Intracranial Vessel Wall MRI Does Not Allow for Accurate and Precise Wall Thickness Measurements: An Ex Vivo Study

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In recent years, MRI sequences have been developed that enabled visualization of the intracranial vessel walls.[1] The measured vessel wall thickness potentially distinguishes between patient and control groups.[1] Unfortunately, the spatial resolution of the used MR acquisitions thwarts reliable thickness measurements, because for reliable measurements walls need to span at least two voxels. This is not feasible as acquisition schemes commonly have voxel sizes between 0.5-0.8 mm, while vessel wall thicknesses of the larger arteries of the circle of Willis (CoW) range between 0.3-0.5 mm. This results in an overestimation of the true vessel wall thickness, as demonstrated in a simulation and phantom study by Antiga et al.[2] We aimed to quantify the accuracy and precision of vessel wall thickness measurements from clinically feasible MR images of post-mortem CoW specimens.

The vessel wall thickness measured on clinically feasible (low-resolution) images was compared to validated thickness measurements acquired on ultra-high-resolution images. Both images were acquired on a 7T MRI scanner with an isotropic voxel size of 0.8/0.11 mm for the low-/ultra-high-resolution images, respectively. Twelve post-mortem CoW specimens were imaged and the vessel wall thickness was measured using a validated full-width-at-half-maximum method. The imaging data is available from the corresponding author upon reasonable request.

Our results show that normal or slightly thickened walls cannot be measured reliably. The measured vessel wall thickness deviates considerably from the true thickness for walls thinner than 1.0 mm. From 0.2-1.0 mm, measurements on the low-resolution images were indistinguishable from each other (median thickness=1.1 mm; interquartile range (IQR)=0.3 mm), confirming the simulations of Antiga et al.[2] with real imaging data. The relatively poor precision, given by the IQR, prevents potential post-hoc corrections of the measured vessel wall thickness. Only walls thicker than 1 mm, e.g. advanced plaques, could be measured accurately from the clinically feasible low-resolution images.

The clinical application of the vessel wall thickness as a biomarker seems unfeasible given these results, as early wall thickening remains undetected. This will likely hold for other acquisitions with different voxel sizes, although the limit of detection might shift slightly. Although the ex vivo nature of this study might not directly translate to clinical in vivo measurements, the accuracy and precision of vessel wall thickness measurements was assessed in a best-case scenario.

In vivo acquisitions are challenged by motion artefacts and blood flow pulsation, which will have an added detrimental effect on thickness measurements. Next to that, the point spread function of the used MR acquisition has a negative effect on the overall image resolution and thickness measurements as well.

Our results, in accordance to the measurements by Antiga et al.[2], pose a significant challenge to the MR community to further improve measurement accuracy. Currently, the signal-to-noise ratio (SNR) and acquisition duration are major limitations for high-resolution

acquisitions. Ongoing technological developments, including higher field strengths and compressed sensing may allow for higher spatial resolutions in the future. Nonetheless, accurate measurements of the thinnest walls theoretically require a resolution of 0.15 mm isotropic. This resolution will likely remain unfeasible for a long period of time as the voxel volume and SNR are an order of magnitude smaller than the currently highest resolution acquisitions. Alternatively, the use of image processing methods such as deep learning, that can learn relevant image features related to the vessel wall thickness, can be explored.

In conclusion, the use of the vessel wall thickness as a biomarker for disease progression should be avoided for walls thinner than 1 mm, given current image resolutions. This ex vivo study confirms the severe overestimation of thickness measurements around and below the acquired voxel size. Additionally, we show that poor precision prohibits post-hoc corrections and prevents distinction between healthy vessel walls and early wall thickening owing to disease.

