

UNIVERSITY *of* WASHINGTON

Part 2: Innovations



Heino Hulseby-Vincent, Latimer Lab



Brain arteriolosclerosis (AS) is common and has significant consequences

- Wall thickening in small (40-150 μm) arterioles in white matter and subcortical structures
- One of the most common pathological findings in the aging brain
- Consequences include:
 - Impaired cognitive performance
 - Microinfarcts and hemorrhages
 - White matter hyperintensities
 - Enlarged perivascular spaces
 - Synergy with neurodegenerative diseases

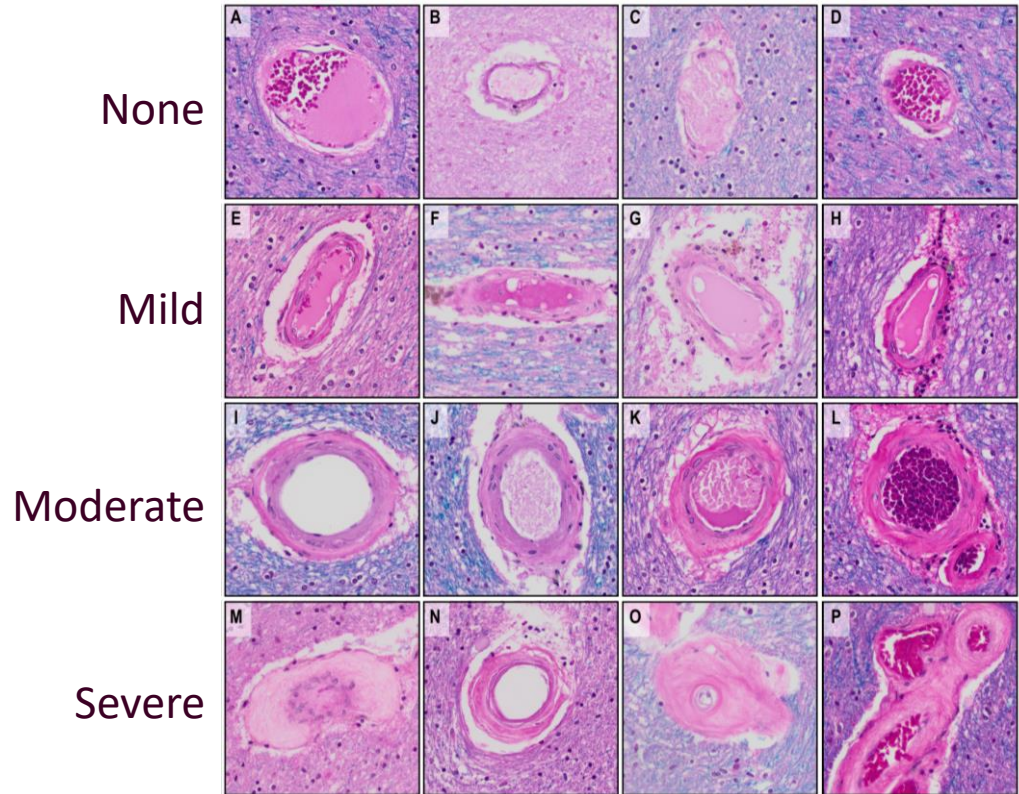


Figure by Lucy P. Evans

Brain arteriolosclerosis (AS) is categorized by the gestalt of the tissue

- Diagnosed as either: None, Mild, Moderate, or Severe
- Interobserver concordance is “moderate”

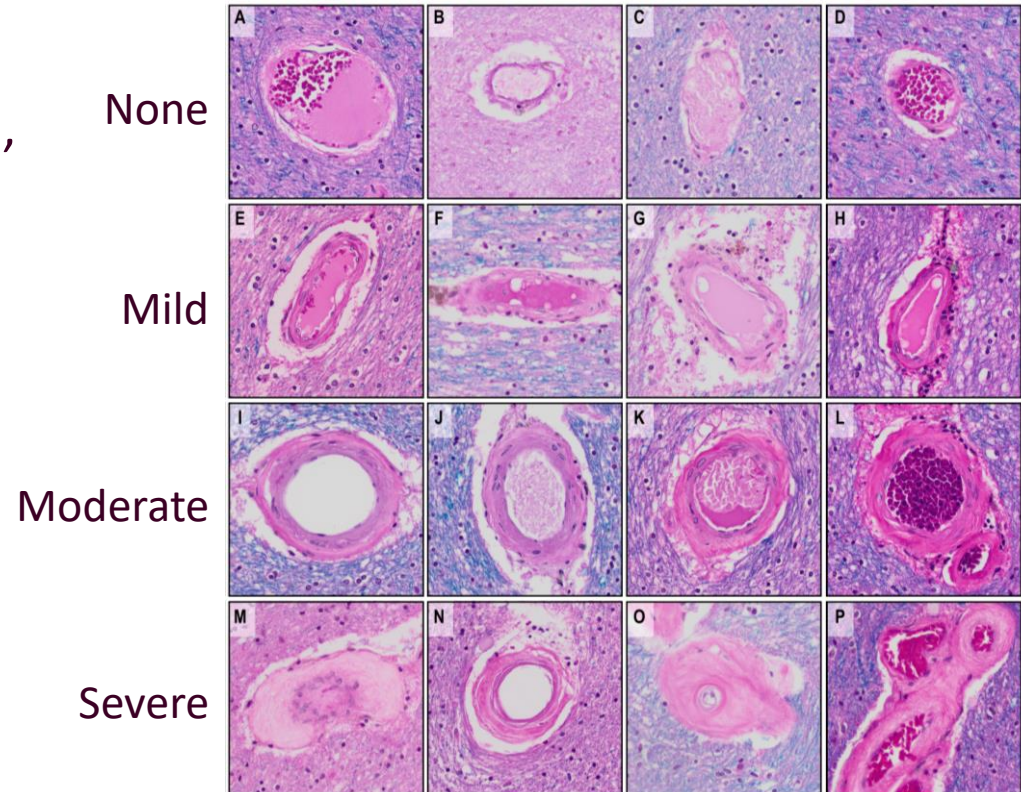


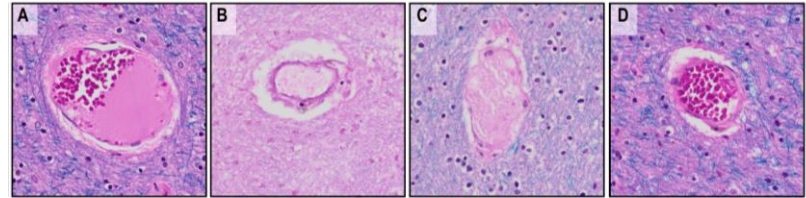
Figure by Lucy P. Evans

We wanted to create an automated way to measure AS

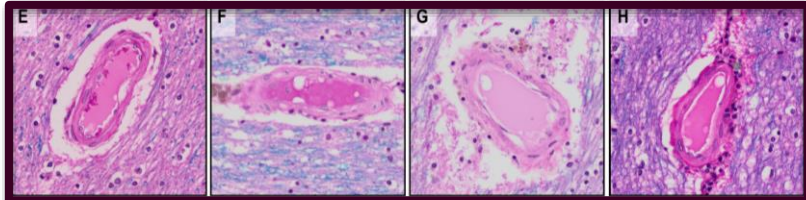
Cohort:

- 10 matched donor pairs (10 mild vs. 10 Severe AS)
- Matched on:
 - Age
 - Sex
 - Alzheimer's Disease pathology
- 2 sections each (MFG + Frontal WM)

