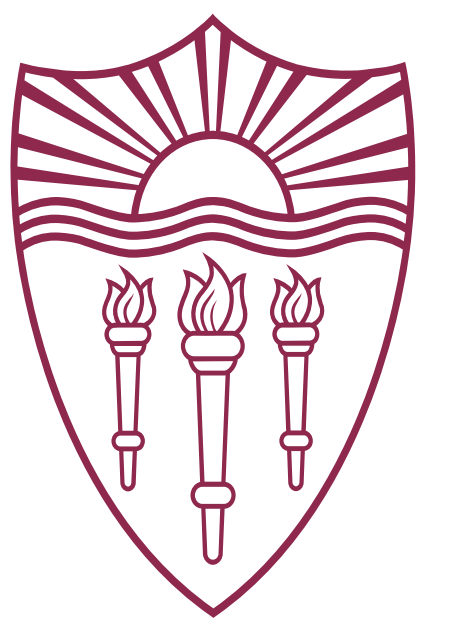


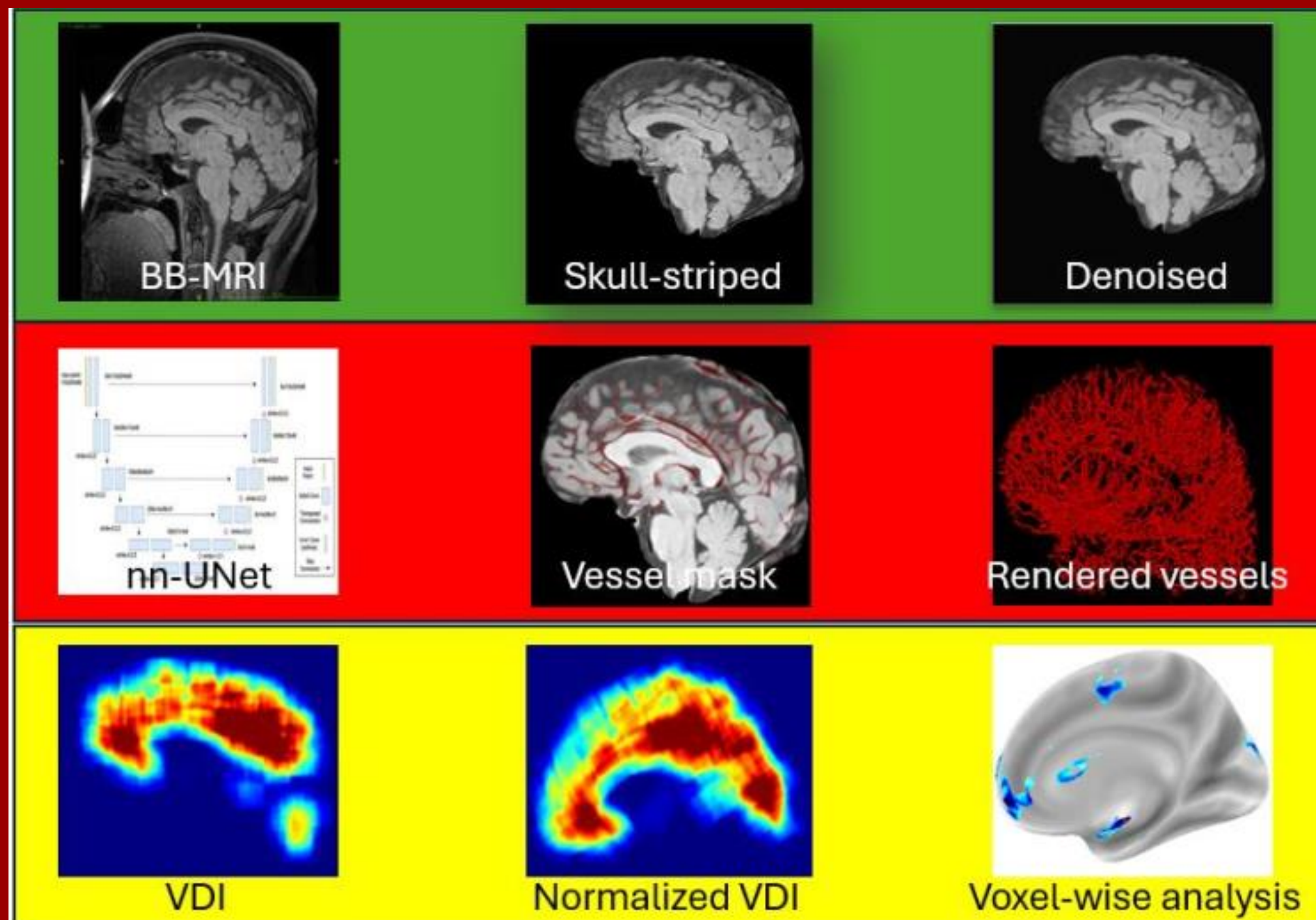


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INTRODUCTION/METHODS

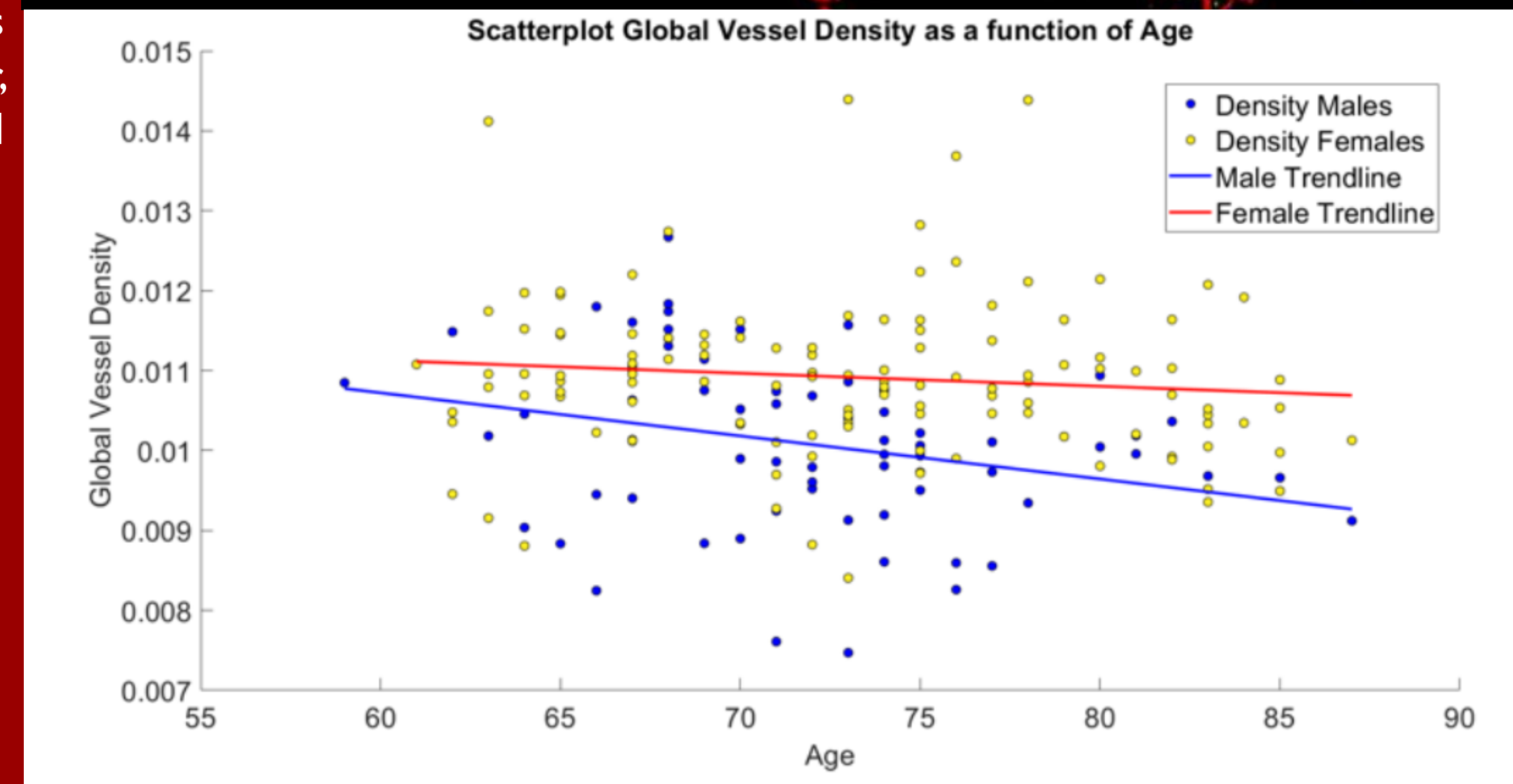
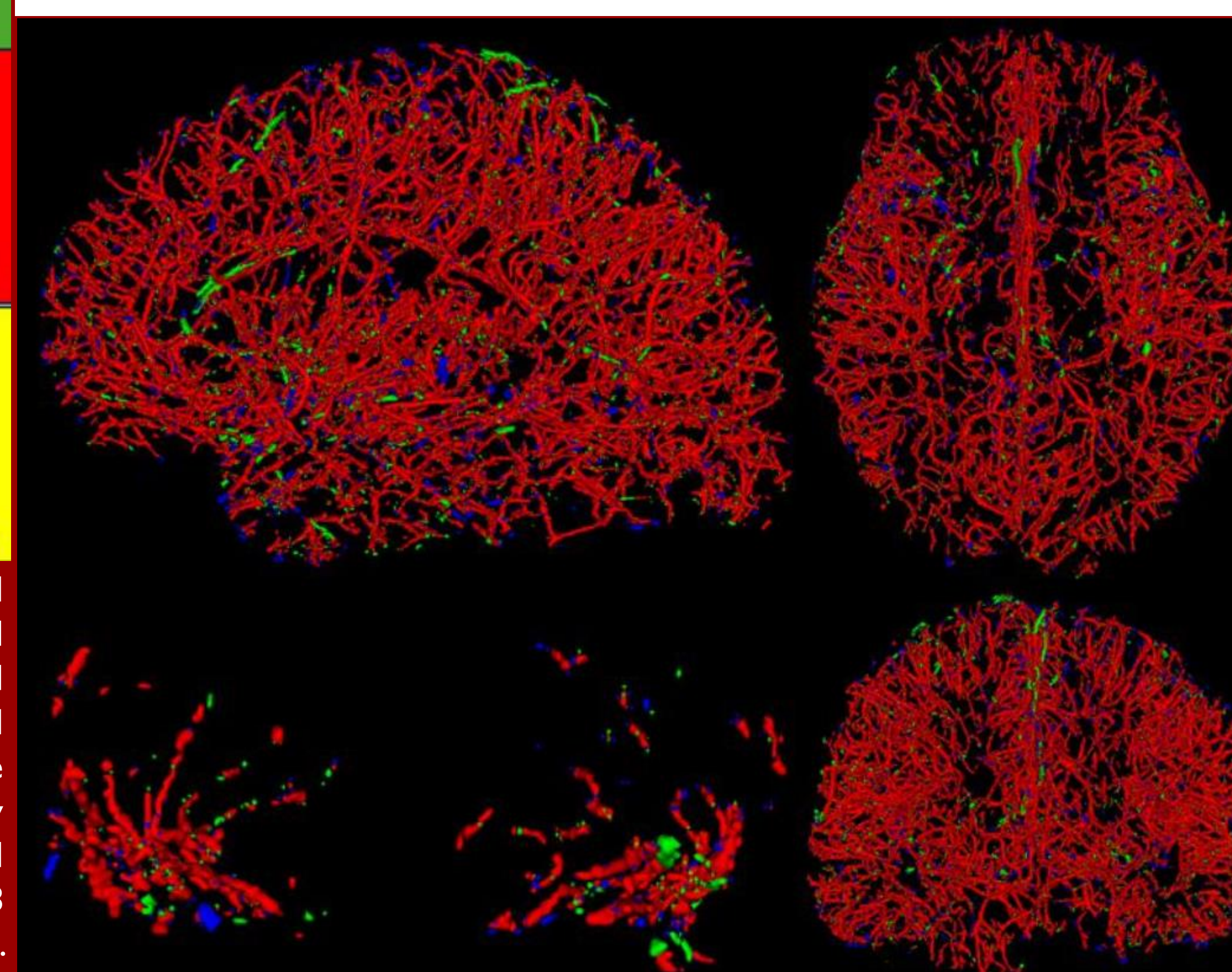