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Disclosures

None

References

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Supplemental methods

Specimen data

In this retrospective, institutional review board approved study, MRI data from previously published work was used.[1] This data consisted of 15 human specimens of the circle of Willis, collected between 2008 and 2015. Thickness measurements were performed on the M1 segment of the middle cerebral artery (MCA). Since the MCA is one of the most common locations of atherosclerosis it should therefore provide a large range of possible thickness values[2,3]. Out of the 15 specimens, three were excluded because of missing both MCAs (n=1), or due to a collapsed MCA (n=2), where no lumen existed between two sides of the vessel wall. The twelve remaining specimens belonged to patients with a mean age of 76 years (range: 66-84 years), of which seven had belonged to symptomatic stroke patients.

MRI acquisition

Imaging was performed at room temperature on a 7T human MRI scanner (Philips, Best, The Netherlands). A custom-made high-density receive coil (16 channels per 70 cm^2, MR Coils BV, Zaltbommel, The Netherlands) was used. For transmission, a volume transmit coil was used. The specimens, embedded on a petri dish in 2% agarose solution, were imaged two at a time, with the receive coils placed above and below the two stacked specimens. All specimens were imaged using an ultra-high-resolution sequence and a clinically used sequence (here further referred to as low-resolution sequence), obtained in the same imaging session (Figure I). The ultra-high-resolution images were acquired with a 3D gradient echo sequence (FOV: 95x130x35 mm^3; acquired resolution: 0.11x0.11x0.11 mm^3; repetition time/echo time: 55/6.2 ms; flip angle: 28 degrees; NSA: 1; acquisition time: 5h46m). For the low-resolution images a clinically used 3D Magnetization Prepared Inversion Recovery Turbo Spin Echo (3D MPIR-TSE[4,5]) scan protocol was used (FOV: 150x150x40 mm^3; acquired resolution: 0.8x0.8x0.8 mm^3; repetition time/echo time : 1700/33 ms; inversion time: 650 ms; flip angle: 90 degrees; NSA: 2; acquisition time: 8m35s).

Image processing

After acquisition, N4 bias field correction was applied to all images.[6] A mask of the vessel walls was acquired by thresholding the ultra-high-resolution images using Otsu's method.[7] By eroding the vessel wall mask, a skeleton was acquired. Thickness measurements were performed on the ultra-high- and low-resolution images at the locations of the skeleton points.

Thickness measurements

For each point on the skeleton, an intensity profile of 5 mm in length was acquired along the surface normal, the line perpendicular to the vessel wall surface. The orientation of the surface normal was computed as the direction of the image gradient vector at the location

of the skeleton point. The image gradient vector was composed of the directional image gradient in the x, y, and z directions. To estimate the wall thickness from the intensity profile, two subsequent mathematical functions were fit to the intensity profile. Initially, a piecewise linear fit was performed, where the piecewise linear function is given by:

$$I_{est}(x) = \begin{cases} B & x < x_1, \\ B + \frac{I-B}{x_2-x_1} \cdot (x - x_1) & x_1 < x < x_2, \\ I & x_2 < x < x_3, \\ B + \frac{B-I}{x_4-x_3} \cdot (x - x_3) & x_3 < x < x_4, \\ B & x > x_4 \end{cases}$$

Where $I_{est}(x)$ is the estimated intensity along x, the location along the intensity profile. B is the background intensity and I is the wall intensity, and x_1, x_2, x_3, x_4 are the knots that determine the position of the slopes along the profile. In several instances, the intensity profile also (partially) included the wall on the other side of the vessel, giving spurious results from our piecewise linear fit. In that case, a bimodal Gaussian fit was performed. For the bimodal Gaussian fit, the mode closest to the center of the intensity profile was taken as fit for the current vessel wall. Finally, the vessel wall thickness was measured as the full-width-at-half-maximum of the piecewise linear- or Gaussian-fit.

Experimental setup

Validation with manual thickness measurements

Validation with manual thickness measurements The vessel wall thickness measured using our automatic algorithm was compared to manual measurements by Harteveld et al.[1] at the same anatomical locations. In their study, the vessel wall thickness was measured on the ultra-high-resolution images from manually drawn inner and outer wall contours. The contours were drawn on multi planar reconstructions (MPR) of the image, along a centerline through the vessel lumen. They reported the average vessel wall thickness per MPR slice. In our study, an MPR of the skeleton image was created along the same centerline. The vessel wall thickness of the skeleton points that were reconstructed to the same MPR slices were averaged.

