Influence of blocks' topologies on endothelial shear stress observed in CFD analysis of artery bifurcation

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It is well known that endothelial shear stress affects occurrence of plaque in arteries. Lack of a method for measuring this physical quantity limits scientific understanding of this phenomenon. Application of numerical methods in this area has considerable amount of experimental verifications in terms of quantities that can be measured (velocity, pressure). On that basis we can rely on the results of endothelial shear stress calculations. The literature mainly documents the application of numerical methods to average geometries. However, arterial bifurcations are patient-specific. Moreover, occurrence of disease significantly complicates the geometry of the arteries and bifurcations. A multiblock concept provides the necessary geometrical flexibility and computational efficiency to generate patient-specific finite element models. For a particular class of problems different topologies of blocks are possible. This paper provides an overview of the possible block topologies required in finite element modeling using multiblock approach. In order to obtain accurate results of endothelial shear stress, two most general topologies are examined by numerical calculations. Favorable topology of the blocks is implemented in in-house software stl2fem.

Key words: artery bifurcation, topology of blocks, endothelial shear stress, CFD, FEM, PAK

1. Introduction

Cardiovascular diseases are one of the major causes of long-term human morbidity and mortality. The nearly epidemic increase in prevalence of such diseases calls for efficient methods of diagnosis and treatment. Non-invasive diagnostic procedures such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are often used in this context [1], [2], but do not provide information on quantities considered to be partially responsible for the formation and development of related pathologies [3]. The key quantities describing flow field are time-dependent velocity, pressure and endothelial shear stress [4]–[6]. The relationship between flow in the arteries, the endothelial shear stress (ESS) distribution and the sites where diseases develop has motivated much research on arterial flow in the last decade. It is now accepted that the sites where shear stresses are extreme or change rapidly in time or space are the ones that are most vulnerable [7], [8]. Endothelial shear stresses cannot be measured. Knowledge of this field would greatly facilitate the prediction of the formation and growth of plaque [9].

According to many authors numerical methods, such as finite element analysis (FEA), allow sufficiently accurate determination of such transient field. The analysis algorithms require discretization of the governing equations into finite element equations. Hence, mesh generation is an interface between physical domain representation and analysis algorithms. The development of finite element codes has increased the demands for quality finite element meshes. It is im-

portant to have realistic and quality geometric models with minimal number of elements for accurate and efficient finite element calculations. The mesh quality plays an important role in finite element simulations [10]. It is well known that poor quality meshes result in poorly conditioned stiffness matrices in finite element analysis. Also, it affects the stability, convergence, and accuracy of finite element solvers. The accuracy of the numerical solution is determined by the nature of the mesh used to represent physical domain [11]. This is especially apparent within the CFD field, where numerical errors, dependent upon the quality of the mesh, become visible in the flow solution. In order to be used for in vitro research, the grid generation process needs automation [12], [13]. There has been tremendous progress in the area of surface reconstruction and 3D geometric modeling, but it still remains a challenging process to generate 3D meshes directly from imaging data [14], [15].
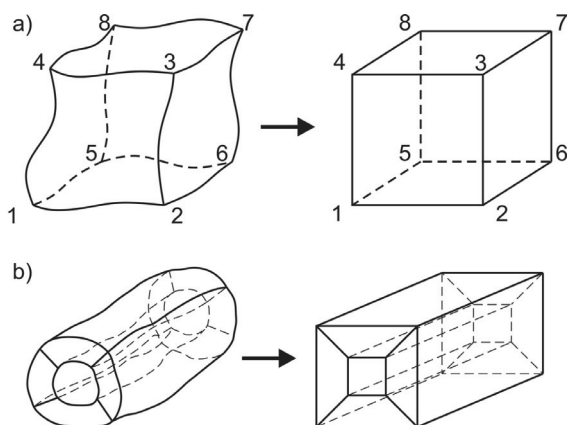

Fig. 1. Mapping of a block from solution domain (SD) to computational domain (CD)

Structured mesh generation is the most appropriate method for discretising domains. The method is based upon a direct mapping from the physical or solution domain (SD) to computational domain (CD) (Fig. 1a). Boundary points prescribed within the solution domain are used to interpolate the interior points within the computational domain. The grid point distribution is generated by the solution of a set of three Poisson equations, one for each coordinate direction. Structured grids use general curvilinear coordinates to produce a body fitted mesh. This has the advantage that boundaries can be exactly described and hence boundary conditions can be accurately modeled. Unfortunately, this approach cannot be used for complex geometries.

