



High-resolution Computational Histology Resolves Ongoing Amyloid-beta Accumulation Beyond the Neuroimaging Plateau

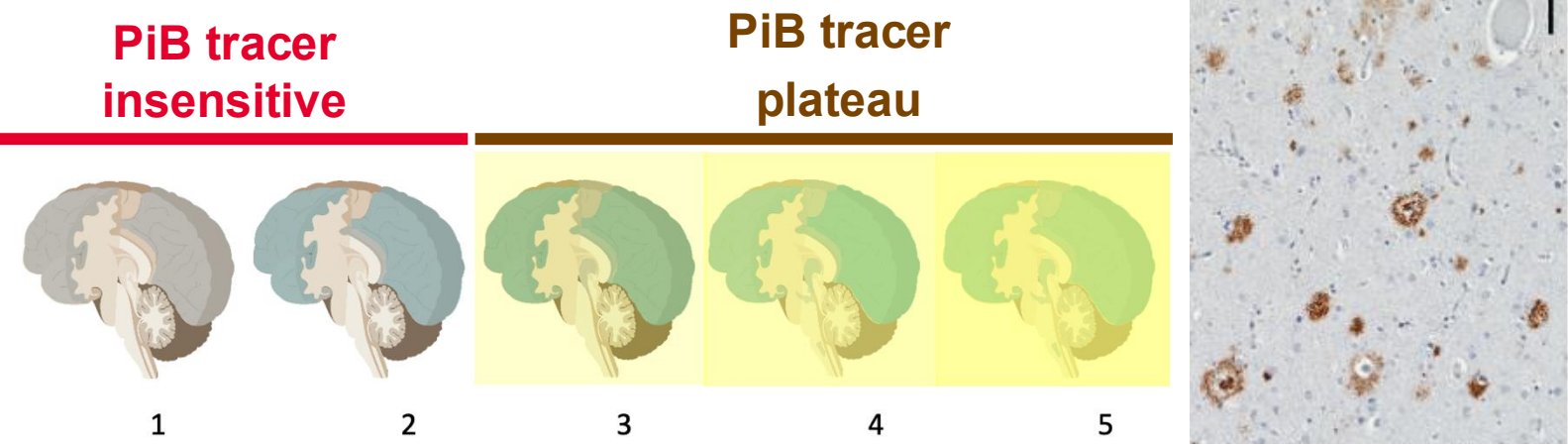
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BACKGROUND

- Alzheimer's disease (AD) is driven by two major hallmarks: extracellular amyloid-beta plaques and intracellular phosphorylated Tau.
- With recent advances in anti-Amyloid antibody treatment, there is an increasing need for an accurate and sensitive monitoring tool to assess disease progression and treatment effectiveness.
- Even the FDA-approved biomarker, like PiB PET tracer, has its limitations in both sensitivity and specificity