Ultra-high- and low-resolution comparison

The main goal of this study was to determine the relationship between the vessel wall thickness measured from the ultra-high-resolution and the low-resolution images. To this end, we compared the vessel wall thickness measured in both images using our algorithm. A one to one comparison between the thickness measurements was made at the same skeleton point locations. In total, skeleton points were generated for 24.000 voxels over all included specimens, on which the thickness measurements were performed in both images.

Results

Validation with manual thickness measurements

The vessel wall thickness obtained with the automatic algorithm was very similar to the manual measurements. On average, the median difference between the thickness measured using our automatic algorithm and the manual measurements was -0.04 mm, with an interquartile range of 0.08 mm.

Ultra-high- and low-resolution comparison

Vessel walls thinner than 1 mm were measured inaccurately on the clinically used low-resolution scans (Figure II). Walls in the submillimeter range appear to have the same thickness given our measurements. For thicker walls, e.g. advanced plaques, the vessel wall thickness can be accurately measured.

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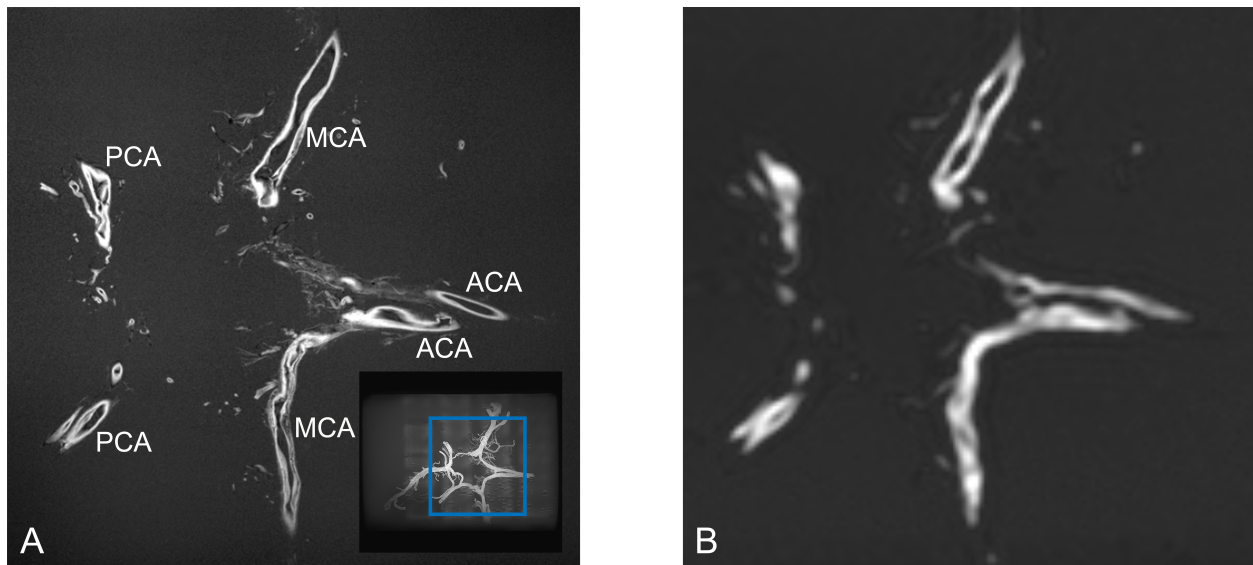
Figures

