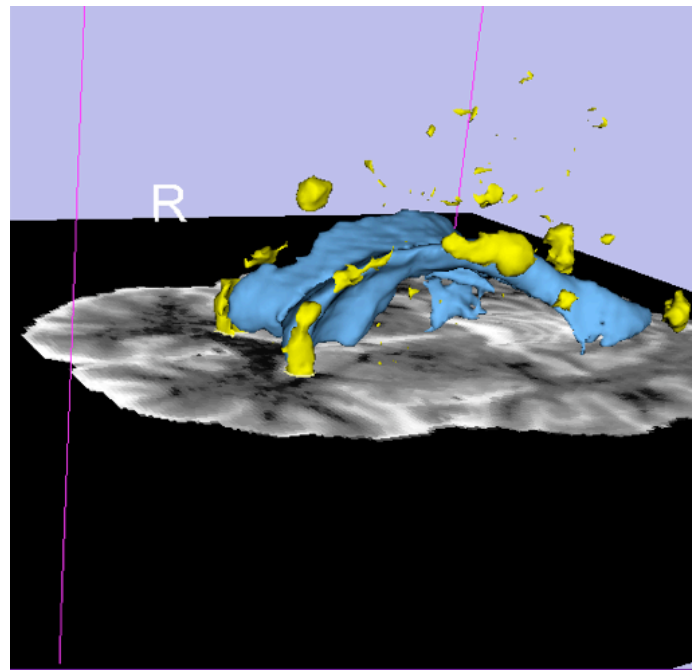


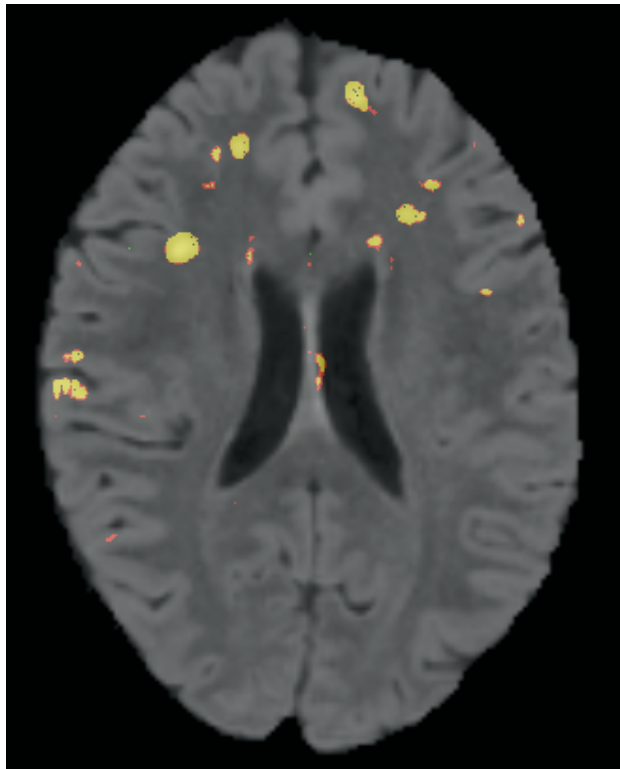
Detecting White Matter Lesions in Lupus



Version 2.3
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Learning objective



This tutorial demonstrates an automated, multi-level method to segment *white matter brain lesions* in lupus.

Following this tutorial, you'll be able to **load scans** into Slicer3, and **segment and measure** the volume of white matter lesions on the provided data-set.



Prerequisites

This tutorial assumes that you have already completed the tutorial **Data Loading and Visualization**. Tutorials for **3DSlicer** are available at the following location:

<http://www.na-mic.org/Wiki/index.php/Slicer3.2:Training>



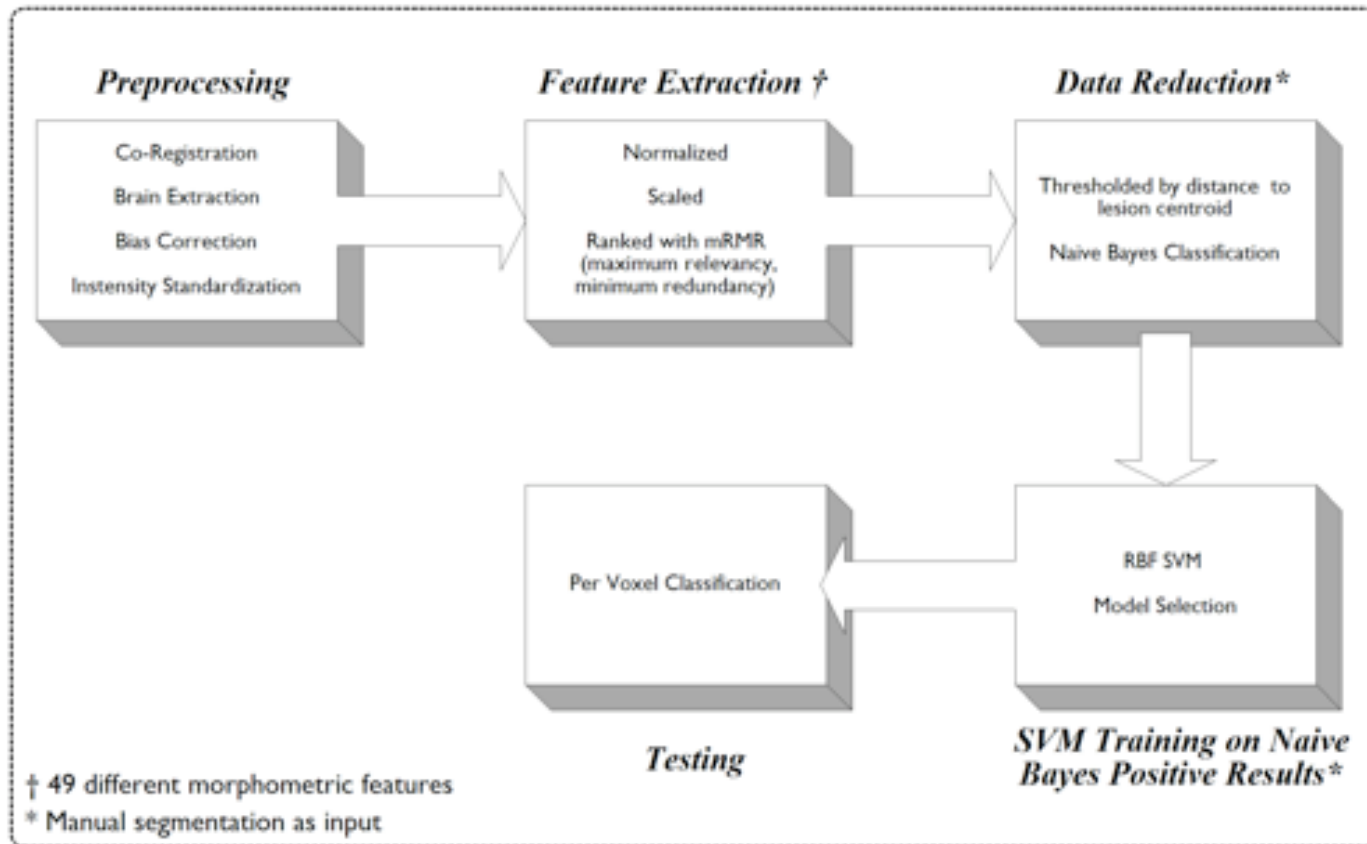
Material

This course requires the following installation:

- The current stable version of 3DSlicer 3.4 Software which can be installed from:
 - <http://slicer.org/pages/Special:SlicerDownloads>
- The White Matter Lesion module extension to 3DSlicer
 - (see follow on instructions on slides 7-9 of this tutorial)
- The Lupus Lesion Tutorial Data, which can be downloaded from:
 - <http://wiki.na-mic.org/Wiki/images/c/c8/LesionSegmentationTutorialData.tgz>
- n.b., a reliable internet connection will be required for downloading the data

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.