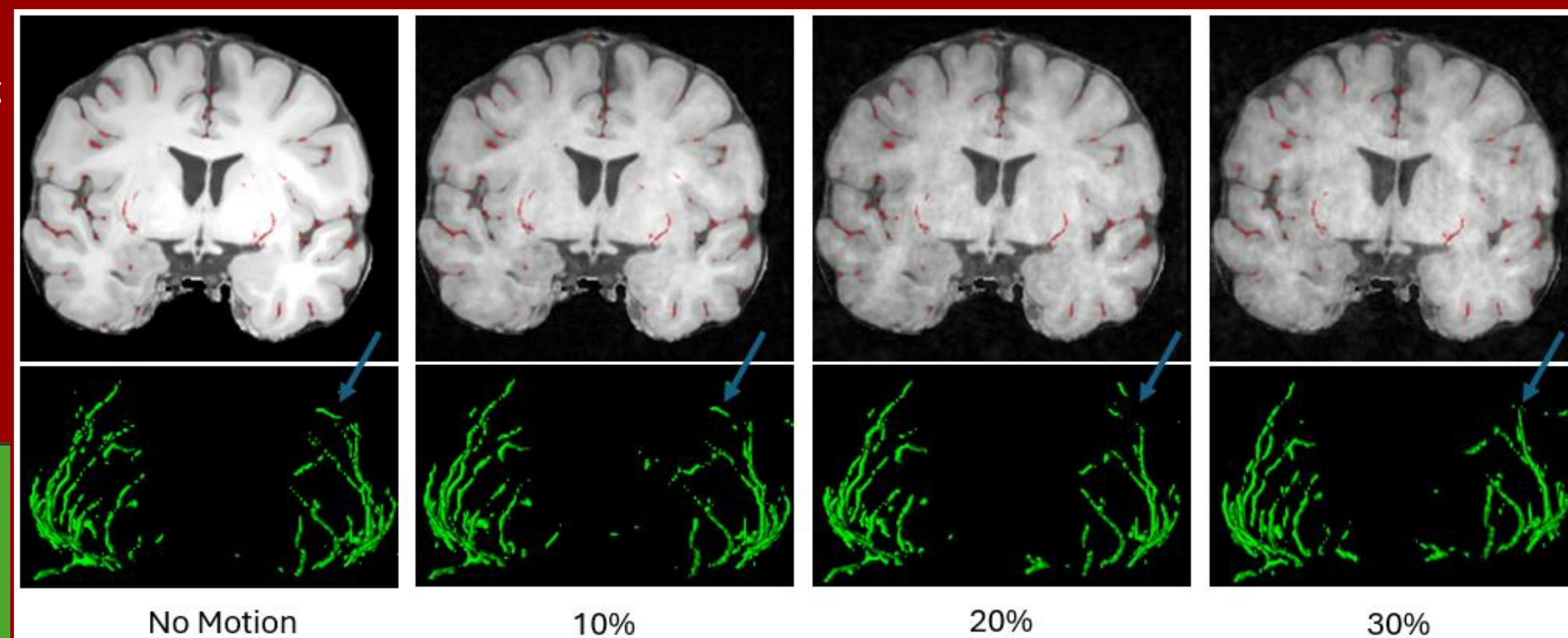
BACKGROUND: Cerebral Small Vessel Disease (cSVD) is the main cause of Vascular Cognitive Impairment and Dementia (VCID). Existing MRI modalities primarily detect parenchymal lesions of cSVD, which reflect downstream changes rather than directly visualizing small cerebral blood vessels. Here, we developed and applied a novel deep learning (DL) based pipeline to segment and quantify small cerebral blood vessels in a cohort of elderly persons at risk of cSVD, based on high-resolution black blood (BB) MRI. By correlating vessel density with cognitive scores, we demonstrate this method's potential as a non-invasive biomarker for VCID.



