

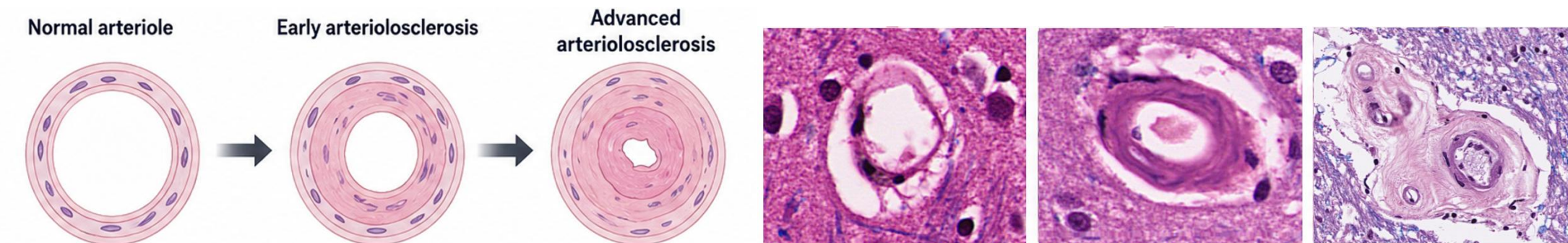
Machine Learning-Based Characterization of Brain Arteriolosclerosis in Neurodegenerative Diseases

Ain Kim¹, Youyou Guo², Shelley L. Forrest^{1,3}, Hidetomo Tanaka¹, Daisuke Taniguchi¹, Akira Arakawa¹, Gabor G. Kovacs^{1,3*}

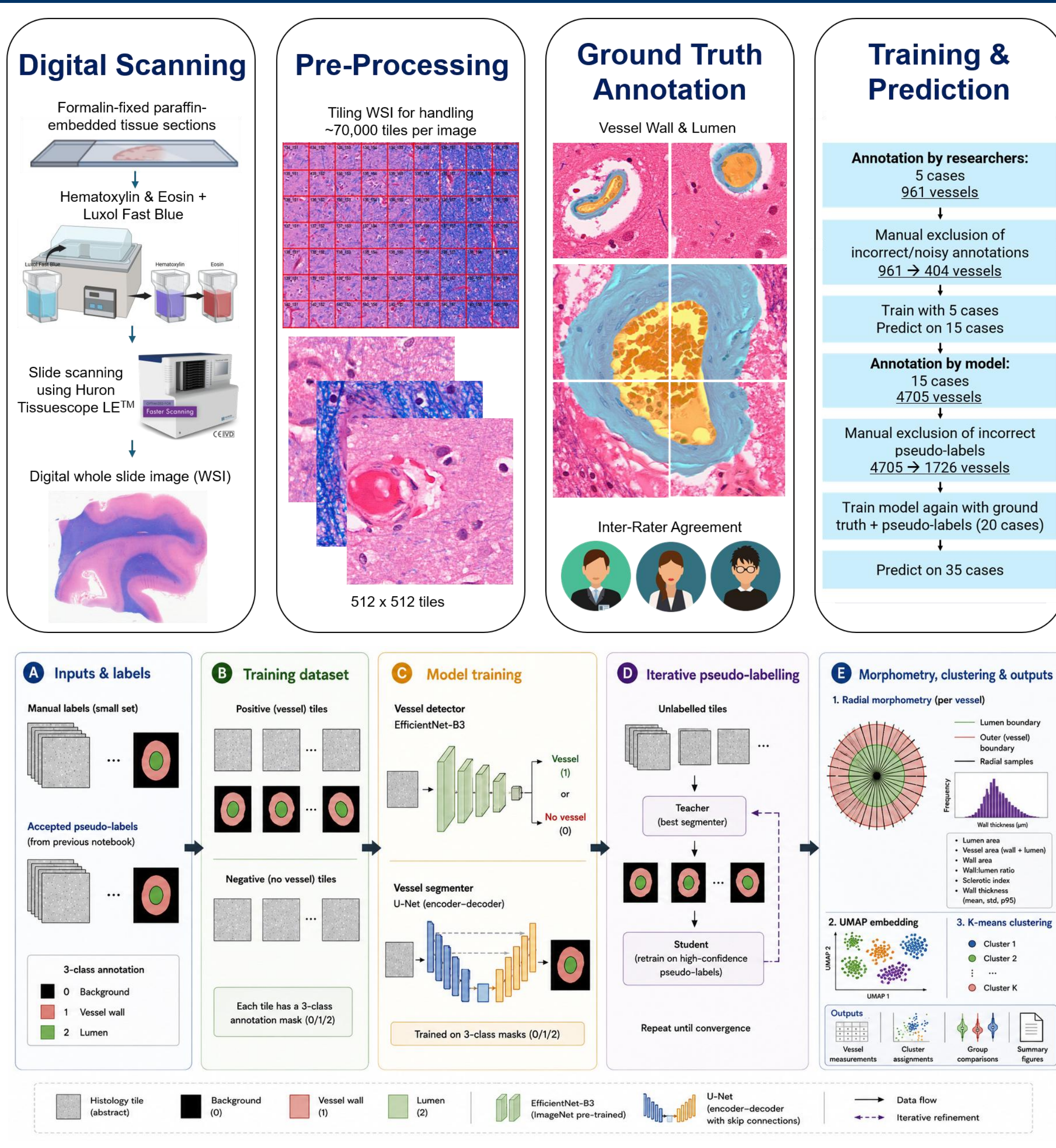
¹Tanz Centre for Research in Neurodegenerative Disease, University of Toronto, Toronto, ON, Canada; ²Department of Computer Science, University of Toronto, Toronto, ON, Canada
³Krembil Brain Institute, University Health Network, Toronto, ON, Canada; *Corresponding Author: gabor.kovacs@uhn.ca

