Ex vivo multi-contrast MRI of the coronary artery wall at simulated in vivo condition

B. Sun[1], D. P. Giddens[1], R. Long[2], W. R. Taylor[3], D. Weiss[3], J. N. Oshinski[1,2]

[1]The Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology/Emory University, Atlanta, GA, United States, [2]Department of Radiology, Emory University, Atlanta, GA, United States, [3]Division of Cardiology, School of Medicine, Emory University, Atlanta, GA, United States

Introduction

Due to technical and signal-to-noise limitations, most previous studies of plaque characterization in coronary vessels have done on preserved specimens [1]. However, *in vivo* conditions are important in determining the tissues' MR properties. Specifically, water diffusion properties may change according to the viability of cells. Therefore, in this study, we propose to image fresh excised human coronary arteries in a tissue culture chamber, which keeps tissue viable under *ex vivo* conditions.

Methods

To approximate the *in vivo* conditions, a custom-designed MR-compatible tissue culture chamber was built to keep the temperature, pressure, PH and nutrient environment at *in vivo* levels. The chamber consists of a 35 mm diameter cylindrical tube made of polycarbonate. End caps are present on each side of the tube. On each cap, there is a cannula which is connected to the inside of the vessel then connected to a long plastic tube which runs outside the bore. A second hole in the end cap accesses the chamber outside the vessel. This access is also connected to a long tube which runs outside the bore. The purposes of these plastic tubes are to perfuse the vessels, to keep a specified internal pressure of 80mmHg, and to independently control pressure inside and outside the vessel. The chamber is filled with tissue culture media during the imaging session. Temperature is kept at 37ºC via warm water circulating around the chamber and it is monitored with an MR-compatible thermocouple.

Five human right coronary arteries harvested from heart transplant patients at Emory University Hospital were scanned for this study within 24 hours of surgery. Four of the vessels were from ischemic patients and had many advanced and complicated plaques (type V and type VI); one was from a non-ischemic patient and had significant intimal hyperplasia but no plaques. The chamber is filled with Medium 199 (T1≈3.4s at 37ºC) during imaging. The vessel is mounted on cannulas and plastic markers with no MR signal are attached to the vessel for the purpose of registering MR images with histology slices in the longitudinal direction. The MR scans are conducted on a 4.7T small animal MR scanner (INOVA, Varian, Inc.) with a 37 mm diameter 16-element birdcage quadrature coil. Proton Density Weighted SE (TE/TR=10ms/3.2s), T2 Weighted SE (TE/TR=60ms/3.2s), T1 Weighted SE (TE/TR=10ms/0.9s) and Diffusion Weighted SE (TE/TR = 31ms/3.5s, diffusion gradient=10 gauss/cm, σ=4ms, Δ=20ms), images were obtained with a FOV of 3cm by 3cm (resolution after zero filling=58.6μm *58.6μm) and slice thickness of 1mm (21 slices with no gap between slices), and four averages were done for each image.

After imaging, the vessels are pressure fixed and Methyl Methacrylate (MMA) embedded. H&E, Trichrome, Smooth Muscle Actin (SMA), and Verhoeff-Van Gieson (VVG) stains are done on each 5μm histological slice. MR images are segmented using a gradient vector flow (GVF) snake on both Diffusion Weighted image and T2 Weighted image to distinguish the vessel wall from background. Spatially penalized fuzzy k-means (PFKM) method is used to segment the tissues of interest based on T1, T2 and proton density weighted images. Tissue labeling in the MR images (fibrous, lipid core, calcium etc.) was done according to criteria from previous studies [1].

Results

The acquired MR images characterized the plaque constituents similar to what has been shown in previous studies [1]. However, the results from the non-ischemic patient revealed a larger lumen diameter in T2W image compared to the other three contrast images in several slices. A typical slice is shown in figure 1. There are no advanced plaques in the vessel wall but a significant level of intimal hyperplasia is present. The diffusion weighted image and T2W image have the largest difference in lumen size. This area difference is identified by subtracting the lumen area in T2 weighted image and that in diffusion weighted image (both lumens detected via GVF snake method). The difference is shown in the upper right of the red rectangle in figure 1. In the lower right of the rectangle, the intima and media layers are identified (as detected with the PFKM clustering algorithm). In the reconstructed 3D model in figure 1, the region that is different between the T2W and diffusion weighted images is labeled brown. Comparison with histology (VVG, color changed for better visualization) in figure 2 shows that this region is part of the neointima but contains a very high level of macrophage and foam cells, which implies initial atherogenesis [2].

Discussion

Diffusion weighted imaging applied to a viable vessel in tissue culture media helps visualize the entire intima that may have an intensity similar to the culture media in the T2 weighted images. T2 weighted images offer the best contrast between plaque constituents.

References

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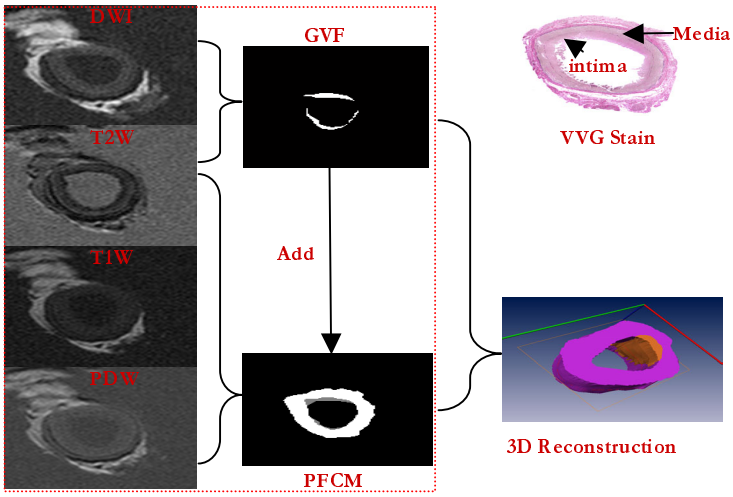

Figure 1. Multi-contrast images, processing results and histology

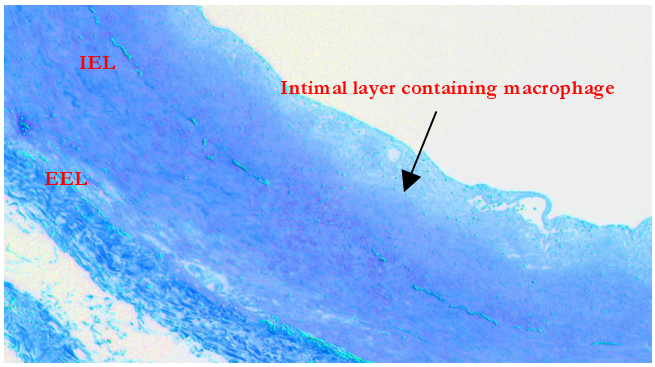

Figure 2. VVG stains of area which is smaller on T2W than diffusion weighted images (color changed for better visualization)