Artery bifurcations may have very complicated configuration [16]–[19]. Lately, the trend is patient-specific modeling [20], [21]. The flexibility required to construct vessel's computational grids has led to the development of a multiblock or composite grid approach. This approach is a very effective tool for generating computational structured grids in biomechanics and engineering since it allows larger, more complex and better quality meshes to be produced. The solution domain is subdivided into a set of blocks [22]. Now, each block in the SD is mapped onto a Cartesian block in the CD (Fig. 1b). Structured mesh techniques are applied to blocks. Blocks are then linked together to produce a much larger mesh. Since multiblock grids are unstructured on block level, information about block connectivity is needed along with the each block. The actual SD on which the governing physical equations are solved is therefore a set of connected, regular blocks in the CD.

Multiblock approach requires definition of block topology. Topology is meant as constructing a wireframe model around volumetric model by placing wireframe points, linking these points, and assigning them to fixed surfaces. The paper analyzes a few cases of blocks' topologies for a complex geometry of artery bifurcation with the minimum possible errors in the numerical solution. The most general principles that make a clear line between the bad and the optimum arrangement of the blocks are presented.

2. Materials and methods

2.1. Topologies of blocks

A procedure we use is based on setting up user-defined sections of the artery geometry. We observe a set of n sections marked as shown in Fig. 2a. For each section the coordinates of barycenter point, normal vector and maximum dimensions of vessel are known. These arrangements of the blocks are observed in each section from the top of the z axis, apropos from head to feet of patient. Blocks' vertices are placed in the section to form a 2D array and are divided into two groups: external and internal ring (Fig. 2b). The external vertices of the block (external ring) are set to lie in the section and outside of vessel at half the maximum dimension of the section from the section center point in directions of local coordinate axes x and y. The internal vertices of a block (internal ring) are placed inside vessel.
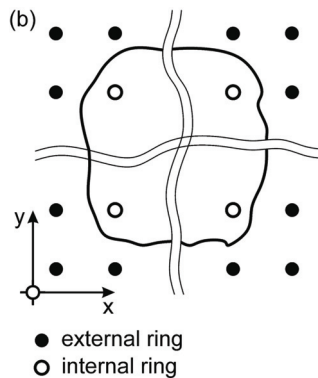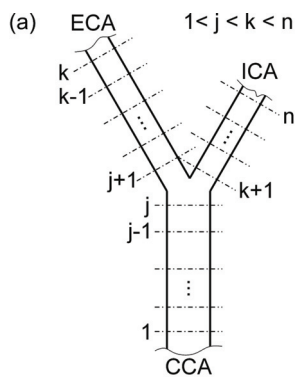
Fig. 2. Vertices of the blocks:
(a) sections containing block vertices
and (b) layout of vertices in each section

Over the vertices different block scheduling strategies may be applied using all or just some of the vertices. Number of division on the block opposite sides must be equal. Let us first consider block scheduling strategy around the straight circular vessel. Only the external vertices (external ring) are used. We consider the case where just one block is used and the number of elements per block's edge is 2 (Fig. 3a). Nodes on the surface described by the point cloud are obtained by projecting the grid points on the point cloud in direction connecting the appropriate grid points of opposing edges of the block. Nodes within the domain are constructed by transfinite interpolation (TFI). Elements closest to the external vertices of the blocks in such a mesh will have an irregular shape, or so-called very large skew angle, so that their shape will affect the quality of results. It should be noted that this case is applicable only to a tube without branching. If there is any branching, this simplest case of the layout of blocks cannot be applied.

If we construct a topology with 3×3 blocks, we get the opportunity to model branching (Fig. 4). Vertices of the blocks are marked with numbers 1–16, where number 1 denotes lower left vertices on internal ring, and number 5 denotes lower left vertices on external ring. Vertices in the following sections always have a numbering increased for 16 compared to the vertices that precede them. The block marked by I denotes the central block. Other blocks are denoted by II to IX. Three blocks on the left and right are used to describe the mesh before and after the branch, and three blocks in the middle exists only before the bifurcation. In this case unfavorable deformed elements are obtained in the blocks that are closest to the external corner vertices (in blocks II, IV, VI, and VIII).
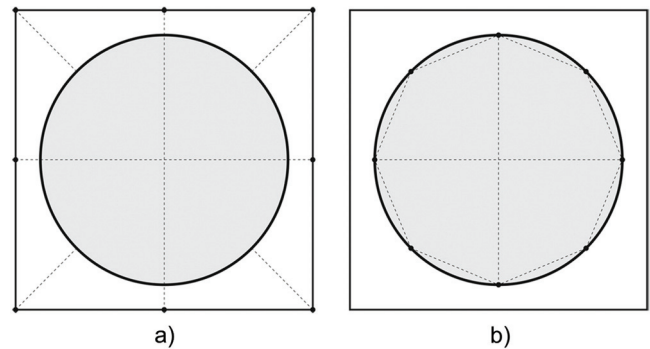

