MR Imaging of Atherosclerotic Plaques with the Iron-oxide-based Contrast Medium VSOP-C184

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Introduction:

Several experimental and clinical studies have shown that intravenously injected ultrasmall superparamagnetic iron oxide (USPIO) particles accumulate in atherosclerotic plaques and produce a signal loss on T2- or T2*-weighted images (1, 2). However, with the currently available USPIO preparations, this signal loss occurs as late as about 24 h after injection and at experimental doses far above the clinically acceptable maximum dose. The aim of the present study was to investigate whether the novel citrate-stabilized very small superparamagnetic iron oxide particles (VSOP) produce signal changes in atherosclerotic plaques early after IV injection and in a dose range that will also be used for clinical MR angiography (3).

Materials and Methods:

Contrast medium: The citrate-stabilized iron oxide preparation VSOP-C184 (Ferropharm GmbH, Teltow, Germany) was investigated. The particles have a total diameter of 7 nm with a core size of 4 nm. T1 and T2 relaxivities at 1.5 T in water are 13.9 and 33.4 l/(mmol*s), respectively. The contrast medium was injected as an IV bolus at a dose of 0.06 mmol Fe/kg.

Animals: A total of five Watanabe heritable hyperlipidemic (WHHL) rabbits aged 15 to 18 months were examined. Five New Zealand white (NZW) rabbits aged 5 to 7 months served as controls.

MR imaging: The studies were performed at 1.5 T on a whole-body MR imager (Siemens Sonata) using the standard extremity coil. Images of the aortic arch including the supra-aortic vessels were acquired with an ECG-triggered gradient-echo sequence (TR=200 msec, TE=3.2 msec, 20 slices, slice thinkness=2 mm) in axial slice orientation. Time points were before and at 10 to 60 min as well as 2 h after contrast medium injection.

Analysis: Images were evaluated qualitatively comparing pre- and postcontrast images for signal loss within the vessel wall using a 3-point scale. All animals were sacrificed after imaging, and the thoracic aorta and supra-aortic vessels were removed en bloc and histologically analyzed. Histologic findings were correlated with imaging results.

Results:

Histologically, all five WHHL rabbits showed atherosclerotic changes of the area investigated whereas a normal vessel wall was found in the NZW rabbits. MR imaging demonstrated a significant signal loss in the atherosclerotic plaques of the WHHL rabbits, starting at 15 min and lasting up to 2 h after injection (Fig 1). No signal loss was found in the vessel wall of the NZW rabbits.

Conclusion:

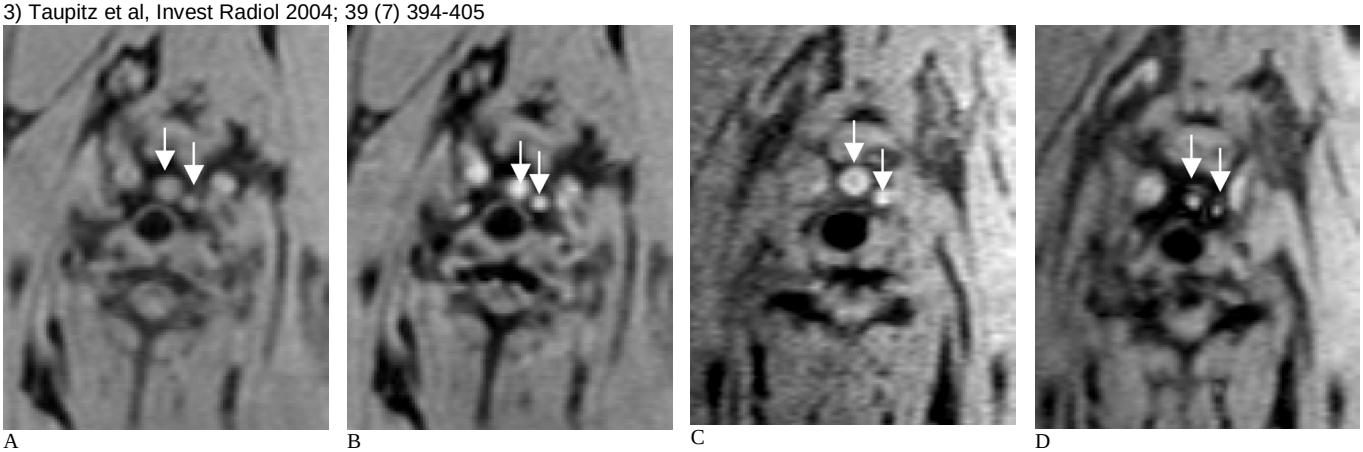
VSOP-C184 produces a significant focal signal loss in atherosclerotic plaques as early as 15 min after IV injection at a dose of 0.06 mmol Fe/kg. This is in the dose range at which VSOP-C184 has been shown to be a suitable blood pool contrast medium for clinical MR angiography. Hence, VSOP-C184 has the potential to enable evaluation of both the vessel lumen and the wall in a single MR examination.

References:

1) Schmitz et al, Invest Radiol 2000; 35 (8) 460-471

2) Ruehm et al, Circulation 2001; 103 (3) 415-422

3) Taupitz et al, Invest Radiol 2004; 39 (7) 394-405



A B C D

Fig 1: Axial MR images at the level of the supra-aortic vessels (arrows) in a control animal (A, before and B, 15 min after IV injection of VSOP-C184) and in a WHHL rabbit (C, before and D, 15 min after IV injection of VSOP-C184). No signal changes in the vessel wall in the control animal (B), pronounced signal loss in the vessel wall in the WHHL rabbit (D) in post contrast imaging.