Flowchart summarizing the *training pipeline* for the white matter lesion classification procedure employed in this tutorial.



Methods

The method makes use of local morphometric features based on multiple MR sequences, including **T1-weighted**, **T2-weighted**, and **Fluid Attenuated Recovery** from ten subjects.

After preprocessing, including co-registration, brain extraction, bias correction, and intensity standardization, 49 features were calculated for each brain voxel based on local morphometry.

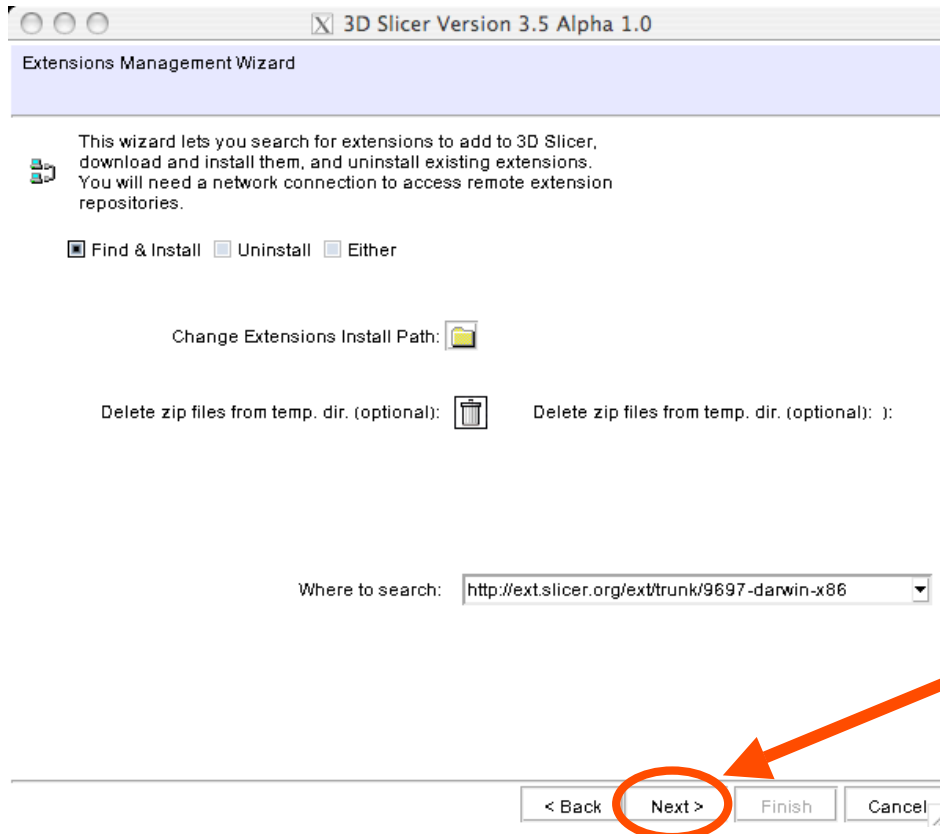
At each level of segmentation a supervised classifier takes advantage of a different subset of the features to conservatively segment lesion voxels, passing on more difficult voxels to the next classifier.

This multi-level approach allows for a fast lesion classification method with tunable trade-off between sensitivity and specificity, with accuracy comparable to a human rater.

When applying the above classifier to novel data sets, such as the sample data in this tutorial, the user should follow 3 steps (described on slides 11-20) to apply the classifier to the data set they wish to predict lesions upon.

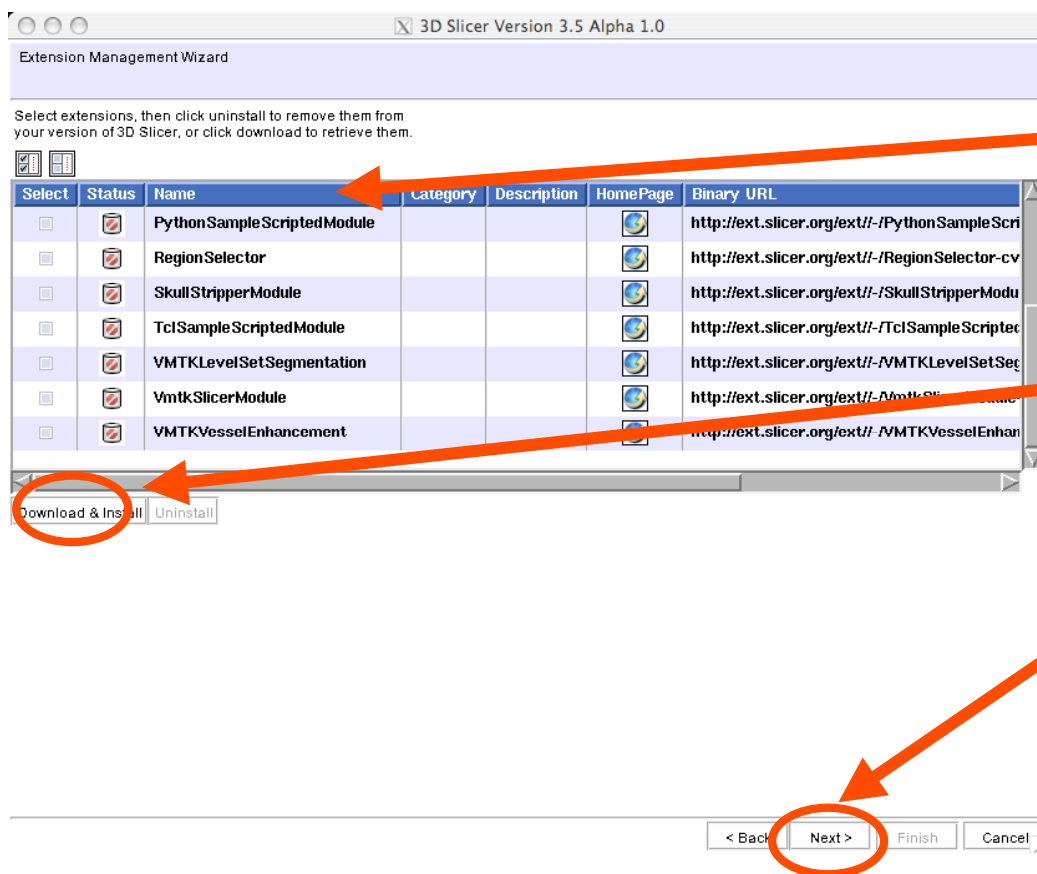


Finding the Module



- To add the external module, Select the **Extensions Management Wizard** from the **View** menu within 3DSlicer.
- Click **next** to search the external site for the appropriate module to install.

