Uncovering Uncertainty in Alzheimer's Disease Biomarkers through Automatic MRI Segmentation

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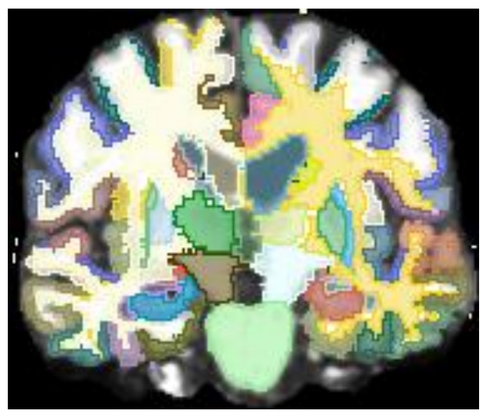
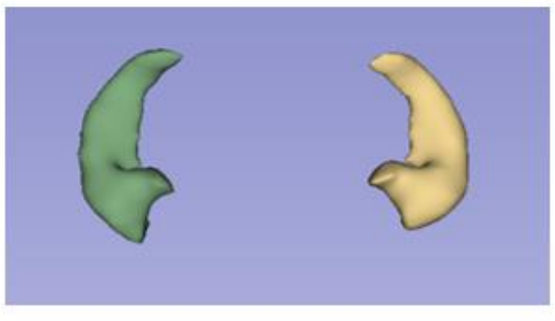
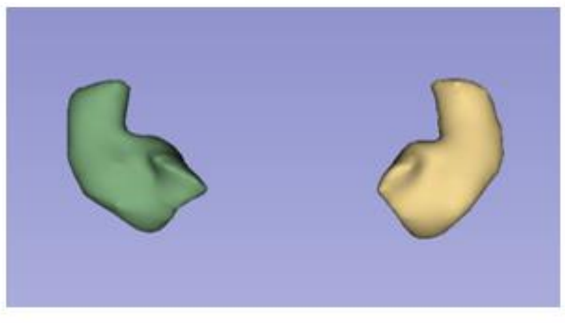


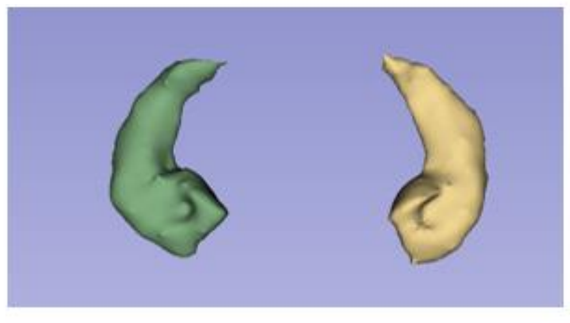
SNT



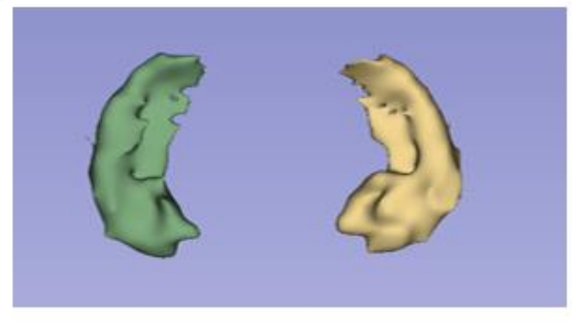
MAPER



MONAI



FreeSurfer



Core Aim:

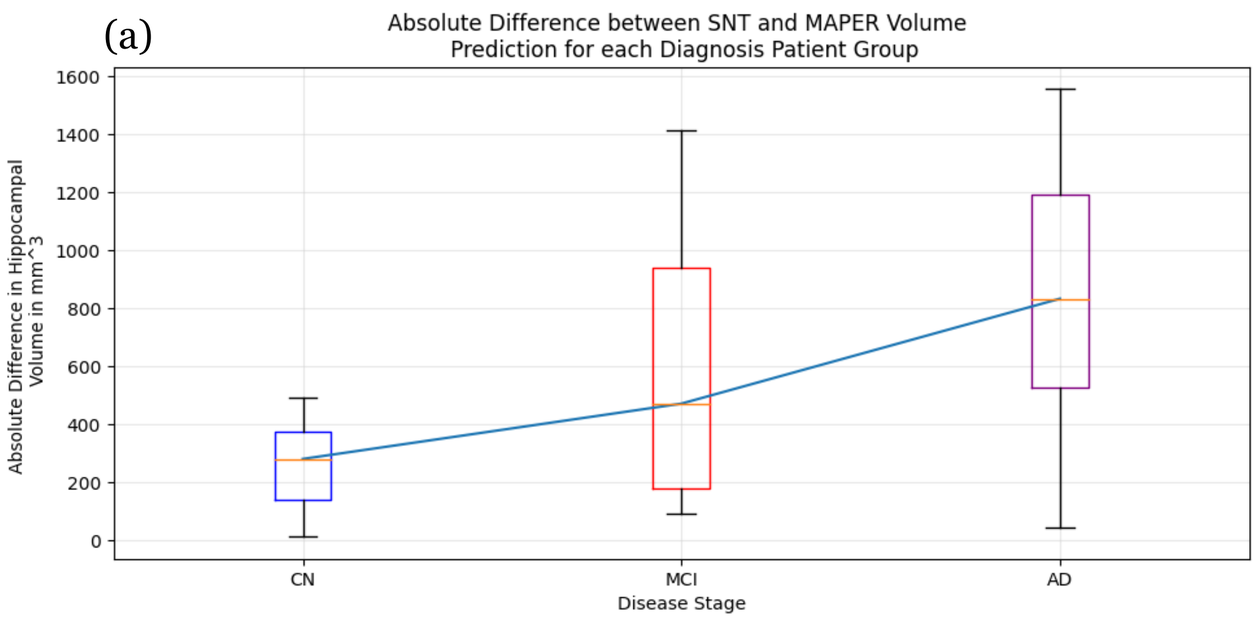
Characterize the uncertainty introduced into neurodegenerative disease predictive models from automated biomarker estimates to improve confidence in diagnosis and assessment of treatment effects.

