Computational simulation of carotid stenosis and flow dynamics based on patient ultrasound data – a new tool for risk assessment and surgical planning

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Conflict of interests

The authors declare no conflict of interests.

Acknowledgments

This work was partially done in the scope of project PTDC/SAU-BEB/102547/2008, “Blood flow simulation in arterial networks towards application at hospital”, financially supported by FCT – *Fundação para a Ciência e a Tecnologia* from Portugal.

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ABSTRACT

Purpose: There is nowadays extensive experimental and computational investigation on the pathophysiology of atherosclerosis, searching correlations between its focal nature and local hemodynamic environment. The goal of this work is to present a methodology for patient-specific hemodynamics study of the carotid artery bifurcation based on the use of ultrasound (US) morphological and blood flow velocity patient data.

Methods: Subject-specific studies were performed for two patients, using a developed finite element code. Geometrical models were obtained from the acquisition of longitudinal and sequential cross-sectional ultrasound images and boundary conditions from Doppler velocity measurements at the common carotid artery.

Results: There was a good agreement between ultrasound imaging data and computational simulated results. For a normal and a stenosed carotid bifurcation the velocity, wall shear stress (WSS) and WSS descriptors analysis illustrated the extremely complex hemodynamic behaviour along the cardiac cycle. Different patterns were found, associated with morphology and hemodynamic patient-specific conditions. High values of time-averaged WSS (TAWSS) were found at stenosis site and for both patients TAWSS fields presented low values within areas of high oscillating shear index and relative residence time values, corresponding to recirculation zones.

Conclusion: Simulated hemodynamic parameters were able to capture the disturbed flow conditions in a normal and a stenosed carotid artery bifurcation, which play an important role in the development of local atherosclerotic plaques. Computational simulations

based on clinic US might help improving diagnostic and treatment management of carotid atherosclerosis.

Keywords: Carotid artery bifurcation; Atherosclerotic plaque; Stenosis; 3D reconstruction and mesh generation; Doppler ultrasound.

1. Introduction

Many studies looking for correlation between local hemodynamics and development of atherosclerosis have been done. Artery bifurcations and curvature regions are prone sites to develop initiation of atherosclerotic plaques, and often present disturbed wall shear stress and flow disruption [1-5]. The common carotid artery (CCA) bifurcation and the proximal external (ECA) and internal (ICA) carotid arteries are prone sites to atherosclerosis associated diseases. Several studies point to a complex interrelationship among vascular geometry, local hemodynamics, vascular aging, and atherosclerosis [2,6-9]. Although the relationship between carotid plaque morphology and stroke pathogenesis is not yet fully understood it is widely accepted that **the wall shear stress (WSS)** plays an important role in the development and progression of atherosclerosis. **WSS** within the stenosis is usually high due to flow acceleration in the reduced lumen. Diseased vessels and post-stenotic regions experience a significantly different biomechanical environment than healthy vessels, due to high Reynolds numbers and the presence of transitional and turbulent flow, which may be responsible for cell damage or plaque disruption [3]. Namely the presence of turbulence associated with high WSS and large spatial WSS gradient is thought to enhance mass transport into the arterial wall and make the plaque vulnerable to rupture [3,4,10].

Most studies aiming to investigate turbulent flow characteristics within stenosed vessels were conducted experimentally and employing numerically idealized stenosis geometries[10-13]. Image-based computational fluid dynamics (CFD) studies of real arterial anatomical geometries appeared in the late 1990s, either using **computed tomography (CT)** and magnetic resonance imaging (MRI) [14-20], or ultrasound (**US**) imaging [21-24]. Non-invasive and inexpensive ultrasound imaging is a widely used instrument for medical diagnosis of arterial diseases, like atherosclerosis; furthermore CCA bifurcation is quite superficial and allows real-time images of endovascular structure with high spatial resolution, and in vivo measurements of velocities with minimal risk for the patient[12,25-27].