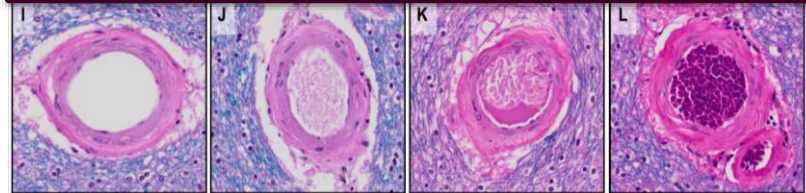
None



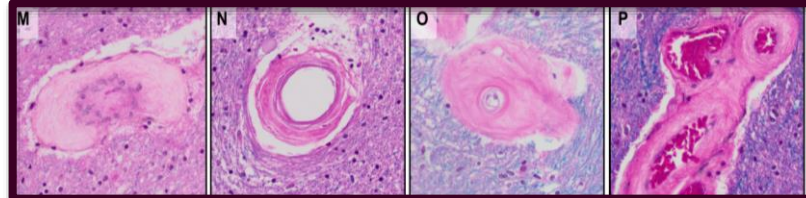
Mild



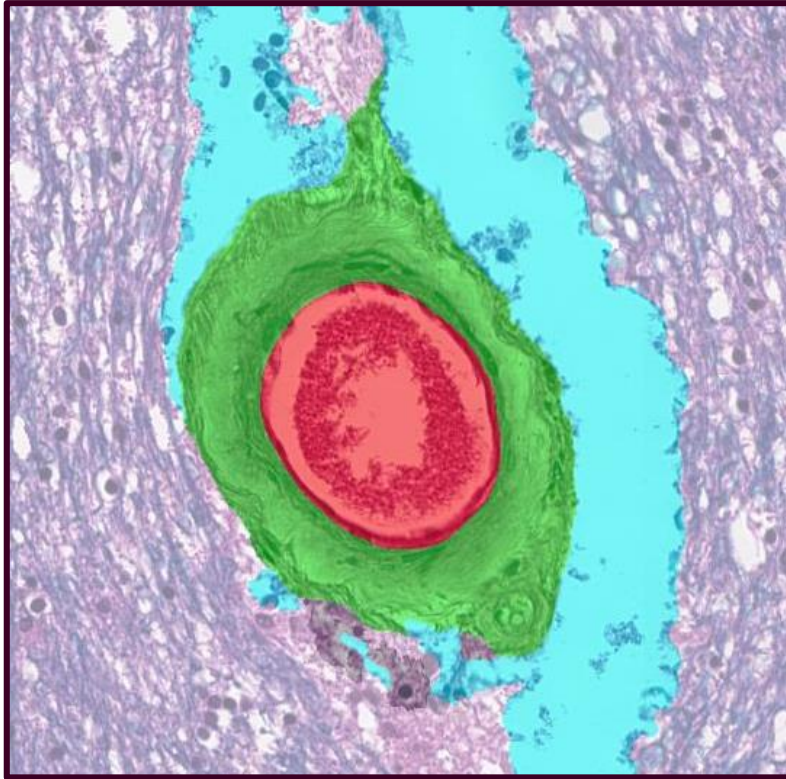
Moderate



Severe

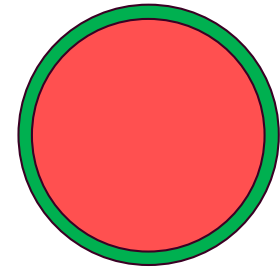


Sclerotic Index (SI) quantifies relative vessel wall thickness

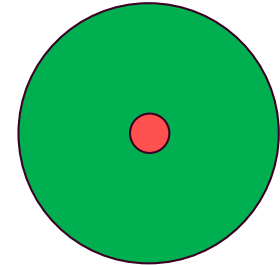


$$SI = 1 - \frac{\text{Internal Diameter}}{\text{Outer Diameter}}$$

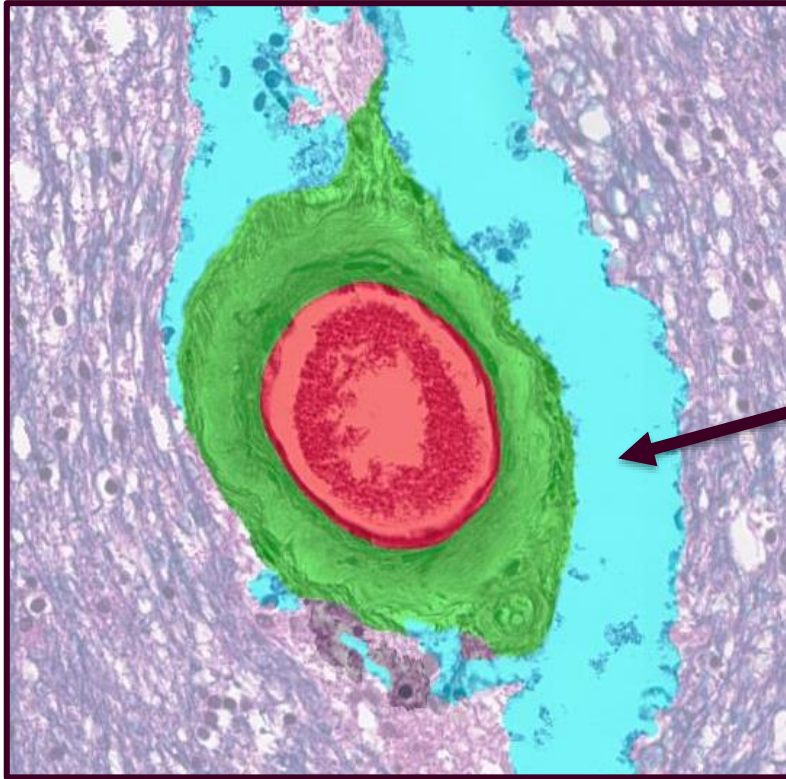
$$0.01 = 1 - \frac{99}{100}$$



