To evaluate the two candidate definitions and methods for calculating vessel wall thickness, we created a test set (n = 62) by selecting images (Supplementary Figure 4) meeting the following inclusion criteria: (1) the image contained only one single vessel, (2) segmentation output showed uninterrupted circumferential labeling of the vessel wall, and (3) segmentation output does not show false-positive satellite lumens and only contains one accurately segmented lumen. A senior neuropathologist (WY) manually measured the vessel wall thickness for each image using ImageJ.29 For these manual measurements, blood vessel wall thickness was defined as the distance between the inner boundary of the vessel endothelium and the outer boundary of the tunica adventitia along a line perpendicular to the wall’s “backbone” or minimum skeleton – the arc equidistant from the outer and inner wall boundaries, which equates to the sum of the widths of the endothelium, tunica intima, tunica media, and tunica adventitia.37 The neuropathologist was asked to complete four vessel wall thickness measurements per image (Supplementary Figure 5).

A collage of images of a cell

Description automatically generated

**Supplementary Figure 4: Example input image and segmentation output pairs in test set used to evaluate the two candidate definitions of vessel wall thickness.** The inclusion criteria for each image were: (1) the image contained only one single vessel, (2) segmentation output showed uninterrupted circumferential labeling of the vessel wall, and (3) segmentation output does not show false-positive satellite lumens and only contains one accurately segmented lumen. The test set included 62 total image and segmentation output pairs.

A close-up of a microscope

Description automatically generated

**Supplementary Figure 5: Example manual vessel wall thickness measurements for one image within the SITE test set.** Four manual measurements were made per image by a neuropathologist (WY). The test set contained 62 total images and segmentation outputs.