Quantitative Medical Imaging for Clinical Research and Practice

Sonia Pujol, PhD, Katarzyna Macura MD, PhD, Kitt Shaffer, MD, PhD, Hatsuho Mamata, MD, PhD, Andriy Fedorov, PhD, Wendy Plesniak, PhD, Ron Kikinis, MD
Quantitative imaging is the extraction of quantitative measurements from medical imaging.

This tutorial is built upon two examples of quantitative imaging:

- **Morphology**: small volumetric changes in slow growing tumors
- **Function**: metabolic activity in squamous cell carcinoma
Quantitative Imaging: Software

- This hands-on tutorial will guide you step-by-step through the use of quantitative imaging modules of the 3DSlicer software.

- 3DSlicer is a freely available open-source platform for medical imaging research supported by the National Institutes of Health.

www.slicer.org
Tutorial Overview

Part 1: Basics of 3D Data Loading and interactive visualization in 3DSlicer

Part 2: Measurement of small Volumetric Changes in meningioma using the Change Tracker module

Part 3: Measurement Metabolic Activity in squamous cell carcinoma using the PET Standard Uptake Value Computation module
Introduction to the 3DSlicer software

Sonia Pujol, PhD
Director of Training,
National Alliance for Medical Image Computing
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3DSlicer is a freely available open-source platform for segmentation, registration and 3D visualization of medical imaging data.

3DSlicer is a multi-institutional effort supported by the National Institute of Health.
3DSlicer

- 3DSlicer version 4.2 is a multi-platform software running on Windows, Linux, and Mac OSX
- Slicer is distributed under a BSD license with no restriction on use
- Slicer is a tool for research, and is not FDA approved

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.
An interdisciplinary platform

An open-source environment for software developers

An end-user application for clinical investigators and scientists

A software platform that is both easy to use for clinical researchers and easy to extend for programmers
3DSlicer History

- 1997: Slicer started as a research project between the Surgical Planning Lab (Harvard) and the CSAIL (MIT)

Image Courtesy of the CSAIL, MIT
3DSlicer History

- 1997: Slicer started as a research project between the Surgical Planning Lab (Harvard) and the CSAIL (MIT)

- 2012: Multi-institution effort to share the latest advances in image analysis with clinicians and scientists
Slicer: Behind the scenes

Slicer is built every night on Windows, Mac and Linux platforms.
Slicer Training

- Hands-on training workshops at national and international venues
- More than 2,000 clinicians, clinical researchers and scientists trained since 2005
Slicer Downloads

Slicer 4 download statistics

Total matching downloads: 46794

Date range: past year

Release type: any

Browser type: desktop

Update
Part I: 3D Data Loading and Visualization

Sonia Pujol, PhD
Wendy Plesniak, PhD
3D Data Loading and Visualization

• This tutorial is a short introduction to the advanced **3D visualization capabilities** Slicer.

• The Slicer4 Minute dataset is composed of an MR scan of the brain and 3D surface reconstructions of anatomical structures.

• The data are part of the SPL-PNL Brain Atlas developed by Talos, Jakab, Kikinis et al. The atlas is available at:

  http://www.spl.harvard.edu/publications/item/view/2037
Welcome to Slicer4

To start Slicer, select Start → Programs → Slicer4.2.0 (Win64) → Slicer
The Graphic User Interface (GUI) of Slicer4 integrates **four components:**
- the Menu Toolbar
- the Module GUI Panel
- the 3D Viewer
- the Slice Viewer
Click on **Welcome to Slicer** in the Modules menu to display the list of modules of Slicer.
Welcome to Slicer4

Slicer4.2 contains more than 100 modules for image segmentation, registration and 3D visualization of medical imaging data.
Slicer4 Minute Tutorial: **Welcome Module**

The **SlicerWelcome** module is the module displayed by default. This module gives an overview of the GUI of Slicer4, and **data loading & saving functionalities**.
Click on the **Load Data** icon, and select **Choose File(s) to Add** and browse to the directory ‘C:\Pujol2012’

