

Automated White Matter Hyperintensity Segmentation in Postmortem Ex Vivo MRI Using Modified U-Net Pipeline

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Introduction

White matter hyperintensities (WMH) are regions that show increased signal intensity on T2-weighted magnetic resonance imaging (MRI). They are often linked to aging, cerebrovascular disease, and neurodegenerative disorders. Measuring WMH burden is commonly used to study brain aging and disease progression. Many automated WMH segmentation tools exist for antemortem MRT; however, these methods are often not suited for postmortem ex vivo MRI. This is due to differences in image contrast, the effects of tissue fixation, and the lack of surrounding skull and cerebrospinal fluid. Manual WMH segmentation is still the standard method for gathering postmortem datasets, but it is time-consuming, labor-intensive, and leads to variable results. Recent advances in deep learning, especially U-Net-based convolutional neural networks, have shown strong performance in medical image segmentation. However, few automated pipelines have been developed specifically for postmortem ex vivo MRI.

The goal of this project was to create a reliable automated WMH segmentation pipeline for postmortem ex vivo MRI using a modified U-Net architecture and multiple types of MRI inputs. By ensuring consistent WMH quantification, this work seeks to support large-scale neuropathological studies that examine the connections among aging, neurodegeneration, and white matter injury.

Methods

MRI Acquisition. Postmortem ex vivo brain specimens from people with Down syndrome (DS, n=9) and other clinical diagnosis (non-DS, n=60) were embedded in agar/sucrose gel [Liou et al. 2025 J Neuropathol Exp Neurol] and imaged using high-field 7T MRI. For each specimen, T1-weighted (T1w, 0.37 mm isotropic resolution) and T2-weighted (T2w, 0.40 mm isotropic resolution) image sequences were acquired and served as inputs for the segmentation pipeline.

Image Preprocessing. Prior to processing the images underwent spatial normalization and multimodal image organization. T1w and T2w volumes were then aligned and formatted to generate standardized inputs suitable for the deep learning analysis.

Modified U-Net Segmentation. A modified U-Net architecture was implemented to perform automated WMH segmentation. The network took both T1w and T2w MRI inputs and produced a binary WMH segmentation mask that identified WMH regions. This architecture was adapted from earlier in vivo work and improved for post-mortem ex vivo MRI datasets.

Quantitative Analysis. WMH volumes were calculated from the generated segmentation masks. Volumes were then log-transformed before statistical analysis to adjust for skewed distributions. Exploratory analysis assessed the relationship between WMH burden and demographic variables, including age, sex, and clinical diagnosis.

