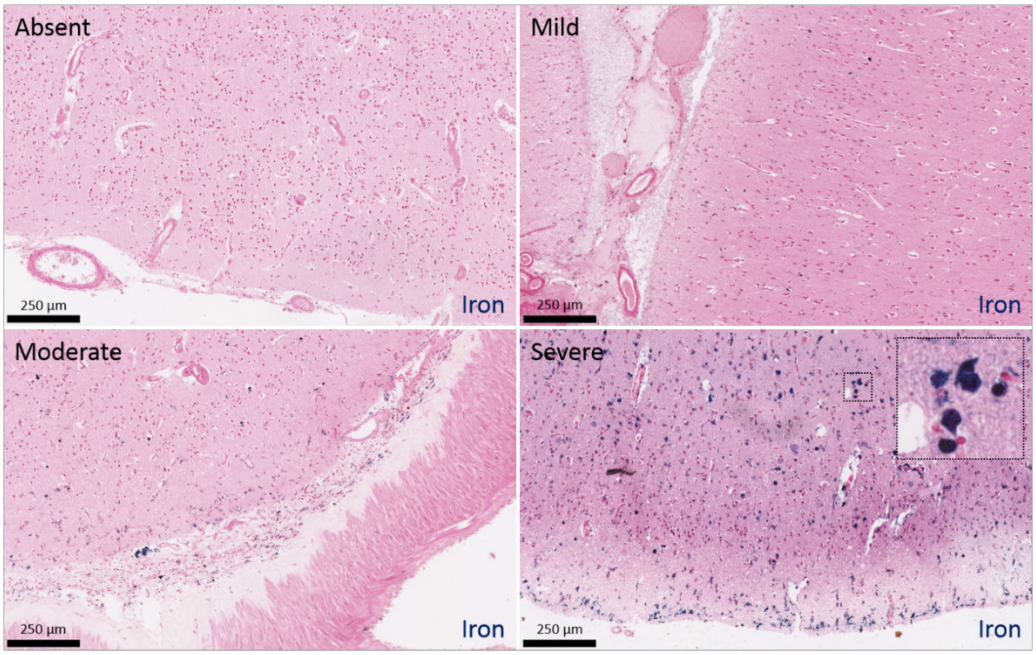
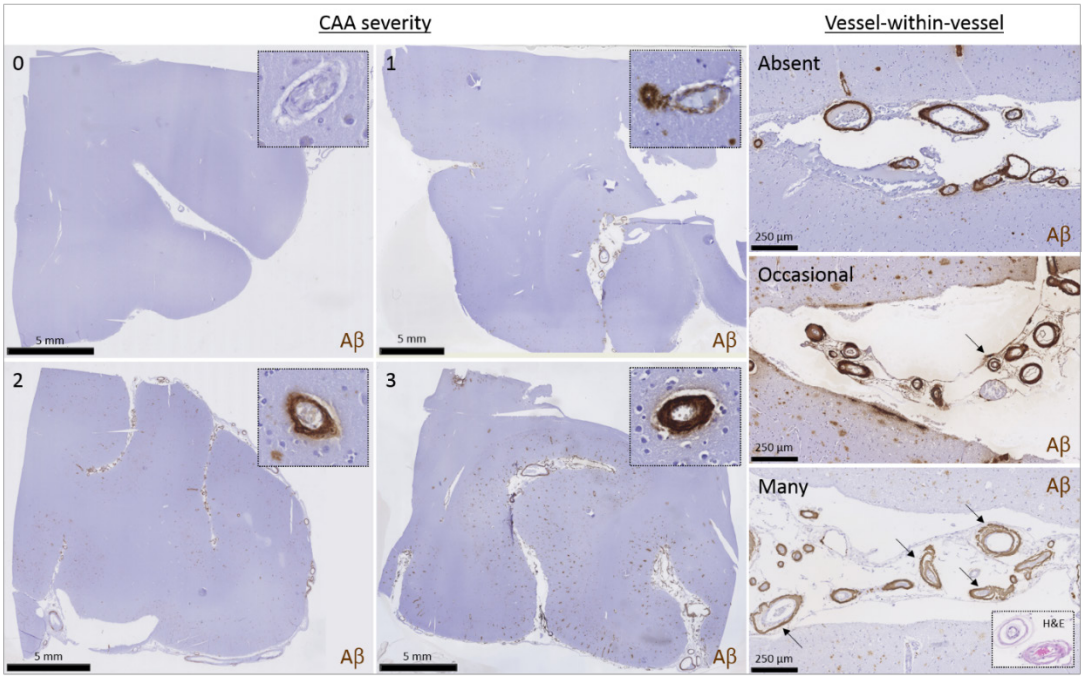
Supplementary Material

