Detection of intracranial vessel wall lesions in an elderly asymptomatic population using 7T MRI

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Introduction: Intracranial atherosclerotic disease (ICAD) is one of the main causes of ischemic stroke and transient ischemic attack (TIA). Furthermore, the presence of ICAD has been associated with a higher recurrent stroke rate compared to the absence of ICAD.[1,2] Development of atherosclerotic lesions occurs silently over a long period, before they become symptomatic. Most studies have attempted to target ICAD when it is already symptomatic. Additional information regarding the prevalence of ICAD in the asymptomatic population would provide us with better insight in its development. Thus far, only transcranial Doppler has been used to assess the presence of ICAD in the asymptomatic population[3]; however, because of arterial remodeling, this technique may result in underdiagnosis of intracranial atherosclerosis. Previous studies have shown that high-resolution magnetic resonance imaging is able to reliably identify intracranial vessel wall abnormalities, even before causing luminal narrowing.[4] The aim of this study was to assess the presence of intracranial vessel wall lesions and enhancement in an asymptomatic population using intracranial vessel wall MR imaging at 7.0 tesla (7T).

Methods: This prospective study was approved by the institutional review board of our institution; all subjects provided written informed consent. Between November 2013 and August 2014, healthy volunteers aged > 60 years, without a history of cerebrovascular or ischemic heart disease, were included in this study. Imaging was performed on a 7T whole-body system (Philips Healthcare, Cleveland, OH, USA) with a 32-channel receive coil and volume transmit/receive coil for transmission (Nova Medical, Wilmington, MA, USA). The imaging protocol included a high-resolution (0.8 mm isotropic) transverse T_1-weighted magnetic preparation inversion recovery turbo spin echo (MPIR-TSE) intracranial vessel wall sequence[5] before and after contrast administration, and a 3-dimensional time-of-flight (TOF) MRA by means of a fast-field echo sequence. The following imaging parameters were used: MPIR-TSE sequence, field-of-view (FOV) 250x250x190 mm^3, acquired resolution 0.8x0.8x0.8 mm^3, TR/TI/TE 3952/1375/36 ms, and scan duration ≈11min; TOF-MRA sequence, FOV 190x190x102 mm^3 in transverse orientation, acquired resolution 0.4x0.5x0.6 mm^3, TR/TE 22/2.4 ms, flip angle 30 degrees, and scan duration ≈10min. Approximately 10 minutes before acquisition of the post-contrast MPIR-TSE sequence, 0.1mL/kg of a gadolinium-containing contrast agent (Gadobutrol, Gadovist 1.0mmol/mL, Bayer Schering Pharma, Newbury, UK) was administered. Image quality was scored with a five point scale (1=poor, 5 =excellent); volunteers with a score <3 were excluded. Two observers independently scored the vessel wall abnormalities and enhancement (location and type (concentric or eccentric, enhancing or non-enhancing)) in all the major artery segments of the circle of Willis (ACA: A1, A2 and ACoM; MCA: M1 and M2; ICA: distal part and bifurcation; PCA: P1, P2, bifurcation P1-P2 and PCoM; BA: bifurcation BA-P1, distal half, proximal half; VA: distal half, proximal half) on the MPIR-TSE scans according to the method previously described by Van der Kolk et al.[5] processing for assessment of the contrast enhancement was performed using MeVisLab (v2.6.1, MeVis Medical Solutions AG, Bremen, Germany). A consensus reading was performed with a third observer, in case of disagreement. The presence of stenosis was scored on the TOF-MRA sequence by one observer.

