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TOWARDS THE PREDICTION OF PLAQUE ONSET AND GROWTH IN CAROTID ARTERIES

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We describe a computational platform to predict atherosclerotic plaque onset and growth in carotids. It integrates *in-vivo* data, Computational Fluid Dynamics (CFD) simulations and a model for plaque growth linearly correlating the plaque progression with low values of time-averaged Wall Shear Stresses (WSS). We show that steady CFD simulations give the same averaged-WSS values as unsteady simulations. Therefore, the model for plaque growth can be coupled with steady simulations, reducing the computational costs. Finally, by comparing the numerical predictions with the *in-vivo* data, we show that a modification must be introduced in the plaque growth model to obtain acceptable results.

Keywords: hemodynamic simulations, atherosclerotic plaque, carotid arteries

1. Introduction

Cardiovascular Diseases (CVD) have emerged as a significant concern for global public health in recent decades due to their high risk, elevated mortality rates, and challenges associated with the diagnosis (Townsend *et al.*, 2016). Atherosclerotic plaque in the carotid arteries is a specific CVD condition that causes the narrowing of the vessel lumen, due to the deposition of substances on the arterial wall. This process obstructs the delivery of blood to downstream organs (Ross, 1999). Consequently, it is imperative to develop strategies aimed at preventing the onset of plaque by identifying key factors and providing healthcare professionals with reliable information (Rafieian-Kopaei *et al.*, 2014). Computational Fluid Dynamics (CFD) simulations, conducted on both idealized and patient-specific geometries, have become a widely utilized tool for analyzing blood flow dynamics and hemodynamic parameters that influence plaque growth. Some of these parameters, such as Wall Shear Stresses (WSS), are challenging to measure directly *in-vivo* (Lopes *et al.*, 2020). CFD simulations, however, need proper geometry definition and boundary conditions. We consider herein the patient-specific geometry and cardiac-cycle flow-rate waveform from *in-vivo* data. Moreover, realistic simulations are three-dimensional in complex geometries and unsteady following the cardiac cycle; therefore, the related computational costs and times are large. Since the growth of atherosclerotic plaques occurs over times much larger than the cardiac cycle period, a possible simplification of the steady flow assumption can be adopted for blood circulation, and the results used to predict plaque growth (Lopes *et al.*, 2020; Marshall *et al.*, 2004). This may allow for a more computationally efficient analysis,

allowing one to model the progression of plaque development over an extended period without prohibitive computational costs (Tang *et al.*, 2008; Gessaghi *et al.*, 2011). Finally, CFD simulations must be coupled with a model predicting the plaque growth.

In this work, we integrate the WSS model by Tang *et al.* (2008) into CFD simulations of patient-specific geometries. To the best of our knowledge, this is the first time this model has been utilized to predict atherosclerotic plaque growth in patient-specific carotid arteries. The plaque growth model establishes a linear correlation between the thickening of the innermost intimal layer of the arterial vessel and the time-averaged WSS exerted on the wall. The thickening of the carotid intimal layer is implemented through morphing (Biancolini *et al.*, 2020; Capellini *et al.*, 2021). We first investigate whether accurate values of WSS can be provided by steady simulations, reducing in this way the computational costs. We evaluate then the capability of this approach in predicting the plaque onset and growth in the considered patient-specific carotid geometry, and we propose a modified version of the model for plaque growth, aimed at improving the agreement with clinical data.

2. Materials and methods

The clinical dataset includes *in-vivo*-measured geometries and flow rates of the diseased right and left carotid arteries from a 78-year-old male patient (Fig. 1a). The diseased geometry is obtained through segmentation of Computed Tomography (CT) scans. The corresponding healthy geometries are derived from the diseased ones by applying an idealized endarterectomy (Fig. 1b). The volumetric flow rates at the inlet Common Carotid Artery (CCA) and the outlets, Internal Carotid Artery (ICA), and External Carotid Artery (ECA) are obtained by interpolating 4D-flow Magnetic Resonance Imaging (4D-MRI) data (Fig. 2).