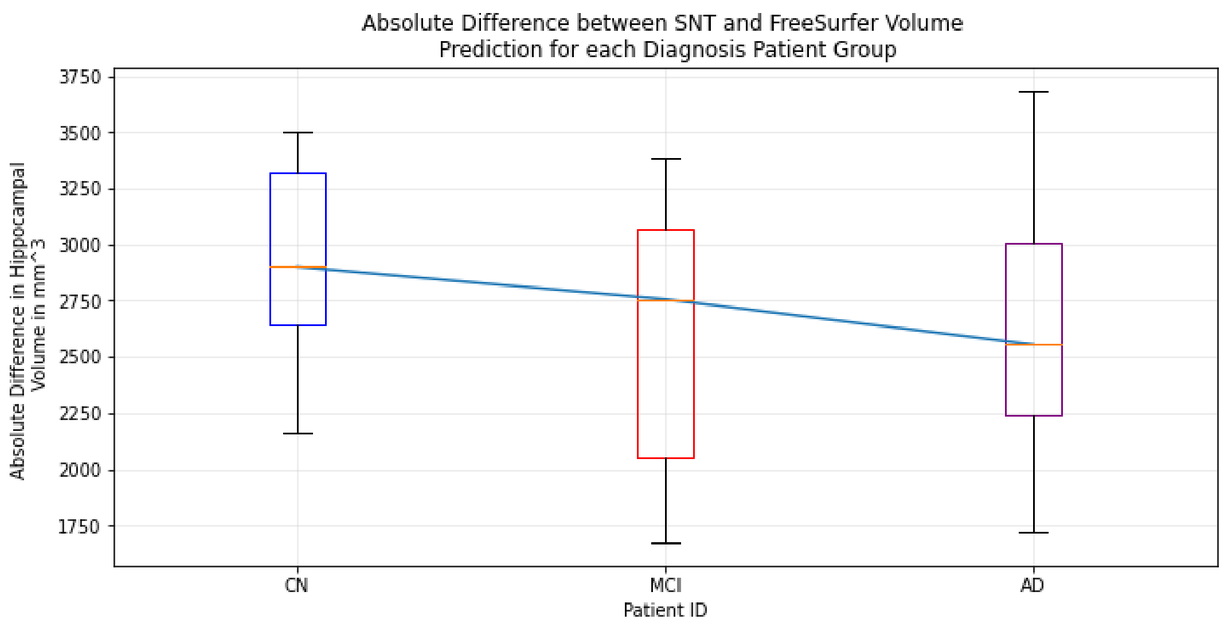
Sub-Aims:

1. Quantify the variability in a hippocampal volumes set obtained from different MRI segmentation models.
2. Investigate a predictive model's uncertainty for different patient groups arising from this variability.

