Diffusion Weighted Imaging (DWI) in the Rabbit Model of Atherosclerosis: Characterization and Quantification of Water Diffusion in Six-Month Old Aortic Plaque

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Introduction: The rabbit model of atherosclerosis is useful for studying treatment models, drug development and longitudinal studies monitoring response or disease progression as well as for development of new imaging techniques. Diffusion imaging has shown promise in atherosclerosis. It has been shown to identify different plaque components in *ex vivo* studies in human [1,2,3] and animals [4], and *in vivo* in human studies [2,5], however, it has not previously been demonstrated *in vivo* in the rabbit model.

Purpose: To investigate the use of diffusion imaging in the rabbit model, we characterize diffusion-weighted imaging (DWI) in 6-month old aortic plaque in the rabbit model that is known to include lipid infiltration, fibro-genesis [6], angiogenesis [7], and increased macrophage content [8], all of which may lead to differences in diffusion characteristics within the plaque. We assess the average diffusion coefficient and the presence of multi-component diffusion. We determine the precision of the diffusion coefficient estimation from in vivo measurements in comparison to diffusion values found for vessel wall and lipid core from the literature.

Methods: Eight male New Zealand White rabbits with atherosclerosis induced by an established method [7,8] were imaged with DWI after 6 months of plaque development. A clinical system (Philips 3 T Achieva) was used with the product 8-channel knee-coil arrayed receiver. The DWI protocol consisted of the following: SE-DW single-shot EPI, TR/TE 3000/68 msec, FOV 160 x 40 mm, 1x1 mm resolution with 3-mm slice thickness, 16 slices in one TR orientated perpendicular to the abdominal aorta inferior to the renal arteries. Images were acquired with 12 different *b*-values equally spaced up to 600 s/mm^2, with diffusion gradients in the slice-select direction. 32 averages were acquired for each image in a total scan time of 19:15 min.

For a representative slice in each animal, an ROI was drawn to encompass the whole vessel wall to measure the mean signal at each *b*-value. In all rabbits there is a substantial drop in signal between the b = 0 s/mm^2 and the first non-zero b-value. The diffusion coefficient was measured by a simple least squares fit to the remaining 11 data points.

Results: Image quality was good in all rabbits scanned (Fig. 1). Diffusion values ranged between 0.83 and 1.87 x10^{-3} mm^2/s, with an average value of 1.19 x10^{-3} mm^2/s. In 1 rabbit it was possible to identify a bimodal relationship. The fast/slow diffusion components had D = 2.90 and 1.10 x10^{-3} mm^2/s (Fig. 2). The average two-tailed span of the 90% confidence interval for the diffusion coefficient was 0.3 x10^{-3} mm^2/s with this DWI protocol.

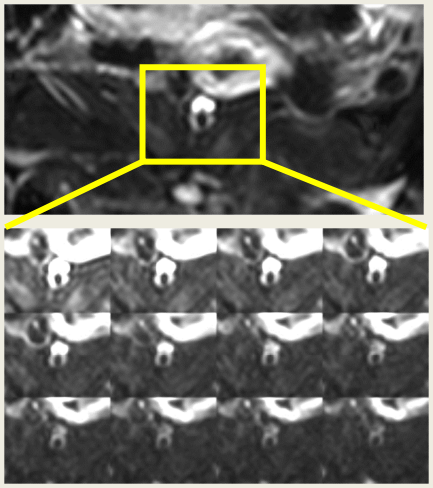

Figure 1: Typical images of diffusion weighting in 6-month old atherosclerotic plaque in the NZW rabbit aorta at a select range of diffusion *b*-values. *Top*: The aorta is shown in the abdomen in a b=0 s/mm^2 image. *Bottom*: All 12 b-values evenly distributed from 0 to 600 s/mm^2 (left-to-right, top-to-bottom; all images displayed at same greyscale; to show higher b-values well, signal at low b-value is saturated.)

Discussion: DWI *in vivo* in the rabbit model is feasible with a 20-min protocol giving up to 16 slices. Image quality was acceptable with diffusion weighting in the range up to 600 s/mm^2. Quantification showed diffusion values consistent with others' measurements in normal vessel wall media [1], the highest diffusion coefficient was less than pure water, which is a physical upper limit for diffusion measurements. DWI was sufficiently sensitive to distinguish bimodal diffusion characteristics in the 6-month old aortic plaque. The precision of diffusion measurements in this study is sufficient to distinguish normal vessel wall, lipid core, and free water (D = 1.54, 0.26, 3.03 x10^{-3} mm^2/s, [1],[9]). Furthermore, it is feasible that this precision would facilitate discrimination of intermediate diffusion values that we speculate could arise in vessel wall with partial lipid infiltration (0.3-1.5 x10^{-3} mm^2/s), and loose matrix or hemorrhage (1.5-3.0 x10^{-3} mm^2/s).

Conclusion: DWI is a feasible technique for quantitative characterization of atherosclerotic plaque in the NZW rabbit model *in vivo* and may provide important information about high-risk plaques.

References:

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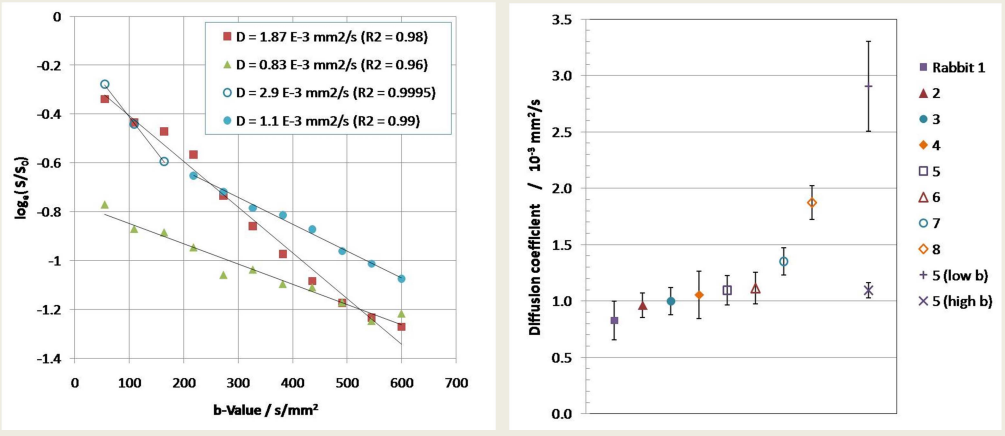

Figure 2: (Left) Diffusion coefficient determination from the plot of log(S/S$_0$) and *b* including the bimodal relationship (circles). (Right) All diffusion coefficient measurements with 90% CI including the separate low and high b-value portions for the bimodal relationship.