Partial volume effect correction by Müller-Gärtner method (pvcPET)

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Requirements

MATLAB 2016 and better (tested in 2022a)

Download and install:

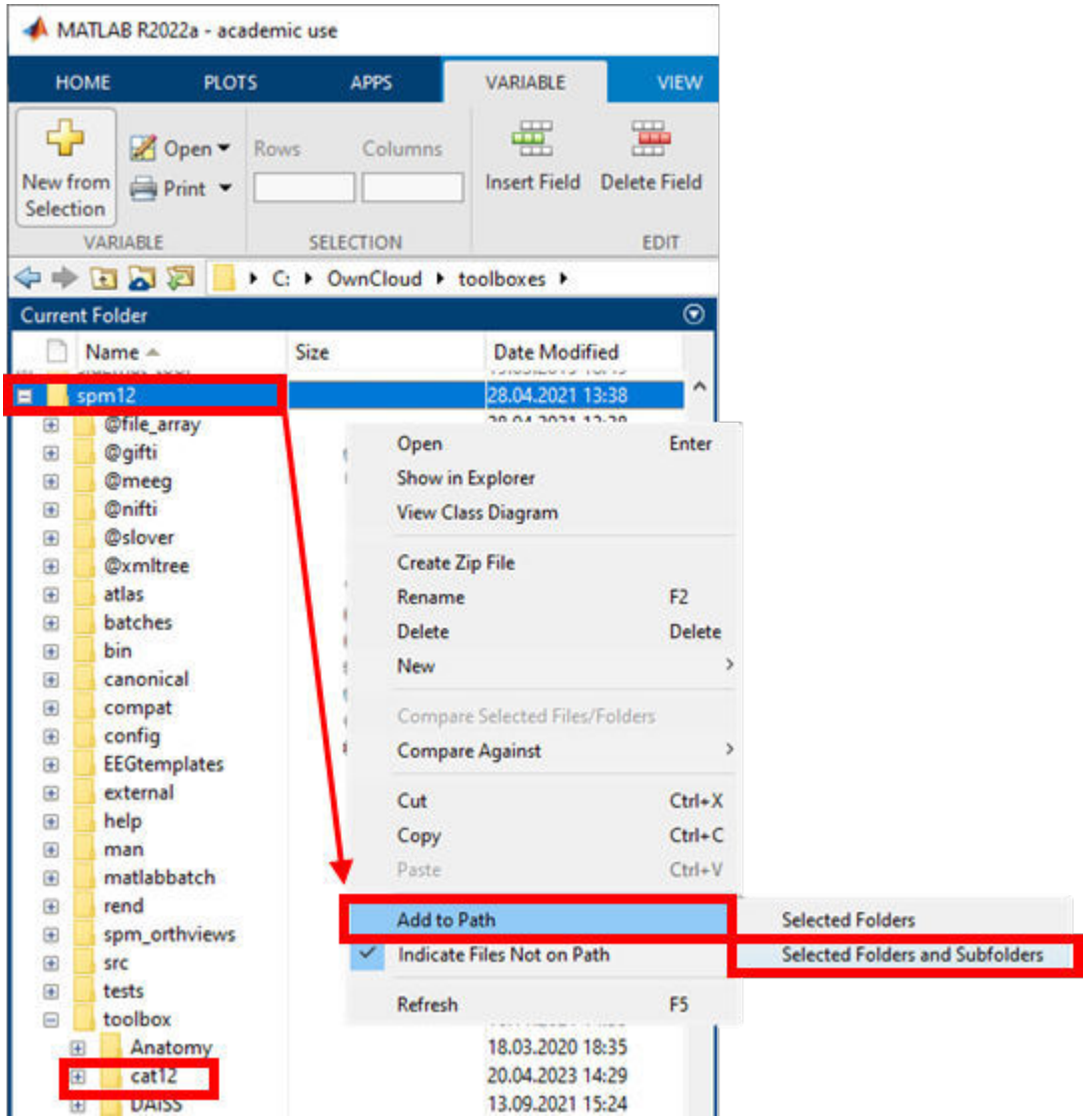
SPM12 toolbox [download]

CAT12 [download] and unpack to ...SPM12/toolbox/CAT12

or

SPM12+CAT12 [google drive]

Add to Path with subfolders:



Download and install external software (Windows, Linux, MacOS):

PETPVC 1.2.10 [download]

3D Slicer 5.2.2 [download]

Download sample data:

RAW data in Nifti formata (T1, T2, FLAIR, PET) [google drive] and unpack them to working directory, e.g., c:\pvcPET\...

Download processed data for skipping time-consuming steps of pipeline:

PROCESSED data (all future results) [google drive] and unpack them to working directory, e.g., c:\pvcPET\...

Final Slicer scene (future result) [google drive]

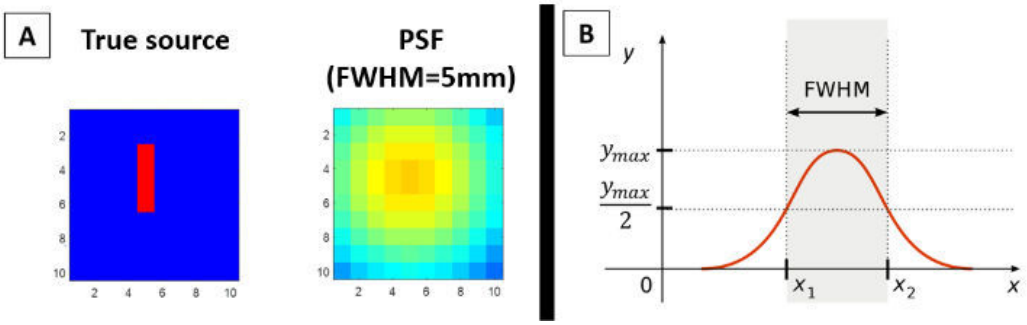
Download main live-script (*.mlx) and functions [google drive]

Introduction

Neuroimaging methods play an important role in presurgical examinations and localization of epileptogenic lesion. Magnetic resonance imaging (MRI) is a neuroimaging technique that is essential to detect structurally abnormal tissue and thus delineate the epileptogenic lesion. Positron emission tomography of 2-deoxy-2-[18F]fluoro-D-glucose radiotracer (FDG-PET) is a functional neuroimaging method that can also significantly contribute to the localization of the epileptogenic lesion. FDG-PET image visualizes the tissue metabolic activity associated with the consumption of glucose. The tissue of epileptogenic lesion often shows decreased metabolic activity (hypometabolism) and in the FDG-PET image it can be recognized as a region with hypointense signal.

