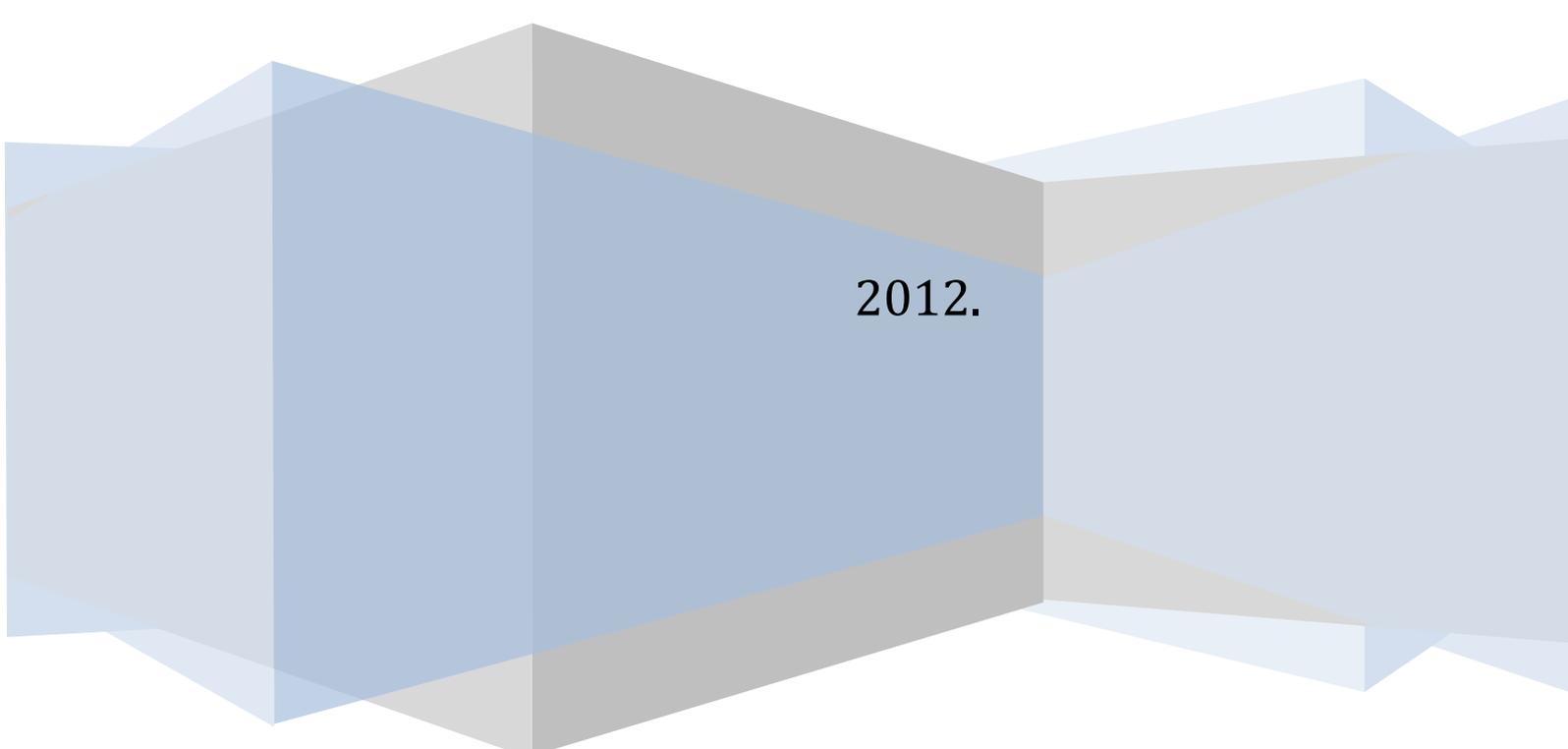


University of Debrecen / ETH Zürich

# Segmenting Brain Tumors with the Slicer 3D Software

Manual for providing expert segmentations for the BRATS-Ch  
Tumor Segmentation Challenge

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# 1. Getting started with Slicer 3D

## 1.1. Downloading Slicer 3D

Slicer 3D 3.x version binaries are available for Linux (32, 64 bit – tested on Ubuntu and Debian), Windows 32-bit, Mac OSX and Solaris. Generally, it is recommended to use 64 bit OS with lots of memory (4-8+ Gb of RAM). The Slicer development team provides daily builds and bug-fixes; however, still it is advisable to run on a stable image-processing workstation. The binaries should run without problems and no 3<sup>rd</sup> party libraries have to be installed, VTK and ITK is included.

Slicer 3.x versions are obsolete and are currently being replaced by Slicer 4. This documentation is based on the GUI and functionality of the 3.x versions. Such binaries can be downloaded from this link:

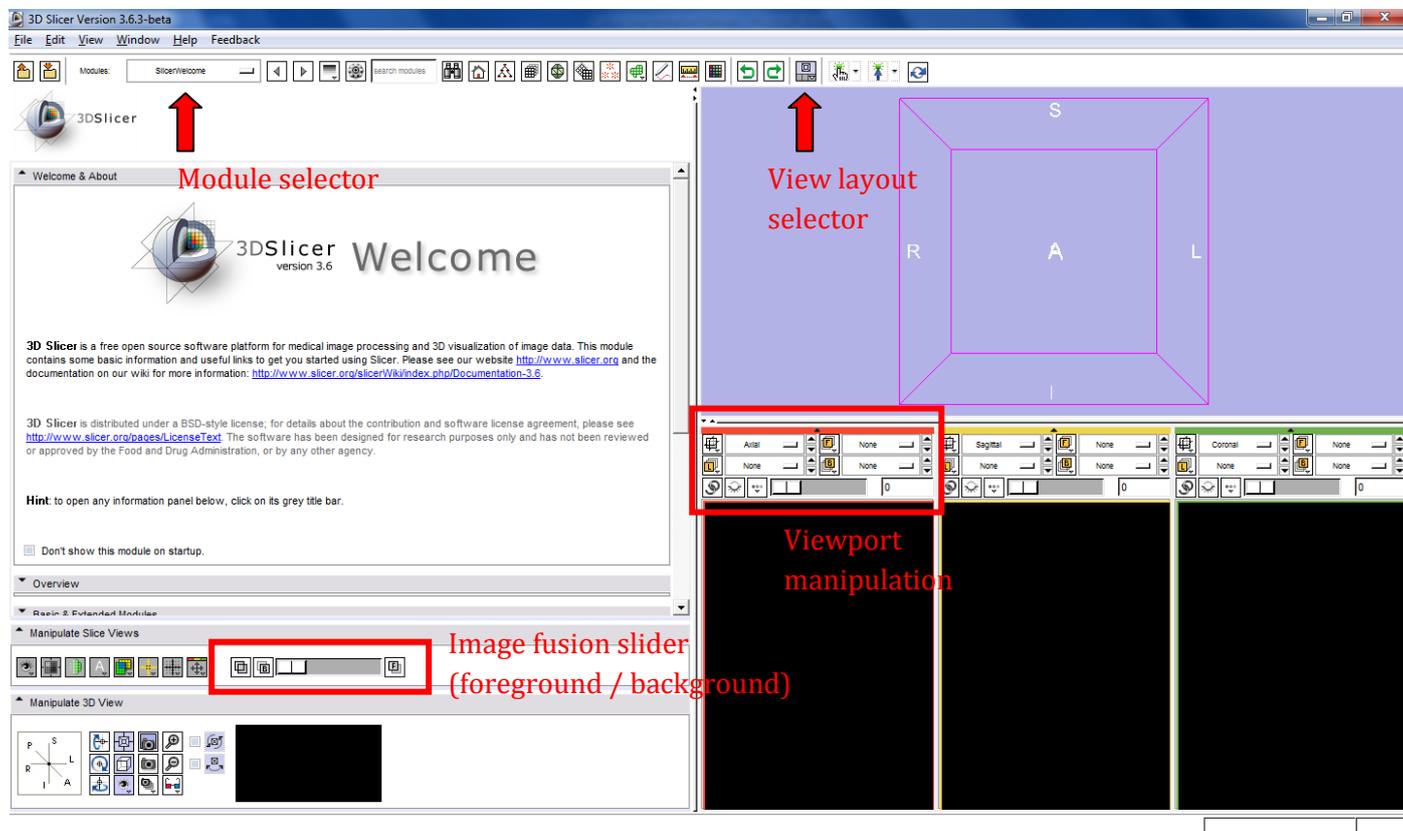
<http://www.slicer.org/pages/Special:SlicerDownloads>

It is recommended to download stable releases. This manual is based on the version 3.6.3. For further tutorials, users are kindly asked to visit the Slicer training pages:

[http://www.slicer.org/slicerWiki/index.php/Slicer\\_3.6:Training](http://www.slicer.org/slicerWiki/index.php/Slicer_3.6:Training)

## 1.2. Graphical interface

Slicer 3D is a state-of-the-art image processing, multi-modal visualization and neurosurgical planning toolkit. It comprises a collection of modules and plugins and an interface for scripting in Tcl or Python. Most of its functionality for segmentation purposes is accessible through a 2D interface. The left panel is the module parameter editor where most functions can be controlled; the right panel is the 2D / 3D display, while you can see an upper strip of tools and the bottom-left panel to manipulate the 3D display. As Slicer handles multimodal image fusions, the entire logic is based on loading multiple radiological volumes into one single “scene”.

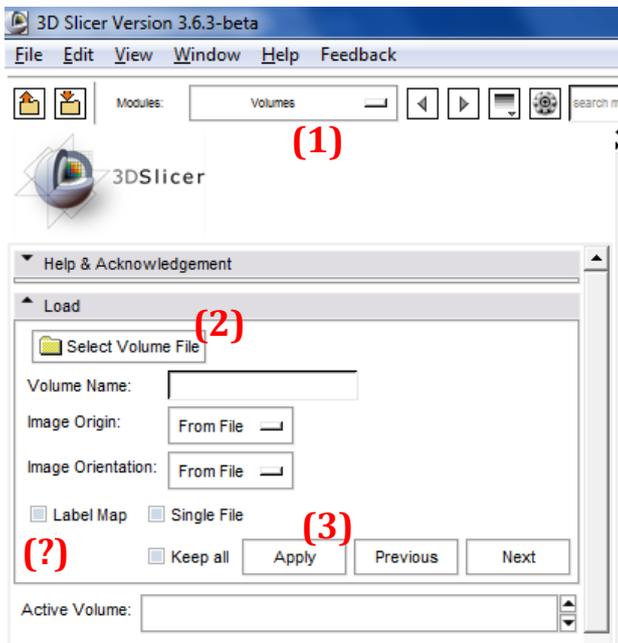


Slicer 3D interface. The basic controls for setting up an image segmentation workspace are marked.

### 1.3. Volumes (loading, saving)

Slicer handles a vast variety of image formats from standard DICOM to NIFTI, Analyze and the .nrrd or raw formats. Most image processing tools use NIFTI, however, for the BRATS workshop, the Meta format is used (\*.mha extension).

