# LC Data Processing

First I download the data using the dcmconv.pl tool in dicom format. This is important because the nifti converter that is used from the data storage does put a weird orientation on the images.

Then, I organized Control data in this folder structure:

./Controls/Controls\_LC\_DATA/data/XXXXXX\_YYYYY/mt

./Controls/Controls\_LC\_DATA/data/XXXXXX\_YYYYY/fmri

./Controls/Controls\_LC\_DATA/data/XXXXXX\_YYYYY/qsm

./Controls/Controls\_LC\_DATA/data/XXXXXX\_YYYYY/r2star

./Controls/Controls\_LC\_DATA/data/XXXXXX\_YYYYY/mp2rage

For the Patient data I have the following:

./Patients/Patients\_LC\_DATA/data/XXXXXX\_YYYYY/mt

./Patients/Patients\_LC\_DATA/data/XXXXXX \_YYYYY/fmri

./Patients/Patients\_LC\_DATA/data/XXXXXX \_YYYYY/qsm

./Patients/Patients\_LC\_DATA/data/XXXXXX\_YYYYY/r2star

./Patients/Patients\_LC\_DATA/data/XXXXXX\_YYYYY/mp2rage

XXXXXX is the date of the scan in this format: 180817 where 18 is the last two digits of the year, 08 is the month, and 01 is the day of the scan.

YYYYY is the WBIC id number that they give once the subject is first registered at the wbic.

## 1. MT processing

All mt data is stored on the mt folder.

1) Navigate to the mt folder. First I convert the data to nifti format using the command:

dcm2nii \*

This will create 4 nifti files for controls and 3 nifti files for patients. Then I just rename them to something more sensible. You should be able to tell what is what from the name they have.

I renamed them in the following way:

INPUT IMAGES:

mt\_01.nii.gz

mt\_02.nii.gz

mt\_03.nii.gz

mt\_no.nii.gz

2) This is the script to combine the mt ON sequences using ANTs:

templateCommandRigid\_MT\_MI\_PT.sh

The structure of this one and all of the main scripts is the following:

1st: some declaration of important directories

2nd: mysubjs is the subjects structure where you just put the name of the subject directory that you want to process. For multiple subjects you just put them all in the same string, each separated by a space such as:

mysubjs="180723\_27287 180803\_27348 180813\_27381 180904\_27435 180912\_27517";

OUTPUT IMAGES:

This script will create a new folder inside the mt folder called: template\_n4MT2

The combined image of the 3 or 2 runs is called: t\_template0.nii.gz.

In this folder you’ll also get all the transforms of each individual mt images to the template, called: t\_mt\_XX00GenericAffine.mat where XX is the run number.

#### 1.1 Putting individual MT images and no MT to the subject specific MT template

Run the following script:

antsRegistration\_individual\_MT\_NoMT\_to\_subj\_mt\_template.sh

1. Make sure that the SUBJDIR directory is correct
2. mysubjs is the array of strings of the subject’s folder name you want to process.

Important OUTPUT files:

All these images will appear in the MT folder.

## 2. MP2RAGE processing

All mp2rage data is stored on the mp2rage folder. The important dicom folders are called:

Series\_XXX\_MP2RAGE\_0.7\_RR\_UniformSens\_MAG

Series\_XXX\_MP2RAGE\_0.7\_RR\_UniformSens\_PHS

Converting them to nifti using dcm2nii \* command, you’ll get two nifti files. Rename these two in the following way:

1st: For the one corresponding to the magnitude (MAG) data:

mp2rage\_magnitude.nii.gz

2nd: For the one corresponding to the phase (PHAS) data:

mp2rage\_phase.nii.gz

Then on the following script:

mp2rage\_processing.sh

1. Make sure that the MATLAB folder directory is correct
2. Make sure that the spm folder directory is correct
3. Make sure that the scriptdir directory is correct
4. Make sure that the fsldir directory is correct
5. mysubjs is the array of strings of the subject’s folder name you want to process.