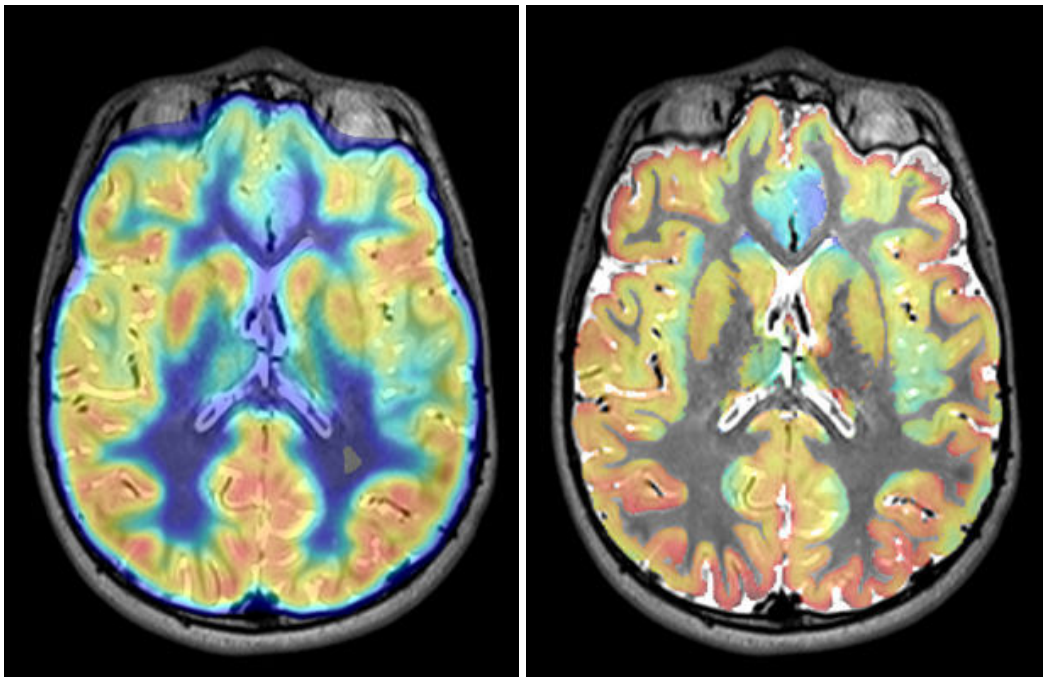
However, the hypometabolic lesions can be very subtle and their identification in the MRI and PET image might be difficult. One of the important effects that limits the use of FDG-PET for precise localization of the subtle hypometabolic lesions is the **low effective spatial resolution** which leads to blurring of the PET image. In comparison, effective resolution of modern 3T MRI is better than 1 mm, but PET effective resolution varies from 3 to 8 mm depends on PET scanner generation and mainly physical limitations. The signals emitted from neighbouring tissue mix together which results in **partial volume effect** (PVE). For example, naturally **metabolic grey matter** is mixed with **hypometabolic white matter** and other tissue, that leads to an underestimation of radiotracer activity in the cortex and blurring of tissue edges. This effect can lead to spurious hypometabolic regions, resulting in an increased amount of false-positive hypometabolic regions, and vice versa.

Partial volume effect can be compensated using **partial volume correction** (PVC) which can additionally increase the effective spatial resolution of the PET image. Various methods for partial volume correction have been proposed [cite]. One of the important inputs for partial volume correction methods is the full width at half maximum (FWHM) of the scanner point spread function (PSF), which defines how much point source is blurred.



Partial volume correction will be performed with Müller-Gärtner method [cite] using implementation from publicly available PETPVC toolbox [cite]. Müller-Gärtner method is one of the post-reconstruction methods for PVC, which performs correction of radiotracer activity for each voxel back to in the grey matter tissue segment. In summary, the technique refocuses PET activity to gray matter well defined in MRI.

PET over MRI-T2: **pvcPET over MRI-T2:**



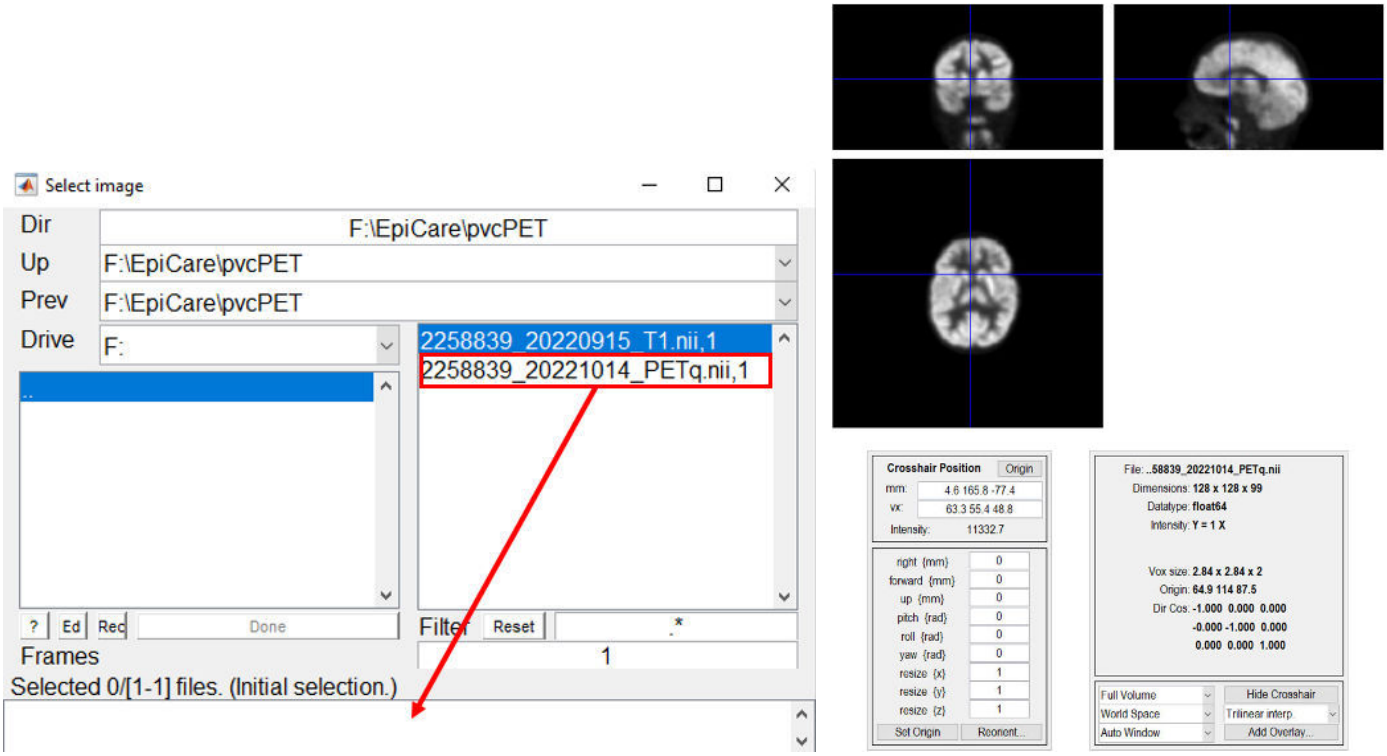
```
clc; close all; clear all;
```

1 Coregistration and resliceing

1.1 Initial checking

The images to coregistration can have the originator of world space far away from the centre of the head and the registration process cannot find starting point for fitting. Typically, the originator of MRI is close to the anterior commissure (AC). However, CT-PET sceners usually use variable origin, e.g., in sternum etc. We suppose that the reference (fixed) image will be MRI (T1) and we want to fit the PET image over MRI. Therefore, the origin of PET must be set manually.

```
spm_image() % run and select '2258839_20221014_PETq.nii'
```



