Sensitivity analysis of 3D MRI-based models with fluid–structure interactions for human atherosclerotic coronary and carotid plaques

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Abstract

Accuracy and reliability are extremely important when computational models are used to analyze biological systems and make diagnostic decisions and clinical predictions. In this paper, sensitivity analysis is performed for magnetic resonance imaging (MRI)-based three-dimensional (3D) models with multi-component plaque structure and fluid–structure interactions (FSI) to quantify effects of various controlling factors on stress/strain distributions in human atherosclerotic coronary and carotid plaques. Our quantitative results indicate that plaque morphology and structure, vessel and plaque material properties, and pressure conditions all have considerable effects on flow and plaque stress/strain behaviors. This FSI multi-component model provides more complete stress/strain analysis and better interpretation of information from magnetic resonance images and may lead to more accurate plaque vulnerability assessment and rupture predictions.

Keywords: Atherosclerotic plaque; Coronary; Carotid; Artery; MRI; Fluid–structure interactions

1. Introduction

Cardiovascular disease (CVD) is the number-one killer in the USA and was responsible for 40% of all deaths in the USA during 2000. Atherosclerotic plaques may rupture without warning and cause acute cardiovascular syndromes such as heart attack and stroke. A large number of victims of the disease who are apparently healthy die suddenly without prior symptoms. About 95% of sudden cardiac arrest victims die before reaching a hospital. Available screening and diagnostic methods are insufficient to identify the victims before the event occurs [1]. Magnetic resonance imaging (MRI)-based computational modeling may provide helpful information non-invasively for early diagnosis and treatment of such diseases.

This paper is a continuation of our ongoing effort investigating stress/strain behaviors in human atherosclerotic plaques to quantify conditions under which plaque rupture may occur [2]. Sensitivity analysis is necessary to establish the models and to identify the controlling factors and critical risk indicators that may be used to predict possible plaque ruptures. We will concentrate on the following: (a) unsteady stress/strain variations under pulsating pressure conditions; (b) effects of material properties of plaque components (large calcifications and lipid-rich necrotic pools); and (c) plaque cap thickness on stress/strain distributions. Our results are preliminary and large-scale patient studies are needed to validate our computational findings.

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2. The model and solution method

2.1. Flow and solid models

The flow is assumed to be laminar, Newtonian, viscous, and incompressible. The incompressible Navier–Stokes equations with arbitrary Lagrangian-Eulerian (ALE) formulation were used as the governing equations, which are suitable for fluid–structure interaction (FSI) problems with frequent mesh adjustments. Both artery vessel material and plaque components in the plaque are assumed to be hyperelastic, isotropic, incompressible, and homogeneous. The fluid and structure models are fully coupled, and no-slip conditions and natural traction equilibrium conditions are assumed at all interfaces. The three-dimensional (3D) non-linear modified Mooney–Rivlin (M–R) model was used to describe the material properties of the vessel wall and plaque components [2,3]. The strain energy function is given by

$$W = c_1(I_1 - 3) + c_2(I_2 - 3) + D_1[\exp(D_2(I_1 - 3)) - 1], \quad (1)$$

where I_1 and I_2 are the first and second strain invariants and c_i and D_i are material constants chosen to match experimental measurements [4]. The following values were chosen for the baseline model (units: dyn cm^{-2} for c_1 and D_1; $c2 = 0$): artery: $c_1 = 92\,000$, $D_1 = 36\,000$, $D_2 = 2$; lipid-rich core: $c_1 = 5000$, $D_1 = 5000$, $D_2 = 1.5$; calcification: $c_1 = 920\,000$, $c_2 = 0$, $D_1 = 360\,000$, $D_2 = 2$.

2.2. 3D reconstruction of plaque geometry

3D ex vivo MRI data sets obtained from human atherosclerotic coronary and carotid plaques were read by VTK [5] and 3D plaque geometry and mesh were reconstructed following the procedure described in Tang et al. [2]. Boundary lines for various plaque components were generated according to segmentation data validated by histological analysis. Figure 1 shows one selected magnetic resonance image from a 36-slice 3D set of a cadaveric human coronary plaque, the component contour plot, and the reconstructed geometry. The vessel was extended at both ends so that it became long enough for computational simulations.

