

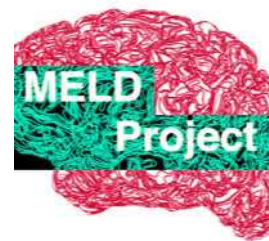
May 17, 2024

Version 2

Protocol 2 - MRI data protocol V.2

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We use this protocol and it's working

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Abstract

The MELD Project is an international collaboration aiming to create open-access, robust and generalisable tools for FCD detection.

This MRI data protocol details

- 1) The MRI data required / desirable for patients and controls in the MELD focal epilepsies project
- 2) How to convert the MRI data from dicom to nifti
- 3) How to ensure all identifiable data is stripped from the header
- 4) How to deface the data
- 5) How to convert the data into BIDS format
- 6) How to send the anonymised data to the study coordinators

Please refer to protocol 1 for inclusion / exclusion criteria and retrieval of necessary anonymised demographic and clinical information.

PLEASE NOTE: To take part in the MELD Project each site will be required to 1) sign our memorandum of understanding and 2) provide a letter from the head of department or local R&D office confirming that they have obtained appropriate ethical approval to share the anonymised data with UCL.

Guidelines

If you have any questions or run into problems, please feel free to contact the MELD project:
(meld.study@gmail.com)



Before start

Ensure that you have "cloned" the MELD file structure and scripts from github. (https://github.com/MELDProject/meld_focal_epilepsy)

To do this, in a terminal window cd into the location you wish to store the data.

```
cd <path>
```

Then "clone" the repository using the following command:

```
git clone https://github.com/MELDProject/meld_focal_epilepsy
```

This will download all of the scripts & template folder structure necessary for the MELD focal epilepsy project.

Initial setup

1 For this protocol you will need to have installed :

- Anaconda
- FSL 6.0
- The meld_focal_epilepsy package
- The mfe_env conda environment

1.1 Install Anaconda & FSL

To check if you already have **anaconda** installed, in your terminal window run:

```
conda --version
```

It should return the version of your current conda installation e.g "conda 4.10.1"

If not, please refer to the following instructions to install anaconda on your computer :

<https://www.anaconda.com/products/individual-d>

To check if you already have **FSL** installed, in your terminal window run:

```
flirt --version
```

It should return the version of your current FSL installation e.g "FLIRT version 6.0"

If not, or if you don't have the version 6, please refer to the following instructions to install FSL 6.0 on your computer :

<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FslInstallation>

1.2 Install meld_focal_epilepsy github & create environment:

1) Open a terminal and move to the folder you want to save the package in:

```
cd <path_to_meld_focal_epilepsy_github_folder>
```

2) Copy from GitHub the package by pasting the following sentence :

```
git clone https://github.com/MELDProject/meld_focal_epilepsy.git
```

Press enter. Your package will be installed

Check if you have a folder called meld_focal_epilepsy in

<path_to_meld_focal_epilepsies_folder>

3) Create the environment :



```
cd
<path_to_meld_focal_epilepsy_github_folder>/meld_focal_epilepsy/sc
ripts
conda env create -f mfe_env.yml
```

4) Activate the environment :

```
conda activate mfe_env
```

you should have "mfe_env" replacing "base" in front of your computer ID on the terminal

e.g

```
(base) mathilde@it-Precision-5820-Tower:~$ conda activate mfe_env
(mfe_env) mathilde@it-Precision-5820-Tower:~$
```

Your meld_focal_epilepsy package is ready to be used !

