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The influence of constitutive law choice used to characterise atherosclerotic tissue material properties on computing stress values in human carotid plaques

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ABSTRACT

Calculating high stress concentration within carotid atherosclerotic plaques has been shown to be complementary to anatomical features in assessing vulnerability. Reliability of stress calculation may depend on the constitutive laws/strain energy density functions (SEDFs) used to characterize tissue material properties. Different SEDFs, including neo-Hookean, one-/two-term Ogden, Yeoh, 5-parameter Mooney–Rivlin, Demiray and modified Mooney–Rivlin, have been used to describe atherosclerotic tissue behavior. However, the capacity of SEDFs to fit experimental data and the difference in the stress calculation remains unexplored. In this study, seven SEDFs were used to fit the stress–stretch data points of media, fibrous cap, lipid and intraplaque hemorrhage/thrombus obtained from 21 human carotid plaques. Semi-analytic solution, 2D structure-only and 3D fully coupled fluid-structure interaction (FSI) analyses were used to quantify stress using different SEDFs and the related material stability examined. Results show that, except for neo-Hookean, all other six SEDFs fitted the experimental points well, with vessel stress distribution in the circumferential and radial directions being similar. 2D structural-only analysis was successful for all seven SEDFs, but 3D FSI were only possible with neo-Hookean, Demiray and modified Mooney–Rivlin models. Stresses calculated using Demiray and modified Mooney–Rivlin models were nearly identical. Further analyses indicated that the energy contours of one-/two-term Ogden and 5-parameter Mooney–Rivlin models were not strictly convex and the material stability indictors under homogeneous deformations were not always positive. In conclusion, considering the capacity in characterizing material properties and stabilities, Demiray and modified Mooney–Rivlin SEDF appear practical choices for mechanical analyses to predict the critical mechanical conditions within carotid atherosclerotic plaques.
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1. Introduction

Carotid atherosclerotic disease is responsible for around 15–20% of all ischemic strokes (Brott et al., 2011), with the luminal stenosis being the only validated diagnostic criterion for patient risk stratification. However, this criterion becomes less reliable in patients with mild to moderate carotid stenoses (Barnett et al., 1998). Increasing evidence has suggested that both the physical characteristics of atherosclerotic plaques and the mechanical loading within the structure may allow greater potential to predict clinical progression than luminal stenosis alone. A vulnerable carotid atherosclerotic plaque is characterized by the presence of intraplaque hemorrhage (IPH) and a large lipid-rich necrotic core, with symptomatic plaques also showing evidence of fibrous cap (FC) rupture. These features have been shown to predict future events in both symptomatic (Altaf et al., 2008; Eliasziw et al., 1994) and asymptomatic (Singh et al., 2009; Takaya et al., 2006) patients. As plaques are continually subject to mechanical loading due to pulsatile blood pressure and flow, FC rupture is thought to occur when loading exceeds its material strength (Richardson et al., 1989; Tang et al., 2009a). FC stress can differentiate symptomatic from asymptomatic patients (Sadat et al., 2011; Zhu et al., 2010) and both plaque deformation and FC stress have been found to be

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associated with subsequent cerebrovascular ischemic events in symptomatic patients (Sadat et al., 2010; Teng et al., 2011, 2013).

There is therefore a need to integrate both plaque morphological and compositional features with the critical mechanical conditions for improved patient risk stratification. However, the reliability of re-predicting the critical mechanical conditions is largely dependent on the accuracy of plaque geometry and the material properties of each atherosclerotic component, including intra-plaque hemorrhage or thrombus (IPH/T), lipid and FC. Accurate reconstruction of plaque geometry is critically dependent on the imaging technique utilized, limited by resolution and tissue discrimination. The behavior of material properties is determined from experimental measurements, but also influenced by constitutive laws. Several potential strain energy density functions (SEDFs) can be used to characterize the material, such as neo-Hookean (Akyildiz et al., 2011; Caille et al., 2002; Lee et al., 1996; Ohayon and Tracqui, 2005), one-term Ogden (Barrett et al., 2009), two-term Ogden (Li et al., 2006, 2007; Tang et al., 2008; Versluis et al., 2006), Yeoh (Cunnane et al., 2015; Lawlor et al., 2011), five-parameter Mooney–Rivlin (Gao and Long, 2008; Maher et al., 2009), Demiray (Chau et al., 2004; Delfino et al., 1997; Kaazempur-Mofrad et al., 2003a), and modified Mooney–Rivlin SEDF (Tang et al., 2009a, 2013, 2014b). These seven SEDFs have been used in numerous studies to model the mechanical behavior of carotid atherosclerotic plaques. However, the effectiveness of each SEDF at characterizing the material properties of carotid atherosclerotic tissue and the resulting variance in predicted critical mechanical conditions within the plaque structure using these different SEDFs remain unexplored.

In this study, the seven selected SEDFs are used to fit the experimental data obtained from uniaxial extension tests performed on human carotid atherosclerotic tissues. The accuracy in computing the mechanical stress within the plaque structure is assessed by using analytical solutions, idealized 2D structure-only and 3D fully coupled fluid-structure interaction (FSI) simulations and the related material stability is discussed.