METHODS: High-resolution (iso-0.5mm) BB MRI using T1-weighted turbo spin-echo sequence with variable flip angles at 3T was performed on 193 elderly participants at risk of cSVD and VCID. An automated pipeline incorporating nn-UNet-based vessel segmentation quantified vessel density imaging (VDI) globally and across cortical regions. The network was trained on data with simulated motion artifacts commonly observed in the elderly population, and its performance was validated using carefully labeled data, yielding average Dice scores of 0.80 +/- 0.08 (shown below) across both motion-simulated and non-simulated data. Voxel-wise regression of VDI with global CDR and MoCA scores was performed using SPM with FDR cluster corrected $p < 0.05$ (age, gender, and global mean VDI included as covariates), after registering the BB MRI volumes to the MNI atlas.

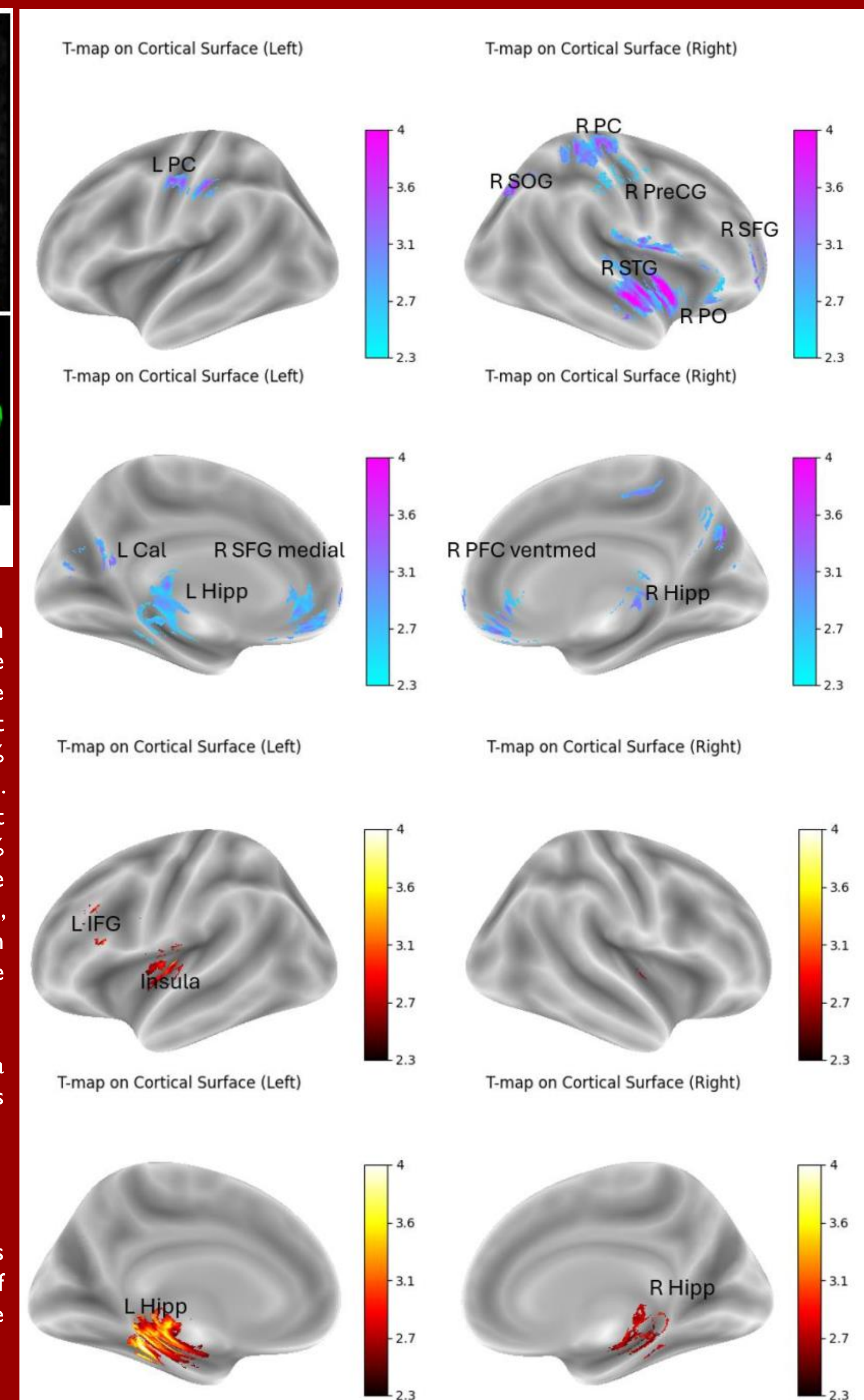
Condition	Dice Score	95% Harsdorff Distance (mm)
DL Denoised	0.832 ± 0.074	0.807 ± 0.606
DL Denoised + 10% Sim	0.784 ± 0.075	0.880 ± 0.525
DL Denoised + 20% Sim	0.762 ± 0.075	0.880 ± 0.415
DL Denoised + 30% Sim	0.727 ± 0.075	1.120 ± 0.510
DL Raw	0.789 ± 0.089	0.878 ± 0.664
Jerman Denoised Image	0.701 ± 0.105	4.180 ± 1.300
Jerman Raw Image	0.463 ± 0.160	6.300 ± 3.500

