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The influence of vascular anatomy on carotid artery stenting: A parametric study for damage assessment

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ABSTRACT

Carotid artery stenting is emerging as an alternative technique to surgery for the treatment of symptomatic severe carotid stenosis. Clinical and experimental evidence demonstrates that both plaque morphology and biomechanical changes due to the device implantation can be possible causes of an unsuccessful treatment. In order to gain further insights of the endovascular intervention, a virtual environment based on structural finite element simulations was built to emulate the stenting procedure on generalized atherosclerotic carotid geometries which included a damage model to quantify the injury of the vessel. Five possible lesion scenarios were simulated by changing both material properties and vascular geometrical features to cover both presumed vulnerable and stable plaques. The results were analyzed with respect to lumen gain and wall stresses which are potentially related to the failure of the procedure according to previous studies. Our findings show that an elliptic lumen shape and a thinner fibrous cap with an underlying lipid pool result in higher stenosis reduction, while large calcifications and fibrotic tissue are more prone to recoil. The shielding effect of a thicker fibrous cap helps to reduce local compressive stresses in the soft plaque. The presence of a soft plaque reduces the damage in the healthy vascular structures. Contrarily, the presence of hard plaque promotes less damage volume in the fibrous cap and reduces stress peaks in this region, but they seem to increase stresses in the media-intima layer. Finally the reliability of the achieved results was put into clinical perspective.

1. Introduction

Atherosclerosic cerebrovascular diseases, in particular carotid artery occlusive disease, have been estimated to be responsible for about 20% of all ischemic strokes (Chaturvedi et al., 2005; Sacco et al., 2006), the second major cause of death and morbidity worldwide (Mathers et al., 2009).

Carotid artery stenting (CAS) is emerging as an alternative technique to surgery (Nallamothu et al., 2011) for the treatment of severe carotid stenosis ($>70\%$) in an elective patient population. The minimally invasive nature, lack of need for general anesthesia and the increased number of trained physicians contribute to the introduction of CAS into routine clinical practice (Halm, 2010). Nevertheless both short- and long-term efficacy of CAS is debated and the causes which lead to procedural failure are yet not completely understood (Brott et al., 2010; SPACE Trial, 2006; Yadav et al., 2004). The peri-procedural risk of stroke is high (SPACE Trial, 2006) and multi-center randomized trials demonstrated that the incidence of restenosis is higher at one year compared to the surgical counterpart (McCabe et al., 2005). Severe restenosis were strongly dependent on poor initial results mostly attributed to inadequate early angioplastic techniques which were also suspected to induce neointimal hyperplasia due to excessive dilation of the vessel. Thus, a balance is needed between post-implant stenosis and vessel dilation (Cosottini et al., 2010).

These clinical results seem to support the hypothesis that restenosis is related to tissue injury and response due to local stress concentrations which initiate the remodeling process leading to re-occlusion of the vessel (Timmins et al., 2011; Wentzel et al., 2003).

Currently, interventional diagnosis is based on the degree of luminal stenosis and plaque severity (ECST Trial, 1991; NASCET Trial, 1991; Ritter and Tyrrell, 2013; Rothwell and Goldstein, 2004). However stenosis alone may not adequately reflect the risk associated with the lesion. High-risk vulnerable plaques are characterized by a large necrotic lipid core, a thin overlying fibrous cap and ulceration while large calcifications seem not to be related to stroke symptoms (Fisher et al., 2005; Stary et al., 1995). Plaque vulnerability is extremely important in the context of CAS, where the plaque is manipulated

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by the endoluminal devices (Hellings et al., 2006). Large randomized trials have shown that the incidence of peri-procedural major adverse events increases with age (Redgrave et al., 2010; van Lammeren et al., 2011). In elderly patients larger lipid cores, and more calcified plaques are present as compared with younger patients which showed more fibrotic plaque tissue (van Lammeren et al., 2011). High prevalence of lipid cores is associated with higher risk of embolism during and after CAS (Uchiyama et al., 2011) and superficially calcified lesion could potentially embolize during deployment causing stroke (Clark et al., 2004).

Numerical simulations seem promising in assessing the plaque rupture risk. Thanks to advances in diagnostic imaging, plaque composition is detectable in vivo allowing the reconstruction of patient specific models for numerical analysis. Fluid–structure interaction and structural finite element analysis (SFEA) of in-vivo MRI based atherosclerotic carotid models were able to relate sites of rupture with plaque structural stresses (Teng et al., 2010), differentiate ruptured and unruptured plaques (Li et al., 2006; Tang et al., 2009b; Teng et al., 2011), refine risk stratification among symptomatic patient with/without hemorrhage or thrombi (Teng et al., 2011), correlate plaque stress and lumen curvature (Li et al., 2007; Li and Tang, 2008) and correlate biomechanical structural stresses with ipsilateral cerebrovascular ischemic symptoms (Sadat et al., 2010). Stress concentration was found to occur at the shoulders and at the thinnest fibrous cap regions while thicker fibrous caps prevent high stresses in the lipid core (Li and Tang, 2008; Loree et al., 1992; Versluis et al., 2006).

Computational frameworks have also been used to analyze the impact of different stent designs and interventional techniques on the outcome of endovascular procedures in various vascular districts (Auricchio et al., 2011; Holzapfel et al., 2005; Mortier et al., 2009; Wu et al., 2007). Although, the effect of anatomical differences and plaque composition on endovascular procedure outcomes has been rarely studied (Pericevic et al., 2009).

