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The influence of axial image resolution on atherosclerotic plaque stress computations

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ABSTRACT

Biomechanical models are used extensively to study risk factors, such as peak stresses, for vulnerable atherosclerotic plaque rupture. Typically, 3D patient-specific arterial models are reconstructed by interpolating between cross sectional contour data which have a certain axial sampling, or image, resolution. The influence of the axial sampling resolution on computed stresses, as well as the comparison of 3D with 2D simulations, is quantified in this study. A set of histological data of four atherosclerotic human coronary arteries was used which were reconstructed in 3D with a high sampling (HS) and low sampling (LS) axial resolution, and 4 slices were treated separately for 2D simulations. Stresses were calculated using finite element analysis (FEA). High stresses were found in thin cap regions and regions of thin vessel walls, low stresses were found inside the necrotic cores and media and adventitia layers. Axial sampling resolution was found to have a minor effect on general stress distributions, peak plaque/cap stress locations and the relationship between peak cap stress and minimum cap thickness. Axial sampling resolution did have a profound influence on the error in computed magnitude of peak plaque/cap stresses ($\pm$15.5% for HS vs. LS geometries and $\pm$24.0% for HS vs. 2D geometries for cap stresses). The findings of this study show that axial under sampling does not influence the qualitative stress distribution significantly but that high axially sampled 3D models are needed when accurate computation of peak stress magnitudes is required.

1. Introduction

Atherosclerosis is characterized by plaque formation in the arterial wall (Virmani et al., 2000). Plaque rupture may lead to thromboembolism, possibly causing acute myocardial infarctions and ischemic strokes (Falk et al., 1995; Yuan et al., 2002). Rupture prone plaques, termed vulnerable plaques, generally consist of a large necrotic core separated from the lumen by a thin macrophage infiltrated fibrous cap (Schaar et al., 2004; Virmani et al., 2006).

To improve clinical decision making for medical treatment much attention has been focused on understanding vulnerable plaque rupture. The biomechanical approach treats plaque rupture as an event of mechanical failure, where stresses in the cap lead to its rupture if they exceed the cap strength (Loree et al., 1992; Sadat et al., 2010; Redgrave et al., 2008; Tang et al., 2009). Finite element analysis (FEA) is often used to provide insight into the stress distribution in plaques and the dependence of plaque stress on morphological and geometrical factors such as cap thickness, necrotic core size, luminal curvature and microcalcifications (Akyildiz et al,. 2011; Gao et al., 2009; Sadat et al., 2011a,b; Vengrenyuk et al., 2006; Teng et al., 2011a, b; Creane et al., 2010a,b; Rambhia et al., 2012; Maldonado et al., 2012). In addition to contributing to understanding of plaque rupture (Gao et al., 2011), biomechanical modeling also shows potential for non-invasive identification of vulnerable plaques using novel risk-stratification criteria (Sadat et al., 2011a, 2011b).

Reliable stress assessment using FEA critically depends on accurate reconstruction of the plaque geometry. The plaque geometry is typically obtained from a range of *in vivo* or *ex vivo* imaging methods including MRI (Kock et al., 2008; Li et al., 2008; Teng et al., 2011a,b; Sadat et al., 2009; Huang et al., 2011), CT (Creane et al., 2010a,b, Maldonado et al., 2012), OCT (Chau et al., 2004), intravascular ultrasound (Ohayon et al., 2001; Kural et al., 2012, Baldewsing et al., 2004) and histology (Huang et al., 2001;

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Akyildiz et al., 2011; Speelman et al., 2011; Ohayon et al., 2007; Vengrenyuk et al., 2010). In the case of 2D FEA simulations, plaque components are delineated in cross sectional images, and a plane strain analysis is performed. For 3D simulations, cross sectional images are predominantly obtained from MRI volume data which typically consist of anisotropic voxels with an in-plane resolution being in the order of 5–10 times higher than the axial resolution (voxel dimensions of 0.2–0.6 mm in-plane vs. 1–2 mm axial) (Yuan et al., 2004). The 3D geometry is reconstructed by axially stacking cross sectional segmented contours with a distance which will be referred to in this study as the axial sampling resolution. For contours derived from volume image data, the axial sampling resolution is equal to the axial voxel dimension while for contours based on histology it is equal to the slice distance. Upon stacking the contours, interpolation is used to generate the 3D arterial geometry.

This study aims to quantify the influence of axial sampling resolution on computed peak plaque and cap stresses using FEA. This will be done by performing stress simulations on a set of histology based atherosclerotic arterial segments. Each segment will be reconstructed in 3D using a high axial resolution and a low axial resolution. For each segment also 2D simulations will be performed and compared to the 3D models.

