Contribution ID: **15** Type: **Talk**

High-resolution Postmortem Image Analysis of the Human Brain to Characterize Alzheimer's Disease and Related Dementias

Wednesday 29 October 2025 11:15 (15 minutes)

Background: Postmortem MRI has opened-up avenues to study brain structure at sub-millimeter ultra high-resolution revealing details not possible to observe with in vivo MRI. Here, we present a novel package (purple-mri) which performs segmentation, parcellation and registration of postmortem MRI. Additionally, we provide a framework to perform one-of-its-kind vertex-wise group-level studies linking morphometry/histopathology in common coordinate system for postmortem MRI.
Method: We developed a combined voxel- and surface-based pipeline combining deep learning with classical techniques for topology correction, cortical modeling, inflation, registration for accurate parcellation of post-mortem cerebral hemispheres (Fig.1 Khandelwal et al. 2024). Moreover, using the GM/WM segmentations derived from postmortem hemisphere and FreeSurfer-processed antemortem MRI, we perform deformable image registration between the two modalities for each brain specimen. Vertex-wise thickness analysis was performed to assess tau and neuronal loss distribution in corresponding specimens of postmortem (7T at 0.3mm3; N=75) and antemortem (3T at 0.8mm3; N=49) MRI (Table 1) with AD continuum diagnosis. The semi-quantitative average tau and neuronal loss ratings were derived from histopathological examination across the brain. All analyses include age, sex, and postmortem (or antemortem) interval as covariates.
Result: Our method parcellates postmortem brain hemisphere using a variety of brain atlases even in areas with low contrast (anterior/posterior regions), profound imaging artifacts and severe atrophied brains (Fig. 1). Our registration pipeline provides one-to-one correspondence between the two modalities. For thickness/pathology associations, small sparse significant clusters in superior temporal and precuneus in antemortem MRI (N=49) were observed. However, postmortem MRI showed much stronger associations across large clusters in the temporal, entorhinal cortex, and cingulate for both the matched cases (N=49) and the full cohort (N=75), regions implicated in ADRD.
Conclusion: Purple-mri paves the way for large-scale postmortem image analysis. Stronger associations between thickness and average tau burden/neuronal loss than antemortem MRI shows that our pipeline (purple-mri) could inform the development of more precise and sensitive invivo biomarkers by mapping information from postmortem to antemortem MRI in a common reference coordinate framework just as is the norm for antemortem studies.

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Session Classification: Session 3: Applications & Clinical Translation