Note : you will have to activate your environment every time you open a new terminal and you want to use the meld_focal_epilepsy package

Retrieval of MRI data

2 Prepare your data

Download the meld_focal_epilepsy_data folder from :

<https://figshare.com/s/763e50f4eb51a4f76f58>

Keep note of where you save this folder as it will be your data folder :

<path_to_meld_focal_epilepsy_data_folder>

You will need to unzip the folder :

```
cd <path_to_meld_focal_epilepsy_data_folder>
tar -xzf meld-focal-epilepsy-data.tar.gz
```

Anonymous participant IDs

During Protocol 1 each participant should have been given an anonymous ID according to the following naming structure:

MELD_[site code]_[patient/control]_number

- 2.1 In the meld_focal_epilepsy_data/participants folder copy the template file structure called meld_template and rename the folder with the participants anonymous ID. This can either be done by right clicking on the folder clicking rename and typing in the anonymous ID OR in your terminal window:

```
cd  
<path_to_meld_focal_epilepsy_folder>/meld_focal_epilepsy/participa  
nts  
mv meld_template <MELD_anonymous_ID>
```

e.g. mv meld_template MELD_H1_P_0001

Further details about the naming structure:

[site code] = site identifier which will be provided to you e.g. H1 for Great Ormond Street Hospital

[patient/control] = P if patient, C if control.

If participant was included in the FCD study and has an ID such as MELD_H1_15T_FCD_0001, the ID should be kept the same. I.e. Use the original FCD flag and scanner flag.

If control was included in the FCD study and has an ID such as MELD_H1_3T_C_0001, the ID should be kept the same.

[number] = 0001, 0002 etc.

Examples of participant IDs:

MELD_H1_P_0001

MELD_H1_C_0002

MELD_H2_FCD_0042

Please make sure to securely keep a spreadsheet at your centre which links the anonymous IDs used in this study back to the IDENTIFIABLE patient data. THIS MUST



NOT BE SHARED and should be kept securely!

- 2.2 The following MRI data should be retrieved off the hospital system / research database for each participant and stored in the relevant folder for each participant:

A	B	C	D	E
MRI scan	Notes on data	Essential / where available	Folder to store data	Data formats accepted
T1-weighted preoperative	3D 1.5T, 3T or 7T	Essential	t1	dicom, nifti
T2 preoperative	3D or 2D coronal	Where available	t2	dicom, nifti
FLAIR preoperative	3D or 2D coronal	Where available	flair	dicom, nifti
DWI preoperative (diffusion weighted data, bval and bvec)	3D	Where available	dwi	dicom, nifti
T1-weighted postoperative	3D 1.5T, 3T or 7T	Essential in operated patients	postop_t1	dicom, nifti

Please note: the MRI data must NOT have contrast (e.g. gadolinium contrast)

Within the meld_template are 1.5T, 3T and 7T folders and within these there are folders to store the MRI data. Please save the patient's MRI data in the correct folder.

If you have MRI data from multiple scanner field strengths for the same patient (e.g. 1.5T and 3T data for a patient) - it would be wonderful to have both, so we can compare how the classifier is able to perform on data from different scanner field strengths.

Here is an overview of the folder structure:

```
meld_template/  
├── 15T  
│   ├── dwi  
│   ├── flair  
│   ├── lesion_mask  
│   ├── postop_t1  
│   ├── t1  
│   └── t2  
├── 3T  
│   ├── dwi  
│   ├── flair  
│   ├── lesion_mask  
│   ├── postop_t1  
│   ├── t1  
│   └── t2  
└── 7T  
    ├── dwi  
    ├── flair  
    ├── lesion_mask  
    ├── postop_t1  
    ├── t1  
    └── t2
```

2.3 Diffusion Weighted Data:

Please note if you are providing the data in nifti format you need to provide the following files:

dwi.nii.gz

dwi.bval

dwi.bvec

If you are providing the data in dicom format, the script in the subsequent section will create these files.

Anonymising MRI data

- 3 Once you have retrieved all your patient / control MRI data and stored it in the MELD_focal_epilepsy file structure, you need to run the "*meld_bidsify_data_step1.py*" script. This script will convert any dicom data into nifti format and save them alongside dicoms

Note : you need to have your mfe_env environment activated : `conda activate mfe_env`

Please note that the ***meld_focal_epilepsy_github_folder*** contains the scripts and is different from the ***meld_focal_epilepsy_data_folder*** which should contain the data.

