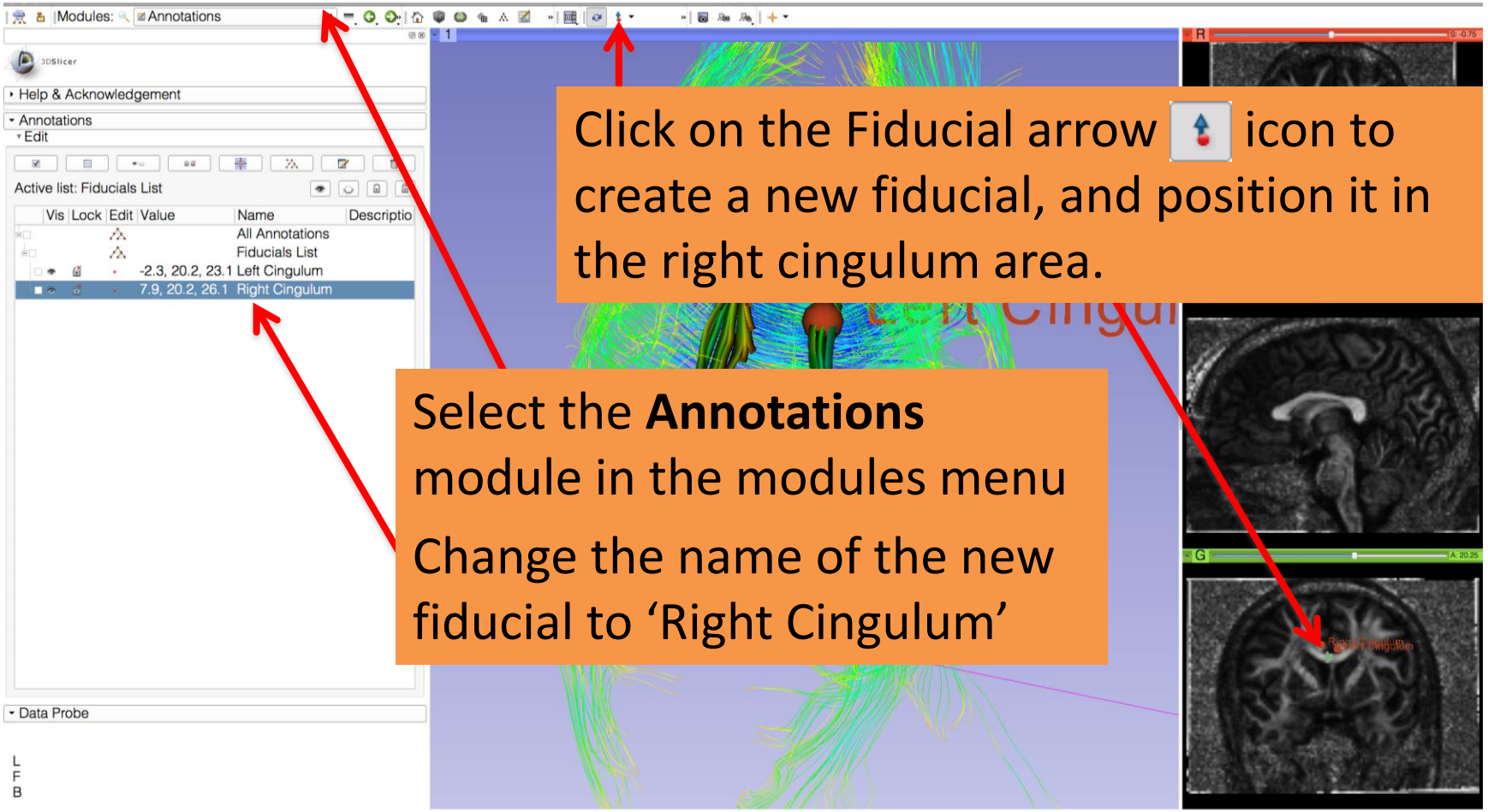
-Maximum number of seeds: 100

-Create Tracts Initially as Tubes

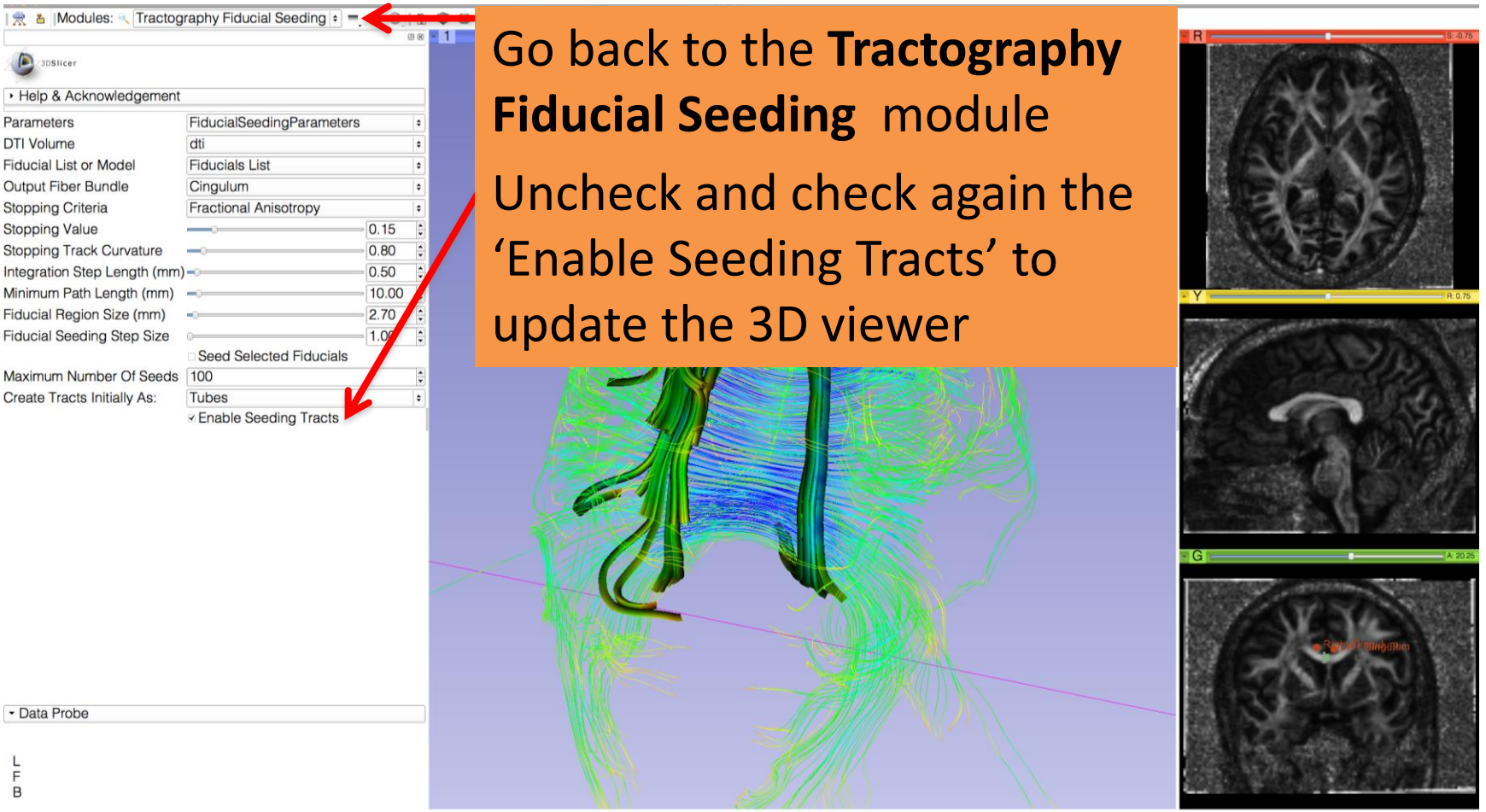