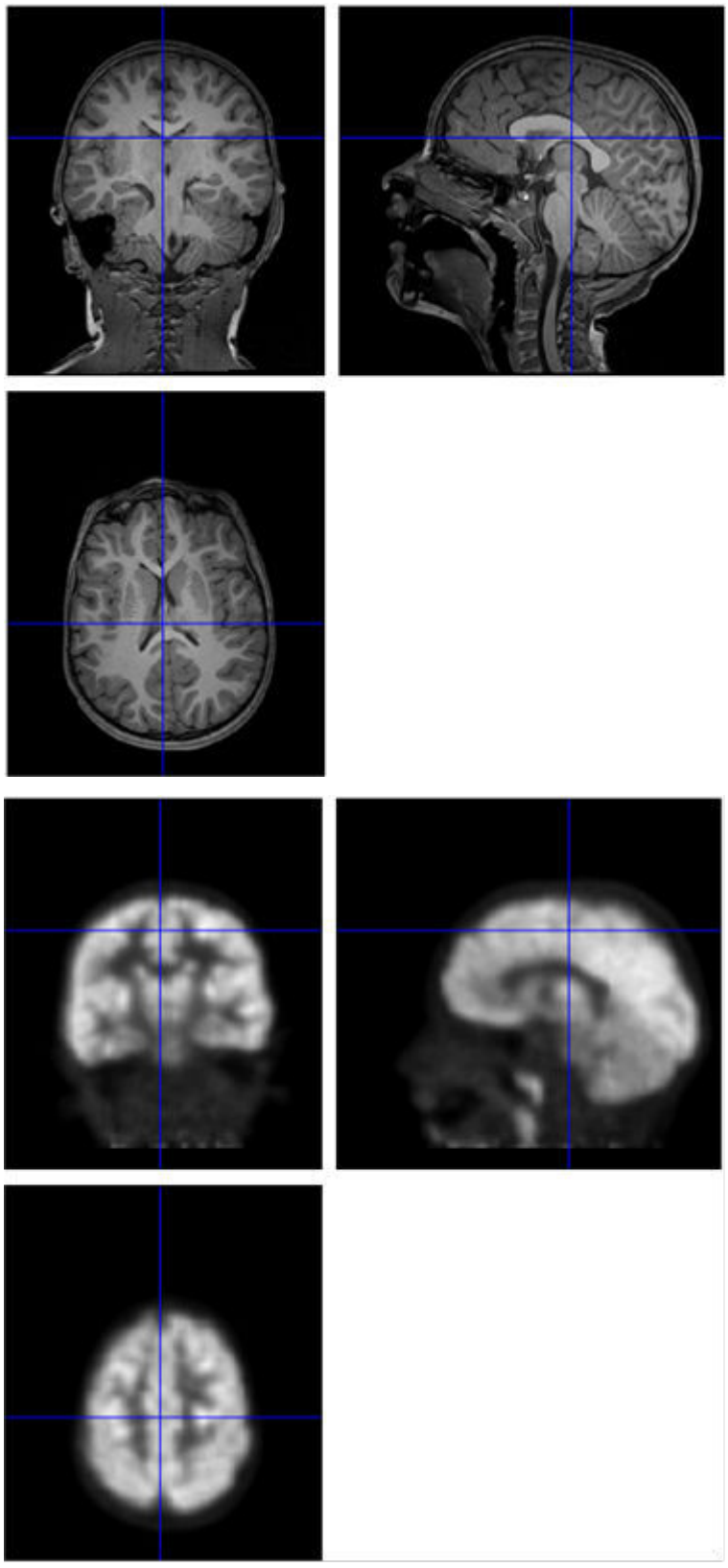
Find the appropriate position of AC and click on **Set Origin**. Save the new origin by clicking on **Reorient**, the selected file will be still PETq volume, confirm by the **Done** button. Video tutorial available at https://www.youtube.com/watch?v=AwNJAUKLhqY&t=185s

1.2 Check registration

```
mri_path = '2258839_20220915_T1.nii';
pet_path = '2258839_20221014_PETq.nii';
```

```
check_list(1).path = mri_path; % MRI path
check_list(2).path = pet_path; % PET path

spm_check_registration(check_list.path); % SPM multivolume viewer
```



You can see that both images (PET and MRI) are partially overlapped in the region of the brain (required). However, the images are not coregistered yet.

1.3 Coregistration and resliceing

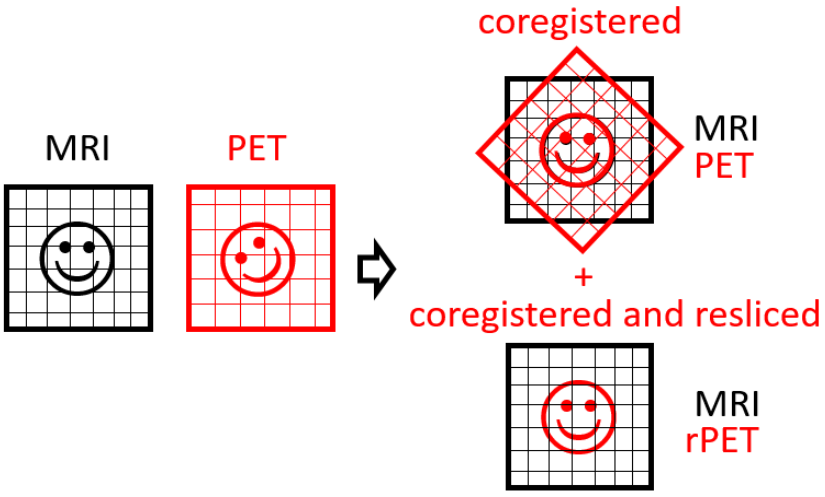
Data matrix is indexed by **IJK cordinates (data space)** which are transformed by **affine transformation** to **word space in millimeters** (typically to RAS or LPS, detailed later). Affine geometric transformation **T** allows translation, reflection, scale, rotation and shear of the data matrix for visualization. Transofrmation **T** contains all information about image: origin of word space, flipping, resolution, orientation and scanner gantry angle. Therefore, each 3D image is coposed from **data matrix and transformation matrix**.

$$\begin{bmatrix} R \\ A \\ S \\ 1 \end{bmatrix} = \mathbf{T} \cdot \begin{bmatrix} I \\ J \\ K \\ 1 \end{bmatrix}; \quad \mathbf{T} = \begin{bmatrix} T_{11} & T_{12} & T_{13} & T_{14} \\ T_{21} & T_{22} & T_{23} & T_{24} \\ T_{31} & T_{32} & T_{33} & T_{34} \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

For the common visualization of MRI and PET, the one of the images must be coregistered to another. MRI is usually selected as the fixed image and PET is the moving image. The algorithm finds rigid body transformation which modifies the transformation **T** of PET so that the both images overlap exactly. **This process is called coregistration**. In SPM-fmri corregistration is done by *Spatial pre-processing* module: Coregister (Estimate). Although the coregistered images (MRI+PET) correspond to each other in the world space, the data matrices are unchaged and still different.

Data matrices of moving image (PET) can be interpolated to mash grid of fixed image (MRI) - **resliced**. The both images then have the same orientation, same transformatin matrix and same size of data matrix. In SPM-fmri reslicing is done by *Spatial pre-processing* module: Coregister (Reslice). Usually, the resliced images are renamed with prefix 'r' (**rPET**).

Both previous steps are done by ***Spatial pre-processing* module: Coregister (Est & Res)**, schematicaly shown below:



As an alternative, it is possible to use SPM12 in the batch mode. The **batch code** is a piece of MATLAB code that can be included into an automatic data processing pipeline. The following batch script performs coregistration and reslicing of PET image to T1 weighted MRI image.

```
% show verbose windoes
try; ifig = spm('CreateIntWin','on'); end
try; gfig = spm_figure('Create','Graphics'); set(gfig,'Visible','on'); end
```

```
% co-registration job initialization
matlabbatch = {};
matlabbatch{1}.spm.spatial.coreg.estwrite.ref = {[mri_path ',1']}; % fix image (MRI)
matlabbatch{1}.spm.spatial.coreg.estwrite.source = {[pet_path ',1']}; % moving image (PET)
matlabbatch{1}.spm.spatial.coreg.estwrite.other = {''}; % default
matlabbatch{1}.spm.spatial.coreg.estwrite.eoptions.cost_fun = 'nmi'; % default
matlabbatch{1}.spm.spatial.coreg.estwrite.eoptions.sep = [4 2];  % default
matlabbatch{1}.spm.spatial.coreg.estwrite.eoptions.tol = ...
                  [0.02 0.02 0.02 0.001 0.001 0.001 0.01 0.01 0.01 0.001 0.001 0.001]; % defaul
matlabbatch{1}.spm.spatial.coreg.estwrite.eoptions.fwhm = [7 7]; % default
matlabbatch{1}.spm.spatial.coreg.estwrite.roptions.interp = 4; % default
matlabbatch{1}.spm.spatial.coreg.estwrite.roptions.wrap = [0 0 0]; % default
matlabbatch{1}.spm.spatial.coreg.estwrite.roptions.mask = 0; % default
matlabbatch{1}.spm.spatial.coreg.estwrite.roptions.prefix = 'r'; % prefix (rPET)

% run job
spm_jobman('run',matlabbatch(1)); % run 1st batch
```

