CHAPTER 3: 3D Slicer extension

As a complementary work to the development and evaluation of the 3DWLS, a GUI extension that implements the algorithm has been created for 3DSlicer [22]. The extension communicates with another software package, the statistical parametric mapping (SPM) *(FIL, Wellcome Trust Centre for NeuroImaging, UCLhttp://www.fil.ion.ucl.ac.uk/spm/)*, to carry out the functionalities required -but not exclusive- to the image correction process i.e. coregistration, segmentation and normalization.

Both 3DSlicer and SPM software suites will be briefly described in the following section. All extension functionalities are described in the 'extension features' section.

3.1 Extension dependencies

- **3DSlicer**

3DSlicer is an open source software platform for the analysis, processing and visualization of medical images widely used in the research field. The 3DSlicer framework facilitates developers the integration of new features and algorithms to the platform in an easy way, as well as creating user interfaces that implements those features for their practical use.

This framework provides native features for importing and exporting data and medical images in multiple formats and for image visualization in 2D and 3D. As a whole, the included features allow visualizing the results obtained from the implemented algorithms, evaluating their performance and introduce any required modifications easily.

The implemented extension makes use of the importation, exportation and visualization features (built on VTK and MRML libraries) as well as on the GUI widgets (built on Qt and CTK libraries) included in the 3DSlicer core. 3DSlicer provides Python wrappers for this features and the extension has been programmed in Python as a scripted loadable module.

- **SPM**

The SPM software is an open source MATLAB collection of functions for the spatial processing and statistical analysis of brain neuroimaging data (PET, fMRI).

The extension makes use of the spatial pre-processing (coregistration, segmentation and normalization) functions provided by SPM v.12. It was decided to use the SPM12 functions instead of the ones available in 3DSlicer because they are currently one of the gold standards for performing the spatial processing over brain images and are extensively used by the research community.

The extension implements an interface for communicating with the SPM MATLAB routines. This communication is based on the generation of batch script text files loadable by SPM and the execution of the batch scripts by a standalone version of SPM (available for download upon request) via a system terminal command. The SPM standalone version is a version of the SPM toolbox that has been compiled by the MATLAB compiler runtime (MCR), which is freely downloadable from the MATLAB webpage. Therefore, the extension does not require a full MATLAB installation to work.

3.2 Features description

The developed extension includes the following functionalities:

➢ **Importation and visualization of the ASL and anatomical images**
➢ Interaction with SPM software package for image **spatial processing**
➢ Optional **importation of an alternative image for** obtaining the **coregistration** transformation
➢ Optional **importation of a label image for computing PVC independently** for each of the labeled regions.
➢ **Regression kernel size selection** as well as **weighting type selection**
➢ **Normalization and smoothing** (by VTK library) **of the PVC results** for future group comparisons.
➢ **Exportation and visualization of the PVC results**.

Fig. 3.1 complete view of the 3DSlicer extension GUI

Importation and visualization of ASL and anatomical images.

The minimum input required for computing the PVC is the ASL image to be corrected and a T1-weighted anatomical high resolution image of the same subject. Currently, the only supported image format is .nii format.

The images are loaded by introducing their file paths in their corresponding file path selectors. The introduction can be done both manually by typing the complete path through the keyboard or by exploring and opening the path in the file explorer window that pops up when clicking in the (…) button. Once a proper file path has been introduced, the corresponding .nii image is automatically loaded and displayed in the 3DSlicer visualization area.

ASL image volume file: lzheimer/suj205/suj205_ASL.nii ▾ | ...

Anatomical MRI image volume file: Alzheimer/suj205/suj205_T1.nii ▾ | ...
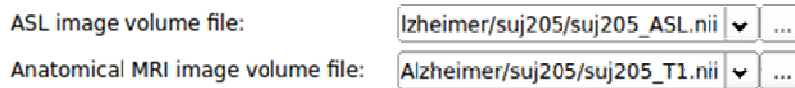
Fig.3.2 image importation widget and example

Image spatial processing

The 3DWLS algorithm requires having the tissue probability maps to estimate the partial GM, WM and CSF intensity contributions to the CBF image. These tissue probability maps are obtained through the coregistration and later segmentation of the anatomical image.