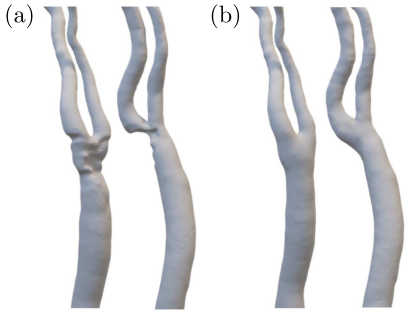

Fig. 1. Patient-specific (a) diseased and (b) healthy right and left carotids geometrical models

CFD simulations are carried out for a laminar and incompressible blood flow ($\rho = 1050\,\mathrm{kg/m^3}$). Blood is considered as a non-Newtonian fluid to capture the shear-thinning effect near the arterial wall that influences the WSS field in medium-small vessels like carotids; the Carreau-Yasuda model is adopted (Weddell *et al.*, 2015). We carry out CFD simulations using a finite-volume commercial code. For simulations involving patient-specific flow-rate waveforms, we conducted unsteady simulations. Conversely, when employing a time-constant inflow condition, we conducted steady-state simulations since the flow remains constant over time. In steady-state simulations, the Navier-Stokes equations are solved in their steady-state formulation, neglecting time derivatives. Conversely, unsteady simulations solve the Navier-Stokes equations as they are, considering time-dependent variables. The fluid domain is discretized by using a polyhedric grid defined after the grid independence study, and the 3D Navier-Stokes equations are discretized through finite volumes. An implicit unsteady time scheme is applied for unsteady simulations. In the steady simulations, we impose a constant fully-developed parabolic velocity profile at the inlet based on the cycle-averaged mean value of the flow rate, as shown in Fig. 2. Furthermore,

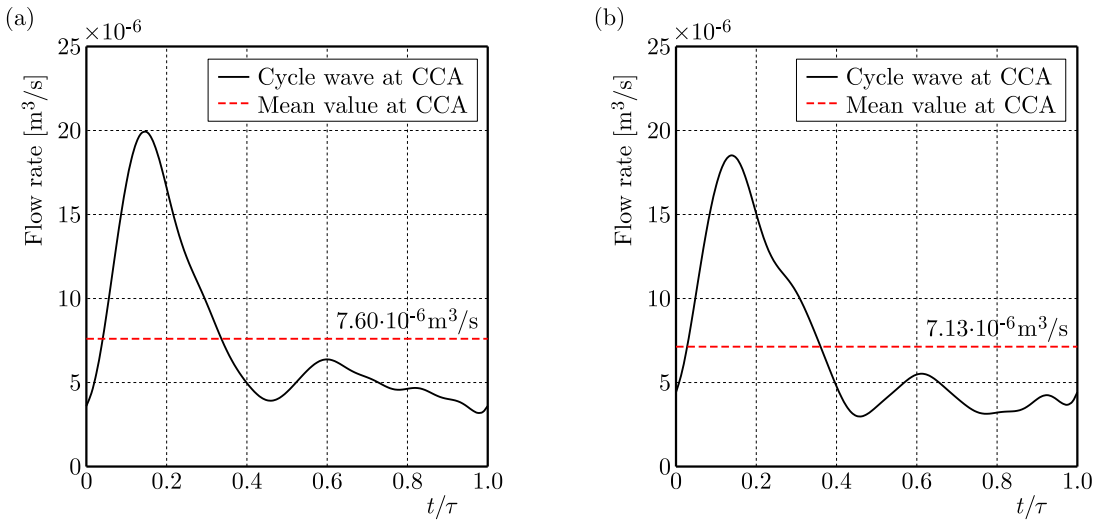

Fig. 2. Patient-specific flow rates: (a) right carotid at CCA and (b) left carotid at CCA

a flow rate split ratio is imposed at the two outlets, ICA : ECA = 0.66 : 0.34 for the right and ICA : ECA = 0.61 : 0.39 for the left carotid (Marshall *et al.*, 2004) with a reference pressure equal to 12438.98 Pa.

CFD simulations are coupled with the WSS-based model of plaque growth from Tang *et al.* (2008) which computes the plaque growth rate $\dot{e}$ as

$$\dot{e} = k_1 - k_2\tau \tag{2.1}$$

where $k_1 = 1.85 \cdot 10^{-2}$ cm/(3months) and $k_2 = 1.73 \cdot 10^{-3}$ cm/(3 months·Pa). Moreover, we have developed a modified version of the model, the WSS_{th} model, that incorporates a threshold value τ_{th}, which confines the plaque growth to regions with low values of τ, thereby preventing plaque onset in the straight portions of vessels, which is unrealistic. The threshold value is set to $\tau_{th} = 0.3$ Pa as suggested in Gessaghi *et al.* (2011). Thus, the updated version of the model is as follows

$$\dot{e} = \begin{cases} k_1 - k_2\tau & \text{for} \quad \tau < \tau_{th} \\ 0 & \text{for} \quad \tau > \tau_{th} \end{cases} \tag{2.2}$$