Fig. 3. Mapping from computation to physical domain
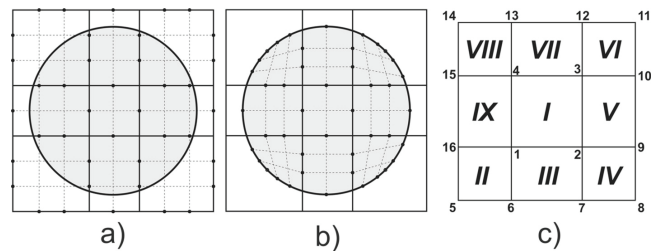for straight vessel

Fig. 4. The first variant: (a), (b) mapping from computational
to physical domain in section, and (c) local numeration
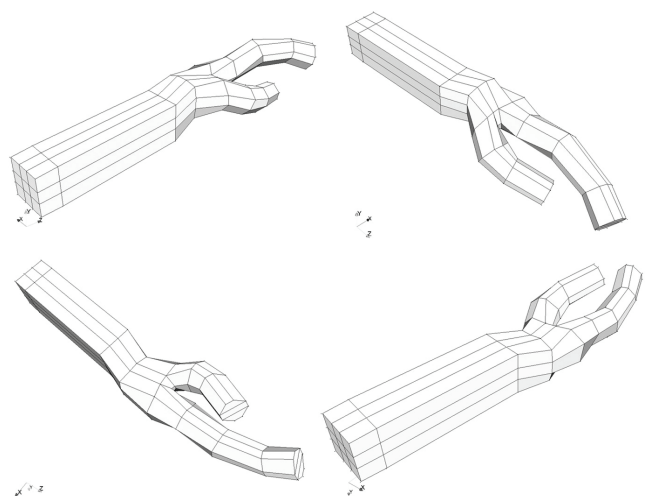of vertices and blocks in section

Fig. 5. Configuration of blocks obtained by the first variant
of topology of blocks

To generate proper elements of the entire domain, it is necessary to apply more sophisticated layout of the blocks. One of the possible topologies is shown in Fig. 6. Vertices of the blocks are marked with numbers 1–8, where number 1 denotes lower left vertices on internal ring, and number 5 denotes lower left vertices on external ring. Vertices in the following sections always have a numbering increased for 8 compared to the vertices that precede them. The block marked by I denotes the central block. Blocks below, right, above, and left are denoted by II, III, IV, and V, respectively.
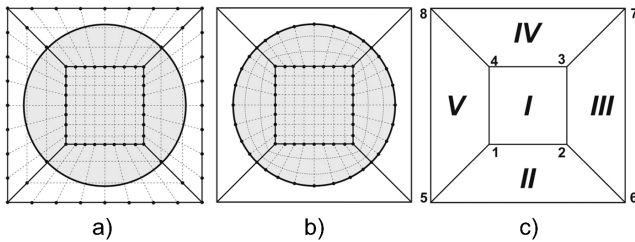

Fig. 6. The second variant: (a), (b) mapping from computational to physical domain in section, and (c) local numeration of vertices and blocks in section