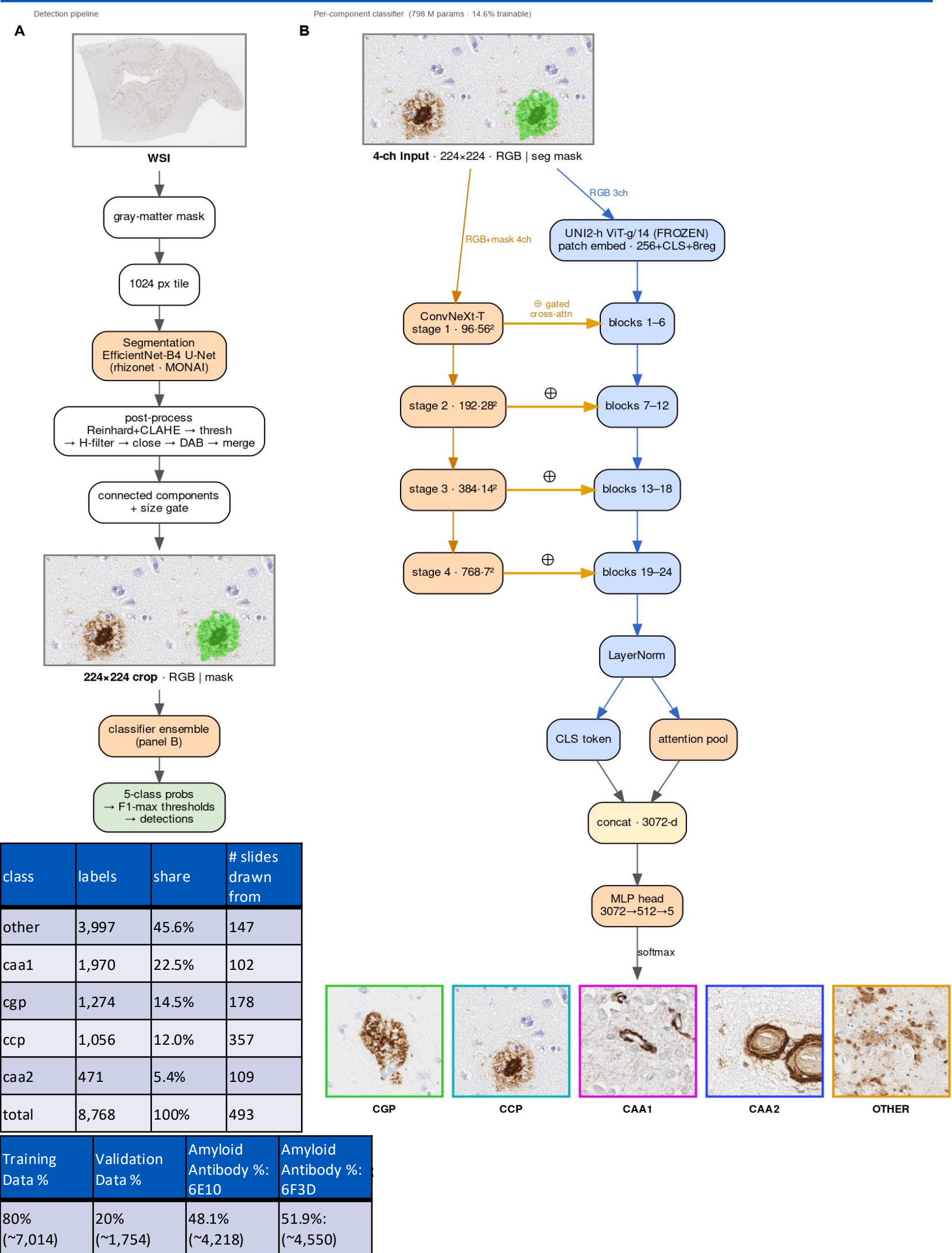
THAL Stage – Amyloid-beta staging



OBJECTIVES

- Developing a computational pathology pipeline to segment and classify various Amyloid beta burden, using high-resolution histological quantification to unmask continuous pathological changes across Thal phases beyond the limitation of PiB PET tracer
- Establishing the relationship between different Amyloid pathologies: Classic Core Plaque (CCP)/Coarse Grained Plaque (CGP)/Capillary CAA (CAA type 1)/Parenchymal CAA(CAA type 2) and Alzheimer's disease progression in different subtypes (like early onset AD vs late onset AD)