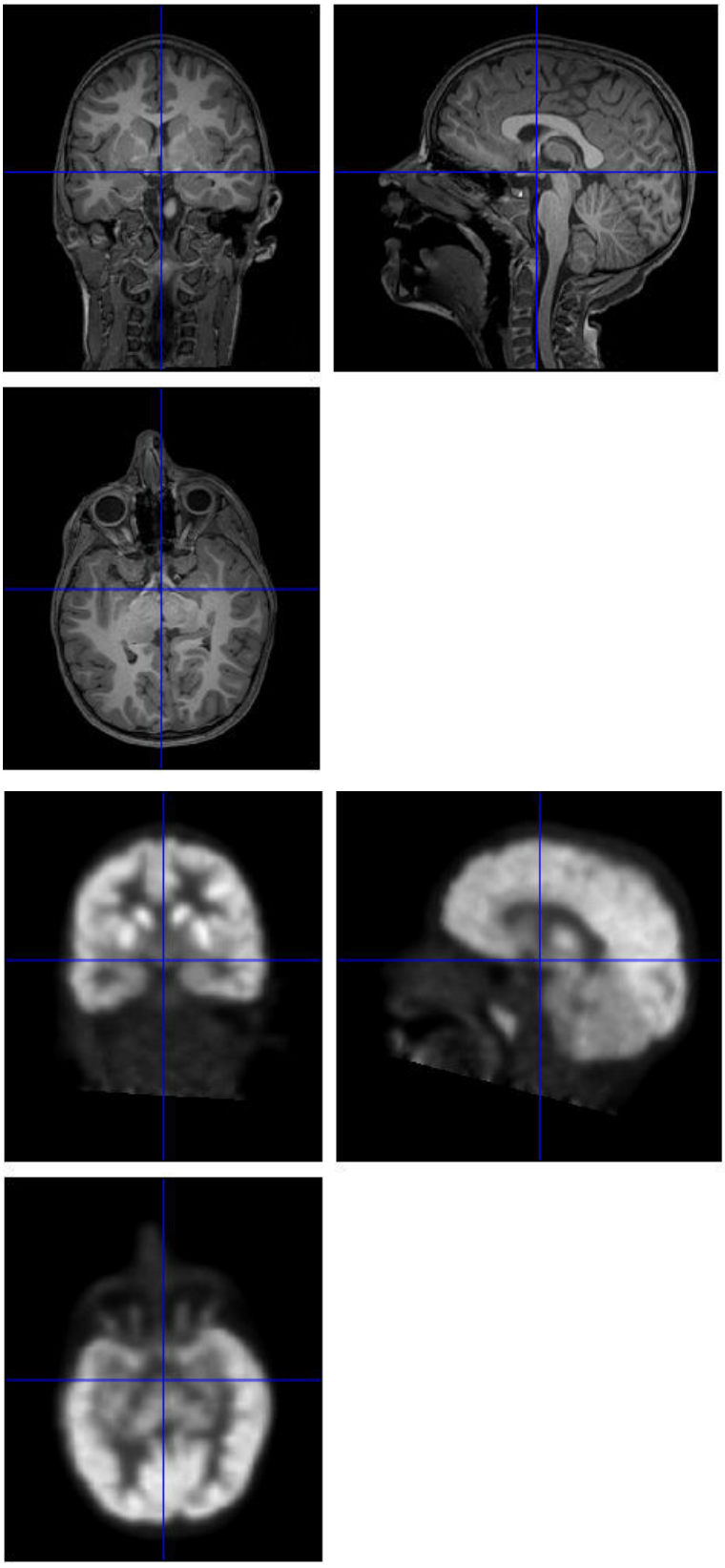
The batch code can be also directly generated from the GUI by selecting **View -> Show .m Code** as shown below. If interested, check SPM12 manual for further details: https://www.fil.ion.ucl.ac.uk/spm/doc/spm12_manual.pdf

WARNING: estimation process change orientation (affine transform) in moving image

1.4 Check registration

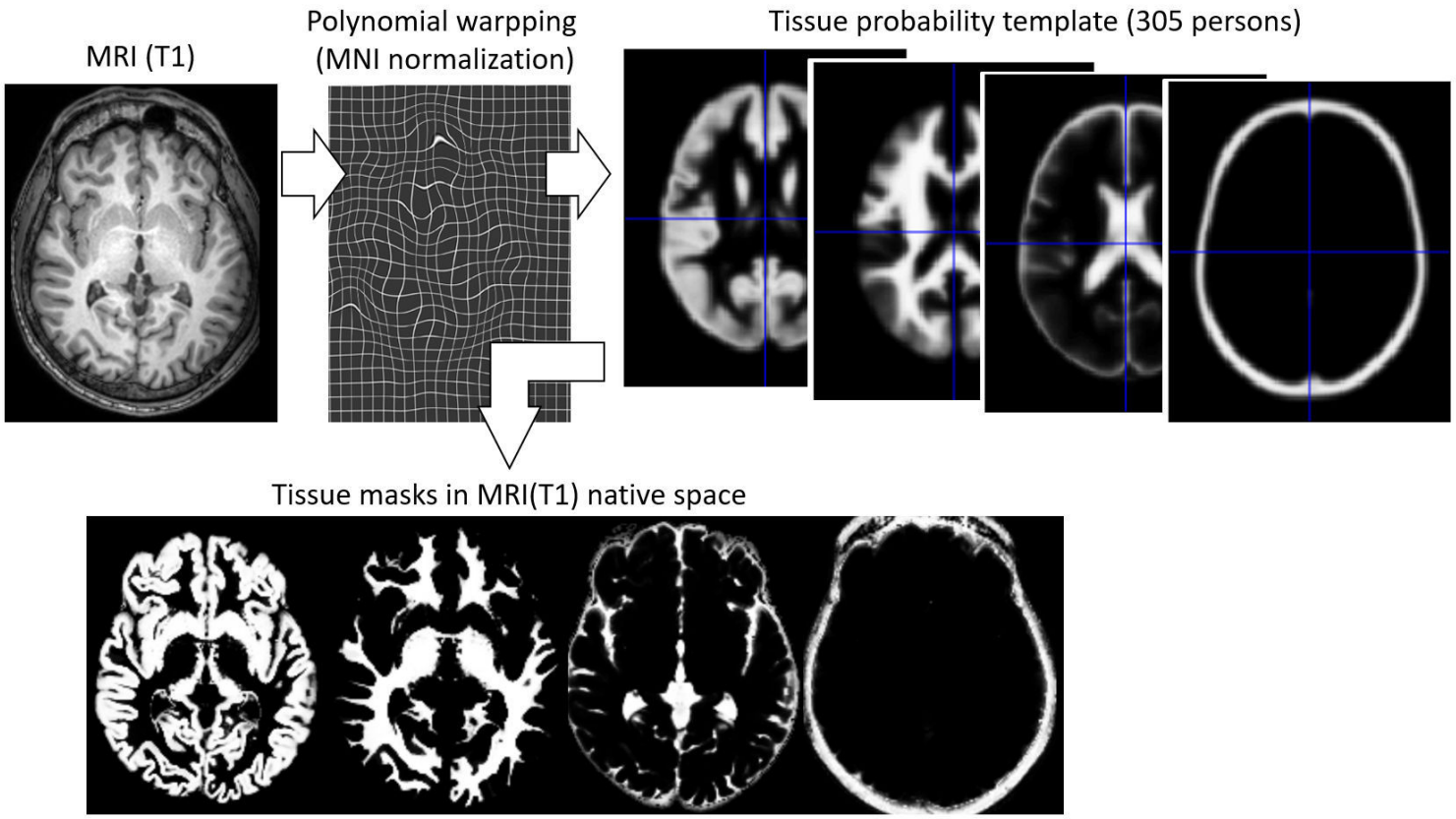
Check the successful process of coregistration.

```
spm_check_registration(check_list.path); % SPM multivolume viewer
```



2 Atlas-based tissue segmentation

The extraction of brain tissue regions is crucial part of the processing. Unfortunately, intesities (color) in MRI - T1 weigted images (**T1**) are similar for different type of the tissues, e.g., gray matter intensity is similar to skin or muscles. Therefore, simple thresholding segmentation can not work correctly. SPM contains probabilistic templates of head tissues (GM, WM, cerebrospinal liquid, bone, skin, air) obtained using MRI images of 305 people. The segmentation algoritm uses generative model, which polynomially warps MRI image to the template (normalization) [cite]. Each intensity in normalised MRI is weigted by template tissue probability, which results in the identification of probability masks of GM, WM, cerebrospinal liquid, bone, etc. The tissue maps are inversely unwarped to native MRI space and saved with prefix: 'c1' for GM, 'c2' for WM, 'c3' for cerebrospinal fluid, etc. The value of the voxel in tissue map represents the posterior probability of the tissue. Therefore, the mask is defined by thresholding a tissue map at level of 0.5 (>50% probability).