Blood flow velocity spectral waveforms at the carotid arteries of older adults are significantly different from those of young adults [28]. For an older adult a common feature is the presence of a strong secondary peak during early systolic deceleration, typically associated with flow disturbances. While for large-scale studies of CCA bifurcation hemodynamics the use of a typical flow waveform shape is sufficient [10,12,20,28], for a single patient study a subject-specific waveform collected in clinical practice yields a more accurate assessment of flow characteristics. Furthermore for image-based hemodynamics studies, the carotid artery domain of interest is always truncated and the application of the inlet and outlet boundary conditions will affect the numerical accuracy of the WSS derived parameters dramatically[17,28,29].

Selecting patient specific CCA bifurcation with stenosis, as diagnosed by ultrasound, the present investigation developed a platform that will provide estimates of disturbed flow conditions and forces at the carotid artery wall towards the link between hemodynamic behaviour and stenosis pathophysiology. Computational simulation of detailed morphological and hemodynamic carotid bifurcation characteristics was

performed using an ultrasound based semi-automatic methodology for reconstruction and structured meshing, and the incompressible Navier–Stokes equations for blood flow modelling. Post-processing results showed WSS and its descriptors to be extremely sensitive to variation in geometry enabling early detection of vessels at risk and prediction of stenotic disease progression. Furthermore, specific carotid bifurcation hemodynamic analysis could be used to model/replicate turbulence conditions at high-grade stenosis where the velocity is very high and ultrasound measurements can suffer from inaccuracies.

The present research was partially done in the scope of a project with a public hospital using simple, inexpensive and non-invasive carotid artery US as a preliminary diagnostic tool for artery disease. Hemodynamic simulation post-processing will allow accurate characterization and identification of patients with high probability for developing cerebral vascular events.

2. Materials and methods

The computational investigation of patient specific arterial morphology and blood flow behaviour using a finite element code requires four sequential steps[30]: 1)acquiring ultrasound morphological and blood flow velocity data of patients' carotid artery cervical segments,2) reconstructing a computational surface of the ultrasound-based carotid image,3)defining a 3D finite element mesh and 4) performing a computational blood flow simulation.

Aiming to study complex flow features near the stenosis two patients volunteered to participate; Patient 1 (P1) was a 57-year-old man with a CCA bifurcation stenosis, and for inter-individual comparison, patient 2 (P2) was a 63-year-old man with no visible carotid atherosclerotic plaque.

Data was obtained at São João Hospital Centre, a university hospital in Porto, Portugal. The study was approved by the institutional ethical committee and informed consent of each volunteer was obtained. Carotid artery examinations were performed according to a proposed created protocol.

2.1. Acquisition of ultrasound morphological and blood flow velocity data of patients' carotid artery cervical segments

Experimental data necessary for the present study were obtained by the same experienced sonographer (R.S.) dedicated to neurovascular ultrasound at the Neurosonology Unit of the Department of Neurology of São João Hospital Centre[30].

Using a commercial colour ultrasound scanner (Vivid e; GE, Milwaukee, WI, USA) and a linear array probe (GE 8L-RS), high-resolution ultrasound images with 256 level of gray scale and pulsed-wave Doppler PW were collected along the CCA, its bifurcation and proximal segments of ICA and ECA from approximately 2 cm before CCA bifurcation, until post-bulbar ICA and ECA, including the bifurcation entrance (APEX). Raw DICOM data were exported from the echography device for offline analysis.

The longitudinal and transversal set of B-mode images were recorded at end-diastole, to control physiologic variations of diameter within cardiac cycle. End diastolic point was visually identified selecting the video frame of the instant of minimum artery diameter. Cross-sectional locations were registered at the longitudinal bifurcation image, to allow the correct reconstruction of the CCA bifurcation luminal surface. In order to minimize flow modelling inaccuracies, tracking of the US probe was done by marking positions along the artery bifurcation relying on the ability to manually guide the US probe. During medical examination of patient P1, ICA stenosis was measured

according to European Carotid Surgery Trial (ECST), the percentage of luminal diameter narrowing at the most stenotic region.