Installing the Module



Select
**LesionSegmentati
onApplications**
from the list

Click **Download &
Install.**

Click **Next** after the
status turns green



Finish Installing Module

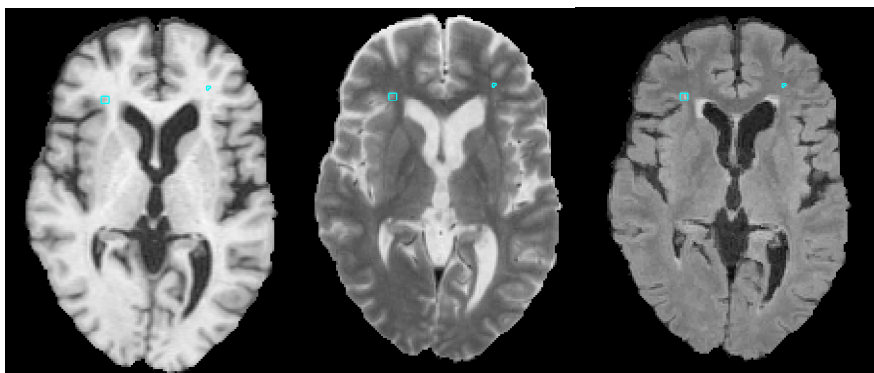


Click **Restart 3D Slicer** now once you have installed the module



Tutorial Data

This course is built upon two scans of patients with lupus that have **T1**, **T2**, and **FLAIR** images. These images have been co-registered and brain extracted outside of the scope of this tutorial. Also, the tutorial data contains model files that support the module introduced in this tutorial. Finally, results files from one subject are included in the tutorial data. The following summary shows the contents of the **LesionSegmentationTutorial** archive once downloaded and uncompressed to your filesystem.



Joint Intensity Standardization Volume.nhdr
Joint Intensity Standardization Volume.raw.gz
Joint Intensity Standardization Volume1.nhdr
Joint Intensity Standardization Volume1.raw.gz
Joint Intensity Standardization Volume2.nhdr
Joint Intensity Standardization Volume2.raw.gz
LesionSegmentTutorial.mrml
Predict Lesions Volume.nhdr
Predict Lesions Volume.raw
Predict Lesions Volume1.nhdr
Predict Lesions Volume1.raw
lesionSegmentation.model
lupus002_FLAIR_reg+bias.nii.gz
lupus002_T1_reg+bias.nii.gz
lupus002_T2_reg+bias.nii.gz
lupus002_brain_mask.nii.gz
lupus003_FLAIR_reg+bias.nii.gz
lupus003_T1_reg+bias.nii.gz
lupus003_T2_reg+bias.nii.gz
lupus003_brain_mask.nii.gz
svm.model



Module Step 1: Setup

The screenshot shows the 3DSlicer application window. The 'File' menu is open, and the 'Load Scene...' option is highlighted with a red arrow. A yellow callout box contains the following text:

Load the scene by selecting File Import Scene feature from the menu. Navigate the filesystem to locate the MRML scene that you have downloaded. By loading the scene you will load the reference data sets that are needed for this tutorial.

The interface includes a menu bar (File, Edit, View, Window, Help, Feedback), a toolbar, and several panels: MRML Tree (showing 'Scene'), MRML Node Inspector, Load & Add Scenes Or Individual Datasets (with 'Load new scene (close current)' and 'Add a scene (to current)' buttons), Manipulate Slice Views, and Manipulate 3D View. The bottom right shows three slice views: Axial (Sp: 1mm), Coronal (Sp: 1mm), and a 3D view. The 3D view shows a green box on a purple plane. The bottom status bar shows 'Load Scene...' and a search icon.



Module Step 1: Results

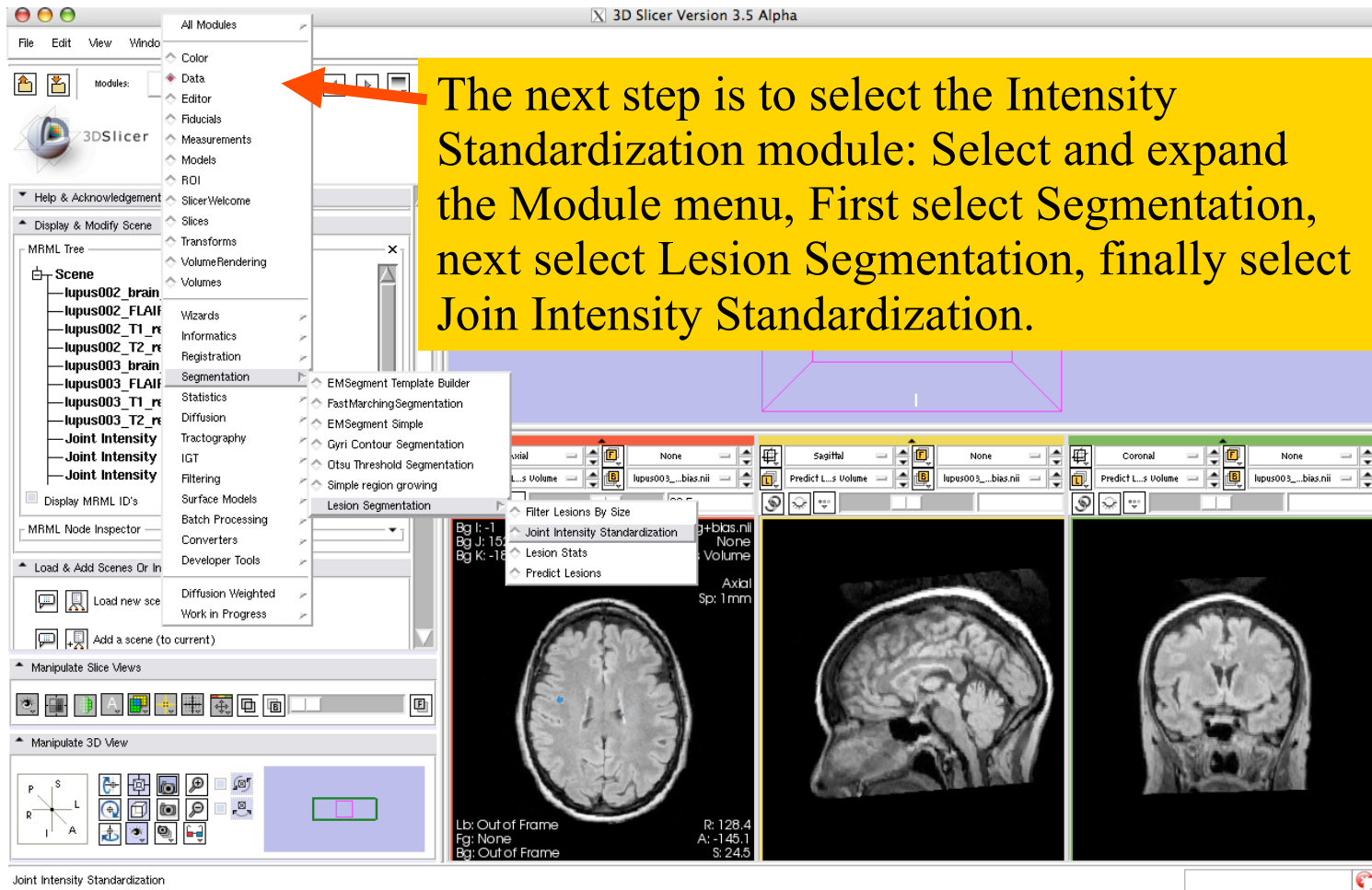
After the scene loads, you will have the data sets that are needed for this tutorial and may continue on to step 2. Confirm that you have the data sets listed in the scene display on the left.

The screenshot shows the 3DSlicer interface. On the left, the MRML Tree panel lists the following data sets under the 'Scene' node:

- lupus002_brain_mask.nii
- lupus002_FLAIR_reg+bias.nii
- lupus002_T1_reg+bias.nii
- lupus002_T2_reg+bias.nii
- lupus003_brain_mask.nii
- lupus003_FLAIR_reg+bias.nii
- lupus003_T1_reg+bias.nii
- lupus003_T2_reg+bias.nii
- Joint Intensity Standardization Volume
- Joint Intensity Standardization Volume1
- Joint Intensity Standardization Volume2

On the right, three MRI slice views are displayed: Axial, Sagittal, and Coronal. The Axial view shows a brain slice with a blue dot indicating a lesion. The Sagittal and Coronal views show the brain in different orientations. The interface also includes a menu bar (File, Edit, View, Window, Help, Feedback), a toolbar, and a status bar at the bottom.