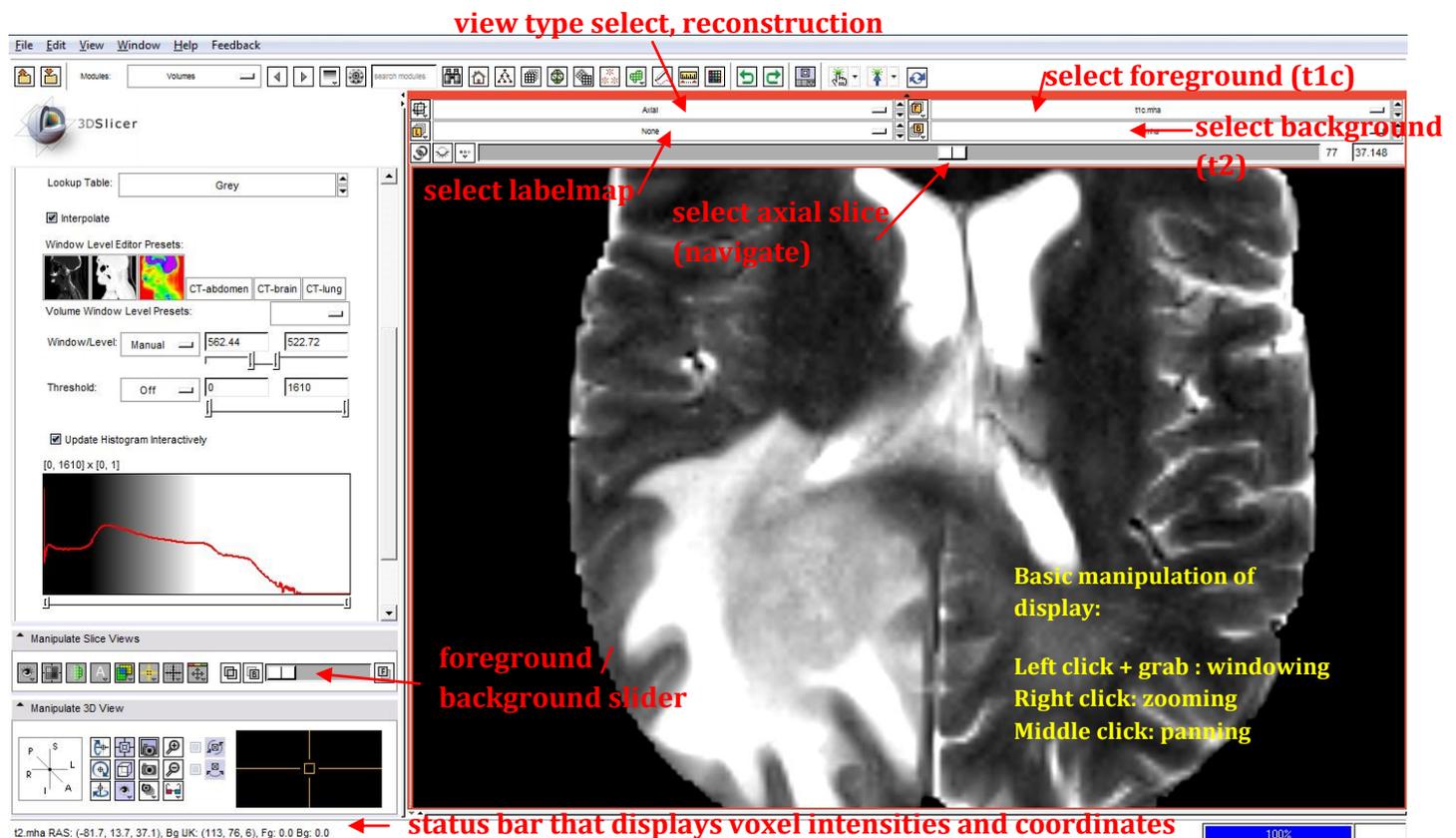
In one scene, Slicer can handle many objects, such as radiological images (=Volumes), labeled images (=Labelmaps), 3D triangulated meshes (=Models), markers (=fiducials) or others like tractography paths etc. Generally, one 2D view handles 3 images in parallel, a foreground (marked with an icon F), a background (B) and a labelmap annotation which is overlaid on the top and displayed in color code or outlines.



Let's load two images from a tumor segmentation study, T1-contrast and T2 MRI. Click on **File / Add Volume**. Alternatively, you can use the **Modules: / Volumes / Select Volume File – Apply** route. If you open radiological (grayscale) images, let the selector as it is, if you are opening annotated labelmaps, tick the “**Label Map**” button.

When you have opened a volume, you can check it at the **Modules / Data** module where all the scene's elements are displayed.

When performing 2D image segmentations, it is recommended to switch to a 2D only (e.g. axial) view. It should look like this:



## Saving files

Everything you do in Slicer is only stored in the memory, no auto-save option exists. You have to save everything manually. Like in every software, sometimes memory leaks and bugs can appear which would cause you big trouble by Slicer instantly exiting. Therefore it is nice to save the labelmaps through the major steps of the segmentation process. Saving is done by using the [File / Save](#) menu and the pop-up window. Here you click each volume you want to save, select its format and give a filename and a path. Note that by default, everything is saved in the Slicer home directory; this has to be changed for each file manually!

### 1.4. Basic manipulations

So, after you have successfully loaded all the volumes you need for segmentation, it is necessary to properly set the display properties. We advise to select a 2D only axial viewport (viewport layout change icon in the upper menu row). Then, you can set the foreground and background volumes to display. Please note that segmentation will be done in the labelmap, the fg / bg display is only for visualization. At this point, there is no need to filter or manipulate the original images.

The windowing function can either be set by clicking and grabbing in the 2D view, or you can use the [Volumes](#) module, where other properties, such as the palette can be modified.

You can either navigate using the slider or by the mouse wheel, or using the left/right arrows on your keyboard. When performing manual segmentations fast, the keyboard becomes especially handy. Please also note that the slice position is displayed in absolute slice number and in world (mm) position as well.

## 2. Segmentation in general

### 2.1. Using the Editor module

The [Editor](#) is the module where basic manual and semi-automatic segmentation tasks can be performed. It is very important to note the basic concept of Slicer's labelmaps: each labelmap is an individual voxelized image, which can contain a discrete label number per voxel. So, you can mark various compartments of the tumor with different colors/values, however, they cannot overlap. A labelmap image is saved as an individual 3D file. It has the same dimensions as its master volume. When working with datasets where images were re-sampled to an identical 1mm iso-voxel space, you don't have to worry about the labelmap parameters. In other cases, you have to create a new labelmap for each image.

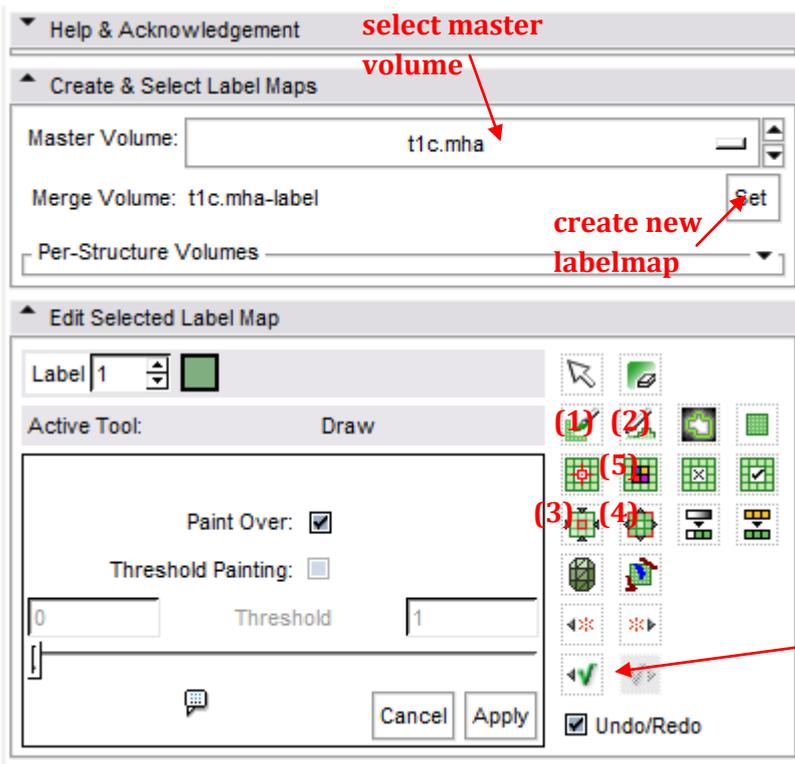
The Editor is found in the [Modules / Editor](#). When you open it up for the first time, it asks for an initial grayscale image to be segmented. Labelmaps cannot be created without a grayscale (radiological) volume; they are required for Slicer to set the dimensionality and other image parameters like voxel sizes etc.

