Quantitative Medical Imaging for Clinical Research and Practice

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Quantitative Imaging Tutorial

- Quantitative Imaging techniques can be used to give radiologists complementary information for interpreting images.
- The hands-on aspect of the course is intended to give clinical researchers a practical experience on the latest methods developed in medical research.
Quantitative Imaging Tutorial

This tutorial is built upon a series of examples of quantitative imaging analysis:

- **Morphology**: volumetric changes in brain and breast tumors
- **Function**: metabolic activity in squamous cell carcinoma
Tutorial Materials

- **Software**: 3D Slicer
- **Datasets**: QuantitativeImaging_Tuesday_Dec2
Tutorial Overview

Part 1: Introduction to 3D Slicer

Part 2: Basics of data loading and 3D interactive visualization

Part 3: Measurement of volumetric changes
- large volumetric change: breast tumor case
- small volumetric change: meningioma case

Part 4: Measurement of metabolic activity
- squamous cell carcinoma case
3D Slicer is a freely available open-source platform for segmentation, registration and 3D visualization of medical imaging data.

3D Slicer is a multi-institutional effort supported by the National Institute of Health.
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)
- 2014: Multi-institution effort to share the latest advances in image analysis with clinicians and scientists
A multi-institution: NA-MIC, NAC, NCIGT

PI: Ron Kikinis, M.D.

PIs: Ferenc Jolesz, M.D., Clare Tempany, M.D.
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
An extensible platform

- 3D Slicer supports plug-ins called Slicer extensions available from the Extension Manager.
- Allows end-users to select extensions useful to them, without having to download the entire extension archive.
- Built Nightly with Slicer.
3D Slicer in practice

- Slicer works on Windows, Linux, and Mac
- Slicer is distributed under a BSD-style license agreement with no restriction on use
3D Slicer in practice

- Slicer works on Windows, Linux, and Mac
- Slicer is distributed under a BSD-style license agreement with no restriction on use
- 3D Slicer is for clinical research use only, and is not FDA approved or CE-marked.
Slicer: Behind the scenes

Slicer is built every night on Windows, Mac and Linux platforms.
An extensible platform

- 3D Slicer supports plug-ins called Slicer extensions available from the Extension Manager.
- Allows end-users to select extensions useful to them, without having to download the entire extension archive.
- Built Nightly with Slicer.
Training Portfolio

- Modular multi-level training for expert and non-expert community
- Tutorials and anonymized datasets for end-users and developers
- Cross platform testing for quality control
Slicer clinical applications

- Applied science oriented toward patient-specific analysis in the presence of pathology
- Driving Biological Projects leading to the development of new tools
Examples of clinical applications

- Radiotherapy: RT-specific analysis dose accumulation and dose comparison (G. Fichtinger et al. Queen’s University, Canada)
Examples of clinical applications

- Diffusion Tensor Imaging tractography for neurosurgical planning
Slicer Training events

Major international conferences

- SfN 2009, 2011
- SPIE 2012, 2013
- CAOS 2010
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Part II: Basics of Data Loading and 3D Visualization
Course Datasets

The QuantitativeImaging_Tuesday_Dec2 directory contains three datasets located in the sub-directories:

- dataset1_MR_Head
- dataset2_ChangeTracker
- dataset3_PETCT

Each dataset is in .mrb file format.
A Slicer mrb file is an archive file that contains all data for loading into Slicer4.

The .mrb file is a .zip file with a different filename extension.
Welcome to Slicer4.4
The Graphic User Interface (GUI) of Slicer4 integrates **four components:**

- the Menu Toolbar
- the Module GUI Panel
- the 3D Viewer
- the Slice Viewer
Welcome to Slicer4.4

Click on Welcome to Slicer in the Modules menu to display the list of modules of Slicer.
Welcome to Slicer4.4

Slicer4.4.0 contains more than 100 modules for image segmentation, registration and 3D visualization of medical imaging data.
Open the directory QuantitativeImaging_Tuesday_Dec2 on the Desktop

Select the directory dataset1_MR-Head

Select the file MRHead_Scene.mrb

This file is composed of an MR scan of the brain and 3D surface reconstructions of anatomical structures, from The data are part of the SPL-PNL Brain Atlas developed by Talos, Jakab, Kikinis et al. The atlas is freely available for download at:

http://www.spl.harvard.edu/publications/item/view/2037
Drag and drop the file **MRHead_Scene.mrb**
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**.
Slicer4 Minute Tutorial: Exploring Slicer’s functionality

To access the Models module, browse through the list of modules...
Slicer4 Minute Tutorial: **Switching to the Models Module**

Slicer displays the GUI of the Models module.
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 model **Skin.vtk**

Click to expand the tab **Display**

Click to expand the tab **Color**

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)
Slicer4 Minute Tutorial: 3D Visualization

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.
Slicer4 Minute Tutorial: 3D Visualization

Select the 3D model **skull_bone.vtk** in the Model Hierarchy.