Using US pulsed-wave (PW) mode with a 2 mm sample volume, axial flow velocity waveforms were obtained at several specific locations from 2 cm before CCA bifurcation to the most distal region of ICA and ECA arteries that could be measured with angle of insonation $\leq 60^\circ$. For each patient flow velocity waveforms obtained from PW images were collected using Matlab. Considering waveform data from three cardiac cycles Fourier analysis allowed the determination of the first seven harmonics coefficients used to set Womersley profiles. Early and mid-diastolic minima and peaks of flow velocity waveforms were found by a forward search from systolic peak for changes in the sign of the derivative. The mid deceleration phase was considered to be the cardiac cycle instant corresponding to half-peak midway between systolic peak and first early-minimum [31].

2.2. Reconstruction of a computational surface of the ultrasound-based carotid image

Given a series of 2D longitudinal and cross-sectional images of the common carotid artery bifurcation, the most obvious method of reconstruction was to outline, either manually or automatically, the boundaries of the lumen and of the artery wall to produce a skeleton of the vessel [30].

The selected 2D longitudinal and cross-sectional images were manually segmented by two neurosonologists (EA, PC). In the plaque region, two contours were delineated for each cross-sectional image, one for the inner arterial wall in contact with the lumen and another for the lumen contour incorporating the plaque surface (Fig. 1). Then, 2D smooth lumen contours were stacked in the axial direction according to each image location obtained during data acquisition. The reconstructed lumen surface was

smoothed in order to reduce misalignment errors due to patient's involuntary movements during scan.

<insert Figure 1 around here>

The obtained polygonal surface was not directly usable for generating a suitable computational mesh. In order to ensure fully developed velocity profiles at the inlet (before bifurcation) and to minimize the influence of outlet(after bifurcation) boundary conditions, cylindrical flow extensions with a length of four times the local diameters were added at the inlet and outlet locations, in the direction of the centerline.

2.3. Definition of a 3D finite element mesh

A structured hexahedral mesh (Fig. 2) of the carotid bifurcation lumen was constructed using grid generation commercial software FEMAP (Siemens PLM software). Although hexahedral meshes are generally more difficult to generate and time consuming, they were employed because for the same accuracy of the result, computer simulations using hexahedral meshes compared to tetrahedral/prismatic meshes converge better, require less computational time, and allow a better calculation of the WSS [16,32].

<insert Figure 2 around here>

The generation of the volume mesh with hexahedral elements started by defining three confining cross-sections, created as artificial separations of the CCA, ECA and ICA. Then the filling of the previously defined surface geometry was performed by

dividing the domain into six parts; each part was meshed independently, maintaining finite elements continuity at each contact surface. Fig. 2 shows a course mesh of the carotid bifurcation model (patient P1). Each vessel was treated independently. Firstly, a 2D quadrilateral mesh was considered in a defined cross-section. Then, a volume mesh of hexahedrons was generated by sweeping or extruding the 2D mesh of a section (quadrilateral) along a path. Using meshes with elements organized along the main flow direction faster convergence and more accurate numerical solutions are acquired, as blood motion in vessels is highly directional [15,32-34].

The grid distribution was not uniform to allow a finer mesh at the bifurcation, near the stenosis and the walls. Calculation precision at the boundary layer was improved gradually employing thinner grids in the radial direction, near the vessel wall [15,32-34]. With the presented semi-automatic technique, it was possible to reduce the required procedure time and the operator intervention aiming a mesh independent solution.