Select the subdirectory ‘QuantitativeImaging_Sunday_Nov25_2012’

Select the directory **dataset1_MR-Head** and click on **Open**
Slicer4 Minute Tutorial: **Load a Scene**

Select the file **MRHead_Scene.mrml** and click on **Open**
Slicer4 Minute Tutorial: Load a Scene

Click on OK to load the data to Slicer
When the scene is finished loading, Slicer displays:

- a **3D model of the head** in the 3D Viewer, and
- anatomical **MR slices of the brain** in the 2D Slice Viewers.
To access the **Models module**, browse through the list of modules...

...or click on the **models icon** in the toolbar.
Slicer4 Minute Tutorial: **Switching to the Models Module**
Slicer4 Minute Tutorial: Basic 3D Interaction

Position the mouse in the 3D Viewer.

Hold down the **left mouse button** and **drag to rotate** the model.
Click on the **Slice Visibility** icon to display the Axial Slice in the 3D Viewer.
Slicer adds a view of the **Axial slice** in the 3D View.
Click on the layout menu in the toolbar, and select the Conventional layout.
Select the **Skin.vtk**
Change the opacity of the model from **1.0** to **0.0**.
The model of the skull bone and eyeballs become visible through the model of the skin in the 3D viewer.

(skin model opacity = 0.5)
The model of the skin becomes invisible in the 3D viewer.

(skin model opacity = 0.0)
(skull model opacity = 1.0)
Click on the **Slice Visibility** icon in the **Green Slice Viewer** to display the Coronal Slice in the 3D Viewer.
The Axial and Coronal Slices are displayed in the 3D Viewer.
Select the 3D model **skull_bone.vtk** in the Model Hierarchy and turn on the Clipping option.
Slicer4 Minute Tutorial: 3D Visualization

Browse through the **coronal slices** to expose the 3D model of the **white matter**, and the left and right **optic nerves**.
Now make the skull invisible.
Scroll the **Coronal Slices** to display the hemispheric white matter model in the context of the image data in the 3D Viewer.
Select the hemispheric white matter model called \texttt{hemispheric\_white\_matter.vtk}

Turn off its \textit{visibility}. 
Slicer displays the optic nerve, optic chiasm and optic tracts overlaid on the MR images of the brain.
Slicer4 Minute Tutorial: 3D Visualization: Zoom the view

**Windows/Linux users:** Position the mouse in the 3D Viewer, hold down the **right mouse button** and move the mouse down to zoom in.

**Mac users:** Position the mouse in the 3D Viewer, hold down the **apple button and the mouse button** and move the mouse down to zoom in (or use two fingers on the touchpad).
Slicer displays a **closer view** of 3D anatomical structures overlaid on 2D MR slices.
Close the existing scene and all its data

Select **File->Close Scene**

This removes any dataset previously loaded into Slicer.

Select **File-> Exit** to exit the software
Part I: Summary

This first part of the tutorial has demonstrated:

• Basic description of the Slicer4 Application Interface
• How to load a scene containing volumes and models
• How to visualize these different datasets together

Next, we will use these building blocks to perform image analysis and visualize quantitative results.
Part II: Analyzing Small Volumetric Changes

Sonia Pujol, PhD  
Kilian M Pohl, PhD  
Andriy Fedorov, PhD  
Ender Konukoglu, PhD  
Ron Kikinis, MD
Conventional measures of tumor response

- Conventional anatomic imaging using CT or MRI are often used to evaluate tumor size and shape.
- Most clinical trials that evaluate new chemotherapeutic drugs use changes in uni-dimensional or bi-dimensional measurements to assess response (e.g. RECIST).
- Slicer has several tools for applying RECIST methodologies.

