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Introduction

Tau PET quantification typically requires structural MRI for reference-region definition, normalization, and segmentation, which imposes a logistical and operational burden. In this study, we evaluated whether low-dose CT can serve as a reliable MRI alternative for tau PET quantification when MRI is unavailable.

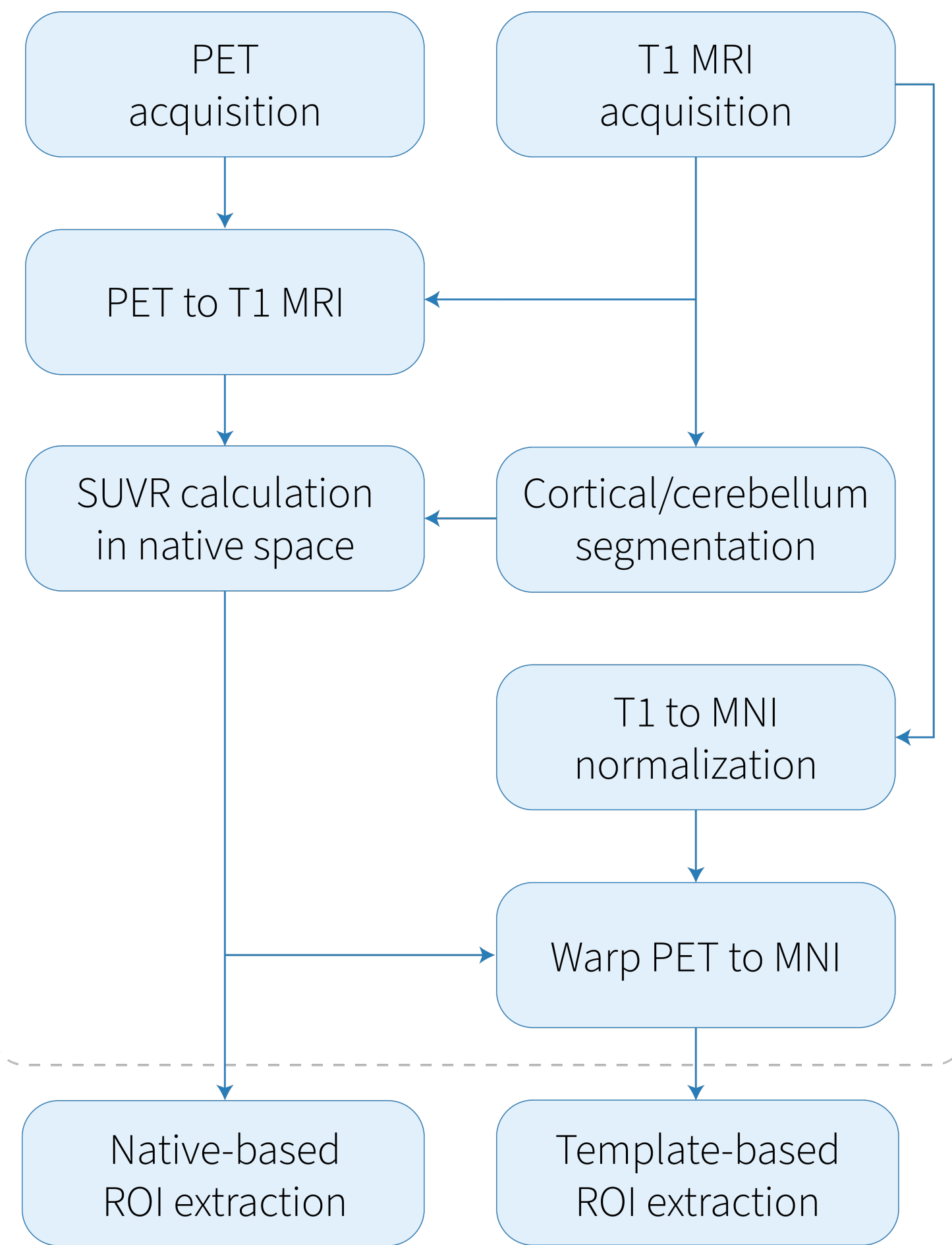
Methods

We developed a PET-CT pipeline using low-dose CT as the sole anatomical reference for tau PET quantification (**Fig. 1**). Participants were recruited from six sites in the HEAD study. The cohort comprised CU young adults (<28 years), CU middle-aged adults (50–65 years), CU older adults (>65 years), and participants with MCI or dementia. Participants underwent [¹⁸F]MK6240 and [¹⁸F]flortaucipir PET-CT, T1-weighted MRI, and Aβ PET. SUVRs were calculated for three composite regions and 34 individual cortical regions using a template-based cerebellar reference and compared with PET-MR pipelines using template-based or FreeSurfer subject-space segmentation. Tau-positivity thresholds were derived separately for each tracer and pipeline using the cognitively unimpaired middle-aged adults as the reference group (mean + 2 SDs). Agreement was assessed using linear regression, intraclass correlation coefficients, and Cohen's kappa (κ) for binary positivity concordance.