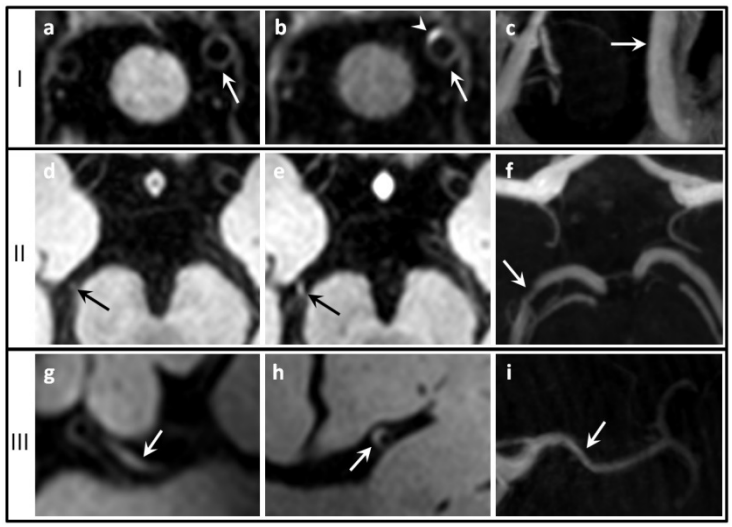

Figure 1. *Three examples of vessel wall lesions. (**I**) 7T pre-contrast (a) and post-contrast (b) transverse MPIR-TSE images of the left proximal vertebral artery with concentric vessel wall thickening (arrow) and focal enhancement (arrowhead), and the corresponding location on the coronal TOF-MRA image(c). (**II**) 7T pre-contrast (d) and post-contrast (e) transverse MPIR-TSE images of the right P2-segment with an eccentric vessel wall lesion (arrow) and focal enhancement, and the corresponding location on the transverse TOF-MRA image (f) showing a stenosis. (**III**) 7T pre-contrast transverse (g) and sagittal (h) MPIR-TSE images of the left M1-segment with an eccentric vessel wall lesion (arrow) without enhancement, and the corresponding location on the transverse TOF-MRA image (i).*

Table 1. *Scoring of vessel wall lesions*

	Lesions	Thickening (#)		Enhancement	MRA-stenosis
	(#)	*eccentric*	*concentric*	(#)	(#)
Anterior circulation	**38**	**27**	**11**	**11**	**1**
ACA	*7*	*5*	*2*	*0*	*1*
MCA	*14*	*8*	*6*	*3*	*0*
ICA	*17*	*14*	*3*	*8*	*0*
Posterior circulation	**62**	**28**	**38**	**25**	**9**
PCA	*11*	*8*	*3*	*2*	*4*
BA	*13*	*6*	*7*	*2*	*0*
VA	*38*	*10*	*28*	*21*	*5*
Total	**100**	**51**	**49**	**36**	**10**

ACA: anterior cerebral artery; BA: basilar artery; ICA: internal carotid artery; MCA: middle cerebral artery; PCA: posterior cerebral artery; VA: vertebral artery.

Results: Twenty healthy volunteers (12 male; age 66 ± 4 years) were included in the current study. Imaging was successful in 17 subjects; three subjects with an image quality score of < 3 were excluded (the distal vertebral arteries were outside the sensitivity reach of the 7T MRI head coil in two subjects, and severe motion artifacts were present in one subject). Figure 1 shows different examples of vessel wall lesions with and without enhancement identified in the study population. Table 1 shows an overview of the number, location and thickening pattern of the identified vessel wall lesions in the main arteries of the circle of Willis, the number of lesions that showed enhancement, and the number of scored stenoses in the TOF-MRA scans. In total 100 intracranial vessel wall lesions were identified in all subjects (median per subject, 5; range, 2-11), of which 36 (36%) enhanced after contrast administration. 51 lesions (51%) were found to be eccentric, and 38 lesions were present in the anterior circulation. Enhancement of the lesions occurred more often in the vessel wall lesions of the posterior circulation (25/62, 40.3%) compared to the anterior circulation (12/38, 31.6%), however, this was not significant (χ^2(1.32), p>0.05). In the anterior circulation the ICA (distal part & bifurcation) showed the highest number of vessel wall lesions (17/38) as well as enhancements (8/11), and in the posterior circulation the vertebral arteries (38/62 vessel wall lesions, 21/25 enhancements). A total of 10 lesions in 6 subjects (35.3% of study population) showed a corresponding stenosis on the TOF-MRA images.

Discussion and conclusion: Intracranial vessel wall lesions were found in all elderly asymptomatic subjects. The total number of identified vessel wall lesions was high, especially for the posterior circulation and specifically the intracranial vertebral artery segments. Only 10% of the lesions showed a corresponding luminal stenosis on the TOF-MRA images. 36% of the detected lesions showed enhancement after contrast injection as an indication for the presence of vasa-vasorum or focal plaque inflammation. We hypothesize that with high resolution 7T MRI vessel wall imaging in asymptomatic patients small atherosclerotic lesions are detected at an early stage without luminal stenosis. Correlation of high resolution *in vivo* and *ex vivo* MRI with histopathology will be needed to validate these findings. In the future, early detection of intracranial atherosclerosis and quantification of the total burden of atherosclerosis may allow for monitoring of therapeutic interventions, proxy imaging outcomes for a faster evaluation of interventions, and provide better insight in the role of ICAD in the development of certain cerebrovascular diseases.

References: [1]Arenillas et al. Stroke 2011; [2]Qureshi et al. Lancet 2013; [3]López-Cancio et al. Atherosclerosis 2012; [4]Dieleman et al. Circulation 2014; [5]Van der Kolk et al. Stroke 2011