Figure I. A) Ultra-high-resolution and B) low-resolution acquisition of a circle of Willis specimen. In the shown cross section, the middle cerebral arteries (MCA), anterior cerebral arteries (ACA), and posterior cerebral arteries (PCA) can be appreciated. Inset in A): Maximum intensity projection of the ultra-high-resolution image with the bounding box in blue marking the region shown in both subpanels.
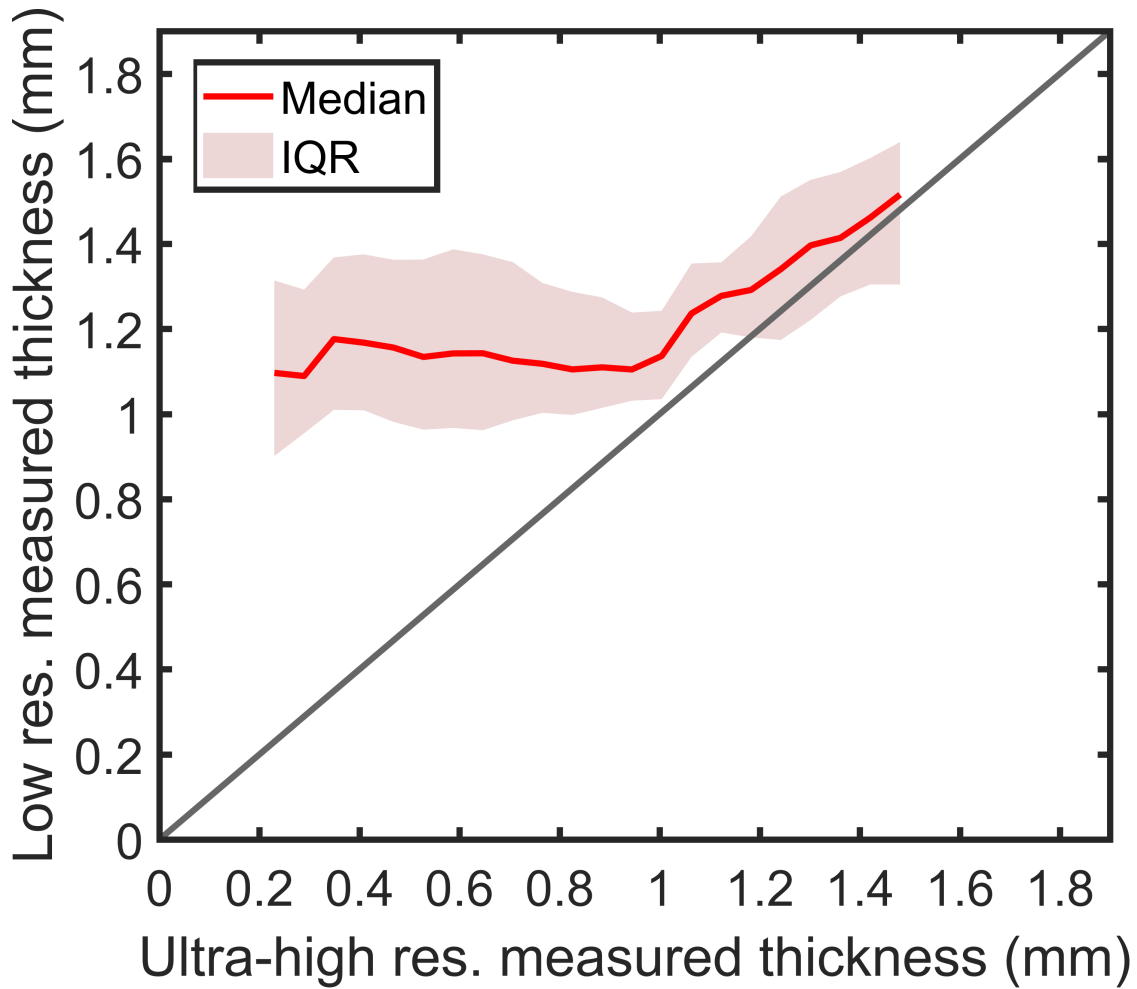
Figure II. The median measured vessel wall thickness (red), calculated from the low-resolution images given against the vessel wall thickness measured from the ultra-high-resolution images. The shaded area indicates the interquartile range of the measurements. The $y = x$ line is given in dark gray. For walls thinner than 1 mm, the thickness cannot be accurately measured from the low-resolution images.