MAGNETIZATION TRANSFER BASED CONTRAST FOR HUMAN ATHEROSCLEROTIC PLAQUE CHARACTERIZATION

Y. Qiao[1], K. Hallock[1], and J. A. Hamilton[1]
[1]Department of Physiology & Biophysics, Boston University, Boston, MA, United States

Introduction

Visualizing the fibrous collagen-rich cap in atherosclerotic plaques is a key to predict plaque vulnerability. To enhance the contrast of the cap from other plaque components, we used magnetization transfer contrast (MTC) with human carotid plaques (*ex vivo*) to evaluate whether MTC provides better contrast to improve the identification of fibrous tissue (collagen-rich region).

Material and Methods

Human carotid artery specimens (n=8) were obtained after resection from patients undergoing endarterectomy. Segments (2-3cm long) were were maintained at 37 C and rinsed with saline, then immersed in PBS solution (0.1M) with Protease inhibitor (Sigma-Aldrich Co., St. Louis, MO) and metalloprotease (MMP) inhibitor (Chemicon GM6001) to prevent protein degradation. All MRI experiments were conducted at 11.7 T on an Avance spectrometer (Bruker, Billerica, MA) at 37 °C within 6 hours after surgery to maintain the relaxation parameters of the *in vivo* tissue.

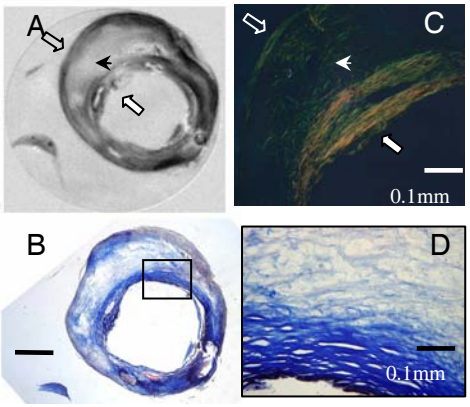

Figure 1: MTC images correlated with histology.

Two sets of T1W RF-spoiled GRE images were acquired with and without the application of a 12 ms 16 μT saturation pulse 10000 Hz off resonance. The other parameters for gradient echo sequence were α=15°, TR=70ms, TE=5ms, FOV=12mm, slice thickness=0.5mm, matrix=128x128. MTR maps were calculated with the following equation: $((M_0-M_s)*100)/M_0$ and pseudo-colored based on the measured MTR value. The histograms analysis was performed for the specimens. To reduce the influence of PBS buffer on the MTR histogram, the minimum MTR was adjust to 8%. The integral of whole signal intensity of histogram was normalized to 1. After imaging, specimens were stained with trichrome and Sirius red for collagen and collagen types identification.

Results and Discussion

Figure 1A shows an MTC image (image with MT subtracted from image without MT) with matched histology. The predominant MT effects (darker regions) corresponded to collagen-rich fibrous tissue, as confirmed by histology (Figure 1B & 1D). The trichrome stain revealed dark blue regions corresponding to the darkest regions in MTC (collagen=blue). Sirius Red stain was used to identify different types of collagens. The dense fibrous tissue, which is rich in collagen type I, is red-yellow colored under PLM (Figure 1C). It is located in the fibrous cap (solid arrow) and deep intima (open arrow). Region that shows small MT effect (Figure 1A, arrow head) is collagen type III rich and overlapped with the green staining under PLM (1C, arrow head).

Figure 2 shows the calculated MTR maps (A and B) with corresponding histograms for two specimens. A higher MTR (40-50%) was observed in collagen-rich regions and pseudo-colored as yellow-red. MTR regions pseudo-colored as cyan (20-30%) correspond to the loose connective tissue region. The relative amount of collagen in the entire tissue can be estimated from the MTR histogram (the # of pixels between MTR of 40 and 50%). For example, the amount of fibrous tissue of specimen in Figure 2B is higher than the one shown in Figure 2A. Therefore, this specimen is more fibrotic (rigid) than the other specimen. Thus, the MTR histograms provide additional information to characterize the plaque based on the collagen concentration.

The results indicate MTC, which is based on differences in macromolecular content rather than relaxation, permits differentiation of densely packed fibrous tissue (collagen, especially type I) from loosely packed connective tissue (collagen type III, proteglycan or other fibrous tissues). Most important, it will enhance visualization of the fibrous cap, a key feature that might predict the vulnerability of the plaque. If successfully translated *in vivo*, it may also permit the non-invasive identification of features of vulnerable plaque (SUPPORTED BY NIH grant P50 HL083801).

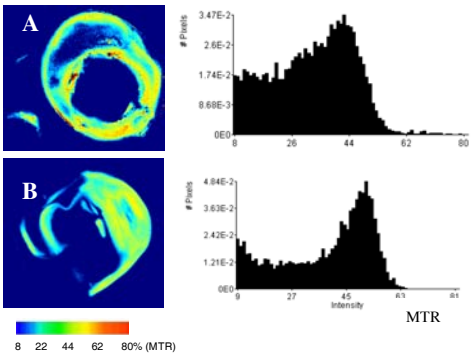

Figure 2: MTR maps with histograms for CEA specimens. Histograms show the signal intensity dispersion for MTR.