As previously said, both processing steps are conducted through SPM. During execution, the extension builds a new batch file from a template batch text file (contained in the extension folder) including the proper code lines with the paths to the current ASL and anatomical images previously imported. This final batch file is executed by sending a system terminal command that calls SPM and MCR over the file.

The user must introduce the paths to the SPM standalone and MCR directories in the system. This introduction only needs to be done once. The extension generates or modifies a text file contained in the extension folder that stores and imports these paths each time the extension is loaded in 3DSlicer.

- **Coregistration**

Image coregistration stands for the spatial alignment of two or more images belonging to the same or different subjects (intra-inter subject) and to the same or different image modality (intra and inter modality). The coregistration process consists in finding a suitable image transformation (rotation, scaling, translation...) which minimizes a cost function (sum of squared differences, correlation, mutual information...) related to the difference between the images after applying the transformation. Depending on whether the coregistration is intra or inter modality a proper cost function must be chosen. Through coregistration, the anatomical image is aligned and downsampled (to

the same size as the ASL image) to obtain a new anatomical image that overlaps to the ASL image.

- **Segmentation**

Image tissue segmentation refers to the classification and separation of the tissue captured in an anatomical image. In the case of brain images, segmentation refers to the classification of brain tissue into GM, WM, CSF and other tissues like bone. Although there are many segmentation approaches, the method implemented in SPM is based on the alignment of the anatomical image to an already classified template image for obtaining the prior probability of the voxel to contain GM, WM or CSF tissues. These prior probabilities are combined with the voxel information to obtain the tissue classification. By segmenting the coregistered anatomical image, the required tissue probability maps P_{gm}, P_{wm} and P_{csf}, are obtained.

The results from the coregistration and segmentation, that is, the coregistered anatomical volume and the three segmentation volumes for GM, WM and CSF tissues, are saved in .nii format inside the output folder specified.

Alternative coregistration

The extension allows the user importing an additional image volume (like a proton density image) for calculating the coregistration transformation to the T1 weighted anatomical image.

This coregistration transformation is later applied over the ASL image so the alternative image volume must be already in alignment to the imported ASL image and have the same matrix size.

Use an alternative image volume for anatomical MRI coreg + reslice: ☐
Alternative image volume file:
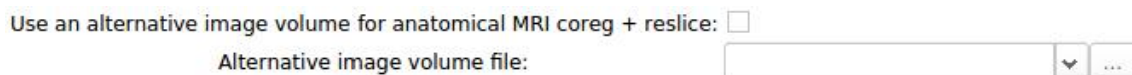
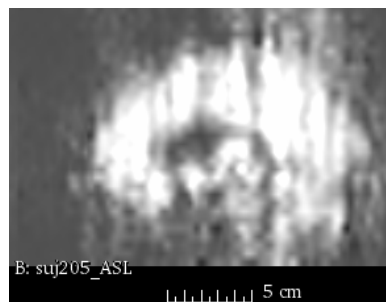*Fig. 3.3 alternative image importation widget*

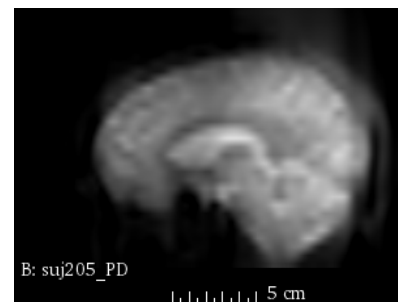To apply this functionality, the option must be checked and a proper image must be introduced.

This feature is sometimes useful for improving the coregistration result, as the ASL image is very noisy and provides a poor anatomical detail.