$$0.99 = 1 - \frac{1}{100}$$



Perivascular Space (PVS) enlarge with age and vascular disease

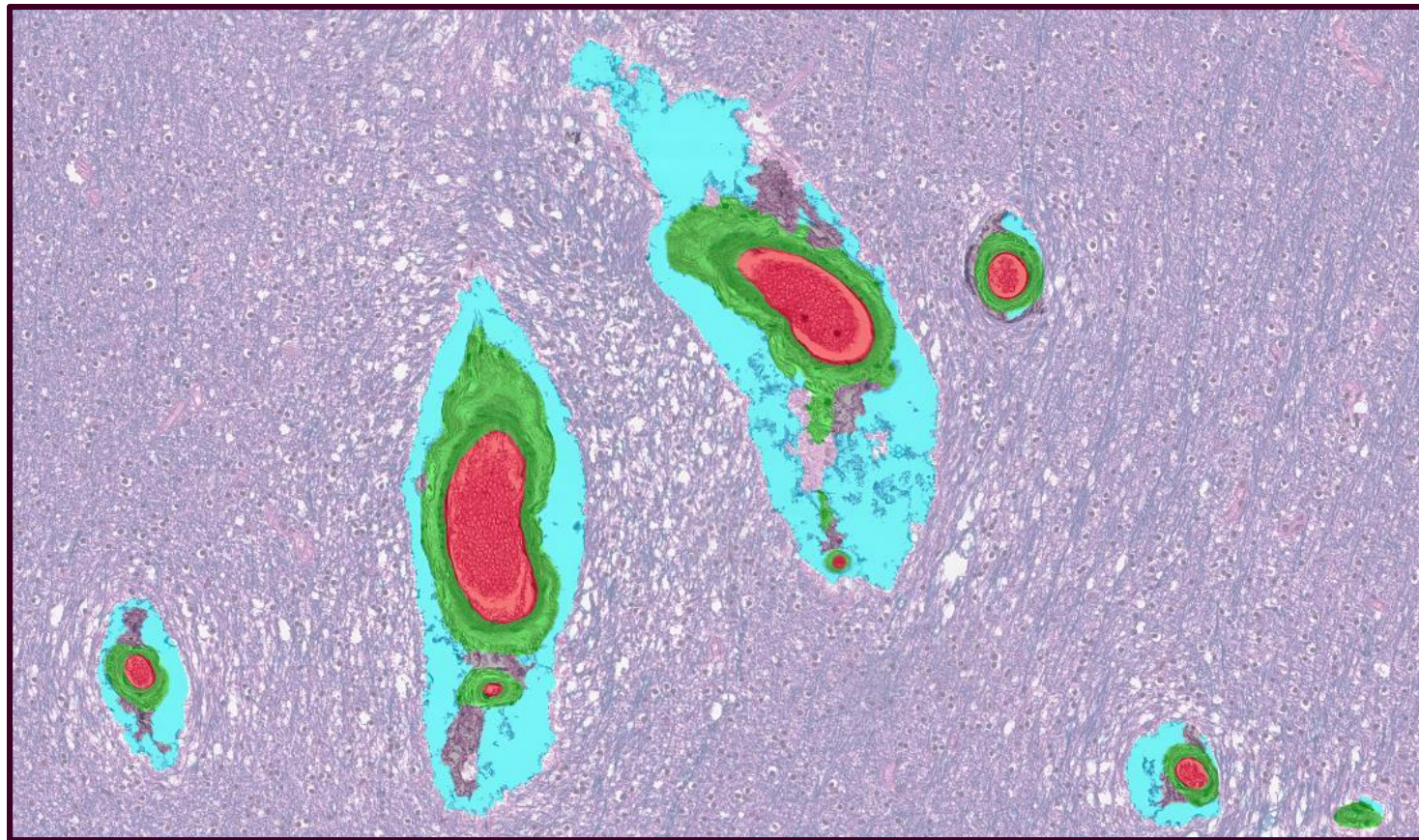


Perivascular Space

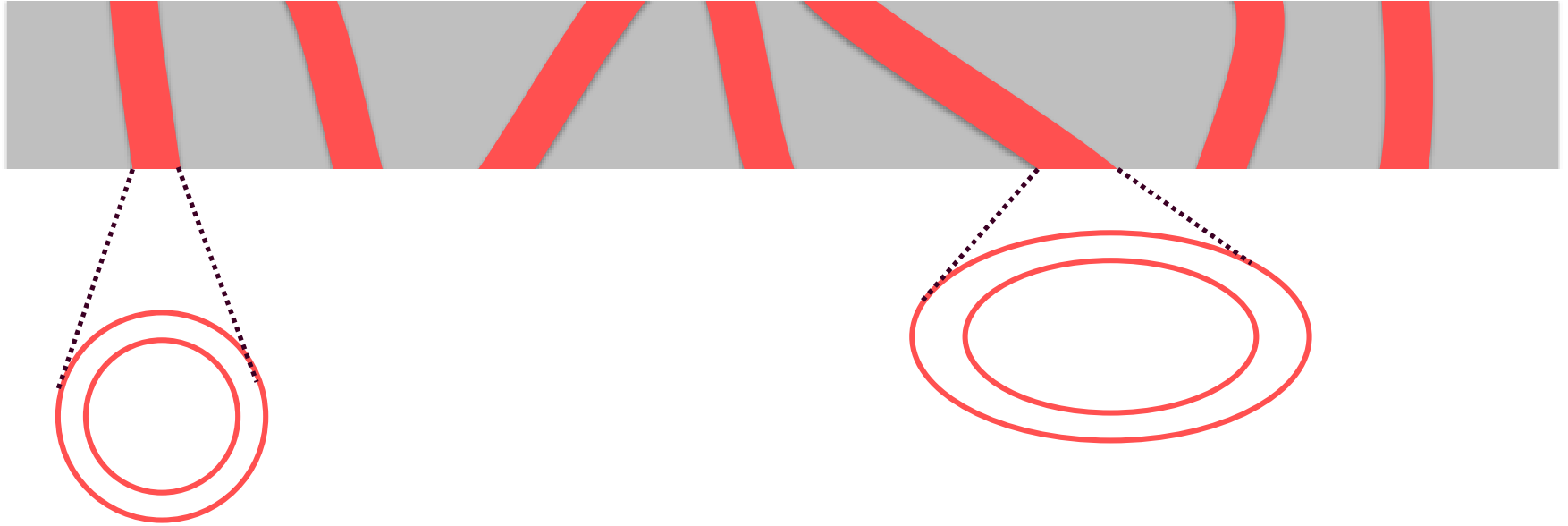
Our lab uses 'HALO' to perform image analysis on slides of postmortem tissue



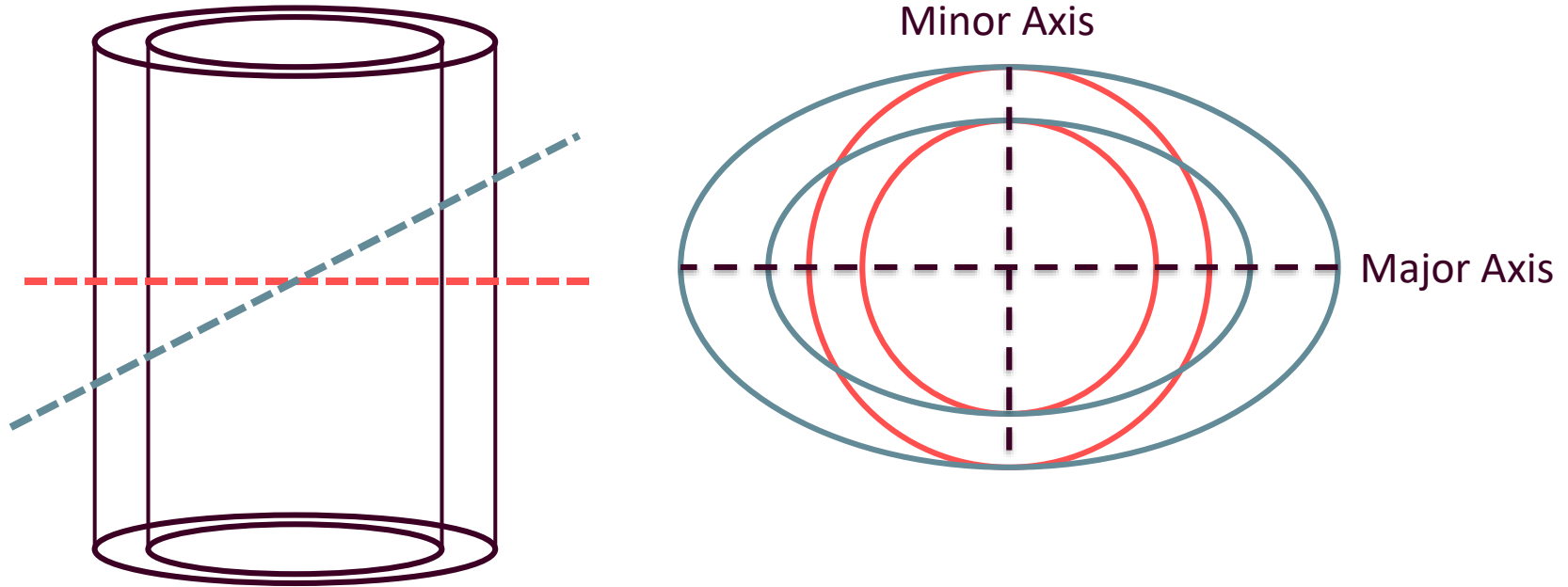
We trained a model to segment blood vessels

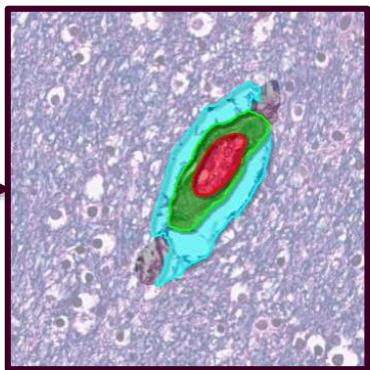
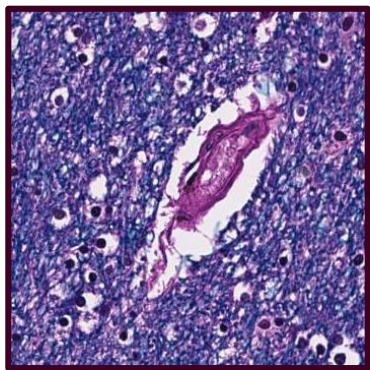