Module Step 2: Setup

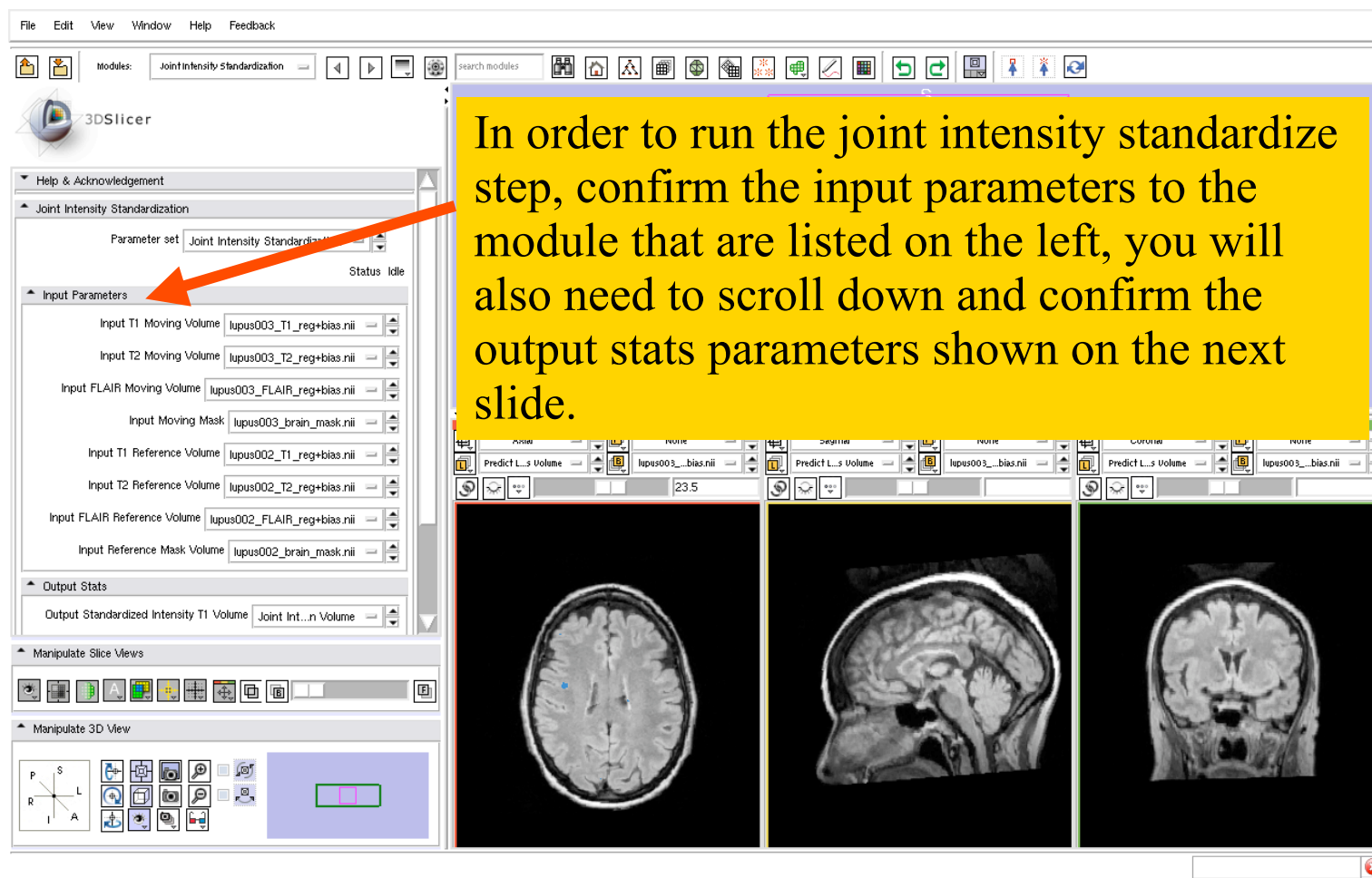


The screenshot shows the 3D Slicer 3.5 Alpha interface. The 'All Modules' menu is open, and the 'Segmentation' module is selected and expanded. The 'Joint Intensity Standardization' module is highlighted. A yellow callout box with a red arrow pointing to the 'Segmentation' menu item contains the following text:

The next step is to select the Intensity Standardization module: Select and expand the Module menu, First select Segmentation, next select Lesion Segmentation, finally select Joint Intensity Standardization.

The interface also shows the MRML Tree on the left, the 'Manipulate Slice Views' and 'Manipulate 3D View' toolbars, and three slice views (Axial, Sagittal, Coronal) at the bottom right. The 'Joint Intensity Standardization' module is active in the bottom panel.

Module Step 2: Setup



In order to run the joint intensity standardize step, confirm the input parameters to the module that are listed on the left, you will also need to scroll down and confirm the output stats parameters shown on the next slide.

The screenshot shows the 3DSlicer interface with the 'Joint Intensity Standardization' module selected. The 'Input Parameters' section is highlighted with a red arrow and contains the following fields:

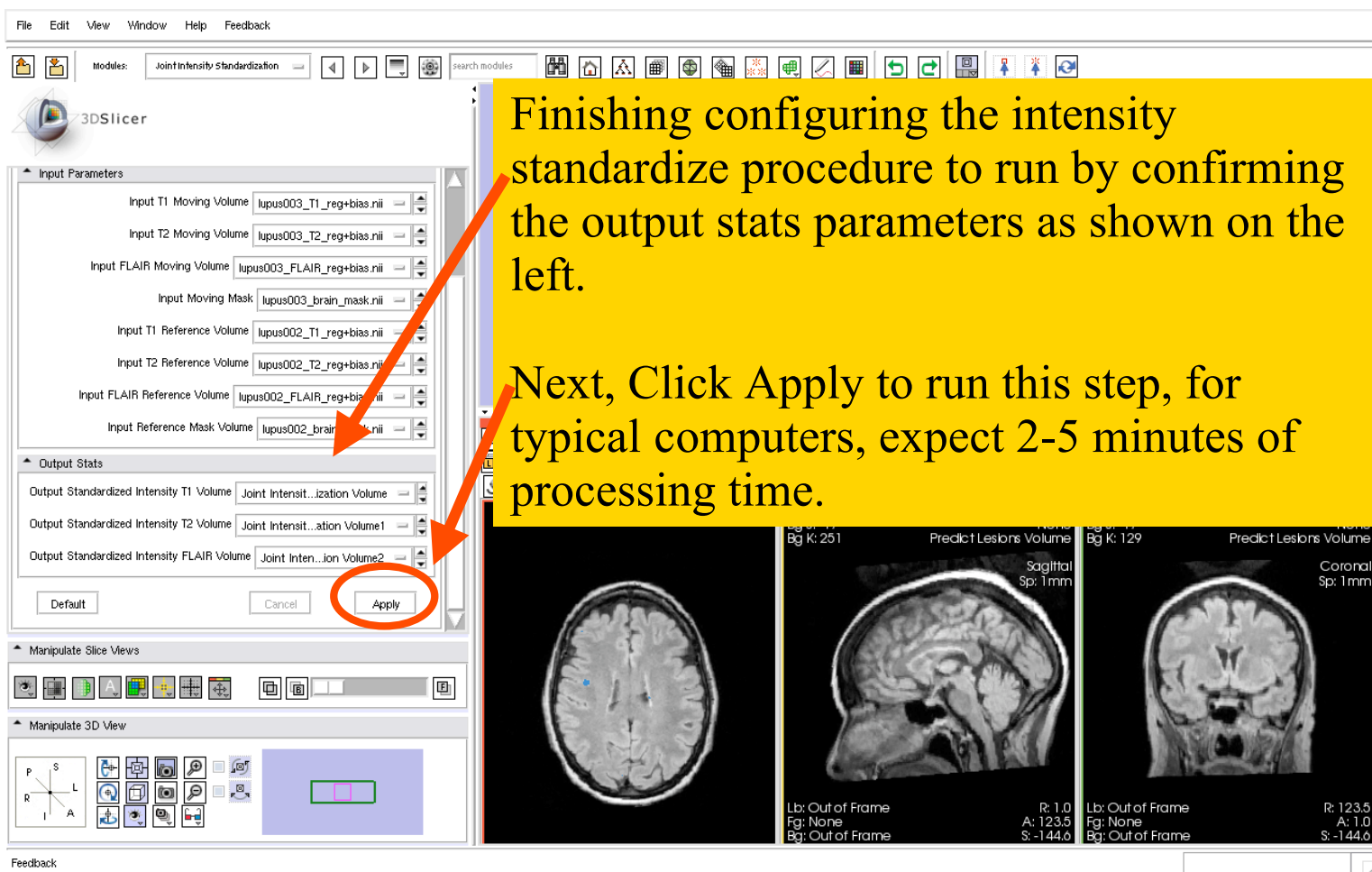
- Input T1 Moving Volume: lupus003_T1_reg+bias.nii
- Input T2 Moving Volume: lupus003_T2_reg+bias.nii
- Input FLAIR Moving Volume: lupus003_FLAIR_reg+bias.nii
- Input Moving Mask: lupus003_brain_mask.nii
- Input T1 Reference Volume: lupus002_T1_reg+bias.nii
- Input T2 Reference Volume: lupus002_T2_reg+bias.nii
- Input FLAIR Reference Volume: lupus002_FLAIR_reg+bias.nii
- Input Reference Mask Volume: lupus002_brain_mask.nii