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Conventional measures of tumor response

3D Slicer Annotations module can be used to measure diameters in a tumor cross section, and to provide interactive numerical annotations.
Baseline radiologist’s clinical impression:
• large falcine lesion is identified.
• measures 3.10 cm anteroposteriorly and 3.51 cm in height.
• enhances moderately on post gadolinium imaging.
Clinical Case: follow-up scan

Follow-up radiologist’s clinical impression:
• left frontal lobe mass appears unchanged on all series.
• measures 3.3 x 3.2 cm in maximum dimension.
• enhances moderately on post gadolinium imaging.
Clinical Case: follow-up scan

Follow-up radiologist’s clinical impression:
• left frontal lobe mass appears unchanged on all series.
• measures 3.3 x 3.2 cm in maximum dimension.
• enhances moderately on post gadolinium imaging.

→ How has the tumor changed?
More accurate and precise methods for understanding volume changes may be useful when:

- **benign tumor change** is being monitored, or
- where **small changes may be clinically significant** but difficult to assess with RECIST
Goal of the tutorial

The following section will guide you step-by-step through the computation of small volumetric changes in a slow growing tumor.

This tutorial is built upon two scans (Axial 3D SPGR T1 post Gadolinium) of a patient with meningioma, and uses the Change Tracker module of Slicer.
ChangeTracker: Load the dataset

Select **File**→**Add Data** in the main menu

Select the directory **dataset2_ChangeTracker** located in **C:\Pujol2012\QuantitativeImaging_Sunday_Nov25_2012**

Select the scene file: **ChangeTrackerScene.mrml** and click on **Open**

Click on **OK** to load the data to Slicer
Loading the data

The datasets of the ChangeTrackerScene appear in the anatomical viewers.
ChangeTracker: exploring small volumetric changes

Using the **Modules Menu** button, select the **ChangeTracker** Module in the **Wizards** category.
The **Workflow Wizard** guides the user through a sequence of steps and has the following components:

- the Step Panel
- the User Panel
- the Navigation Panel
Step 1: Select input scans

- Click to expand the tab ‘1. Select input scans’
- Set the Baseline scan to 2006-spgr1
- Set the Follow up scan to 2007-spgr1

Click on the green arrow to the next step of the workflow
Step 2: Define Region of interest

A Volume of Interest (VOI) Box Widget appears in the anatomical viewers, and in the 3D viewer.
Step 2: Define Region of interest

- Browse through the Axial, Sagittal and Coronal slice viewers to get a close-up view of the tumor.

- **Zoom in** (Right mouse down and push/pull).

- **Pan** (Middle mouse down and move).
Step 2: Define Region of interest

Center the VOI first:

Position the square in the center of the tumor in the slice viewer.
Step 2: Define Region of Interest

Next, resize the VOI:

Use the colored handles to change the VOI extent
Step 2: Define Region of interest

The VOI box and volume rendering of tumor in yellow appear in the 3D Viewer.
Step 2: Define Region of interest

Note: VOI Widget range sliders are color-coded to match VOI box Widget handles in 3D Viewer.

Fine-tune the VOI using the VOI Widget range sliders or by moving the VOI Widget handles in 3D view.
Step 2: Define Region of Interest

Select the viewing mode ‘Conventional Widescreen’
Step2: Define Region of interest

Slicer shows a closer view of the volume rendered tumor region.
Step 2: Define Region of interest

Zoom in and out, and rotate the volume rendered image to explore the tumor region in 3D.
Step 2: Define Region of interest

Select 'Four-Up Quantitative' to return to the initial view mode.

Click on the green arrow to move to the next step.
Step 3: Segment the tumor

Click on the pin icon in the top left corner of the red slicer viewer to display the names of the two volumes that Slicer has generated automatically: `baselineROI` and `baselineROI_segmentation`
Step 3: Segment the tumor

'baselineROI' (background viewer) is the subvolume that corresponds to the previous VOI

'baselineROI_segmentation' (labelmap viewer) is the current segmentation of the tumor.

In the current settings, Slicer displays the segmentation overlaid on the spgr volume.

