Hemodynamic conditions of patient-specific carotid bifurcation based on ultrasound imaging

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Abstract

The purpose of this paper is to complement the characterization of patient-specific carotid artery bifurcation hemodynamics based on image data obtained by Doppler ultrasound imaging. A methodology for patient-specific 3D luminal surface reconstruction followed by structured hexahedral meshing of the volume and blood flow simulation is presented. Quantitative descriptors of the flow based on wall shear stress (WSS) are used to compare healthy and stenosed carotid bifurcation hemodynamic disturbances. Independently on the presence of stenosis, the internal carotid artery has been identified as a region of abnormal high values of oscillating shear index and relative residence time, and low values of time averaged-WSS. For the healthy carotid bifurcation, WSS descriptors manage to capture flow disturbances at the external carotid artery. This work addresses the lack of quantitative analysis on anatomically realistic stenosed carotid bifurcations.

Keywords: Carotid artery bifurcation; 3D reconstruction; mesh generation; computational fluid dynamics; image-based analysis
1. Introduction

Most diseases and their treatments involve complex physical responses and interactions between biological systems. Simulation methods can therefore, dramatically increase our understanding of these diseases, improve their treatment and follow-up. Computational simulations have evolved as a powerful tool in studies of the role of hemodynamics in the disease development (Li et al. 2005; Stuhne et al. 2004; Evegren et al. 2010) as well as design of medical devices (Qiao et al. 2006) and prediction of the outcomes of surgeries (Migliavacca et al. 2006; Soerensen et al. 2007).

Image-based computational fluid dynamics studies of anatomically realistic arterial geometries appeared in the late 1990’s, either using magnetic resonance imaging (Krams et al. 1997; Botnar et al. 2000; Ladak et al. 2001; Zhao et al. 2002) or ultrasound imaging (Chandran et al. 1996; Gill et al. 2000; Lee et al. 2004). Nowadays, there is extensive experimental and computational investigation on the pathophysiology of atherosclerosis looking for correlations between its focal nature and local hemodynamics (Schumann et al. 2008; De Santis et al. 2010; Morbiducci et al. 2010; Rocha et al. 2010; De Santis et al. 2013; Anastasiou et al. 2012).

Ultrasound imaging of the carotid artery is a common procedure when screening for cardiovascular disease, as the vessel is particularly prone to atherosclerosis and easily accessible with ultrasound probes. Furthermore, ultrasound imaging is a fast and inexpensive technique, presenting minimal risk for the patient, and providing real-time images of endovascular structure and accurate information on flow velocities in a non-invasive manner.

The analysis of anatomically realistic blood flow simulations performed by the finite element method has the potential to enhance our understanding of how hemodynamic factors are involved in atherosclerotic disease. The main goal of this
paper is to present a methodology for patient-specific study of carotid bifurcation hemodynamics using Doppler ultrasound image data. The computational pipeline adopted includes geometric reconstruction, structured meshing of the carotid bifurcation, blood flow simulation and hemodynamic analysis. In order to improve the link between hemodynamic changes and stenosis pathophysiology, hemodynamic simulations of a diseased and a healthy image-based carotid bifurcation were carried out under pulsatile conditions. Results generated by blood flow simulation of patient-specific reconstructed model (Sousa et al. 2012a; Sousa et al. 2012b) were compared with Doppler ultrasound blood flow measurements at particular positions of the common (CCA), internal (ICA) and external (ECA) carotid arteries showing a good agreement. There is considerable inter-individual variation in arterial geometry and variation in arterial flow patterns between the two studied subjects is expected. As in previous works (Lee et al. 2007; Lee et al. 2009; Morbiducci et al. 2011), our findings show WSS and its derived parameters to be extremely sensitive to variation in geometry. Furthermore, this study shows that these parameters are also able to detect abnormal flow. The present research was partially done in the scope of a project with a public hospital and aims to early detect vessels at risk and to predict further atherosclerotic disease progression.

2. Methods
Reconstruction of carotid artery bifurcation and blood flow environment from ultrasound images of patients with nearly-planar carotid bifurcation requires four sequential steps: acquisition of anatomical data of the arterial section via ultrasound imaging, segmentation of the acquired B-mode images and surface reconstruction, 3D finite element mesh definition and computational blood flow simulation.
2.1. Acquisition of anatomical in vivo data

Two middle aged volunteers underwent ultrasound carotid examinations: P1 presenting a visible carotid stenosis and P2 with no visible stenosis. Examination of the extracranial carotid system was performed using a commercial color ultrasound scanner (model Vivid-e ultrasound system from GE Healthcare, United Kingdom) and a linear array probe (model 8L-RS from GE Healthcare). All data requested for the present study were obtained by the same experienced sonographer technician exclusively dedicated to neurovascular ultrasound studies at the Neurosonology Unit of the Department of Neurology of Hospital São João, in Portugal. A protocol for this study has been approved by the local institutional ethical committee and informed consent of each volunteer was obtained.

