Contrast-enhanced MRI at 3T of experimental atherosclerotic lesions using QIR-FSE and DTPA(Gd)

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Introduction Atherosclerosis is the underlying cause of both heart disease and stroke. It is caused by the formation of lipid-filled inflammatory lesions in the arteries of the vascular system. These lesions can narrow the lumen of these arteries and decrease blood flow to downstream tissues, such as the heart and brain. Conventional (T2w, T1w and PDw) MRI of atherosclerotic lesions can provide information of both lesion size and structure; the latter being thought of as the more important of the two for determining patient risk of clinical events. To improve our ability to characterize lesions in terms of both size and structure, contrast-enhanced MRI using DTPA(Gd) has been attempted in both animals and humans. In humans, this results in significant improvement in determinations of fibrous cap thickness and/or amount of neovascularization, two important variables of plaque stability[1-3]. However, to our knowledge, similar success in animal models, particularly non-balloon injured models (i.e. intact endothelial barrier), of the disease has been limited. In the present work, we used a cholesterol fed (no balloon injury) rabbit model of atherosclerosis and a quadruple inversion recovery fast-spin-echo (QIR-FSE) sequence that allows accurate estimations of T1-enhancement[4, 5], to assess peak enhancement and wash-in/wash-out kinetics of DTPA(Gd) in aortic lesions.

Methods New Zealand White rabbits (n=3) were fed a cholesterol-supplemented (0.25%) diet for 18 months to promote the formation of human-type atherosclerotic lesions. Typically, five axial T1-weighted aortic images were acquired on a 3.0 T CV/i GE MR scanner interfaced with a customized two-channel phased array RF coil using a QIR-FSE sequence (TE=16.8 ms, TR=800 ms, TI=520 ms, ETL=6, BW=+/-11.9 kHz, FOV=5 cm, Matrix=256x192, Slice Thickness=5 mm, NEX=2, Scan time~ 4:25). Images were acquired before and after injection of DTPA(Gd) (Magnevist, 0.1 mmol/kg), between 1 minute and approximately 2 hours post-injection. Manual tracing of inner and outer vessel wall boundary was used to calculate signal intensity change over baseline (% enhancement) within the vessel wall.

Results DTPA(Gd) administration enhanced atherosclerotic vessel wall in low-dose cholesterol-fed rabbits with peak enhancement occurring approximately 10 to 20 minutes post-injection (Figure 1 and 2). Peak signal within the vessel wall was on average 86.3% above values at baseline (Figure 2). Typically enhancement of vessel wall occurred throughout the plaque, however, some select focal areas within the vessel wall appeared to enhance more than others. After 20 minutes, vessel wall enhancement began to decline and an exponential fit to the wash-out portion of the data yielded an average decay constant of 170.8 minutes (average $R^2 = 0.848$), with full clearance therefore requiring on the order of 6 hours (Figure 2). Signal intensity values within the vessel wall 24 hours after administration were essentially equal to pre-contrast values, supporting this kinetics analysis.

Discussion Here we show the first evidence of DTPA(Gd) enhancement of non-ballooned injured experimental atherosclerotic lesions. Similar to results in patients, we found enhancement typically occurred within the first 10 minutes following gadolinium administration and remained elevated over the next 10 minutes[3]. Interestingly, compared to enhancement patterns seen in carotid plaques in patients[2] we found contrast administration enhanced rabbit vessel wall to a greater extent (30% in fibrous regions of carotid vs ~85% in entire rabbit vessel wall). Future work will focus on looking at regional differences of enhancement and comparative histological classification. Typically double inversion recovery (DIR-FSE) black-blood imaging is employed to enhance the conspicuity of enhancement using Gd-based agents. However, to obtain a black-blood image following contrast agent administration, the inversion time must be shortened compared to pre-contrast TI times to compensate for T1 shortening effects in blood. This change in TI value complicates the quantitative measurement of percent enhancement values[4]. The use of the QIR-FSE sequence is therefore advantageous for the specific requirement of accurate determination of percent enhancement values while still maintaining a consistent, high-contrast black-blood image. Finally, this work forms the basis for quantitative assessment of novel gadolinium-based agents (macromolecular, protein-binding, enzyme-activatable, etc), which may yield additional information about plaque structure and composition over that provided by conventional DTPA(Gd).