The 'Output Stats' section shows:

- Output Standardized Intensity T1 Volume: Joint Int...n Volume

The bottom of the interface displays three axial MRI slices of a brain, with the central slice showing a blue dot indicating a point of interest.

Module Step 2: Running



File Edit View Window Help Feedback

Modules: Joint Intensity Standardization

3DSlicer

Input Parameters

- Input T1 Moving Volume: lupus003_T1_reg+bias.nii
- Input T2 Moving Volume: lupus003_T2_reg+bias.nii
- Input FLAIR Moving Volume: lupus003_FLAIR_reg+bias.nii
- Input Moving Mask: lupus003_brain_mask.nii
- Input T1 Reference Volume: lupus002_T1_reg+bias.nii
- Input T2 Reference Volume: lupus002_T2_reg+bias.nii
- Input FLAIR Reference Volume: lupus002_FLAIR_reg+bias.nii
- Input Reference Mask Volume: lupus002_brain_mask.nii

Output Stats

- Output Standardized Intensity T1 Volume: Joint Intensity Standardization Volume
- Output Standardized Intensity T2 Volume: Joint Intensity Standardization Volume1
- Output Standardized Intensity FLAIR Volume: Joint Intensity Standardization Volume2

Default Cancel **Apply**

Manipulate Slice Views

Manipulate 3D View

Feedback

Finishing configuring the intensity standardize procedure to run by confirming the output stats parameters as shown on the left.

Next, Click Apply to run this step, for typical computers, expect 2-5 minutes of processing time.

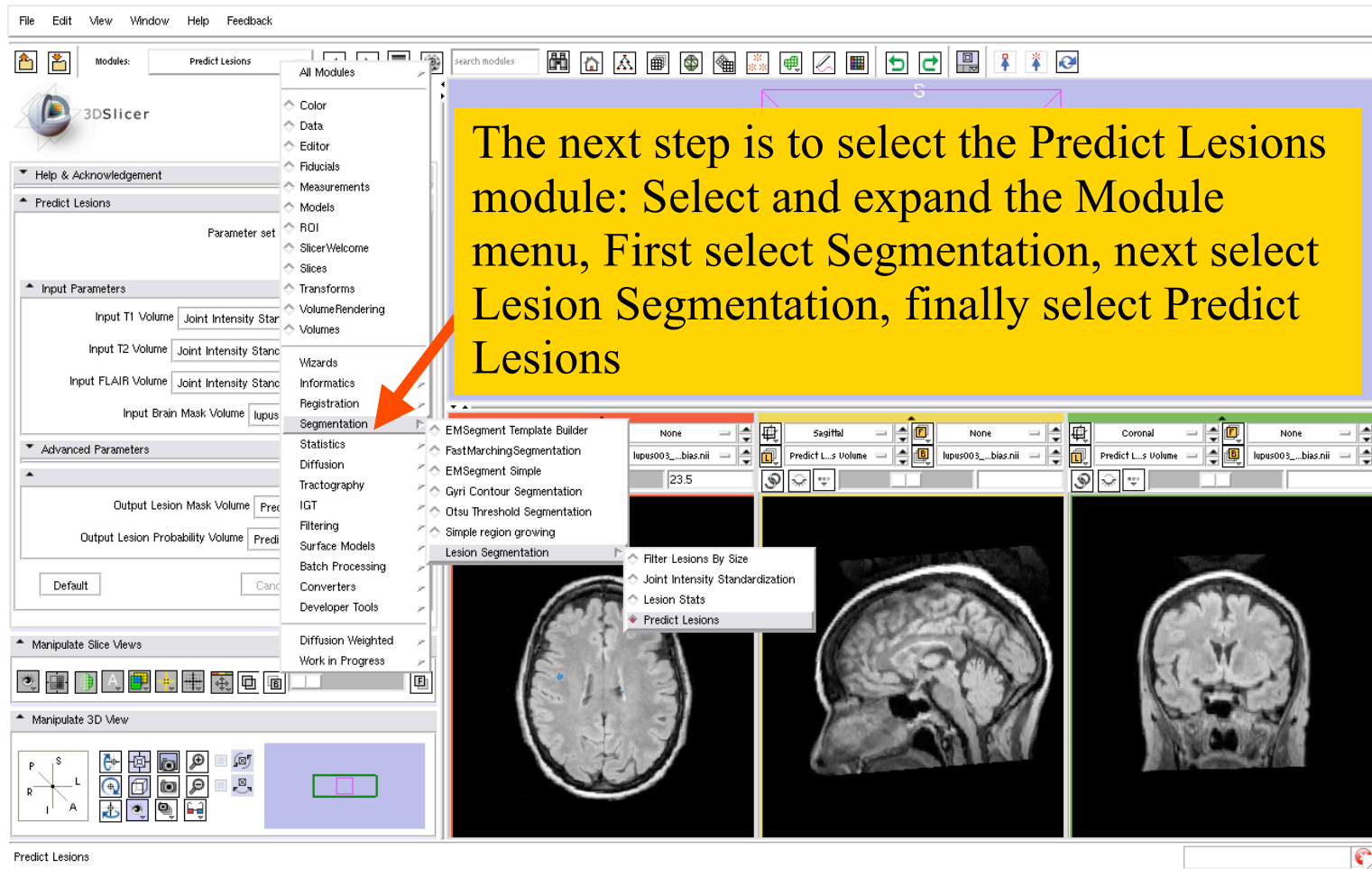
Axial View: Sagittal Sp: 1 mm
 Sagittal View: Predict Lesions Volume, Bg K: 251, Sagittal Sp: 1 mm, Lb: Out of Frame, R: 1.0, A: 123.5, S: -144.6, Fg: None, Bg: Out of Frame
 Coronal View: Predict Lesions Volume, Bg K: 129, Coronal Sp: 1 mm, Lb: Out of Frame, R: 123.5, A: 1.0, S: -144.6, Fg: None, Bg: Out of Frame



Importance of Intensity Standardization

- At this stage, intensity standardization is now complete. This preprocessing is needed because the scale and range of intensities within each of the **T1**, **T2**, and **FLAIR** sequences vary across individuals, the intensity standardization attempts to normalize the intensities within each sequence. The normalized intensity values are the input for the next phase, step 3 which classifies the input images from step 2 to predict where white matter lesions are present in the given data set.

