A4 Tau PET Processing Details

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Tau PET and MRI data were downloaded from LONI following the “Quick Guide to A4 Imaging Data” document. Briefly, the “pre-processed” flag was set on LONI and “Flortaucipir” was used as a search term – this imaging data was downloaded as well as the accompanying collection csv file generated by LONI, which provides a list of participants. This csv list of participants with tau PET data was then entered into the “Subject ID” field and “T1*” was entered in the image description field, returning the MPRAGE data for only participants with Flortaucipir data. These data are for 447 participants.

This document describes the two following files:

	Filename	File label	
1	imaging_Tau_PET_Stanford.csv	Imaging - Tau PET SUVR (Stanford Pipeline)	Tau SUVrs
2	imaging_Tau_PET_PetSurfer.csv	Imaging - Tau PET SUVR (PetSurfer Pipeline)	Tau SUVrs with partial volume correction

Stanford Tau PET Processing Pipeline – published in Young et al., JAMA Neurol 2022.

The processing steps were as follows:

1. Reconstruction to create 2D surfaces and segmentations were run on all the T1 data using Freesurfer’s recon-all command. The important output were nu.mgz and aparc+aseg.mgz files.
2. PET 5-minute frames were realigned and summed. As noted in the “Quick Guide to A4 Imaging Data” file, some data were reconstructed into a single frame, but per A4 recommendations, the data were used as provided.
3. 111 participants presumably from a single site had very noisy looking tau PET data. For these subjects, FSL was used to apply 4 mm FWHM smoothing to the tau PET data only.
4. PET scans were coregistered to their MRI scans using SPM. The MRI and corresponding aparc+aseg data were moved into PET space.
5. The mean values from the summed PET file were extracted across all aparc+aseg regions. A csv file was created with all mean values along with each region’s total volume to enable regions to be combined.
6. We additionally created bilateral regions taking a volume weighted average across hemispheres. These are provided for in the bi_* columns.
7. For tau PET, we used a gray matter only cerebellum reference region (volume weighted across hemisphere using Mean.Left.Cerebellum.Cortex, Mean.Right.Cerebellum.Cortex, Volume_mm3.Left.Cerebellum.Cortex, and Volume_mm3.Right.Cerebellum.Cortex columns). Because the values in the tau PET csv files are normalized to this gray matter only cerebellum reference region, the values in this column (“bi_Cerebellum.Cortex”) are 1.

Tau PET Processing – PVC

PVC was completed using the PetSurfer pipeline.

1. Anatomical segmentations for the geometric transfer matrix were created for each participant using Freesurfer’s gtmseg command. The important output is gtmseg.mgz.
2. The lta_convert command was used to create an LTA Freesurfer transformation format file from the same realigned and summed PET file that was used in the non-PVC pipeline (lta_convert –initla identity.nofile –src PET.nii.gz –trg brainmask.mgz –outlta PET.lta).

PVC was applied using FreeSurfer's mri_gtmpvc command (mri_gtmpvc –i PET.nii.gz –reg PET.lta –psf 6 –seg gtmseg.mgz –default-seg-merge –mask PET_bin.nii.gz –no-reduce-fov –mgx 0.01 –rescale 8 47 –o gtmpvc.output). The realigned and summed PET file was used as the input. The PET.lta file maps PET to anatomical. The PSF was assumed to be 6 for all participants. The 'default-seg-merge' flag applies the default schema for merging ROIs. The mask file was created by binarizing the PET image. The 'no-reduce-fov' flag maintains the FoV. The 'mgx 0.01' flag runs Muller-Gartner analysis with 0.01 as the GM threshold. The '—rescale 8 47' flag uses regions 8 (Left-Cerebellum-Cortex) and 47 (Right-Cerebellum-Cortex) for rescaling. As expected, PVC values are systematically higher than non-PVC values since higher SUVRs likely have more atrophy.