For each volunteer, a C-mode image was acquired along the longitudinal plane to delineate the carotid environment. To allow the correct reconstruction of the carotid bifurcation luminal surface, B-mode longitudinal images were also acquired and complemented with B-mode images of the carotid vessels and the bifurcation along the transverse plane registered at end-diastole to control physiologic variations of vessel diameter along cardiac cycle. A longitudinal and a transverse Doppler grayscale image for volunteer (P1) are presented in Figure 1.

Using PW-mode, velocities were determined at distal, mid, and proximal portions of the carotid bifurcation identified by B-mode imaging. Pulsatile spectral waveforms, and peak systolic frequency were obtained at the centerline of the distal common carotid artery (D-CCA) approximately 2 cm before bifurcation, at the
bifurcation entrance (APEX) and at the most proximal regions of the internal (P-ICA) and external carotid arteries (P-ECA) without relevant flow disturbances. Angle correction was activated and an angle of insonation of 60° was maintained whenever possible.

2.2. Geometrical 3D surface reconstruction

DICOM files were imported into MATLAB framework (The Mathworks Inc. Natick, MA, USA), and the B-mode images were segmented to produce smooth lumen and plaque contours by using an image segmentation propose-developed MATLAB algorithm (Santos et al. 2012; Santos et al. 2013). The referred algorithm for the automatic segmentation of the lumen and bifurcation boundaries of the carotid artery in ultrasound B-mode images uses the hypoechogenic characteristics of the lumen and bifurcation of the carotid artery. Each input image is initially processed with the application of an anisotropic diffusion filter for speckle noise removal, and morphologic operators are employed in the detection of the relevant ultrasound data regarding the artery. The information obtained is then used to define two initial contours, one corresponding to the lumen and the other one regarding the bifurcation boundaries, for the application of the Chan-Vese level set segmentation model (Chan et al. 2001; Lanktom et al. 2008; Santos et al. 2012; Santos et al. 2013).

For the 3D reconstruction process, the segmented 2D images, i.e. the segmented boundary contours, were modelled using commercial software. Specific points of the lumen-intima and media-adventitia boundaries were identified on the longitudinal images in order to construct splines A, B, C and D for ICA, ECA and CCA boundary definition, as shown is Figure 2.
The centerlines of CCA, ECA and ICA were defined by creating a curve associated to equidistant points from splines A to B, A to C and D to B. Segmented transverse contours were then positioned and oriented in 3D space; each contour was then realigned so that its centroid coincided with the defined arteries centerlines. Figures 2 and 3 show the main steps of the proposed 3D surface reconstruction for the patient P1.

To minimize the influence of boundary instabilities and to facilitate the application of boundary conditions for the computational model simulation, cylindrical flow extensions with a length of four times the local radius were added at the inlet and outlets in the directions of the centerlines.

2.3. Structured mesh generation

A structured hexahedral mesh of the lumen of the nearly-planar carotid bifurcation was constructed, as depicted in Figure 4. This type of mesh was adopted as computer simulations using hexahedral meshes have shown to converge better, require less computational time, and more competence for the calculation of the wall shear in comparison to tetrahedral/prismatic meshes (Verma et al. 2005; Antiga et al. 2008, Swillens et al. 1012).
Using FEMAP software, 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 branches at the bifurcation. Then, the filling of the carotid surface geometry was performed by dividing the domain in six parts and each part meshed independently maintaining finite elements continuity at each contact surface; Figure 4 illustrates the mesh generation method showing a coarse mesh for the carotid bifurcation of patient P1. In order to mesh elements along the main flow direction, each branch was treated independently according to the following procedure: first, a 2D quadrilateral mesh was considered in the three confining sections; then, by sweeping or extruding a 2D mesh of a section (quadrilateral) along a path, a volume mesh was generated (hexahedrons). It should be noted that blood motion in vessels is highly directional and the use of computational meshes with well-organized elements along the main flow direction assures faster convergence and more accurate numerical solutions (Almeida et al. 2000; Frey et al. 2003; Müller et al. 2005; Antiga et al. 2008; De Santis et al. 2010).