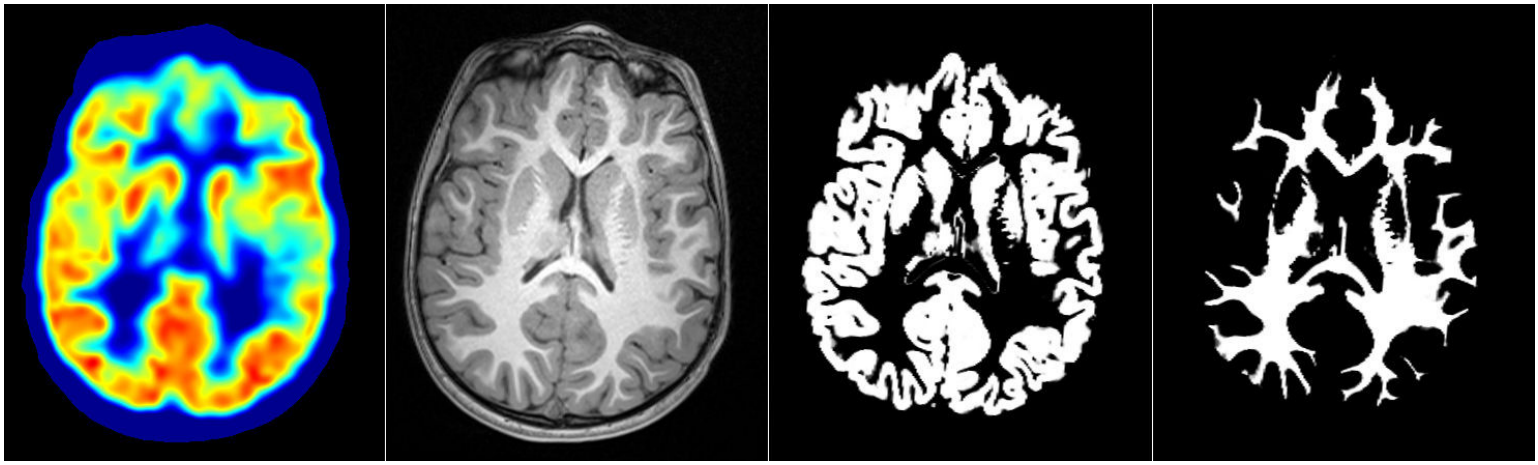
In SPM-fmri segmentation is done by *Spatial pre-processing* module: **Segment.** The batch code below performs segmentation of T1 weighted MRI image. The processing time depends on many factors (MRI resolution, CPUs) and can be from units to tens of minutes.

```
segmentation_method='cat12';
% ... 'spm' faster (Ryzen 2700x CPU: 5 min.), but unprecise for child brain and inhomogencus MR
% ... 'cat12' time-consuming (Ryzen 2700x CPU: 20 min.), but much better rusult (recommended)
switch segmentation_method
    case 'spm'
        segment_job_newSegment(mri_path); % SPM job batch is inside function
    case 'cat12'
        segment_job_cat12(mri_path); % SPM job batch is inside function
end
```

3 PET partial volume effect correction

Anatomically based PVC methods were proposed that incorporate anatomical information and tissue homogeneity constraints. The aim of anatomically based PVC methods is to utilize structural information from other imaging modalities (MRI) as a priori information in order to suppress the noise and artifacts. These modalities achieve better effective spatial resolution (FWHM < 1mm), and therefore better depict the edges in the image and provide more accurate information about the high-frequency components of the image. Anatomically based PVC methods are therefore principally based on the use of tissue segmentation of the structural image.

FDG-PET: MRI-T1 MRI-grey matter mask MRI-white matter mask



The **PETPVC** implementation requires segmented tissue in a single Nifiti file form as a binarized mask. Therefore, the c1*.nii (grey matter) and c2*.nii (white matter) will be fused to the 4D matrix and thresholded from probabilistic values of tissue to binary mask.

NOTE: When you forget install it on the start, here is link to dovnload: PETPVC 1.2.10 [download].

```
 % create 4D segmented MRI volume (for PETPVC toolbox)
% mri_path = '2258839_20220915_T1.nii';
mask_path = 'c12_segments_4D.nii';

matlabbatch={};
matlabbatch{1}.spm.util.cat.vols = {['c1' mri_path]; ['c2' mri_path]};
matlabbatch{1}.spm.util.cat.name = mask_path;
matlabbatch{1}.spm.util.cat.dtype = 0;
matlabbatch{1}.spm.util.cat.RT = NaN;
spm_jobman('run',matlabbatch(1));


% binarize 4D matrix  ----------------
for c=1:2 % for c1 and c2 separately
    v=spm_vol([mask_path ',' num2str(c)]); % read header
```

```
    vol=spm_read_vols(v); % read data matrix

    vol(isnan(vol))=0; % replace NaN values by zeros (if exist)
    vol=vol>=0.5; % set voxel with >50% probability of tissue to 1, else 0

    spm_write_vol(v,vol); % write data
end
```

3.1 Point spread function (PSF)

PSF describes the response of a PET scanner to a point source, that is the blurring of the point source in the resulting PET image. In general, PSF of the PET scanner is spatially variant — meaning that the PSF depends on the position of the point source in the field of view of the scanner. However, a spatially invariant PSF is usually assumed and the reconstructed PET image can be considered as a result of convolution of the true metabolic activity distribution with the PSF. Therefore, PSF of PET scanner is often modelled as a Gaussian distribution that is uniquely defined by its full width at half maximum (FWHM), which can be different in different spatial directions. However, the true value of FWHM is hard to obtain objectively and depends on many factors (patient's morphology, its movement in a scanner, etc.). Presented effective resolution of PET scanner producers is measured using ideal phantoms and filtered back-projection reconstruction, which is different with respect to real clinical practice.

For example, we measured SIEMENS Biograph Vison **PSF@2.5-3.2 mm** for high-resolution reconstruction and **PSF@5.4-6.8** mm for quantitative reconstruction (with 4 mm Gaussian filter) (in radial distance 1 - 10 cm). Based on our experiences and unpublished results, the precise knowledge of FWHM value for PVC is not critical, but the best result is for FWHM in the 100-150% range of real value. Although the effective resolution of quantitative reconstruction is worse, **quantitative PET protocols** are more appropriate for epileptic patients and PVC for hypometabolism search. A high-resolution protocol is more appropriate for oncology patients with hypermetabolic lesions.

In this case, FWHM 6 mm was selected in the middle range.

```
fwhm=6; % 6 mm isomorphic
```

TIP: When the PSF is unknown or unavailable for your PET scans, use 5 mm for the last generation of scanners and 7-8 mm for older type.