Module Step 3: Setup



The next step is to select the Predict Lesions module: Select and expand the Module menu, First select Segmentation, next select Lesion Segmentation, finally select Predict Lesions

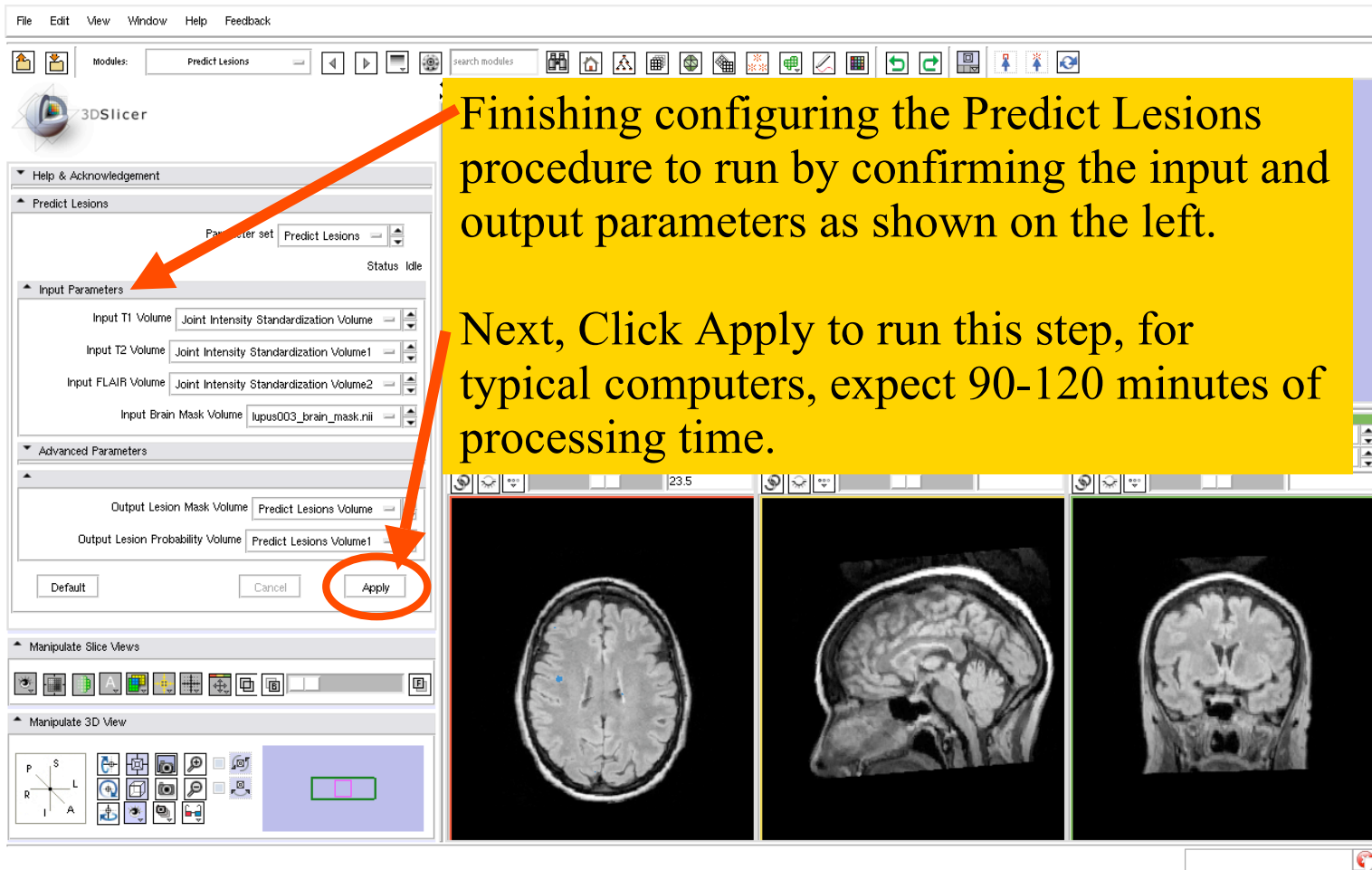
File Edit View Window Help Feedback
 Modules: Predict Lesions
 3DSlicer
 Help & Acknowledgement
 Predict Lesions
 Parameter set
 Input Parameters
 Input T1 Volume Joint Intensity Star
 Input T2 Volume Joint Intensity Stanc
 Input FLAIR Volume Joint Intensity Stanc
 Input Brain Mask Volume lupus
 Advanced Parameters
 Output Lesion Mask Volume Prec
 Output Lesion Probability Volume Predi
 Default Cancel
 Manipulate Slice Views
 Manipulate 3D View
 Predict Lesions

All Modules
 Color
 Data
 Editor
 Fiducials
 Measurements
 Models
 ROI
 SlicerWelcome
 Slices
 Transforms
 VolumeRendering
 Volumes
 Wizards
 Informatics
 Registration
 Segmentation
 Statistics
 Diffusion
 Tractography
 IGT
 Filtering
 Surface Models
 Batch Processing
 Converters
 Developer Tools
 Diffusion Weighted
 Work in Progress

None Sagittal None
 lupus003...bias.nii Predict L...s Volume lupus003...bias.nii
 23.5
 None Coronal None
 Predict L...s Volume lupus003...bias.nii
 23.5
 None
 Predict L...s Volume lupus003...bias.nii
 23.5

EMSegment Template Builder
 FastMarchingSegmentation
 EMSegment Simple
 Gyri Contour Segmentation
 Otsu Threshold Segmentation
 Simple region growing
 Lesion Segmentation
 Filter Lesions By Size
 Joint Intensity Standardization
 Lesion Stats
 Predict Lesions