Since the behavior of the solution close to the wall is of great interest for hemodynamics, as it is directly linked to wall shear stress and derived quantities, it is desirable that the mesh has a high element density near the wall, and that elements are aligned with the local orientation of the boundary surface (Almeida et al. 2000; Frey et al. 2003; Müller et al. 2005; Antiga et al. 2008; De Santis et al. 2010). In practice, this is often obtained with a locally refined mesh creating one or more layers of prismatic elements having smaller thickness. An accurate description of the flow field was obtained in the vicinity of the vessel wall with thinner elements of 0.1 mm.
2.4. Blood flow model

In order to solve the governing equations of blood flow in the carotid bifurcation, the finite element method was adopted. Time-varying 3D velocity fields were computed using a developed finite element code (Sousa et al. 2012a; Sousa et al. 2012b). The nonlinear system of equations derived from the discretization of the flow equations were solved using the upwinding method. The backward Euler implicit time integration scheme was implemented to obtain the solution at each time step of the time-dependent problem.

Blood was modeled as isotropic, incompressible, homogeneous and Newtonian viscous fluid with a density of 1060 kg/m$^3$. The rheological behavior of blood was simulated considering a constant dynamic viscosity value of 0.0035 kg/(m.s), a reasonable assumption for bulk flow metrics (Lee et al. 2007; Morbiducci et al. 2011). Newtonian rheology is reasonable in the context of currently available levels of geometric precision, and assumptions and uncertainties related to the inlet boundary conditions fluid (Seung et al. 2008; De Santis et al. 2010; De Santis et al. 2011; Morbiducci et al. 2011).

At the CCA inlet Womersley velocity profiles were imposed. A common approach was applied at the outlets by imposing Dirichlet velocity conditions at ICA (Womersley profiles) and stress-free boundary condition at the ECA section (Lee et al. 2008; Kim et al. 2009; Hoi et al. 2010; Morbiducci et al. 2010). Both CCA and ICA Womersley velocity profiles were derived from the pulsatile spectral waveforms obtained by pulsed Doppler.

To ensure mass conservation, the outlet flow rates were corrected using the instantaneous flow rate ratio ICA/ECA and maintaining the CCA flow (Hoi et al. 2010). This need to resolve inlet/outlet flow discrepancies is mainly due to uncertainties in
measurements and to the existence of small branches. Another contribution comes from the assumption of rigid wall in the simulations since the consideration of distensible arteries might reduce instantaneous flow mismatches at the bifurcation (Hoi et al. 2010).

A long standing hypothesis that correlates fluid dynamic forces and atherosclerotic disease has led to numerous analytical, numerical, and experimental studies over the years. Much of what inspired these studies is the observation that atherosclerotic disease is focal, typically occurring at sites of complex hemodynamics with low wall shear stress (WSS) regions, such as arterial bifurcations (Botnar et al. 2000; Lee et al. 2004; Evegrena et al. 2010; Hoi et al. 2010; Anastasioua et al. 2012). Since computed values associated to flow and WSS patterns might suggest locations of formation and progression of atherosclerotic plaque, mesh sensitivity and time step analyses were conducted based on ICA flow and maximum nodal WSS in order to assure solutions to be grid independent. Convergence has been carefully tested following previous works (Sousa et al. 2012a). Refinement of both spatial and temporal resolutions was performed until changes in predicted velocities and WSS became insignificant (less than 1.5%). For this intended performance, the transient simulation was performed with a mesh of 55 thousand hexahedrons and using constant time step size configuration of $2.5 \times 10^{-3}$s. For each bifurcation, simulation computations were carried out requiring approximately 20 hours of CPU.

### 2.5. WSS-based hemodynamic descriptors

A variety of metrics has been used to model the flow patterns of the carotid bifurcation. The most widely used wall shear stress (WSS) based descriptors are the time averaged WSS (TAWSS), the oscillating shear index (OSI) and the relative residence time (RRT) computed as follows (Ku et al. 1985; Lee et al. 2009):
\[
TAWSS(s) = \frac{1}{T} \int_0^T |WSS(s, t)| \, dt
\]

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

\[
RRT(s) = \frac{1}{(1-2_OS).TAWSS}
\]

where \( T \) is the total time of the cardiac cycle, \( s \) is the location on the vessel wall and \( t \) is the time.