Click to expand the tab **Visibility** in the Display pannel.

Turn on the **Clip** option.
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 hemispheric_white_matter.vtk

Turn off its visibility.
Slicer displays the **optic nerve**, **optic chiasm** and **optic tracts** overlaid on the **MR images** of the brain.
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
Summary

This first part of the tutorial has demonstrated:

- Basic description of the Slicer4 Application Interface
- How to load a .mrb file 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 Volumetric Changes
Example 1: Large volumetric change

- Clinical case: 45 y-o woman presenting with an infiltrating ductal carcinoma in left breast

- Pre- and post-treatment imaging shows large volumetric difference in tumor size

Case Courtesy of Dr. Macura, JHU
PreTherapy acquisition

Pre-Gad High resolution MR scan

Post-Gad High resolution MR scan
Quantitative Imaging Processing Pipeline

Step #1: Non-rigid Registration of pre-Gad image to post-Gad image
Step #2: Subtraction of registered pre-Gad image to the post-Gad image
Step #3: Semi-automated segmentation of the subtracted image
Step #4: 3D model creation
Step #5: Tumor volume computation

Processing time ~5-7 min
Pre-therapy analysis (May 2013)

Subtract

Pre-Gad

Post-Gad

Tumor volume (May): 75 cm³
PostTherapy acquisition

Pre-Gad High resolution scan

Post-Gad High resolution scan
Post-therapy analysis (Oct. 2013)

Subtract

Pre-Gad

Post-Gad

Tumor volume (Oct): 0.9 cm³
Example 1: Large Volumetric Change

Tumor volume (May): 75 cm³

Tumor volume (Oct): 0.9 cm³
Example 2: Small volumetric change

The second example is built upon MR datasets of a meningioma case.

The following section will guide you step-by-step through the computation of small volumetric changes between the baseline (2006) and follow-up (2007) using the Change Tracker module.

MR Scan1 2006

(Voxel dimension: 0.94mm x 0.94mm x 1.20mm, FOV: 240mm, Matrix: 256 x 256)

MR Scan2 2007
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.
Conventional measures of tumor response

The **Annotations** module of 3D Slicer can be used to measure diameters in a tumor cross section, and to provide interactive numerical annotations.
Clinical Case: baseline scan (2006)

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 (2007)

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
**ChangeTracker: Load the dataset**

Drag and drop the file `ChangeTrackerScene.mrb` located in the directory `dataset2_ChangeTracker` into Slicer.

Click OK to load the .mrb file into Slicer.
Loading the data

The datasets of the ChangeTrackerScene appear in the anatomical viewers.

Click on **Welcome to Slicer** and select the module **Data**.
Loading the data

The Slicer scene contains two scans 2006-spgr1 and 2007-spgr1.
ChangeTracker: exploring small volumetric changes

Using the **Modules Menu** button, select the **Wizards->ChangeTracker**.
ChangeTracker: a note about the Workflow wizard

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 Panel**

- 1. Select input scans
  - Select the baseline and follow-up scans to be compared.

**User Panel**

- Baseline scan: Select a Volume
- Followup scan: Select a Volume

**Navigation Panel**

- Back
- Next
Step 1: Select input scans

Click to expand the tab ‘1. Select input scans’

Click on **Select a Volume** next to **Baseline Scan**
Select the volume **2006-spgr1**

Click on **Select a Volume** next to **Follow up Scan**
Set the volume **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).

**Position the mouse cursor** in a viewer, **hold the shift** button down on the keyboard, and move the mouse to display the corresponding location in the two other viewers.
Step 2: Define Region of interest

Center the VOI first:

Left click on the central yellow dot and hold the mouse cursor down to move the VOI.

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
Step2: 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’ 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 viewer (next to the letter R)
Click on the double arrow icon (>>)
to display the names of the two volumes that Slicer has generated automatically:
baselineROI_segmentation and baselineROI
Segment the tumor

Step 1: VOI definition

Step 2: VOI extraction

Step 3: Segmentation
Step 3: Segment the tumor

The 3D Viewer shows the corresponding 3D volume-rendered image of the tumor.
Step 3: Segment the tumor

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

In the Basic Settings Tab: 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 Basic Setting
‘Intensity Difference Change Detection (FAST)’

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

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
Step 4: Select the Analysis Method

Click on links icon in the Red Slice Viewer menu to link all three viewers.
Click on the icon to adjust the size of the image to the size of the window, and browse through the slices to display the images.
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

• BaselineROI: Six consecutive slices for the ROI in Baseline Scan (top row), and

• FollowupROI: Six corresponding consecutive slices for the ROI in Follow Up Scan (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

The metrics calculated indicate the volume and percentage of tumor growth between the two time points.
Change Tracker module

- The 3D Slicer ChangeTracker module is a research tool for evaluating volumetric changes and bring additional complementary information to RECIST measurements.