In this topology, the set of 8 vertices are assigned the smallest number of blocks that provide the proper elements. Since grid point is always projected in the direction that connects the two corresponding grid points of opposing edges of the block, this way ensures that each unit generates proper hexahedral elements. Block configuration obtained by the second variant of block topology is given in Fig. 7.
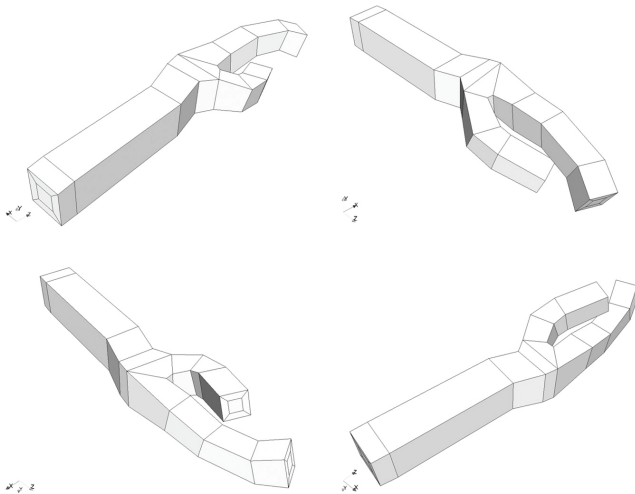

Fig. 7. Configuration of blocks obtained by the second variant of topology of blocks

2.2. Mesh generation

An automatic method of subdividing the flow domain into blocks has been implemented in software [23]. Once the topology definition has been done, grids are produced automatically starting in-house stl2fem, which uses an algorithm to extract quality hexahedral meshes directly from volumetric data. Software employs a multiblock meshing scheme aimed at hexahedral mesh generation. No relaxation based technique is deployed to improve mesh quality. The final numerical models contain elements that are exactly fitted on the border. The modeled carotid artery bifurcation for both variants of block topology is presented in Fig. 8.
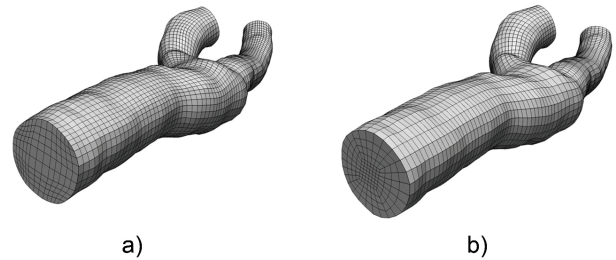

Fig. 8. Blocks' topologies applied to carotid artery bifurcation model: a) the first variant, b) the second variant

2.3. Numerical analysis

This section explores the influence of block topologies in the study of hemodynamic characteristics of carotid artery bifurcation. Software used for blood flow simulation is PAK-F Explicit. This solver involves modules for steady and transient incompressible fluid flow with heat transfer. It is developed on finite element method and corresponds to the fundamental equations of viscous fluid flow. Programming language FORTRAN, especially suited for numerical computations, was used to develop basic subroutines of PAK-F Explicit. The calculation results obtained are written in several file formats such as FEMAP neutral file, IDEAS graphics file, and VTK Paraview format (*.vtk file) [24].

Basic differential equations that govern the flow of an incompressible fluid [25]–[27], [4] are the Navier–Stokes equations given by the expressions

$$\rho\left(\frac{\partial v_i}{\partial t} + v_j v_{i,j}\right) = \sigma_{ij,j} + f_i^V, \qquad (1)$$

$$v_{i,i} = v_{1,1} + v_{2,2} + v_{3,3} = 0. \qquad (2)$$

Equation (1) represents the second Newton's law applied to the mass of fluid in control volume and (2) represents the continuity equation of fluid flow.

Constitutive relations for stress in Newtonian fluid are described by the following equation

$$\sigma_{ij} = -p\delta_{ij} + \tau_{ij} \tag{3}$$

where p is the pressure of fluid, δ_{ij} the Kronecker delta symbol and τ_{ij} is the shear stress. Shear stress is proportional to the strain rate tensor as

$$\tau_{ij} = 2\mu\dot{e}_{ij} \tag{4}$$

where $\dot{e}_{ij}$ is the strain rate tensor defined as

$$\dot{e}_{ij} = \frac{1}{2}(v_{i,j} + v_{j,i}). \tag{5}$$

Replacing the constitutive relation for the stress (3) in equation (1) and applying the continuity equation (2) next relation is obtained

$$\rho\left(\frac{\partial v_i}{\partial t} + v_j v_{i,j}\right) = -p_{,i} + \mu v_{i,jj} + f_i^V, \tag{6}$$

where ρ is the fluid density, v is the velocity of fluid, p is the pressure of fluid, μ is the dynamic viscosity and f_i^V are the volume forces. Using the Galerkin method, with appropriate interpolation functions

$$v_i = h_I V_i^I \quad I = 1, 2, ..., N, \tag{7}$$

$$p = \hat{h}_I P_I \quad I = 1, 2, ..., M, \tag{8}$$

and integration by volume of finite element, a matrix form of equations (6) and (2) is obtained such as