INTRODUCTION

- One of the major concepts of neurodegenerative diseases is the presence of co-existing proteinopathies/cerebrovascular disease
- Brain arteriolosclerosis (thickening and narrowing of cerebral arterioles) is a common age-related small vessel pathology
- Vascular Cognitive Impairment Neuropathology Guidelines (VCING) and the National Alzheimer's Coordinating Center Neuropathology Data Set uses semi-quantitate scores (none, mild, moderate, severe)
- The occipital white matter is considered a reliable region for assessment
- Semi-quantitative scoring may not fully capture the continuous spectrum of vascular pathology
- Disease is spatially heterogeneous, and inter-rater agreement is variable
- Machine learning approach may improve characterization of vascular pathology and whether vascular phenotypes are associated with distinct patterns of neurodegenerative co-pathology

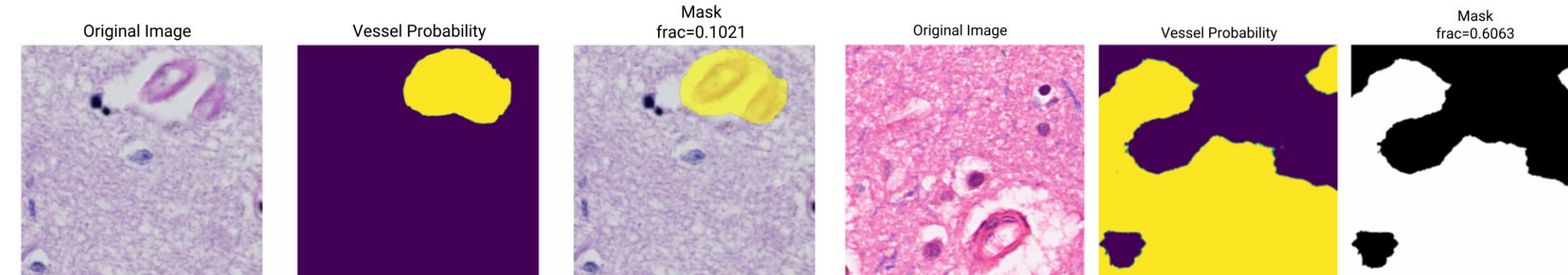


MATERIALS & METHODS



RESULTS

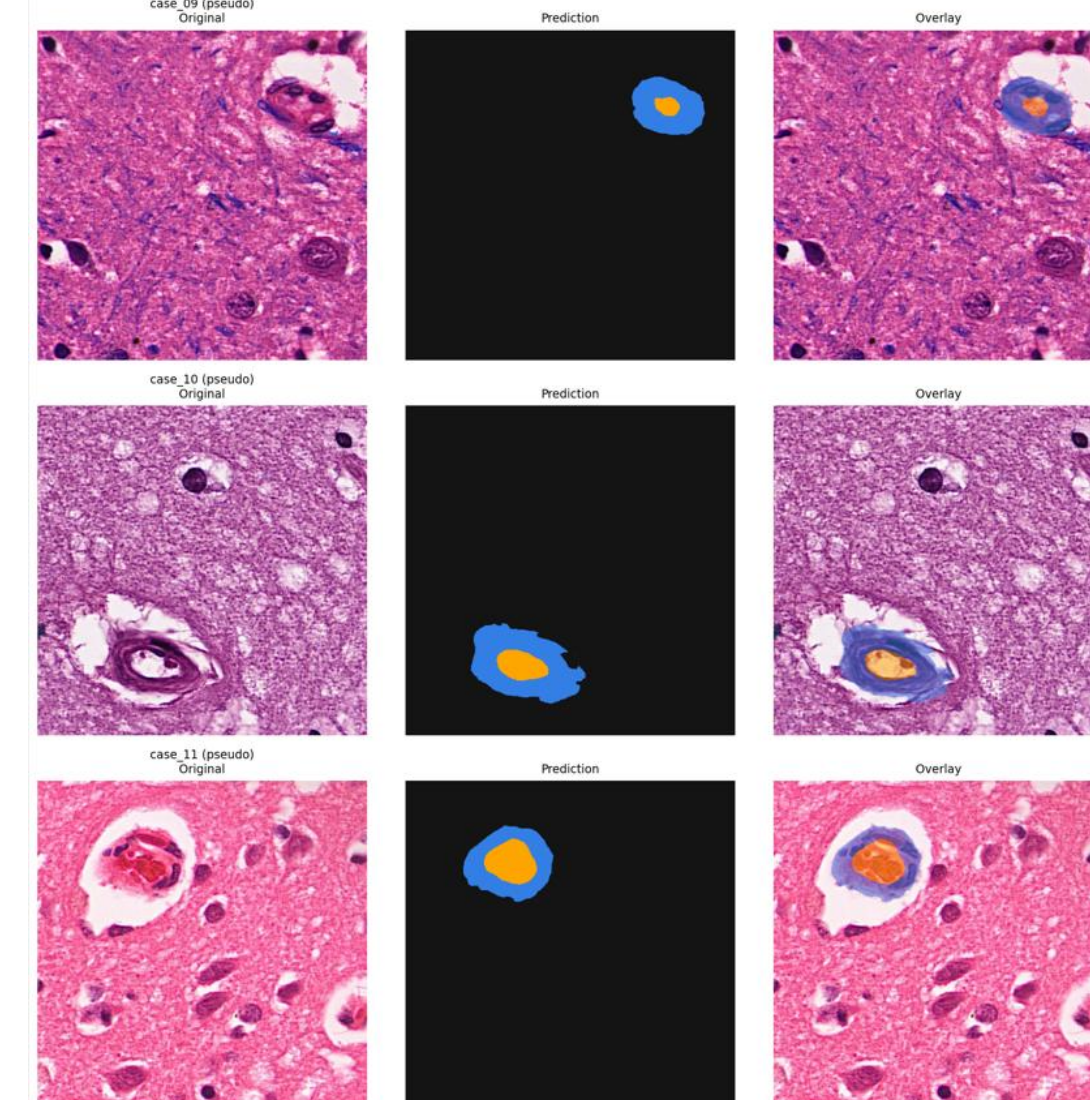
1 Limited generalizability of machine learning models



ArtSeg-VasMorph model applied to H&E staining shows accurate detection of vessels
ArtSeg-VasMorph model applied to H&E with LFB staining shows high level of false positivity