2. Methods

2.1. Histology and segmentation

To investigate the influence of axial sampling resolution on computed stresses, we needed a data set of diseased arteries with a sufficiently high resolution that can serve as a gold standard. We used a histological set of human coronary arteries with an axial slice distance of 0.5 mm. We selected 4 arterial segments with a length of 3 mm (7 slices). The selection criteria were such that each segment had at least one large necrotic core and at least one thin cap. Before sectioning, the arteries were decalcified and perfusion fixated with formalin at 100 mmHg and stained with a Movat pentachrome staining to enable segmentation of the plaque components. Manual segmentation of the lumen, necrotic cores, media and adventitia layers was performed (Fig. 1).

2.2. Geometry reconstructions

To reconstruct the 3D geometries, the slices were stacked vertically by alignment of the luminal center of gravity. For each arterial segment, a reference geometry using all 7 histological slices spaced 0.5 mm apart was created, referred to as the high sampling (HS) model. A low sampling (LS) geometry was created to mimic the in vivo imaging situation which had only 4 slices spaced 1.0 mm apart. The most extreme case of low sampling would be the use of only a single slice, thus resulting in a 2D formulation. To investigate and compare results of this lowest possible sampling resolution to the HS models, four 2D models were created from the same four slices used for the LS geometry (Fig. 2). Non-uniform rational basis spline interpolation in Gambit (Fluent Inc., ANSYS, Canonsburg, Pennsylvania) was used to interpolate between slices. To avoid reading out values at the boundary of the simulated domain, an additional top and bottom end slice were added to each 3D model before geometrical interpolation.

2.3. Material properties and computational analysis

All tissues were assumed to be homogeneous, hyperelastic and incompressible. The intima and lipid core tissues were assumed to be isotropic and modeled with the Neo-Hookean material model. The media and adventitia tissues were modeled with an anisotropic material model (Gasser et al., 2006). The same material constants were used as in Akyildiz et al. and are listed in Table 1 (Akyildiz et al., 2011).

All FEA were performed using Abaqus (Version 6.11.1, Dassault Systèmes Simulia Corp., Providence, RI, USA). The models for the 2D simulations were meshed with four-node linear hybrid elements (~100.000 elements). For 3D simulations, four-node linear hybrid tetrahedral elements were used. All 3D meshes were created using an iterative adaptive remeshing procedure allowing for small elements in high stress regions while keeping the total mesh size below 2 million elements. All models contained at least 3 layers of elements in every thin cap and yielded mesh independent solutions. The initial stress was calculated using the backward incremental method (de Putter et al., 2007; Speelman et al., 2011). A static intraluminal pressure of 15 kPa (~110 mmHg) was applied as the loading condition for all models. The 2D models were based on a plane strain assumption whereas the boundary conditions for the 3D models consisted of restraining the z-component of the deformation at the axial boundaries.

2.4. Analysis

The maximum principal stress, stress-P_1 [kPa], was used as the stress scalar quantity in this study (Kock et al., 2008). Quantitative comparisons were performed only at cross sections matching the slices used to create the HS models. Four out of seven of these slices are *shared* in all models (HS, LS and 2D) while the other three represent *interpolated* cross sections for the LS models

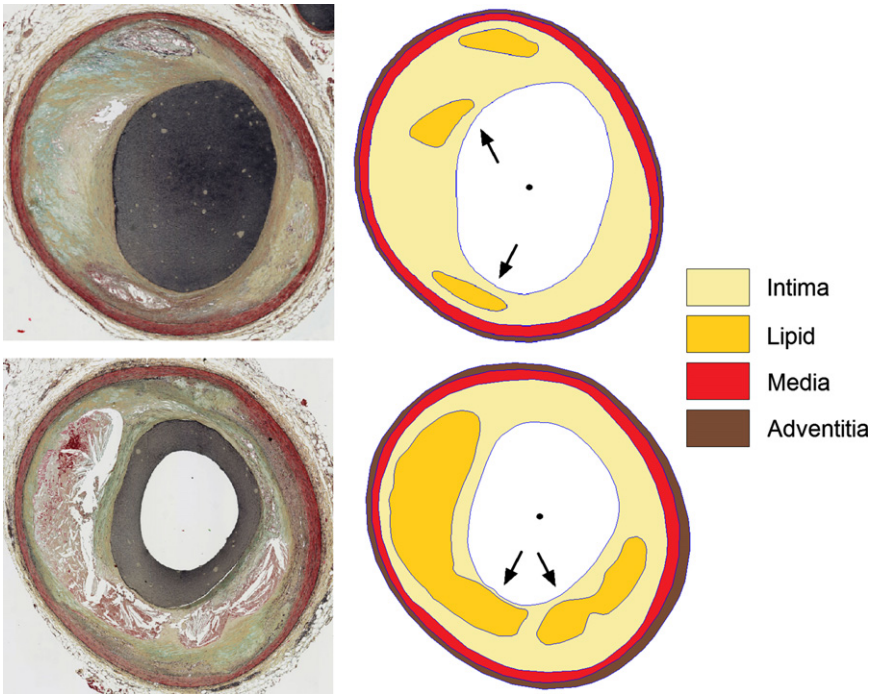

Fig. 1. Histological cross sections and their delineated contours. Cap regions are indicated by black arrows.