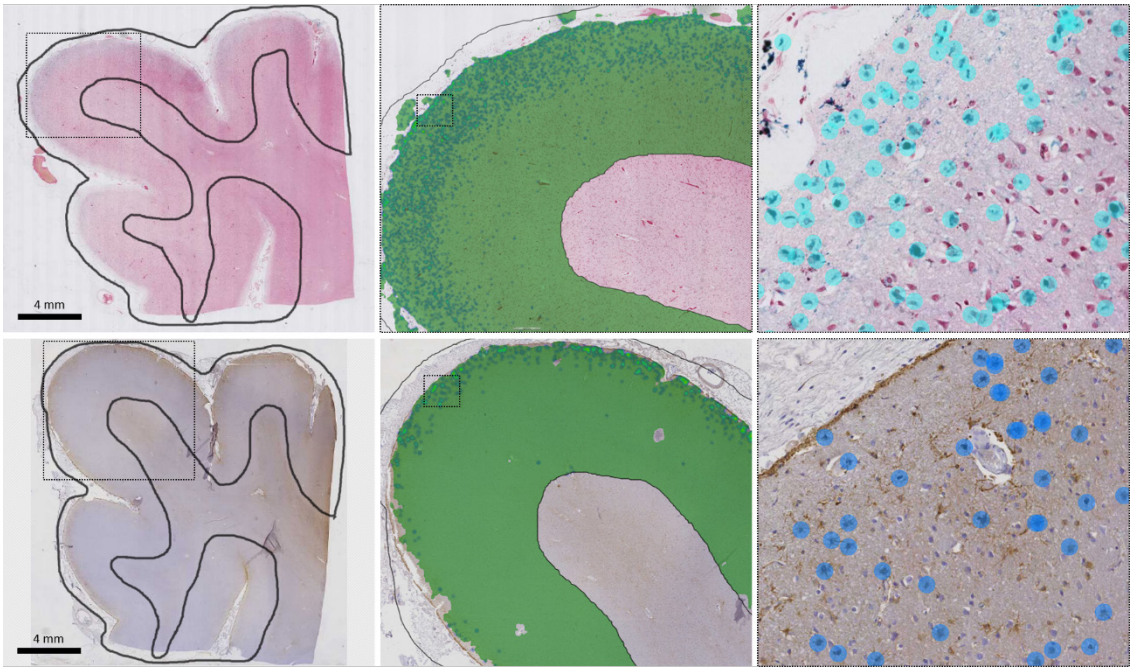


Supplemental Figure 1. Templates for the assessment of Iron deposits on histopathology. Presence and severity of Iron positive (blue) deposits was assessed on Perls' Prussian blue-stained sections using a 4-point scale: absent (0), mild (1), moderate (2), or severe (3).



Supplemental Figure 2. Templates for the assessment of cerebral amyloid angiopathy burden on histopathology.

Cerebral amyloid angiopathy (CAA) severity was assessed on Aβ-stained sections using a 4-point scale; absent (0), scant Aβ deposition (1), some circumferential Aβ (2), widespread circumferential Aβ (3), following proposed consensus criteria with minor modifications (Love *et al.,* 2014). Vessel-within-vessel pathology was determined as absent (0), occasional vessel (1), or many vessels (2).



Supplemental Figure 3. AI-guided detection of Iron deposits and reactive astrocytes for quantitative assessment.

To perform quantitative assessment of cortical superficial siderosis and astrogliosis, an AI was trained to identify tissue and Iron positive deposits on Perls' Prussian blue-stained sections (top row) and to identify tissue and reactive astrocytes on GFAP-stained sections (bottom row). Note that the AI correctly identified tissue and objects of interest in the manually outlined regions of interest.

Supplemental Table 1. Multivariable logistic regression models of the association between cortical superficial siderosis (cSS) presence and burden with CAA severity in cortical and leptomeningeal vessels, across all MRI-targeted and untargeted sections within the CAA cases combined (n=65 sections).

Model	**OR (95% CI)**	**p-value**
-cSS presence		
Moderate-to-severe cortical CAA	0.39 (0.11-1.42)	0.156
Moderate-to-severe leptomeningeal CAA	9.22 (1.82-49.73)	0.007
-cSS presence		
Moderate-to-severe cortical CAA	0.39 (0.1-1.58)	0.188
Presence of leptomeningeal vessel-within-vessels	13.16 (3.53-49.07)	<0.0005
Many leptomeningeal vessel-within-vessels	13.25 (3.01-58.35)	0.001

All models are also adjusted for age at death and anatomical area (=block) and source brain (=case ID).