TIP: Prefer quantitative reconstruction (smoothed) before high-resolution/high-definition (more noisy)

3.2 PETPVC

Create command for PETPVC tool. Eaxmple below is for Windows, edit for your OS:

```
% ========================================================
% set path to executable file of PETPVC (*.exe for Windows, *.bin for Linux, ? for MacOS)
exe_path = [fullfile('PETPVC', 'bin', 'petpvc.exe'), ' '];
% ========================================================


% put together command for cmd
```

```
resliced_pet_path = ['r' pet_path]; % coregistered and resliced PET (r*_PET.nii)
pvc_out_path = [pet_path(1:end-4) '_pvcPET.nii']; % name of output file (pvcPET)
input = ['--input "' resliced_pet_path '" ']; % rPET
mask = ['--mask "' mask_path '" ']; % 4D matrix of GM and WM segmented tissue
output = ['--output "' pvc_out_path '" ']; % output file
method = '--pvc MG '; % Müller-Gärtner method
% point spred function of scaner:
psf = ['-x ' num2str(fwhm,'%.1f') ' -y ' num2str(fwhm,'%.1f') ' -z ' num2str(fwhm,'%.1f')];

command = [exe_path input mask output method psf];   % final command for windows cmd
disp(command)
```

Call command to system commander through MATLAB.

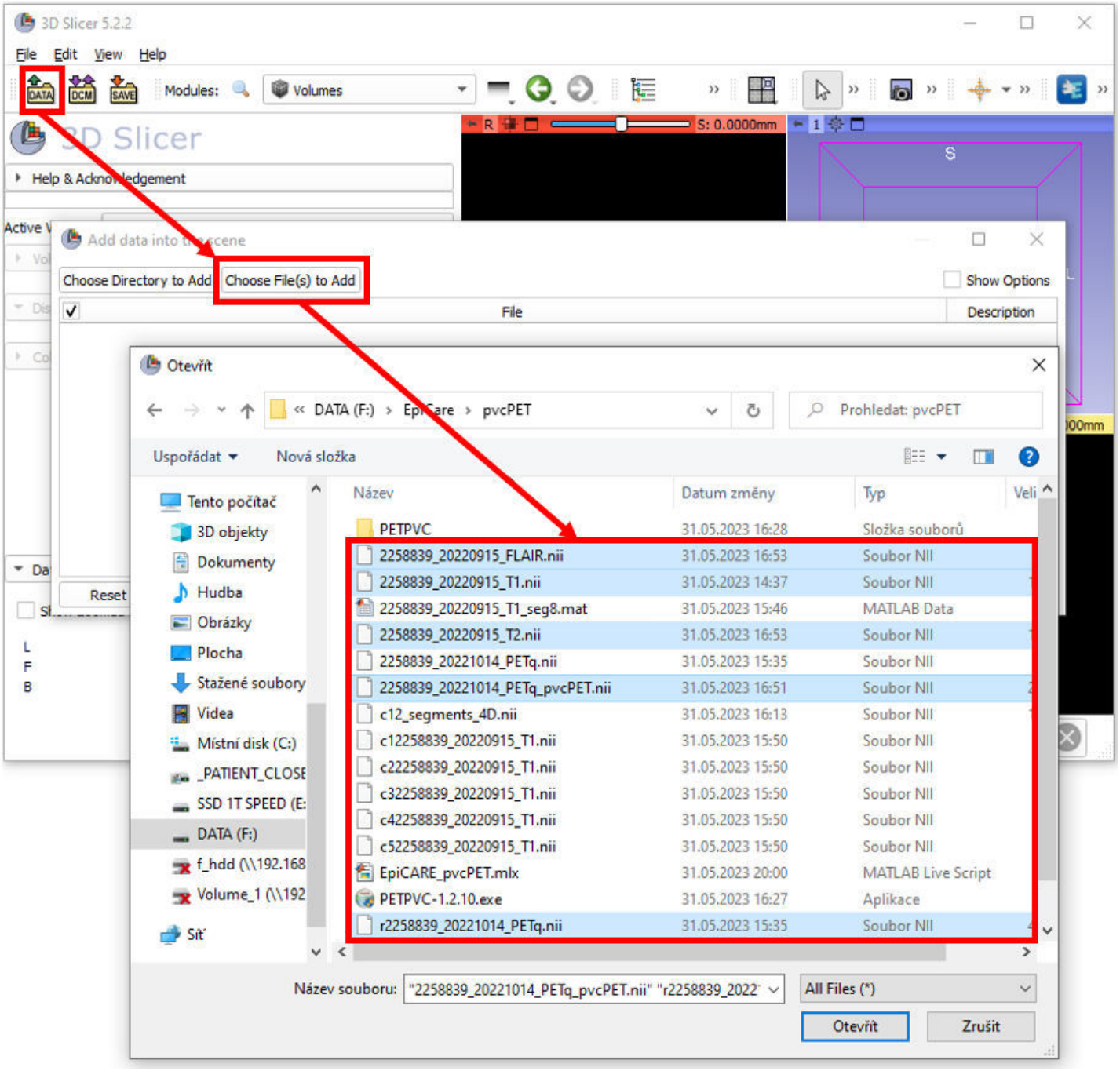
```
status = system(command);   % call cmd exe through matlab, run PETPVC
```

File "..._pvcPET.nii" should be created.

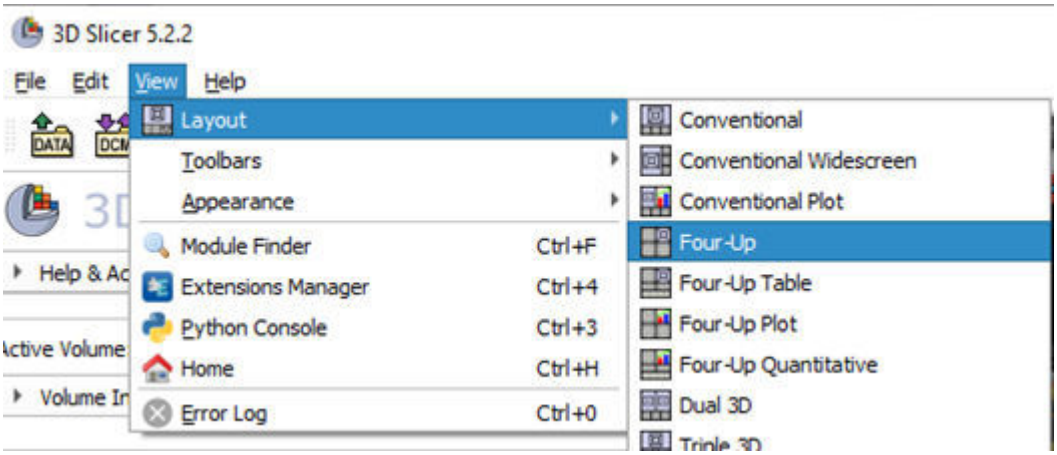
4 Visualization in 3D Slicer

4.1 Run 3D Slicer and read data:

1. File/Add Data
2. Choose Files(s) to Add
3. Select MRI of Epi protocol (T1, T2, FLAIR), coregistered and resliced PET (r...PET.nii) and pvcPET (...pvcPET.nii)