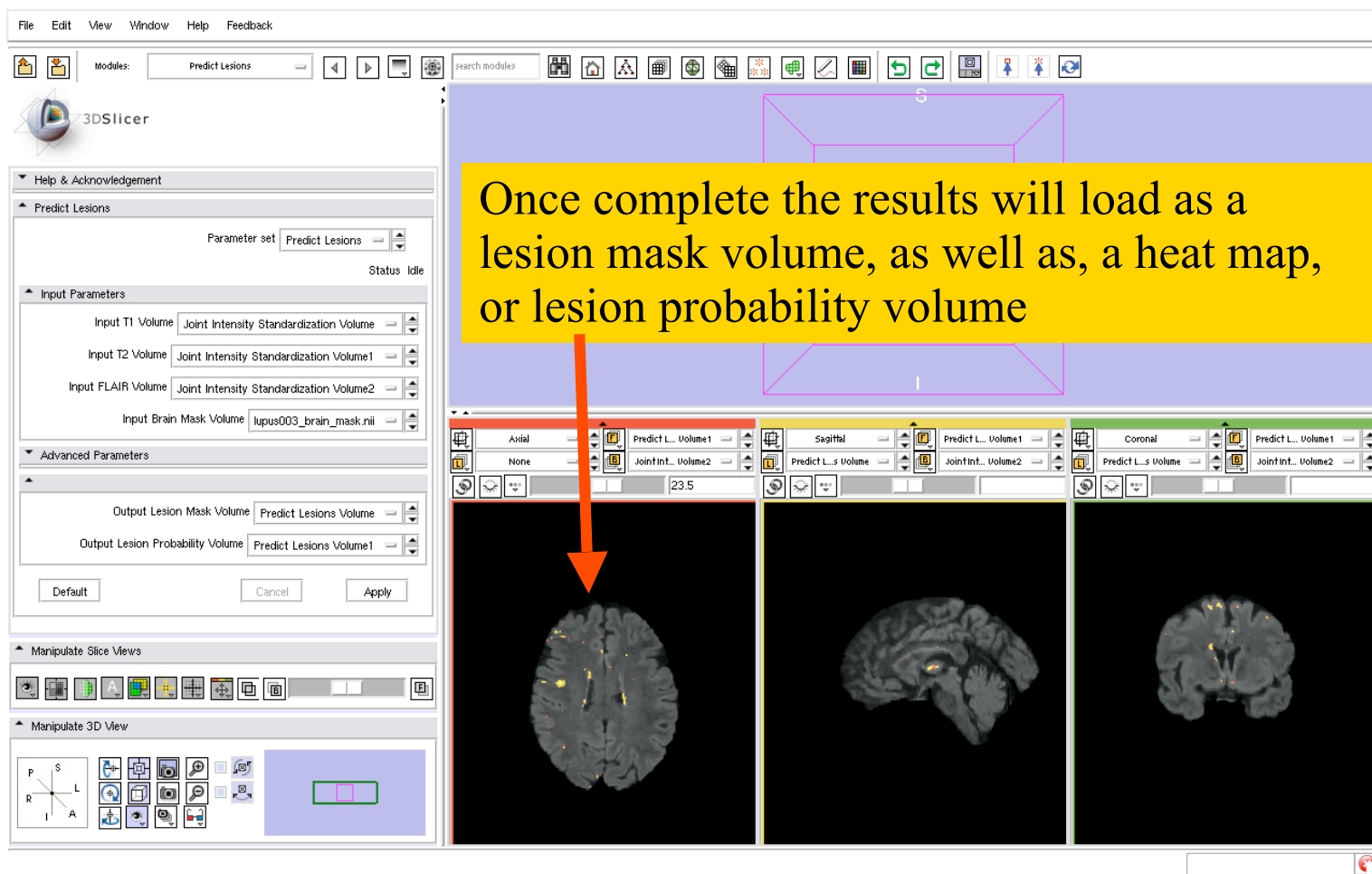
Module Step 3: Running



Finishing configuring the Predict Lesions procedure to run by confirming the input and output parameters as shown on the left.

Next, Click Apply to run this step, for typical computers, expect 90-120 minutes of processing time.

Module Step 3: Results



File Edit View Window Help Feedback

Modules: Predict Lesions

3DSlicer

Help & Acknowledgement

Predict Lesions

Parameter set: Predict Lesions Status: Idle

Input Parameters

Input T1 Volume: Joint Intensity Standardization Volume

Input T2 Volume: Joint Intensity Standardization Volume1

Input FLAIR Volume: Joint Intensity Standardization Volume2

Input Brain Mask Volume: lupus003_brain_mask.nii

Advanced Parameters

Output Lesion Mask Volume: Predict Lesions Volume

Output Lesion Probability Volume: Predict Lesions Volume1

Default Cancel Apply

Manipulate Slice Views

Manipulate 3D View

Once complete the results will load as a lesion mask volume, as well as, a heat map, or lesion probability volume

Axial Predict L... Volume1 Joint Int... Volume2 23.5

Sagittal Predict L... Volume1 Joint Int... Volume2

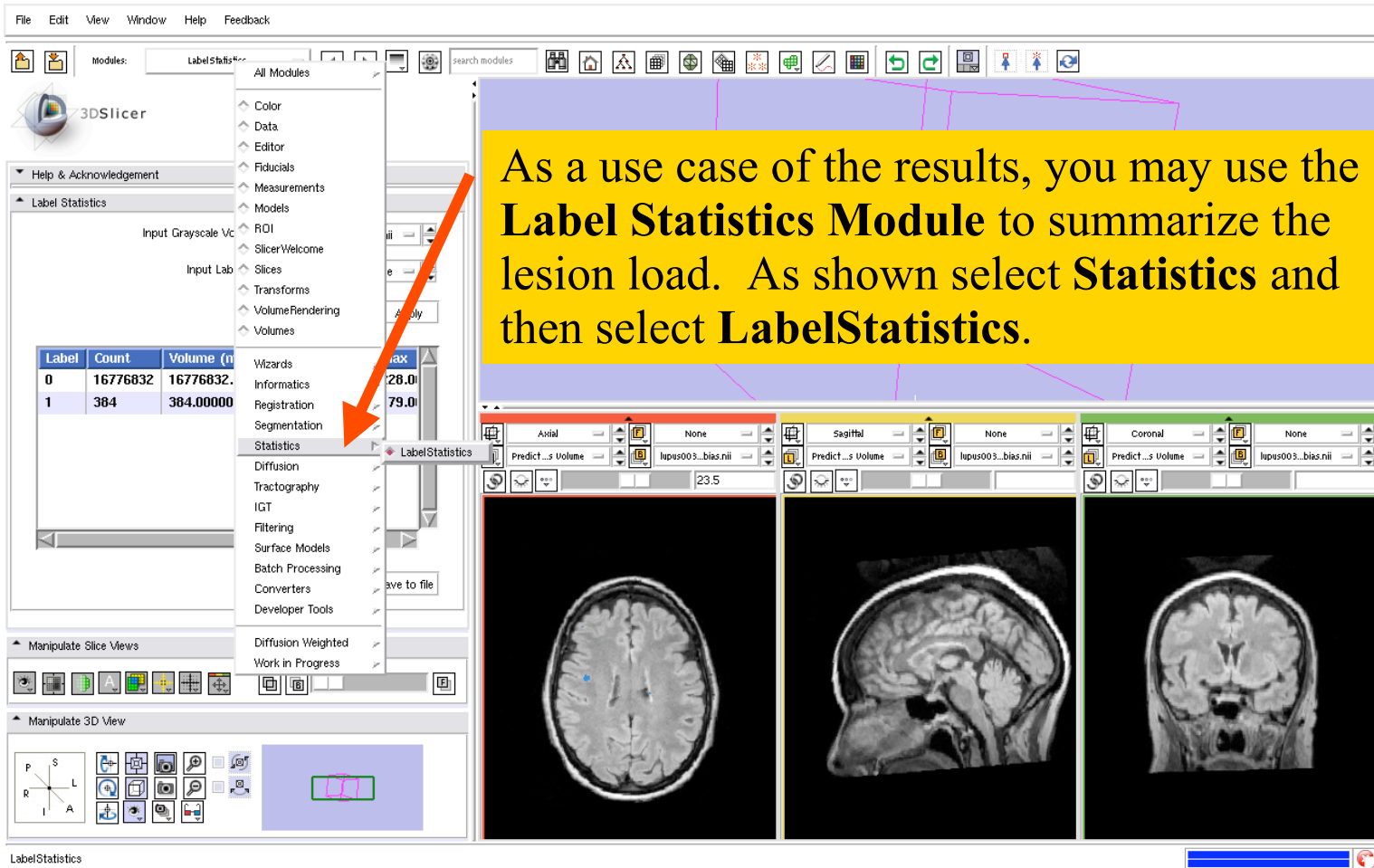
Coronal Predict L... Volume1 Joint Int... Volume2



Predicted Lesions

Following Stage 3, you now have both volumes and probability images that represent where white matter lesions are predicted for the given data set. The remainder of this tutorial will show you first how you may use the volume data to measure the lesion load, and also how the data can be rendered to visualize the location and extent of lesions for the given data set.