To run this script on all participants: Open a terminal window and type:

```
cd
<path_to_meld_focal_epilepsy_github_folder>/meld_focal_epilepsy/scripts
python meld_bidsify_data_step1.py -d
<path_to_meld_focal_epilepsy_data_folder>/meld_focal_epilepsy_data
```

Note :

This script also coregister FLAIR volumes to T1 if both available, and saves it in the 'flair' folder

You can now use the nifti T1 volume, and the additional coregistered FLAIR volume to create the lesion mask if not already provided.

Lesion Masking

4

This section (Substeps 1 - 7) details how to create a lesion mask in ITK-SNAP and save it as a Nifti file.

Lesion masks should ideally be created for all patients included in the MELD Project EXCEPT patients with:

- hippocampal sclerosis
- or patients who are MRI negative

If your centre has an established method to create lesion masks / has already created lesion mask:

*You do not need to redo them or change your method. The lesion masks will need to be converted to Nifti format. Please save the lesion mask as **lesion.nii.gz** or **lesion.nii** in the **lesion_mask** folder. If the lesion mask was created based on a 1.5T scan, please save in the 1.5T folder. If the lesion mask was created based on a 3T scan, please save in the 3T folder etc.*

4.1 How to create a lesion mask:

The lesion mask should be done on the 3D T1-weighted scan but other scans e.g. FLAIR and the post-operative T1-weighted can be used to assist in defining the lesion. We

provide the FLAIR coregistered (FLAIR_coreg.nii) which can be used to help delineate the lesion.

You may need assistance from a neuroradiologist at your centre for the subtle lesions.

If you have multiple T1-weighted scans at different field strengths - please create the lesion mask based on the T1-weighted scan you can visualise the lesion best on.

If the patient has hippocampal sclerosis OR is MRI negative there is no need to create a lesion mask.

If the patient is MRI-negative but with histological confirmation, the post-operative scan and other corroborative evidence such as EEG, PET, sEEG etc. can be used to help define where the lesion was on the preoperative scan in order to create the lesion mask.

If it is NOT possible to create a lesion mask. Please still include this patient in the study. In the RedCap Participant information survey under the question "Have you provided a lesion mask for this patient?" Click No

If you have any questions or run into problems, please feel free to contact the MELD project: (meld.study@gmail.com).

4.2 **Downloading ITK-SNAP:**

Click on the link below and download version 3.8.0 for windows / mac / linux depending on your workstation:

<http://www.itksnap.org/pmwiki/pmwiki.php?n=Downloads.SNAP3>

Follow the tutorial provided for the installation:

<http://www.itksnap.org/pmwiki/pmwiki.php?n=Documentation.TutorialSectionInstallation>

4.3 **Before starting manual lesion masking:**

We advise watching part of the ITK-SNAP webinar:

If you start at 9minutes 57 seconds and watch until 12 minutes 5 seconds, you can watch the part of navigating an image in ITK-SNAP and manual segmentation. You may want to pause / rewatch the manual segmentation example as it is very fast but shows you 3 tools you can use to help create your lesion masks - polygon; paintbrush and smart brush

<https://www.youtube.com/watch?v=Wob8beX88Ks>

Here is a useful introductory guide on how to use ITK-SNAP:

<http://www.itksnap.org/pmwiki/uploads/Train/RSNA2016-Manual-Guido-Final.pdf>

Slides

11-14: Image navigation

16-22: Manual segmentation

24: Loading and saving manual segmentations

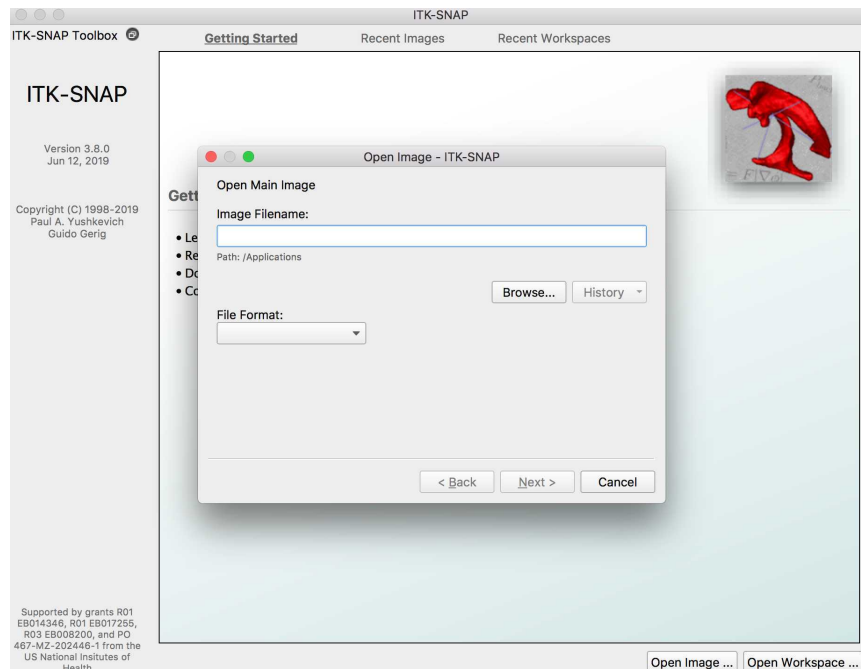
There are also many other useful youtube tutorials on how to manually segment using ITK-SNAP. Here is a longer (18 minute) but much more detailed webinar which is very useful. In this example they use segmentation of the hippocampal subfields as an example.

https://www.youtube.com/watch?v=OpYJiY_GoeY

4.4 **Example manual segmentation of a FCD Type IIB - Opening the MRI scans and navigating through them**

Open ITK-SNAP and click open image

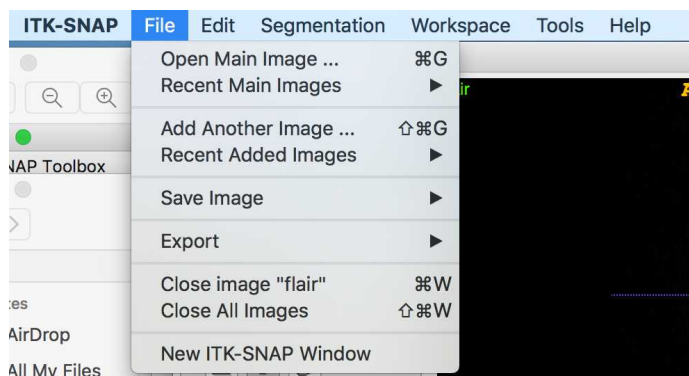
Then search for the MRI image (usually T1-weighted) of the patient who's lesion you are going to segment



In this example I have opened a 3T FLAIR image:



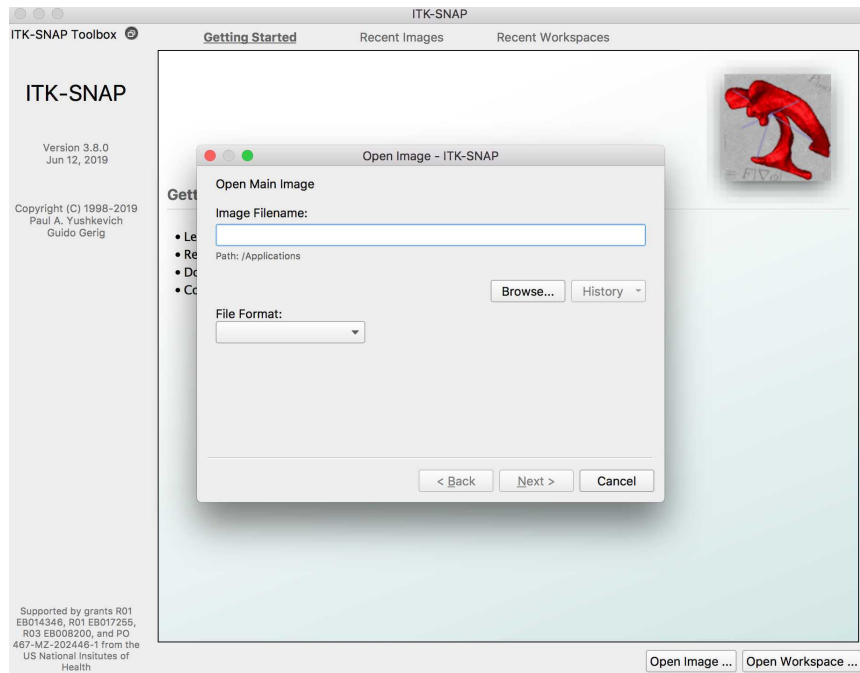
On the toolbar, the cursor is clicked, so I can navigate through the MRI to find the lesion.
If I want to add another MRI scan (e.g. the co-registered 3T T1-weighted), I can click file
→ add another image



4.5 Example manual segmentation of a FCD Type IIB - Opening the MRI scans and navigating through them

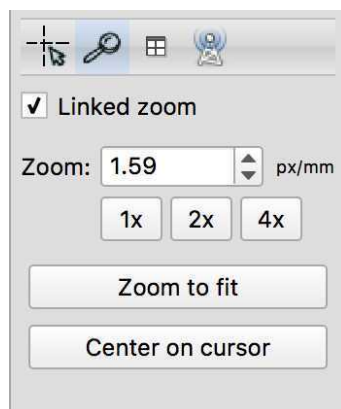
Open ITK-SNAP and click open image

Then search for the MRI image (usually T1-weighted) of the patient who's lesion you are going to segment

