The Impact of Automatic Tau PET Processing On Uptake Variability and Power Analysis in AD

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Introduction

- **Spatial distribution** of phosphorylated Tau [1] is a fundamental hallmark of **Alzheimer's Disease** (AD). PET with [18F]-AV-1451 (Tau-PET) probes in-vivo such distribution. For motion-robustness and comparability across imaging protocols, Tau-PET uptake is often summarised over composite regions, for example: Braak stages [Braak;Neuropathology;2006].
- Beyond **Braak composites**, regional Tau-PET uptake **might locally better differentiate** Cognitively Normal (CN), Mild Cognitive Impaired (MCI) and AD.
- However, **the impact of pre-processing** on **group classification performances** is unclear at both resolution levels.

AIM → Explore SUVR variability arising from different image pre-processing tools, namely for image registration

KEYWORDS: Tau-PET, Alzheimer's disease, pre-processing, registration impact

Methodology

Data source ADNI (http://adni.loni.ucla.edu)

- A total of 96 ADNI subjects (34 normal controls, 29 mild cognitively impaired, 33 AD) randomly selected
- Dynamic 6x5min Tau-PET frames ([18F]-Flortaucipir)
- Tau-PET regional SUVR measures obtained from ADNI-core
- T1w-MRI volumes (1.0x1.0x1.2 mm)

Image pre-processing

- T1w-MRI data was anatomically segmented with LEAP [Wolz;NeuroImage;2009] .
- Rigidly registered into native Tau-PET space (motion corrected saturated image) implementing two approaches:
  1. IRTK-based [Schnabel;MICCAI;2001]
  2. ANTs-based [Avants;NeuroImage;2011]
- Regional Tau-PET SUVR measures were obtained composing the 142 LEAP regions obtained for each subject into 68 bilateral cortical composites in addition to three Braak-like composites (one per staging level). Reference region = Cerebellum grey matter.

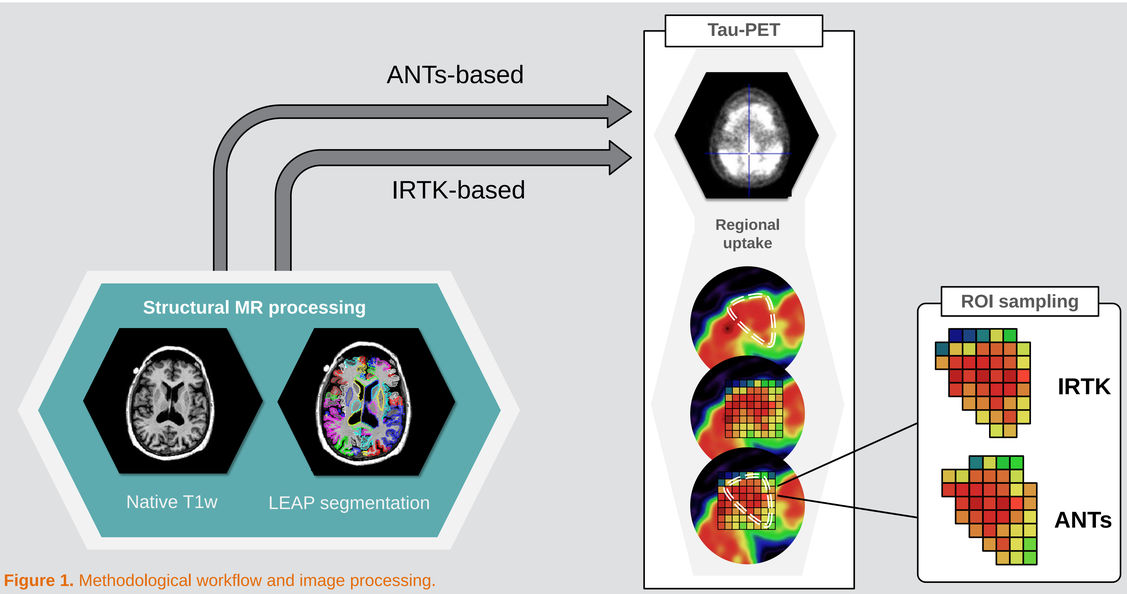

Figure 1. Methodological workflow and image processing.