The majority of these studies suffers of different limitations: 2D or simplified 3D geometries not taking into account the complex plaque morphology, inadequate material descriptions which do not reflect the anisotropic behavior of both diseased and healthy tissues (Holzapfel et al., 2004) which lead to significantly different results compared to isotropic material models (Auricchio et al., 2012). The assumption of an anisotropic model can be sufficiently general to study the pathophysiological atherosclerotic condition (Kiousis et al., 2009) but over-stretching of the artery induces damage which can influence the biomechanical interpretation of the interactions between vessel and devices (Balzani et al., 2006).

Thus, procedure related conditions and adequate anatomical and material models challenge a complete accurate computational analysis that captures the correct mechanics of the interventional procedure.

In order to gain further insight on CAS, a virtual environment based on SFEA was built to emulate the stenting procedure on generalized carotid models with inhomogeneous plaque composition focusing on anatomical changes. Different morphology and composition of the atherosclerotic plaque (lipidic, fibrotic, calcified) were considered, incorporating a damage model to describe the vessel injury due to the angioplasty and stenting procedure.

2. Material and methods

2.1. Carotid models

2.1.1. Mesh generation

Three realistic carotid bifurcation models were created using the open-source script based program pyFormex (http://www.nongnu.org/pyformex). For all models, a fixed diameter of 7 mm was chosen for the common carotid lumen, while internal and external carotid were smoothly reduced to 5 and 4 mm respectively (Krejza et al., 2006). Vessel wall thickness was assumed to be 30% of the lumen diameter (Sommer et al., 2010a, 2010b).

The geometries were designed to have an eccentric plaque with minimum cross-section area of 15% of the original lumen (corresponding to 85% stenosis) and 20 mm length. The stenosis is smoothly reduced until restoring the normal diameter using a normalized gaussian shaped function. Only two layers were considered for the healthy vessel (adventitia, media-intima) in order to apply experimentally derived material model data (Sommer et al., 2010a, 2010b), while fibrotic media, lipid pool, fibrotic cap regions were considered for the lesion.

Assuming a circular vessel shape with a fibrous cap of 0.25 mm as baseline, the other geometries were modified (i) to increase the fibrous cap to 0.5 mm and (ii) create an elliptic lumen shape (to account for lumen curvature changes) as shown in Figs. 1 and 2. The mesh was generated with hexahedral elements. The density of the elements was increased at the plaque location, while coarser seeding was applied elsewhere (Fig. 1).

2.1.2. Material model

To mimic the mechanical response of the diseased vessel, we implemented the anisotropic hyperelastic constitutive model proposed by (Gasser et al., 2006) in a dedicated Abaqus subroutine to define anisotropic materials (VUANYSOHYPER). This model describes the hyperelastic strain energy function Ψ as the addition of the isotropic contribution of the tissue matrix Ψ_{mat} and the anisotropic contribution of two families of collagen fibers Ψ_{fib}.

$$\Psi = \Psi_{mat} + \Psi_{fib}$$

$$\Psi_{mat} = C_{10}(I_1 - 3)$$

$$\Psi_{fib} = \sum_{i=4,6} \frac{k_1}{k_2} \exp(E_i)$$

$$E_i = (1-\rho)(I_1 - 3)^2 + \rho(I_i - 1)^2$$

where C_{10}, k_1, k_2 are material parameters and ρ controls the dispersion of the fibers.

To allow for an explicit solution scheme, a dilatational component was added to the strain energy function Ψ

$$\Psi_{dil} = \frac{1}{D}\left(\frac{J^2-1}{2} - \ln(J)\right)$$

where J is the elastic volume ratio and D is a parameter dependent on the bulk modulus.

To account for the rupture of collagen fibers upon stretch, we included a damage model as described by Famaey et al. (2012) motivated in previous studies (Balzani et al., 2006). In this model, Ψ_{mat} and Ψ_{fib} are multiplied by a scalar damage value $(1-d)$

$$\Psi = \sum_{i=mat,\, fib_4,\, fib_6} (1-d_i)\Psi_i$$

where d_i is function of the undamaged strain energy

$$d_i = \gamma_i\left(1 - \exp\left(\frac{-\beta_i(\Psi_i)}{\tau_i}\right)\right)$$

$$\beta_i = \sup(\Psi_i^t - \Psi_i^{ini}),\ \forall\ t$$

in these expressions, β_i keeps track of the maximum occurrence of the undamaged function Ψ_i and Ψ_i^{ini} is an initial offset. The maximum value of the damage is determined by γ_i, whereas τ_i is a scaling constant.

The parameters of the vascular material models were taken from literature for both the healthy carotid (Sommer and Holzapfel, 2012) and the atherosclerotic

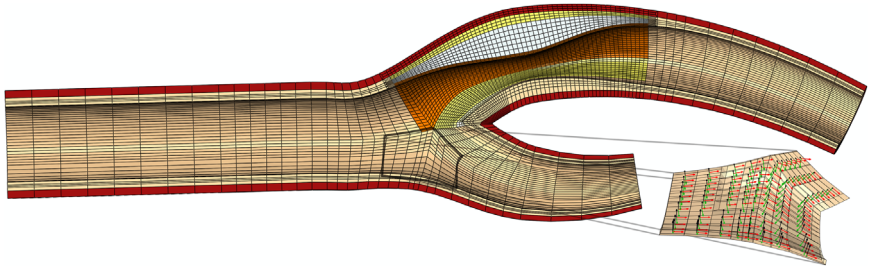

Fig. 1. Axial section of the baseline model with a detail of the elements local coordinate system.