

## High quality 7T MRI of atherosclerotic plaque in the significantly stenosed carotid artery

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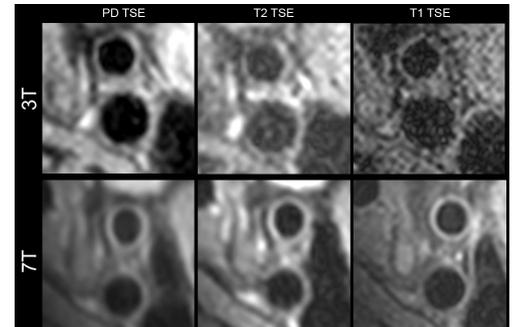
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**Targeted audience** Researchers involved in carotid atherosclerosis imaging.

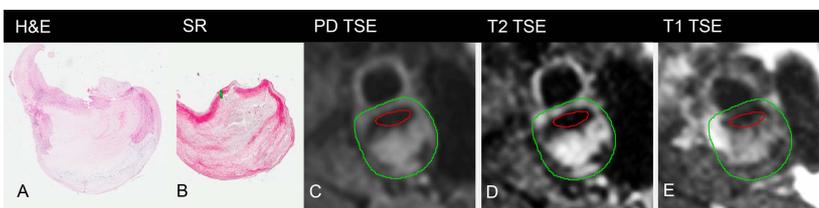
**Purpose** Several studies have shown that specific plaque components predict vulnerability of atherosclerotic plaque. For example intraplaque hemorrhage (IPH) and a thin fibrous cap on top of a lipid rich necrotic core (LRNC) can be used for risk stratification of the occurrence of cerebrovascular events. In vivo identification of this plaque vulnerability may enable to specify subgroups of patients with a high risk of cerebrovascular ischemia. High field strength MRI can visualize different components, like IPH, LRNC and fibrous cap thickness. However, since these components sometimes have sub-millimeter dimensions, it is important to aspire the highest possible spatial resolution. Previous technical development studies have shown the accuracy of ultra-high field strength MRI in vessel wall imaging of the common carotid artery in healthy volunteers. However, extensive data on patients is lacking. Aim of the current study was to test the feasibility of carotid plaque MR imaging in a series of patients with a high-grade carotid artery stenosis, scheduled for carotid endarterectomy (CEA). For this purpose the black blood (BB) sequences available at 7T MRI were used.

**Methods** Institutional Review Board approval was obtained for this prospective study.[1] Seventeen patients with a symptomatic >70% stenosis of the carotid artery, scheduled for CEA, were scanned at 7T one day prior to surgery. During surgery the plaque was collected for histological assessment of plaque components. All subjects gave written informed consent. Ultra-high field strength imaging was performed on a 7T whole body MRI system (Philips) with a leaky waveguide transmitter and high-density receive array (MR Coils B.V.) [2] The imaging protocol consisted of a dual-echo TSE sequence (voxelsize 0.5x0.5x2.0mm, TR 3000ms, equivalent TE 27/70ms, scantime 4:36min) and a T1-weighted TSE sequence (voxelsize 0.4x0.4x1.5mm, TR 1000ms, equivalent TE 19ms, scantime 3:52min). Six healthy volunteers were scanned at 3T and 7T for signal to noise (SNR) comparison. For the healthy volunteers the same 7T MRI scanner and protocol was used. High field strength imaging was performed on a 3T whole body MRI system (Philips) with an eight-channel phased-array coil (Shanghai Chenguang Medical Technologies Co.) dedicated for carotid artery imaging. The 3T scanning protocol was conform the 7T protocol. The accuracy to determine luminal and vessel wall area was evaluated in VesselMass (Dept. of Radiology Leiden University Medical Center, Leiden, the Netherlands) by two observers, both well trained in VesselMass. For evaluation of the intra-observer reproducibility, one observer (AR) performed the analysis twice with two weeks in between. The Interclass Correlation Coefficient (ICC) was used to determine the intra- and inter-observer reproducibility. Additionally, signal intensities of the plaque were determined as hypo-, iso- or hyperintense relative to the signal intensity of adjacent muscle. Signal intensity distribution was correlated with different plaque components seen with histopathology.

**Results & discussion** The SNR analysis was performed in all six healthy volunteers, (mean age 26years, range 23-33; 2 male) and resulted in a mean SNR of 42 (SD 12) in the vessel wall of the first echo of the dual TSE sequence at 7T compared to a mean SNR of 24 (SD 4) at 3T ( $P < 0.05$ ; Paired-Samples T-test). In Figure 1 MR images of one healthy volunteer are shown. The ICC's, based on luminal and vessel wall determination in both healthy volunteers (3T and 7T) and patients (Figure 2), were measured with a two-way random effects model where both people effects and measures effects are random. For both inter- and intra-observer agreement the ICC's were good. In all categories scores were above 0.900, except for the inter-observer agreement of the 7T data in healthy volunteers (Lumen: ICC = .867, 95% CI = 0.804 – 0.901,  $P < .001$ ; Outer vessel wall: ICC = .837, 95% CI = 0.701 – 0.905,  $P < .001$ ). In 12 patients of whom histopathology analysis was available, image quality of the proton density weighted sequence (PDW) was sufficient for signal intensity analysis. Simple binary logistic regression analysis demonstrated that the odds of having calcification in the atherosclerotic plaque of the culprit lesion decreased proportionally to the increase of MR signal hyperintensity in the corresponding slice of the carotid plaque ( $R^2 = .452$  (Nagelkerke),  $X^2 = 4.7222$ ,  $P = .030$ , OR = .929 (95% CI = 0.00 – 0.98,  $P = .021$ ) per percentage difference in hyperintensity). The  $P$  value and 95% CI were based on a bootstrap of 1947 samples. Although in 4 out of these 12 patients IPH was seen on histopathology, a similar analysis could not demonstrate a significant relation between signal intensity of the atherosclerotic plaque (on the PDW images) and IPH. Neither a relation between signal intensity and macrophage infiltration and lipid accumulation in the culprit lesion could be demonstrated.



**Figure 1.** 3T and 7T carotid images of a 28 year old healthy female.



**Figure 2.** Hematoxylin and eosin staining (A) and Sirius red staining, first echo (proton density weighted, C) and second echo (D) of Dual TSE sequence and T1 weighted TSE sequence of the culprit lesion of a 69 year old male. The green line marks the outer vessel wall and the red line marks the lumen.

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**Conclusion** To the best of our knowledge this is the first study showing the feasibility of carotid plaque imaging at 7T in a series of patients with a symptomatic carotid artery stenosis of >70%. No correlation could be confirmed with IPH. However, the available BB sequences at 7T seem accurate to demonstrate that an increasing hyperintensity of the MR signal in the carotid plaque on the PDW sequence is inversely proportional to the absence of calcification in the atherosclerotic plaque. Carotid plaque MRI at 7T enables to increase SNR significantly, compared to 3T, which results in accurate luminal and vessel wall determination, both in healthy volunteers and in a series of high-risk patients. Future development of BB sequences is needed for extensive plaque component imaging at 7T MRI.

**References:** 1. Den Hartog et al. *Current cardiology reviews*, 7, 28-34 (2011). 2. W. Koning et al. *MRM*, 69, 1186-93 (2013)