2.4. Computer simulation of the blood flow

The time-varying 3D velocity and wall shear stress fields were computed using a finite element solver developed in our university [30,35-37]. Considering isothermal conditions, the time dependent incompressible blood flow is governed by the Navier-Stokes equations given as:

$$\rho \left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = \nabla \cdot \boldsymbol{\sigma} + \mathbf{f} \quad \text{and} \quad \nabla \cdot \mathbf{u} = 0 \quad (1)$$

where $\mathbf{u}$ and $\boldsymbol{\sigma}$ are the velocity and the stress fields, ρ the blood density and $\mathbf{f}$ the volume force per unit mass of fluid. Blood flow was modelled as an isotropic, incompressible, homogeneous, Newtonian viscous fluid, with a specific mass value equal to 1060 kg/m³ and a constant dynamic viscosity value equal to 0.0035 kg/(m.s); Blood is a complicated

non-Newtonian fluid with shear thinning and viscoelastic properties, especially when the shear rate is low. However the flow field of the carotid bifurcation usually covers a wide range of shear rate typically between 250 and 450 s⁻¹ averaged over the cardiac cycle, and blood exhibits mainly Newtonian property [10,15,16,38,39]. The components of the stress tensor are defined by the Stokes' law:

$$\boldsymbol{\sigma} = -p\mathbf{I} + 2\mu\boldsymbol{\epsilon}(\mathbf{u}) = -p\mathbf{I} + \mathbf{S} \quad (2)$$

where p is the pressure, $\mathbf{I}$ the unit tensor, μ the dynamical viscosity $\boldsymbol{\epsilon}(\mathbf{u})$ the strain rate tensor and $\mathbf{S}$ the deviatoric stress. Given appropriate boundary and initial conditions, the equation system Eq. (1) can be solved for the velocity and the pressure. In this study the biochemical and mechanical interactions between blood and vascular tissue were neglected. In diseased vessels wall motion is further reduced as the arteries are less compliant and the assumption of zero wall motion and the non-slip imposed condition reflected the intended hemodynamic conditions. At the flow entrance Dirichlet boundary conditions were considered prescribing the Womersley velocity profile for the time dependent value u_D of the velocity on the portion τ_D of the boundary $\mathbf{u}(\mathbf{x}, t) = \mathbf{u}_D(\mathbf{x}, t)$, $\mathbf{x} \in \Gamma_D$. At the outlets, a common approach was applied by imposing Dirichlet velocity conditions at ICA (Womersley profiles) and stress-free boundary condition at the ECA section [28,40-42].

$$\left(-p\delta_{ij} + \mu \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \right) n_j = h_i \quad i, j = 1, 2, 3 \text{ on } \Gamma_N \quad (3)$$

where n_j are the components of the outward pointing unit vector at the outflow boundary. The numerical procedure for the discretization in space uses the Galerkin-finite element interpolation of mixed type [35-37].

In order to solve the nonlinear system of equations derived from the discretization of the flow equations on the computational grid, the upwinding method was applied and

the backward Euler implicit time integration scheme was implemented to obtain the solution at each time step of the transient analysis.

At CCA inlet and ICA outlet of the carotid geometry, physiologically realistic boundary conditions were imposed. Womersley velocity profiles were derived from the pulsatile velocity waveforms obtained by pulsed Doppler images and imported as input data into the developed software.

Womersley introduced an approach on pulsatile blood flow[43]. Considering a Poiseuille flow, the longitudinal velocity, $v(r, t)$ of an incompressible fluid in a circular pipe with radius R , is given as a function of the distance r from the axis and of the time t :

$$v(r, t) = \frac{AR^2}{i\mu\alpha^2} \left(1 - \frac{J_0\left(i^{3/2}\alpha\frac{r}{R}\right)}{J_0\left(\frac{3}{2}\alpha\right)} \right) e^{i\omega t} \quad (4)$$

where J_0 is the Bessel function, α the Womersley number and the term $A = \frac{1}{\rho} \frac{\partial p}{\partial x}$ is the pressure gradient. Substituting in the previous equation the measured velocity at the lumen center, $v(0, t)$ and as $J_0(0)=1$, equation (4) becomes:

$$v(0, t) = \frac{AR^2}{i\mu\alpha^2} \left(\frac{J_0\left(i^{3/2}\alpha\right)-1}{J_0\left(\frac{3}{2}\alpha\right)} \right) e^{i\omega t} \quad (5)$$