- However, three current requirements are needed for Change Tracker to produce adequate measurements:
  1) Clear Tumor boundaries
  2) Contrast enhanced images only
  3) Homogenous enhancement across timepoints

- The Change Tracker module has not been tested for tumors with changing necrosis.
Clear the scene and its data

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

Select **File->Exit** and restart Slicer
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 follow-up studies.

Next, we will demonstrate combined visualization of PET/CT studies and SUV computation.
PET/CT Visualization and Analysis

Part III: PET/CT Analysis

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Goal of the tutorial

The goal of this tutorial is to guide you step-by-step through the Standard Uptake Value (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

\[
\text{SUV} = \frac{\text{Tissue Concentration of Radioactive Tracer}}{\text{Patient Weight}} \times \frac{1}{\text{Injected Dose}}
\]

- Under certain circumstances, 18-F Fluorodeoxyglucose (FDG) SUV correlates with metabolic rate of glucose and/or the number of viable tumor cells
Tutorial Case

- 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.
PETCT tutorial: Clinical Case and Data

The datasets are located in \dataset3_PETCT

The directory contains two .mrb files

- PET_CT_pre-treatment.mrb corresponds to the baseline
- PET_CT_post-treatment.mrb corresponds to the follow-up scan.
Loading the PETCT scene

Drag and drop the file **PETCT_pre-treatment.mrb**

Click OK to load the .mrb file into Slicer
Loading the PETCT scene

Select the module **Data**

The CT dataset appears in the anatomical viewer
Left click on the pin icon in the top left corner to display the red slice viewer menu.

The **CT1** volume is displayed in the Foreground viewer.

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

Use the slider to fade between the Bg viewer and the Fg viewer to display the PET volume overlaid on the CT volume.
Visualization of PETCT data

Change the opacity of the CT1 volume to 0.50 to display the CT images overlaid on the PET images.
Visualization of PETCT data

Hold the left mouse button down, and move the mouse cursor up/down and left/right to adjust the window and level of the PET images
PET uptake findings

Note an intense uptake in
1) left oropharyngeal mass involving the base of tongue and left glossotonsillar fossa (Axial -139 mm)
2) in left level IIa/III lymph nodes as well as a small adjacent left level III node (Coronal 65 mm)
3) a possible small metastasis in the left retropharyngeal region at level of C1 (Sagittal -19 mm)
For the purpose of this tutorial, we have pre-segmented the lymph nodes uptake region (PET1_label). 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

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’**
PET SUV Computation

Step 2: Path to the DICOM PET header

Click on C:/RSNA Hands-on/S401AB/RCA23 Pujol/Slicer-4.4.0-win-amd64-RSNA
PET SUV Computation

Browse to the \PET1 directory located under

C:\Users\Adminstrator\Desktop\QuantitativeImaging_Tuesday_Dec2\QuantitativeImaging_Tuesday_Dec2\dataset3_PETCT

Click on Choose to select the PETDICOM volume path
Step 3: SUV Computation
Click on **Apply** to compute the SUV in the segmented region.
PET SUV Computation

**SUV Computation Results:**

\[ \text{SUVmax} = 7.53385 \text{ mg/ml} \]
\[ \text{SUVmean} = 5.01805 \text{ mg/ml} \]
\[ \text{SUVmin} = 3.39015 \text{ mg/ml} \]
Select File → Close Scene in the main menu.
Loading the PETCT scene

Drag and drop the file **PETCT_post-treatment.mrb** located in **dataset3_PETCT**

Click OK to load the .mrb file into Slicer
Set the opacity of the CT2 images to 0.5 in the anatomical viewers, and use the left mouse button to adjust the Window and Level of the images.
Observe a mild uptake in larynx and pharynx that are likely due to radiation effect.
Note that there is no remaining uptake in the area of the primary tumor or nodes after treatment.
Conclusion

• This tutorial has demonstrated the 3D Slicer modules for quantitative imaging

• Continuous advances are being made in imaging technology and post-processing software tools

• The intersection of quantitative and clinical sciences offers great promise to help improve outcome prediction and tumor response to therapy
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3DSlicer at RSNA 2014

Quantitative Imaging Reading Room, Exhibit LL-QRR3007

• Tue. Dec.2-Fri. Dec.5, 8:00-6:00

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

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