Important OUTPUT files:

n4mag0000\_PSIR\_skulled\_std.nii : this is the mp2rage combined in standard orientation.

n4mag0000\_PSIR\_skulled\_std\_struct\_brain.nii : this is the brain extracted mp2rage.

n4mag0000\_PSIR\_skulled\_std\_struct\_brain\_mask.nii.gz : this is the brain mask.

### for subject with OLD MP2RAGE:

The important dicom folders are called:

Series\_013\_mp2rage\_sag\_p3\_0.75mm\_UNI\_Images

Converting them to nifti using dcm2nii \* command, you’ll get one nifti file. Rename these two in the following way:

1st: For the one corresponding to the magnitude (MAG) data:

mp2rage\_old.nii.gz

Use the following script:

mp2rage\_processing\_old\_mp2rage.sh

1. Make sure that the MATLAB folder directory is correct
2. Make sure that the spm folder directory is correct
3. Make sure that the scriptdir directory is correct
4. Make sure that the fsldir directory is correct
5. mysubjs is the array of strings of the subject’s folder name you want to process.

Important OUTPUT files:

n4mp2rage\_old\_std.nii : this is the mp2rage in standard orientation.

n4mp2rage\_old\_std\_struct\_brain.nii : this is the brain extracted mp2rage.

n4mp2rage\_old\_std\_struct\_brain\_mask.nii.gz : this is the brain mask.

## 3. QSM processing

All qsm data is stored on the qsm folder. The important dicom folders are called:

Series\_XXX\_T2star\_0.7\_6echo\_WTCrecon3Dgrappa\_UniformSens\_MAG

Series\_XXX\_T2star\_0.7\_6echo\_WTCrecon3Dgrappa\_UniformSens\_PHAS

Converting them to nifti using dcm2nii \* command, you’ll get two nifti files. Rename these two in the following way:

1st: For the one corresponding to the magnitude (MAG) data:

t2star\_mag.nii.gz

2nd: For the one corresponding to the phase (PHAS) data:

t2star\_phas.nii.gz

Then on the following script:

QSM\_processing.sh

1. Make sure that the MATLAB folder directory is correct
2. Make sure that the spm folder directory is correct
3. Make sure that the scriptdir directory is correct
4. Make sure that the fsldir directory is correct
5. mysubjs is the array of strings of the subject’s folder name you want to process.

Important OUTPUT files:

Three folders will be created in the qsm folder called /lambdaXXX.XXXX/. The most important is the lambda501.182.

Inside that folder the most important file is called:

qsm\_INTEGRAL\_4\_MSDI\_l501.1852.nii.gz

This is the qsm map.

## 4. R2star processing:

Use the following script:

antsRegistrationMP2RAGE\_to\_MT.sh

This script will pull some of the files from step 3 (qsm processing) and will compute all things in the r2star folder.

Make sure that in the r2star folder you see ARLO\_R2s.nii.gz and ARLO\_T2s.nii.gz files as output.

## 5. Registration of MP2RAGE to MT template images:

Use the following script:

antsRegistrationMP2RAGE\_to\_MT.sh

1. Make sure that the SUBJDIR is correct.
2. mysubjs is the array of strings of the subject’s folder name you want to process.

Important INPUT files:

You need to run step 1 and 2 first.

Important OUTPUT files:

(…..)/”Subj”/mp2rage/n4pmp2rage\_to\_t\_template0\_XXXXX

n4pmp2rage\_to\_t\_template0\_0GenericAffine.mat -> This is the affine matrix from mp2rge to mt subj template space

n4pmp2rage\_to\_t\_template0\_Warped.nii.gz -> This is the mp2rage image in mt subj template space

### for subject with OLD MP2RAGE:

Use the following script:

antsRegistrationMP2RAGE\_to\_MT\_old\_mp2rage.sh

Important INPUT files:

Same as before

Important OUTPUT files:

Same as before.

## 6. Registration of QSM + R2star to MT template images:

Use the following script:

antsRegistration\_QSM\_2\_MP2RAGE\_2\_MT.sh

1. Make sure that the SUBJDIR is correct.
2. mysubjs is the array of strings of the subject’s folder name you want to process.