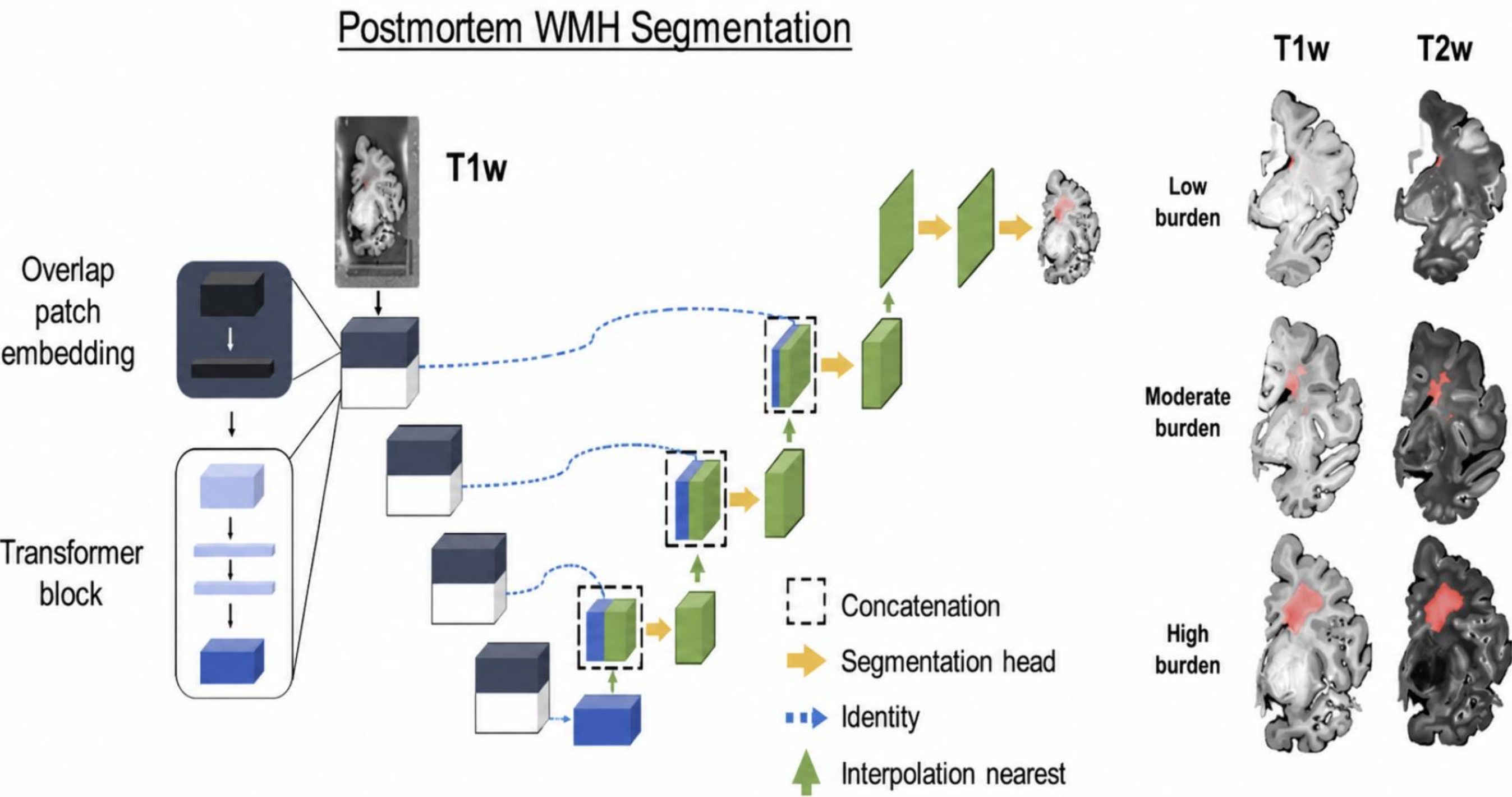


Figure 1. T1-weighted (T1w) and T2-weighted (T2w) postmortem ex vivo MRI volumes were provided as multimodal inputs to a modified U-Net architecture. The network generates binary segmentation masks. Representative outputs are shown for low, moderate, and high WMH burden cases.