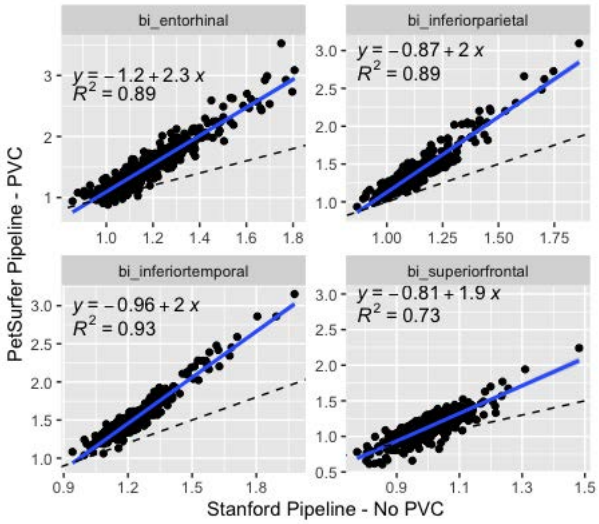

Figure 1. Relationship between tau SUVRs using the Stanford processing pipeline detailed above (x-axis) and SUVRs using the PetSurfer pipeline with partial volume correction (y-axis). Dashed line represents identity line. Solid blue line represents the regression line.

The PetSurfer without PVC pipeline values are not shared here, but they are very comparable to the no-PVC pipeline detailed above.

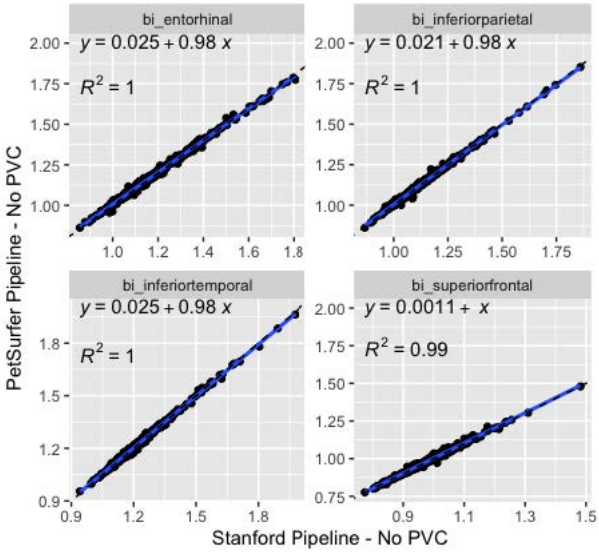

Figure 2. Relationship between tau SUVRs using the Stanford processing pipeline detailed above (x-axis) and SUVRs using the PetSurfer pipeline without partial volume correction (y-axis). Dashed line represents identity line. Solid blue line represents the regression line.

8. The PVC values were extracted across all aparc+aseg regions. A csv file was created with all PVC values (PVC_*) along with each region's number of voxels (NumVoxels_*) to enable regions to be

combined.

9. We additionally created bilateral regions taking a voxel weighted average across hemispheres. These are provided for in the bi_* columns.
10. We used a gray matter only cerebellum reference region (voxel weighted across hemisphere using PVC_Left.Cerebellum.Cortex, PVC_Right.Cerebellum.Cortex, NumVoxels_Left.Cerebellum.Cortex, and NumVoxels_Right.Cerebellum.Cortex columns). Because the values in the tau PET csv files are normalized to this gray matter only cerebellum reference region, the values in this column ("bi_Cerebellum.Cortex") are 1.

Appendix

Note that B34660963 has off-target binding outside of the brain that is inflating tau SUVRs in the frontal lobe. Consider excluding this subject based on study focus.

References

Young, C. B., Winer, J. R., Younes, K., Cody, K. A., Betthauser, T. J., Johnson, S. C., Schultz, A., Sperling, R. A., Greicius, M. D., Cobos, I., Poston, K. L., Mormino, E. C., & Alzheimer's Disease Neuroimaging Initiative and the Harvard Aging Brain Study. (2022). Divergent Cortical Tau Positron Emission Tomography Patterns Among Patients With Preclinical Alzheimer Disease. *JAMA Neurology*. https://doi.org/10.1001/jamaneurol.2022.0676