**Keihaninejad Pipeline – Generic – 11/12/20**

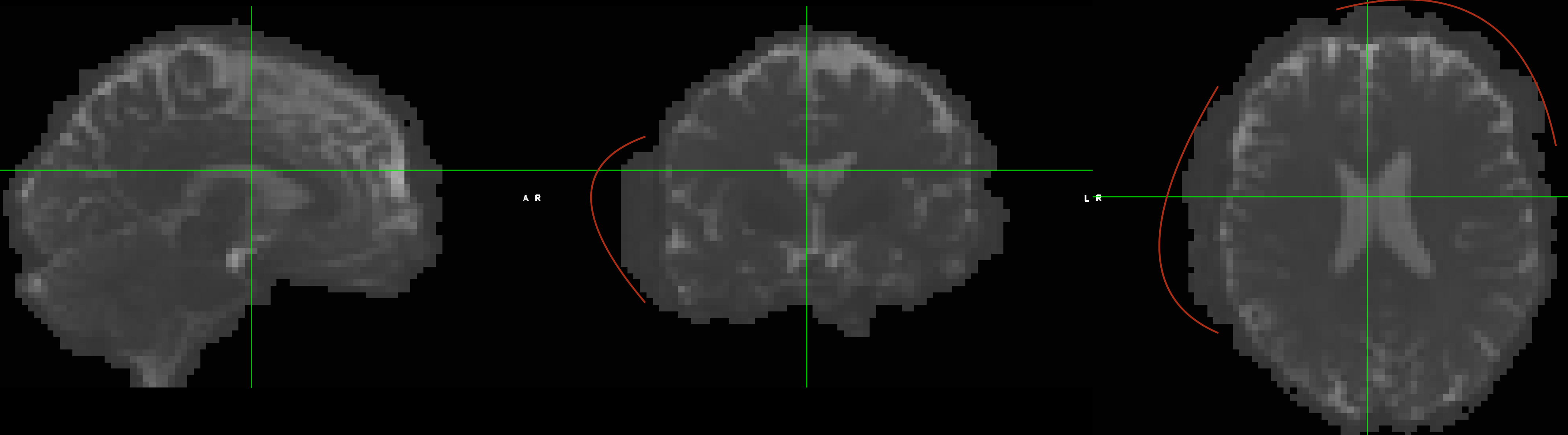
**Note**: Many images are scaled down in size to save space and help this document stay organized. Use the zoom function in order to close up on images.

**Note**: Run all scripts manually and change paths when needed.

* **Prepping Tensors for Registration**:
  + Note: All following steps are accomplished via **1\_Preproc\_Tensor\_Prep.sh**
    - It is necessary to run this manually.
  + File Organization: In order to generate tensor files for later registration, the following files are required:
    - The preprocessed nifti, the associated bvec and bval files.
    - A screenshot of a cell phone

      Description automatically generated
    - This is done in 1\_Preproce\_Tensor\_Prep.sh section 1
  + **BET: 1\_Preproce\_Tensor\_Prep.sh section 2**
    - It is necessary to skull strip the preprocessed diffusion nifti output by PyDesigner; this step is **extremely important** as a bad skull strip will negatively affect registration.
    - During this step, dwi\_preprocessed.nii files are skull stripped and a mask is created.
    - A screenshot of a cell phone

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    - A QC folder is also created with all skull stripped files. If skull stripping is not sufficient, the skull stripping threshold (-f # in the script) can be modified.
      * Depending on the dataset, BET can be highly customized to achieve appropriate skull stripping.
      * Due to the nature of tensor files and default scales in many image viewers, just looking at the skull stripped tensor with default scale settings may be deceptive:
      * A picture containing cat, looking, sitting, screen

        Description automatically generated
      * The above image appears appropriately skull stripped but by overlaying the mask onto it, we see that it is not skull stripped correctly:
      * 
      * Once you refine the BET process, the mask overlay should look more like this:
      * A picture containing cake, table, sitting, white

        Description automatically generated
  + **Tensor Prep: 1\_Preproce\_Tensor\_Prep.sh section 3**
    - 3.a - dtifit – dtifit is an FSL tool that takes preprocessed niftis and associated bvec/bval files and creates tensor.nii files. This step also requires the BET mask created in the previous step.
      * A screenshot of a cell phone

        Description automatically generated
    - 3.b – fsl\_to\_dtitk – fsl\_to\_dtitk is a DTI-TK tool that converts FSL output files into DTI-TK format. This step creates many extraneous files. The file required to proceed is called dti\_dtitk.nii
      * A picture containing screenshot, screen, sitting, black