Results

We analyzed 387 participants (205 [53%] women, 182 [47%] men; six [2%] aged 19–25 years, 130 [34%] aged 50–65 years, and 251 [65%] aged 66–89 years). Average brain maps showed visually similar spatial patterns of tau deposition between PET-CT and PET-MR for both the tracers (**Fig. 2**). Against the template-based PET-MR pipeline, CT-derived standardized uptake value ratios showed near-perfect linear correspondence with the template-based PET-MR pipeline for MK6240 (R^2 0.925–0.975) and flortaucipir (0.925–0.964, **Fig. 3**), with high absolute agreement (intraclass correlation coefficient 0.976–0.985 for MK6240 and 0.955–0.978 for flortaucipir). Against the FreeSurfer subject-space pipeline, correspondence remained strong for MK6240 (R^2 0.952–0.971) and flortaucipir (0.909–0.949). Mean R^2 across 34 cortical regions was 0.917 (SD 0.049) for MK6240 and 0.874 (0.057) for Flortaucipir. Tau-positivity concordance was high (92.0–96.6%; κ 0.802–0.895; all $p < 0.0001$; **Fig. 4**), with discordant cases near the classification threshold. Associations with amyloid burden and memory were preserved across pipelines (Steiger's test, all $p > 0.05$). Equivalence between pipelines was confirmed by two one-sided tests (all $p < 0.001$).