2.3. Solution method

The coupled fluid and structure models were solved by a commercial finite-element package ADINA (ADINA R & D, Inc., Watertown, MA, USA) that has been tested by hundreds of real-life applications and has been used by Tang and colleagues in the past several years [2,4]. ADINA uses unstructured finite-element methods for both fluid and solid models. Non-linear incremental iterative procedures are used to handle FSIs. The governing finite-element equations for both the solid and the fluid models are solved by the Newton–Raphson iteration method. Proper mesh was chosen to fit the shape of each component, the vessel, and the fluid domain. Finer mesh was used for thin plaque cap and components with sharp angles to get better resolution and to handle high stress concentration behaviors. The artery was stretched axially and pressurized gradually to specified conditions. More details for the model and solution methods can be found in [2,3,4].

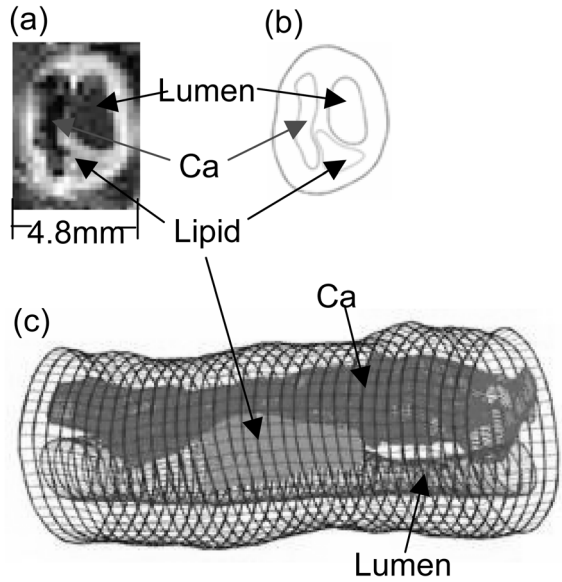


Fig. 1. Coronary plaque sample with large calcification block and a lipid-rich necrotic pool. (a) Selected MRI slice from a 36-slice set; (b) corresponding segmentation based on histological data with contour plots for calcification, lipid core, and lumen area; (c) reconstructed 3D plaque geometry. The position of the vessel is rotated for better viewing.

3. Results and conclusion

3.1. Location and plaque structure sensitivity: stress/strain variations under pulsating pressure

Blood vessel and atherosclerotic plaque are subjected to strong pulsating pressure conditions. Corresponding stress/strain behaviors are worth investigating. Using the critical points selected from various sites (Fig. 2), a cardiac pressure profile with a 90–150-mm Hg range was used in the simulation to observe stress/strain variations under pulsating pressure. Downstream pressure (P_{out}) was chosen so that flow rate was physiological (2–15 ml/s).

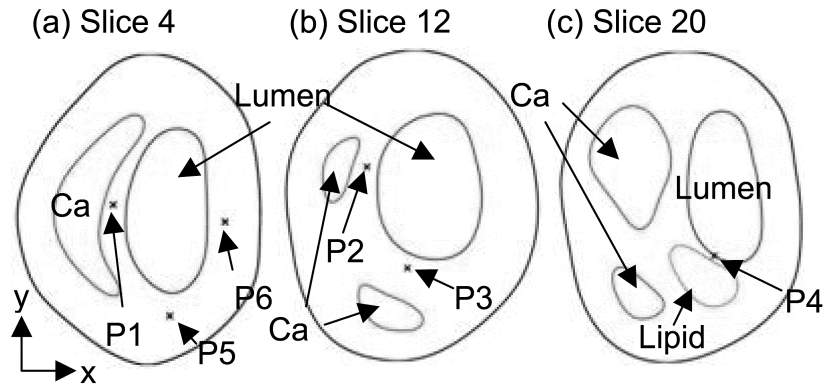


Fig. 2. Selected normal and critical points to track stress/strain variations. P1, from calcification cap; P2, from a thicker Ca cap; P3, from a thicker Ca cap; P4, from a thin lipid core cap (most vulnerable site); P5, normal point to observe stress-xx; P6, normal point to observe stress-yy. (a)–(c) give locations of the six points and three slices from the plaque sample (see Fig. 1).