Fiducial Seeding



Fiducial Seeding



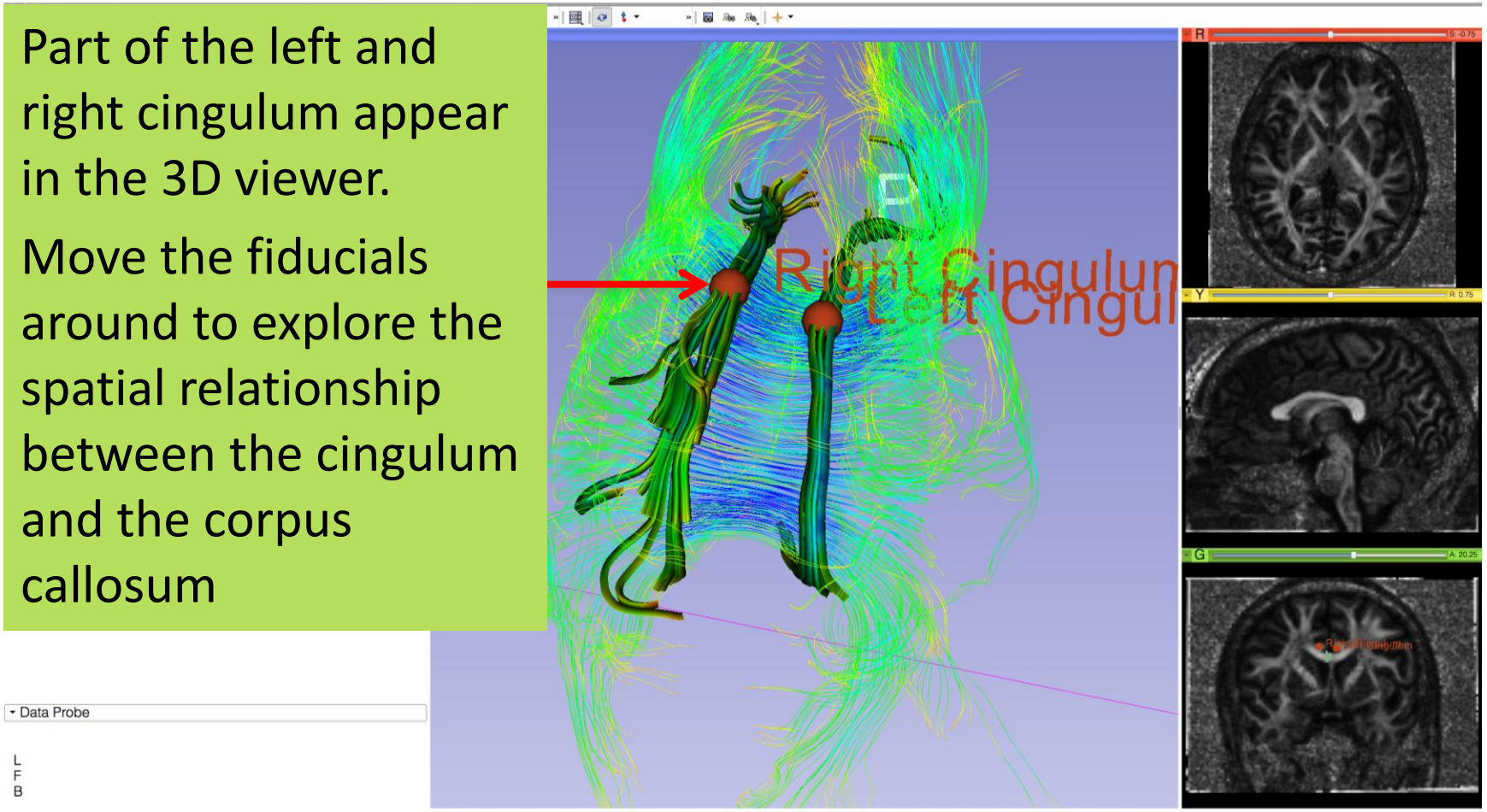
Fiducial Seeding