Approximating the Doppler axial velocity $v(0, t)$ by a Fourier cosine series, $v(0, t) = k \cos(\omega t + \phi)$ with k and ϕ being the magnitude and the phase, and expressing the pressure gradient as a periodic function of time using Fourier series, $|A|$ can be obtained:

$$|A| = |v(0, t)| \left| \frac{i\mu\alpha^2}{R^2} \frac{J_0\left(\frac{3}{2}\alpha\right)}{J_0\left(i^{3/2}\alpha\right)-1} \right| \quad (6)$$

and

$$\phi(A) = \phi(v(0, t)) + \phi\left(\frac{i\mu\alpha^2}{R^2} \left[\frac{J_0\left(i^{\frac{3}{2}}\alpha\right)}{J_0\left(i^{3/2}\alpha\right)-1} \right]\right) \quad (7)$$

The true pressure gradient is the real part of the complex pressure gradient and is given by:

$$\frac{1}{\rho} \frac{\partial p}{\partial x} = |A| \cos(\omega t + \phi(A)) \quad (8)$$

Fig. 3 shows the selected ultrasound images used to calculate the inlet CCA Womersley velocity profiles for patients P1 and P2.

<insert Figure 3 around here>

Flow discrepancies due to small branches or uncertainties in measurements and the assumption of rigid wall in the simulations outlet blood flow velocities, were corrected using the instantaneous blood flow velocity ratio ICA:ECA and maintaining the CCA flow. It is, however, possible that the distensible arteries produce instantaneous flow mismatches at the bifurcation [28,31].

For patient P1 a mesh sensitivity analysis was carried out under steady conditions to assure grid independence[36]. The imposed inlet flow corresponds to the systolic peak. Five meshes were created with a number of elements ranging from 40 to 60 thousand hexahedrons and a mesh of 55245 hexahedrons and 60340 nodes was chosen based on ICA flow and maximum nodal WSS. For the transient analysis, and using the selected mesh, temporal convergence was studied and time step refinement was performed until changes in velocities and maximum nodal WSS became insignificant between the adopted and finer time steps (less than 1.5%). Due to the large amount of involved computational work, we limited the transient study to the chosen mesh, adopting a constant time step equal to 2.5×10^{-3} s. For each patient a complete study can be

performed within one day as clinical examinations take around one hour, model definition and mesh generation 2 hours, and computational convergence of the finite element simulation approximately 15 hours running on a PC (3.3GHz Intel, CPU 16 GB Ram).

2.5. WSS-based hemodynamic descriptors

In this work three hemodynamic WSS based descriptors were used, the time averaged WSS (TAWSS), the oscillating shear index (OSI) and the relative residence time (RRT). These descriptors have been found to be the best metrics for measuring low and oscillating shear at the carotid bifurcation [2,30,44]:

$$TAWSS(\mathbf{s}) = \frac{1}{T} \int_0^T |\mathbf{WSS}(\mathbf{s}, t)| dt \quad (9)$$

$$OSI(\mathbf{s}) = 0.5 \left[1 - \left(\frac{\left| \int_0^T \mathbf{WSS}(\mathbf{s}, t) dt \right|}{\int_0^T |\mathbf{WSS}(\mathbf{s}, t)| dt} \right) \right] \quad (10)$$

$$RRT(\mathbf{s}) = \frac{1}{(1-2 \cdot OSI) \cdot TAWSS} = \frac{T}{\left| \int_0^T \mathbf{WSS}(\mathbf{s}, t) dt \right|} \quad (11)$$

where T is the total time of the cardiac cycle, $\mathbf{s}$ is the location on the vessel wall and t is the time.