PET-MR Pipeline



PET-CT Pipeline

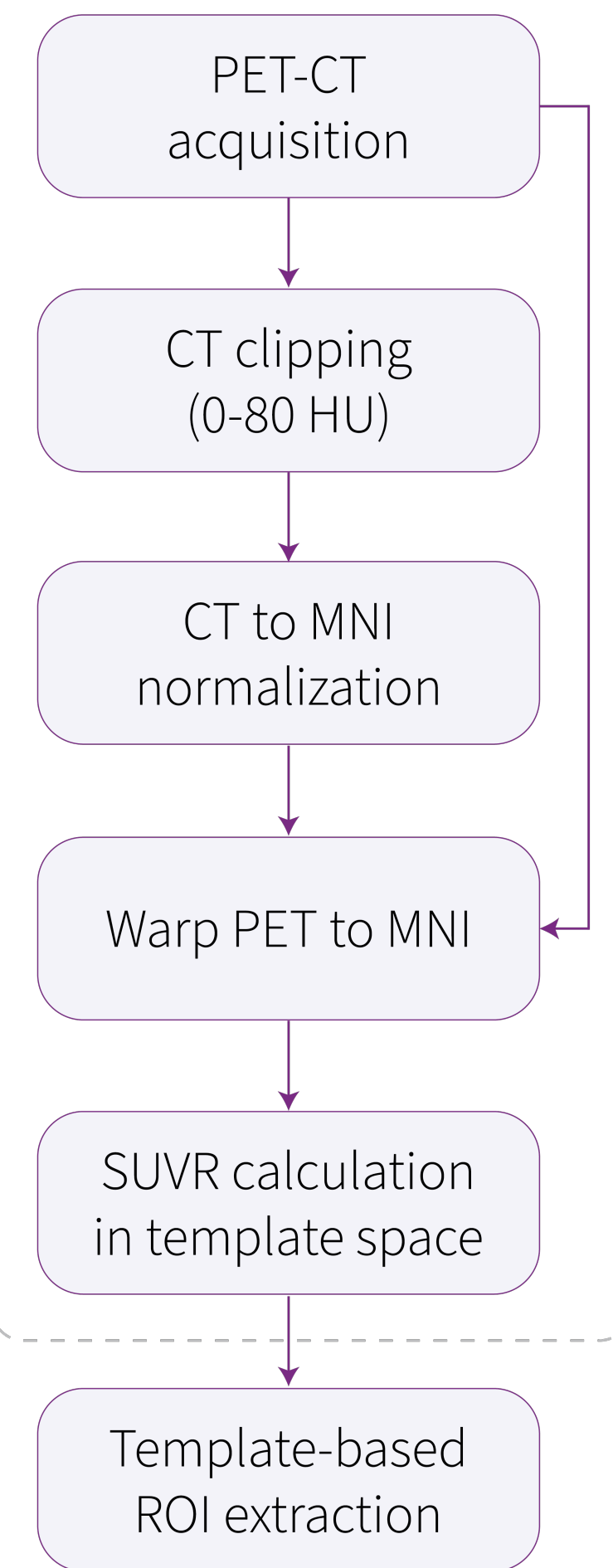
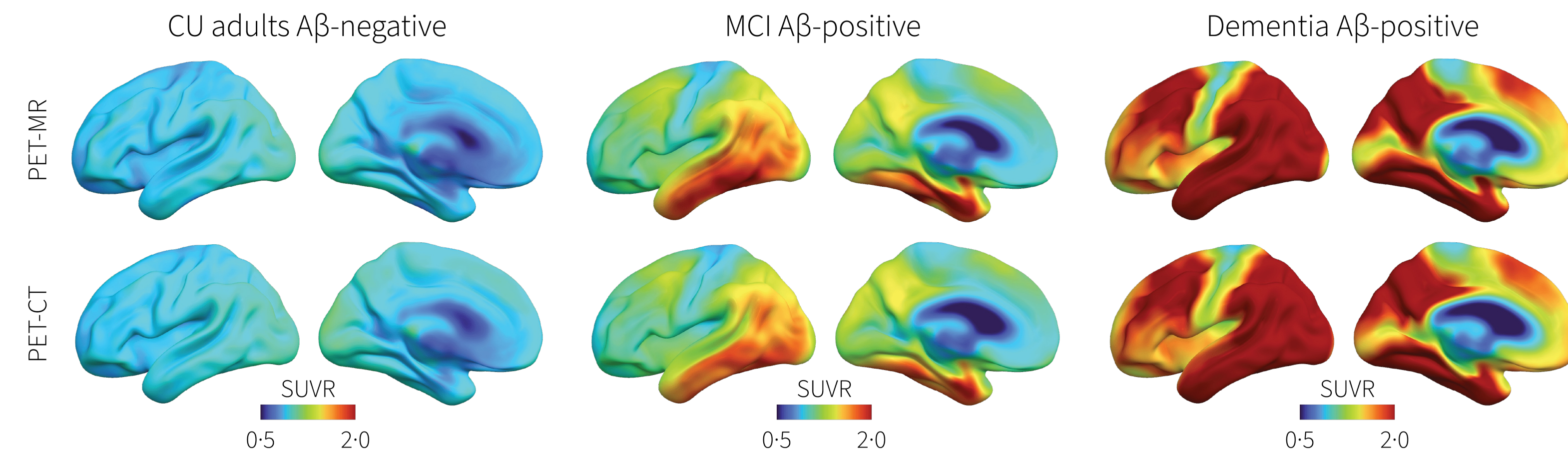


Figure 1. PET-MR and PET-CT image processing pipelines.