METHODS



RESULTS

Figure 1. Training Data Processing + Augmentation + Attention Map

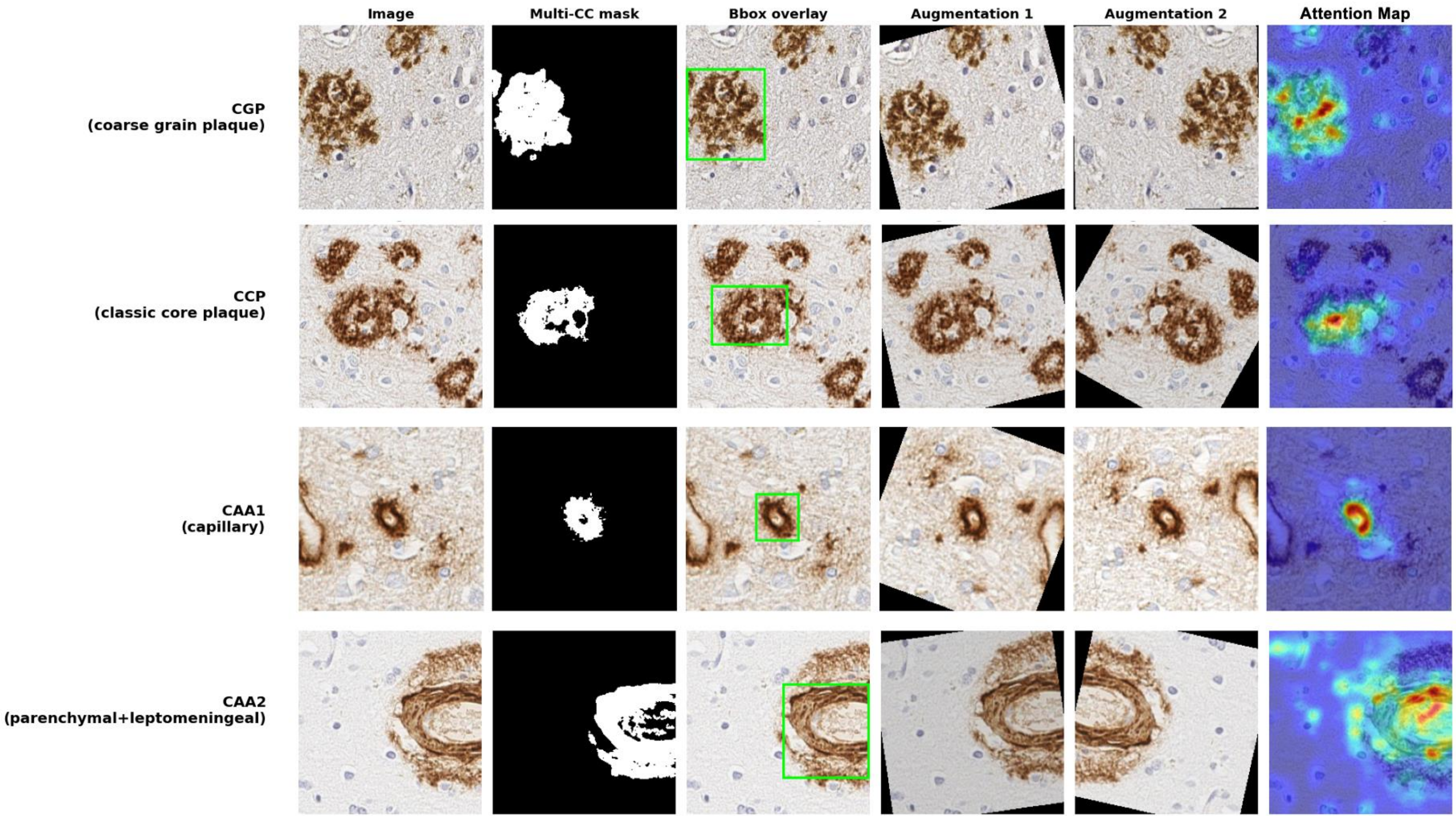
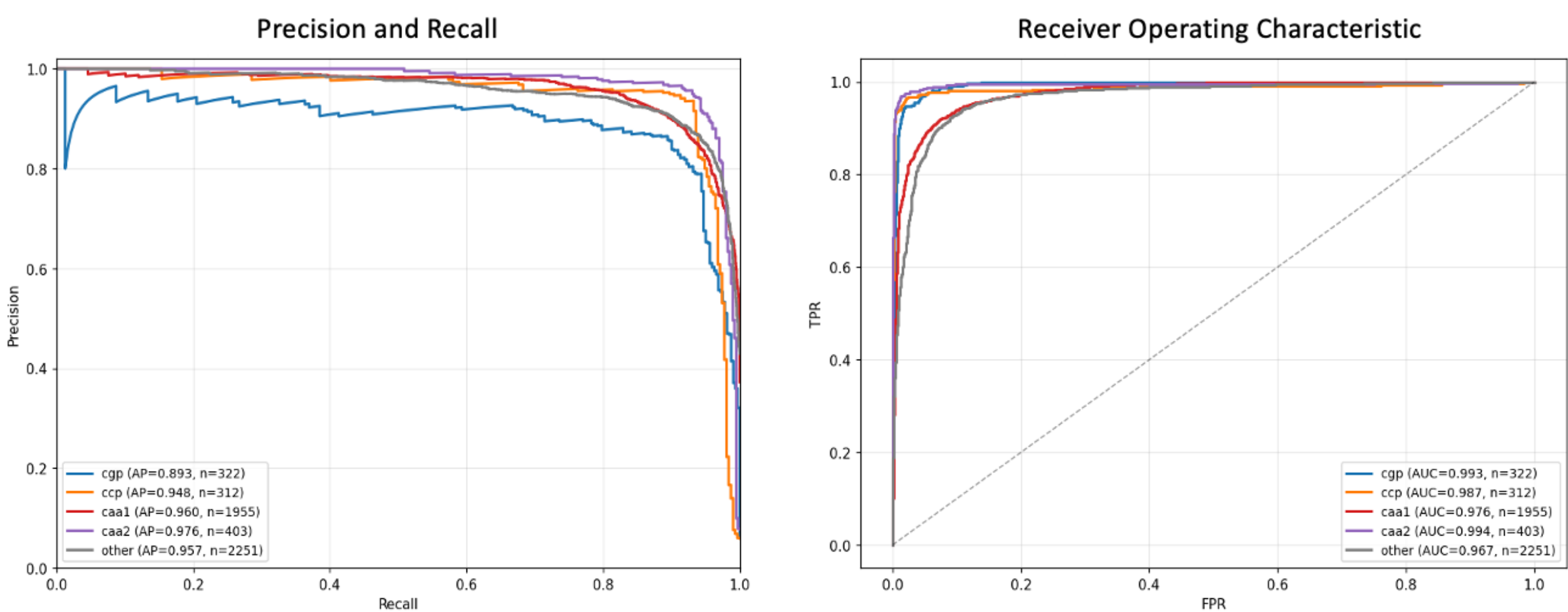