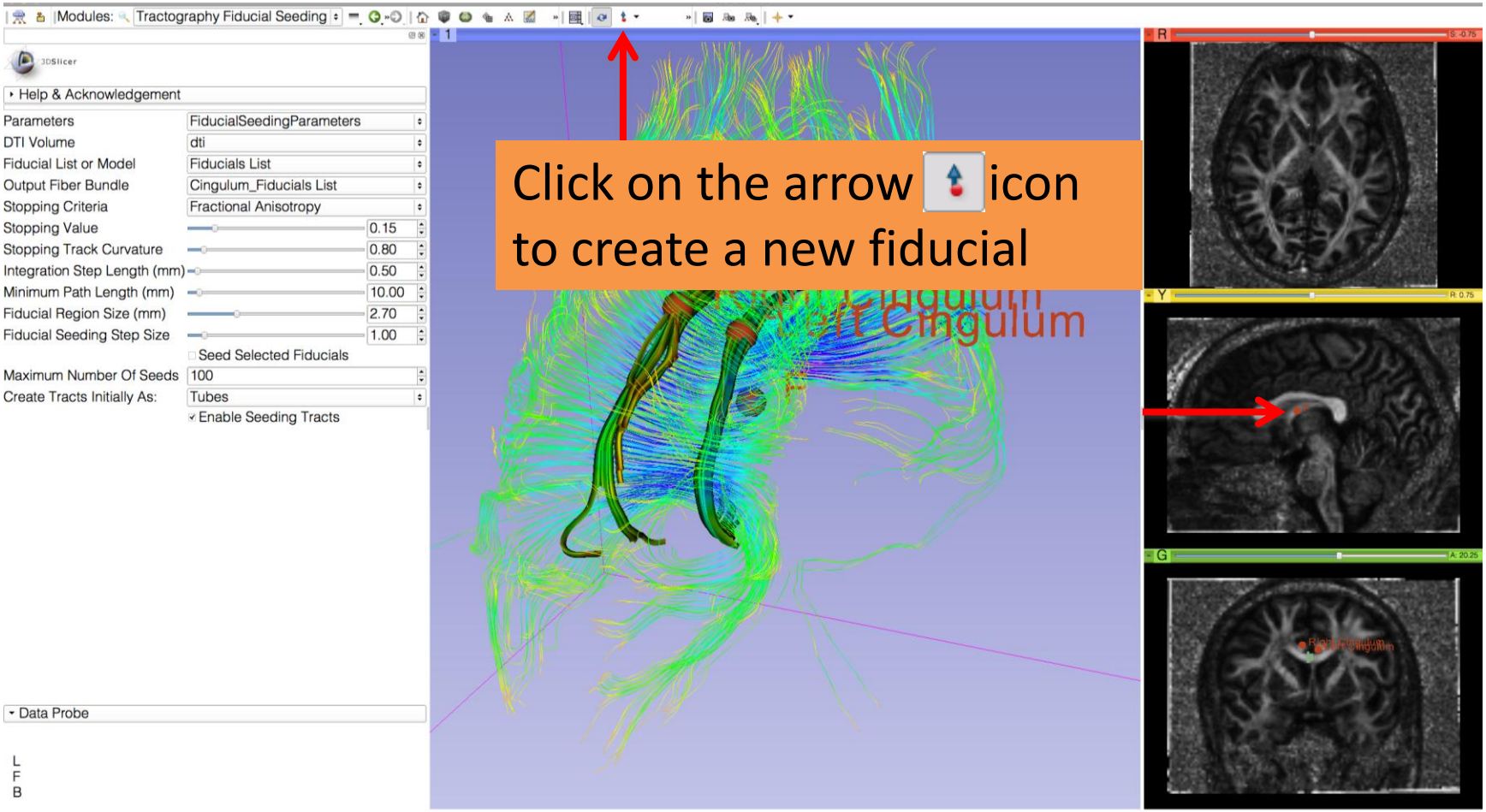
Fiducial Seeding

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

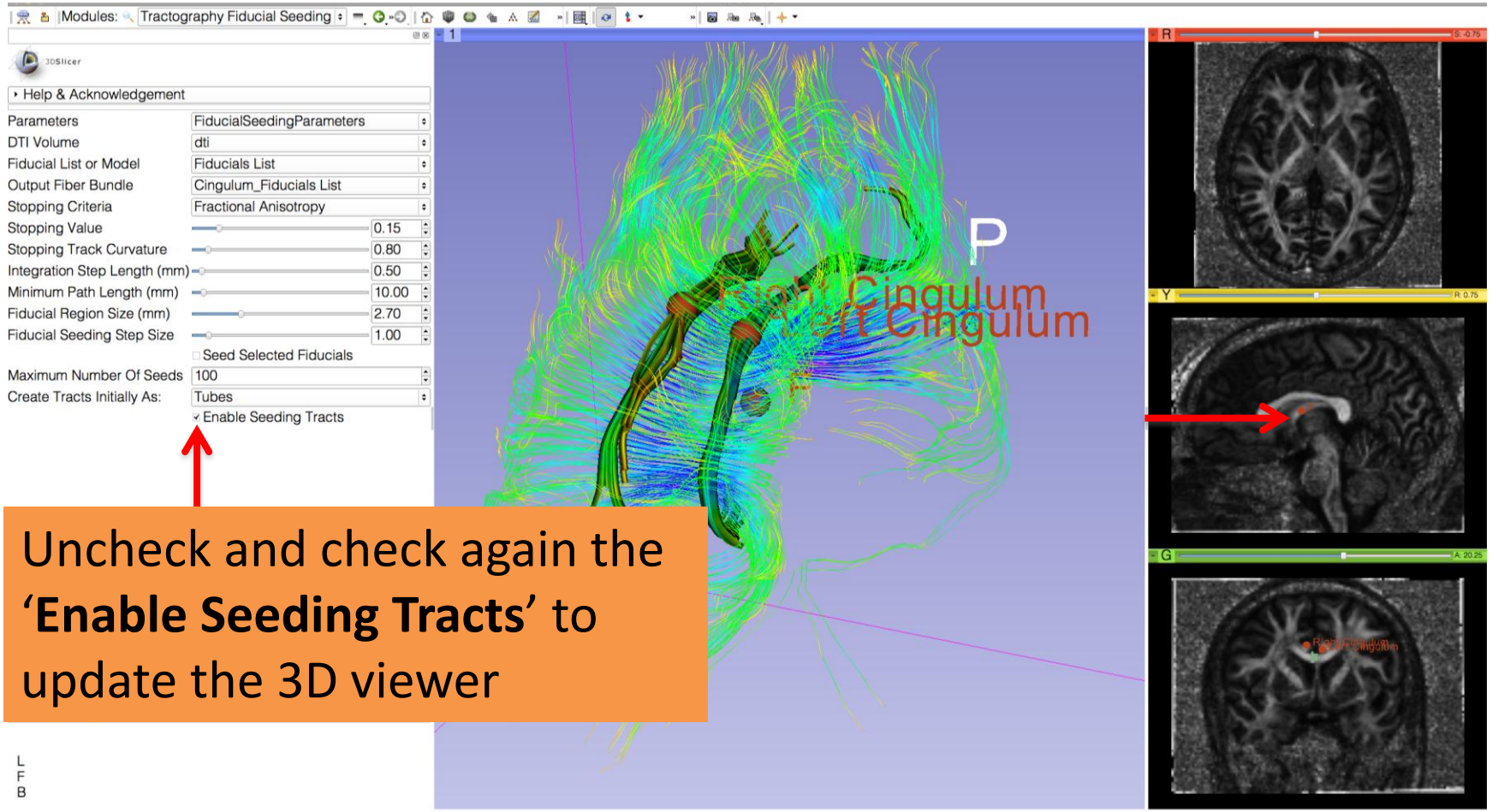
Move the fiducials around to explore the spatial relationship between the cingulum and the corpus callosum



