Effects of Fibrous Cap Thickness on Peak Circumferential Stress in Model Atherosclerotic Vessels

Howard M. Loree, Roger D. Kamm, Richard G. Stringfellow, and Richard T. Lee

It is likely that factors other than stenosis severity predispose some atherosclerotic plaques to rupture. Because focal increases in circumferential stress may be an important mechanism of plaque rupture, we examined peak circumferential stress of atherosclerotic lesions by using finite element analysis based on idealized two-dimensional cross sections of diseased vessels similar to intravascular ultrasound images. The study was designed to test the hypothesis that subintimal plaque structural features such as thickness of the fibrous cap are more important factors in the distribution of stress in the plaque than stenosis severity. The analysis incorporated equilibrium biomechanical parameters from normal and diseased vessels and determined the stress distribution within the plaque at a mean luminal internal pressure of 110 mm Hg. With a constant luminal area reduction of 70%, maximum circumferential stress (σmax) normalized to luminal pressure (σmax/P) increased from 6.0 to 24.8 as the thickness of the lipid pool was increased from 38% to 54% of the plaque thickness because of the thinner fibrous cap over the lipid pool. When the lipid pool thickness was constant, increasing the stenosis severity from 70% to 91% by increasing the fibrous cap thickness decreased σmax/P from 24.8 to 4.7. When no lipid pool was present and the stenosis severity was increased from 70% to 99%, σmax/P decreased from 5.3 to 4.7. Thus, reducing the fibrous cap thickness dramatically increases peak circumferential stress in the plaque, whereas increasing the stenosis severity actually decreases peak stress in the plaque. The critical dependence of peak circumferential stress on subintimal structure may explain why some atherosclerotic plaques that rupture and cause myocardial infarction are not angiographically severe. (Circulation Research 1992;71:850–858)

KEY WORDS • atherosclerosis • myocardial infarction • coronary disease • biomechanics

Fracture of the surface of an atherosclerotic plaque is a common cause of acute myocardial infarction and unstable angina, and the sequence of events leading from plaque rupture to luminal thrombosis to myocardial necrosis has been well described. A number of clinically successful strategies for limiting infarction size are directed at these events, including thrombolytic therapy, acute mechanical intervention, and acute β-adrenergic blockade. However, the ability to identify unstable atherosclerotic lesions and to intervene successfully before acute plaque rupture occurs has been an elusive goal. Although coronary angiography provides some prognostic information, factors other than stenosis severity predispose some atherosclerotic plaques to rupture. For example, Little et al found that the angiographic severity of coronary stenosis poorly predicted the subsequent location of infarction. Based on a retrospective analysis of preinfarction angiograms, a study by Ambrose et al has also suggested that myocardial infarction frequently develops from the rupture of angiographically nonsevere coronary lesions.

The biomechanical mechanism of plaque rupture is controversial. Mechanisms that have been proposed include shear stress injury, transient collapse of the stenosis, rupture of the vasa vasorum, turbulent plaque injury, and mechanical shear stress. One mechanism that is strongly supported by pathological data is fracture caused by increases in circumferential stress within the plaque. Because some components of the diseased vessel are stiffer than others, regions of “stress concentration” develop. Richardson and colleagues have identified stress-concentration regions by finite element modeling; these regions correlate with locations of plaque fracture in autopsy specimens. Thus, subintimal structure, rather than stenosis severity, may be critical in determining overall plaque stability, explaining why coronary angiography has not been a reliable method for predicting future myocardial infarction. This study was designed to test the hypothesis that subintimal plaque structural features such as thickness of the fibrous cap and size of lipid pools are more important factors in the distribu-
tion of circumferential stress in the plaque than stenosis severity.