DEEP LEARNING TECHNICAL VALIDATION



Jann, K., Shao, X., Ma, S. J., Cen, S. Y., D'Orazio, L., Barisano, G.,...Staffaroni, A. M. (2021). Evaluation of cerebral blood flow measured by 3D PCASL as biomarker of vascular cognitive impairment and dementia (VCID) in a cohort of elderly Latinx subjects at risk of small vessel disease. *Frontiers in neuroscience*, 15, 627627.

CLINICAL APPLICATIONS



Top: A validation case with different motion levels, we see good segmentation despite noise. The only significant differences appear with 30% motion, with the smaller vessels. Motion simulation at different levels, from no motion to 30% represents progressively more motion as the scan progresses, with 30% representing motion happening about 30% of the time.

Middle: Error map of a representative subject, 52 years old, female
Red - Correct segmentation
Blue - False Negative
Green - False positive
We see relatively few regions where we have errors; most of the regions show reliable segmentation.

Bottom: Global VDI decreases with age ($\tau = -2.37$, $p < 0.019$) and is higher in females compared to males ($\tau = 5.68$, $p < 0.001$). The blue trendline (representing males) is notably steeper than the red trendline (representing females). The general trends align with similar perfusion studies between elderly males and females (Jann, 2021)

Top: Surface-based statistical maps illustrating negative associations between regional vessel density and CDR-GS score. T-maps are projected onto the left and right cortical surfaces, shown in lateral (top row) and medial (bottom row) views. Significant cluster is observed in the right Superior Temporal Gyrus (L STG), right Superior Occipital Gyrus (R SOG), left Ventromedial Prefrontal Cortex (L SFGM), right Superior Frontal Gyrus (R SFG), left Postcentral (L PC), right Postcentral (R PC), right Superior Frontal Medial Orbital (SFG medial), left Calcarine (L Cal), left Hippocampus (L Hipp), right Hippocampus (R Hipp), right Posterior Orbital (R PO). Color bars represent T-statistics (range ≈ 2.3–4.0). All results were voxel-level thresholded to $p < 0.01$ and FDR-corrected at $q < 0.05$ (cluster size > 901 voxels).

Bottom: Surface-based statistical maps illustrating positive associations between regional vessel density and MoCA score. T-maps are projected onto the left and right cortical surfaces, shown in lateral (top row) and medial (bottom row) views. Significant clusters are observed in the left hippocampus (L Hipp), Insula, left inferior frontal gyrus (L IFG), and right hippocampus (R Hipp). Color bars represent T-statistics (range ≈ 2.3–4.0). All results are voxel-level thresholded at $p < 0.01$, and FDR corrected $q < 0.05$ (cluster size > 1103 voxels).

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