

SCAN/CLARiTI MRI-free Tau PET Processing

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Summary

A goal of SCAN (Standardized Centralized Alzheimer’s & Related Dementias Neuroimaging) is to generate PET data that could be merged with other multisite studies, such as ADNI. However, the ADNI PET pipeline¹ requires an MRI, and many SCAN PET images do not have an accompanying MRI available. Similarly, the CLARiTI (ADRC Consortium for Clarity in ADRC Research Through Imaging) study, which recruits through the ADRCs, does not require participants to undergo MRI acquisition, resulting in acquired PET images without an accompanying MRI. For these reasons, we have implemented MRI-free processing for SCAN and CLARiTI PET images; all numerical data provided in these datasets have been calculated without the use of an MRI for definition of ROIs. It is important to understand that the MRI-free pipeline does not yield quantitative values that are identical to values produced from an MRI-based pipeline. However, the values are quite similar and linearly related. Further down in this document, we explain how to transform MRI-free data to equivalent MRI-based data.

The MRI-free tau PET processing pipeline builds on our previously validated MRI-free PET processing methods² by employing an approach that can be used across multiple tau PET tracers (¹⁸F-Flortaucipir (FTP), ¹⁸F-MK-6240). *The tau PET tracer ¹⁸F-PI-2620 will also be processed as part of SCAN and CLARiTI, but an MRI-free pipeline is currently being validated for this tracer.* Our MRI-free PET pipelines consist of (1) a linear registration of individual PET scans to a MNI152 T1 template, (2) non-linear spatial normalization to a tracer-dependent PET template, (3) mean intensity quantification within regions of interest (ROIs), and (4) intensity normalization to create standardized uptake value ratios (SUVRs) in relation to a reference region.

Methods

Accessing SCAN/CLARiTI tau PET images in LONI Repository

We download SCAN and CLARiTI FTP and MK-6240 images from LONI in the most fully pre-processed format (Step 4; frames realigned and averaged, linear transformation to straighten out the head, standardized voxel size and smoothed to 6mm resolution). In the table below, LONI series descriptions are listed for each tracer and corresponding standardized acquisition window (Table 1).

Table 1. SCAN/ CLARiTI tau PET LONI Series Descriptions. Primary acquisition times are in bold.

<u>Tracer</u>	<u>Acquisition Time</u>	<u>LONI Series Description</u>	
		<u>SCAN</u>	<u>CLARiTI</u>
FTP	80-100	T80 Coreg, Avg, Rigid Reg to Std Img/Vox Size, 80-100*, 6mm Res	T80 Coreg, Avg, Std Img and Vox Siz, Uniform 6mm Res 80-100
MK-6240	90-110	M62 Coreg, Avg, Rigid Reg to Std Img/Vox Size, 90-110*, 6mm Res	M62 Coreg, Avg, Std Img and Vox Siz, Uniform 6mm Res 90-110

Tau PET templates

FTP and MK-6240 scans with MRIs from other studies were used to create the tau PET templates. A set of n=200 of images for each tracer were transformed to MNI-152 space using participant - specific MRIs. Samples between tracers were matched for a similar distribution of sex, age, diagnosis, and amyloid status as best as possible for the cohorts we had available to us (Table 2). The FTP template was created using a subset of Alzheimer's Disease Neuroimaging Initiative (ADNI: 50 A β -negative and 50 A β -positive unimpaired; 50 A β -negative and 50 A β -positive impaired males and females) participants. For the MK-6240 template, we used scans from the Alzheimer's Association U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (U.S. POINTER: 50 A β -negative and 50 A β -positive) for unimpaired participants and scans from Cerveau Technologies (Cerveau: 41 A β -negative and 59 A β -positive) for impaired participants with MCI or AD. Each set of images were preprocessed by the University of Michigan and downloaded as "Step 4" images through LONI in the same method as SCAN and CLARiTI images. Template space PET scans were intensity normalized and averaged together for each tracer to create tau PET templates (Figure 1). These templates are used for spatial normalization of SCAN and CLARiTI tau PET images as part of the MRI-free processing pipeline.