Materials and Methods

Design of Models

Ten idealized models were designed to test the effects of plaque geometry on circumferential stress fields in the diseased vessel. All models represented cross sections of typical atherosclerotic human coronary arteries with eccentric intimal plaques. As illustrated in Figure 1, the artery is modeled as a thick-walled cylinder with an inner radius of 1.8 mm and an outer radius of 2.0 mm. The lumen is modeled as a circular hole of varying radius R with an eccentricity of 0.5 mm with respect to the artery center. Fibrous plaque occupies the region between the luminal wall and the inner wall of the artery. The assumption was made in these idealized models that the fibrous cap was continuous with the fibrous plaque and had the same material properties as the fibrous plaque. In some models, a subintimal lipid pool exists as a 140° crescent with inner radius a and outer radius 1.75 mm with respect to the lumen center. Only radius R and radius a varied in the 10 models described below.

The ends of the lipid pool are hemicircular. The portion of plaque between the lumen and the lipid pool is the fibrous cap. A static pressure of 110 mm Hg (14.6 kPa) acts along the luminal wall, representing mean physiological blood pressure in the coronary arteries. Table 1 gives the dimensions of models A–J. In models A–D, fibrous cap thickness is varied by changing the lipid pool size (changing radius a) at a constant stenosis severity; the outer radius of the lipid pool remained constant, so the lipid pool increased in size by thinning of the fibrous cap. In models E–G, stenosis severity is varied with no lipid pool present. In models A, H, I, and J, fibrous cap thickness is varied by changing the stenosis severity (changing radius R) with a constant lipid pool size (as in model A).

Material Properties

Both the plaque and artery are modeled as orthotropic materials with linear elastic properties. Although finite element codes can accommodate nonlinear incremental solutions, little nonlinear biomechanical testing data from atherosclerotic plaque tissue are available. In the absence of reliable nonlinear parameters, the estimates of linear elastic parameters were used. Since these tissues have similar properties in the circumferential (θ) and axial (z) directions, which differ from the properties in the radial (r) direction, they belong to a class of orthotropic materials termed "transversely isotropic" with r-θ and θ-z as the principal planes. Therefore, five material parameters completely describe the mechanical properties of the material:15: E_r, E_z, ν_rθ, ν_rz, and G_θz. E_r and E_z are Young’s moduli in the r and θ directions, respectively, where E_r is the ratio of normal stress in the i direction to normal strain in the i direction. ν_rθ and ν_rz are the Poisson ratios in the r-θ and θ-z planes, respectively, where ν_i is the ratio of transverse strain in the i direction to imposed normal strain in the j direction: ν_i = −Δstrain_j/strain_i. G_θz is the shear modulus in the r-θ plane, where G_i is the ratio of the i-j component of shear stress to the i-j component of shear strain.

![Diagram showing geometry of idealized atherosclerotic coronary artery cross section. Eccentric plaque has lumen of radius R and subintimal crescent-shaped lipid pool with inner radius a.](image-url)

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**Table 1. Geometry of 10 Finite Element Models Based on Schematic of Idealized Atherosclerotic Coronary Artery Cross Section in Figure 1**

<table>
<thead>
<tr>
<th>Model</th>
<th>R  (mm)</th>
<th>a  (mm)</th>
<th>Stenosis severity (% area reduction)</th>
<th>Fibrous cap thickness (mm)</th>
<th>Maximum lipid pool thickness (% maximum plaque thickness)</th>
<th>Peak stress (σ_max/P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.00</td>
<td>1.05</td>
<td>70</td>
<td>0.05</td>
<td>54</td>
<td>24.8</td>
</tr>
<tr>
<td>B</td>
<td>1.00</td>
<td>1.15</td>
<td>70</td>
<td>0.15</td>
<td>46</td>
<td>9.2</td>
</tr>
<tr>
<td>C</td>
<td>1.00</td>
<td>1.25</td>
<td>70</td>
<td>0.25</td>
<td>38</td>
<td>6.0</td>
</tr>
<tr>
<td>D</td>
<td>1.00</td>
<td>1.50</td>
<td>70</td>
<td>0.50</td>
<td>19</td>
<td>5.3</td>
</tr>
<tr>
<td>E</td>
<td>1.00</td>
<td>...</td>
<td>94</td>
<td>...</td>
<td>...</td>
<td>5.3</td>
</tr>
<tr>
<td>F</td>
<td>0.45</td>
<td>...</td>
<td>94</td>
<td>...</td>
<td>...</td>
<td>4.6</td>
</tr>
<tr>
<td>G</td>
<td>0.18</td>
<td>...</td>
<td>99</td>
<td>...</td>
<td>...</td>
<td>4.7</td>
</tr>
<tr>
<td>H</td>
<td>0.90</td>
<td>1.05</td>
<td>75</td>
<td>0.15</td>
<td>41</td>
<td>8.8</td>
</tr>
<tr>
<td>I</td>
<td>0.80</td>
<td>1.05</td>
<td>80</td>
<td>0.25</td>
<td>38</td>
<td>5.6</td>
</tr>
<tr>
<td>J</td>
<td>0.55</td>
<td>1.05</td>
<td>91</td>
<td>0.50</td>
<td>19</td>
<td>4.7</td>
</tr>
</tbody>
</table>

