

Using Neuroimaging to Quantify Tau in the Spinal Cord of Alzheimer's Disease Patients: A Novel Neuroimaging Approach

Matthew Kirshner*, Carolyn Fredericks**

Department of Neurology, Yale School of Medicine, New Haven, CT, USA

*Presenting author, **Principle Investigator



Introduction

The current models of Alzheimer's disease (AD) pathology are limited to supraspinal models of the disease. Recent findings suggest AD involvement in regions of the spinal cord, primarily through immunohistochemical quantification (**Figure 1**) and volumetric analysis (**Figure 2**).^{1, 2}

Current models of AD pathology do not explain these findings in the spinal cord, rendering the pathological model of AD incomplete alongside unexplained symptoms with profound impact on patient quality of life. It is necessary for the AD pathology model to be expanded to include the spinal cord to develop a more complete understanding of AD pathology in addition to improving patient treatment quality.

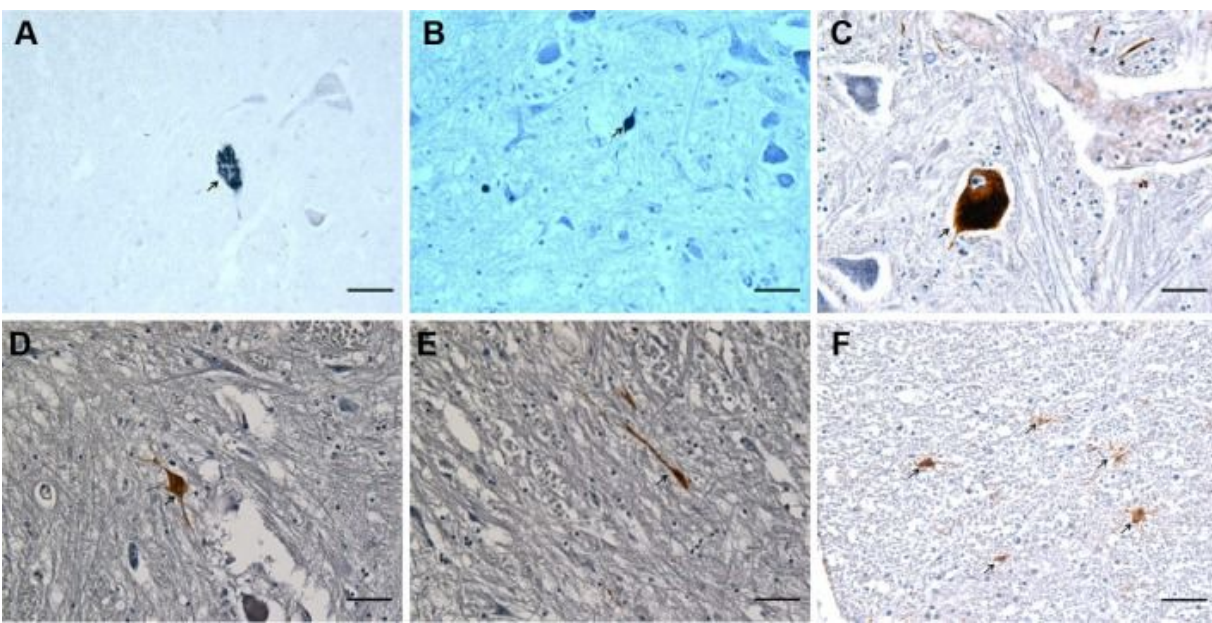


Figure 1: Wang et al., 2015

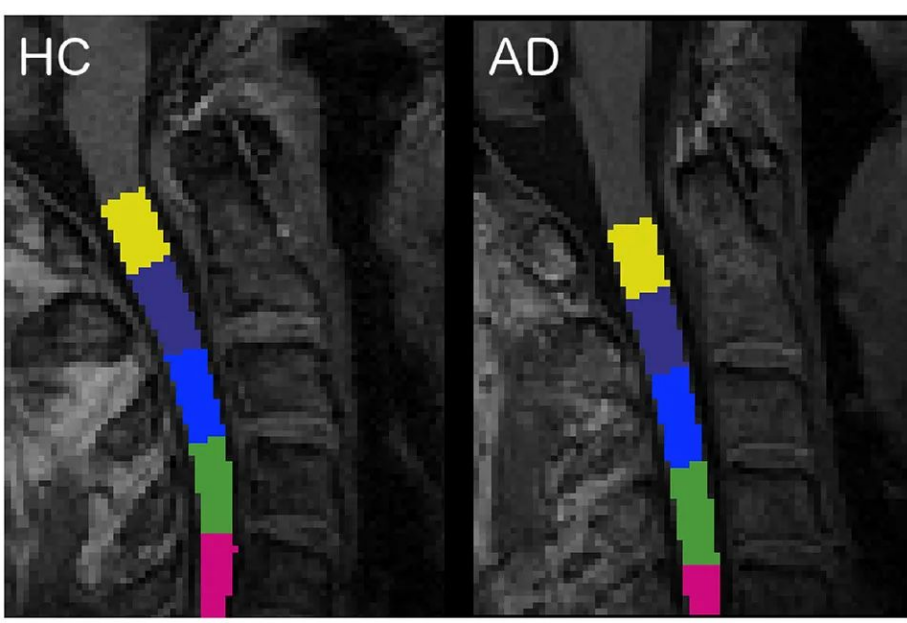


Figure 2: Lorenzi et al., 2020

Methods

Data Access & Usage:

Baseline ¹⁸F-AV1451 (Flortaucipir) PET and T1-W MPRAGE MRI Scans were sourced from the Alzheimer's Disease Neuroimaging Initiative (ADNI) accessed via the University of Southern California Image and Data Archive (IDA).³

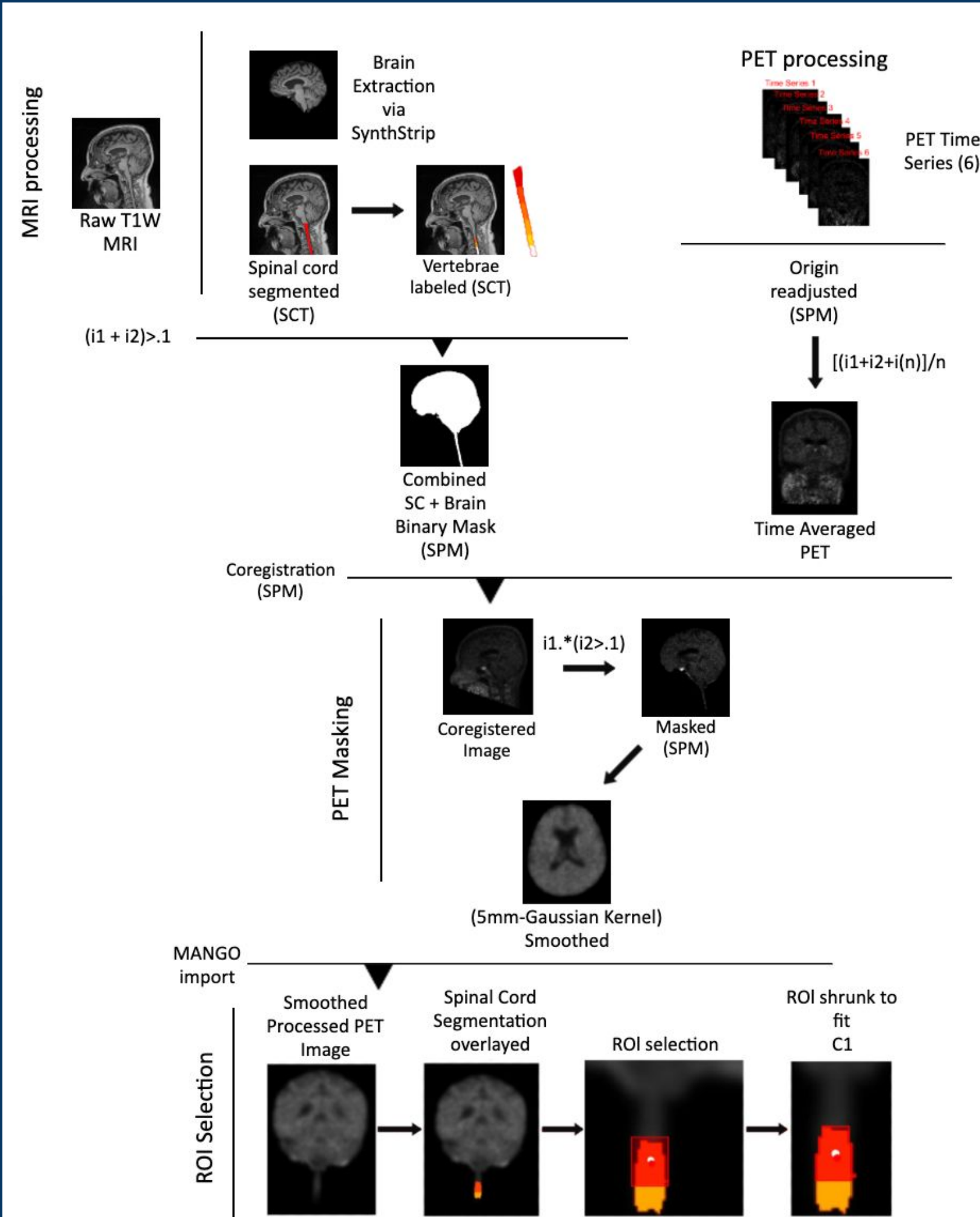
Cohort Selection:

Two cohorts, consisting of AD and Cognitive Normal (CN), were derived from the ADNI3 and ADNI4 imaging cohorts, each consisting 10 subjects (n=10). Subjects possessed both a baseline (bl) ¹⁸F-AV1451 tau PET image and bl T1-W MPRAGE MRI image. ADNI3 and ADNI4 images were manually inspected for viability and image quality, eliminating scans without C1 or more of the spine visible, and those with artifacts, such as tumor.

Pipeline Construction:

A novel PET preprocessing pipeline was created using a combination of functions from 4 distinct softwares: Statistical Parametric Mapping (SPM) 25, Spinal Cord Toolbox (SCT), SynthStrip, and Multi-Image Analysis GUI (MANGO).

Pipeline



Results & Discussion

Figure 3: CN vs AD Mean Tau UV

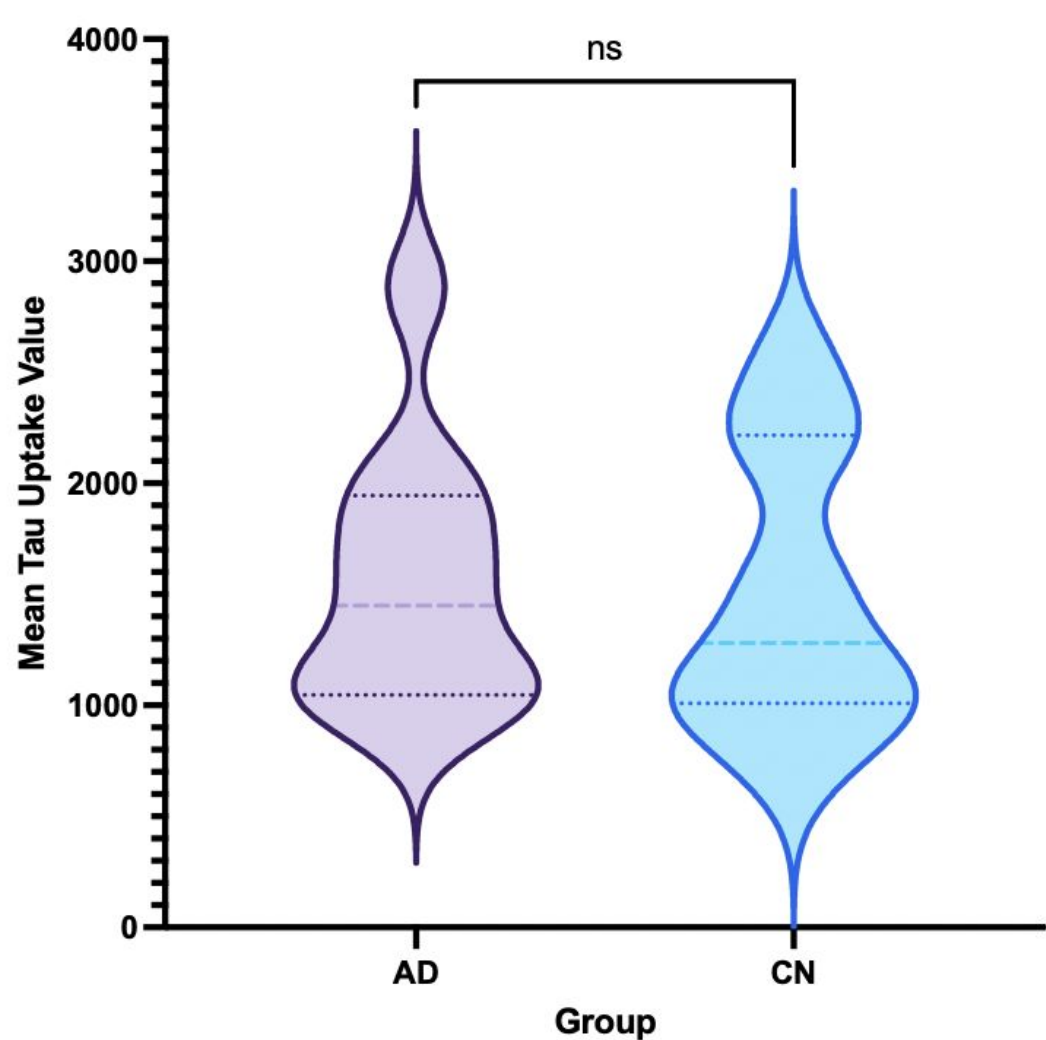
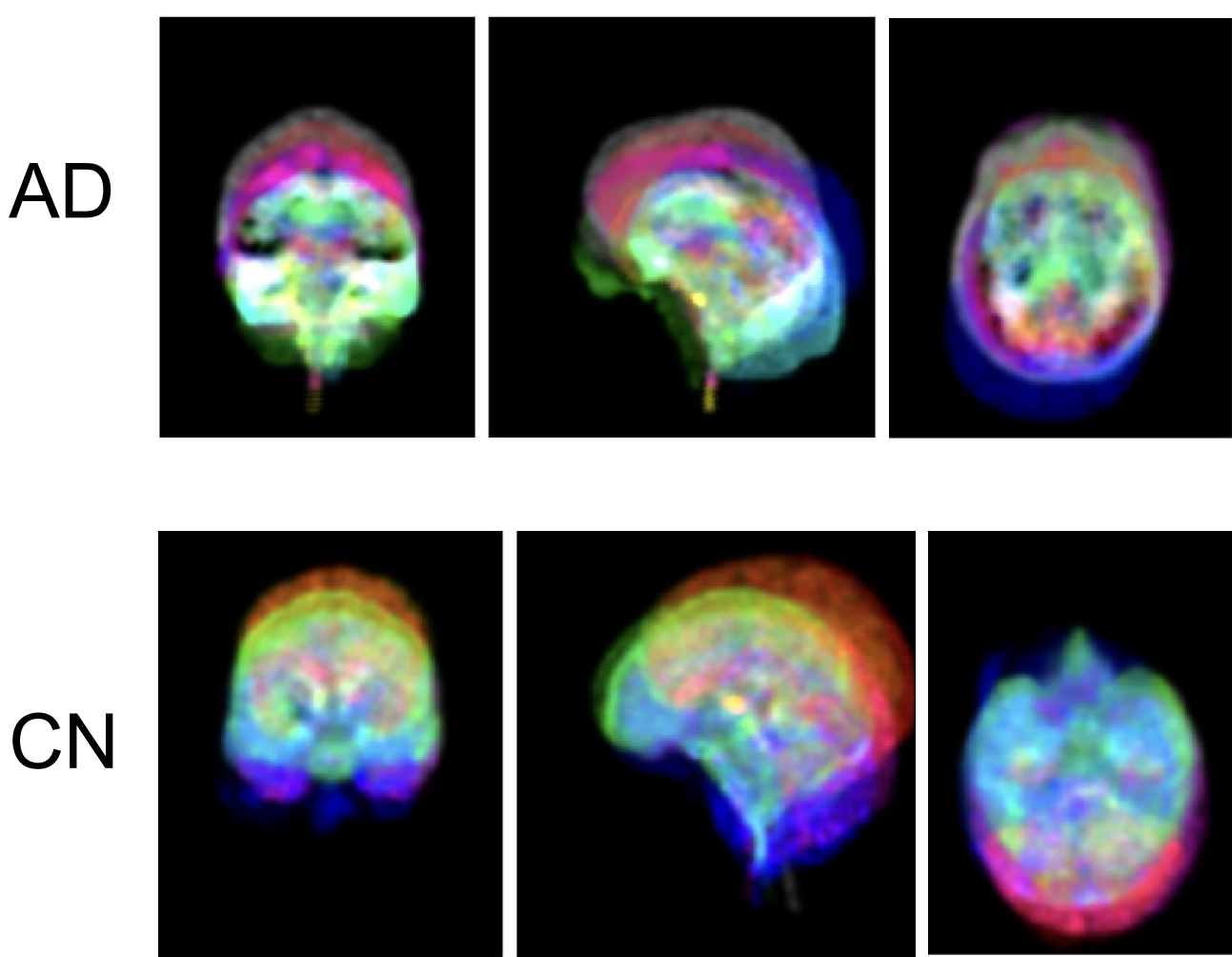