Let's click on [Apply](#) when it asks for the color palette. Then, you select the [Master volume](#) of which Slicer would take the labelmaps parameters. Let it be t1c, our T1 image. As you see, it instantly created a new labelmap, called t1c.mha-label. You can select it in the viewport via the zone near the small L icon. Always only 1 labelmap is displayed.

When segmenting anything, the following logic should be used:

1. Select the proper Master volume and the merged (labelmap volume) to manipulate
2. Select the label color (the value which it would assign to the voxels)
3. Use a tool
4. Click apply or press enter to apply the current segmentation to the labelmap

At this point, you would need the following tools in the Editor:



**1. Paint** (like a paintbrush with n-voxel diameter).

1/a. paint with threshold painting is very useful.

**2. Draw** (thin free-hand outlines)

**3. Erode tool** (shrinks the label and erases small islands)

**4. Dilate tool** (dilates all voxels to the neighbors)

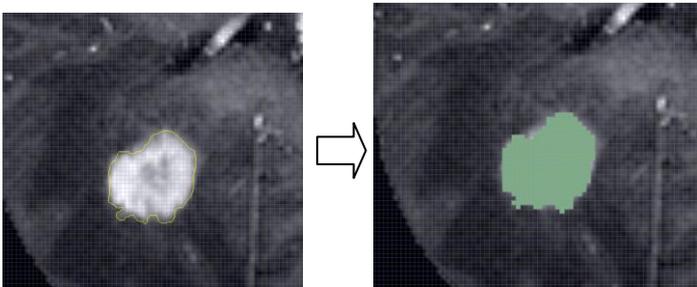
**5. Change island.**

Note that there is undo functionality in the editor and each segmentation task can be cancelled.

## 2.2. Morphometric operations and segmentation tools

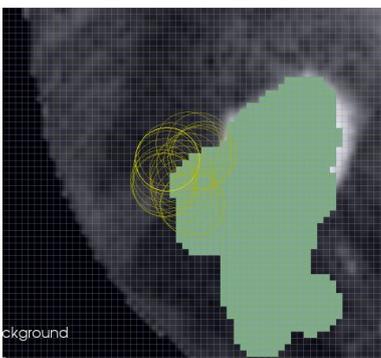
In this paragraph, we will go through the very basic manual and semi-automatic segmentation tools in the Editor module. The simplest are the draw and paint functions.

### Draw



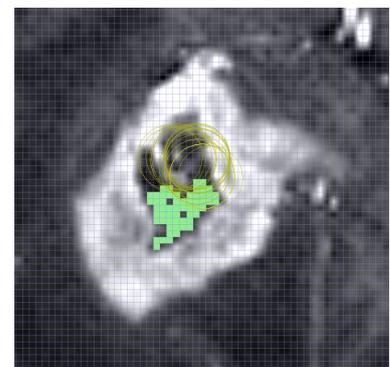
Drawing is a manual, slice-by-slice segmentation tool where you are outlining the region of interest. After the yellow border is ready, press enter to apply the drawing. You can undo the result or you can switch to label color "0" where you draw zero values and can correct or erase the segmentations.

### Paint and threshold painting



Normal painting

Paint uses a circular brush of N-voxel diameter. First select the diameter of the brush with the slider. A special option is **threshold painting** where you can practically use a large gross brush but only voxels within a signal intensity range will be segmented. If you put your cursor on an MRI voxel, the current value is displayed in the bottom status row. This is very handy when you have to delineate, for instance, contrast enhancing small spots or necrotic regions.



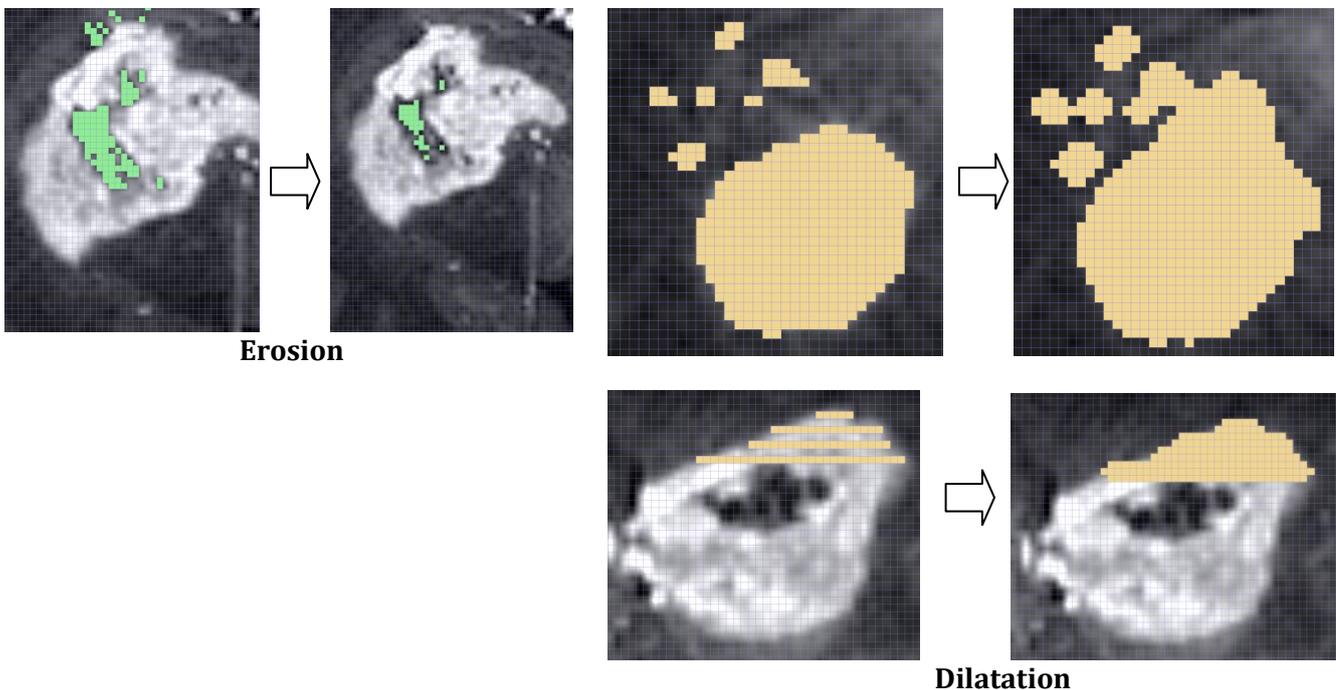
Threshold painting necrotic areas (upper threshold of 300)