Fiducial Seeding

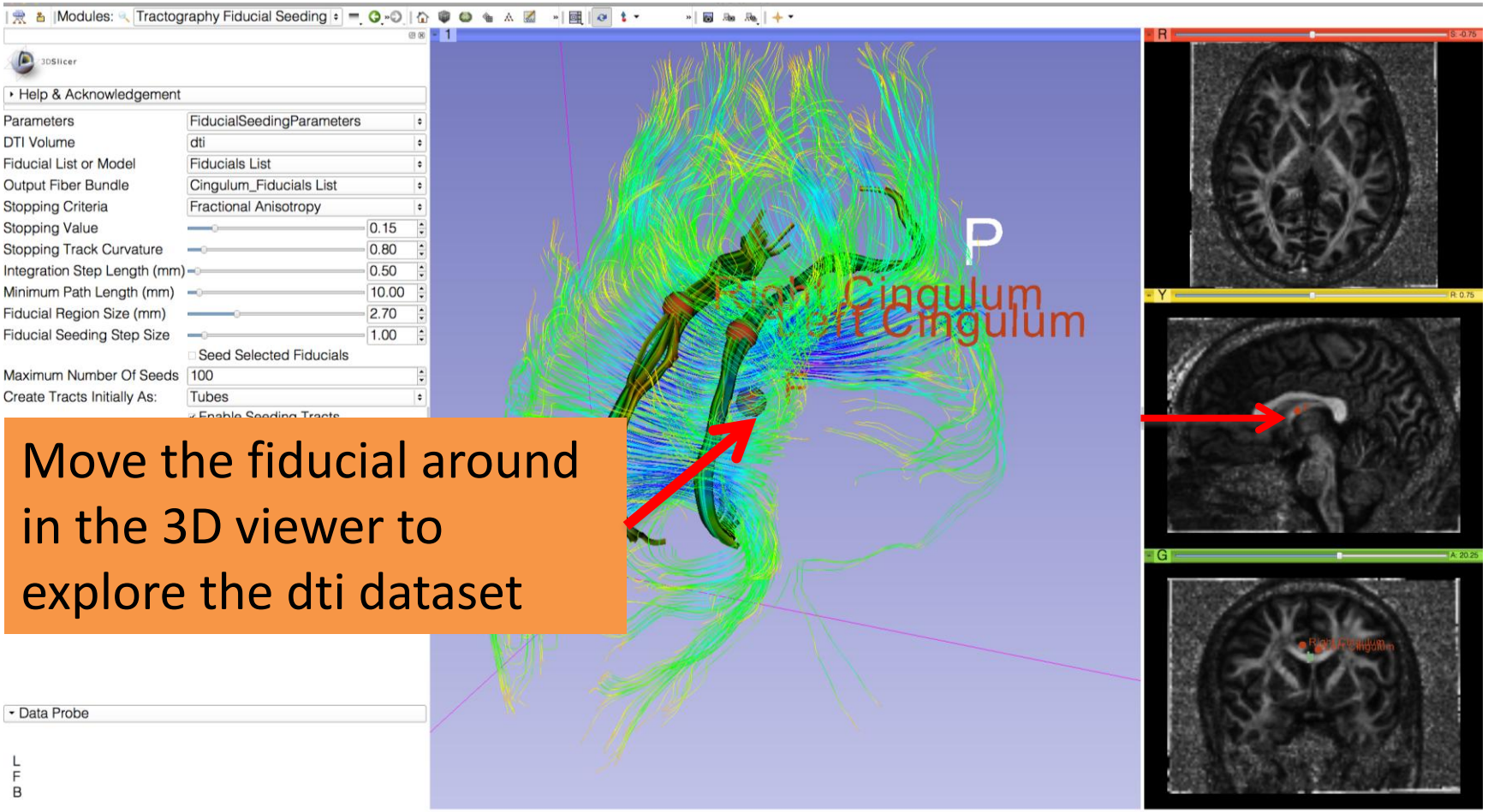


Fiducial Seeding



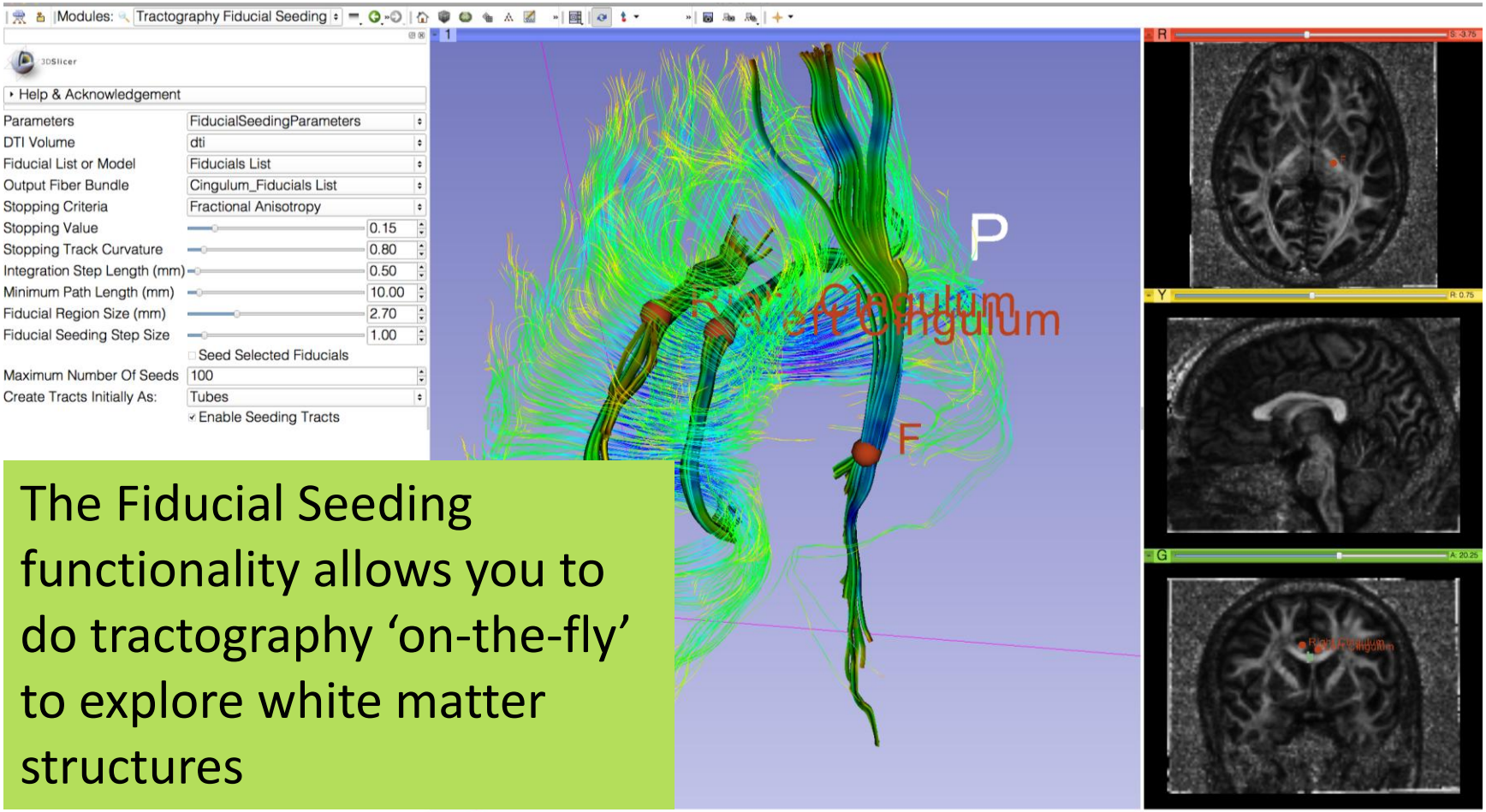
Uncheck and check again the '**Enable Seeding Tracts**' to update the 3D viewer