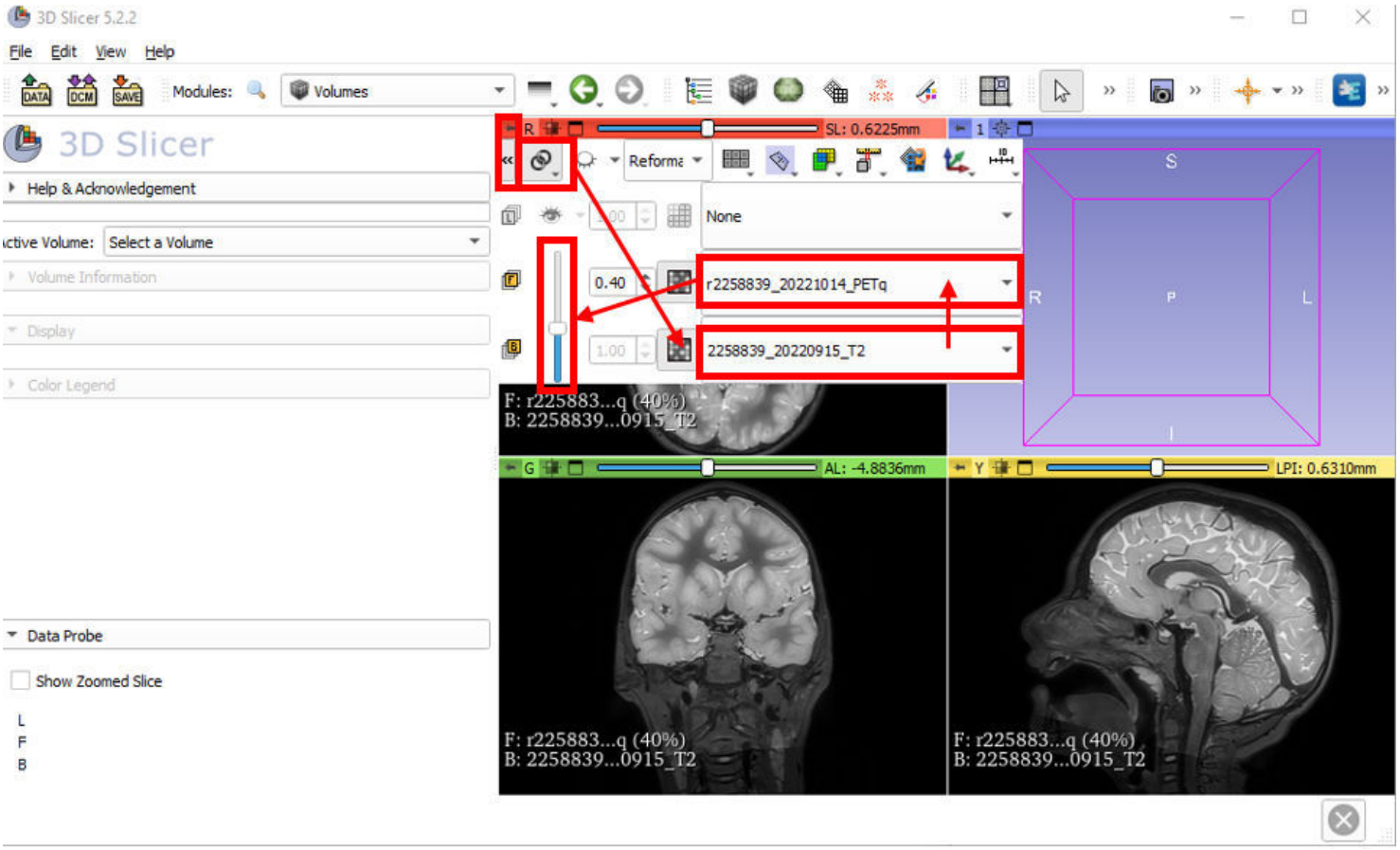


Select the layout of windows displacemnts: View / Layout / Four-Up (recommended)



4.2 Set backkround image (MRI) and foreground image (PET):

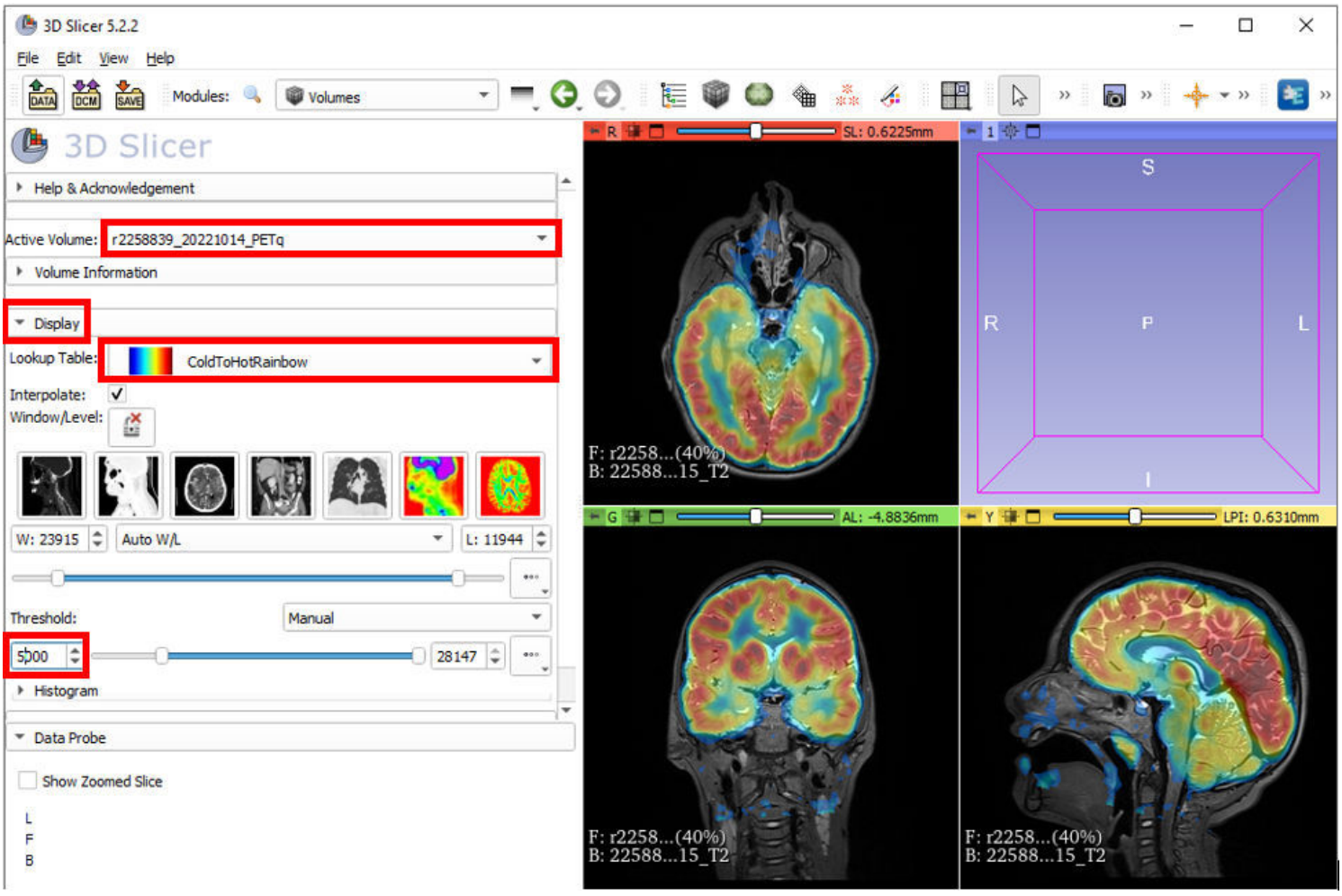
1. Go by cursor over pin symbol
2. Expand menu by << symbol
3. Click on chain sybol and lock all layouts
4. Select backround image T2 (bottom)
5. Select foreground image coregistered a resliced rPET (middle)
6. Set overlay (transparecy) of foreground to 40%