## Erode

Erode and dilate are related algorithms. They shrink or expand the currently segmented voxels. Erode has an important implication: when you erode with a  $4 \times 4$  kernel, all small islands will be deleted and performing dilatation will recover the original geometry without the islands. Please note that erode and dilate can only be performed on one labelmap color at one time. Additionally, the eroded areas are filled up by either zero or you can choose a labelmap color. By default, erode and dilate are performed in 3D. If you want to switch to 2D, you have to change [Scope: all](#) to [Scope: visible](#).

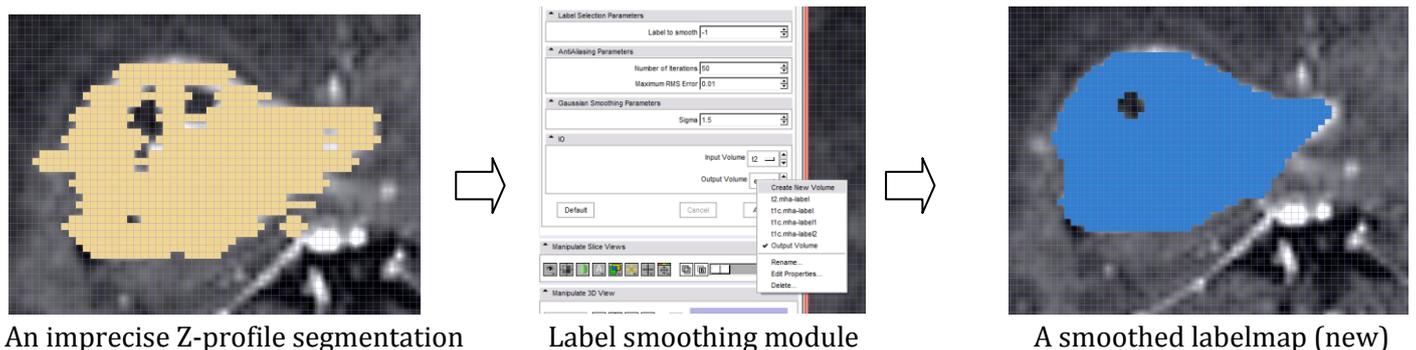
## Dilate

Dilate is the opposite of erode. Dilatation is very useful when you assume that the differences in your labelmaps are not very different among neighboring slices. When delineating object with large Z scale, it is possible to only segment every 2<sup>nd</sup> or 3<sup>rd</sup> slice, and then perform Dilatation and Erosion to fill up these in 3D. After this, it is advisable to perform smoothing of the labelmap, as the Z profile of your segmentation will look zigzagged.



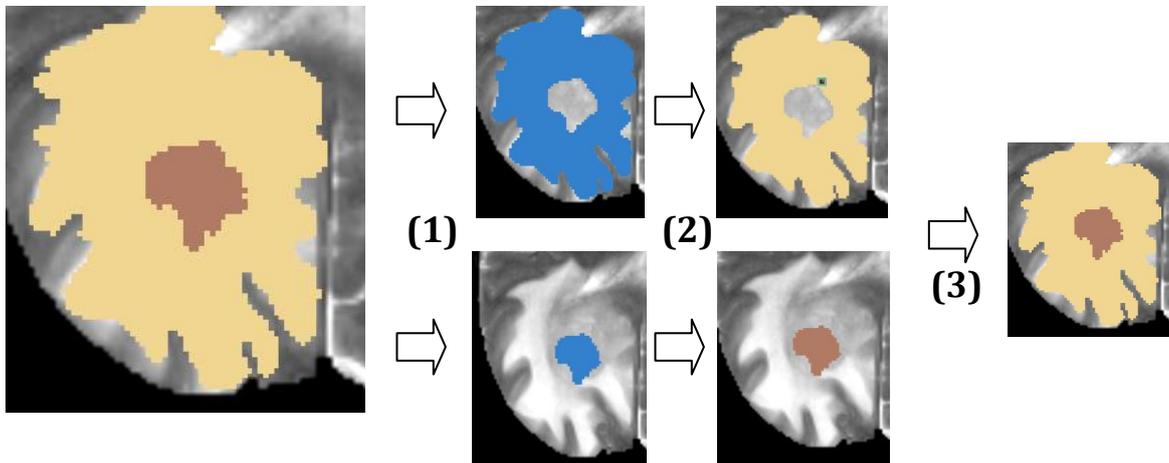
## Label map smoothing function

When delineating very large regions (i.e. brain edema affecting multiple lobes) and where the Z-detail of the delineation is not crucial, you may use hand segmentation of every 2<sup>nd</sup> or 3<sup>rd</sup> slice and interpolate in between. One workaround for interpolation is to use Dilatation + Erosion and then smoothing the labelmap. A smoothing filter is implemented in Slicer and is found in [Modules / Surface Models / Label map smoothing](#). An important parameter is the sigma value of the Gaussian kernel of the smoothing function. You may set it to 1 – 1.2.



## Smoothing multiple labelmaps

Unfortunately the Label map smoothing module can only smooth one label value / color at one time; all the others will be ignored and deleted in the new resulting labelmap. To smooth multiple values (i.e. the tumor core and the edema separately), you need to change the [Label selection parameters / Label to smooth](#) the certain value. After that, you create a new labelmap image, named Output Volume – Output Volume1, etc. You can repeat this for all the label values, and then you can use [Filters / Image label combine](#) module where label A and B are combined to a new image called Output Label Map by default. This workaround is a bit time consuming, so therefore we suggest applying this to only the first two initial label categories.



The major steps are the following. You have to smooth each label value from an initial labelmap into two new, separate images (step 1). Then due to the fact that the algorithm replaces all label values with 1, you have to use the [Editor](#) and the [Change Island](#) or [Change labels](#) tool to replace the values to their original color (like in the illustrated image, step 2). Then you combine the two images with the “top” overwriting the “bottom” to a new labelmap with the [Image label combine](#) (step 3). Alternatively, you may delineate components separately and smooth them separately, as suggested by the work-flow in 3.9.