Fig. 3.4 T1 image (sagittal slice)   *Fig. 3.5 ASL image (sagittal slice)*   *Fig. 3.6 PD image (sagittal slice)*

Independent PVC per brain regions

The extension allows the user importing a label image volume containing a parcellation of specific brain regions. In a label image, voxel intensities represent region classification, i.e all voxels belonging to the same region will share the same intensity value. The regions are interpreted from the intensity values using a look-up table (LUT). As a default, the extension loads (from a text file in the extension folder) the LUT characteristic to Freesurfer, which is one of the most used software packages to estimate brain parcellation. Nevertheless any custom LUT defined by the user can be imported, provided it is given in a text file with a proper format readable by 3DSlicer.
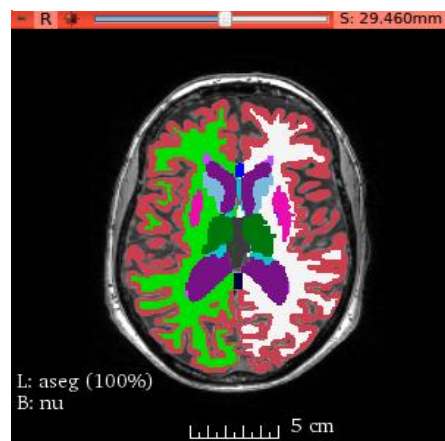

Fig. 3.7 *label image and LUT importation widget*

Once loaded, the label image volume is displayed in the 3DSlicer visualization area with the colors and labels defined by the selected LUT file.

Fig. 3.8 *label image displayed over a T1 anatomical image*

If a label image is imported, it will also be coregistered to the ASL image so the coregistered label image will be also in alignment to the tissue probability maps. If this option is checked and a proper label image is introduced, the PVC will be done independently for each of the labeled regions.

For each region, a mask is applied to the ASL image to preserve only the voxels corresponding to that region and then the PVC is run. The final GM, WM and CSF corrected volumes result from the integration of the analogous individual maps for all the regions into single image volumes.

In addition, by applying this functionality, the extension dumps specific data(mean GM, WM and CSF perfusion and total mean perfusion)relative to each of these regions in the output data file (described later).

This feature was included taking into account an hypothesis by which the perfusion uniformity assumption will hold more likely along voxels of the same region rather than for voxels close in distance but belonging to different cerebral regions.

One drawback of this feature is that, as PVC runs over it region at a time, the computing time is longer than when applying the PVC to the whole image with a single shot.

Regression kernel size and weighting type selection

The user can select the regression kernel $\vec{x}, \vec{y}$ and $\vec{z}$ size (row, column and slice directions respectively) in pixels in increments of two, starting from the lowest size (3x3x1). The real size in mm of the selected kernel is displayed below the kernel size selector and it is calculated from the voxel size information contained in the ASL image .nii file.

The user can also select between the distance weighting types discussed before: inverse of the distance, inverse exponential of the distance and Gaussian of the distance.

Kernel size in pixels (x,y,z):	3	3	3
...in mm (x,y,z):	5.62 x 5.62 x 12.00		
Choose weighting kernel type:	Exponential		

Fig. 3.9 kernel size and weighting type selection widgets

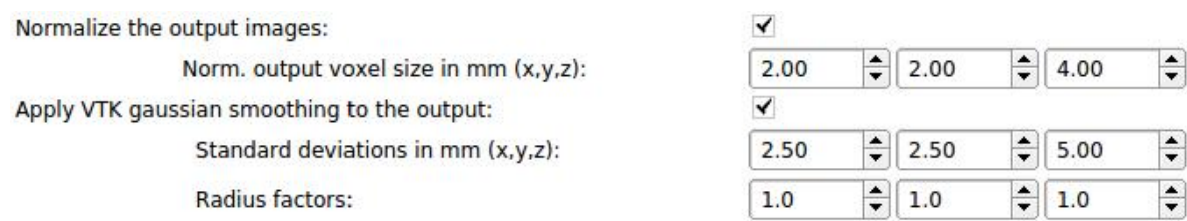### Normalization and smoothing of PVC results

Normalization consists in anon-rigid transformation by which an image is deformed commonly to match the shape of a certain image template. Normalization is done via SPM through a batch file executed through a terminal command, like coregistration and segmentation steps. The segmentation step requires a previous normalization of the coregistered anatomical image to a template. This normalization transformation is stored and used for the normalization of the PVC output maps, the anatomical map and the original ASL image, if the user has checked the normalization option. The user can also select the voxel size of the images resulting after normalization.