R, radius of lumen; a, inner radius of subintimal lipid pool; σ_max/P, maximum circumferential stress normalized to luminal pressure.
TABLE 2. Orthotropic Material Parameters for Plaque and Artery Used in Finite Element Models

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Plaque</th>
<th>Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>E₁ (kPa)</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>E₀ (kPa)</td>
<td>1,000</td>
<td>100</td>
</tr>
<tr>
<td>G₀ (kPa)</td>
<td>500</td>
<td>50</td>
</tr>
<tr>
<td>νₑ</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>νₐ</td>
<td>0.27</td>
<td>0.27</td>
</tr>
</tbody>
</table>

E₁ and E₀, Young's moduli in the radial (r) and circumferential (θ) directions, respectively; G₀, shear modulus in the r-θ plane; νₑ and νₐ, Poisson ratios in the r-θ and θ-z planes, respectively, where z is the axial direction.

The selection of material properties for the models is described in Table 2; although these parameters vary from specimen to specimen, estimations of typical values were made. Note that these are estimates for static, not dynamic, parameters, because the finite element solutions in this study evaluate stresses caused by mean arterial pressure. E₁ for fibrous aortic plaque and E₀ for normal artery were measured in static uniaxial compression between a radial stress of 30 mm Hg (−4.0 kPa) and 90 mm Hg (−12.0 kPa), as previously reported.16,17 E₀ for fibrous plaque was estimated from previous reports of static tensile properties of human aortic atherosclerotic plaque.18 For the coronary artery was based on previously published studies of normal arteries using inflation or ultrasound techniques19,20 as well as additional previous reports (reviewed in Reference 21). The Poisson ratios for plaque and artery were based on a previously measured value of νₑ = 0.27 in the canine aorta.22 νₑ was then chosen to satisfy the requirements for positive diagonal entries in a positive definite-stiffness matrix. To evaluate the effects of potential errors in parameter estimation, a sensitivity analysis of the effects of varying plaque E₂, νₑ, and νₑ and other parameters on maximum circumferential stresses was performed (Table 3).

The G₀ shear moduli for plaque and artery were estimated based on a limit argument. The upper bound for G₀ was chosen to be the larger of the elastic moduli E₀. If G₀ were greater than E₀, then the layers of fibers within plaque or artery would more easily stretch than slide over one another; in the plaque, this is unlikely since the bonds between collagen fibers form a highly rigid structure. The artery wall is less rigid than the plaque, so that higher G₀ relative to E₀ may be possible. However, sensitivity analysis demonstrated little effect of increases in G₀ for artery on circumferential tensile stress. The lower bound for G₀ was established by modeling plaque and artery as incompressible isotropic materials with E₀ = E₀ and then solving for G₀ = E₀/3. For plaque, the predicted range was 17 kPa < G₀ < 1,000 kPa, and for artery, the predicted range was 3 kPa < G₀ < 100 kPa.