Not all blood vessels are perpendicular to how the tissue was cut



We can still get accurate measurements if we use the minor axis



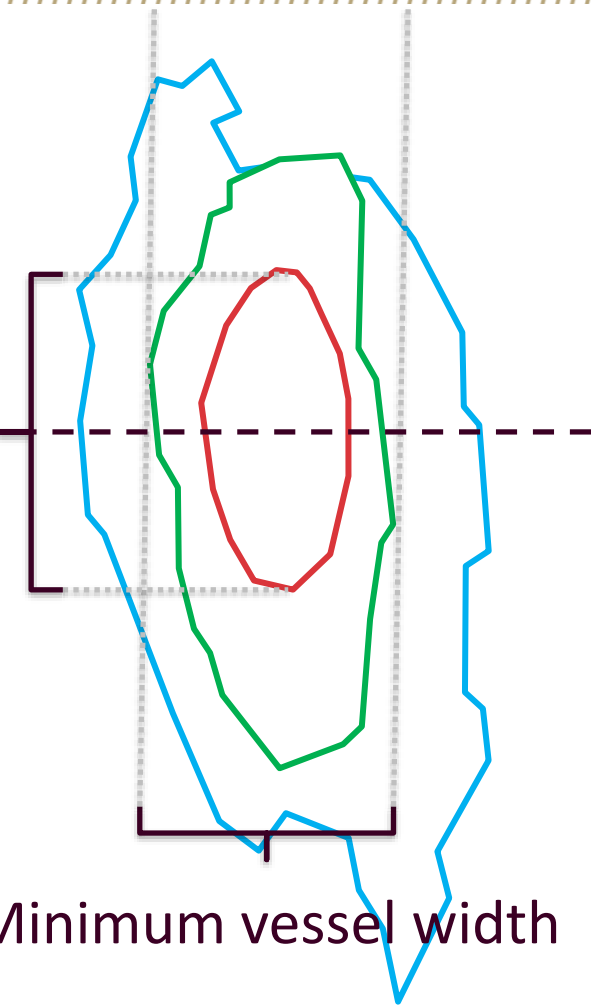




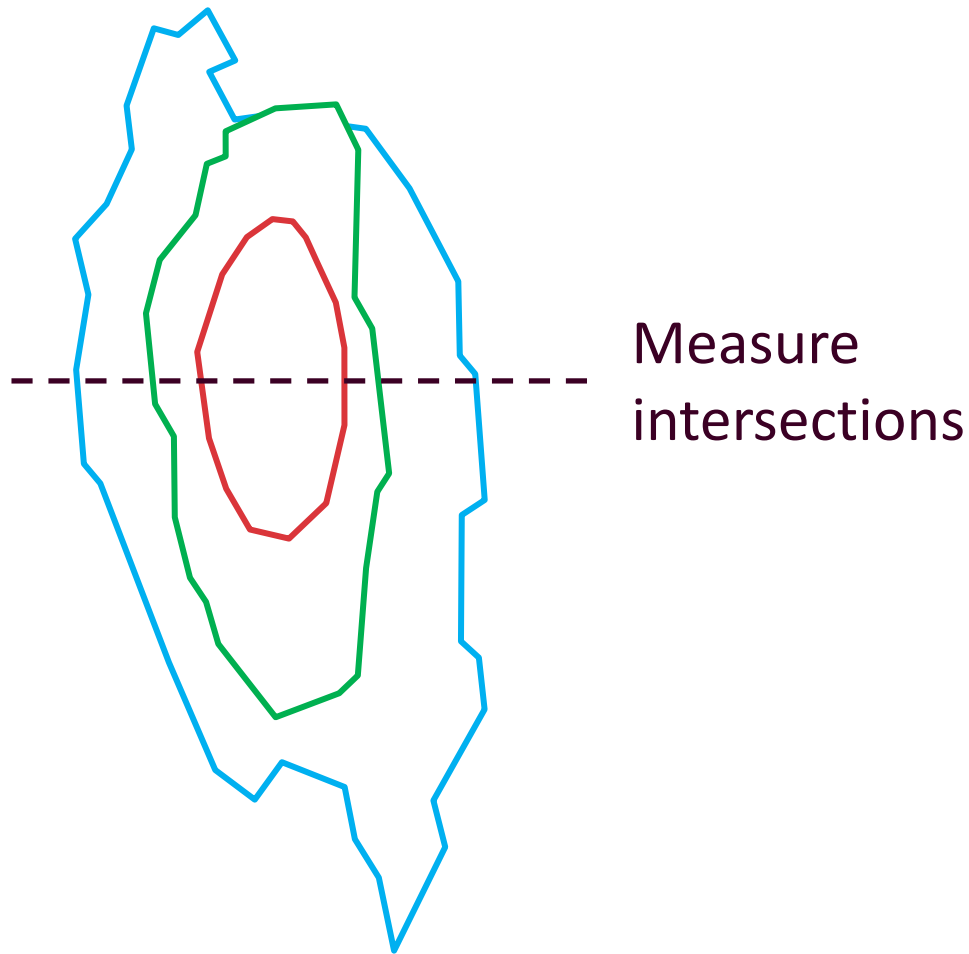
Find lumen mid point

Measure intersections

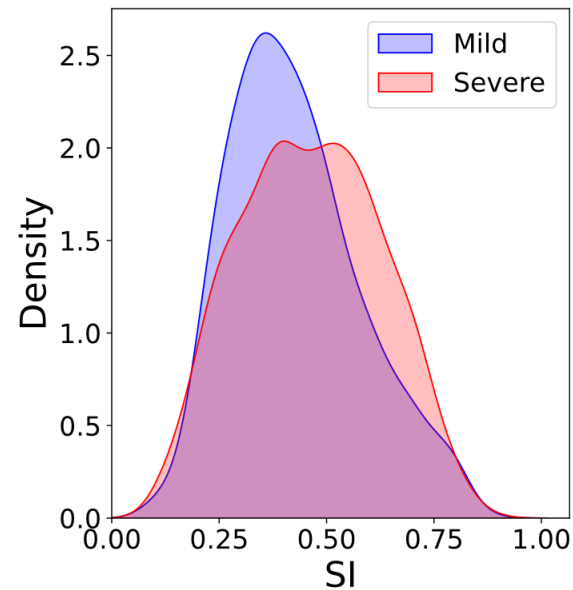
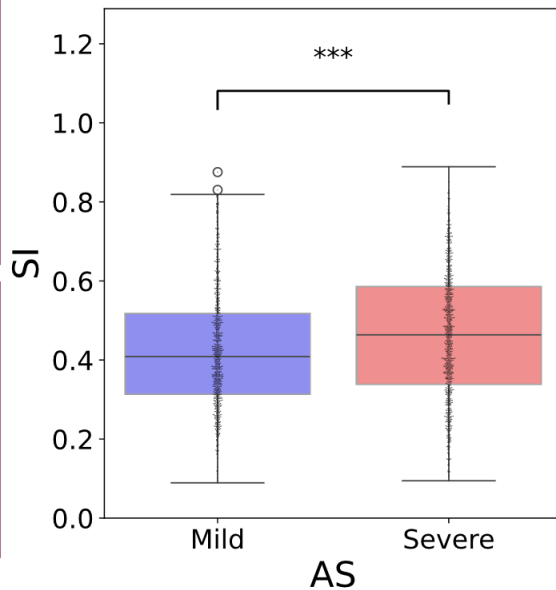
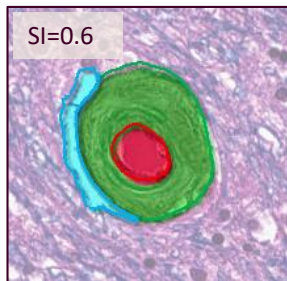
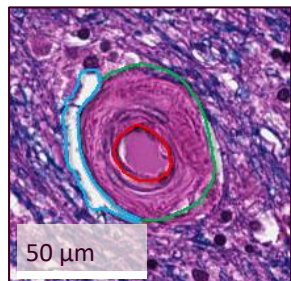
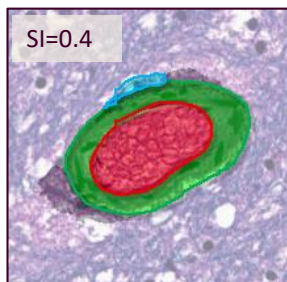
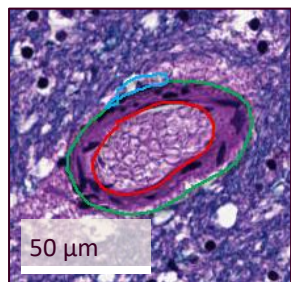
Minimum vessel width