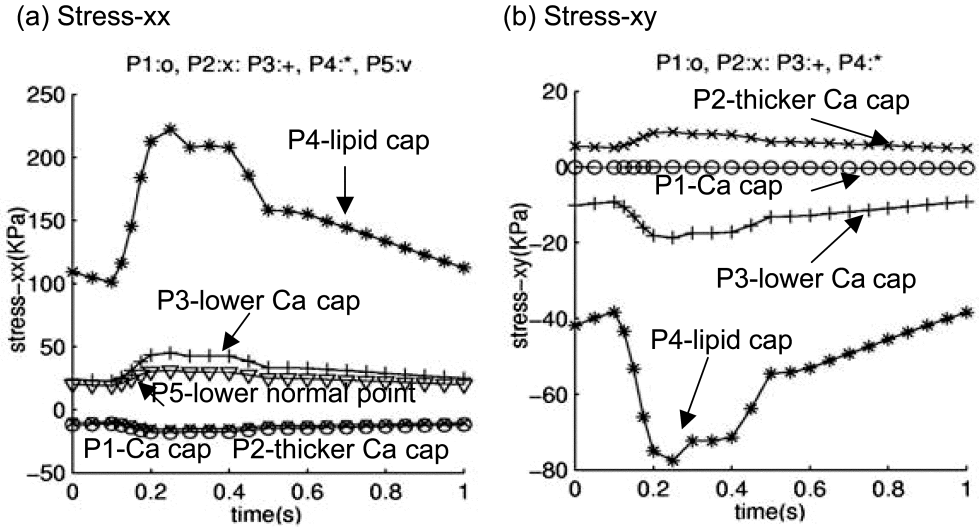
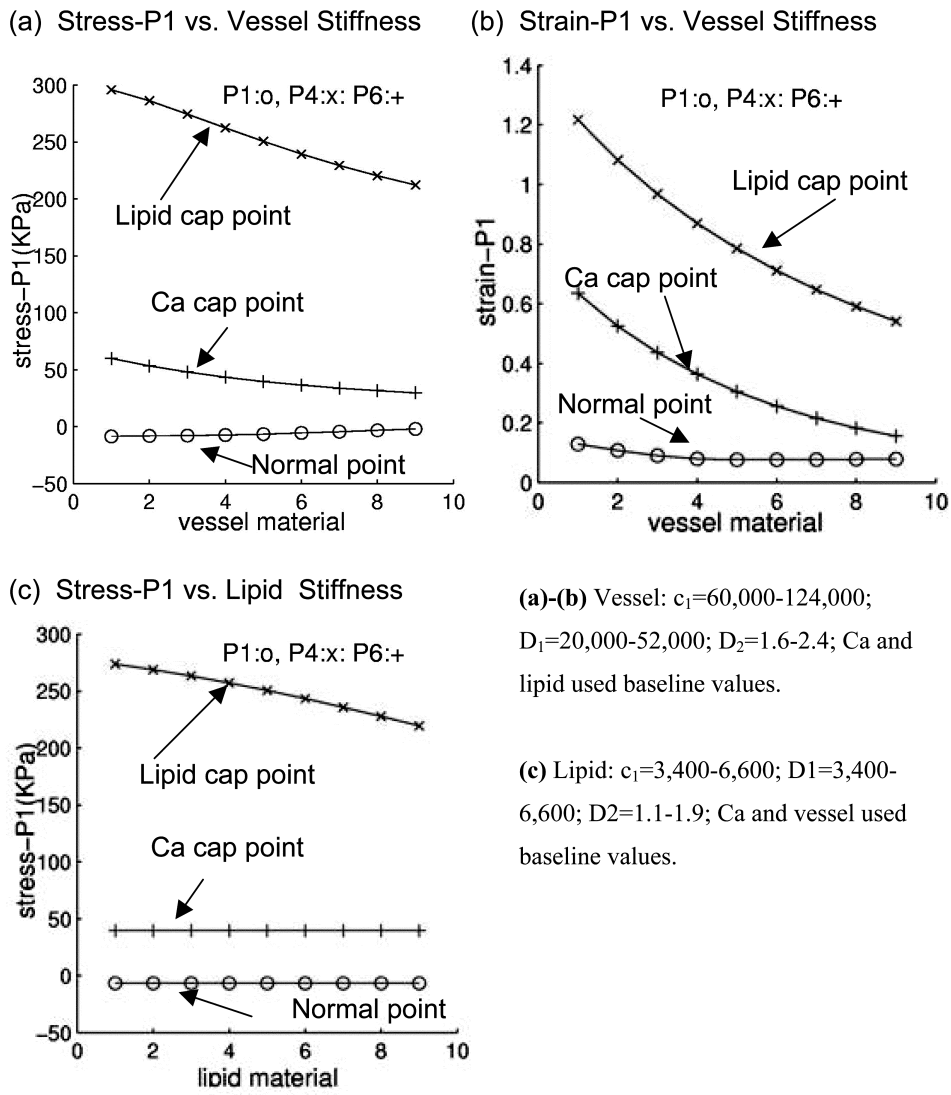