Fiducial Seeding



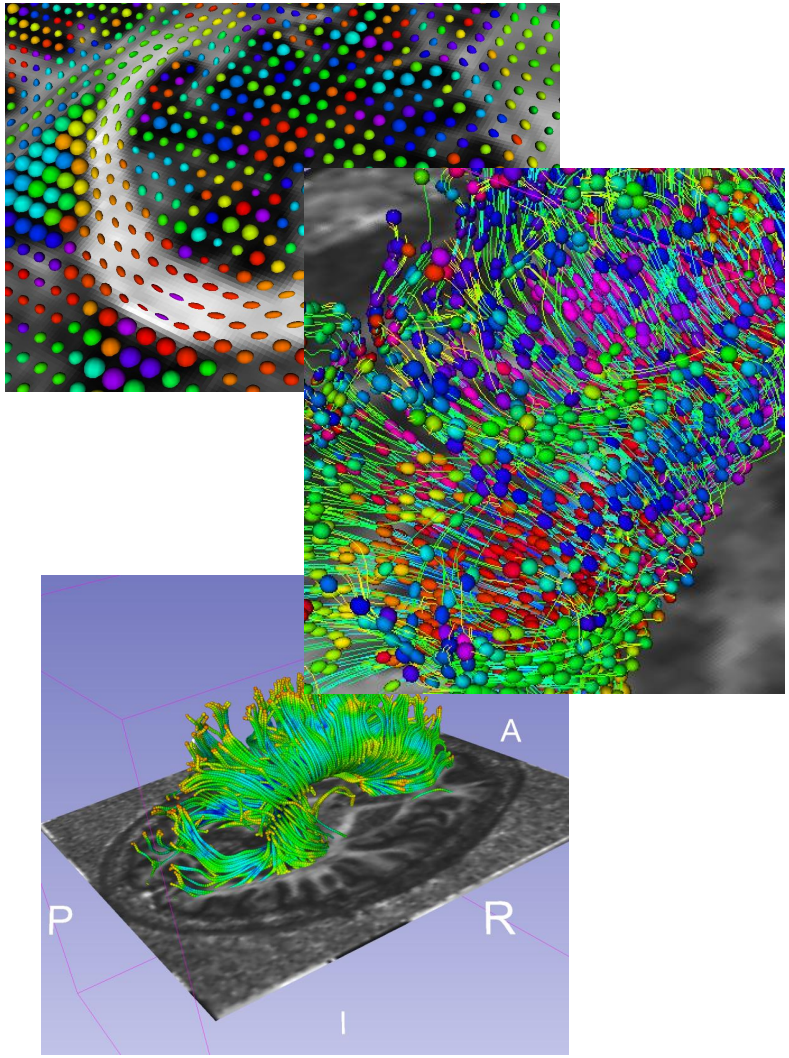
Move the fiducial around in the 3D viewer to explore the dti dataset