Mesh Generation and Model Solution

All finite element meshes were designed using SDRC IDEAS software on a DEC MicroVax II computer. Regions were defined and then automatically meshed with eight-noded quadrilateral plane-strain elements using a free-meshing algorithm designed to minimize element distortion. The assumption of plane strain was made because the axial dimension of atherosclerotic lesions is on the order of the vessel diameter. Plane-strain models would be more appropriate if axial dimensions were very small relative to the vessel diameter. Models A and E were also analyzed with plane-strain elements (data not shown); these results were not significantly different from those of the plane-strain models. The average element dimension was 0.1 mm. Because of symmetry, only half of the artery and plaque system was analyzed, with nodes along the center line restrained to move only in the r direction and one node on the outer wall of the artery completely restrained. The origin of the r-θ coordinate system was defined as the center of the lumen.

To improve the accuracy of the finite element stress analysis, each mesh was refined by using an adaptive remeshing algorithm. This remeshing algorithm increases the number of elements in regions of high strain energy, providing a more accurate finite element solution. A simplified isotropic shell element model with the artery assigned an E of 100 kPa and ν of 0.27 and the plaque assigned an E of 1,000 kPa and ν of 0.27 was solved for strain energy in each element. The elements with the top 15% strain-energy gradients were then divided into smaller triangular or quadrilateral elements. Examples of finite element meshes following the adaptive remeshing process are illustrated in the top panels of Figures 2–5. The refined finite element models with orthotropic linearly elastic material properties and plane-strain elements were then solved using HKS ABAQUS 4.9 software on a CRAY-2 or CRAY X-MP supercomputer. Contour plots of circumferential stress (the bottom panels of Figures 2–5) were displayed using

TABLE 3. Sensitivity of Maximum Circumferential Stress in Model D to Changes in Various Orthotropic Material Parameters

| Parameter | Change in parameter (%) | Change in σₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉᵉぇeeeeeeeee
ABAQUS POST on a graphics terminal (model 4107A, Tektronix).

Results

The results of the finite element analyses for several of the plaque models are shown in the bottom panels of Figures 2–5. Circumferential stress is plotted linearly with respect to the color scale. The regions of maximum circumferential stress lie either in the plaque cap over the subintimal lipid pool or on the luminal wall near the thinnest plaque section. Small compressive circumferential stresses occur in the subintimal lipid pool (range, 0.3–2.0 kPa; mean, 0.8±0.6 kPa). Peak compressive circumferential stresses were found in the plaque at the lipid pool tip (shown as the largest negative stress in the bottom panels of Figures 2–5).

Values were determined for $\sigma_{\text{max}}/P$, where the maximum circumferential stress in each model ($\sigma_{\text{max}}$) is normalized by luminal pressure (P). By adjusting plaque cap thickness and stenosis severity across the range of geometries studied, $\sigma_{\text{max}}/P$ varied from 4.7 to 24.8. As shown in Figure 6, for a constant stenosis severity, $\sigma_{\text{max}}/P$ decreased from 24.8 to 5.3 as cap thickness increased from 0.05 to 0.5 mm because of the decreasing lipid pool size. When plaque cap thickness was increased by increasing the stenosis severity with constant lipid pool geometry, slightly lower values of $\sigma_{\text{max}}/P$ resulted. As shown in Figure 7, for a constant lipid pool geometry, $\sigma_{\text{max}}/P$ decreased from 24.8 to 4.7 as stenosis severity increased from 69% to 91%; this effect is due to the increase in fibrous cap thickness as the stenosis severity.

FIGURE 2. Top panel: Diagram showing geometry of model A: stenosis severity, 70%; fibrous cap thickness, 0.05 mm; maximum lipid pool thickness, 54% of maximum plaque thickness. There were 1,283 plane-strain elements: 957 plaque, 166 artery, and 160 lipid. Bottom panel: Contour map of circumferential (CIRCUM) stress in model A (in pascals). Maximum circumferential stress normalized by luminal pressure ($\sigma_{\text{max}}/P$) was 24.8 (arrowhead), with $P=110$ mm Hg.
becomes more severe. For models without a lipid pool, $\sigma_{\text{max}}/P$ decreased from 5.3 to 4.7 as stenosis severity increased from 70% to 99%. Additional analyses of the effect of increasing lipid pool size toward the adventitia (with constant fibrous cap thickness of 0.15 mm) were performed (data not shown); this caused very little increase in circumferential stress.