A Average brain maps for MK6240



B Average brain maps for Flortaucipir

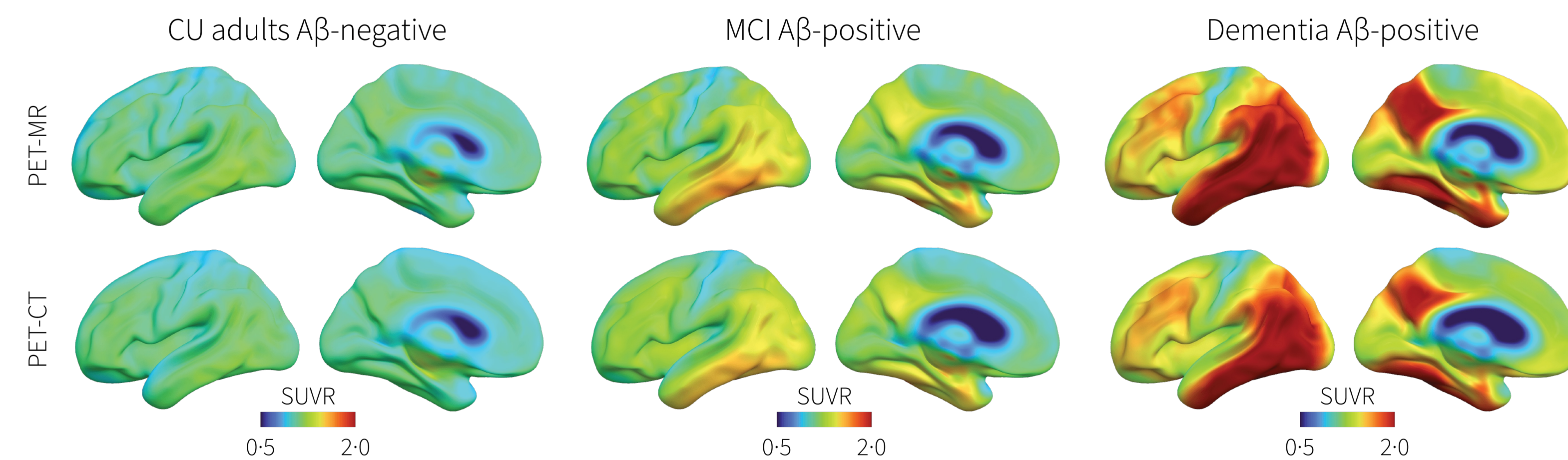


Figure 2. Average tau PET brain maps for the PET-MR and PET-CT pipelines.