$$\mathbf{M}\dot{\mathbf{V}} + \mathbf{K}_{vv}\mathbf{V} + \mathbf{K}_{vp}\mathbf{P} = \mathbf{F}_v, \tag{9}$$

$$\mathbf{K}_{vp}^T\mathbf{V} = 0. \tag{10}$$

Components of this matrix and vectors from (9) and (10) are

$$\overline{\mathbf{M}}_{IJ} = \rho\int_V h_I h_J dV, \tag{11}$$

$$(\overline{\mathbf{K}}_{vv})_{IJ} = \int_V h_I v_j h_{J,j} dV + \int_V \mu h_{I,j} h_{J,j} dV, \tag{12}$$

$$(\mathbf{K}_{vpi})_{IJ} = -\int_V h_{I,i}\hat{h}_J dV, \tag{13}$$

$$(\mathbf{F}_{vi})_I = \int_V h_I f_i^V dV + \int_S h_I(-p\delta_{ij} + \mu v_{i,j})n_j dS. \tag{14}$$

By grouping equations (9) and (10), the system of differential equations is presented as

$$\begin{bmatrix} \mathbf{M} & 0 \\ 0 & 0 \end{bmatrix}\begin{bmatrix} \dot{\mathbf{V}} \\ \dot{\mathbf{P}} \end{bmatrix} + \begin{bmatrix} \mathbf{K}_{vv} & \mathbf{K}_{vp} \\ \mathbf{K}_{vp}^T & 0 \end{bmatrix}\begin{bmatrix} \mathbf{V} \\ \mathbf{P} \end{bmatrix} = \begin{bmatrix} \mathbf{F}_v \\ 0 \end{bmatrix}, \tag{15}$$

or

$$\hat{\mathbf{M}}\dot{\mathbf{U}} + \hat{\mathbf{K}}\mathbf{U} = \mathbf{F}. \tag{16}$$

The system of equations (15) is a symmetrical system of nonlinear differential equations of first order by unknown values in nodes $\mathbf{V}$ and $\mathbf{P}$. The matrix $\mathbf{K}_{vv}$ (12) is nonlinear, since it depends on velocity.

Endothelial or wall shear stress is a hemodynamic factor of great importance to the study of the problem of blood flow. It is calculated based on the equation

$$^t\tau_{ij} = \mu\frac{\partial^t v_t}{\partial n}\bigg|_{wall} \tag{17}$$

where τ_{ij} is the endothelial shear stress, v_t is the tangential velocity and n is the direction of a unit vector normal to the wall at the moment t. The tangential velocity is first calculated at the integration points near the wall surface, and then the velocity gradient $\partial^t v_t / \partial n$ is numerically evaluated.

The calculation of fluid flow through carotid artery bifurcation was performed in 30 steps (10 by 0.02 s and 20 by 0.03 s). Total time is 0.8 s. The average flow velocity in the inlet, density of blood, and coefficient of dynamic viscosity are adopted according to [28], [29]. Time function is a standard phase of systole and diastole of one human cardiac cycle (Fig. 9) [28], [29].
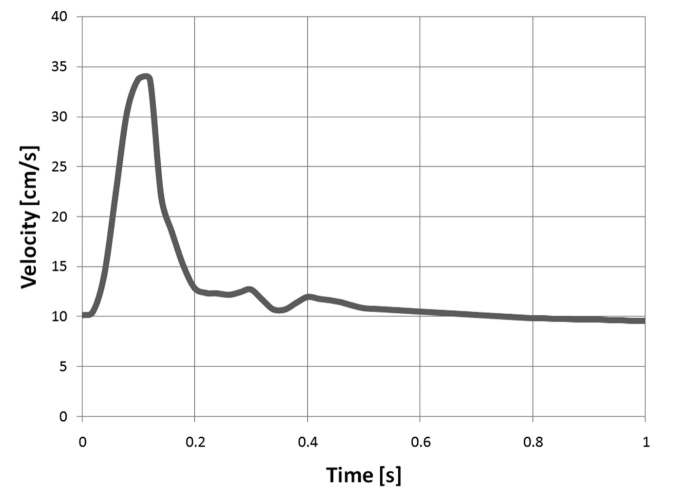

Fig. 9. Input flow waveform for one human cardiac cycle

The boundary conditions for the calculation model are:

• inlet velocity profile is a paraboloid (analogy with fluid flow through a circular tube),

• on the walls of the artery fluid velocity is set to zero (no-slip condition),

• on the outlet surfaces of artery surface forces are set to zero.

