General

createSheet

This function creates csv files summarizing all available scans across all subjects. It also writes individual csv files to each subject's directory. The master MRI and PET tables will be used to save QC info and index which scans to use for each subject. It will be written to a folder called spreadsheets in your project folder. 'spreadsheets' will be made automatically if it doesn't exist.

Note: Sometimes NIfTI images may not have the header field specifying field strength. If the code doesn't find a field strength specified, it will assume 3T.

MRI pre-processing

Individual pre-processing

dicomRecon - reconstruct DICOM files to a single NIfTI file. This will also create a 'dicom' subdirectory within the scan folder and move the DICOM files into it.

reorientAC - the goal of this step is to manually set the origin of the image to the anterior commissure, and make sure the head is oriented upright in the frame, by adjusting the roll, pitch and yaw. Andrew Jahn has a good tutorial here for those new to imaging. Ideally, save the .mat file specifying the reorientation for future reference. The newly reoriented file will be saved with an 'ac*' prefix and zipped in case pre-proc needs to be rerun.

checkVoxels - this will add the voxel sizes of each image to the master MRI spreadsheet. It will also ask you to decide whether to perform co-register: estimate only, or co-register: estimate and re-slice. Generally, if all images have the same or similar voxel dimensions co-register: estimate only will work fine. If there is a wide variety of voxel sizes across your dataset, sometimes re-slicing may be helpful. This is explained further in the SPM manual, section 4.

coreg - perform co-registration (estimate only or estimate and re-slice, depending on the output of the previous checkVoxels step). You need to specify an image to co-register to that has the orientation and or dimensions you would like. The enhanced TPM could be used if needed.

longitudinalRegistration - perform serial longitudinal registration for each subject. This will create a midpoint average image to use as the reference scan, instead of choosing an individual timepoint image as the reference. If you have multiple MRI scans of the same weighting and field strength (e.g. 3T T1-weighted) that were collected on the same day, it will also create intra-averages (an average for a specific timepoint) which will be used during midpoint average creation instead of the timepoint images.

segment - this step will segment MRI images into grey matter, white matter, CSF and other tissue compartments using segmentation in CAT12. This step also saves out imported segments (rp1 and rp2) which are required by geodesic shooting to create the population template. A bias corrected image will also be output. Different versions of CAT12 may cause issues with the segmentation module if CAT12's segmentation parameters change with subsequent updates.

MRI segmentation QC

summarizeSegQC - This adds the CAT12 Image Quality Rating (IQR) that is output during segmentation. The IQR's are added to the MRI master csv file. For subjects that don't have an IQR value, -1 means that the data is cross sectional (and the code was run in avgMode or to exclude cross sectional subjects), -10 means the segmentation is missing (was not run), and -100 means that segmentation failed for that subject.

redoSegProblems - Any subjects who failed or were missed during segmentation (-10, -100) can be re-run with a higher processing accuracy.

MRI template creation

buildCustomTemplate - population-specific template creation with geodesic shooting (optional). The custom template will be copied into a new directory within the project folder called (project_name)_shoot_template. This step will also output y_*.nii files that can be used to warp each subject's native space image into the population template space.

addToShoot - this step will perform nonlinear registration of each subject's data to an existing template, and output the y_*.nii files as above. If you are running this step without a population specific template created in the previous step, specify a path to an existing template in the shootTemplateOverride variable in the run_preproc.m file.

invertY - during CAT12's segmentation, it will output a deformation field (y file) that specifies the transformation from a subject's native space into the CAT12 geodesic shooting MNI template. This module will invert this Y file, to give the transformation from MNI → native space. Not required for pre-processing, but may be useful for native space ROI analyses.

**Longitudinal modulation and spatial normalization**

multiplyJacobian - For each subject, multiply the Jacobian determinant created for each timepoint during longitudinal registration by the specified tissue segment. This will produce Jacobian modulated grey matter (jacp1*.nii), white matter (jacp2*.nii), or CSF (jacp3*.nii) segments, depending on what tissue compartment you specify in the tissue_compartments variable of the run_preproc.m. These are output to the timepoint directories for each subject.

warpToShoot - normalize native space images to the shoot template space. You can specify to modulate or not modulate the images during warping in the warpType variable of the run_preproc.m file. If you are performing modulated warping, the code defaults to looking for the Jacobian-modulated (jacp*.nii) files in AvgMode or the tissue segment specified in tissue_compartments in indMode. You can alternatively update the warpPath and warpFilt variables to change which file will be spatially normalized depending on your goal. Note: if you need to warp the p1 midpoint average files (for between subject QC), set warpPath = {['midpoint_average', filesep, 'mri']} and warpFilt = {'p1'}.