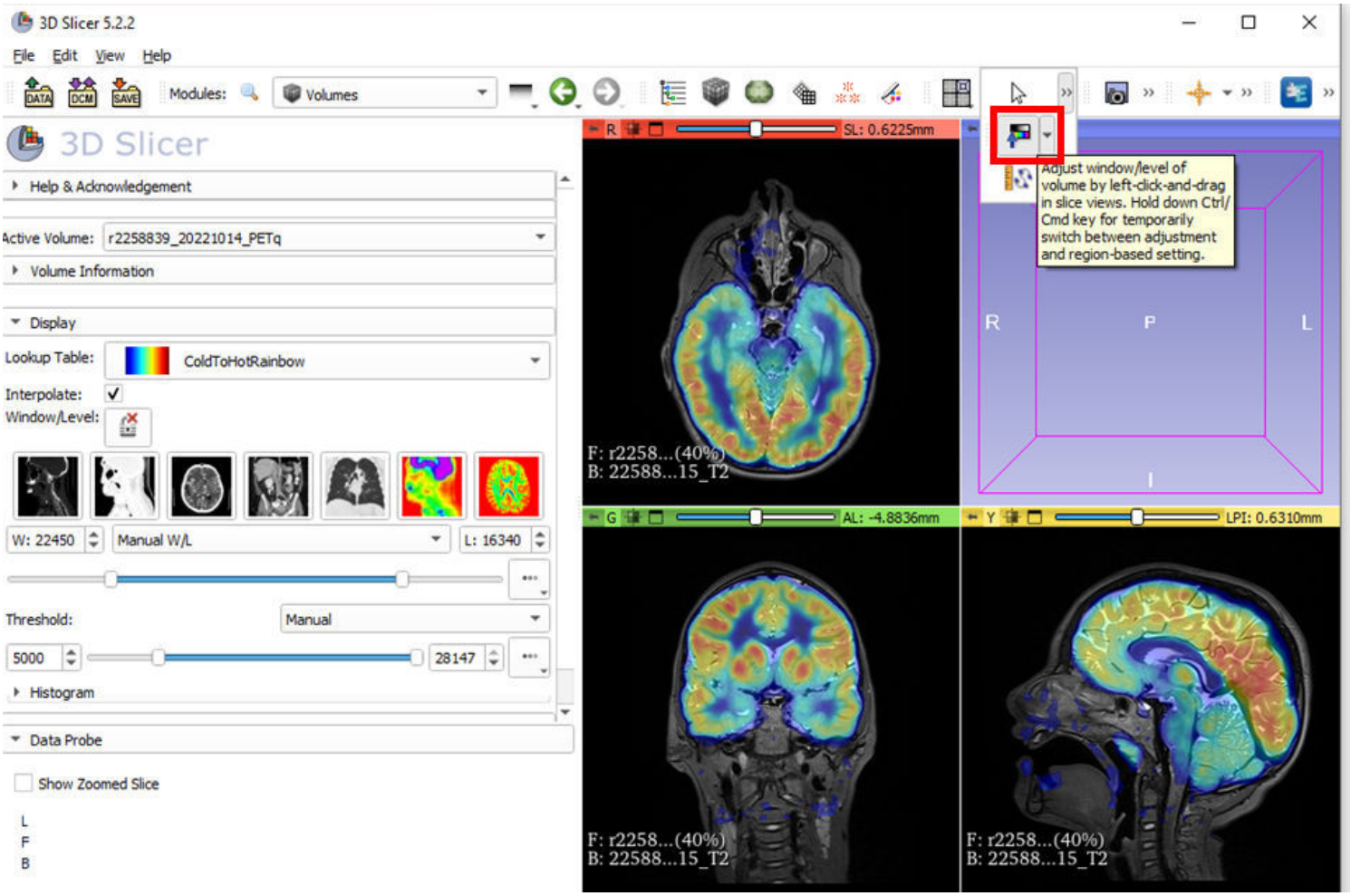
4.3 Lookup table (colormap)

Change colormap of PET images from greyscale to rainbow. Switch to module: Volumes

1. Select Active volume: r...PET
2. Expand Display menu
3. Select Lookup Table: ColdToHotRainbow
4. Set lower-threshold as 5000 to hide low-metabolism of air and skin (optional)

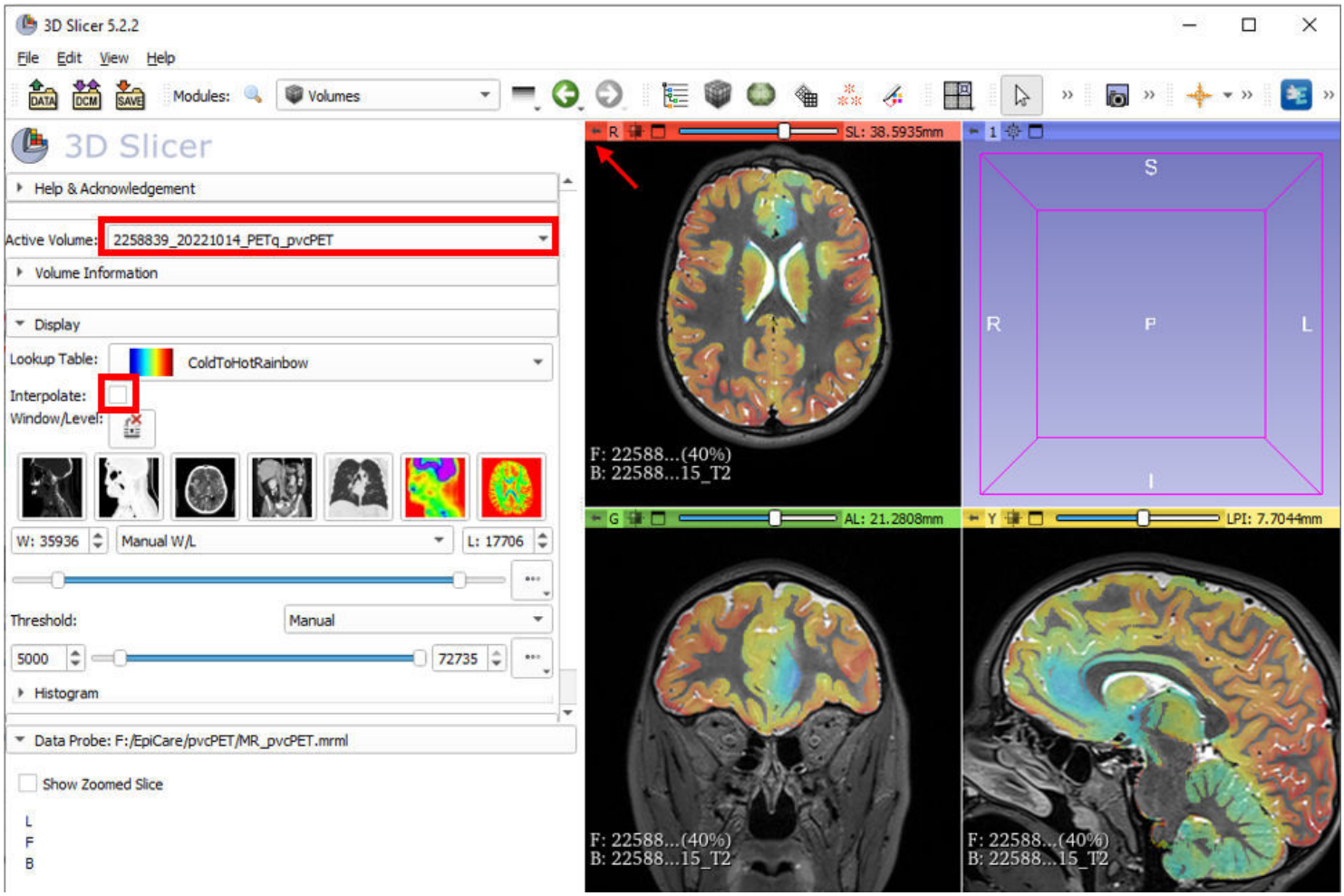


Turn-on Adjust window/level mode and set color (brightness/contrast equivalent) by hold mouse over slice and move up-down, left-right. For the setting of backround colors, set overlay to 0%, set color of MRI and increse back overlay to 40%.



Repete it for ... pvcPET by instruction from section 4.2.

Turn-off interpolation by uncheck **Interpolate** option.



4.4 Save the project to one-file