The first, TAWSS, is used to evaluate the total shear stress exerted on the wall throughout a cardiac cycle; OSI is a measure of directional changes in WSS over the cardiac cycle and its maximum value equal to 0.5 indicate regions with the high oscillating shear stress and greater susceptibility to develop atherosclerosis. Both metrics are related to the amount of shear stress distributed across the carotid wall. The third parameter, RRT, is a measurement of how long the particles will stay near the wall.

3. Results

Hemodynamic results obtained for the two patients are presented. For patient P1, presenting an ECST grading of stenosis equal to 50%, systolic values of numerical and Doppler measured velocities at six different locations are shown in Fig. 4. At all positions in the carotid bifurcation there was a good agreement between the simulated flow velocities and those obtained by Doppler ultrasound measurements and the maximum deviation equal to 5% was found in ICA, downstream stenosis(location 4 in Fig.4)

<insert Figures 4 and 5 around here>

Differences were found between CCA flow rates for the two patients, with mean rates varying by 20% (395 ml/min for P1 and 323 ml/min for P2). Inter-individual variation in flow dynamics at the carotid artery bifurcation was performed comparing the described stenosed bifurcation (P1) with the carotid bifurcation from a subject without stenosis (P2). Fig. 5 shows the velocity distributions at two instants of the cardiac cycle, systolic peak and mid-deceleration phase, for the two patients. In the enlarged bulb region high velocity gradients can be observed and a stagnation zone, larger during deceleration phase, was detected for the two patients. Particularly, for the patient P1 at the stenosis, high velocities were observed throughout the whole area. The increase in the cross-sectional area, just distal to the stenosis, contributed to the blood flow velocity heterogeneity observed. In distal sections, the blood flow velocity lumen distribution was still influenced by the stenosis. Peak high velocity gradients were detected at ECA during systolic phase for the two patients..

<insert Figure 6 around here>

WSS distribution near peak systole for the two volunteers is shown in Fig. 6. Due to the geometrical asymmetry of the bifurcation, results are presented from both anterior and posterior vessel walls. For P1, maximum WSS values of approximately 30 and 42 Pa were observed within the ICA stenosis (P1) at systole, in outer and inner walls respectively, while for patient P2, the maximum WSS, 22 Pa, was located in the inner wall of ECA proximal to the bifurcation apex. Although low values were concentrated around both bifurcations, for P1 low WSS values were found in the bulb region of ICA and also in the outer and inner walls of ICA upstream and downstream the stenosis identifying abnormal flow. For P2, low WSS patches in the CCA were contiguous with the carotid bulb low WSS region.

<insert Figure 7 around here>

WSS-based descriptors were evaluated throughout a cardiac cycle at the end of the simulation. The distributions of three flow indicators on the luminal surface of volunteers P1 and P2 are shown in Fig.7. As commonly, apparent flow disturbances were captured at the same sites by TAWSS (low values) and OSI and RRT (high values) and areas of high OSI and RRT lie within areas of low TAWSS. Regions of high OSI values up to 0.5 were found at the ICA origin for both bifurcations and downstream stenosis for patient P1.

4. Discussion

A qualitative comparison between hemodynamic of stenotic (P1) and a healthy (P2) carotid bifurcation was performed. Different patients exhibited different velocity

patterns associated with their morphology and hemodynamic patient-specific conditions. For patient P1 maximum velocity gradients, associated with reduction in lumen section, occurred at the stenosed ICA during systolic peak. For both patients high velocity gradients were detected at ECA probably due to the sharp unevenness of the vessel wall.

The WSS distributions near peak systole obtained for the two patients, shown in Fig. 6, presented significantly different WSS patterns. The main features expected from fluid dynamics as recirculation zones characterized by patches of low WSS in ICA bulb region, were successfully captured. For P1 low WSS values could also be observed in ICA outer and inner walls, distally to stenosis associated with stenosis-induced heterogeneity of blood flow velocities near the inner and outer walls. The same recirculation zones downstream the ICA stenosis could be noticed in the velocity distribution presented in Fig. 5. For P2, low WSS patches in CCA were contiguous with the carotid bulb low WSS region. Extremely high WSS values of approximately 42 Pa were observed within the ICA stenosis (P1) at systole, in outer and inner walls, corresponding to high velocity-gradients with a skewed velocity profile. Relatively high WSS values were observed in ECA inner wall for the two patients according with the observed high velocity gradients.