If you are running this step without a population specific template, specify a path to an existing template in the shootTemplateOverride variable in the run_preproc.m file.

createAvg - This is intended for visualization only. It can be used to create an average of all subjects' spatially normalized midpoint average images so that you have a nice quality MRI scan in the template space to project any statistical results onto. You can also visually assess if there were glaring issues in spatial normalization,

based on whether the average image looks like one image, or if you can see rings suggesting the images did not align across subjects. In the example PET images, the average image on the left shows mis-alignment across subjects, while the average image on the right looks like spatial normalization worked generally well.
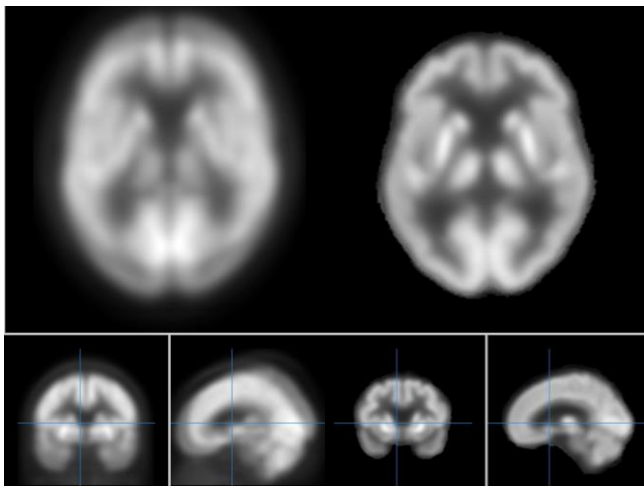
Final MRI QC

withinSubQC - uses CAT12's check covariance function to assess the covariance between each of the Jacobian modulated tissue segments for a given subject. This could help identify (for example) if a subject has one individual timepoint image that was low quality relative to their remaining images.

betweenSubQC - uses CAT12's check covariance function to assess the covariance across all subjects. If a subject has very low covariance, there may have been an issue during segmentation and/or spatial normalization. The covariance is typically checked on the spatially normalized midpoint average grey matter segment for each subject. See instructions under warpToShoot module for how to do this.

summarizeQC - this step will summarize all of the QC variables created during MRI preprocessing into one variable to make it easier to exclude subjects who failed QC during statistical analyses. Subjects with low withinSubQC or betweenSubQC values will be displayed for visual inspection by the user, and the user will indicate whether they would like to include or fail the subject. In avgMode, summarizedAvgFails (0 = pass, 1 = failed) will be written to the MRI master sheet. In IndMode, the variable is called summarizedTimepointFails.

extractICV - this will add the subject's intracranial volume (ICV) to the master sheet. ICV may be needed during stats to control for head size.

PET pre-processing

****Not recommended for use with true dynamic PET data. Multiple steps required for dynamic data (e.g. checking motion) are not implemented. If you have multiple frames of PET data collected during the static period the code can handle that, but again, not recommended.*

within-subject registration

dicomRecon, **reorientAC** and **checkVoxels** function similarly to what was described in the MRI section. See above for more details. In the case of **reorientAC** for PET data that is 4D, make sure you save the reorientation matrix so that it can be applied to all PET frames.

remove4D - splits a 4D NIfTI file into multiple 3D files, which is needed for further preprocessing steps.

Realign frames - uses the SPM re-align (estimate and write) to align dynamic PET data or longitudinal static data within each subject.

coregMR - co-register: estimate and re-slice the PET data to the subject's reference MRI data. The reference MRI data is specified in the mri_ref variable. If you had T1-weighted longitudinal MRI data processed using longitudinal registration, this would be specified by setting mri_ref = {'avg', 'T1'};

spatial normalization, SUVR calculation & (optionally) PVC

warpToShoot - using the subject's deformation field estimated during MRI preprocessing, spatially normalize the PET image into the shoot template space.

makeMasks - make a grey matter mask from the template image, binarized at p >= 0.5. This will also make a whole brain mask, to calculate average whole brain uptake.

computeSUVR - for this step, you need to have created a reference region mask, and normalized it to your template space. Your reference region mask should be a binary file where 1s indicate voxels within the mask. The mask name is specified in the ref_mask variable, and the directory containing the ROI mask is specified by the roi_dir variable.

pvc - perform partial volume correction with the Müller-Gärtner (MG) method (optional). Whether or not to perform this step depends on what tracer you are using, the study population and possibly whether the PET data is longitudinal or cross sectional.

createAvg - see description in MRI section.

PET QC

getSUVRfails - this will add a binary variable to the PET master table indicating whether each image was able to be SUVR'd. This variable will mainly filter out subjects who don't have MRI data that passed QC. 1 = image failed SUVR step.

withinSubQC and **betweenSubQC** function similarly as to with MRI, except you are instead checking the covariance of the warped, SUVR'd PET images.

summarizeQC - this creates a summary variable in the PET master table indicating who failed overall QC, considering all steps involved in the PET QC process. In this variable, 1 indicates that an image failed QC and should be excluded. Images that are marked as fails will be displayed for the user to inspect and manually indicate if they agree that the subject should be excluded.

checkReg - this step pulls up the PET images for random subjects who passed QC using SPM's check registration module. This allows the user to visually inspect the images and ensure that registration looks accurate across images.

At this point, the MRI and PET pre-processing is complete, and data can be entered into voxel-wise or ROI based statistics. If you are using voxel-based stats, you will likely want to smooth your data beforehand, which can be easily done in SPM.