2. Material and methods

2.1. Strain energy density functions

Human carotid atherosclerotic tissues exhibit non-linear stress–strain behavior at low stretch levels (Maher et al., 2009; Mulvihill et al., 2013; Teng et al., 2014c). These complexities need to be accommodated by specific SEDFs/hyperelastic material models. Several SEDFs were adopted/developed for this purpose, including neo-Hookean, one- and two-term Ogden, Yeoh, 5-parameter Mooney–Rivlin, Demiray and modified Mooney–Rivlin models, with details as follows:

neo-Hookean model

$$W = C_1(\bar{I}_1 - 3) + \kappa(J-1)$$

one-term Ogden model

$$W = \frac{\mu_1}{\alpha_1}(\lambda_1^{\alpha_1} + \lambda_2^{\alpha_1} + \lambda_3^{\alpha_1} - 3) + \kappa(J-1)$$

two-term Ogden model

$$W = \sum_{p=1}^{2} \frac{\mu_p}{\alpha_p}(\lambda_1^{\alpha_p} + \lambda_2^{\alpha_p} + \lambda_3^{\alpha_p} - 3) + \kappa(J-1)$$

Yeoh model

$$W = \sum_{i=1}^{3} C_i(I_1 - 3)^i + \kappa(J-1)$$

5-parameter Mooney–Rivlin model

$$W = C_{10}(I_1-3) + C_{01}(I_2-3) + C_{11}(I_1-3)(I_2-3) + C_{20}(I_1-3)^2 + C_{02}(I_2-3)^2 + \kappa(J-1)$$

Demiray model

$$W = D_1\left[e^{D_2(I_1-3)} - 1\right] + \kappa(J-1)$$

modified Mooney–Rivlin model

$$W = C_1(\bar{I}_1 - 3) + D_1\left[e^{D_2(\bar{I}_1-3)} - 1\right] + \kappa(J-1)$$

Ogden material models are expressed in terms of principal stretches, $\lambda_j (j = 1, 2, 3)$, while the others are expressed in terms of invariants of Cauchy–Green deformation tensor. $\bar{I}_1 = J^{-2/3} I_1$ and $\bar{I}_2 = J^{-4/3} I_2$ with I_1 and I_2 being the first and second invariant of the unimodular component of the left Cauchy–Green deformation tensor,

$$I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2, \quad I_2 = \lambda_1^2\lambda_2^2 + \lambda_2^2\lambda_3^2 + \lambda_3^2\lambda_1^2$$

in which λ_i $(i = 1, 2, 3)$ is the principal stretch. $J = \det(\boldsymbol{F})$ and $\boldsymbol{F}$ is the deformation gradient. κ is the Lagrangian multiplier for the incompressibility and the remainder are material constants which will be determined by fitting experimental measurements.

2.2. Material testing and data fitting

Endarterectomy carotid plaque samples from 21 symptomatic patients were collected during surgery. The local ethics committee approved the study protocol and all patients gave written informed consent. Details of tissue preparation, testing protocol and equipment used have been described previously (Teng et al., 2014c). In total, stress–stretch curves were obtained successfully from 65 media strips from 17 samples, 59 FC strips from 14 samples, 38 lipid strips from 11 samples and 21 IPH/T strips from 11 samples. An energy-based average strategy (Teng et al., 2014c) was used to obtain the representative stress–stretch curve for each atherosclerotic tissue as shown in Fig. 1 and Fig. S1 in the Supplemental material.

Cauchy stress in terms of principal stretches can be obtained from each SEDF,

$$\sigma_{ii} = \lambda_i \frac{\partial W}{\partial \lambda_i} + \kappa, \; (i = 1, 2, 3) \tag{1}$$

where W is the part in SEDFs without the incompressible term, $\kappa(J-1)$. In the case of simple uniaxial extension with an incompressible tissue strip,

$$J = 1, \; \lambda_1 = \lambda, \; \lambda_2 = \lambda_3 = 1\frac{}{\sqrt{\lambda}} \text{ and } \; \sigma_{22} = \sigma_{33} = 0$$

The stress–stretch relationship can be therefore derived,

$$\sigma_{11} = \lambda_1 \frac{\partial W}{\partial \lambda_1} - \lambda_2 \frac{\partial W}{\partial \lambda_2} \tag{2}$$

and material constants can be obtained by minimizing the following objective function,

$$S = \sum_{j=1}^{N} |\sigma_{11j} - \sigma_{11j}^e| \tag{3}$$

The relative error is used to assess the fitting quality,

$$\gamma = \frac{\sum_{j=1}^{N} |\sigma_{11j} - \sigma_{11j}^e|}{\sum_{j=1}^{N} |\sigma_{11j}^e|} \times 100\%$$

in which σ_{11} and σ_{11}^e are the predicted and measured stress, respectively; and N is the number of data points. In this study, all material constants were constrained to be positive as one or some negative material constants might lead to unphysical phenomena, e.g., an increased stretch leads to a decreased stress.

2.3. Material stability

The material stability should be taken into account when a SEDF is used to describe the material properties and to calculate mechanical conditions within the plaque. The material stability is material constant- and loading-dependent (Adina, 2013; Ogden, 2003).

Convexity is one of the criteria for assessing the material stability to some extent defined as,

$$W''(\lambda_i) > 0 \tag{4}$$

implying the stress being a monotonic increasing function of the stretch ratio. If Eq. (4) holds for all $\lambda_i > 0$, W is globally strictly convex. However, convexity depends on the measures being employed, such as stretch ratio, true strain and Green strain. Convexity in one measure does not necessarily guarantee material stability, but failure of convexity may have undesirable consequences for the development of numerical schemes (Ogden, 2003).

The material stability can also be partially characterized by using stability curves under certain loading conditions (Adina, 2013). Considering an incompressible solid that undergoes homogeneous deformations, the equilibrium requires the equality of the external and internal virtual work as,

$$\lambda_i \frac{\partial W}{\partial \lambda_i} + \kappa = R_i \lambda_i \quad \text{(no sum on } i\text{)}$$

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