Fig. 3. Tracking of stress components at selected sites under pulsating pressure, showing that the critical point from the thin lipid cap has much greater stress variations. (a) Normal stress in x-direction (stress-xx); (b) shear component (stress-xy).

Fig. 3 shows that the thin cap point (P4) has much greater ($> 400\%$) stress variation than other points. Shear component showed similar patterns, with negative peak values (Fig. 3b).

3.2. Sensitivity analysis for material property variations

For a normal vessel of circular shape made of one uniform and homogeneous material, our calculation found that material stiffness variations cause the vessel to expand more or less (i.e. cause strain variations), but the stress components are affected very little (less than 2%). However, for diseased arteries with large plaque components, such as the plaque sample shown in Fig. 1, material properties have much more considerable impact on stress distributions. Starting from the baseline model, material parameters for vessel, calcification, and lipid-rich core were varied (changing one material property while holding the other two unchanged) incrementally within a specified range; stress-P1/strain-P1 values from three selected points are plotted in Fig. 4. Stress-P1 at the lipid cap decreased by about 40% with about 100% vessel stiffness increase (Fig. 4a), decreased 6% with 100% calcification stiffness increase (not shown), and decreased by 18% with 100% lipid core stiffness increase (Fig. 4c). Strain-P1 at the lipid cap



(a)-(b) Vessel: c_1=60,000-124,000; D_1=20,000-52,000; D_2=1.6-2.4; Ca and lipid used baseline values.

(c) Lipid: c_1=3,400-6,600; D1=3,400-6,600; D2=1.1-1.9; Ca and vessel used baseline values.

Fig. 4. Plots of maximal principal stress (stress-P1) at three selected points with different material parameters showing that material properties have considerable effect on stress distributions. P_{in} = 150 mm Hg, P_{out} = 126 mm Hg, preaxial stretch = 10%. For each material, nine cases were computed, with Case 1 being the softest and Case 9 being the stiffest.

decreased by about 60% for the same vessel stiffness increase (Fig. 4b). Changes at the other two locations are less noticeable. Our quantitative study indicates that obtaining accurate material property information is important for the accuracy of computational simulations. Plaque structure and component size are also important factors.

3.3. Sensitivity of stress/strain distributions to plaque cap thickness variations and plaque cap erosion

Simulations were also conducted using another plaque [2] with plaque cap thickness reduced incrementally (ten steps) from 0.44 to 0.04 mm to observe stress/strain behaviors. Stress-P1 at the cap tracking point increased exponentially from about 35 KPa to 70 KPa, a 100% increase. To see the effect of plaque cap erosion/weakening, we reduced the stiffness of the plaque cap (half of cap thickness, on the lumen side) by 50% and ran the simulation. It was observed that stress level did not change much (less than 1%), but strain-P1 (maximal principal strain) at the tracking point increased from 0.466 to 0.706, a 50% increase. More detailed results will be presented at the conference and are omitted here.

4. Conclusion

Our sensitivity analysis and parameter evaluations indicate that vessel and plaque material properties, plaque component size (lipid and calcification), and plaque cap thickness and weakening have large impacts on stress/strain distributions. Considerably higher stress/strain variations under pulsating pressure are observed at thin plaque cap. Relevance of these findings with respect to plaque vulnerability needs to be established using histopathological and clinical data. Large-scale patient studies are needed to identify and validate potential stress/strain risk indicators for plaque vulnerability assessment.

Acknowledgments

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