2 Vessel detection accuracy of new model

Segmentation Visual Check

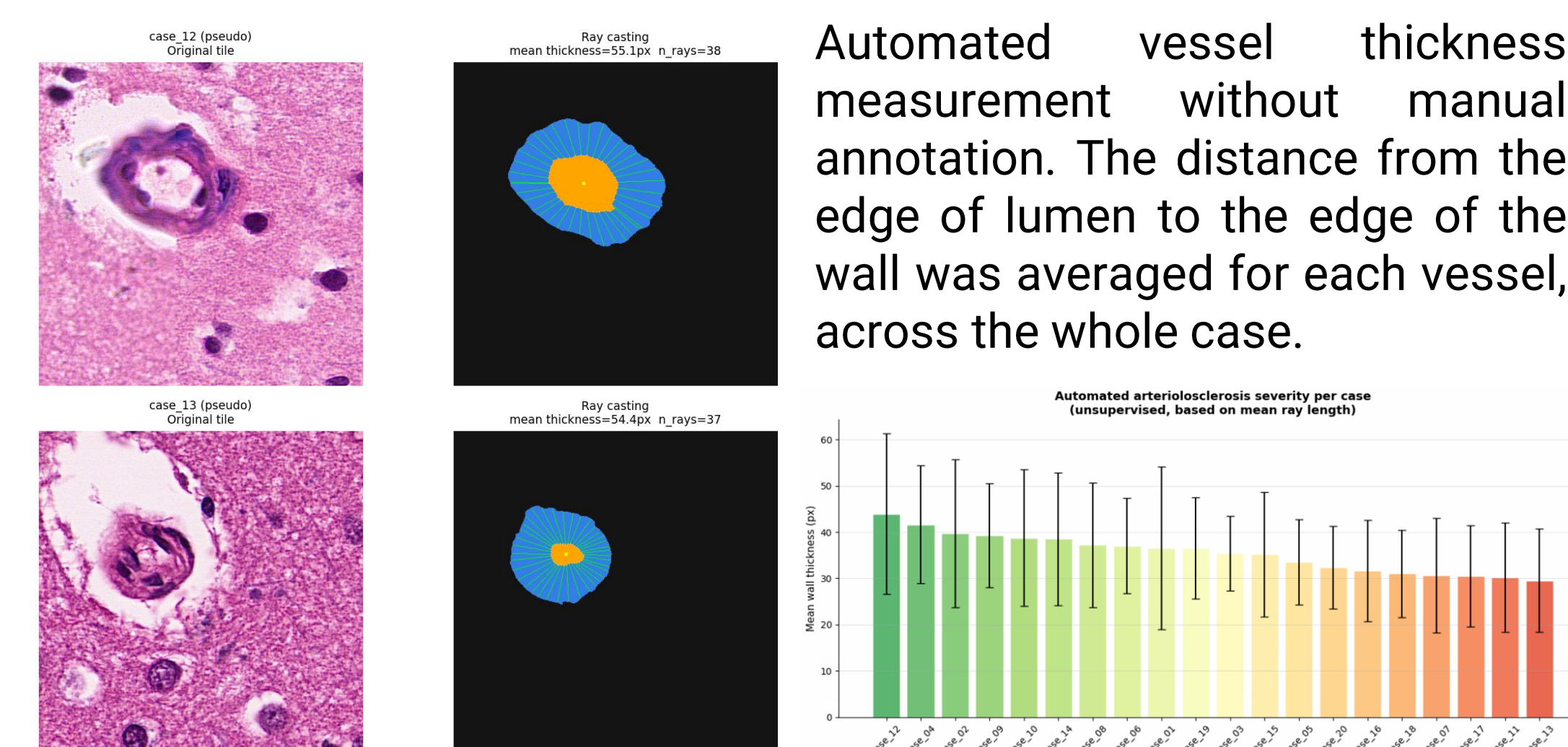


Held-Out Test Accuracy

	Overall	Wall	Lumen
DICE	0.91 ± 0.10	0.84 ± 0.10	0.89 ± 0.11
IOU	0.85 ± 0.13	0.73 ± 0.13	0.81 ± 0.15
PRECISION	0.86 ± 0.13	0.77 ± 0.14	0.90 ± 0.13
RECALL	0.99 ± 0.02	0.95 ± 0.03	0.89 ± 0.13
F1	0.91 ± 0.10	0.84 ± 0.10	0.89 ± 0.11