Tractography ‘on-the-fly’



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

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

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Neuroimage Analysis Center
NIH P41RR013218

Slicer Community

- www.slicer.org

- Mailing lists:

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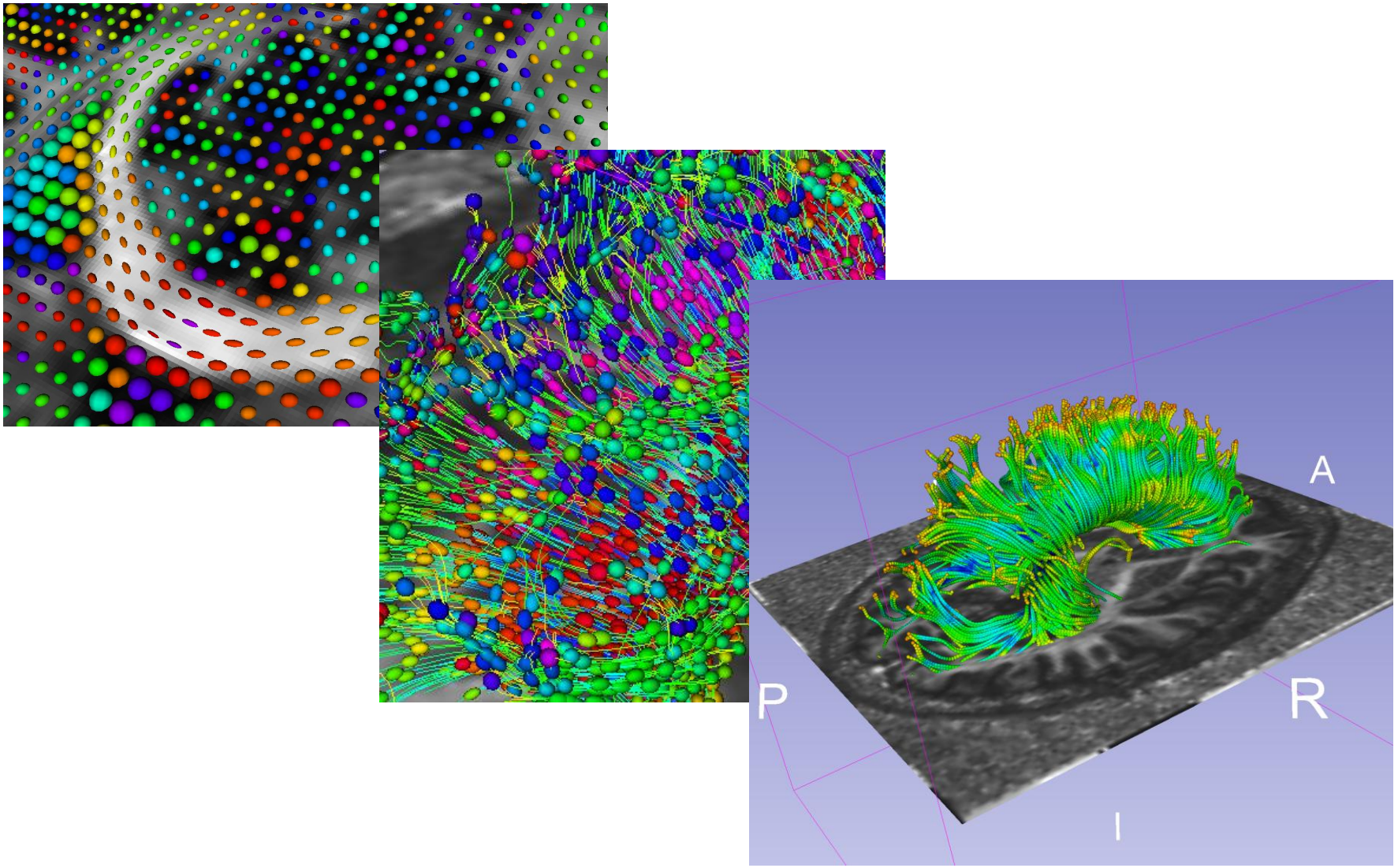

Contact: spujol@bwh.harvard.edu