**Sensitivity Analysis**

An analysis of sensitivity of maximum circumferential stress to changes in plaque orthotropic properties is shown in Table 3. The range of $E_x$ tested corresponds to typical values obtained through experimentation. The ranges of $\nu_y$ and $\nu_{yt}$ tested correspond to values satisfying the necessary condition of a positive definite-stiffness matrix. Thus, reasonable errors in estimation of these material parameters would not significantly influence the primary conclusions of this study.

**Discussion**

**Plaque Rupture**

Although many questions about the initiating events of myocardial infarction remain unanswered, it is likely that the increases in circumferential stress within the plaque proposed by Richardson et al\textsuperscript{14} play an important role. In this study of idealized atherosclerotic vessels, increasing the stenosis severity actually decreased circumferential stresses in the absence of a lipid pool, but the effect was small and may be biologically

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**Figure 3.** Top panel: Diagram showing geometry of model C: stenosis severity, 70%; plaque cap thickness, 0.25 mm; maximum lipid pool thickness, 38% of maximum plaque thickness. There were 962 plane-strain elements: 663 plaque, 166 artery, and 133 lipid. Bottom panel: Contour map of circumferential (CIRCUM) stress in model C (in pascals). Maximum circumferential stress normalized by luminal pressure ($\sigma_{\text{max}}/P$) was 6.0 (arrowhead), with $P=110$ mm Hg.
insignificant. On the other hand, decreasing the thickness of the fibrous cap over a subintimal lipid pool (either by decreasing stenosis severity or increasing lipid pool size toward the lumen) dramatically increased peak circumferential stresses.

An important question is raised by this study and the study of Richardson et al.14 How high are these stresses relative to failure stresses of human atherosclerotic tissues? Preliminary investigations24 and our data (unpublished observations) indicate that the fracture stresses of stable human fibrous caps have a broad range that is generally two to 10 times peak static stresses predicted by finite element analysis (depending on geometry and subintimal structure). Nonulcerated aortic plaques generally do not fracture at tensile circumferential stresses lower than 300 kPa.24 Three important factors may explain why fracture stresses are higher than predicted stresses. First, myocardial infarctions do not occur randomly throughout the day, and it is likely that at least some infarctions are “triggered” by significant elevations in blood pressures, which will increase circumferential stresses.25 In the linearly elastic model used in this study, increases in mean blood pressure would lead to directly proportional increases in circumferential stress; it is conceivable that large sustained increases in blood pressure could raise stresses into the fracture range. Second, repetitive dynamic stresses will be caused by pulsatile pressure; these dynamic stresses may cause “fatigue” of the plaque. It is also possible that fatigue through repetitive bending of the artery during the cardiac cycle occurs; this mechanism cannot be studied with the plane-strain model. Third, the

FIGURE 4. Top panel: Diagram showing geometry of model E: stenosis severity, 70%; no lipid pool. There were 874 plane-strain elements: 696 plaque and 178 artery. Bottom panel: Contour map of circumferential (CIRCUM) stress in model E (in pascals). Maximum circumferential stress normalized by luminal pressure ($\sigma_{\text{max}}/P$) was 5.3 (arrowhead), with $P=110$ mm Hg.
plaque is a biologically active environment, where macrophages, smooth muscle cells, platelets, and other cells participate in secretion and remodeling of the extracellular matrix. Lendon et al. have demonstrated that macrophage-rich regions of plaque will fracture at lower stresses than macrophage-poor plaques. In addition, evidence for stromelysin mRNA has been found in human atherosclerotic plaques; this protease may be one of the macrophage proteases causing plaque weakening.