Methods

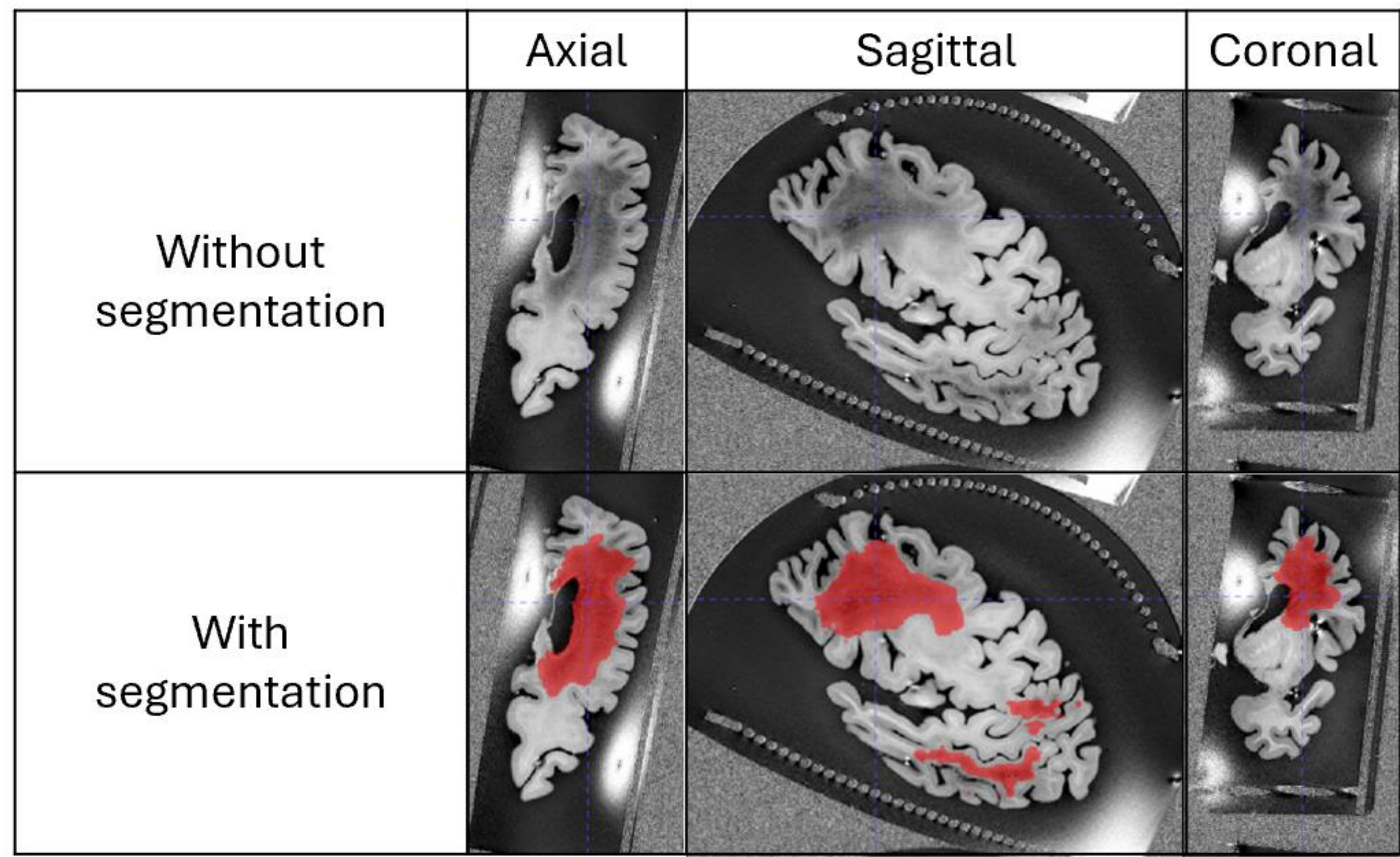


Figure 2. Example postmortem MRI T1w slices before and after automatic segmentation. Red overlays indicate WMH regions identified by the modified U-Net model. The automated approach successfully localized WMH lesions across multiple imaging planes.