Figure 4: Seven Image Compilation



References

1. Lorenzi RM, Palesi F, Castellazzi G, et al. Unsuspected Involvement of Spinal Cord in Alzheimer Disease. *Frontiers in Cellular Neuroscience*. 2020;14. doi:https://doi.org/10.3389/fncel.2020.00006
2. Wang L, Guo Y, Zhu M, et al. Detection of hyperphosphorylated tau protein and α -synuclein in spinal cord of patients with Alzheimer's disease. *Neuropsychiatric Disease and Treatment*. Published online February 2016:445. doi:https://doi.org/10.2147/ndt.s90735
3. ADNI | Alzheimer's Disease Neuroimaging Initiative. ADNI. <https://adni.loni.usc.edu/>

Conclusion

Spinal cord quantification of tau is possible:

Mean uptake values yielded by MANGO ROI analysis in conjunction with manual ROI selection indicate that the quantification of mean uptake value in the cervical spine is possible through this pipeline.

Methodological advance in the study of AD spinal cord pathology:

The accessibility and efficacy of the pipeline enables its further usage in application to AD PET and MRI scans.

The pipeline requires further construction, calling for more research in AD spinal cord imaging:

While accuracy may be decreased through hindrances such as PVE and limited scan visibility in application of this pipeline, the absence of a solution in AD spinal cord imaging but not in AD cortical imaging suggests that more involvement in AD spinal cord imaging research is necessary.

Clinical and pre-clinical impact:

Achieving a more comprehensive image and understanding of the extend of AD pathology contributes to treatment of under-explained symptoms and treatment of AD as a whole.