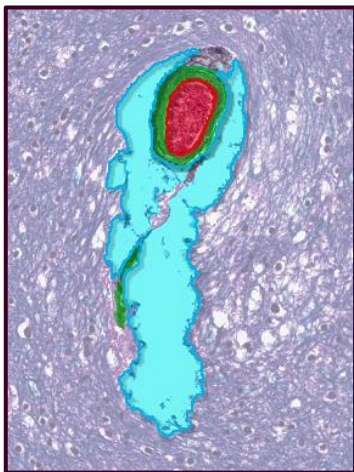
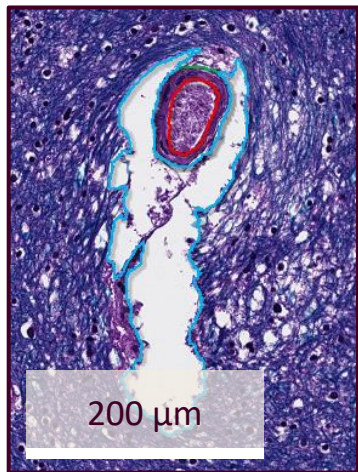
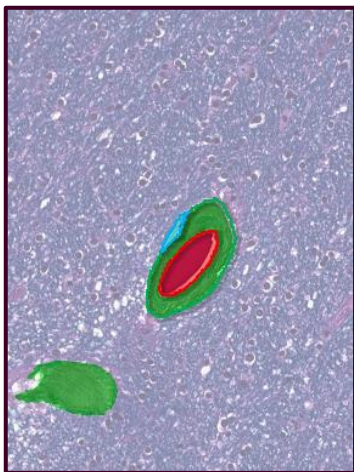
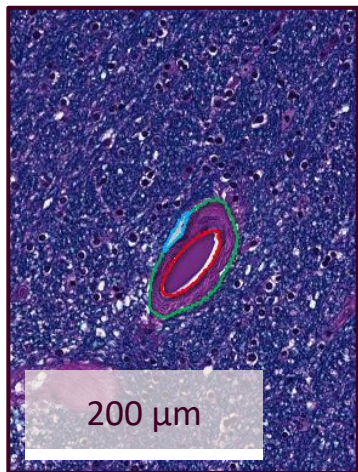


1. Width of: PVS, vessel wall, and lumen
2. Vessel SI
3. Area of: PVS, vessel wall, and lumen
4. Vessel circularity

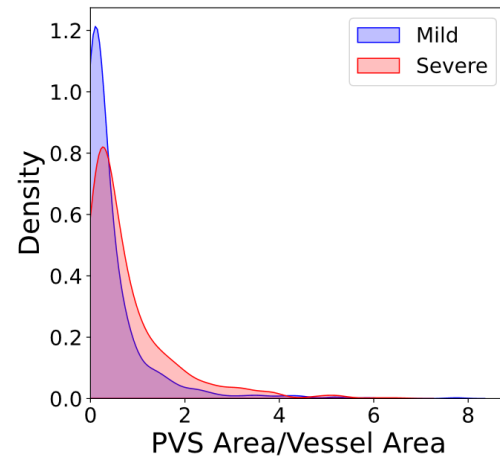
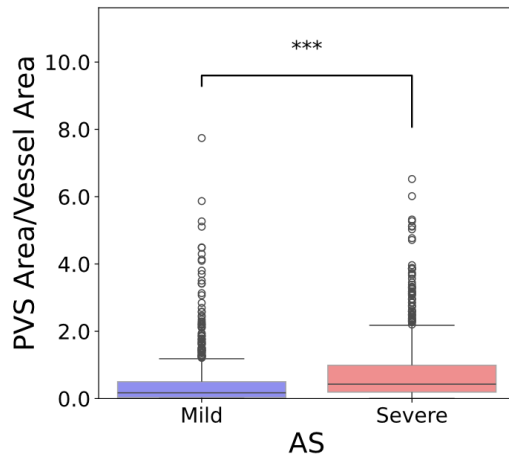


Comparing our metric (SI) to pathological diagnosis

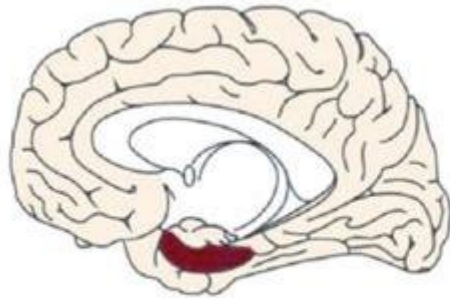




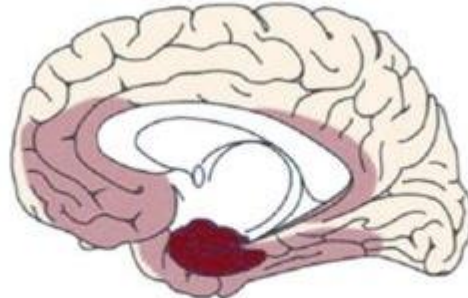
Comparing our metric (PVS) to pathologist categorizations



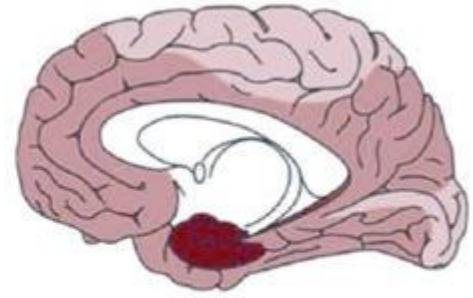
Tau pathology is traditionally described used Braak and Braak staging system



Transentorhinal (I/II)

