T2 and ADC Values of Coronary Atherosclerotic Plaques under Fresh and Preserved Conditions

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Introduction: Quantitative T2 and ADC values are valuable in characterizing atherosclerotic plaque components[1] and in optimizing pulse sequences for multi-contrast MRI. Currently, plaque constituents are usually labeled based on their relative contrasts in a set of multi-contrast MR images (T1, T2, proton density, etc). This makes the plaque labeling susceptible to imaging parameter changes. In contrast, quantitative T2 and diffusivity measurements combined with prior knowledge of the T2 and diffusivity distribution of typical plaque components may be a more effective means to label plaque constituents because they depend only on magnetic field and temperature. In addition, knowledge of T2 values of plaque components could serve as the basis in optimizing sequences and parameters.

In the present study, we evaluated the T2 and ADC values of typical plaque constituents on both "fresh" and "preserved" human coronary arteries. The MR scans were conducted on freshly-excised coronary arteries under simulated *in-vivo* conditions by using a custom designed tissue culture chamber. Preserved scans were conducted on the same vessels after preserving them in formalin. T2 and ADC distributions of each plaque constituents were measured using the pixels that corresponding to the specific tissue type based on histological sections.

Methods: Eight human coronary arteries harvested from heart transplant patients were examined in this study. All MR scans were performed in a custom-designed tissue culture chamber filled with tissue culture media M199 at 37±1C°. The MR scan of fresh vessels was accomplished within 24 hours of surgery to ensure the vessel viability. After this scan, vessels were preserved in 10% buffered formalin for 48 hours and scanned again following the same imaging protocol of the scans on fresh vessels. Within the vessels, typical plaque constituents including intact initima, necrotic core, calcification, fibrous tissue, fibrocellular (fibrous cap) and adipose fat were present.

The MR scans were conducted on a 4.7T small bore MR scanner (*INOVA, Varian, Inc., USA*) using a 37-mm-diameter 16-element birdcage quadrature coil. Three to five spin echo MR images with TR = 3.5s and TE = 15-70ms were used to reconstruct the quantitative T2 MR map. Both read re-focusing and phase encoding gradients were placed after the 180 degree pulse to minimize the diffusion effects of imaging gradient. This modified sequence was tested on tissue media M199 and showed improvement in T2 quantification. The T2 values of M199 calculated using traditional, modified and CPMG spectroscopic sequences were 128ms, 798ms and 823ms, respectively.

Quantitative ADC maps were reconstructed using two to five pulse field gradient (PFG) diffusion-weighted images (b = 0-300s/mm^2). In order to eliminate the diffusion arising from the cross-terms between the diffusion and imaging gradients, we adapted the bipolar PGF scheme[2] in the diffusion pulse sequence. With this scheme, the calculated the ADC values of water at room temperature on all three gradient orientations were all 2.5 x 10^{-5}cm^2/s, which is similar to those in literature. For all the MR scans, in-plane resolution after zero filling was 58.6µm x 58.6µm and slice thickness was 1mm. Eighteen to twenty-one slices were acquired per vessel with no gap and four signals were averaged for each image.

After imaging, the vessels were embedded in Methyl Methacrylate (MMA) and 5µm serial sections were obtained. Histological stains including Hematoxylin and Eosin (H&E), Masson's Trichrome, Smooth Muscle Actin, and Verhoeff-Van Gieson were performed on each section. With the guidance of these histological sections, T2 and ADC values for each plaque constituent were measured on the quantitative MR maps by picking up pixels belonging to the tissue type over all slices and vessels. 500-2000 data points were measured for each component and Gaussian distribution was assumed for T2 and ADC values. Two-tailed, student t-test was performed for each plaque constituent in evaluating the changes that might be introduced to the T2 values by preservation.

Results and Discussion: The measured T2 and ADC values for typical plaque constituents of both fresh and preserved stages are summarized in Figure I. Intima and fibrous tissues in initial and advanced plaques were analyzed separately to avoid misinterpretation. The student t-test on T2 values shows a small, but significant difference in all plaque constituents between fresh and preserved stages. The media in both initial and advanced plaques showed the most significant changes in T2 after preservation. The fibrous tissue in both fresh and preserved vessels showed no difference between initial and advanced plaques. In an previous study, Dalager-Pedersen[3] et al. reported that formalin will introduce significant T2 changes in media at room temperature. From their data, they also reported no significant differences in T2 values of initima and adventitia layer between fresh and preserved vessels. This difference may be due to the fact that the fresh vessels they used were frozen and no longer viable during the scan. It is noteworthy to point out that similar to previous research, our results with T2 values showed limited contrast between necrotic core and fibrous tissues.

Our measured ADC values of fibrous tissue and media are similar to that of collageneous cap measured by Toussiant et al[4]. In our study, we did not differentiate the fibrous cap and media because both their ADC and T2 appear comparable. The ADC value of our adipose fat region is similar to the ADC value of lipid core measured by previous studies[1,4], however, our measured ADC values in necrotic core region show a higher diffusivity. This can be explained by the limited presence of excellular lipid in these necrotic cores.

Conclusions: We evaluated the T2 and ADC values in typical coronary artery plaque constituents both before and after formalin preservation. The measured T2 values for all plaque constituents showed small, but significant changes between fresh and preserved vessels. T2 and ADC values of plaque constituents can potentially be used to assist plaque characterization and pulse sequence optimization in multi-contrast MRI.

TABLE I
T2 AND ADC MEASURED ON PLAQUE CONSTITUENTS OF FRESH AND PRESERVED VESSELS

	T2 (ms)		ADC (cm^2/s)	
	Fresh	Preserved	Fresh	Preserved
Media (Initial)†	49.7±9.7	58.0±12.5	1.9±0.8	2.3±1.1
Fibrous Tissue (Initial)	28.6±8.9	32.1±9.0	1.7±0.9	1.6±1.2
Fibrous Tissue (Advanced)	28.8±8.7	32.9±7.8	1.3±0.8	1.5±0.7
Necrotic Core	30.6±7.0	34.9±5.1	0.9±0.6	1.1±0.4
Media (Advanced)†	54.7±10.7	62.4±10.1	2.2±0.8	1.9±0.5
Adipose Fat	43.2±6.3	40.7±6.7	0.24±0.05	0.25±0.06

Media and fibrous tissue layers in initial and advanced plaques were separately measured
† Media in both initial and advanced plaques shows very significant change in T2 values after preservation ($p < 10^{-18}$)

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