3. Results

Simulation of blood flow through the carotid artery bifurcation was carried out on realistic three-dimensional numerical models generated by a procedure described in the previous section. The results of ESS for the first and the second variant of finite element mesh are shown in Fig. 10. There is a low value

of endothelial shear stress on the external carotid artery (ECA), where cross section is bigger and flow velocity is smaller. In these areas there is a possibility of the atherosclerosis occurring. From the results obtained by analyzing the two models of the carotid artery bifurcation it can be seen that the quality of finite element meshes affects a lot endothelial shear stress field. For the first variant of the finite element mesh ESS field has bad results displayed as a line that runs along the entire artery. In the second variant of the finite element mesh, the results are good and show that the ESS have maximum at constriction of blood vessel.

4. Discussion

For medical purposes, local endothelial shear stress is one of the most fundamental factors influencing endothelial structure and function, and it is the central factor responsible for the localization of atherosclerotic plaque formation and progression. Current developments in the technology used to characterize local ESS and vascular remodeling in vivo provide a rationale for innovative diagnostic and therapeutic strategies for patients that aim to prevent clinical syndromes. Early identification of local ESS patterns, local plaque morphology, and local remodeling responses will probably enable identification of the early stages of plaques that will evolve into a high-risk, rupture prone lesion [30]. Early identification of these lesions may provide the framework and justification for pre-emptive strategies to interrupt the natural history of these high-risk plaques. To date, the methodologies for characterizing local shear stress distribution and other hemodynamic parameters in circulation have been used for research purposes only, because no tools are available to provide this information in a routine manner.

All these facts point to the great importance of arterial bifurcation rapid modeling. In the conventional methods of model generation, the time needed for ESS profiling depends on the time needed to segment the artery wall components, to obtain a 3D reconstruction and mesh generation, and to perform the computational fluid dynamics. Attempts are underway to speed up the patient-specific model generation techniques by improving the specific steps. Our mesh generator stl2fem is one of them. It uses composite or multiblock approach as the best way to generate finite element mesh with minimum errors in the numerical solution. One of the phases of the software develop-
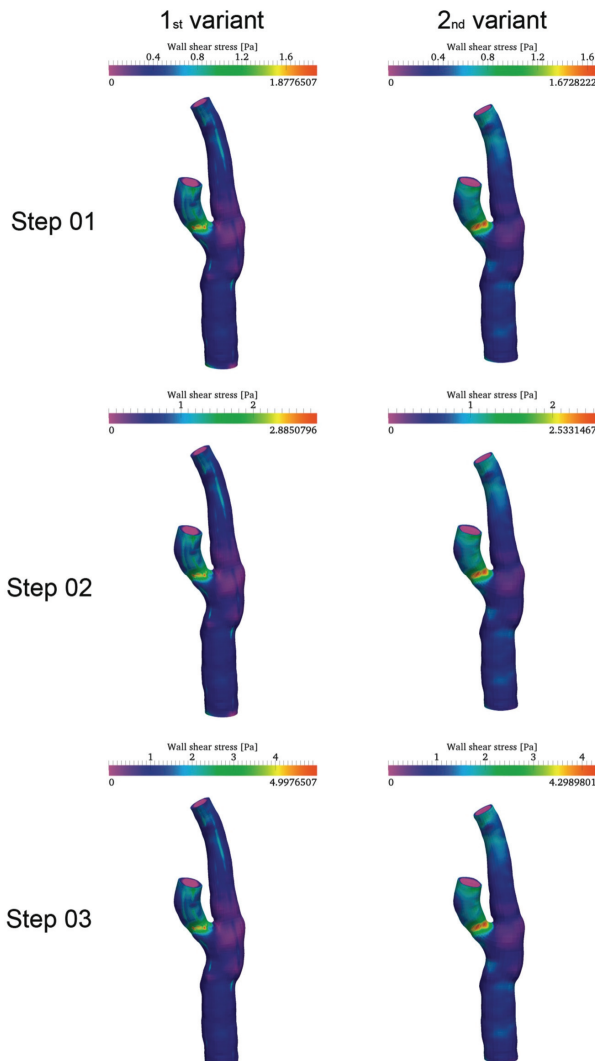

Fig. 10. Endothelial shear stress calculation results for both variants of FE mesh in steps 01, 03 and 05

ment is presented in this paper. Our goal was to determine the most optimal topology of blocks which gives exact solutions. The analysis presented shows that the first variant of block topology has elements with very large skew angle and this configuration results in bad calculation results of ESS. Otherwise, the second variant of block topology being favorable, is adopted and implemented in in-house mesh generator stl2fem. Baseline of this approach is that the time-consuming 3D surface reconstruction phase is skipped, thus the process of generating a 3D finite element model can be completely programmed and performed in routine manner.