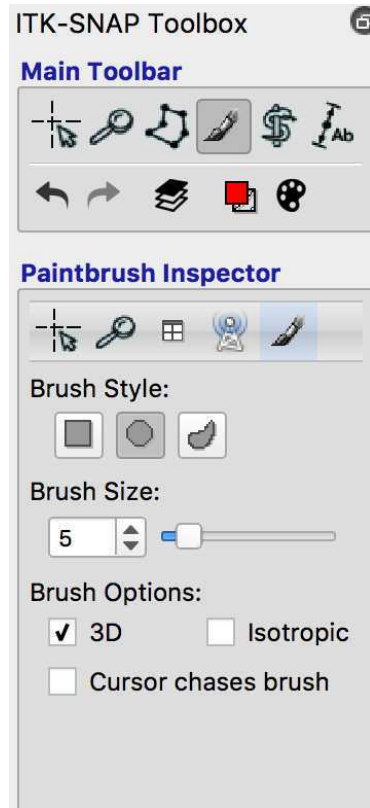


Example manual segmentation of a FCD Type IIB

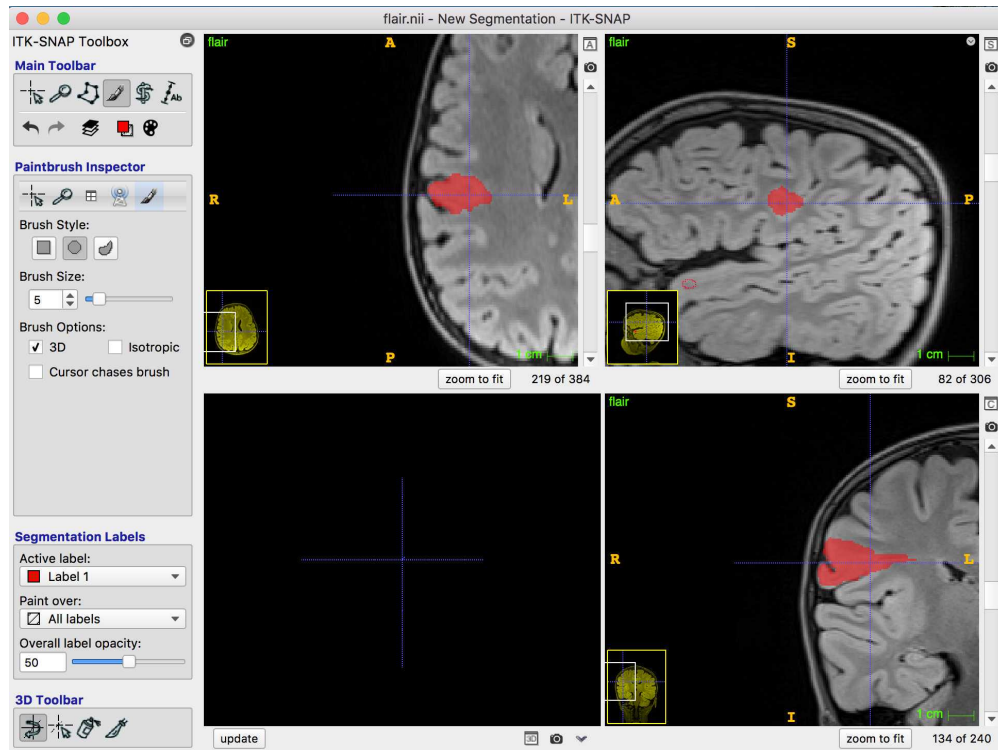
Once you have identified the lesion, you may want to zoom in on it. Click the magnifying glass and increase the zoom until you can clearly see the lesion



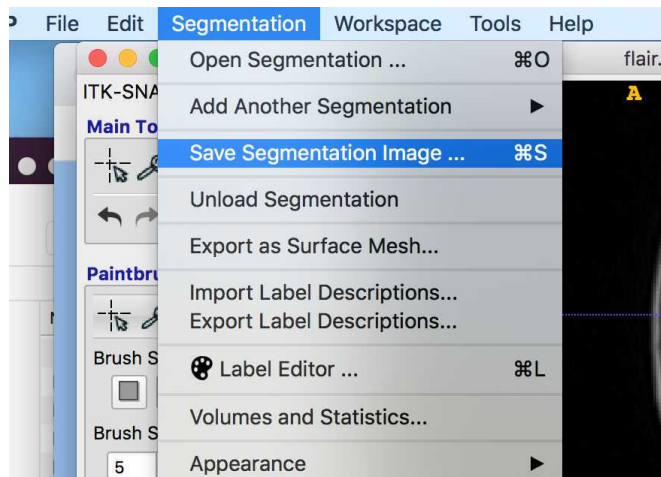
Then click the paintbrush and choose your brush style (I use the circle), and brush size. To create your lesion mask in 3D click 3D, to mask slice by slice, unclick the 3D button.



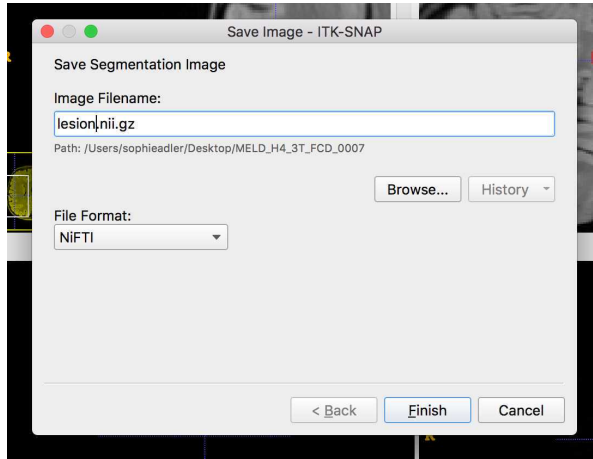
You can now start to mask your lesion. As you can see the "Active label" is 1 - this means that the voxels of the lesion will all have a value of 1. If you make a mistake and want to delete some of the voxels you have labelled, you can right click on them.