3. Results and discussion

In Fig. 3, we compare the results of steady and unsteady simulations. Specifically, Fig. 3a shows the time-averaged WSS fields $\overline{\tau}$ obtained from patient-specific unsteady simulations. In Fig. 3b, the WSS field τ for the steady simulation is depicted, and in Fig. 3c, the difference $\overline{\tau} - \tau$ is illustrated. The differences are negligible. Therefore, we can conclude that steady simulations with the time-averaged patient-specific inflow flow rate give WSS that are identical to time-averaged WSS obtained in realistic unsteady simulations. Thus, in the following, the plaque growth will be evaluated on τ with reduced computational costs.

The CFD-predicted values for the plaque onset and early-stage growth are shown in Figs. 4a,c for the WSS-based model from Tang *et al.* (2008) and in Figs. 4b,d for the modified version. The results report the displacement Δe of the intimal layer thickness over a year.

The original version of the WSS-model from Tang *et al.* (2008) lacks precision in predicting the onset location, as it suggests the plaque growth throughout, including in the straight branches of the carotid with high values of τ. Conversely, the modified version of the WSS-model,

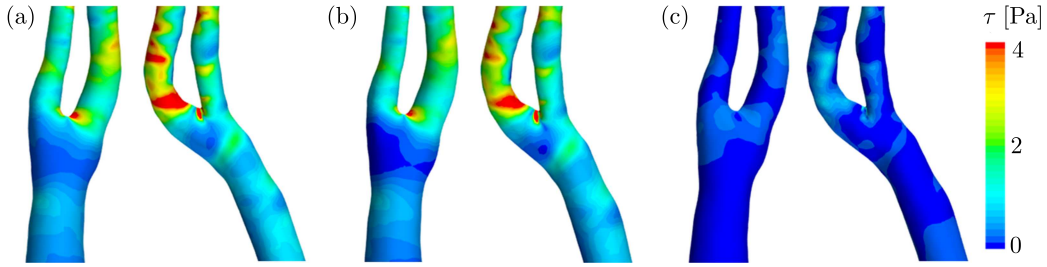

Fig. 3. WSS fields for right and left carotids: (a) $\overline{\tau}$, (b) τ, and (c) $\overline{\tau} - \tau$

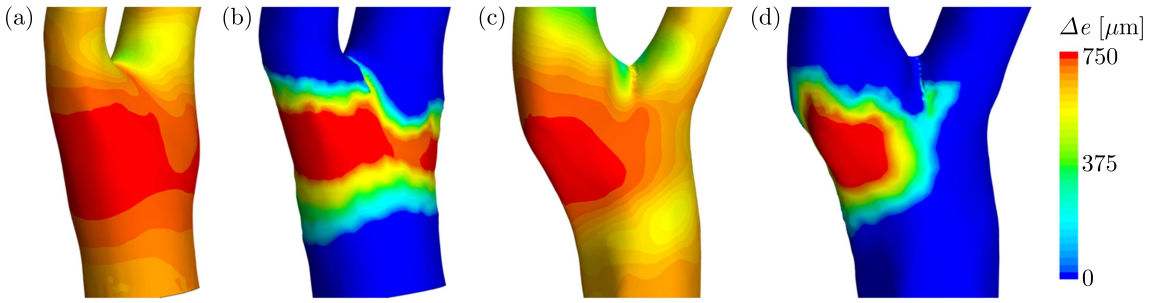

Fig. 4. Displacement fields of the plaque for right and left carotids: (a) WSS model, (b) WSS_{th} model, (c) WSS model, and (d) WSS_{th} model

incorporating the threshold, better delineates and identifies the onset region. The plaques indeed tend to develop near the bifurcation with low values of τ, where the plaques have actually formed in the patient (refer to Fig. 1a). Regarding the plaque growth, both versions of the WSS-model provide overestimated predictions for the plaque growth rate $\dot{e}$, and consequently, for Δe after one year (in comparison, for instance, with the data from the review paper by Lopes *et al.* (2020)). Therefore, while the modified WSS-model effectively identifies the plaque onset, both are inadequate for precise quantitative predictions of the plaque growth without additional calibration of the model constants. Therefore, future work could be devoted to (i) calibrating the constants of the WSS-based model to obtain a more accurate growth rate and (ii) considering more complete plaque growth models, such as the one proposed in Gessaghi *et al.* (2011).

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