The 3D Viewer shows the corresponding 3D model of tumor.
Step 3: Segment the tumor

Select the layout FourUp in the layout menu to display the volume rendered segmentation.

Modify the segmentation of the tumor by moving the threshold range slider.
Step 3: Segment the tumor

Scroll through the slices until the segmentation appears optimal.

Click on the green arrow to move to the next step.
Step 4: Select the Analysis Method

Select the ROI Analysis Method:
‘Intensity Difference Change Detection (FAST)’

Click on the green arrow to move to the next step.
Final Step: Change Tracker Results

Left click on the slice menu to display the volumes that have been generated:

- **followupROI** correspond to the subvolume that has been extracted around the tumor in the 2007-spgr_1 dataset

- **changesVolume_IntensityDifferenceMetric** corresponds to the change between the 2006 and 2007 scans
Final Step: Change Tracker Results

The change in volume is shown overlaying the tumor image and in the 3D Viewer:

- **magenta** = growth
- **green** = shrinkage
Visualization of the change in pathology

The results of the analysis are displayed in the “Compare View” layout:

- Six consecutive slices for the VOI in Scan1 (top row), and
- Six corresponding consecutive slices for the VOI in Scan2 (bottom row).
- A zoomed view of the axial slice in the red slicer viewer.
Visualization of the change in pathology

The Crosshairs in Compare View show corresponding voxels in Scan1 and Scan2 for voxel-wise comparison.
Change Tracker Results

Growth: 1.69 mL (16423 pixels), or 1.08%
Shrinkage: 0.00 mL (0 pixels), or 0.00%
Total: 1.69 mL (16423 pixels), or 1.08%
Change Tracker module

• This tutorial demonstrated the use of the change tracker module in Slicer on axial 3D SPGR T1 post Gadolinium scans

➢ Tumor boundary should be clear
➢ Only for contrast enhanced images
➢ Need homogenous enhancement across timepoints.

• The Change Tracker module has not been tested for tumors with changing necrosis.
ChangeTracker: Exploring small volumetric changes

This tutorial demonstrated:

- a method to quantify small volumetric changes in pathology.
- visualization of these changes in the anatomical context
- use of Slicer’s “Compare Viewer” to simultaneously explore baseline and followup studies.

Next, we will demonstrate combined visualization of PET/CT studies and SUV computation.
Clear the scene and its data

Clear the previous scene.
Select **File->Close Scene**

This removes any datasets previously loaded into Slicer.
Select **File→Exit** to restart Slicer
Goal of the tutorial

The goal of this tutorial is to guide you step-by-step through the SUV computation of PETCT data of a squamous cell carcinoma case pre- and post-treatment.
FDG-PET SUV

- Standardized Uptake Value (SUV) is a semi-quantitative measure derived from the determination of tissue activity obtained from a clinical PET study

\[
\text{SUV} = \frac{\text{Tissue Concentration of Radioactive Tracer} \times \text{Patient Weight}}{\text{Injected Dose}}
\]

- Under certain circumstances, 18-F Fluorodeoxyglucose (FDG) SUV correlates with metabolic rate of glucose and/or the number of viable tumor cells
• Pathology: poorly differentiated squamous cell carcinoma

• Treatment: radiotherapy and chemotherapy (weekly cis-platin)

• Two 18F-FDG PET and CT scans acquired within a 5-month interval.
The datasets are located in

C:\Pujol2012\QuantitativeImagingSunday_Nov25_2012\dataset3_PETCT

- PETCT1 dataset is located in the pre-treatment directory corresponds to the baseline
- PETCT2 dataset is located in the post-treatment directory corresponds to the follow-up scan.
Select DICOM Database Directory

Click on Load DICOM Data in the panel of the Welcome to Slicer module.
Select DICOM Database Directory

The DICOM Details window appears.
Select DICOM Database Directory

The window **Select DICOM Database Directory** appears when you use the DICOM module for the first time.