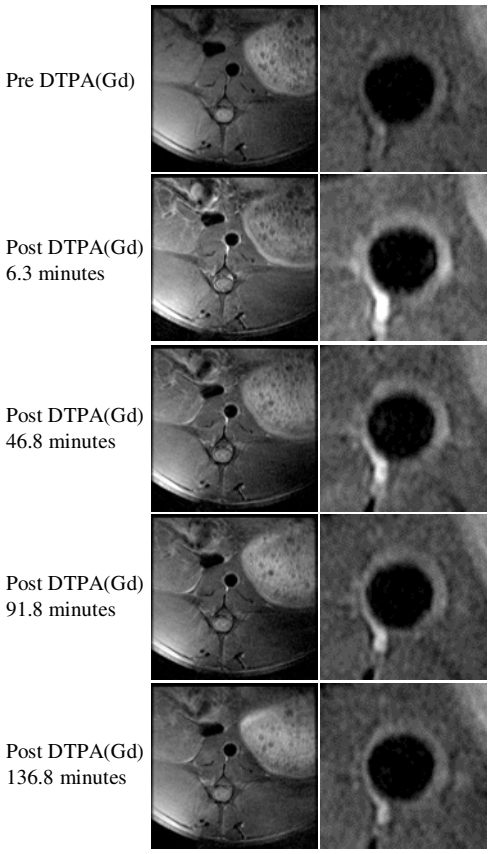

Figure 1 Enhancement of experimental atherosclerotic lesion using DTPA(Gd). Selected axial T1-weighted QIR FSE images of an aortic location in a cholesterol fed rabbit showing enhancement of the vessel wall. Images are before and after (6.3, 46.8, 91.8 and 136.8 minutes) injection of DTPA(Gd) (0.1 mmol/kg). Left panel is of acquired images and right is magnified view of aorta. Also, note the clear ability of the QIR-FSE sequence to null blood at early time points despite significant T1-shortening following DTPA(Gd) administration.

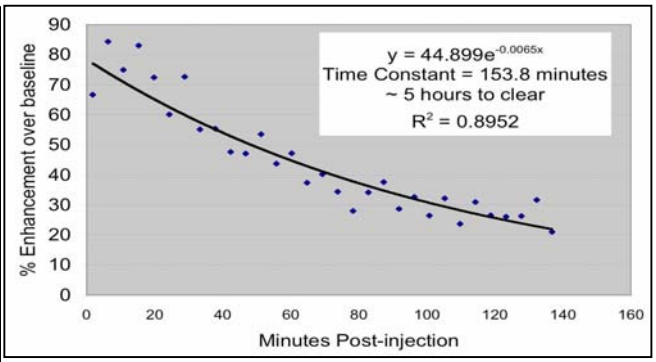

Figure 2 Kinetics of DTPA(Gd) enhancement of experimental atherosclerotic lesions Vessel wall signal enhancement (% over baseline) at a representative single aortic location following administration of DTPA(Gd). Enhancement tended to peak at approximately 10 to 20 minutes post-injection. Exponential fits of the data revealed clearance at this aortic location would occur approximately 5 hours following administration.

References 1. Yuan C, Kerwin WS, Ferguson MS, Polissar N, Zhang S, Cai J, Hatsukami TS. Contrast-enhanced high resolution MRI for atherosclerotic carotid artery tissue characterization. J Magn Reson Imaging. 2002;15:62-67. **2.** Wasserman BA, Smith WI, Trout HH, 3rd, Cannon RO, 3rd, Balaban RS, Arai AE. Carotid artery atherosclerosis: in vivo morphologic characterization with gadolinium-enhanced double-oblique MR imaging initial results. Radiology. 2002;223:566-573. **3.** Wasserman BA, Casal SG, Astor BC, Aletras AH, Arai AE. Wash-in kinetics for gadolinium-enhanced magnetic resonance imaging of carotid atheroma. J Magn Reson Imaging. 2005;21:91-95. **4.** Yarnykh VL, Yuan C. T1-insensitive flow suppression using quadruple inversion-recovery. Magn Reson Med. 2002;48:899-905. **5.** Yarnykh VL, Yuan C. Multislice double inversion-recovery black-blood imaging with simultaneous slice reinversion. J Magn Reson Imaging. 2003;17:478-483.