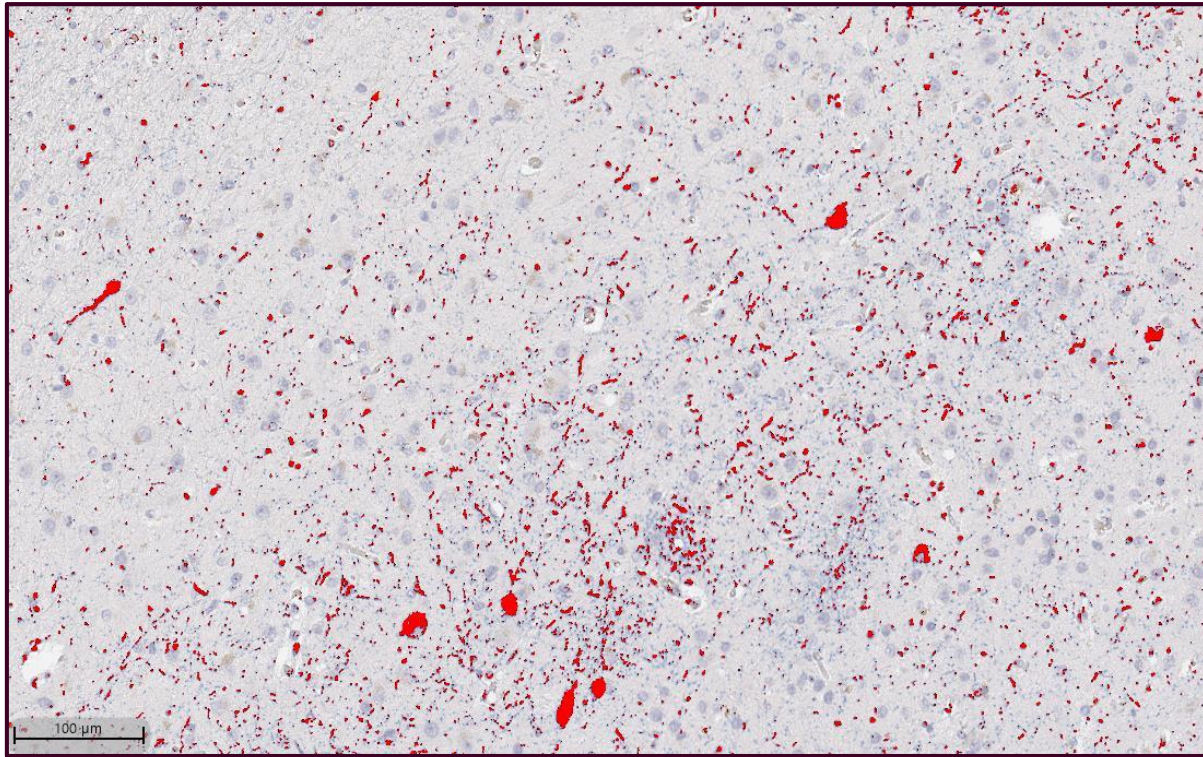


Limbic (III/IV)

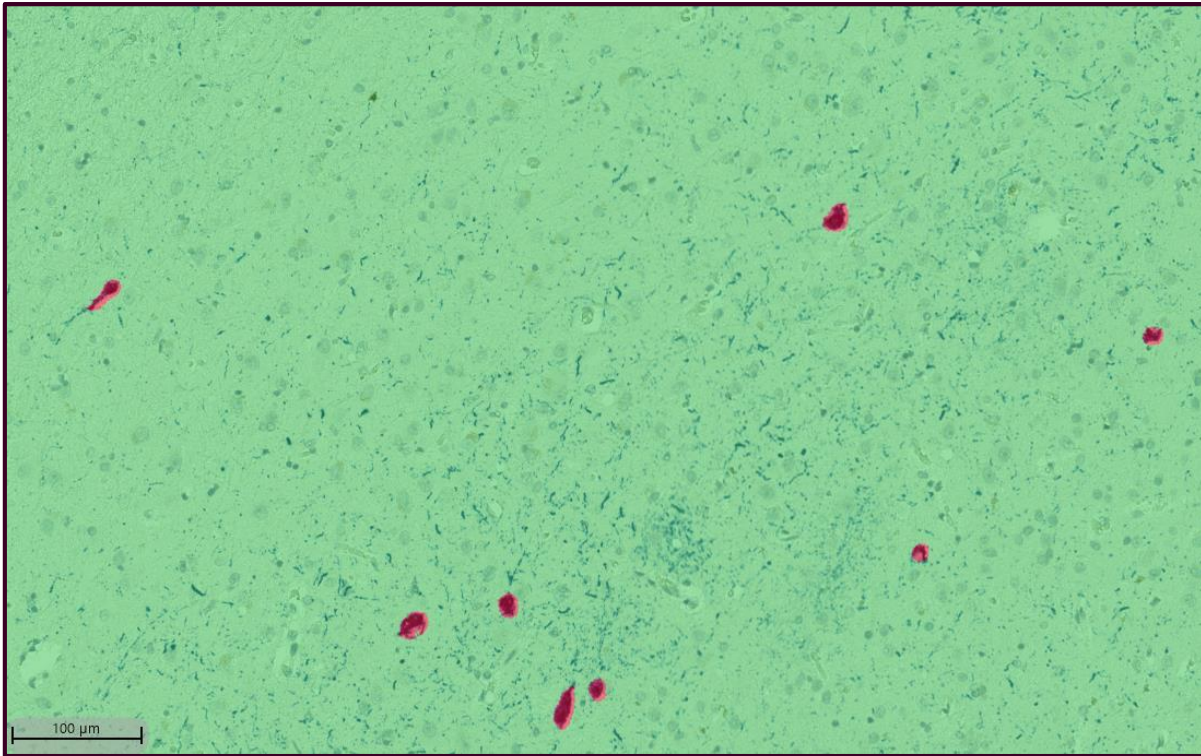


Neocortical (V/VI)

Tau burden can be quantified through thresholding

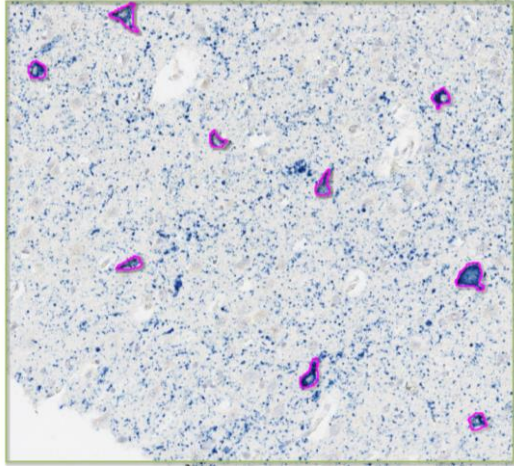


By counting tangles, we can exclude the diffuse tau

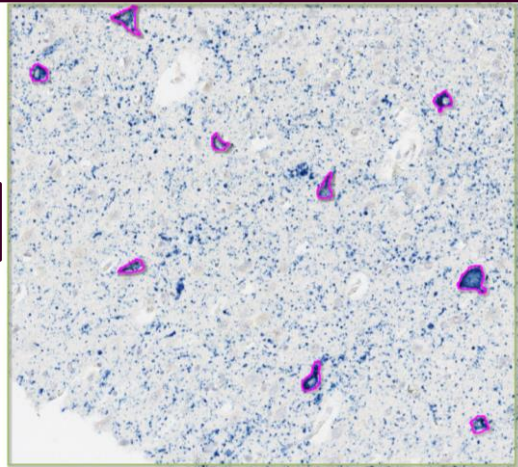


Outline Tangle/Pretangles

(Novice)