Two different view angles of TAWSS distributions obtained for the two volunteers are shown in Fig. 7. While for the non-stenosed patient, low TAWSS values at ICA origin were contiguous with bulb region, for patient P1 low values were found in the outer wall downstream and upstream the stenosis identifying turbulence.

In this study and for the two patients, areas of high OSI lying within areas of low TAWSS were located on the outer wall of ICA of patient P1 (Fig. 7), which correspond to recirculation zones consistent with other studies [39,42,44]. OSI fields showing high values were also located on the outer wall of the ICA origin for both patients, which

once more is found in other studies [39,42,44]. Following the same behavior RRT distribution captured the main features of both TAWSS and OSI presenting high values at ICA origin for both patients and downstream the stenosis for patient P1, indicating localized flow reversal or varying flow direction.

For both patients, the three WSS indicators were able to capture disturbed flows to the same surface regions. This finding is in agreement with recent studies that recommend the RRT as a robust single metric of low and oscillatory shear [39,42,44].

WSS-based descriptors identified ICA origin as the region of abnormal flow for both a normal and a stenosed carotid bifurcation. For carotid bifurcation with no visible stenosis, our findings were consistent with the previous works that only study normal carotid bifurcations [7,39,44]; this finding is in agreement with the fact that plaques tend to occur at the ICA. Results of the stenosed ICA showed that the existence of plaques can be associated with local disturbed haemodynamics that might be important in further progression of the lesions and direct endothelial injury with increase of the risk of thrombosis [42]. These findings are consistent with previous studies with normal carotid bifurcations.

Flow disturbances at the ECA branch were also captured by the three descriptors for the two carotid bifurcations studied, at extended sites in the normal ECA. According to Lee [41] this might be associated with branch geometry and tortuosity occurring at the inner wall of ECA leading to high OSI values where the jet impinges on the wall.

The assumption of rigid walls, justified by the age of patients and the presence of a stenosis, and the consideration of Newtonian rheology are, among others, limitations of this work introduced as well by other researchers [8,9,10,15,16,28,29,41]. Uncertainties arising from these assumptions have a minor effect on the resulting carotid bifurcation flow dynamics and are less important than the uncertainty from the geometric

reconstruction of the model [10,15,16,38,45]. Furthermore, Newtonian fluid simulations require less CPU effort and storage compared with non-Newtonian fluid simulations due to the calculation of the diffusion matrix at every time step and is commonly considered for large vessels [10,15,16].

The adoption of straight flow extensions in order to minimize the influence from outlet boundary conditions and to ensure fully developed velocity at the CCA inlet, is a general practice to justify the adoption of Womersley theory valid for long straight tubes; this assumption, still debated whether it can influence bulk flow topology, may introduce errors in the estimation of flow patterns and WSS at the bifurcation [29,42,45]. However in recent works [29,46] it was concluded that at least three CCA diameters reconstructed length is sufficient to model normal carotid bifurcation hemodynamics. On the other hand, due to flow disturbances downstream ICA stenosis the consideration assuming a Womersley profile at the ICA outlet, while considering a 4 diameter flow extension, may influence the numerical solution of carotid hemodynamics [29,42,45]. Another limitation of this study is the correction of measured outlet flow rates by scaling the CCA flow according to the instantaneous ICA:ECA flow [28]. This assumption intends to minimize uncertainties in ultrasound measurements, small branches and the assumption of rigid walls. Other studies present hemodynamic of carotid artery bifurcation considering different outflow conditions [42,45]: multiscale boundary conditions (MS) and considering flow velocity waveform at the ICA outlet section equal to a fixed fraction of the CCA waveform, obtaining 50:50, 60:40, and 70:30 flow rate ratios between ICA and ECA; these simulations, performed without direct constraints on the shape velocity profiles of ICA outlet demonstrate that RRT and TAWSS are sensitive to outflow boundary conditions, showing RRT similar results to MS for the case of the fixed 60:40 and 70:30 flow rate partitions.