Results

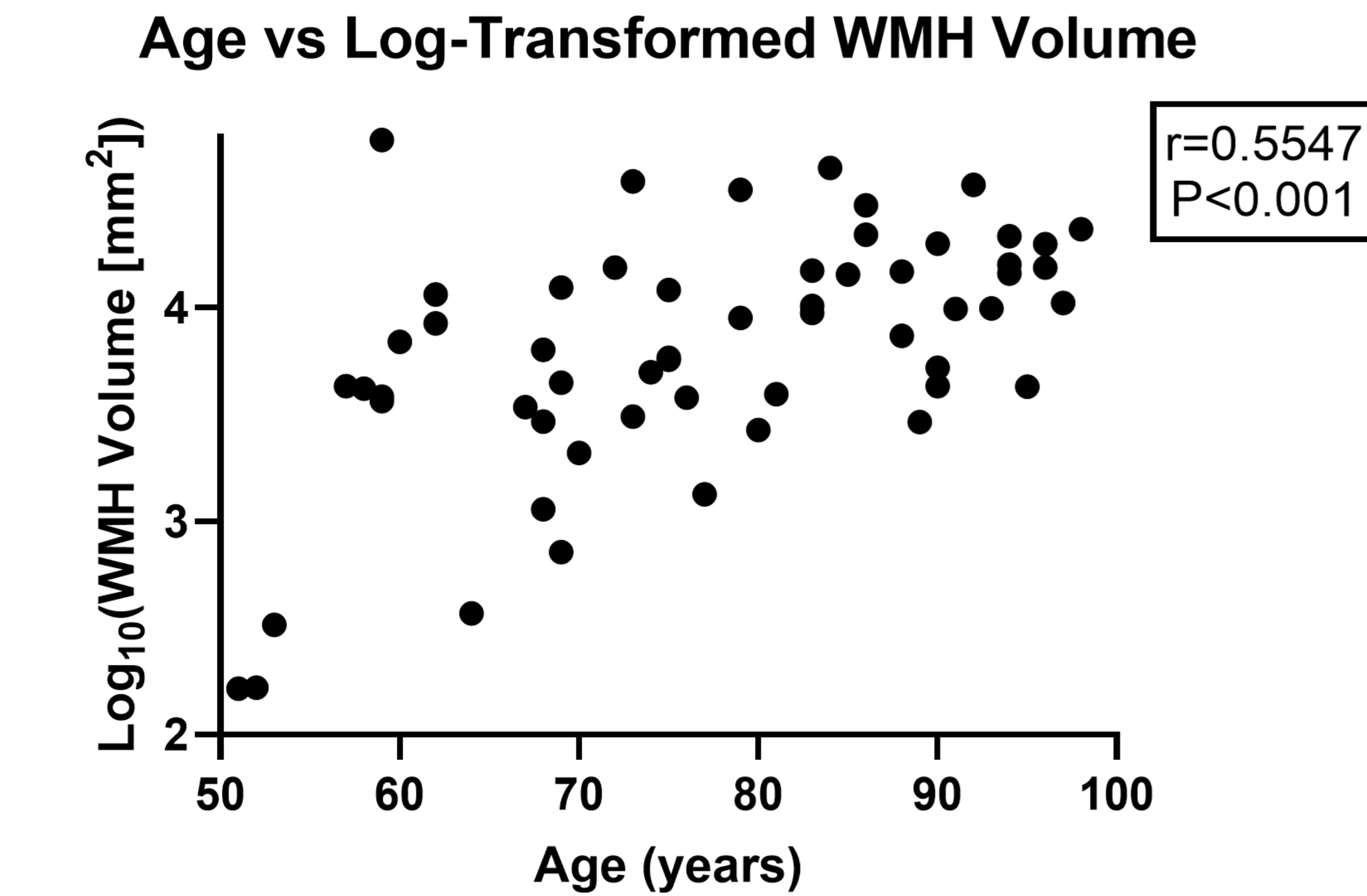


Figure 3. The log-transformed WMH volume showed a positive correlation (n=69, r=0.5547, p<0.001) with age across the cohort, indicating WMH burden grows as age progresses.

