Characterization of Plaque Components in Gadofluorine M-Enhanced Rabbit Atherosclerosis: Toward Quantification of Plaque Progression with Biomechanics

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INTRODUCTION

The risk of atherosclerotic plaque disruption is thought to closely relate to plaque components and rupture triggers (mechanical forces). Gadofluorine M-enhanced MR imaging has shown better detection of atherosclerotic plaque components in experimental animal studies [1,2]. However, local mechanical features of plaques have yet to be assessed using MR images. It is hypothesized that addition of the numerical modeling of stress/strain distribution in the plaque will significantly improve capability of MR imaging to detect vulnerable plaques, and provide a valuable tool to understand the mechanism of plaque progression. The aim of this study was thus first to characterize the signal features of Gadofluorine M-enhanced plaque images in a double-injury rabbit model and then to study the possibility of assessment of plaque progression with both MRI morphology and biomechanical forces.

MATERIALS AND METHODS

Double-injury Rabbit Model Focal femoral atherosclerosis was induced in New Zealand White rabbits (3.6 ± 0.5 kg) by either overstretch balloon injury (n=1, the first rabbit) or endothelial denudation with nitrogen gas (n=3) followed by feeding a diet enriched with cholesterol [3,4]. After 4-6 weeks, the induced lesions were injured by balloon overstretch to simulate plaque disruption. All rabbits were maintained on cholesterol diet supplementation after the second injury.

MRI Protocol MRI studies were performed twice, at one week and 12 weeks, after the second injury, except for the first rabbit, in which MRI study was conducted at 12 and 24 weeks after the second injury. A conventional turbo-spin-echo (TSE) sequence was used to obtain multi-contrast T_1-, T_2-, or proton-density (PD)-weighted cross-sectional images with a spatial resolution of 0.19 x 0.19 mm^2. Inferior and superior radiofrequency (RF) saturation pulses were used to null the signal from flowing blood in the veins and arteries. A dose of 50 µmol/kg of Gadofluorine M (Schering AG, Berlin, Germany) was injected intravenously 24 hours before each MRI session. All imaging procedures were performed on a 3 T Siemens Allegra system using a phased-array head coil.

Histopathology After the completion of all MRI studies, the injured femoral arteries were dissected, fixed, and embedded in paraffin, step cross-sectioned (5 µm) at 100 µm intervals, and stained with hematoxylin and eosin (H&E) and Verhoffs van Gieson (VVG) stain for elastin.

Data Analysis The matched slices between two MRI scans in each rabbit were further segmented using the multi-contrast image data sets and novel segmentation software developed in our lab. Histopathology was used as the gold standard to identify plaque components. Contrast-to-noise ratios (CNRs) between different plaque components and normal fibrous tissue were measured. The change in the area of each plaque component during the plaque progression was obtained. 2D stress and strain maps were calculated for the first rabbit with a newly developed biomechanical model [5].

RESULTS

The plaque components in the rabbit lesions were mainly fibrous connective tissue, loose matrix material containing smooth muscle cells, and lipid-containing foam cells. The foam cells were located primarily at the base of the plaques, but few macrophages and intraplaque thrombosis were observed. MR images were thus segmented into four components: lumen (L), fibrous (F), loose matrix (LM), and foam cells (FC). There were a total of 30 MR image slices to compare between two MRI scans. The following Table shows the CNR results of these segmented components over 30 slices. The lumen was better delineated in T_1w images, whereas LM and FC had the greatest contrasts in T_2w images. PDw images provide little help for the plaque discrimination. Between two MRI scans during the plaque progression (Fig.1), plaque lumen was slightly reduced (11%) and the areas of loose matrix increased the most (63%), followed by increases in the areas of FC (30%) and F (4%). The biomechanical calculations suggested that both shear strain and stress (xy) increased significantly, whereas maximal principal and normal strain and stress showed moderate increases (Fig.2).

Table. CNR of Plaque Components relative to F

	L (%)	LM (%)	FC (%)
T1w	**-59 ± 9**	40 ± 17	106 ± 43
T2w	-51 ± 16	**57 ± 29**	**175 ± 56**
PDw	-57 ± 9	41 ± 17	86 ± 31

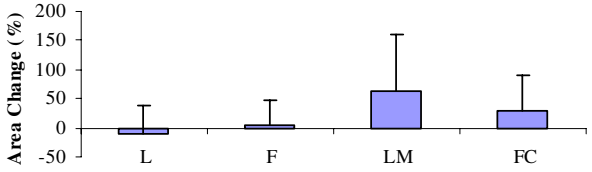
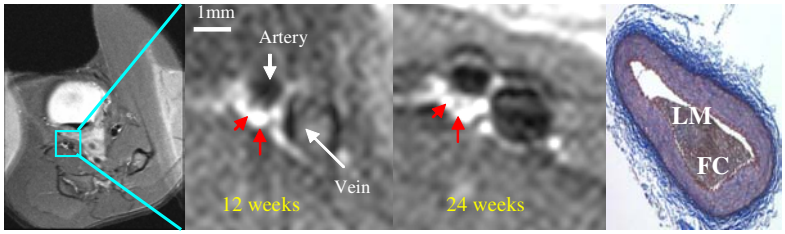


Figure 1. Morphology change during the plaque progression



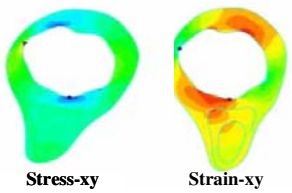


Figure 2. The progression of the first rabbit atherosclerotic plaques (T_1w images) and the histopathology (VVG). Gadofluorine M greatly enhanced large plaque areas. The shear stress and strain maps are also demonstrated.

CONCLUSION

Despite limited spatial resolution, the major plaque components in rabbit femoral artery can still be differentiated with T_1w and T_2w images in Gadofluorine-enhanced MRI. While lumen shows little change, significant increases in loose matrix and foam cells were observed during the plaque progression. This resulted in significant increases in the shear stress and strain within the plaques.

REFERENCES

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