

Cerebral microinfarcts determined at 7T MRI are associated with a thin fibrous cap in ipsilateral carotid atherosclerotic plaque

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Targeted audience Researchers involved in atherosclerotic plaque imaging.

Purpose Carotid lesions may be classified as HIGH RISK based on plaque characteristics and the presence of INFARCTS in the brain parenchyma downstream to these lesions. Patients with infarcts and cerebral symptoms seem to profit more from carotid endarterectomy compared to patients with ocular symptoms.[1] Sensitive detection of brain lesions in patients with carotid artery disease may therefore identify patient (sub)groups with the highest risk of recurrent stroke who might benefit most from carotid surgery. This sensitive detection of the total burden of cerebral infarcts including very small cerebral infarcts is nowadays possible with stronger MRI field strengths. From pathology studies it is known that many infarcts are in the <4mm range (microinfarct range). These microinfarcts (<4mm) typically remain undetected at 1.5T and 3.0T MRI field strength. Recently, a combined in-vivo and post-mortem correlative study showed the ability of 7T MRI to detect cerebral infarcts in the microinfarct range.[2] The aim of the present study was twofold. First, the use ultra-high field 7T MR imaging to visualize the total burden of cerebral infarcts (both macro- and microinfarcts) was evaluated. Second, the presence of micro- and macroinfarcts was correlated with histopathology of carotid artery plaque.

Methods Institutional Review Board (IRB) approval was obtained for this prospective study.[3] In 15 patients, 7T MR images of the brain were obtained. All patients were scheduled for CEA because of a symptomatic carotid artery stenosis of >70%. MRI images were obtained one day prior to surgery. Exclusion criteria were inability to undergo 7T MRI, due to metallic implants not approved for ultra-high field strength MR imaging. All patients gave written informed consent. Ultra-high field strength MRI was performed on a 7T MRI scanner (Philips) with a 32-channel receive-coil and a volume transmit/receive coil for transmission (Nova Medical Inc.). The MRI protocol consisted of a T₂ weighted fluid attenuated inversion recovery (FLAIR) sequence of 12 minutes and 56seconds with the following parameters: FOV 0.8x0.8x0.8mm, TR/TE 8000/300ms, equivalent TE 212ms and TI 2250ms.[4] Carotid plaques, removed during surgery, were subjected to histopathological analysis of lipid core, fibrous cap thickness, intraplaque hemorrhage, calcification and presence of macrophages. In addition, plaques were classified according to the modified American Heart Association classification. On the MR images the number of macro- and microinfarcts were scored, where microinfarcts were defined as infarcts <4mm (Figure).

Results Based on histopathology a fibrocalcified plaque was identified in 6 out of 15 patients. In 4 patients the plaque was classified as a fibrous cap atheroma, in 4 patients a thin fibrous cap atheroma and in 1 patient a thin fibrous cap atheroma with plaque rupture. Pairwise comparison of medians using a Wilcoxon signed rank test showed thinner fibrous cap with an increasing total number of infarcts, in the ipsilateral hemisphere ($Z = -2.666$; $P = 0.008$). The Wilcoxon signed rank test exhibited no significant difference between number of ipsilateral infarcts and macrophages, calcification or lipid in the carotid plaque. In the hemisphere ipsilateral to the symptomatic carotid artery stenosis macroinfarcts were present in 9 of the 15 patients and microinfarcts were present in 4 of the 15 patients. These four patients with microinfarcts showed both ipsilateral micro- and macroinfarcts. The number of microinfarcts was significant related to the number of macro infarcts ($\tau = .41$, P (one-tailed) = .037). In the contralateral hemisphere macroinfarcts were present in 4 patients (1 infarct in each patient) and microinfarcts were found in 3 of these patients.

Conclusion This study shows that a histopathological thinner fibrous cap is associated with more infarcts (both micro and macroinfarcts) in the hemisphere ipsilateral to a >70% symptomatic carotid artery stenosis. Other histopathological plaque characteristics were not related to infarcts (micro and macro). Microinfarcts are common in this patient group with symptomatic carotid artery stenosis but are most often found in combination with macroinfarcts.

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References 1. Howerd et al. 44, 734-9 (2013). 2. Van Veluw et al. *J Cereb Blood Flow Metab*, 33, 322-9 (2013). 3. Den Hartog et al. *Current cardiology reviews*, 7, 28-34 (2011). 4. Visser et al. *MRM*, 64, 194-202 (2010).

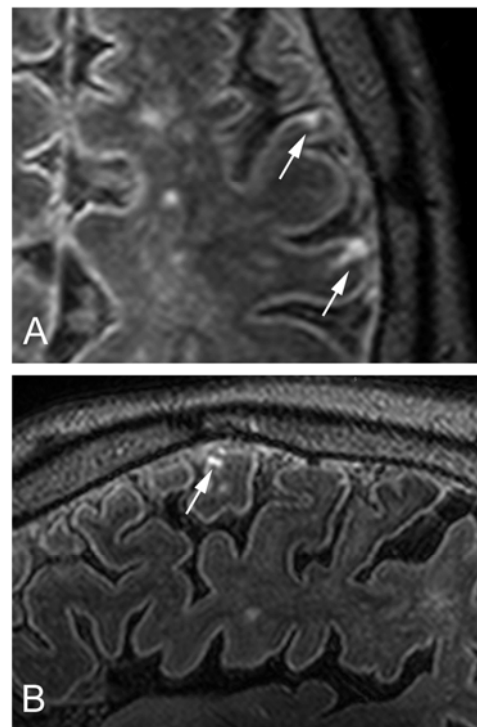


Figure. T₂ weighted FLAIR images of a 74-year-old male with a symptomatic high-grade stenosis of the left carotid artery scheduled for CEA. In figure A two cortical microinfarcts (arrows) ipsilateral to the symptomatic carotid artery are visualized in a transversal plane. The upper one is also visualized in a sagittal plane (B).