Compartmental Assessment of Gadofluorine Contrast Agent Deposition in Atherosclerotic Plaque of WHHL Rabbits and Its Correlation to Lipid Content

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Introduction: Recent advancements in magnetic resonance imaging technology allow for high resolution, *in vivo* visualization of atherosclerotic plaque and its complex composition in humans and animals (1-3). The introduction of new molecular or cellular contrast agents which may improve the signal to noise and/or contrast to noise ratios of plaque subcompartments (e.g. media, intima, fibrous cap) would be of great clinical interest. One such potential contrast agent is Gadofluorine which has been used to enhance the detection of lipid rich atherosclerotic plaques (4). The exact mechanism by which Gadofluorine accumulates within atherosclerotic plaque is unknown. The present study was undertaken to more definitively assess the accumulation of Gadofluorine within specific regions of atherosclerotic plaque in Watanabe rabbits and to quantitatively examine the correlation between contrast agent uptake and cholesterol content in these lesions.

Materials and Methods: *In vivo* imaging of thoracic aorta from aged WHHL rabbits (~36 months) was performed prior to and 24 and 48 hours post-Gadofluorine (Schering AG, Berlin) administration (100-200 μmo/kg). Imaging was performed at 4.7T using a 20 cm diameter volume resonator. Transverse T_1 weighted gradient echo (TR/TE = 382/4 ms, FOV = 11×11 cm, matrix = 256 × 256, slice thickness = 4 mm, NEX =8) images were acquired from approximately 1 cm superior to the aortic arch through to ~ 4 cm inferior of the arch. Aortas were perfused fixed in situ and harvested immediately after the final imaging session.

High resolution, *ex vivo* MRI of the thoracic aorta was performed at 9.4T using transverse, multi-slice T_1 weighted spin echo (TR/TE =180/4 ms, FOV = 10×10 mm, matrix = 256 × 256, slice thickness = 0.5 mm, NEX =8) and gradient echo (TR/TE = 350/4 ms, FOV = 10×10 mm, matrix = 256 × 256, slice thickness = 0.5 mm, NEX =8) imaging sequences. T_1 maps were generated using a spin echo imaging sequence (TR/TE=500/15 ms, FOV=10×10 mm, matrix=256 x 256, slice thickness = 0.5mm, NEX = 4). Following the imaging protocol, absolute Gadofluorine and cholesterol content in vessels was analytically assessed.

Results: *In vivo* signal intensity of the thoracic aorta was increased at 24 hrs post-Gadofluorine administration and remained elevated at 48 hrs. There was significant signal enhancement observed in the plaque intima on the *ex vivo* GE images from Gadofluorine administered rabbits (Fig. 1). There was a dose dependent uptake of Gadofluorine in the thoracic aorta which was associated with a significant reduction in tissue T_1 in the intima, but not in the media at the high dose (Fig. 1 and 2). Gadofluorine content in the aorta was correlated to intima T_1 ($r=-0.81$, $P<0.001$), but not to media T_1 ($r=-0.41$, $P=0.18$). More importantly, the Gadofluorine content in the aorta was not associated with plaque volume ($r=-0.03$, $P=0.91$), or cholesterol content ($r=0.05$, $P=0.85$).

Conclusion: These data suggest that although the Gadofluorine contrast agent does associate with the plaque intima, the MRI signal enhancement observed can not be used to quantitatively assess the lipid content of the vessel.

References:

1) Misselwitz B, et al., Radiology 2004; 231:682.
2) Bendszus M, et al., Ann Neurol 2005; 57:388.
3) Sirol M, et al., Circulation 2004; 109:2890.
4) Koktzoglou I, et al., Proc. of the 13th Annual ISMRM, 2005, (abstract 113).

Figure 1

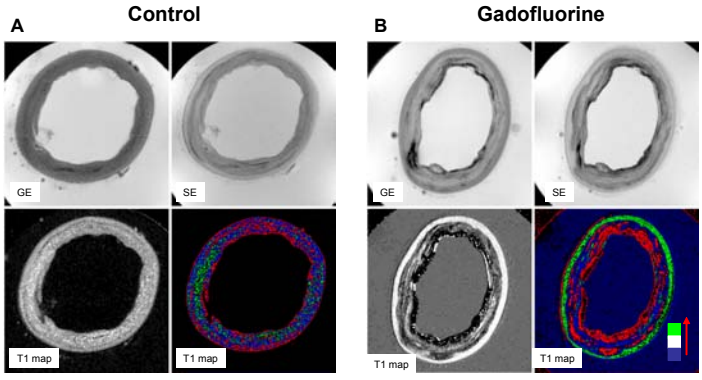

Figure 2