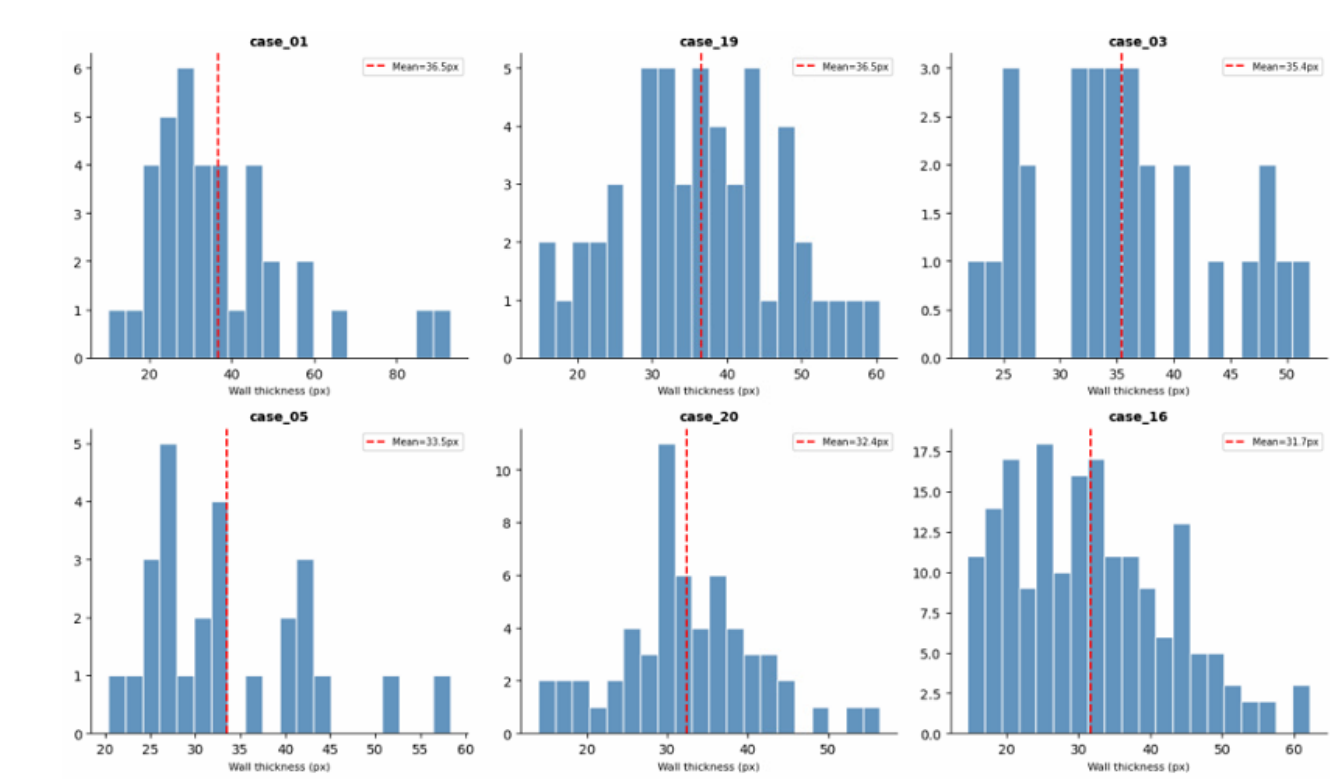
1 case was used for held-out test, where overall DICE score = 91%