Example Measurement



As a use case of the results, you may use the **Label Statistics Module** to summarize the lesion load. As shown select **Statistics** and then select **LabelStatistics**.

Label	Count	Volume (mm ³)
0	16776832	16776832.0
1	384	384.00000

The screenshot shows the 3DSlicer interface with the 'Label Statistics' module active. The 'Statistics' menu item is highlighted in the 'All Modules' list, and 'LabelStatistics' is selected. The main window displays three orthogonal views of a brain MRI scan: Axial, Sagittal, and Coronal. The 'Label Statistics' table is visible in the lower-left corner of the interface.



Example Measurement

After selecting *Flair* as input **Grayscale Volume** and *Predict Lesions Volume* as the **Input Labelmap**, a summary of the volume is provided in the Label Statistics. In this example, the total lesion volume is 384 mm³ for lupus003 subject.

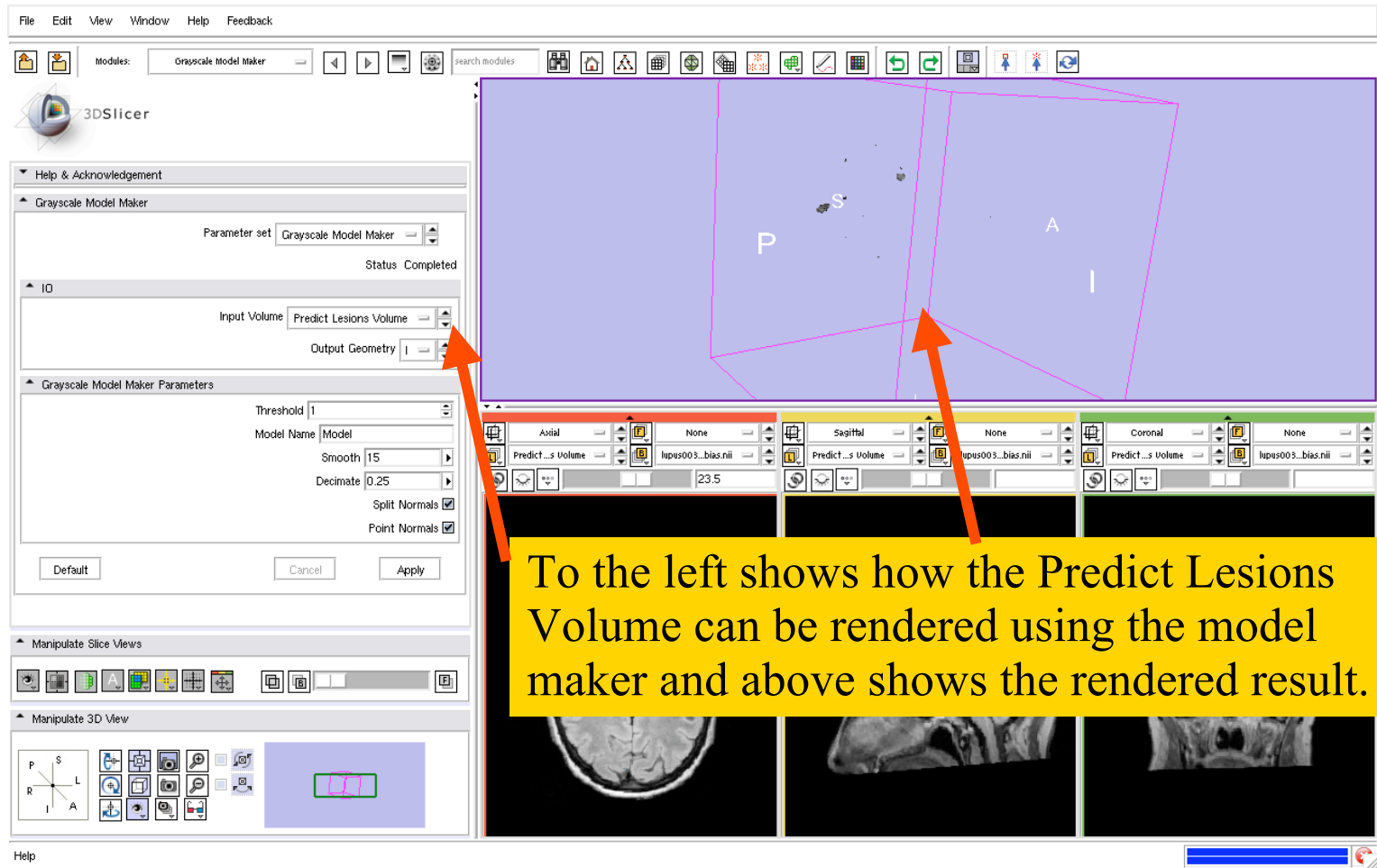
Label	Count	Volume (mm ³)	Min	Max
0	16776832	16776832.000000	0.000000	228.0
1	384	384.000000	113.000000	179.0



Setup Example Model

The screenshot shows the 3DSlicer software interface. The 'Grayscale Model Maker' module is selected in the 'All Modules' list. A yellow callout box with an orange arrow pointing to the 'Grayscale Model Maker' option in the menu contains the text: 'You may also create a model of the classified lesions by using the Model Maker module. To do this, select **Surface Models** and then select the **Grayscale Model Maker**.' The interface also displays three orthogonal MRI slices (Axial, Sagittal, Coronal) and a 3D view of the brain model.

Results Example Model



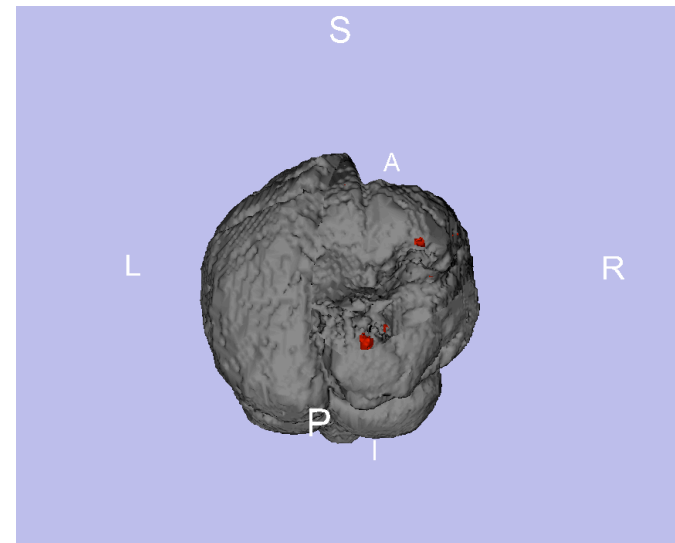


Discussion

- This concludes the objective of the tutorial; however, since the tool has produced a label map, as shown in the example, you may now measure the volumes of the automatically labeled lesion tissue or summarize the anatomical location of lesions for other cases in the tutorial data set. Since, the lesion load is associated with symptom severity and can be used to guide treatment and care.
- You may use the lesion label maps as input to the change tracker capability in Slicer to assess time course of the illness (change in lesion size, number over time).
- You may use the label maps to assess either perfusion or diffusion deficits through co-registration of the lesion maps with pMR, ASL, or DTI.

Conclusion

- This capability provides an intuitive graphical user interface to interact with the data
- The tool has been built in an open-source environment and is readily available to the scientific community





For More Information

- Register as a user of this 3dSlicer Module using the NITRC resource to keep updated on any changes or additions to either the capability or tutorial
 - <http://www.nitrc.org/projects/lupuslesion/>
- You may also send e-mail message with any questions or concerns to Jeremy Bockholt (jbockholt@mrn.org)



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