

Characterization of Coronary Atherosclerotic Plaque Using Multi-Contrast MRI Acquired Under Simulated In-vivo Conditions

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Introduction: Multi-contrast MRI holds the promise of identifying major constituents and morphologies in atherosclerotic plaques. Because of technical limitations, multi-contrast MRI of coronary arteries is usually done under *ex-vivo* conditions^{1,2}. A concern of this approach is that the preserved vessel specimens may have different MR properties compared to the *in-vivo* situation, and this may influence the plaque characterization. Therefore, accessing the effects of preservation is important to ensure that multi-contrast characterization techniques developed on preserved vessels can be used for *in-vivo* imaging.

In the present study, multi-contrast MR scans of freshly-excised coronary arteries was performed under simulated *in-vivo* conditions by using a custom designed tissue culture chamber. In this chamber, vessels were maintained at the approximate temperature, pressure and metabolic environment of *in-vivo* coronary vessels. Multiple MR scans with different contrast mechanisms were performed. Scans were repeated after preservation in formalin. Plaque components were classified using a Fuzzy C-Means (FCM) clustering technique with spatial information incorporated via penalty terms. Plaque component classification results from “fresh” and “preserved” scans were compared with corresponding histological sections to evaluate the influence of preservation on plaque characterization.

Methods: Eight human coronary arteries harvested from heart transplant patients were examined in this study. The first multi-contrast MR scan was performed on these vessels in a custom-designed tissue culture chamber within 24 hours of surgery. After this scan, vessels were preserved in 10% buffered formalin for 48 hours and scanned a second time following the same protocol of the first scan to evaluate the influence of vessel preservation process on multi-contrast MRI of plaques. Three of the eight vessels were from patients with non-ischemic heart failure and were characterized by concentric intimal hyperplasia without plaques. Five of the eight vessels were from patients with ischemic heart failure and contained lipid-laden plaques, thrombus and calcification.

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. Proton density-weighted spin echo (TR/TE=3.5s/15ms), T2-weighted spin echo (TR/TE=3.5/50-60ms), T1-weighted spin echo (TR/TE=0.9-1.4s/15ms) and diffusion-weighted ($b=234s/mm^2$) images were obtained. In-plane resolution after zero filling was 58.6 μm x 58.6 μm 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. Imaging parameters for the preserved vessels were the same as those under the fresh conditions to facilitate comparison.

After imaging, the vessels were MMA embedded and serially sectioned. H&E, Masson’s Trichrome, Smooth Muscle Actin and Verhoeff-Van Gieson stains were then performed on each 5 μm histological slice. The histological slices serve as the gold standard in evaluating plaque components characterization. Manual segmentation identified vessel tissues including lipid/necrotic core, fibrocellular, dense fibrous, thrombus and calcification.

Automatic characterization of the multi-contrast MR images was performed based on a spatial penalized, fuzzy c-means clustering algorithm. The classification results of multi-contrast MRI acquired under fresh and preserved conditions were compared with histology after manually registering them with the help of markers and morphological landmarks. Quantitative comparison of characterization results was performed on component ratio¹ of each plaque constituents (fibrous tissue, fibrous cap, calcification, necrotic core and thrombus) defined as $Component\ ratio = (Component\ Area / Overall\ slice\ Area) \%$.

Results: In general, the appearance of the multi-contrast results from scans under fresh and preserved conditions is similar. An example is shown in Figure 1. The only noticeable change in signal can be identified is the adipose fat, whose T2 value is reduced after preservation as can be seen on T2 and proton density weighted images. The classification results obtained with the SPFCM algorithm for both fresh and preserved scans are shown along with corresponding histological slice in Figure 2. Calcification, dense fibrous tissue and necrotic core regions were color-coded in black, blue and yellow, respectively. The grey level intensity shows tissues with different ratio of smooth muscle cells to collagen. Visually, both results correspond well with the histology in component ratios as well as spatial locations. The paired sample, two tailed, t-test for the grouped component ratios in the classification suggests there is no significant difference between fresh and preserved samples.

SNR of plaque constituents in proton density and T2-weighted MR images acquired under preserved conditions were 1.8%-17.5% greater than SNR acquired under fresh conditions. These small changes in SNR may imply small changes in tissue’s MR properties.

Discussion and Conclusions: We found that multi-contrast MRI on fresh and preserved coronary vessels were similar. We applied an automatic clustering approach to characterize plaque constituents, and for most plaque constituents, the classification results yielded by the technique shows no significant difference of fresh and preserved scans with histological gold standard.

A primary result of this study is that multi-contrast MRI plaque characterization techniques developed on *ex-vivo* scans can be adapted to later *in-vivo* studies. An exception was noticed on fresh thrombus, whose intensity changed apparently on T2 and diffusion weighted images after preservation because the iron product breakdown.

Reference

1. Itskovich VV, et al. *Magn Reson Med* 2004; 52(3) : 515-523.
2. Clarke SE, et al. *Magn Reson Med* 2003; 50(6) : 1199-1208.

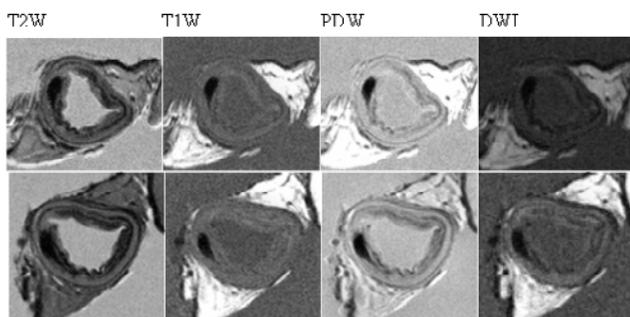


Fig. 1. Comparison of multi-contrast (T2-, T1-, Proton Density and Diffusion Weighted) MRI acquired under fresh and preserved conditions for the same location.

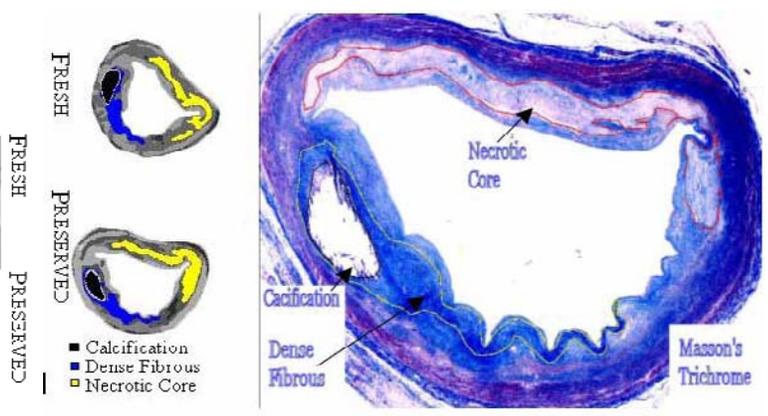


Fig. 2. SPFCM results from multi-contrast MRI under fresh and preserved conditions compared with manual segmentation of the Masson's trichrome stain