Statistical Modelling

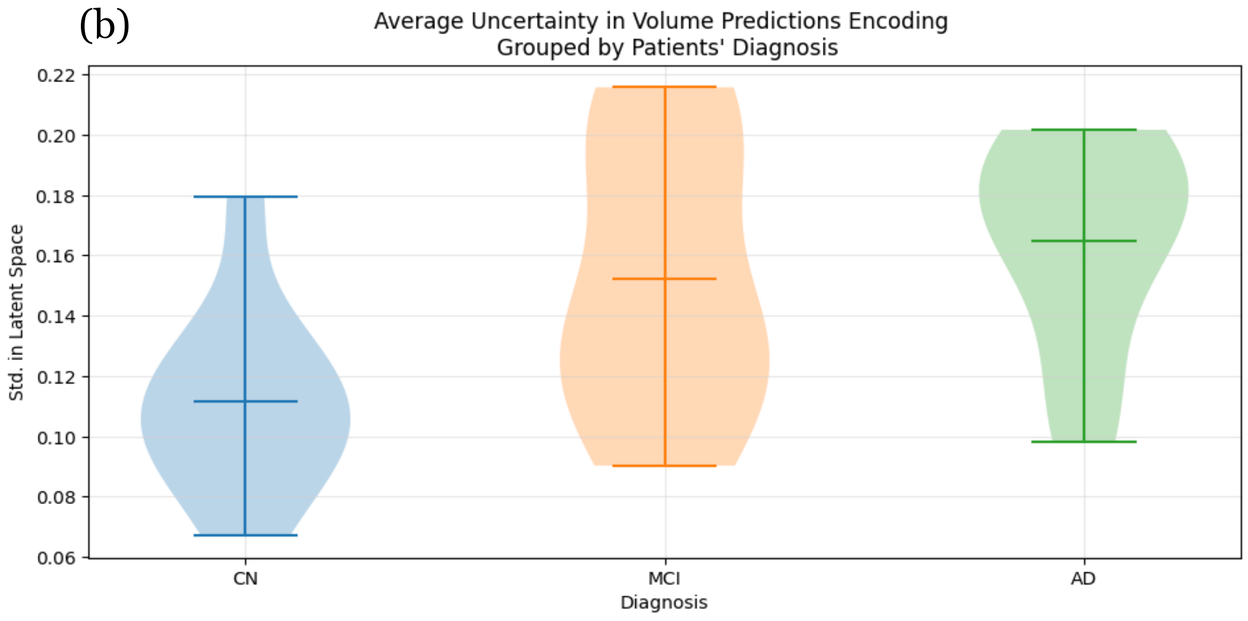
(a)



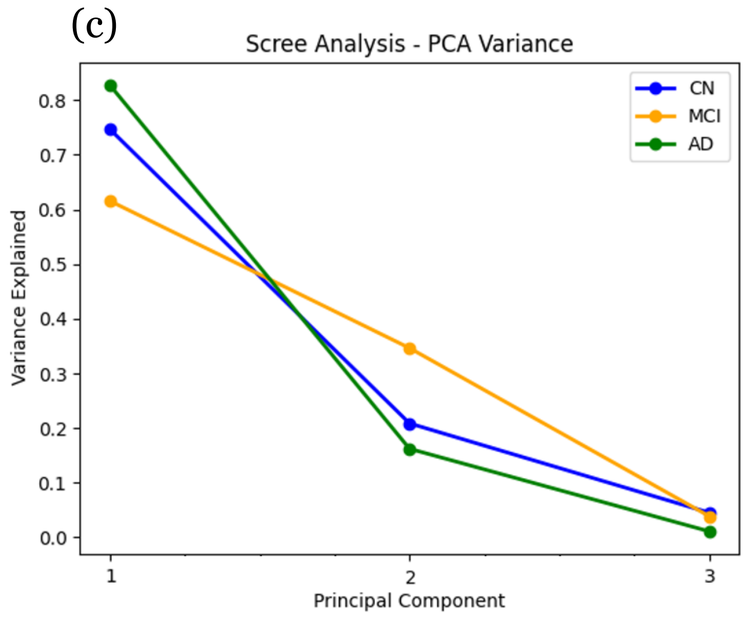


Predictive Modelling

(b)



(c)



(a) Differences in predicted volumes of MAPER and FS with gold standard SNT.
(b) VAE latent uncertainty in patients' volume encodings.
(c) Compressibility of patients' volumes using Principle Component Analysis (PCA).

Summary

This study provides a characterization of the bias and variability in the hippocampal volumes extracted with three automatic MRI segmentation models, FreeSurfer, MAPER, and MONAI's 'Wholebrainseg Large Unest', and SNT's semi-manual model on an authentic MRI dataset from the Alzheimer's Disease Neuroimaging Initiative (ADNI). The biomarker predictions were analyzed statistically and modeled predictively using a Variational Autoencoder (VAE) to quantify the extent of variability and uncertainty present as well as to understand possible impacts on subsequent disease predictive models.
Patterns in variability were identified that correlate with the patients' disease stages: Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer's Disease (AD). These findings suggest that some patient demographics, particularly in progressed disease stages, were described less confidently than others due to intrinsic bias in the automated segmentation models. Thus, this study proposes to characterize patients using a set of plausible biomarker estimates obtained from different tools to counteract individual segmentation model biases with the aim of improving prediction confidence in subsequent Alzheimer's Disease diagnostic and prognostic models.