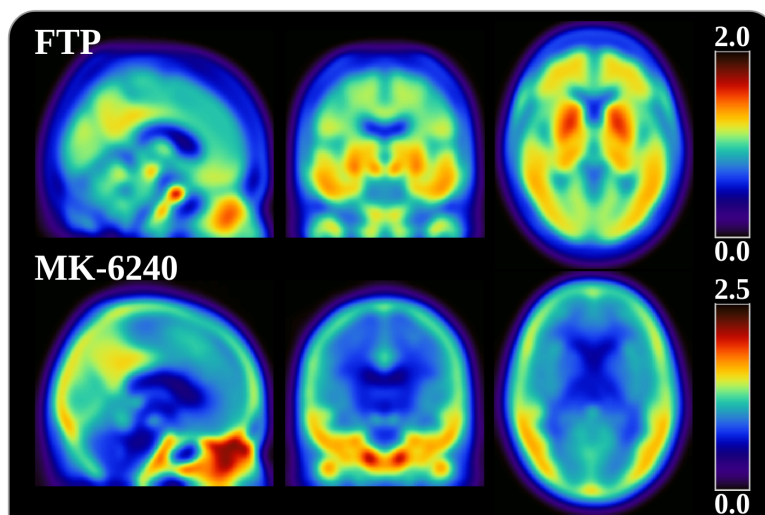


Figure 1. Tau PET templates used for spatial normalization to MNI-152 space.

Table 2. Distribution of total subjects, age, and sex by diagnosis and amyloid status for FTP and MK-6240 Tau PET templates. CN: Cognitively Normal, CI: Cognitively Impaired.

<u>Tracer</u>		<u>CN / Aβ+</u>	<u>CI / Aβ+</u>	<u>CN / Aβ-</u>	<u>CI / Aβ-</u>
FTP	n	50	50	50	50
	Age	73.8 (7.2)	75.4 (6.4)	71.6 (6.6)	73.9 (7.0)
	Sex (M)	40%	52%	40%	62%
MK-6240	n	50	59	50	41
	Age	69.7 (4.8)	73.3 (7.9)	67.7 (4.9)	71.6 (8.8)
	Sex (M)	50%	49%	50%	44%

Calculation of SUVRs

Once images are warped to their respective PET template, we sample regional means within template space ROIs. A whole brain atlas was developed to sample template space Desikan-Killiany ROIs equivalent to those produced by Freesurfer in native space (Figure 2; for more information see NPDKA section below). This was done to reduce differences between our MRI-free and MRI-dependent pipelines so that datasets could more easily be compared. From this atlas, two primary ROIs (temporal MetaROI, entorhinal cortex) and two reference regions (inferior cerebellar gray matter, eroded hemispheric white matter) are placed at the “front” of the dataset, but SUVRs for all NPDKA regions are provided. **The tau PET dataset is intensity normalized by the inferior cerebellum, visible as a column of 1’s for this region. Any SUVR can be renormalized once by dividing the region by another.**

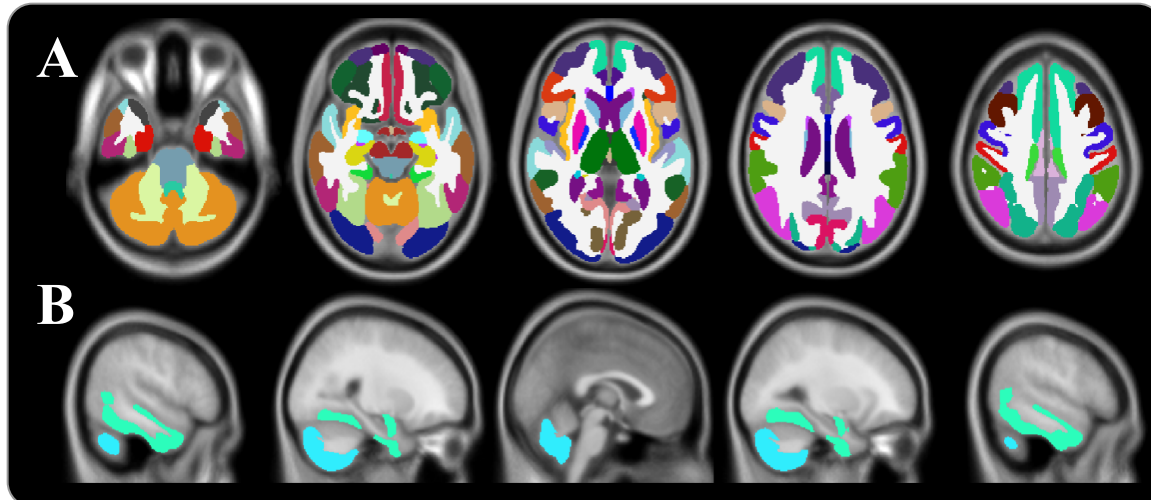


Figure 2. (A) Normalized Probability Desikan-Killiany atlas (NPDKA) based on the Desikan-Killiany atlas and derived from an average of 200 Freesurfer 7.1 segmentations. (B) Inferior cerebellar grey matter and meta-temporal masks. These masks exist in MNI-152 space and are used to sample SUVrs from tau PET images after MRI-free spatial normalization.