Important INPUT files:

You need to run step 1 2, 3 and 4 first.

Important OUTPUT files:

All outputs will be in qsm/lambda501.1872/ folder

And in

r2star/ folder

there wil be the affine and the warp files for images to MP2RAGE space and to subj MT template space.

### for subject with OLD MP2RAGE:

Use the following script:

antsRegistration\_QSM\_2\_MP2RAGE\_2\_MT\_old\_mp2rage.sh

Important INPUT files:

Same as before

Important OUTPUT files:

Same as before.

## 7. Registration of MP2RAGE to MNI space:

We have decided to use he MNI152 2009 template for this data. This is given both at 1mm and 0.5mm resolution. These templates are in the template folder in:

/home/cr439/scratch/LocusCoeruleus/templates/MNI/

The script you need is:

wrapper\_antsRegistration\_MP2RAGE\_to\_MNI.sh

You must run the step 2 from above first to run this.

Also:

1. Make sure that the SUBJDIR folder directory is correct
2. Make sure that the scriptdir directory is correct
3. Make sure that on the fixed mask (which is the MNI template mask) is correct (essentially you ll need to change the directory)
4. Make sure that the fixed image (which is the MNI template ) is correct
5. mysubjs is the array of strings of the subject’s folder name you want to process.

NOTE: this will run with slurm. It may surprise you that it runs very quickly but processes are running in the cluster, in the background. After some hours youll probably find that on the mp2rge folder there will be files appearing, namely:

n4pmp2rage\_To\_MNI152\_T109b\_FSL\_bbox\_mask0GenericAffine.mat

n4pmp2rage\_To\_MNI152\_T109b\_FSL\_bbox\_mask1InverseWarp.nii.gz

n4pmp2rage\_To\_MNI152\_T109b\_FSL\_bbox\_mask1Warp.nii.gz

n4pmp2rage\_To\_MNI152\_T109b\_FSL\_bbox\_maskInverseWarped.nii.gz

n4pmp2rage\_To\_MNI152\_T109b\_FSL\_bbox\_maskWarped.nii.gz

The slurm dump output wll be stored on a slurm-XXXXX.out file inside the mp2rage directory. You can check if it has finished by looking at the last line. It should say:

Total elapsed time: 3.771e+04

Where the number changes slightly. If it says ERROR, something went wrong….please investigate!

### for subject with OLD MP2RAGE:

Use the following script:

wrapper\_antsRegistration\_MP2RAGE\_to\_MNI\_old\_mp2rage.sh

Same rules apply as before. All is run with slurm commands.

LC Segmentation

It is necessary that now you do the LC segmentation:

For each subhect you should gather the MT template data, the No MT in template space, the QSM data in mt template space. I thik we talked about where and whoe this data is called.

I have this order of drawing the ROIs in itksnap:

1 – LC left ROI

2 – LC right ROI

3 – Reference Region

4 – This is the segmentation of the 4th ventricle done by hand. It is not very difficult but it improved significantly the fmri resoluts. Just start at the very first bottom slice that includes the LC and go all the way up to the top of the LC. Segment on the no-mt data.

Then I save the segmentation with the name:

LCrois.nii.gz

(This is important!)

Then save the LCrois.nii.gz in the mt folder of each subject.

Then run the following script:

antsRegistration\_LCROIs2MNI.sh

----🡪 check subjdir is correct and modify the subjs directories that you want to process.

## 8. fMRI processing

STEP 1:

The first part of the fMRI processing is run in matlab directly because it was what Kamen setup for me. Scripts are in the fMRI folder. It will be good that you run this for all the patients because it takes quite a lot of time.

Download all the dicom data necessary and place it in the fmri folder. You should have 6 subfolders with similar names to this:

Series\_016\_MB\_GRE\_1.1\_RS\_MB5\_SBRef

Series\_017\_MB\_GRE\_1.1\_RS\_MB5

Series\_018\_MB\_GRE\_1.1\_RS\_MB5\_PhysioLog

Series\_019\_MB\_GRE\_1.1\_RS\_MB5\_rev\_SBRef

Series\_020\_MB\_GRE\_1.1\_RS\_MB5\_rev

Series\_021\_MB\_GRE\_1.1\_RS\_MB5\_rev\_PhysioLog

Convert them to nifti.

