In Vivo Atherosclerotic Plaque Visualization and Assessment of functional vessel wall parameters in the murine aorta using high resolution MRI at 17.6T

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Introduction:

Genetically engineered mouse models provide enormous potential for investigation of the underlying mechanisms of atherosclerotic disease. However, at present, in vivo plaque characterization is limited to the visualization of lesions without analyzing any functional parameters. This study demonstrates the feasibility of in vivo murine aortic lesion assessment in combination with functional parameters such as aortic blood flow velocity and vessel wall strain using MR microscopy at 17.6 T.

Methods:

All measurements were performed on a Bruker Avance 750 spectrometer with a maximum gradient strength of 1.0T/m and a 20mm Bruker birdcage coil. 9 ApoE(-/-) knockout mice (Charles River, Belgium) at the age of 8-9 weeks were fed a fat diet for a period of 12 weeks. MR data were acquired 0, 6 and 12 weeks after the start of the fat diet. During the measurements, mice were anesthetized using 1.0 – 1.5 vol.% isoflurane inhalation. ECG triggering and respiratory gating was applied for all MR measurements [1]. For visualization of atherosclerotic lesions, a Multi-Slice-Multi-Spin-Echo sequence was applied. Two interleaved datasets of 8-10 slices perpendicular to the ascending aorta were acquired successively, thereby covering the entire aortic arch. Inflowing blood signal was suppressed by acquiring MR data during systole when blood flow velocity is at a maximum. Thus, excited fast flowing blood is not refocused during data acquisition allowing for a black blood image contrast. Image parameters were: TE 9 ms, TR 1 s, FOV 2.0x2.0 cm^2, slice-thickness 0.4 mm, resolution 78x78 μm^2, signal averages 3. Circumferential strain values were measured by using an optimized segmented FLASH sequence with velocity compensation in all gradient directions. The image slice was positioned perpendicular to the ascending aorta. Imaging parameters were: TE 2.0 ms, TR 4.0 ms, FOV 2.2x2.2 cm^2, slice-thickness 1.1 mm, resolution 86x86 μm^2, signal averages 6. Software aided ROI analysis was used to measure the cross section of the ascending aorta and thus to calculate the time dependant radii. Circumferential strain was computed by [2]:

$$E_{\theta\theta}(t) = \frac{1}{2}\left[\left(\frac{r_{(t)}}{R_0}\right)^2 - 1\right]$$

where R_0 is the smallest measured radius and $r_{(t)}$ is the radius at any other point in time during the heart cycle. Motion encoding was achieved by preparing the spin phase using a bipolar gradient, which causes the moving spins to accumulate a velocity-dependent net phase with respect to stationary spins. Velocity was measured perpendicular to the image slice using three different flow encoded data sets.

Results:

After 12 weeks of fat diet, atherosclerotic plaque could be observed in the interior region of the aortic arch which is depicted in figure 1B. Figure 1A shows the corresponding image slice acquired right after starting the fat diet. The increased wall thickness after the fat diet can also be observed in the Cine Flash images, one of which is depicted in figure 1D. Table 1 shows the calculated maximum blood flow velocity and the maximum circumferential strain for the three different time points. The strain values indicate a significant change in the vessel wall elasticity during the 12 weeks of fat diet. Changes in the maximum blood flow could not be observed after 12 weeks.

Conclusion:

In our study, we have demonstrated the feasibility of high field MR microscopy to visualize atherosclerotic lesions in the murine aorta and to further evaluate additional functional parameters such as circumferential strain and aortic blood flow velocity. The MR measurements confirmed that the development of atherosclerotic lesions is accompanied by a decrease of vessel wall elasticity.

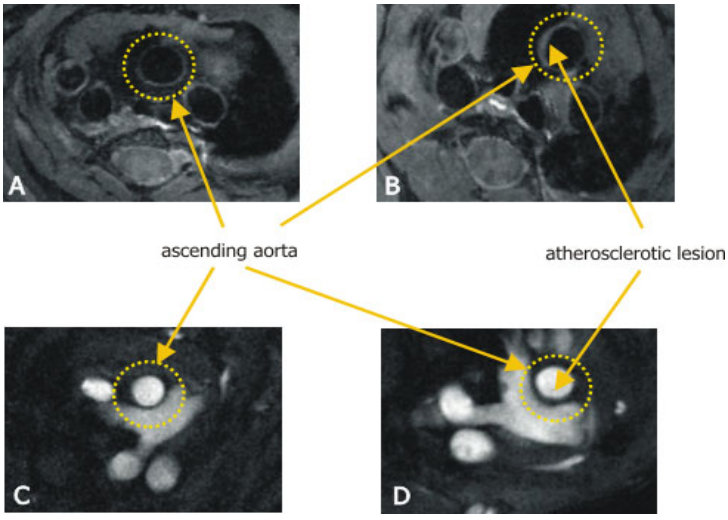

Figure 1 : a) Black blood SE image of the ascending aorta at the beginning of the fat diet; b) same as a) after 12 weeks of fat diet. c) Cine FLASH image at the beginning of the fat diet. d) same as c) 12 weeks after fat diet.

number of weeks after starting the fat diet	circumferential strain (mean ± SD)	max. blood flow velocity [cm/s] (mean ± SD)
0	0.24 ± 0.03	78 ± 4
6	0.17 ± 0.04	81 ± 4
12	0.12 ± 0.04	80 ± 5

Table 1: Development of circumferential strain and max. blood flow velocity in the ascending aorta of ApoE (-/-) knockout mice fed with a fat diet for a period of 12 weeks.

References:

[1] Rommel E. et al., SMR 3rd Meeting [1995]; 938.
[2] Wedding KL et al. J Magn Reson Imaging [2002]; 15:418-428.

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