The TAWSS is used to evaluate the total shear stress exerted on the wall throughout a cardiac cycle and OSI is a measure of directional changes in wall shear stress over the cardiac cycle. OSI is a dimensionless quantity reaching a maximum value of 0.5 in regions with the high oscillating shear stress indicating the greater susceptibility of these regions to develop atherosclerosis. Both metrics are related to the amount of shear stress distributed across the carotid wall. The RRT is a measurement of how long the particles will stay near the wall. These descriptors have been found to be the best metrics for measuring low and oscillating shear at the carotid bifurcation.

3. Results

The computational results showed that flow velocities calculated using the developed approach agreed well with the Doppler measured velocities. For the patient with no visible stenosis (P2) a detailed analysis was conducted at three specific locations named APEX, P-ICA and P-ECA. Figure 5 presents the identification of those regions on a B-mode image and their measured relative distances.

<insert Figure 5 around here>
Figures 6 to 8 allow the comparison between the Doppler flow velocity waveforms obtained within the sample volume at each one of the observed locations and the calculated ones using the patient-specific simulation model for one cardiac cycle. Here, the considered time $t/tp$ was normalized using the acquired cardiac cycle duration time $tp$. At all three locations, there is a good agreement in shape between the obtained blood flow velocities waveforms and those obtained experimentally by Doppler ultrasound measurements in clinical practice. For the same locations, the peak systolic and end diastolic velocities were obtained from the Doppler data and by computational simulation, Table 1. At all the three positions, there is a good agreement (differences $< 10\%$) between the simulated flow velocities and those obtained experimentally by Doppler ultrasound measurements in clinical practice. This agreement allows a study on the accuracy of the carotid bifurcation blood flow simulation method.

<insert Figures 6 to 8 around here>

<insert Table1 around here>

The inter-individual variation in flow dynamics at the carotid artery bifurcation was also analyzed. For blood flow simulation, boundary conditions were imposed. At inlet, Womersley velocity profiles were derived from centerline velocities based on CCA pulsed Doppler measurements and similarly at ICA outlet boundary conditions were calculated. The patient-specific D-CCA input velocity waveforms and simulated velocity fields at two cardiac cycle instants, peak systolic and mid deceleration phases are shown in Figure 9 for patients P1 and P2. It can be observed in this figure a strongly
skewed axial velocity in the proximal internal carotid artery (enlarged bulb region) with high velocity gradients at the internal divider wall. Near the outer bulb wall (the wall opposite the divider wall), a stagnation zone (larger during deceleration phase) was detected by the developed code for the two patients. Peak high velocity gradients were also detected at ECA during systolic, due to the sharp unevenness of the vessel wall.

Along with blood flow simulation WSS values were calculated. The WSS contours detected near peak systole for the two patients are shown in Figure 10. This figure depicts regions of low shear stress located on the lateral surface just prior to bifurcation. The main features expected from fluid dynamics, such as low WSS values in the bulb region of the ICA and high WSS in the inner wall of ECA proximal to the bifurcation, were successfully captured. Nevertheless, different WSS patterns were found for the two individuals, mainly due to the effect of patient-specific geometric variability.

Flow indicators were evaluated throughout a cardiac cycle at the end of the simulation. The distributions of the WSS-based descriptors obtained on the luminal surface of volunteers P1 and P2 are shown in Figure 11. A common feature that can be seen is that TAWSS (low values) and OSI and RRT (high values) mainly captured apparent flow disturbances at the same sites: areas of high OSI lie within areas of low
TAWSS, indicating localized flow reversal or varying flow direction. Regions of high OSI values up to 0.5 were found at the ICA origin for both bifurcations.

4. Discussion

The WSS distributions near peak systole obtained for the two patients are shown in Figure 10 where significantly different WSS patterns can be detected for the two individuals.

For P1, high WSS values of approximately 14 Pa were observed within the stenosis, and low WSS values were found in the bulb region of ICA and also in the outer and inner walls of ICA downstream the stenosis. For P2, low WSS patches in the common carotid artery (CCA) were contiguous with the carotid bulb low WSS region. For both patients, the maximum WSS was located in the inner wall of ECA proximal to the bifurcation apex, 35 Pa and 22 Pa for patients P1 and P2, respectively.

Two different view angles of TAWSS distributions obtained for the two volunteers are shown in Figure 11. Although low values were concentrated around both bifurcations, the patterns were different as for the non-stenosed ICA low values were also found at bulb region. Furthermore, for the stenosed ICA, low TAWSS were found in the outer wall downstream stenosis identifying abnormal flow.