Rapid modeling of patient-specific artery bifurcation opened up new avenues in the investigation of the role of ESS in the natural history of atherosclerosis and in the future we hope it will be powerful tool in everyday medical practice in decision making process for a single patient. This methodology not only allows detailed characterization of arterial plaque at a single point in time but, if studied in serial manner, now allows prognostic insight into how plaques change over time and what antecedent features predict the future behavior of the plaque. Ultimately, this information may be useful for collective teams of medical clinicians, scientists and engineers to facilitate translation to improved bifurcation stent designs or techniques. Better understanding of the interplay between local flow conditions and the formation and progression of plaque in bifurcations may define areas of angiographic interest in high-risk patients, enhance our ability to prospectively identify regions most likely to be inflicted by plaque and possibly facilitate deployment of hemodynamically-driven treatment strategies with better clinical outcomes [31].

Acknowledgements

References

[1] ZHANG Y., BAJAJ C., *Adaptive and quality quadrilateral/hexahedral meshing from volumetric data*, Computer Methods in Applied Mechanics and Engineering, 2006, Vol. 195, 942–960.

[2] ZHANG Y., BAJAJ C., SOHN B.S., *3D finite element meshing from imaging data*, The special issue of Computer Methods in Applied Mechanics and Engineering on Unstructured Mesh Generation, 2005, Vol. 194, 5083–5106.

[3] LONG Q., XUA X.Y., COLLINS M.W., BOURNE M., GRIFFITH T.M., *Magnetic resonance image processing and structured grid generation of a human abdominal bifurcation*, Computer Methods and Programs in Biomedicine, 1998, Vol. 56, No. 3, 249–259.

[4] KOJIC M., FILIPOVIC N., STOJANOVIC B., KOJIC N., *Computer modeling in Bioengineering*, John Wiley & Sons Ltd., 2008.

[5] RENEMAN R., ARTS T., HOEKS A., *Wall Shear Stress – an Important Determinant of Endothelial Cell Function and Structure in the Arterial System in vivo*, Journal of Vascular Research, 2006, Vol. 43, 251–269.

[6] MARIUNAS M., KUZBORSKA Z., *Influence of load magnitude and duration on the relationship between human arterial blood pressure and flow rate*, Acta of Bioengineering and Biomechanics, 2011, Vol. 13, No. 2, 67–72.

[7] ZARINS C.K., GIDDENS D.P., BHARADVAJ B.K., SOTTIURAI V.S., MABON R.F., GLAGOV S., *Carotid bifurcation atherosclerosis. Quantitative correlation of plaque localization with flow velocity profiles and wall shear stress*, Circulation Research, 1983, Vol. 53, 502–514.

[8] SCHULZ U.G., ROTHWELL P.M., *Major Variation in Carotid Bifurcation Anatomy: A Possible Risk Factor for Plaque Development*, Stroke – Journal of the American Heart Association, 2001, Vol. 32, 2522–2529.

[9] RINDERU P.L., RINDERU E.T., GRUIONU L., BRATIANU C., *A FEM Study of Aortic Hemodynamics in the Case of Stenosis*, Acta of Bioengineering and Biomechanics, 2003, Vol. 5, No. 2.

[10] ZHANG Y., BAJAJ C., XU G., *Surface smoothing and quality improvement of quadrilateral/hexahedral meshes with geometric flow*, Proceedings of 14th International Meshing Roundtable, 2005, 449–468.

[11] GARCIA E., SERON F., BALDASSARRI S., *The challenge of hexahedral meshing of arterial geometry*, Machine Graphics & Vision International Journal, 2008, Vol. 17, No. 1, 35–55.

[12] GEORGE P.L., *Automatic mesh generation: application to finite element methods*, Wiley, 1991.