Label colors can be modified by using the [change island](#) tool by clicking inside “islands” – this is also useful when wholes or confluent regions have been left out of the segmentation. Please note that it works as “flood filling” in 3D, therefore waterproof labels are needed. However, in the [Editor](#), there is a possibility to just replace any label value with another one – [Change labels](#).

## 3. Tumor segmentation protocol

### 3.1. Image types used for segmentation

For tumor segmentation, we provide the following images. All images are co-registered to the T1 post-contrast image and resampled to 1 mm. However, the original acquisition parameters are heterogeneous.

**t1.mha** : T1-weighted, native image, sagittal or axial acquisitions, variable slice thickness from 1 to 5 mm.

**t1c.mha**: T1-weighted, post Gd image. Axial 3D acquisition, 1 mm isotropic voxel size.

**t2.mha**: T2-weighted image, axial 2D acquisition, 2-4 mm slice thickness.

**t2f.mha**: T2-weighted FLAIR image, axial or coronal or sagittal 2D acquisitions.

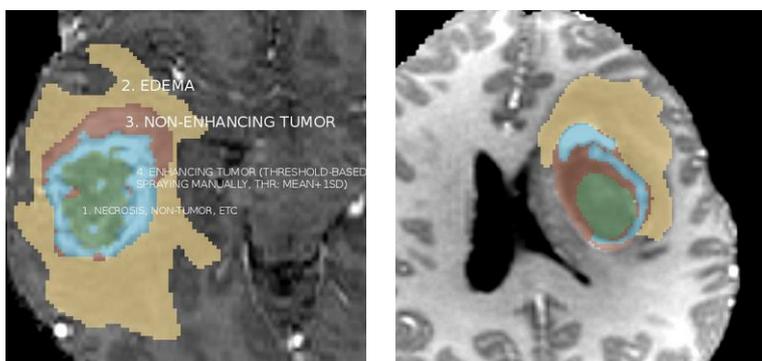
The native T1 images are sometimes taken from 3DT1 images and sometimes they are the fast spin echo T1 or even just the localizers, therefore they might not be suitable for segmentation. It is advisable to use the t1c and

t2 volumes. Note that the images were taken from multiple centers and multiple scanners, therefore image quality and acquisitions differ.

### 3.2. Label definitions

The latest effort is to define four types of intra-tumoral regions. Although the general problem of defining tumor borders in infiltrative tumors still exists, peculiar radiological criteria can be set to define such subdomains. These domains do not reflect strict biological correspondence and homogeneity but are rather placeholders for similarly-looking regions. For instance, the definition of the “active” tumor could simply be the high signal intensity regions on T1 Gd images. However, in high grade tumors, there are non-necrotic, non-cystic regions that do not enhance but they can be clearly separable from the surrounding edema. Another problem is the definition of tumor center in low grades. In such cases, a certain delimitation of the T2 hyperintense surrounding edema and the growing tumor is sometimes possible, but they do not enhance. Therefore we have decided to set the following four label definitions.

#### Overview



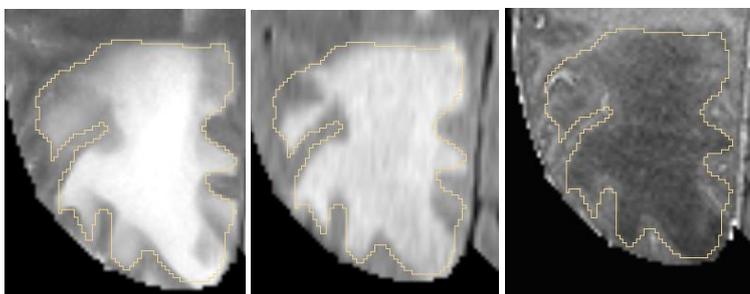
**Label 1.** Non-brain, non-tumor, necrosis, cyst, hemorrhage

**Label 2.** Surrounding edema

**Label 3.** Non-enhancing tumor part

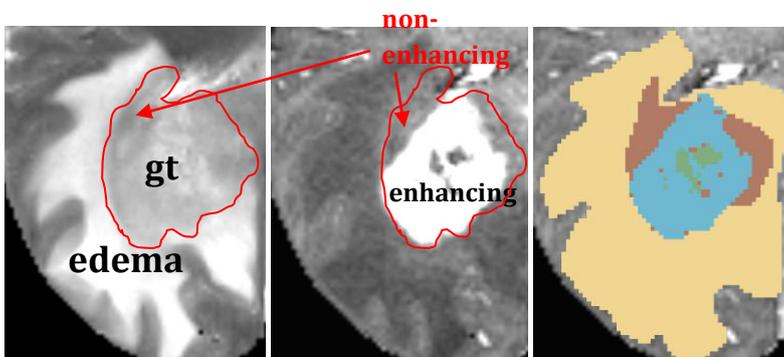
**Label 4.** Enhancing tumor core

#### Label 2. Edema surrounding the tumor



This is fairly easily defined on the T2 weighted images. Hyperintense regions with homogeneous signal distribution on T2 images or low signal on T1. We include mainly the white matter edema, i.e. the glove-like digitations of edematous white matter into the subcortex of the gyri are segmented. It is important to distinguish it from cystic regions or even the ventricles.

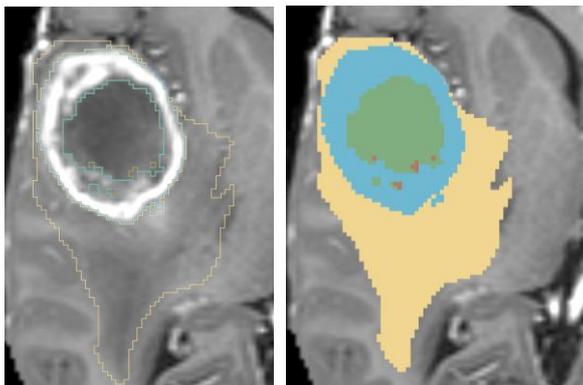
#### Label 3. Non-enhancing gross abnormality



It is possible to find such regions by the parallel viewing of T1 and T2 images. Some parts of the high-grade tumor do not enhance, but they are clearly distinguishable from the surrounding edema on T2 as they have lower signal intensity and heterogeneous texture, as in the Figure. In this case, edema is marked with yellow while non-enhancing tumor, based on T2 is marked with brown. Note that the enhancing core was also illustrated with blue.

Moreover, in low grade gliomas, this is the only category used for delineating tumor centers.