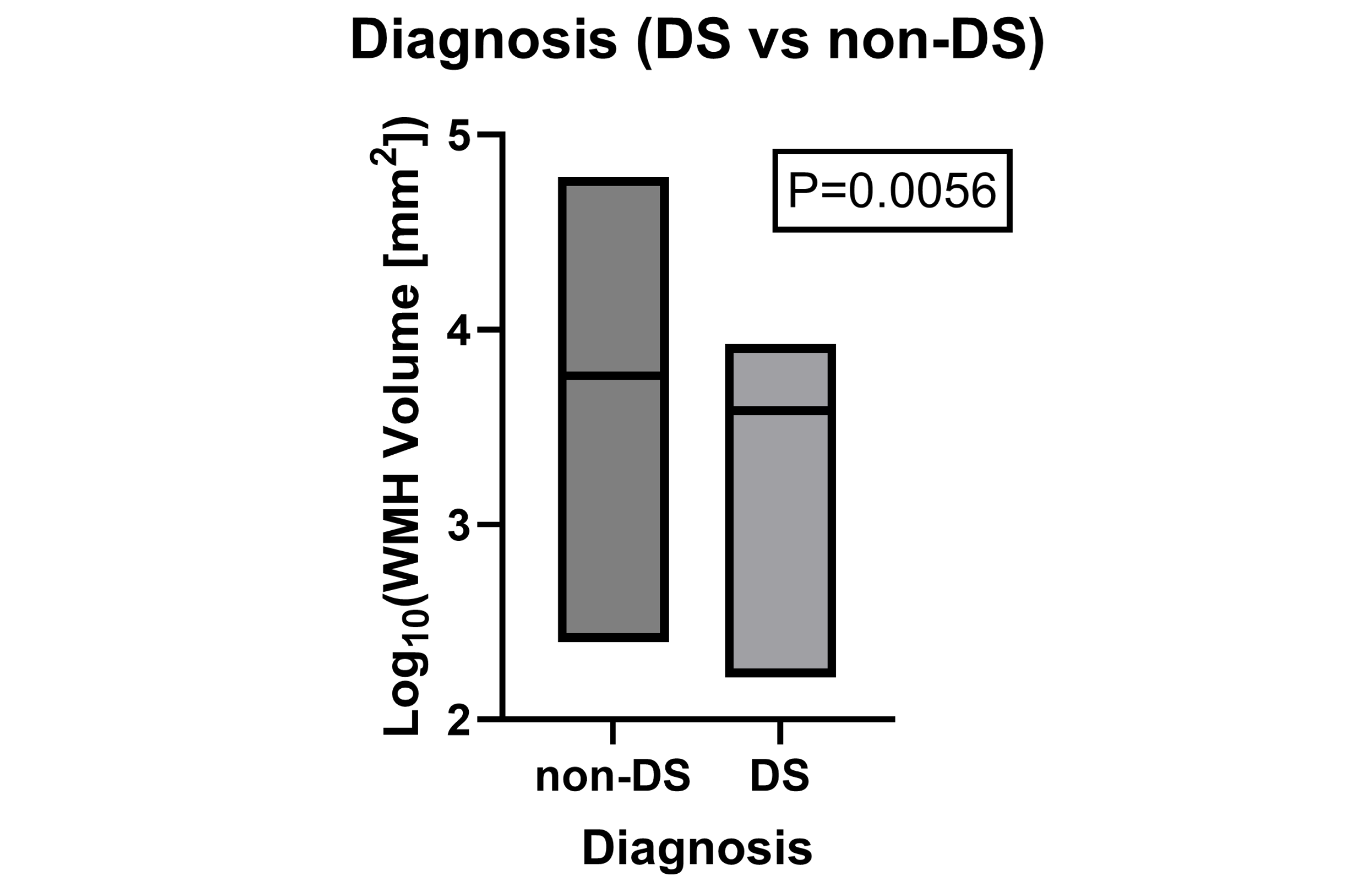


Figure 4. Non-DS (n=60) exhibited significantly higher WMH volumes than DS participants (n=9) (p=0.0056).