NPDKA Summary and Regional SUVrs

The purpose of the normalized probability Desikan-Killiany atlas (NPDKA) was to provide template-space SUVrs for the 111 Freesurfer-defined ROIs used in our MRI-dependent, native space pipeline³. The NPDKA temporal MetaROI and regional SUVrs are intensity normalized to a template space inferior cerebellum mask created from a subset of voxels in the Desikan-Killiany cerebellar gray matter, detailed methods described in Baker, et al (2017)⁴. The inferior cerebellum reference region is recommended for cross-sectional analyses. The eroded hemispheric white matter is another common reference region provided in our dataset and was created from the hemispheric white matter mask in the NPDKA atlas by smoothing the binary mask with an 8mm³ Gaussian kernel and threshold at 0.9 units. We recommend evaluating the eroded hemispheric white matter as a reference region for longitudinal analyses.

The NPDKA (Figure 2) was derived from Freesurfer v7.1 Desikan-Killiany segmentations of 200 cognitively normal, A β -negative ADNI participants³. Template-space probability maps were created for each region first by 1) warping each segmentation to MNI-152 space using the parameters from the T1 (SPM12 normalize), 2) lightly smoothing each ROI mask with a 1.5mm FWHM gaussian kernel to clean the edges, 3) averaging the ROI masks across the 200 subjects, and 4) normalizing each ROI between 0 and 1 by dividing out the highest voxel probability. ROI probability maps were combined into a single whole brain atlas by assigning each voxel to the ROI whose probability map was the highest for that voxel. We used FTP data from ADNI and MK-6240 data from POINTER (unimpaired) and Cerveau (impaired) cohorts to compare MRI-free and MRI-dependent SUVrs to evaluate the correspondence of the MRI-free atlas and normalization (see Table 3 and Figure 3).

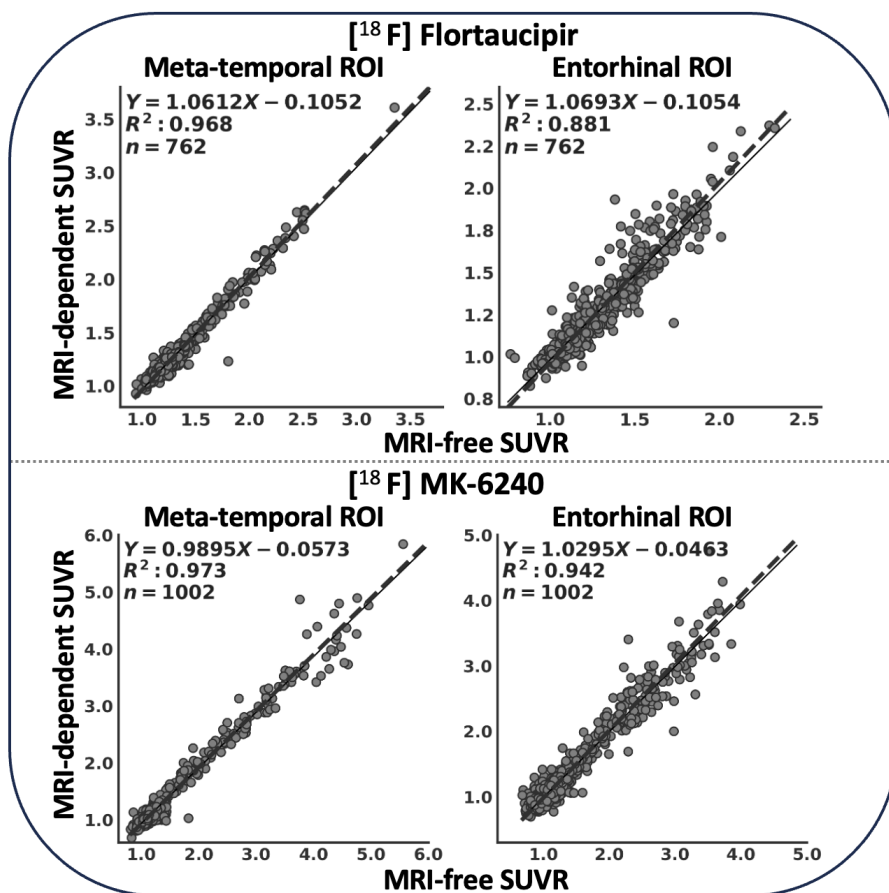


Figure 3. Regressions between MRI-dependent and MRI-free temporal MetaROI and entorhinal ROI SUVRs (normalized to inferior cerebellum) using the NPDKA volumes in FTP and MK-6240.