Image normalization is necessary when making a group comparison. Human brains have significant differences in shape and size between different subjects. Due to this fact, the functional images of each of these subjects must be deformed to match a common image template if a physiological feature (in our case, blood flow) over a region is to be compared between the subjects.
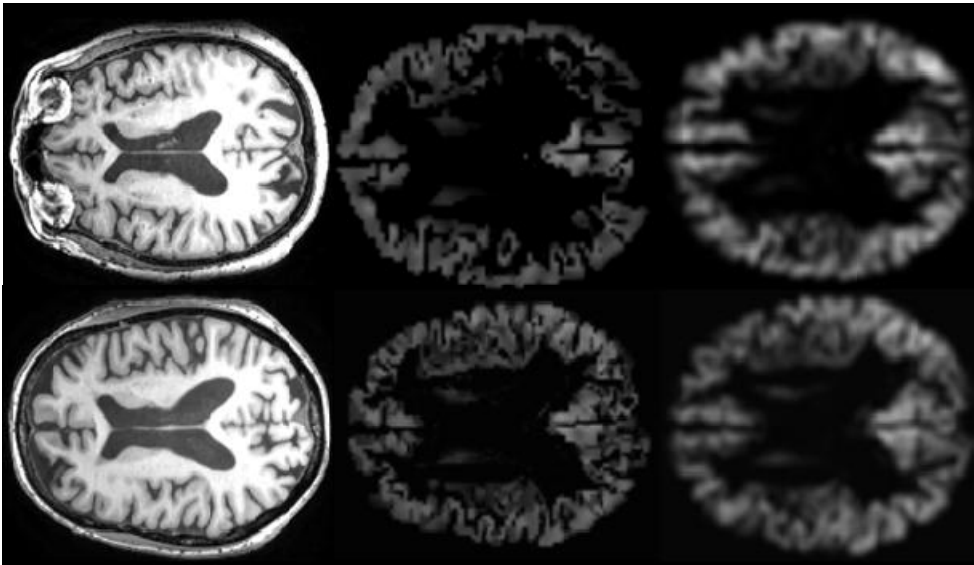
Image smoothing can also be useful in group comparisons by reducing the effect of both structural differences and random noise, although it also reduces the image spatial resolution. Smoothing is provided in the extension by making use of the Gaussian blurring function already implemented inside the VTK library, an open source

software package for image processing and visualization. The user can select the desired parameters of the VTK Gaussian smoothing, namely, the radius factor and the standard deviation of the Gaussian filter.

Normalize the output images:	✔					
Norm. output voxel size in mm (x,y,z):	2.00		2.00		4.00	
Apply VTK gaussian smoothing to the output:	✔					
Standard deviations in mm (x,y,z):	2.50		2.50		5.00	
Radius factors:	1.0		1.0		1.0	

Fig. 3.10 *normalization and smoothing widgets*

Fig. 3.11 *example of normalized output. Each row is a different subject. The columns from left to right represent subject anatomical image, subject GM perfusion after correction and norm. GM perfusion*

Together with the normalization template, the extension folder contains its corresponding label and tissue segmentation volumes. By selecting the normalization feature, both are coregistered to the corrected perfusion images and then stored in the output folder.

As normalization step is posterior to the correction, the template label volume does not influence the correction step, but is used for obtaining the mean perfusion values of each of the brain regions defined in the label map. These values are exported to the text data file for their comparison between different subjects.

Exportation and visualization of PVC results

By default, the extension creates the output folder inside the ASL image directory but the user can select any alternative directory.

Output directory:

Fig. 3.12 output folder selector widget

The images of interest resulting from the computation pipeline are loaded into the 3DSlicer scene for their visualization.

The extension exports the following data to the output folder:

- ➢ The individual perfusion maps for GM, WM and CSF resulting from PVC.
- ➢ The coregistered anatomical T1 image.
- ➢ The tissue probability maps resulting from segmentation
- ➢ The coregistered label volume, if label option is checked
- ➢ The normalized anatomical, segmentation and   perfusion   maps   if   the normalization option is checked
- ➢ A text data file containing the following information:
  -The paths to the imported files
  -The options and parameters selected by the user
  -Mean GM, WM and CSF intensity values for the whole image; and for each of the regions if label option was checked
  -The date and time at which the job execution was started and finished.

In the text file, the values are separated by single blank spaces and lines so that the information contained in the file is easily importable in calculus sheet software like Microsoft Excel or LibreOffice Calc.

3.3 Extension workflow diagram