MRI evaluation of carotid morphology and function in a rabbit constriction model of atherosclerosis: a feasibility study

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Introduction: Atherosclerosis is a major cause of morbidity and mortality in the western world. In order to investigate the role of potential anti-atherosclerotic agents, reliable animal models of the disease itself are needed, along with noninvasive imaging techniques to monitor the onset and progression of disease. Placing a soft silicon collar around the rabbit common carotid artery has been shown to induce intimal thickening within a shorter period of time than that produced by high cholesterol diet alone and with a morphology more relevant to the human species [1]. Previous MR investigations of the rabbit carotid artery performed at low field strengths (1.5-2T) showed that high in-plane resolution (< 200μm) is essential for monitoring the onset and progression of disease [2,3]. In addition, although it is well accepted that hemodynamic factors play a crucial role in the initiation of atherosclerosis [4], flow measurements in animal models are still not widely reported. The aim of this study was to show that high-field high-resolution MRI can be used to visualize the wall of the rabbit carotid artery three days after surgical placement of the collar, when intima-media thickening is expected to be minimal, and to demonstrate the feasibility of spatially- and temporally-resolved flow measurements using a cine phase contrast pulse sequence.

Methods: Non-occlusive, biologically-inert, soft silicon collars (ARK Therapeutics, Kuopio, Finland) were surgically implanted around the left common carotid artery of nine female New Zealand white rabbits (3.5-4.5kg). Imaging was performed three days after surgery using a 4.7T Bruker BioSpin system containing a gradient insert delivering 100mT·m^{-1}. A 2cm diameter single-channel surface coil positioned on the neck of the rabbit was used for signal detection. After localization of the collar, a rapid acquisition with relaxation enhancement (RARE) pulse sequence was used to obtain a series of fat-suppressed 2mm-thick T_2-weighted images spanning the whole length of the collar. A 64mm field of view and matrix size of 512^2 were used, yielding a 125μm in-plane resolution. Other imaging parameters were: TE = 65ms; TR = 4458ms; echo train length = 8; NEX = 5. A T_1-weighted IR-prepared fat-suppressed fast low-angle shot (FLASH) pulse sequence (TE = 5.4ms; TR = 1184ms; TI = 1000ms; flip angle = 90°; NEX = 1) was used to attenuate the signal from the perivascular interstitial fluid within the collar in order to improve visualization of the vessel wall. The geometry was the same as for the T_2-weighted acquisition. Images were acquired with a 256^2 matrix size and zero-filled to 512^2 to obtain the same reconstructed in-plane resolution as the T_2-weighted images. An ECG-gated 2D cine phase contrast pulse sequence was used to acquire velocity maps proximal and distal to the collar (TE = 7.9ms; TR = 21ms; flip angle = 30°; NEX = 1; field of view = 50mm; matrix size = 256^2). Imaging slices were prescribed orthogonal to the vessel in order to minimize flow artifacts. A velocity sensitivity of 120cm/s and temporal resolution of 1×TR yielding 10-15 cardiac phases per R-R interval (typically 250-350ms) were used. The whole protocol was completed in approximately one hour.