3 Vessel thickness measurement



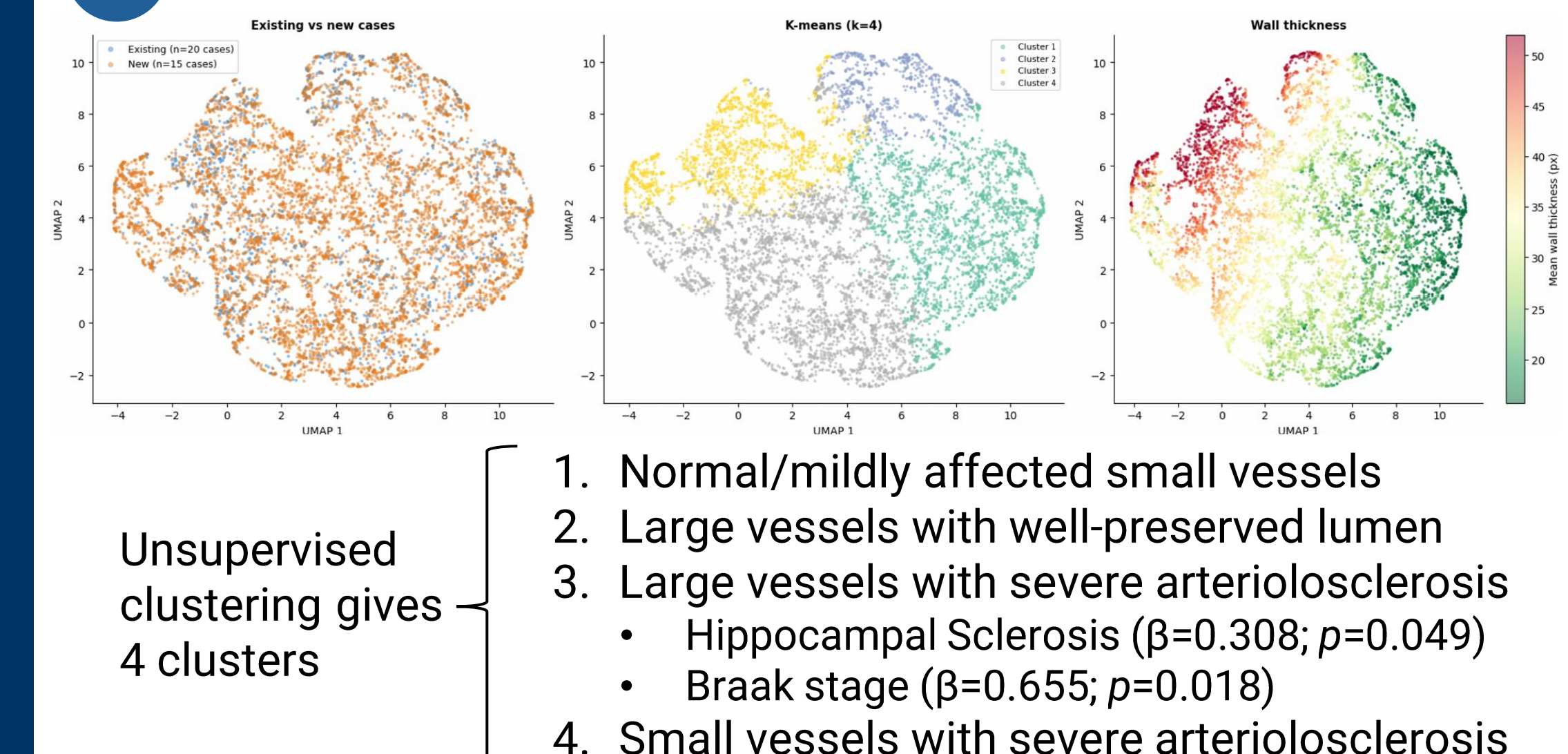
Vessel thickness varies within each case.

Evaluation of all vessels detected allows more averaged measurement of the severity and therefore, categorization into mild, moderate and severe arteriolosclerosis.



RESULTS

4 Unsupervised clustering based on vessel thickness



CONCLUSIONS

- Variability in staining quality, type of staining and tissue preparations make **generalizability** of machine learning models challenging
- Filtering manual annotations and training the model with accurate data yields higher vessel detection accuracy
- Vessel thickness is not consistent within a case; taking the **distribution** of vessel thickness can give an averaged quantification
- We confirm the positive correlation between vessel wall thickening **Braak stage** and **Hippocampal Sclerosis** as reported in the literature. Expanding this analysis could improve our understanding of the association between brain arteriolosclerosis and neurodegenerative diseases.

Limitations: hyaline fibrosis, loss of smooth muscle cells, lumen stenosis and subtypes (i.e., hyaline vs hyperplastic) were not specified in the training data and could be used to further stratify neurodegenerative disease.

ACKNOWLEDGEMENT

The authors particularly acknowledge the patients and their families for their donation. This project was funded by the National Institutes of Health under award number 1U24NS133945-01.

We thank the undergraduate researchers, Ruby Chen and Bilal Assadi for assisting with vessel annotations.

REFERENCES

Lou JJ, Chang P, Nava KD, et al. Applying machine learning to assist in the morphometric assessment of brain arteriolosclerosis through automation. *Free Neuropathol.* 2025 Jun 2;6:12. doi: 10.17879/freeneuropathology-2025-6387. PMID: 40510864

Blevins BL, Vinters HV, Love S, et al. Brain arteriolosclerosis. *Acta Neuropathol.* 2021 Jan;141(1):1-24. doi: 10.1007/s00401-020-02235-6. Epub 2020 Oct 24. PMID: 33098484

Contact: ain.kim@utoronto.ca