Browse to the directory:

C:\Pujol2012\QuantitativeImaging_Sunday_Nov25_2012

Select the sub-directory **dicom-database**

Click on **Choose**
Select DICOM Database Directory

Slicer’s local DICOM database is now set to:

C:/Pujol2012/QuantitativeImaging_Sunday_Nov25_2012/dicom-database
Mac Users: Click on the directory next to Local Database, and browse to the location of the QuantitativeImaging_Sunday_Nov25_2012 directory, located in the 3DSlicer-Data_RSNA2012 directory
Loading a DICOM Volume (Mac Users)

Select the directory **dicom-database** and click on **Choose**
Loading a DICOM Volume

Click on **Import** and browse to the location of the directory:
C:\Pujol2012\QuantitativeImaging_Sunday_Nov25_2012

Click on the dataset **dataset3_PETCT** located in this directory, and select the subdirectory **pre-treatment**
Loading a DICOM Volume

Select the **pre-treatment** directory and click on **Import**
Loading a DICOM Volume

Click to expand the list of DICOM volumes accessible via the DICOM browser
Loading a DICOM Volume

Select the series **PET Skull to MID Thigh Plus DCT Chest W Ini**

Slicer displays the list of DICOM volumes located in the pre-treatment directory:
- ‘**SOFT**’ is the CT dataset
- ‘**HEAD NECK_2D AC**’ is the PET dataset
  (note: this may take a few minutes)
Loading a DICOM Volume

Slicer displays a snapshot of the DICOM volumes:
- ‘SOFT’ is the CT dataset
- ‘HEAD NECK _2D AC’ is the PET dataset

Click on Load Selection to Slicer
The PET dataset appear in the anatomical viewer

Select the layout **Conventional** in the layout menu
Loading a DICOM Volume

Select the module **Data** in the modules menu.

Right click on the volume ‘3: SOFT’ and rename it **CT1**

Right click on the volume ‘401: HEAD NECK_2D AC’ and rename it **PET1**
Loading a PETCT dataset

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

The **PET1** volume is currently displayed in the Background viewer.

Click on the **links** icon to link all three views together, and change the selected volume to **CT1**.
Select the module **Volumes** and use the sliders in the **Display tab** to adjust the Window and Level of the CT images.
Visualization of PETCT data

Set the **Active Volume** to **PET1** and select the **PET1** image in the background viewer.
Visualization of PETCT data

Select the **Lookup table to PET-Heat**
Visualization of PETCT data

Select File → Add Data in the main menu
Select Choose File(s) to Add and browse to the pretreatment directory

Select the file PET1-label.nrrd and click on Open to load it in Slicer
Visualization of PETCT data

Check the ‘Show Options’ box, and check that the option ‘Label Map’ is selected.
Select the file PET1-label.nrrd and click on OK to load it in Slicer.
Visualization of PETCT data

Select the outline mode for the PET1-label segmentation in the labelmap viewer.

The outline of a lesion appears in the anatomical viewers.
Visualization of PETCT data

Set the **CT1** dataset in the foreground viewer, and change the opacity of the CT images to 0.50 to display the CT images overlaid on the PET images.
Visualization of PETCT data

Check on the slice visibility icon 🕵️‍♂️ in the red and yellow viewers to display the axial and sagittal slices in the 3D viewer.
Note an intense uptake in
1) left oropharyngeal mass
involving the base of tongue
and left glossotonsillar
fossa and,
2) in left level IIA/III lymph
nodes as well as a small
adjacent left level III node.
3) a possible small
metastasis in the left
retropharyngeal region at
level of C1
PET SUV Computation

For the purpose of this tutorial, we have pre-segmented the lymph nodes uptake region. In the next section, we will compute the SUV for this area.