Then you need to change the name of the nifti file corresponding to the fmri sequence (which is in this case series 19: Series\_017\_MB\_GRE\_1.1\_RS\_MB5) to the name:

fmri.nii

Then you need to change the name of the nifti file corresponding to the fmri reversed phase encode sequence (which is in this case series 20: Series\_020\_MB\_GRE\_1.1\_RS\_MB5\_rev) to the name:

fmri\_rev.nii.gz

Note that one is nii and other is nii.gz. This is necessary.

Then, copy the subject\_info.xlsx from the controls directly into the patients directory. Inset the relevant info for all the Patients as was done for the controls.

Then open the following script in matlab:

LC7T\_preproc\_pipeline.m

Change the root\_dir according to the patients directory:

In my case was:

S.project.root\_dir = '/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/';

Then you should be able to run everything. This will take a while for each subject.

STEP 2:

This is a bit tricky! If you are brave enough it would be great if you run the registration of the fmri data aleady preproc to mni space. Because these do too take some time.

You’ll need the script:

FSLRegistration\_fMRI\_2\_MNI.sh

Make sure all the directories on the first bit of the script are correct. Go through them very carefully.

This will also run with slurm. I found out that registering bits of 100volumes was ok rather than doing the 354 volumes altogether.

So that is what is happening. I haven’t figured out a way to make the script waiting for this before merging all the 4 bits of registered fmri to MNI together (final line of code) so you might need to rerun only this line after you’ve seen that in the fmri folder the

a\_flip\_rflip\_fmri\_uw\_00\_2\_MNI.nii.gz

a\_flip\_rflip\_fmri\_uw\_01\_2\_MNI.nii.gz

a\_flip\_rflip\_fmri\_uw\_02\_2\_MNI.nii.gz

a\_flip\_rflip\_fmri\_uw\_03\_2\_MNI.nii.gz

were already finished to create.

### for subject with OLD MP2RAGE:

Use the following script:

FSLRegistration\_fMRI\_to\_Structural\_old\_mp2rage.sh

Same details apply as before.

NOTE: I Think from here on down things can improve still so I wouldn’t run these scripts just now…

STEP 3:

Coming to the end of the limited time to process this data I was very sloppy with the programming. You’ll notice there are many defined directories in the middle of the scripts… not good! Please take care of this otherwise your scripts wont run because of incorrect directories.

The script you want to run is:

LC\_preproc\_step2.sh

This has many intricate things, and probably you need to create a sub-one for the patients scans.

STEP 4:

GLM analysis of fMRI scans per subject

## 9. MT template creation

This is to create a template of all the subjects MT data.

To do this you’ll need to have run the step 1 because for this template we need all subject specific mt combined data.

The script you want to run is:

ants\_build\_multivariatetemplate2\_MT.sh

1. Making a target directory: this is the directory where the output will be saved. I’ve created the following directory:

~/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/MT\_results/template/

1. On this directory you’ll need to create a text file called:

images\_mt\_template.txt

you can see the example on the controls data, but essentially this text file contains for each line the data you want to use for the template. This is the example for the Controls template:

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180611\_27124/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180711\_21271/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180718\_21520/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180816\_26997/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180817\_27363/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180821\_13663/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180824\_27417/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180919\_24379/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/180921\_27518/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/181003\_27602/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/181005\_26839/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/181009\_27620/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/181011\_27634/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/181016\_27663/mt/template\_n4MT2/t\_template0.nii.gz

/data/cr439/LocusCoeruleus/Controls/Controls\_LC\_Sorted\_DATA/data/181018\_27383/mt/template\_n4MT2/t\_template0.nii.gz

you need to create one for the patients where you have the full path to the t\_template0.nii.gz of the patients data.

Then you should be ready to run the script. This will take a very long time to process. The 15 subjects took me about 4 days, so just let the window open and carry on with other things.