Results

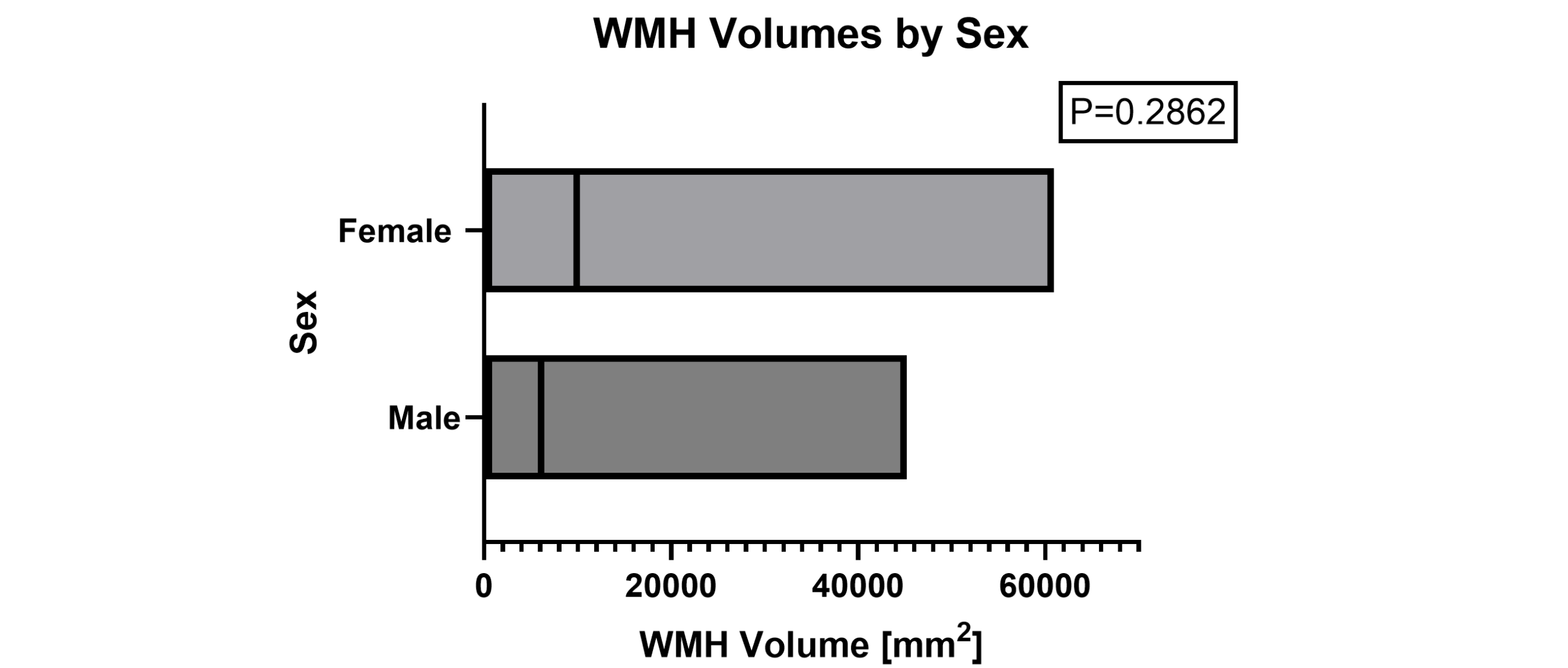


Figure 5. WMH showed high variability between male (n=31) and female (n=27), showing no significant difference (p=0.2862).

The automated pipeline successfully produced WMH binary segmentation masks across postmortem ex vivo MRI datasets. These segmentation outputs allowed for volumetric quantification of WMH burden without needing manual delineation. A positive association was noted between age and log-transformed WMH volume, showing that WMH burden increases with age. Comparisons between male and female subjects showed similar WMH distributions. Analysis of clinical diagnosis revealed that WMH burden was comparable between Down syndrome (DS) and non-DS subjects. The automated method provided consistent segmentation outputs and supported scalable WMH analysis on postmortem imaging studies.

The results show that a modified U-Net architecture can effectively automate WMH segmentation in postmortem ex vivo MRI. The use of multimodal T1w and T2w inputs enabled the network to identify WMH regions and produce reproducible volumetric measurements. Automated segmentation significantly cuts down the time needed for WMH analysis compared to manual methods and improves consistency across datasets. Preliminary findings suggest that WMH burden increases with age, which aligns with previous research on age-related white matter injury. No noticeable differences were found between sex or diagnosis groups in current samples; however, larger cohorts are needed to see if clinically significant group differences exist.

Summary

This work introduces a reliable automated WMH segmentation pipeline designed for postmortem ex vivo MRI. It uses a modified U-Net architecture and multimodal MRI inputs to create WMH probability maps, binary segmentation masks, and volumetric measurements that are ready for further analysis. This approach offers a scalable framework for studying WMH burden in neuropathological research and supports future studies linking white matter injury to aging and neurodegenerative diseases.

Ongoing Effort

- Expand the training and validation datasets.
- Compare automated segmentations with expert manual annotations.-
- Evaluate segmentation performance with quantitative metrics.
- Explore WMH burden across additional diagnostic groups.
- Release the pipeline and documentation to encourage reproducible research.

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