Carotid artery geometry can affect the blood flow pattern through the artery, which, in turn, significantly affects the risk of atherosclerosis [6,7]. Previous works show that variations in waveform shape among healthy subjects have a relatively minor influence on variations in the distributions of WSS derivative parameters [4,44] as compared to the influence of uncertainty in the reconstructed geometry. In this study patient-specific geometry and blood flow velocity waveforms were employed and further studies with a larger sample of patients should be performed in order to clarify the relation between WSS parameters and atherosclerosis.

5. Conclusions

This study combined computational 3D geometry reconstruction, finite element meshing and simulation of blood flow characteristics in CA bifurcation based on Doppler images. Using patient-specific carotid artery ultrasound data collected in hospital practice, a semi-automatic generation of a structured and conformal hexahedral mesh of a carotid bifurcation was presented in this work. There was a good agreement between the simulated blood flow velocities and those obtained by Doppler ultrasound measurements. The simulation demonstrated several complex flow features near the stenosis associated with the diseased vessel geometry. Namely, stenosed carotid bifurcation, as compared with a stenosis-free case, showed a high wall shear stress, particularly during the systolic phase. All WSS-based descriptors, assigned highly disturbed flows at the same artery surface regions; namely they were able to capture abnormal flow at carina for the two patients and upstream and downstream ICA stenosis for patient P1.

CFD analysis could also be used to identify deficiencies in Doppler velocimetry of high-grade stenosis, where velocities are very high, aliasing renders determination of

the peak systolic velocity impossible or irregular calcified plaques obscure the true lumen (space) of the carotid artery.

Although the presence of the plaque may greatly reduce wall compliance, further research will be needed to understand the effect of wall compliance on the blood flow patterns of specific severely diseased carotid arteries, as the irregular 3D shape may heighten the effects of wall compliance. In order to elucidate the role of carotid hemodynamics on plaque development and plaque vulnerability, further larger studies should be done, providing clinically relevant information for risk assessment and surgical planning. Once such relationships are understood, hemodynamic simulations might allow testing hypotheses and improving diagnostic and treatment of carotid atherosclerosis. Understanding blood flow patterns in different carotid geometries can, therefore, lead to the identification of people vulnerable to stroke pathogenesis.

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Figure Captions

Fig.1. Segmented cross-sectional B-mode image (section S1) and reconstructed lumen surface.

Fig.2. Carotid artery bifurcation mesh: 2D quadrilateral meshes of the central structure (left), and structured mesh obtained by extruding each 2D mesh along each branch (center and right).

Fig.3. Inlet CCA velocity flows for patients P1 and P2: pulsed-wave Doppler image (left) and pulsatile velocity waveform used to set the Womersley approach (right) - flow waveform obtained from PW images (red) and Fourier approximation (black line).

Fig.4. Simulated and Doppler measured systolic velocities (**cm/s**) at locations explored during ultrasound examination.

Fig.5. Velocity fields (**cm/s**) at systolic peak (top) and mid deceleration phases (bottom) for patients P1 and P2.

Fig.6. WSS contours (Pa) near peak systole for carotid bifurcations P1 and P2: anterior (left) and posterior (right) side of the carotid artery.

Fig.7. WSS based descriptors for patients P1 and P2: anterior (left) and posterior (right) side of the carotid artery.

Figure 1

Figure 2

Figure 3

Figure 4

	LOCATION					
Velocity [cm/s]	1	2	3	4	5	6
Calculated Max	49.0	42.0	65.4	99.3	91.4	103.5
Measured Max	47.8	40.3	63.5	104.6	93.0	115.0

Figure 5

Figure 6

Figure 7