One potential scenario of the events leading to plaque rupture is raised by these studies. The plaque grows with a necrotic lipid pool so that it is structurally unstable. Macrophage infiltration, perhaps promoted by activation of endothelial cells, leads to a focal weakening of the plaque structure. Pulsatile and mean circumferential stresses further weaken this area until rupture occurs. If the balance of thrombosis and thrombolysis favors thrombus formation, an occlusive thrombus may ensue; however, if the thrombus is not severe enough to occlude the lumen, relief of the peak circumferential stress may allow the plaque to remodel, perhaps with lower levels of stress concentration than before rupture occurred.

An approach that may allow identification of plaques with thin fibrous caps overlying lipid pools before rupture is intravascular ultrasound. Catheter-tipped ultrasound imaging transducers provide information about subintimal structure that has previously been unavailable ante mortem. These images can provide informa-
this study assumed a constant plaque eccentricity, a smooth and round luminal surface, and a smooth boundary between plaque and lipid pool. This was necessary to isolate the effects of fibrous cap thickness and stenosis severity on stresses in the plaque. It is likely that small cracks or irregularities in the plaque surface as well as local variations of moduli could result in much greater stress concentrations than those described in this study. Further studies of specific fatal coronary lesions may demonstrate the importance of lesion geometric irregularities; these studies are complicated by the assumptions made during reconstruction of rupture geometries. In addition, because of the complexity of atherosclerotic lesions, three-dimensional modeling may be essential in some cases; preliminary evidence suggests that intravascular ultrasound may be a feasible approach for obtaining three-dimensional structure.

Plaque and artery were modeled as transversely isotropic linearly elastic biomaterials for the range of stresses encountered in this study. Atherosclerotic changes are likely to influence the distribution and orientation of fibers; thus, transverse isotropy is an approximation. Biomaterials typically are not linearly elastic in the physiological range, and it is unlikely that any component of the plaque behaves in a linearly elastic fashion, especially under the high stresses imposed by percutaneous balloon angioplasty. Very limited experimental data regarding nonlinearity of plaque within the physiological range are available, so nonlinear orthotropic modeling was not performed in this study. It is also likely, given the range of moduli found within a histological class of plaque, that nonuniformities within the fibrous cap or variabilities between different fibrous caps will affect stress concentrations. However, the sensitivity analyses performed in this study indicate that relatively minor changes in stress result from major changes in material properties. In addition, the lipid pool was modeled as a soft, nearly incompressible material. Because necrotic core components of the lipid pool are variable, the stiffness of the lipid pool is probably also different from lesion to lesion. However, the lipid pool will bear very little circumferential stress under any conditions because of its semifluid nature, so that the precise choice of material parameters for this region will not significantly affect the distribution of stress in the plaque. Thus, the results of this study indicate important increases in circumferential stress due to variations in fibrous cap thickness. It is important to note that major changes in material properties may affect the shear stresses between layers and also contribute to high stress concentrations.

This study examined circumferential stresses resulting from the static load of mean luminal pressure. The plaque and artery have dynamic characteristics related to tissue viscoelasticity and poroelasticity that will determine the stresses related to pulsatile flow. These dynamic parameters are variable within the range of physiological heart rate, so modeling these time-dependent effects is a formidable task. Much further work should be done regarding the fracture properties of atherosclerotic tissues, including the potential for dynamic modes of failure from pulsatile flow. Unfortunately, fracture studies of human atherosclerotic tissues are difficult because of the heterogeneous nature of human plaque.
Conclusions

Although acute plaque rupture is a major cause of death in developed countries, no therapeutic strategies have been developed specifically to prevent plaque rupture. Instead, most therapies for myocardial infarction are directed at the events that follow acute plaque rupture by thrombolysis or limiting myocardial oxygen demands. This study demonstrated that the maximum stresses in the plaque are critically dependent on subintimal structure of the lesion, suggesting that angiography alone will not provide sufficient information to stratify lesions by structural stability. By understanding the importance of plaque structural features, particularly subintimal structure, and with improved coronary imaging modalities, identification of unstable lesions before rupture may become feasible.

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