Results

Regression analysis: Braak-SUVR across registration tools (x = SUVR_ANTs, y = SUVR_IRTK)

- High linear correlation between Braak-SUVR estimates: slope / offset / determination coefficient (R^2) = 1.09 / -0.09 / 0.97 [Figure 2.A]
- Relative SUVR difference not significantly different between groups; avg +/- std = 2.7 +/- 3.6 % [Figure 2.C]

→ In a **power analysis** to distinguish clinical groups (power: 80%, alpha: 0.05, 2-sides, balanced groups), the **sample size (# subjects)** required for statistical significance would be **338 samples using ANTs-based** pipeline or **583 samples using IRTK-based pipeline. Note**: with this small effect sizes (Cohen's d = 0.22 / 0.17 respectively from ANTs / IRTK pipelines, full ADNI: d = 0.72) → accurate pre-processing gets resource-critical.

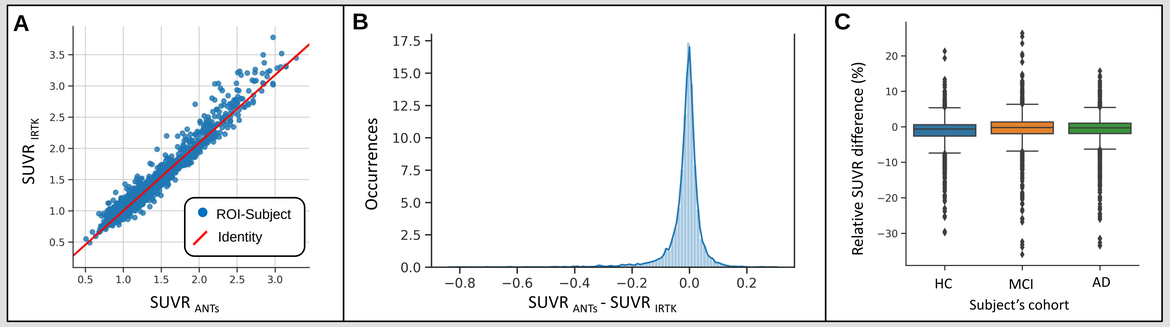

Figure 2. **(A)** Scatter plot representation across all ROIs and subjects between SUVR estimated with an ANTs or IRTK-based approach. **(B)** Actual SUVR difference within-ROI between registration approaches reporting a long left tailed distribution suggesting few high-SUVR outliers differencing the tools. **(C)** Boxplot of the relative SUVR difference between methods grouped by subject's cohort.

Paired-condition SUVR absolute difference was **not correlated with the subject's** group (Spearman's r=-0.01,p>0.05).

- **SUVR differences** between pre-processing tools **not correlated with pathology** [Figure 2.B]

Limited within-region variability in terms of relative SUVR difference (100 x ($SUVR_{ANTs}$ – $SUVR_{IRTK}$)/ ($SUVR_{ANTs}$ + $SUVR_{IRTK}$)/2) [Figure 3].

- Inter-quartile range: -2.26 to 0.84%, 75% of values differed less than 3.31% in relative absolute terms.

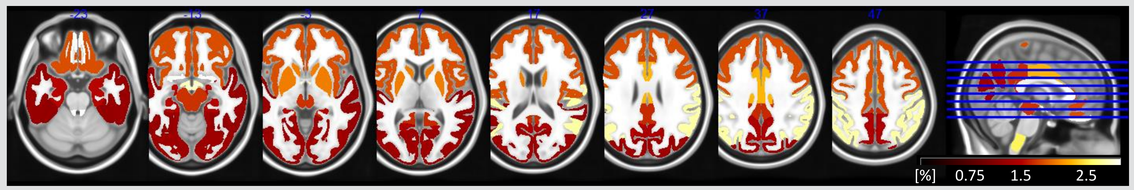

Figure 3. Spatial distribution of relative SUVR difference between registration approaches (%). Regions exhibiting highest SUVR differences between approaches include mid-posterior occipital sections of the cortex peaking at 3% (|relative SUVR difference| scale from 0.75%-dark red to 3%-white).

Conclusions

- Tau-PET ([18-F]-AV-1451) offers performances **robust to pre-processing differences.**
- It nevertheless requires **accurate registration** to anatomical-MRI for **repeatable endpoint generation.**
- We found that the variability introduced by different registration schemes is possibly under the typical scan-rescan variability
- Under small effect size condition, this difference can nevertheless translate in substantially different sample requirements based on accurate consideration of alternative processing schemes.