Following Lee et al. (2009), lumen surfaces exposed to significant disturbed flow can be identified with high OSI values. In this study, OSI fields showing high values within areas of low TAWSS were located on the outer wall of the ICA, which corresponds to recirculation zones and is consistent with other studies (Lee et al. 2009; Morbiducci et al. 2010; Morbiducci et al. 2011; Gallo et al. 2012).
The results shown in Figure 11 also confirm that the RRT distribution captured the main features of both TAWSS and OSI presenting high values at ICA origin for both patients and downstream stenosis for patient P1. For both patients, the three WSS indicators assigned disturbed flows to the same surface regions. This finding is in agreement with recent studies that recommend the relative residence time (RRT) as a robust single metric of low and oscillatory shear (Lee et al. 2009; Morbiducci et al. 2010, Morbiducci et al. 2011).

For the normal carotid bifurcation (P2), flow disturbances at the ECA branch were captured by the three descriptors. This might be associated to branch geometry and tortuosity occurring at the inner wall of proximal ECA leading to high OSI values where the jet impinges on the wall (Lee et al. 2008).

In this work, WSS-based descriptors identified ICA origin as the region of abnormal flow for both a normal and a stenosed carotid bifurcation; this finding is in agreement with the fact that plaques tend to occur at the ICA and that even small plaques can be associated with local disturbed hemodynamic that might be important in further progression of the lesions.

For carotid bifurcation with no visible stenosis, our findings are consistent with the previous works that only study normal carotid bifurcations (Lee et al, 2007; Lee, 2009; Morbiducci et al. 2011). For the stenosed carotid bifurcation, WSS-based descriptors did not capture abnormal flow in ECA and future further research applicable to large-scale studies of hemodynamic factors in atherosclerosis is demanded.

5. Conclusions
A full understanding of hemodynamic changes caused by the carotid bifurcation is meaningful for clinical research. Simulated hemodynamics of two patient-specific
carotid artery bifurcations was presented and validated using experimental data obtained by Doppler measurements.

Study of blood flow hemodynamics based on three wall WSS descriptors was presented. Our findings revealed that the WSS-based descriptors are significantly correlated and extremely sensitive to variation in geometry, and are able to capture flow disturbances at the same sites. This identification might allow testing hypotheses and to address important clinical vascular problems, improving diagnostic and treatment of carotid atherosclerosis.

In future, the influence of geometric features of the bifurcation on WSS and its derived parameters should be investigated in more depth.

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Conflict of interest statement

All authors hereby declare no conflicts of interest.

References


FIGURE CAPTIONS

Figure 1. Segmented Doppler ultrasound images of the carotid artery bifurcation region (patient P1): longitudinal (on the left) and transversal (on the right) scans.

Figure 2. Geometrical definition of the artery centerlines associated to equidistant points from splines A to B, A to C and D to B, and cross-sections (patient P1).

Figure 3. Reconstructed surface of carotid bifurcation using the defined cross-sections.

Figure 4. Carotid artery bifurcation mesh: 2D quadrilateral meshes (on the left), detailed central structure connecting the three branches (on the center) and structured coarse mesh obtained by extruding the 2D meshes (on the right).

Figure 5. Carotid artery bifurcation of patient P2: B-mode and Pw Doppler image (on the left), locations of anatomic references (on the right).

Figure 6. Blood flow velocity waveform at APEX (P2): Doppler measurement (on the left), simulated velocities (on the right).

Figure 7. Blood flow velocity waveform at P-ICA (P2): Doppler measurement (on the left), simulated velocities (on the right).

Figure 8. Blood flow velocity waveform at P-ECA (P2): Doppler measurement (on the left), simulated velocities (on the right).

Figure 9. Patient-specific D-CCA velocity waveform (on the left), velocity fields near systolic peak (on the center) and at mid deceleration phase (on the right), for the two patients.

Figure 10. Systolic peak WSS distribution in the carotid bifurcation for the two patients (P1, P2).

Figure 11. WSS-based descriptors for the two patient-specific models (P1, P2): TAWSS (on the left), OSI (on the center) and RRT (on the right).
TABLE CAPTIONS

Table 1. Simulated and Doppler measured velocities (cm/s).
FIGURES

Figure 1

Figure 2

Figure 3
Figure 4

Figure 5

Figure 6
Figure 10

Figure 11
Table 1. Simulated and Doppler measured velocities (cm/s).

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