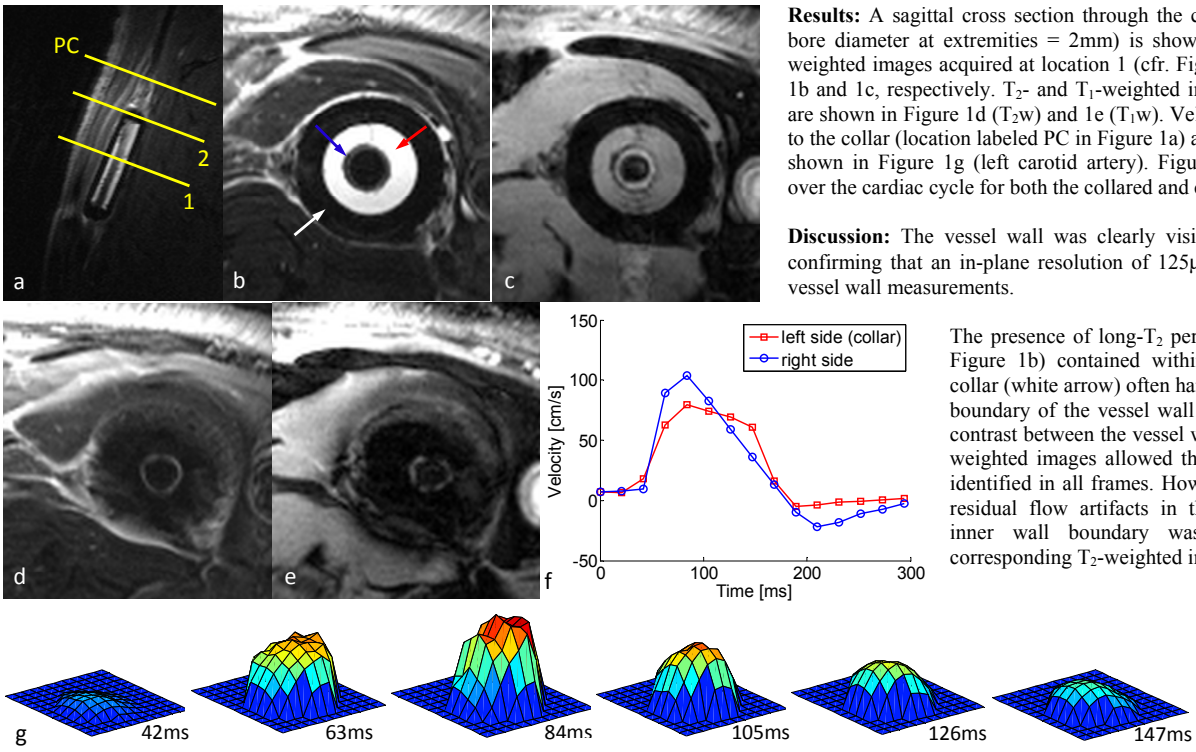

Figure 1

Results: A sagittal cross section through the collar (length = 2.5cm; inner bore diameter at extremities = 2mm) is shown in Figure 1a. T_2- and T_1-weighted images acquired at location 1 (cfr. Figure 1a) are shown in Figure 1b and 1c, respectively. T_2- and T_1-weighted images acquired at location 2 are shown in Figure 1d (T_2w) and 1e (T_1w). Velocity profiles acquired distal to the collar (location labeled PC in Figure 1a) at different cardiac phases are shown in Figure 1g (left carotid artery). Figure 1f shows velocity curves over the cardiac cycle for both the collared and collar-free sides.

Discussion: The vessel wall was clearly visible on most of the images, confirming that an in-plane resolution of 125μm was adequate to perform vessel wall measurements.

The presence of long-T_2 perivascular fluid (red arrow in Figure 1b) contained within the central region of the collar (white arrow) often hampered detection of the outer boundary of the vessel wall (blue arrow). The improved contrast between the vessel wall and outer fluid in the T_1-weighted images allowed the outer wall boundary to be identified in all frames. However, due to the presence of residual flow artifacts in the T_1-weighted images, the inner wall boundary was best delineated on the corresponding T_2-weighted images.

Despite the lower in-plane resolution of phase contrast images, spatially- and temporally-resolved velocity maps were obtained in most rabbits (8 out of 9). The main limitation of this study, which was found to affect the velocity data in particular, was the limited field of view of the coil, which occasionally produced low SNR images depending on the relative position between the coil and the collar.

Conclusions: We have shown that high-field high-resolution MRI can be used to visualize the vessel wall in a rabbit model of collar-induced atherosclerosis and that spatially- and temporally-resolved flow data can be acquired using an ECG-gated cine phase contrast pulse sequence. The nine rabbits included in this feasibility study are part of a larger cohort of rabbits (19) on a high-cholesterol diet undergoing surgical placement of the collar. All the animals will be imaged again at 8, 12 and 16 weeks to monitor the onset and progression of disease. Histological and biochemical examinations will be performed on the excised carotid arteries to validate the MR findings.

References: [1] De Meyer GRY, et al. ATVB 1997; 17:1924-1930; [2] Carpenter TA, et al. MRI 1991; 9:365-371; [3] Ma ZL, et al. Eur Radiol 2008; 18:2174-2181; [4] Nixon AM, et al. J Neurosurg 2010; 112(6):1240-1253.