        Description automatically generated
      * From the DTI-TK site: “a script that takes a FSL-generated DTI eigensystem volumes (*non-brain tissue already removed*) and converts them into fully DTI-TK compatible DTI volumes, i.e., both in the correct format and [correctly preprocessed](http://dti-tk.sourceforge.net/pmwiki/pmwiki.php?n=Documentation.BeforeReg).”
      * It is possible to check that adjustments have been made to the image by comparing the old image header information with the new image header information  
        A screenshot of a cell phone

        Description automatically generated
* **DTI-TK Image Registration: 2\_DTI-TK\_Norm.sh**
  + **Within-Subject Registration: 2\_DTI-TK\_Norm.sh section 1**
    - This section does the following:
      * Renames the dti\_dtitk.nii file to be called “[subjectID]\_dti\_dtitk.nii”
      * Creates a new folder inside of the 01\_Tensor\_Prep folder called “Within-Subject”
      * Creates an individual subject folder for each subject’s BL and FU image inside of “Within-Subject”
      * Copies the newly renamed files into this folder (BL and FU go into the same folder)
      * Creates a subj.txt file in each folder for further processing
        + A black sign with white text

          Description automatically generated
        + A close up of a black background

          Description automatically generated
      * Inside of a for-loop, each set of BL and FU images are registered to an average space (see flowchart for further details)
        + A screenshot of text

          Description automatically generated (zoom to see registration output file list)
      * QA registration by overlaying registered images after registration is complete.
      * A new folder called “02\_Tensors” is created and the subject tensors that had been registered to within-subject space are now copied to the new folder and renamed to [SubjectID}\_wi\_subj.nii
        + A picture containing food, drawing, player, game

          Description automatically generated
  + **Between-Subject Registration: 2\_DTI-TK\_Norm.sh section 2**
    - A subj.txt file is created within the 02\_Tensor folder to include all subjects, much like the subj.txt file shown above but with all subjects instead of a single subject’s BL and FU
    - The same registration process carried out in the last step is now carried out on between-subject data. The output file list is the same as the output file list above, except it will now include all subject data.
    - QA registration by overlaying registered images after registration is complete.
* **Scalar Map Warping: 3\_Scalar\_Map\_Prep.sh**
  + **File Organization: 3\_Scalar\_Map\_Prep.sh section 1**
    - Scalar maps generated via preprocessing program are copied into a new folder called 01\_Scalar\_Prep
    - A picture containing street, city, drawing, phone

      Description automatically generated
  + **Within-Subject Scalar Map Warps: 3\_Scalar\_Map\_Prep.sh section 2**
    - Scalar maps have their origin set to 0 0 0 and the transformation matrices that were generated via the within subject tensor registration method are applied to the scalar maps on a subject by subject basis to move the scalar maps into within-subject space.
  + **Between-Subject Scalar Map Warps: 3\_Scalar\_Map\_Prep.sh section 3**
    - The transformation matrices that were generated via the between subject tensor registration method are applied to the scalar maps on a subject by subject basis to move the scalar maps into between-subject space.
  + **File Organization: 3\_Scalar\_Map\_Prep.sh section 4**
    - Scalar maps in between subject space are moved into a new folder called 03\_TBSS for further processing
    - Files are organized in folders via metric type:
    - **A picture containing building

      Description automatically generated**
* **TBSS prestats: 4\_TBSS\_4.sh and 5\_TBSS\_4B.sh**
  + 4\_TBSS\_4 copies the stats folder from the DKI folder to the WMM folder and runs tbss\_4\_prestats with a threshold of 0.4 for WMM skeletonization setup
  + 4\_TBSS\_4B runs tbss\_4\_prestats with a threshold of 0.2 for DKI skeletonization setup
  + Both steps generate mean\_FA\_skeleton\_mask and mean\_FA\_skeleton\_mask\_dst based on respective thresholds
  + A screenshot of a computer

    Description automatically generated
* **Non-FA files combined and skeletonized: 6\_non-FA\_all\_files.sh**
  + **Non-skeletonized 4D map creation: 6\_non-FA\_all\_files.sh section 1**
    - Fslmerge is used to create 4D niftis of non-skeletonized maps for both DKI and WMM metrics
    - **A picture containing screenshot, sitting, black, screen

      Description automatically generated**
  + **Skeletonized 4D map creation: 6\_non-FA\_all\_files.sh section 2**
    - Tbss\_skeleton is used with mean\_FA\_skeleton\_mask\_dst to create 4D niftis of skeletonized maps for both DKI and WMM metrics
    - A screenshot of a computer

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  + QCing non-skeletonized maps is a good way to QC overall image registration. It is also worthwhile to QC the skeletonized maps to ensure that skeletonization was done appropriately.
  + A picture containing indoor, looking, fruit, sitting

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