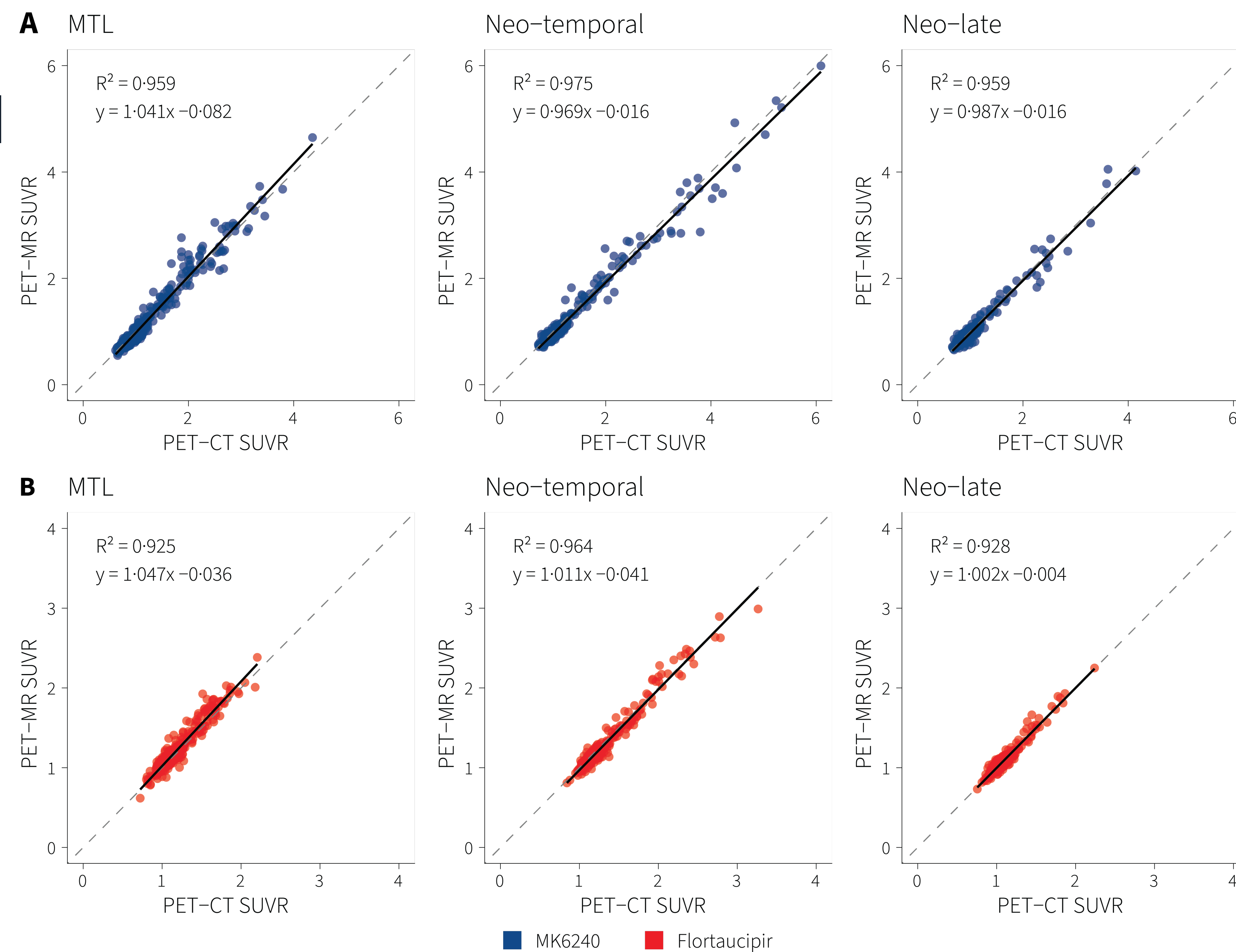
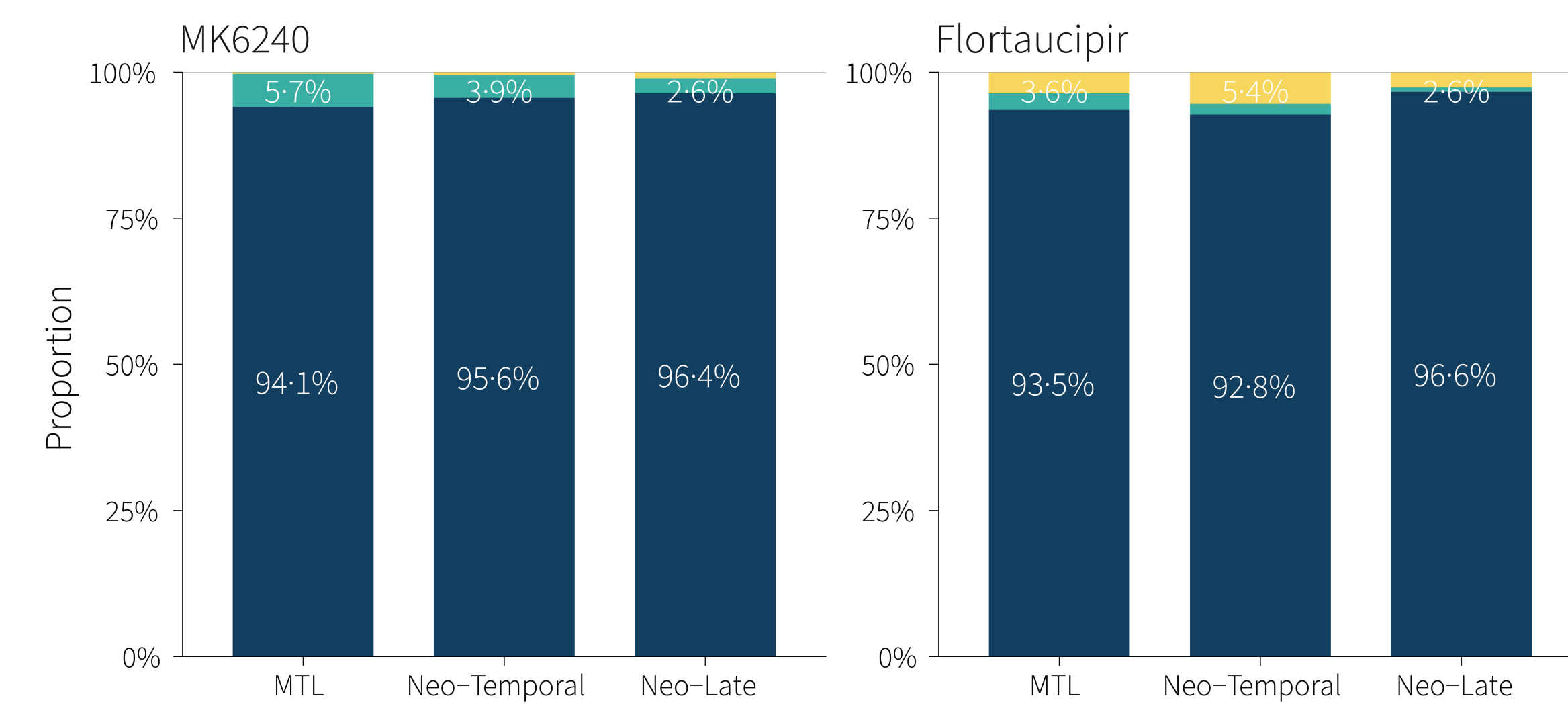


Figure 3. Agreement between PET-CT and PET-MR SUVR estimates.