4.6 Saving the lesion label

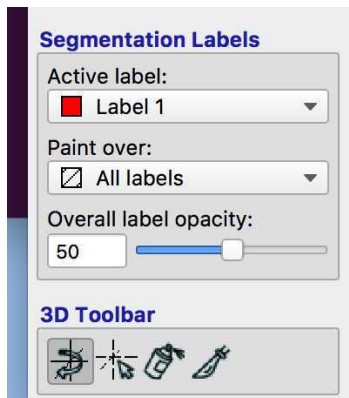


Click Segmentation → Save Segmentation Image

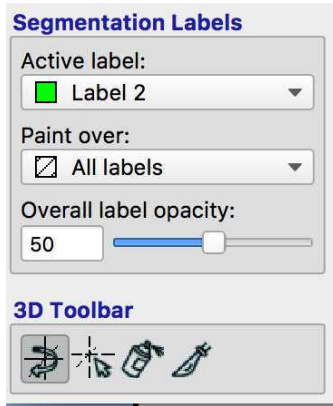


Save image as lesion.nii.gz in the patient's MELD folder e.g.
MELD_H1_0001/3T/lesion_mask

4.7 **Creating the lesion label if there is more than 1 lesion e.g. FCD IIIA where you have a hippocampal lesion and a cortical lesion**



Mask one lesion using active label 1. Then change the label to 2 and mask the other lesion:



Save the lesions as before as "lesion.nii.gz". The first lesion mask will have values of 1 and the second will have values of 2.

Convert in BIDS and zip

5 Run `meld_bidsify_data_step2.py` to convert in BIDS format

Once you have placed the lesion nifti file into the right lesion_mask folder, you need to run "`meld_bidsify_data_step2.py`" script. This script will :

1. Reorganise MRI data into BIDS structure saved into meld_bids folder
2. Strip any identifiable header information from the scans
3. Deface the MRI data
4. Compress the meld_bids folder into different batchs

To run this script you need to provide a txt file with the list of participants you want to include in the batch.

To create the list of participants :

- 1) Open a terminal window

```
cd
<path_to_meld_focal_epilepsy_data_folder>/meld_focal_epilepsy_data
nano list_participants_batch_<date_as_ddmmyyyy>.txt
```

Then type the MELD IDs of the participants you would like to run the script on. Press enter between each participant_id:

e.g.

MELD_H1_3T_P_0001

MELD_H1_3T_P_0002

MELD_H1_15T_P_0001



MELD_H1_15T_C_0002

File handling in nano

Ctrl+S Save current file

Ctrl+X Close buffer, exit from nano

Alternatively use any text editor to save your list of participant ids at
list_participants_batch_<date_as_ddmmyyyy>.txt.

Once you have the participants file, type:

```
cd
<path_to_meld_focal_epilepsy_github_folder>/meld_focal_epilepsy/scripts

python meld_bidsify_data_step2.py -d
<path_to_meld_focal_epilepsy_data_folder>/meld_focal_epilepsy_data
-ids
<path_to_meld_focal_epilepsy_data_folder>/meld_focal_epilepsy_data
/list_participants_batch_<date as ddmmyyyy>.txt
```

You can find your new bids folder and its zipped batches at
<path_to_meld_focal_epilepsy_data_folder>/meld_focal_epilepsy_data/meld_bids
The files to share begin with: "share_data_part"

Note : remember to keep track of the subjects you have already converted with the participants list file.

Sending MRI data

6 Note: Dropbox is now deprecated and files will be shared via File Request on OneDrive

Please contact meld.study@gmail.com and provide the email(s) of the person(s) who will be uploading the data. We will send you a file request to upload the data to a secure drop-only folder.

Upload each zipped batch



Please note – due to the file sizes, it may take a while to upload!

A member of the MELD team will confirm the reception of the files

REMINDER: ONLY SEND ANONYMISED DATA OVER