Transformation Between MRI-free and MRI-dependent Pipeline Results

The MRI-free meta-temporal SUVRs can be transformed to be compatible with the MRI-dependent meta-temporal SUVRs (generated by our MRI-dependent pipeline) using the **MRI-Dep SUVR $\leftrightarrow$ MRI-Free SUVR** transformation equations listed in Table 3. These reversible equations are based on the MRI-free to MRI-dependent total least squares regressions shown in Figure 3. Users may convert to MRI-dependent or MRI-free units depending on their specific projects. Note that these transformation equations apply to MRI-free and MRI-dependent data that is intensity normalized by the inferior cerebellum.

Table 3. Relationships between MRI-dependent and MRI-free NPDKA Meta-temporal and Entorhinal ROI SUVRs, normalized to the inferior cerebellum reference region.

<u>Tracer</u>	<u>MRI-dep SUVR $\leftrightarrow$ MRI-free SUVR</u> <u>temporal MetaROI</u>	<u>MRI-dep SUVR $\leftrightarrow$ MRI-free SUVR</u> <u>Entorhinal ROI</u>
FTP	(FTP MRI-dep SUVR)=1.0612(FTP MRI-free SUVR)-0.1052	(FTP MRI-dep SUVR)=1.0693(FTP MRI-free SUVR)-0.1054
MK-6240	(MK-6240 MRI-dep SUVR)=0.9895(MK-6240 MRI-free SUVR)-0.0573	(MK-6240 MRI-dep SUVR)=1.029 (MK-6240 MRI-free SUVR)-0.0463

FAQs

1. Are the ROI-wise SUVR values in these datasets already intensity normalized?

Yes. The SUVRs are already normalized by the inferior cerebellum. This is observable as a 1.000 SUVR in the column “INFERIORCEREBELLUM_SUVR”.

2. Can I intensity normalize the SUVRs using a different region?

To use a different reference region, re-normalize once with the provided values (divide original SUVRs by new reference region mean). For more information, see the “Calculation of SUVRs” section above.

3. Can I merge SCAN/CLARiTI data with ADNI data?

Yes, but ADNI SUVRs were generated using a different pipeline that depends on the use of an MRI, so it is important to ensure the SUVRs being merged are on the same numerical scale. To merge MRI-free SCAN/CLARiTI tau PET data with MRI-dependent ADNI data, transform the MRI-free SUVRs to their MRI-dependent equivalents using the MRI-free vs. MRI-dependent regression equations listed in Table 2 and plotted in Figure 3.

4. Can I merge SCAN/CLARiTI data with PET data from other studies?

SCAN and CLARiTI data can be merged with PET data from other studies that have been analyzed using an MRI-dependent pipeline identical to that used at UC Berkeley to process ADNI and POINTER PET data, using the strategy described above. To merge SCAN/CLARiTI data with PET data from other studies using other another method, there are two options: (1) the SCAN/CLARiTI images can be analyzed using the other study’s analysis methods in order to calculate a linear transformation equation that describes the relationship between SCAN/CLARiTI SUVRs and the other study’s SUVRs for the same individuals, and this relationship can be used to convert SCAN/CLARiTI data SUVRs to be compatible with the other study’s SUVRs, (2) process the other study’s PET data using UC Berkeley’s SCAN/CLARiTI MRI-free methods.

Version Information

This version of the tau PET MRI-free processing methods document for SCAN and CLARiTI was updated April 2026.

Dataset Information

This methods document applies to the SCAN and CLARiTI tau MRI-free NPDKA datasets that have been made available through the National Alzheimer’s Coordinating Center (NACC). To work with SCAN/CLARiTI tau PET data, researchers can submit a data request using the following link: <https://www.naccdata.org/data-request-process/>. Real-time dashboards showing data availability can also be found on [NACC Data Front Door](#).

References

1. Landau, SM, Murphy, A, Lee, JQ, et al. Florbetapir (AV45) processing methods. *LONI ADNI*. 2022; 1-7.
2. Landau, S. M., Ward, T. J., Murphy, A., Iaccarino, L., Harrison, T. M., La Joie, R., ... & Alzheimer's Disease Neuroimaging Initiative. (2022). Quantification of amyloid beta and tau PET without a structural MRI. *Alzheimer's & Dementia*.
3. Landau, S. M., Harrison, T. M., Baker, S. L., Boswell, M. S., Lee, J., Taggett, J., Ward, T. J., ... & for the U.S. POINTER Study Group and for the Alzheimer's Disease Neuroimaging Initiative. (2025). Positron emission tomography harmonization in the Alzheimer's Disease Neuroimaging Initiative: A scalable and rigorous approach to multisite amyloid and tau quantification. *Alzheimer's & Dementia*.
4. Baker, S. L., Maass, A., & Jagust, W. J. (2017). Considerations and code for partial volume correcting [^{18}F]-AV-1451 tau PET data. *Data in brief*, 15, 648–657.

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