[13] RUIZ-GIRONÉS E., *Structured and Semi-Structured Algorithms for Hexahedral Mesh Generation*, Universitat Politècnica de Catalunya, Barcelona, PhD Thesis, 2009.

[14] http://www.truegrid.com/

[15] GROSLAND N.M., SHIVANNA K.H., MAGNOTTA V.A., KALLEMEYN N.A., DEVRIES N.A., TADEPALLI S.C., LISLE C., *IA-FEMesh: An open-source, interactive, multiblock approach to musculoskeletal finite element model development*, Computer Methods and Programs in Biomedicine, 2009, Vol. 94, No. 1, 96–107.

[16] ZHAO S.Z., ARIFF B., LONG Q., HUGHES A.D., THOM S.A., STANTON A.V., XU X.Y., *Inter-individual variations in wall shear stress and mechanical stress distributions at the carotid artery bifurcation of healthy humans*, Journal of Biomechanics, 2002, Vol. 35, 1367–1377.

[17] SOULIS J., FARMAKIS T., GIANNOGLOU G., LOURIDAS G., *Wall shear stress in normal left coronary artery tree*, Journal of Biomechanics, 2006, Vol. 39, 742–749.

[18] NGUYEN K.T., CLARK C.D., CHANCELLOR T.J., PAPAVASSILIOU D.V., *Carotid geometry effects on blood flow and on risk for vascular disease*, Journal of Biomechanics, 2008, Vol. 41, 11–19.

[19] OWIDA A.A., DO H., MORSI Y.S., *Numerical analysis of coronary artery bypass grafts: An overview*, Computer Methods and Programs in Biomedicine, 2012.

[20] GOUBERGRITS L., AFFELD K., FERNANDEZ-BRITTOY J., FALCON L., *Investigation of geometry and atherosclerosis in the human carotid bifurcations*, Journal of Mechanics in Medicine and Biology, 2003, Vol. 3, No. 1, 31–48.

[21] SHIVANNA K.H., ADAMS B.D., MAGNOTTA V.A., GROSLAND N.M., *Towards Automating Patient-Specific*

Finite Element Model Development, Proceedings of the Computational Biomechanics for Medicine Workshop at MICCAI, 2006.

[22] Shirsat A., Gupta S., Shevare G.R., *Generation of multi-block topology for discretization of three-dimensional domains*, Computers & Graphics, 1999, Vol. 23, 45–57.

[23] Blagojević M., *STL2FEM – Software for automatic mesh generation of patient-specific artery bifurcations*, University of Kragujevac, Faculty of Engineering, Kragujevac, Serbia, 2011.

[24] Blagojević M., Nikolić A., Živković M., *Visualization of field of fluid flow calculated by fem software PAK-F in post-processing software ParaView*, [in:] YU INFO 2012, Kopaonik, Serbia, 2012.

[25] Bathe K.J., *Finite element procedures in engineering analysis*, Englewood Cliffs, Prentice-Hall, New Jersey, USA, 1996.

[26] Kojić M., Filipović N., Živković M., Slavković R., Grujović N., *PAK-F, Program for FE Analysis of Fluid Flow with Heat Transfer*, University of Kragujevac, Faculty

of Mechanical Engineering, Laboratory for Engineering Software, Kragujevac, Serbia, User's Manual, 1999.

[27] Kojić M., Slavković R., Živković M., Grujović N., *Finite element method I – Linear analysis*, (in Serbian), 1st ed., Kragujevac, Serbia: University of Kragujevac, Faculty of Mechanical Engineering, 1998.

[28] Perktold K., Resch M., Florian H., *Pulsatile non-Newtonian flow characteristics in a tree-dimensional human carotid bifurcation model*, Journal of Biomechanical Engineering, 1991, Vol. 113, 464–475.

[29] Perktold K., Resch M., Peter O., *Three-dimensional numerical analysis of pulsatile flow and wall shear stress in the carotid artery bifurcation mode*, Journal of Biomechanics, 1991, Vol. 24, 409–420.

[30] Stone P.H., Feldman C., *In vivo assessment of the risk profile of evolving individual coronary plaques: A step closer*, Circulation, 2011, Vol. 124, 763–765.

[31] Giannoglou G., Antoniadis A., Koskinas K., Chatzizisis Y., *Flow and atherosclerosis in coronary bifurcations*, EuroIntervention, 2010, Vol. 6, J:J16-J23.