Figure 2. Model Performance Metric



Figure/Table 3. Model Validation: Agreement to pathologist scoring

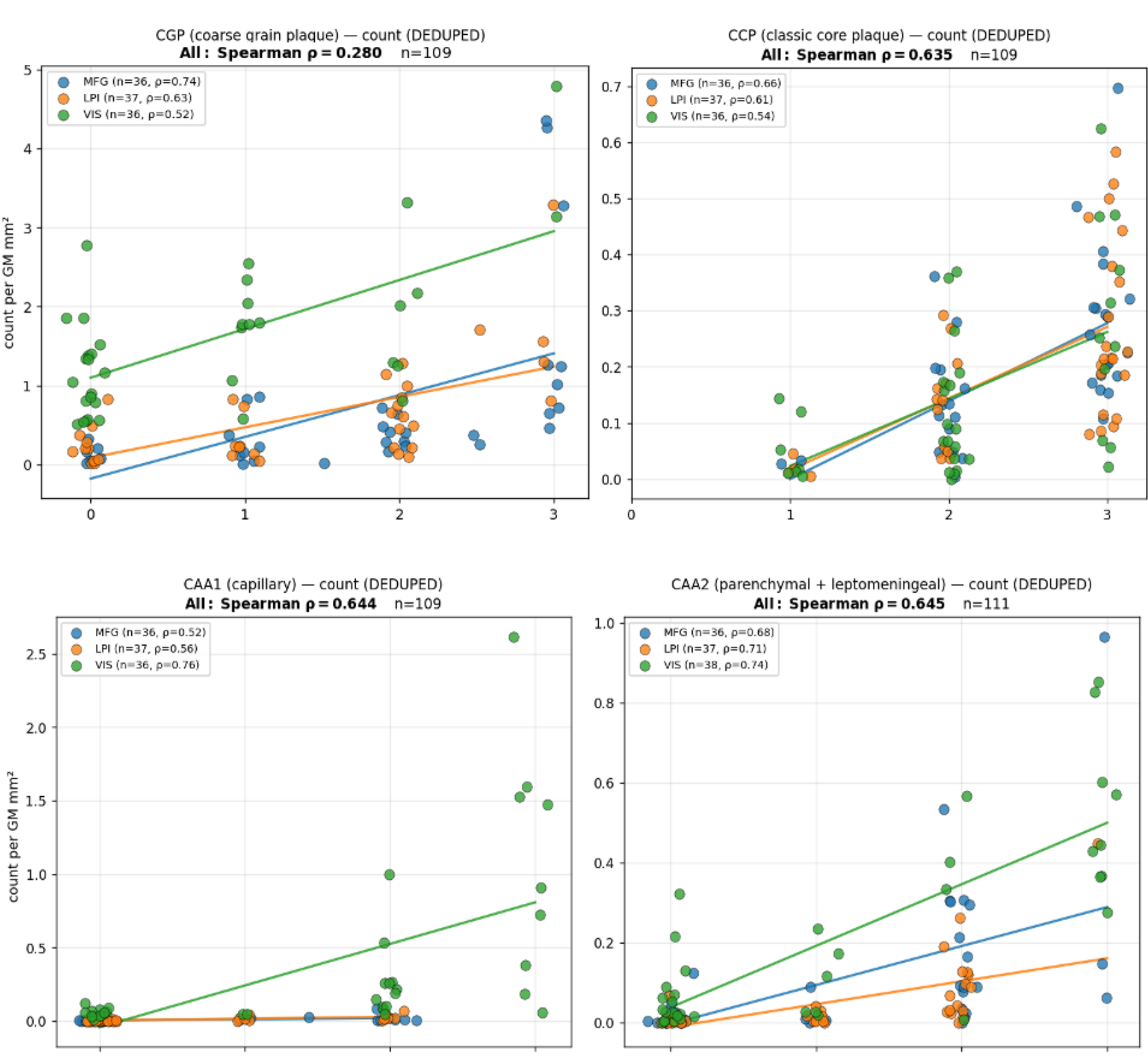


Figure 4. Model Multiclass Inference Demo

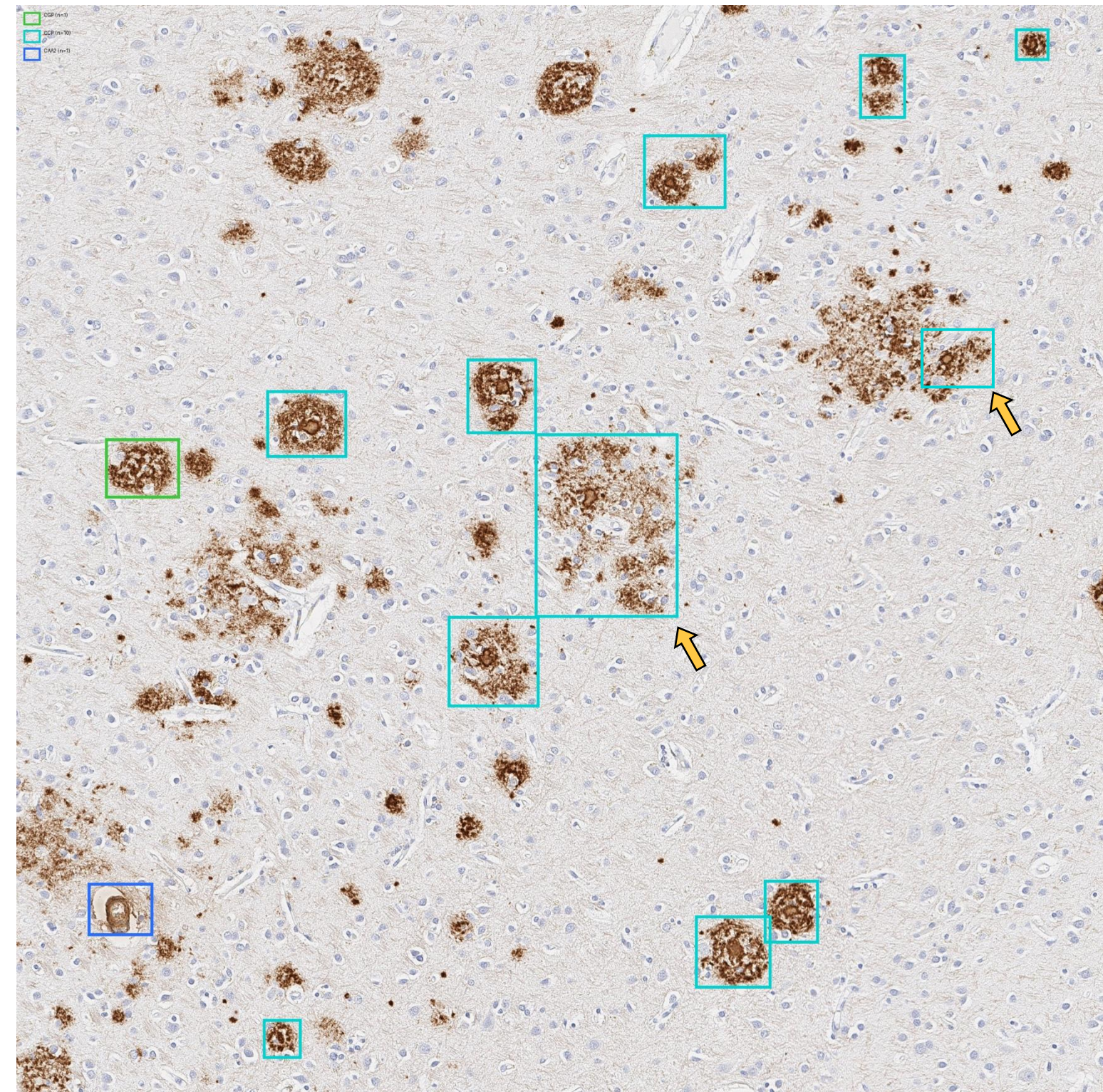


Figure 4 shows an ROI result of the entire WSI (whole slide inference). Here, you can see three classes are detected accurately: CAA type 2 (parenchyma CAA) in blue, CCP (core plaque) in cyan, and CGP (coarse-grained plaque) in green. FRCNN, the specialized contextual detector is more capable in finding core plaque hiding within other amyloid (yellow arrows), where the UNet segmentation model is providing most of the pathology detection as well as all the segmentation masks for the classifier.

CONCLUSIONS

- AI-assisted digital pathology quantification reveals distinct spatial trajectories of various pathology and subtypes
- Amyloid pathology does not plateau at MCI
- Classifier deployed in other amyloid staining slides and continue to improve with dataset expansion (CGP class have the weakest F1: 0.89)
- Inference batch-processing with speed

REFERENCES

Tools/Algorithms	Citations
ViT-Adapter	Chen et al., <i>Vision Transformer Adapter for Dense Predictions</i> , ICLR 2023
UNI / UNi2-h	Chen et al., <i>Towards a general-purpose foundation model for computational pathology</i> , Nat Med 2024
ConvNeXt	Liu et al., <i>A ConvNet for the 2020s</i> , CVPR 2022
EfficientNet	Tan & Le, <i>EfficientNet</i> , ICML 2019
U-Net	Ronneberger et al., <i>U-Net</i> , MICCAI 2015
MONAI	Cardoso et al., 2022
Focal loss	Lin et al., <i>ICCV</i> 2017
CutMix	Yun et al., <i>ICCV</i> 2019
Reinhardt + Macenko + CLAHE	Reinhardt 2001; Macenko 2009; Zuiderveld 1994
SAM	Kirillov et al., <i>ICCV</i> 2023
CTransPath	Wang et al., <i>Med Image Anal</i> 2022

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