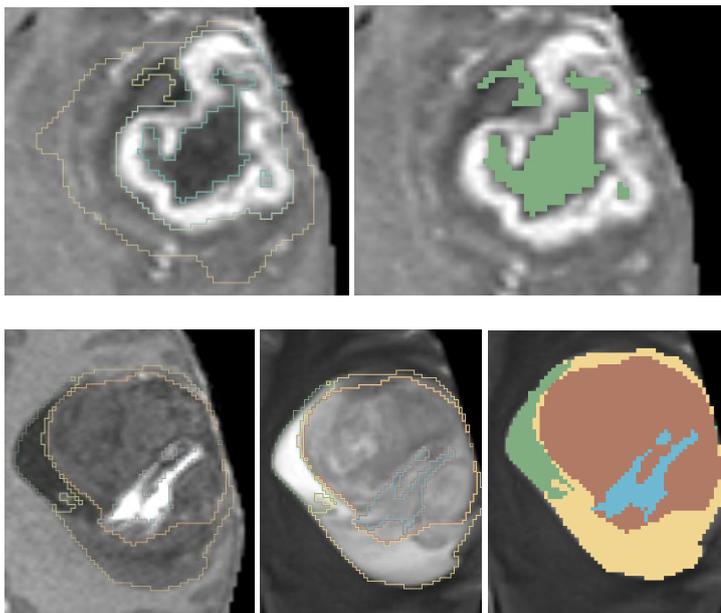
#### Label 4. Enhancing tumor core but not the necrotic center



This is a relatively easy definition, the enhancing regions within the gross tumor abnormality. We find it necessary to exclude the necrotic center out of this. The threshold for setting this should be done subjectively. Vessels should not be included, e.g. see the adjacent vessels running in the lateral sulcus in the Figure.

Color code: yellow: edema (2), blue: enhancing (4), green: necrotic center (1)

#### Label 1. Non-brain, non-tumor region including the necrotic center or necrocyst in high grade gliomas



This is a placeholder for the following categories. The necrotic center of high grades, within the enhancing rim is included, which sometimes appears cystic. Furthermore, large confluent regions of hemorrhage or non-identifiable tissue and post. op. cavity is included. We provide two examples, a typical necrosis (top images) and a fluid surrounding the tumor which is not the lateral ventricle or subarachnoid space (bottom images). Based on the T2 and FLAIR signal, it is obvious that this is fluid and not edema (case 4 in the BRATS database).

Color code: yellow: edema (2), brown: non-enhancing tumor (3), blue: enhancing tumor (4), green: necrotic center and fluid collections (1)

### 3.3. Proposed work-flow

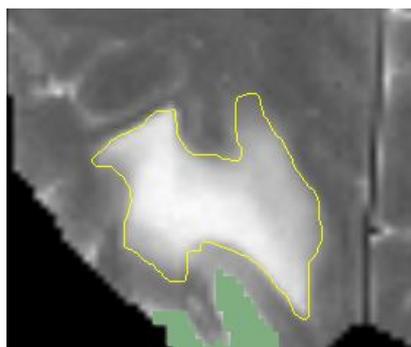
Using the above mentioned criteria, it is already possible to provide similar ground truth delineations. However, we suggest using the following logic when creating the labelmaps. This is mainly due to saving time. It is noteworthy that the various tissue elements (edema, non-enhancing, enhancing, necrosis) usually follow an outside – inside sequence therefore one should start from the outside and delineate regions within the previous labels. Due to this “Mozart Kugel” appearance, it is enough to always delineate what is outside and the internal borders should not be delineated, i.e. you should only draw a circle and not a torus, the remaining label types remain enclosed. We suggest total manual delineation of the edema and gross tumor while the enhancing spots and necrosis can be outlined using semi-automatic tools as well.

In most cases, it is enough to load the T1C and the T2 images. The following work-flow is demonstrated with the case HG0003.

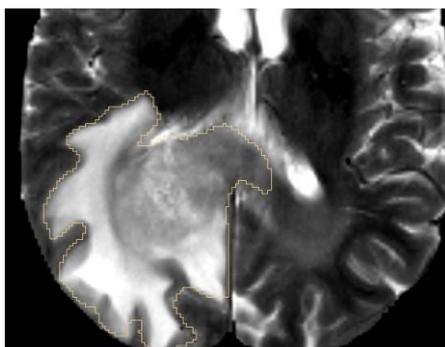
### 3.4. Segmenting the edema on T2 images

Load the T2 images. Create a new label map for the edema. Start from superior. As edema is usually very voluminous and its shape is relatively smooth, it is enough to delineate every 3<sup>rd</sup> slices and use interpolation tricks to fill the labelmap up. Hence after each drawing, use the cursor left to navigate inferiorly. After drawing these slices, use the Editor’s dilatation and erosion to fill the gaps between the axial slices. We suggest using a

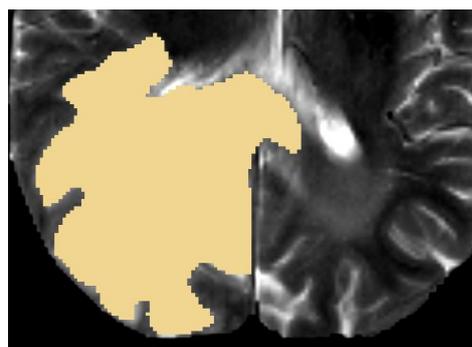
smoothing filter with a Gaussian kernel, sigma 1.0 after that to smooth the zigzagged coronal profile. Remember that this will result in a new labelmap.



Delineating edema

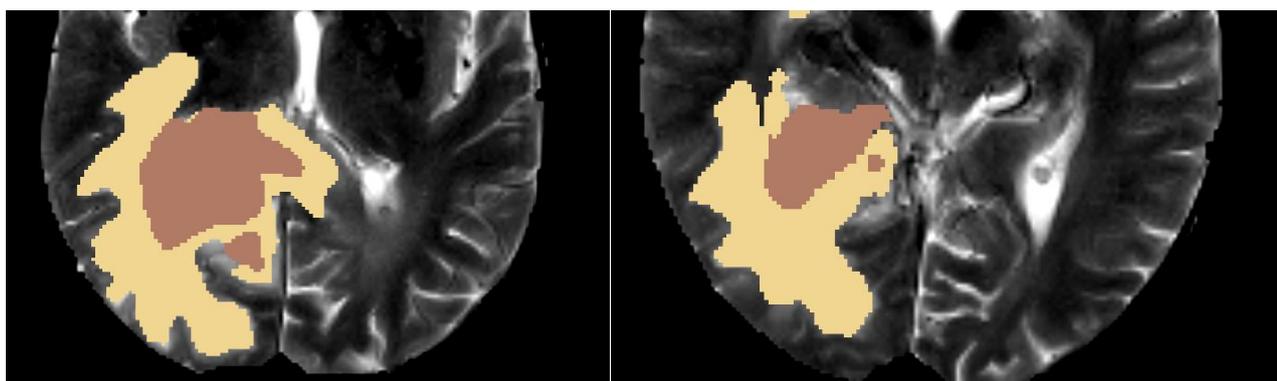


Edema label should enclose all the next label areas inside, no need to draw very concave labels.