A PET-CT vs PET-MR with template-based segmentation



B PET-CT vs PET-MR with subject-space (FreeSurfer) segmentation

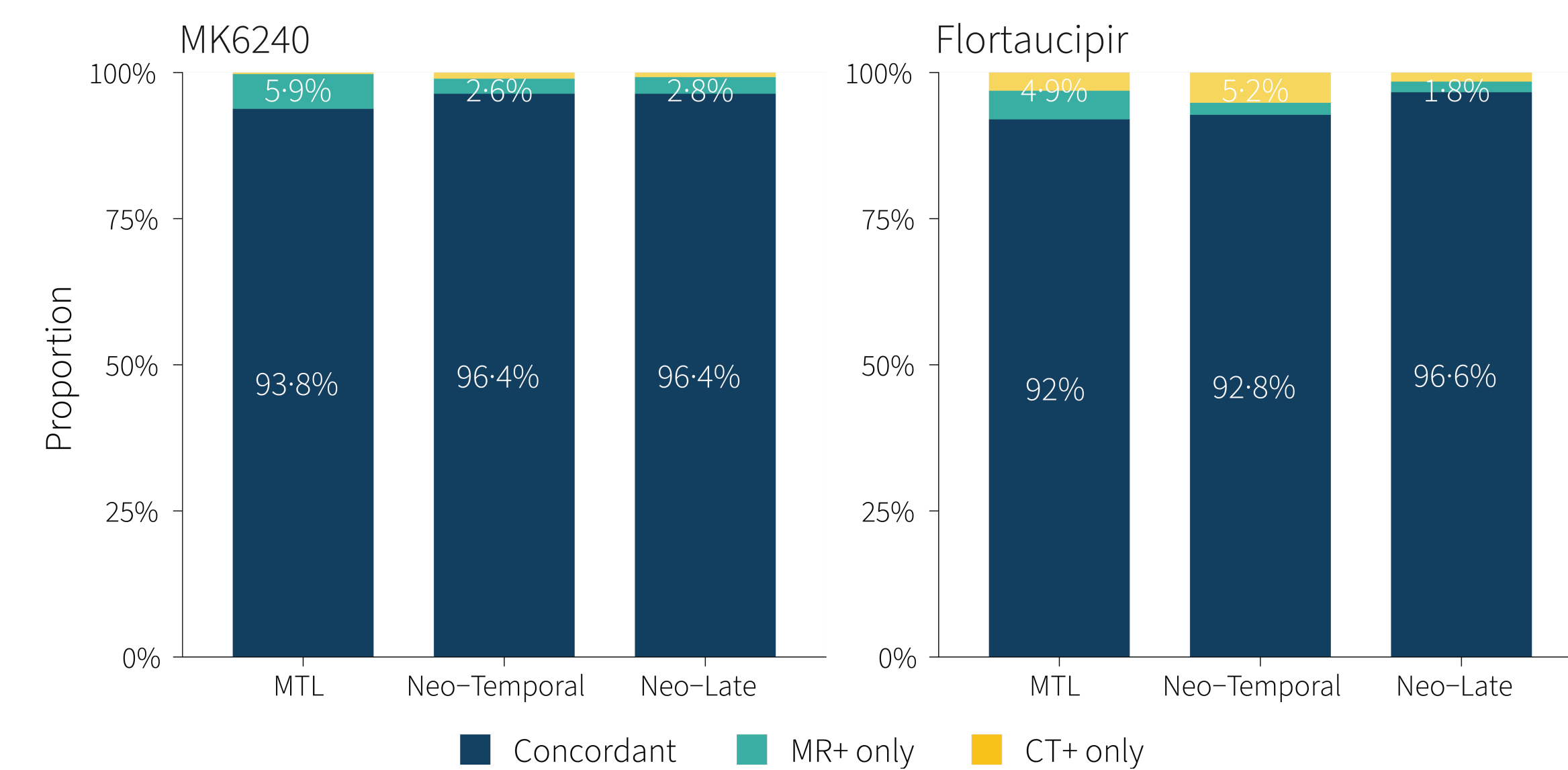


Figure 4. Concordance of tau-positivity between PET-CT and PET-MR.

Conclusion

CT-only processing enables robust tau PET quantification, comparable to standard MRI-based pipelines, including computationally intensive FreeSurfer-based approaches. This method was validated across different radiotracers and represents a reliable alternative when MRI is unavailable or contraindicated. Because low-dose CT is routinely acquired during PET-CT sessions, this approach enables quantification of legacy datasets without MRI, broadens participant inclusion in clinical trials, and can reduce imaging costs in settings where MRI is not clinically indicated.

Acknowledgments:

