T2* value correlates with iron concentration in atherosclerotic rabbit aorta

R. P. Joensuu[1], A. E. Larsson[1], L-M. Gan[2], M. Palmér[2], and P. D. Hockings[1]
[1]DECS Imaging, AstraZeneca R&D Molndal, Mölndal, Sweden, [2]Integrative Pharmacology, AstraZeneca R&D Molndal, Mölndal, Sweden

Introduction

Intravenously administered ultrasmall superparamagnetic iron oxide (USPIO) particles are known to accumulate in atherosclerotic vessel walls [1]. Several attempts have been reported to visualize [2], quantify [3], and to model [4] USPIO-labeled atherosclerotic plaques by applying MRI-based relaxation effects. Here we show that the concentration of USPIO iron in an atherosclerotic rabbit's vessel wall can be quantified from the T_2^* map.

Methods

Five 5 month old NZW rabbits on high fat diet for 11 weeks were given 500 µmol/kg USPIO i.v. (Sinerem®/Combidex®; Guerbet/AMI, France/USA). Seven days after the injection the animals were killed and the cardiovascular system was flushed with phosphate buffer. The aorta was dissected out and kept post fixed in neutral buffered formaldehyde. MR images of the samples were acquired at 9.4T (WB-400; Bruker, Germany) with a Micro-2.5 gradient set and a standard RF volume coil. The acquisition sequence was a 3D multi gradient-echo with the following imaging parameters: TR = 100 ms, TE = {3.22, 7.7, 12.18, 16.66, 21.14, 25.62} ms, single average, and with the resolution of 0.1x0.1x0.2 mm^3. T_2^* was determined from successive reformatted slices along the aortic arch and decending aorta where the view of the aorta was always kept axial. 3 to 19 adjacent slices were first summed depending of the straightness of the aorta (Fig. 1) and T_2^* was measured on a pixel-by-pixel basis by fitting a three-parameter monoexponential curve to the signal intensities as a function of the echo time. Inner and outer surfaces of the vessel wall were manually delineated and the mean T_2^* value of the enclosed area was assigned to every slice. The measurement was repeated in multiple successive slices starting from the aortic arch right after the last of the thoracic arteries branching off and continuing towards the decending aorta until about 30 mm of the aortic length was covered. The mean T_2^* value of the whole aorta was calculated by taking the thickness-weighted average of the T_2^* 's over the slices. The iron content in the aorta from the analysed section was also determined by using the EPA methods 200.7 (ICP-AES) and 200.8 (ICP-SFMS) [5], the reported accuracy being ≤ 3 ppm (Analytica AB, Sweden).

Results and Discussion

Highly linear correlation (Pearson, r = –0.98, 95%CI = –0.999…–0.715, p<0.004) was found between the measured T_2^* values and the iron concentration obtained by plasma spectroscopy (Fig. 2). Analysing iron content directly from tissue rather than relying on the injected dose is obviously important, here a 10-fold difference in iron concentrations was found between tissue samples from different animals although the USPIO dose was the same. USPIO particles contain a dextran coating which can make analysis methods that involve a chemical reaction challenging. In this respect plasma spectroscopy has the advantage of measuring the iron concentration by optical means from plasma and the result is not dependent on the chemical environment. Use of thin slices in MR acquisition is a preferred technique because it reduces the effect to measured T_2^* values from unwanted sources, for example macroscopic susceptibility variations. T_2^* parametric mapping method is also immune to systematic nonlinearities in general and does not, e.g. require a reference signal or T_1 corrections.

T_2^* maps were acquired here with a gradient echo technique with relatively short echo times which makes the method also applicable to high-resolution in vivo imaging even if the target is moving, e.g. imaging arteries that are close to heart. If the relationship is ascertained between the USPIO load and the inflammatory status in atherosclerotic lesions, T_2^* mapping can potentially be used to monitor treatment response.

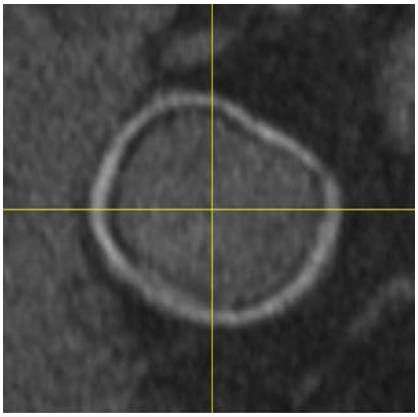

Fig 1. An axial view of rabbit aorta, 7 slices summed.

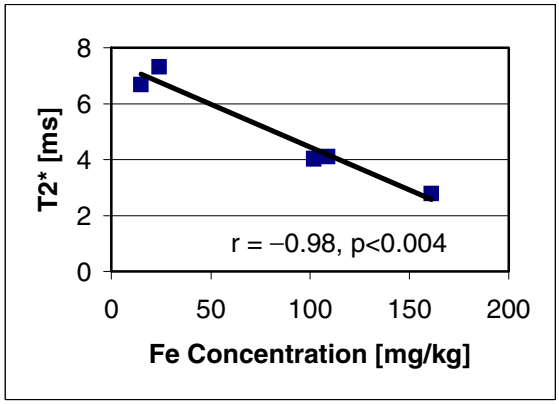

Fig 2. Correlation of iron concentration measured by plasma spectroscopy and T_2^* mapping.

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