Select the module PET Standard Uptake Value Computation in the category Quantification in the modules’ menu.
PET SUV Computation

Step 1: Input volumes selection
Select Input PET Volume ‘PET1’
Select Input VOI Volume ‘PET1-label’
Step 2: Path to the DICOM PET header

Click on /Applications in the PET DICOM volume path, and select the PET1 subdirectory located under C:/Pujol2012/QuantitativeImaging_Sunday_Nov25_2012/dataset3_PETCT/pre-treatment/PET1
**PET SUV Computation**

**Step3: SUV Computation**
Click on **Apply** to compute the SUV in the segmented region
PET SUV Computation

**SUV Computation Results:**

\[\text{SUV}_{\text{max}} = 7.53385 \text{ mg/ml}\]
\[\text{SUV}_{\text{min}} = 5.01805 \text{ mg/ml}\]
\[\text{SUV}_{\text{mean}} = 3.39015 \text{ mg/ml}\]
PET SUV Computation

Select File→ Close Scene in the main menu
Loading the post-treatment dataset

1) Select the module **DICOM**, and click on **Show DICOM Browser**

2) Click on **Import** and select the dataset **post-treatment** located in the directory

C:/Pujol2012/
QuantitativeImaging_Sunday_Nov25_2012/
dataset3_PETCT/post-treatment/
Loading the post-treatment dataset

Click to expand the DICOM files tree
Select the 2nd series **PET SKULL-MID THIGH PL** and click in **Load Selection to Slicer** to load the follow-up PET and CT scans to Slicer
Loading the post-treatment dataset

Select the module Data and rename the CT scan ‘3:SOFT’ to CT2 and the PET scan ‘5: HEAD NECK_2D AC’ to PET2
Loading the post-treatment dataset

Select the module **Volumes**
Select the **Active Volume PET2**
Set the Lookup table to **PET-Heat**
Loading the post-treatment dataset

Set the **Active Volume to CT2**

Click on the links icon and set the **CT2** volume in **Foreground** in the anatomical viewers.
Set the opacity of the CT2 images to 0.5 in the anatomical viewers, and use the sliders to adjust the Window and Level of the images.
Observe a mild uptake in larynx and pharynx that are likely due to radiation effect.
PET uptake findings

Note that there is no remaining uptake in the area of the primary tumor or nodes after treatment.
Conclusion

- This tutorial has demonstrated how to do 3D data visualization, quantitative measurement of small changes in tumor size, and PET CT SUV computation in Slicer.

- 3DSlicer is for research use only, and is not FDA approved.

- 3DSlicer is a free open-source software for medical image computing and supported by the NIH.
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- Tobias Penzkofer, MD, Brigham & Women’s Hospital, RWTH Aachen University
- Marianna Jakab, MS, Brigham & Women’s Hospital
Hands-on courses:

• Tues. Nov. 27, 12:30 pm - 2 pm: 3D Visualization of DICOM images for Radiological Applications. Sonia Pujol, PhD, Kitt Shaffer, MD, PhD, Ron Kikinis, MD (SCD401)

• Wed. Nov. 28, 10:30 am – 12:00 pm: The NIH/NCI Cancer Imaging Archive (TCIA): A Comprehensive Source of DICOM Imaging Data for Research – Hands-on. C. Carl Jaffe MD, John B. Freymann BS, Justin Kirby, Fred William Prior, PhD, Lawrence R. Tarbox PhD
Oral presentations:


- Mon. Nov 26, 02:30-04:00: Open Source Applications for Medical Imaging Research (SCD401). Ricardo Avila, MS  Wesley Turner  PhD, Julien Finet MSc
Quantitative Imaging Reading Room Exhibit QIRR 3007

- Sun. Nov 26-Fri. Nov 30, 8:00-6:00

3DSlicer: An Open Source Platform for Segmentation, Registration, Quantitative Imaging, and 3D Visualization of Multi-Modal Image Data.

Sonia Pujol, PhD, Steve Pieper, PhD, Andriy Fedorov, PhD, Ron Kikinis, MD,
# 3DSlicer at RSNA

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