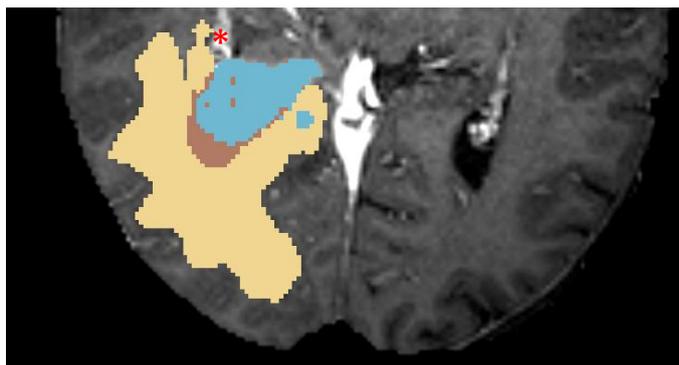
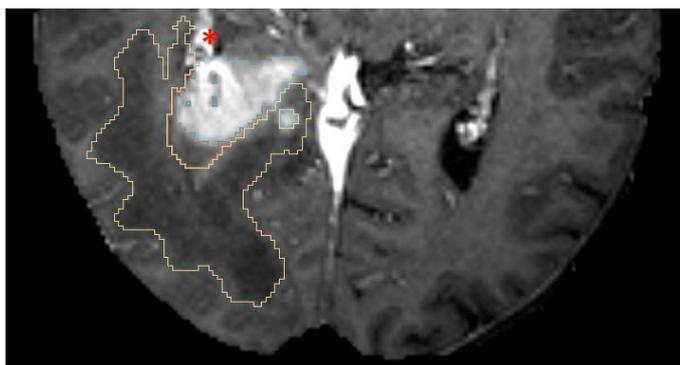
### 3.5. Segmenting the gross tumor outline

Create a new labelmap. Sometimes this category can be skipped, but as illustrated in 3.2., it is necessary to check if there are tumor-appearing non-enhancing regions. Either it exists or not, delineate the gross tumor borders on every 2<sup>nd</sup> slice. Use dilatation and erosion to fill the gaps and then use the Gaussian smoothing filter with sigma of 1.0. Now you have two separate labelmaps, one is the outside edema, smoothed; another one is the gross tumor, also smoothed. Before merging these two labels, make sure you set the correct label value (edema: 2, gross tumor: 3). After that, as suggested in 2.2., merge the two labelmaps together, with the gross tumor overwriting the edema so that it will be on the top. It is quite advisable to save this merged, 2-way segmentation. At this point, your delineation should look like this:



### 3.6. Segmenting the enhancing tumor regions

You can use the T1C image and the already delineated 2-way segmentation. To delineate the high grade gliomas enhancing rim, you may use a paint tool with a threshold set. Make sure you use the label 4 for doing this, and this will overwrite the underlying label values. This label at this point should enclose the necrosis inside. The delineation should look like this with 3 labels. The red asterisk is the chorioid plexus, not to be labeled.



### 3.7. Segmenting the necrotic areas

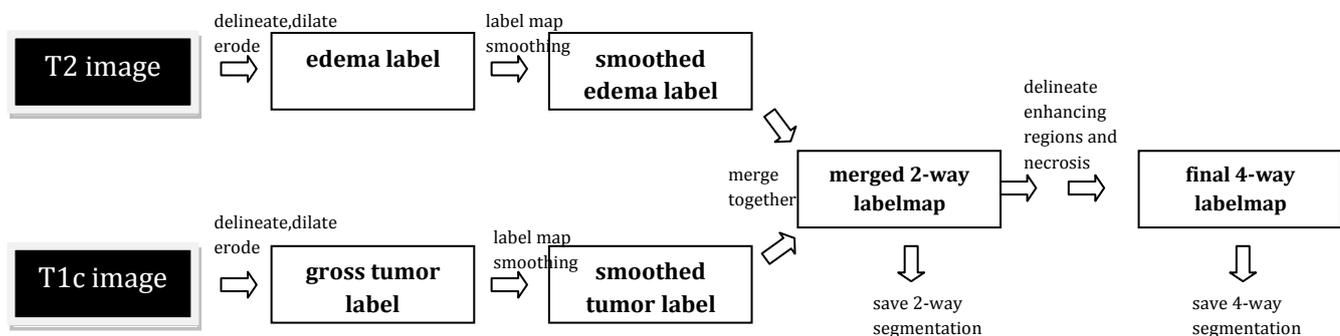
You should use the previous results and use a thresholded paint tool to mark the low intensity necrotic (and very tortuous) regions within the enhancing rim. Make sure to use the label 1. This label should be used for hemorrhages where you can identify such. It is very rare in the tumor dataset. You should save the resulting 4-way segmentation as a single .mha format labelmap.

### 3.8. Remarks on low grade gliomas

For low grade gliomas, the edema segmentation should be the same. After that, the label:2 should be used to separate the tumor mass from the clearly identifiable edema. This is either done by observing the texture or the intensity on T2 images. Label 1 and 4 should not be used. In small astrocytomas, there is no marked tumor center, here you may use the tumor label:2 only.

### 3.9. Summary of work-flow and specific remarks

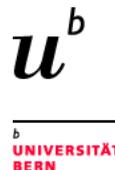
Although in the beginning the work-flow might seem complex, most of the time consuming steps can be learnt easily and the entire procedure should not take more than 20-30 minutes per case.



## 4. Credits

The Slicer 3D is developed by the Brigham and Women's Hospital Surgical Planning Lab, Harvard Medical School. For credits, see the Slicer webpage or the about menu. The tumor segmentation dataset the result of the concerted efforts of the following people and institutions:

**Bjoern Menze** (ETH Zürich), **András Jakab** (ETH Zürich / University of Debrecen), **Stefan Bauer** (University of Bern), **Mauricio Reyes** (University of Bern), **Marcel Prastawa** (University of Utah), **Koen Van Leemput** (Harvard Medical School, Technical University of Denmark).



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