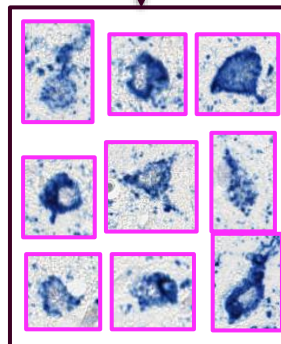


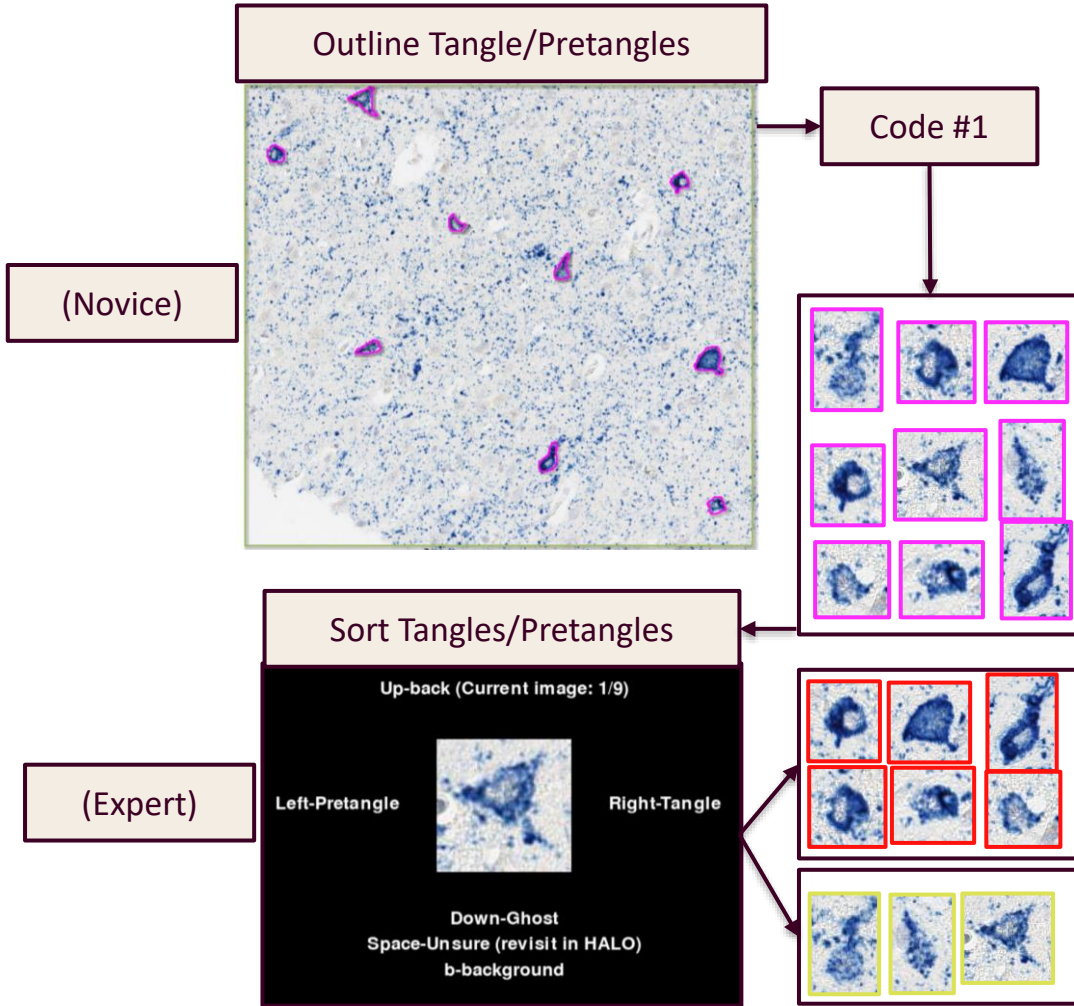
Outline Tangle/Pretangles

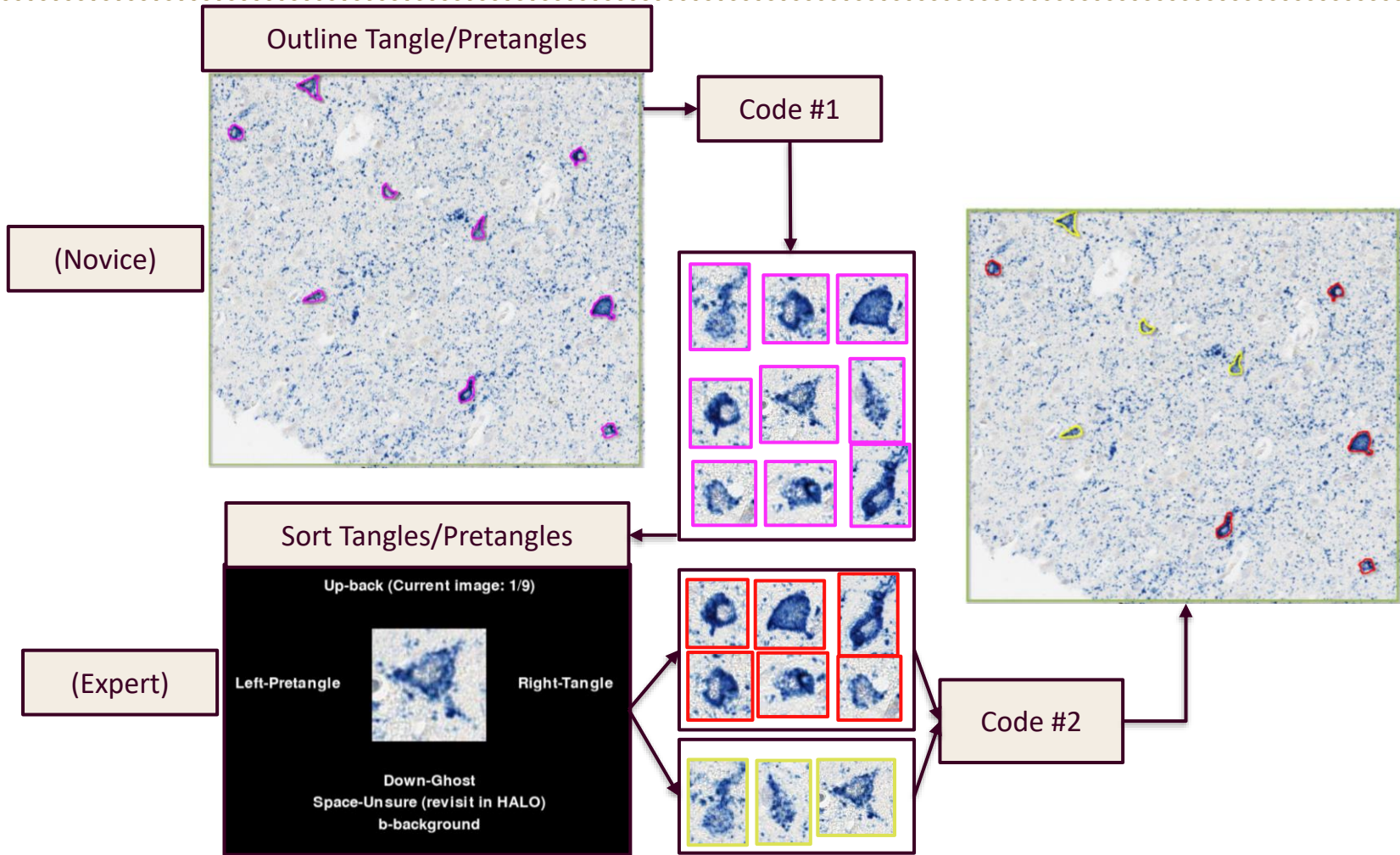


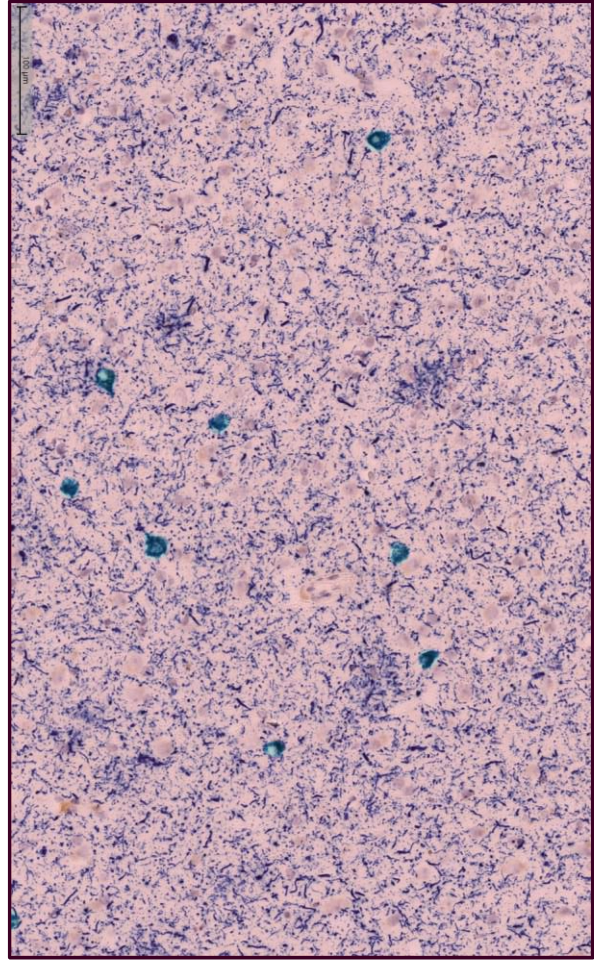
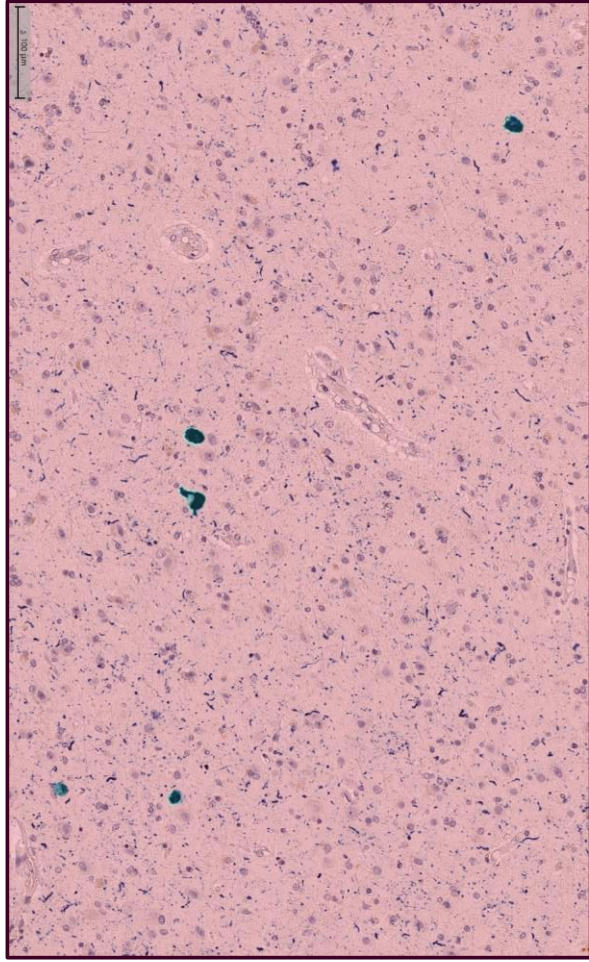
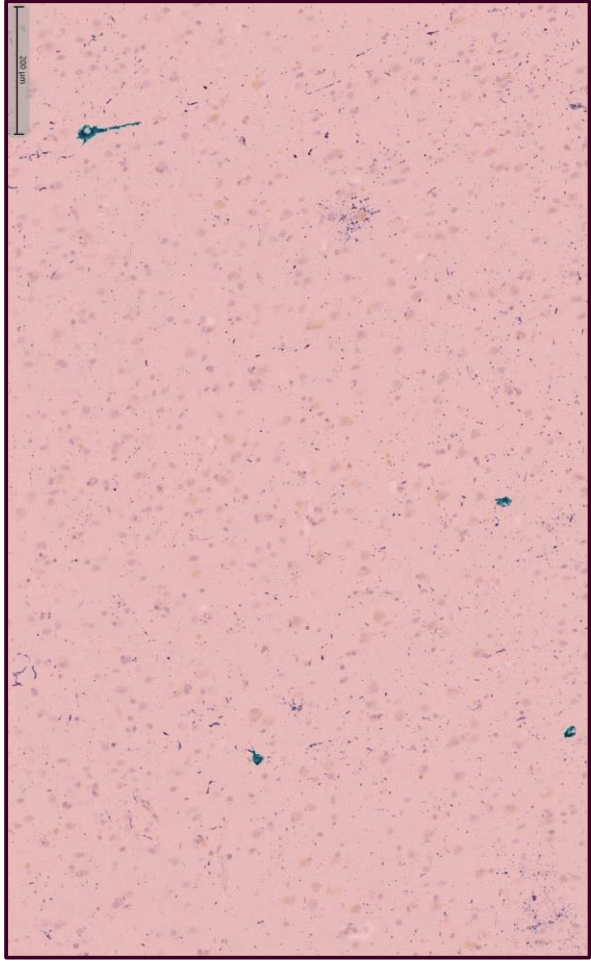
(Novice)

Code #1

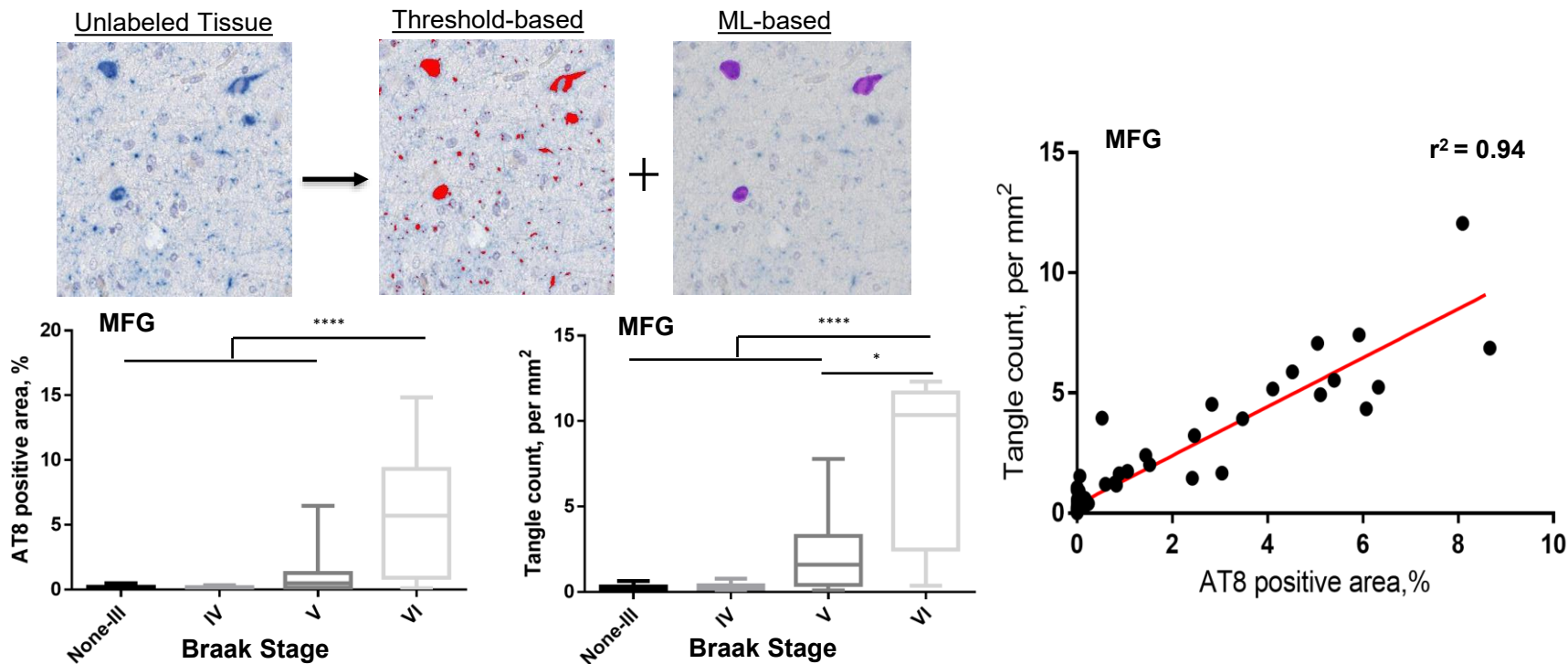




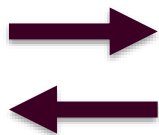




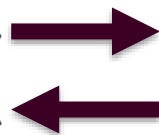
The tangle classifier correlates to Braak stage



We can use Open Neural Network Exchange (ONNX) to share our models outside of HALO, **and** import models to HALO



ONNX



Contributions

- Automated process to measure SI and PVS size in HE-LFB sections.
 - *A similar approach can be developed for Cerebral Amyloid Angiopathy (CAA).*
- Automated process to count tangles

Acknowledgements

ACT Participants

ACT Study Team

Paul Crane, M.D., M.P.H.

UW BRaIN Lab

Dirk Keene, M.D., Ph.D.

Caitlin Latimer, M.D., Ph.D.

Nadia Postupna, M.D., Ph.D.

Lucy Evans, M.D., Ph.D.

Josh Russell, Ph.D.

Ming Xhao, Ph.D.

Swati Levendovszkyc, Ph.D.

Angela Wilson, M.S.

Amanda Kirkland, B.S.

Sora Oyaizu, B.S.

