Delayed enhancement MRI of an *in vivo* model of atherosclerotic plaque using a blood-pool contrast agent

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Introduction. The use of both extravascular and blood-pool MRI contrast agents has been used to study neovessel-rich plaques [1,2]. While these studies have concentrated on the first several minutes after contrast injection, this study compares this enhancement to that seen 24 hours after the injection of a blood-pool agent in an animal model of atherosclerosis. Vessel wall enhancement immediately after contrast injection could reflect altered vessel wall permeability to albumin, while delayed imaging may reveal the extent and leakiness of intramural microvasculature that is not accessible to contrast in the first pass.

Methods. A group of 4 New Zealand white rabbits were fed a 6% peanut oil and 0.25% cholesterol diet for 20 weeks concurrently with intramuscular injections of rhVEGF (R&D Systems) of 4 µg/kg given at weeks 5 and 9 [3]. At week 10, the infrarenal abdominal aorta and right iliac of each animal were injured with a 3F Fogarty arterial embolectomy balloon catheter (Edwards Lifesciences). The catheter was advanced from the right femoral artery to the renal branches, inflated and pulled back 3 times. The animals were imaged at weeks 9, 15 and 20 using a GE 3.0T EXCITE MR system and a 5" custom receive-only coil with a 3-D, axial, high-resolution (374 µm × 374 µm in-plane and 1.6-2.0 mm slice thickness), T1-weighted, fast spoiled gradient-recalled echo sequence. The sequence has a low *b* value diffusion pulse to attenuate the signal from through-plane blood flow.

At all imaging time-points, the abdominal aorta was imaged both before and 10 minutes after a Vasovist injection (0.2 ml/kg, Bayer Schering Pharma). At week 20, imaging of the aorta was repeated approximately 24 hours after Vasovist injection to obtain delayed enhancement images. The thoracic aorta was imaged post-injection to serve as an uninjured control in each rabbit. Following sacrifice at week 20, the aorta from below the aortic arch to the iliac bifurcation was excised, fixed in 10% neutral buffered formalin, and cut into blocks of 5 mm length. Each block was sectioned and stained with H&E.

Results. The MR images of the thoracic aorta (uninjured controls) at week 20 acquired 30 minutes after contrast injection display an enhancing ring of uniform thickness assumed to be the vessel wall (image *c* in Fig. 1). At 24 hours post-contrast, the ring has a similar appearance, though not as pronounced (*e*). In two of the rabbits, the immediate post-contrast images of the abdominal aorta show additional enhancing circumferential regions hypointense to and surrounding the usual enhancing ring, separated by a dark region (*b*). After 24 hours (*d*), the regions of immediate positive enhancement remain enhanced to a lesser degree and are of similar signal intensity. H&E sections corresponding to this enhancement pattern demonstrate extensive microvasculature infiltrating the media and adventitia (*h*), while microvessels are confined to the adventitia layer of the uninjured control vessels. Microvessels not detectable by H&E staining may be present within the intimal plaque of the injured vessels.

Discussion. During the minutes following Vasovist injection, vessel wall enhancement primarily consists of a continuous ring that may correspond to the leakage of contrast agent across the macrovessel endothelium. Additional circumferential enhancement surrounding this ring correlates with the presence of extensive microvasculature in the media and adventitia. The dark region between the enhancing layers may be explained by an intimal lipid-rich layer next to a superficial fibrous layer on the corresponding H&E sections. At 24 hours after contrast injection, the signal intensity difference between the inner and outer rings of enhancement becomes minimal, suggesting that contrast agent delivered by microvessels to the media and adventitia contributes more to signal enhancement at this later time-point.

Conclusion. Vasovist enhancement emphasizes the adluminal surface of the vessel wall during the first several minutes after blood-pool contrast injection, while 24 hour delayed enhancement highlights areas of microvessel infiltration within the vessel wall.

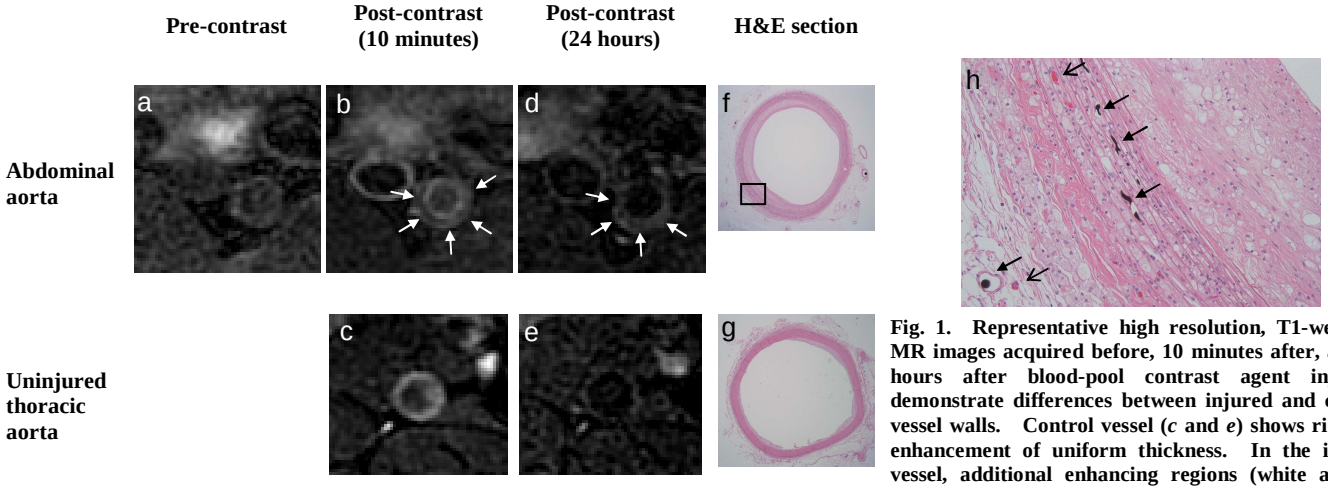

Fig. 1. Representative high resolution, T1-weighted MR images acquired before, 10 minutes after, and 24 hours after blood-pool contrast agent injection demonstrate differences between injured and control vessel walls. Control vessel (*c* and *e*) shows ring-like enhancement of uniform thickness. In the injured vessel, additional enhancing regions (white arrows) appear at both time-points after contrast injection and correspond with medial and adventitial microvasculature on the matching H&E section (*f* and *h*). Image *h* is an enlarged version of the rectangle outlined in *f*. Identified vessels contain injected silicone compound (solid arrows) or red blood cells (open arrows).

References

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