Wall motion and hemodynamics in intracranial aneurysms

Marcelo A. Castro
CONICET. Universidad Tecnológica Nacional, Facultad Regional Buenos Aires
Grupo de Investigación y Desarrollo en Bioingeniería
Medrano 951, Ciudad Autónoma de Buenos Aires, CP 1179, Argentina

E-mail: marcelo.a.castro@gmail.com

María C. Ahumada Olivares
Universidad Favaloro, Facultad de Ingeniería, Ciencias Exactas y Naturales
Solís 453, Ciudad Autónoma de Buenos Aires, CP 1078, Argentina

Christopher M. Putman
Inova Fairfax Hospital, Fairfax Radiological Consultants
3300 Gallows Road, Falls Church, VA 22042, USA

Juan R. Cebral
George Mason University. College of Sciences
4400 University Drive, Fairfax, VA, 22030, USA

Abstract. The optimal management of unruptured aneurysms is controversial and current decision making derived from the International Study of Unruptured Intracranial Aneurysms is based on aneurysm size and location. Wall shear stress triggers biomechanical responses of endothelial cells, which are associated to cerebral aneurysm initiation, progress and bleeding. Early identification of potential risk factors may contribute to decide the treatment and improve patient care. Previous studies have shown associations between high aneurysm wall shear stress values and both elevated risk of rupture and regions of aneurysm growing. Based on the assumption that damaged regions of the endothelium have different mechanical properties, regions with differentiated wall displacement amplitudes are expected. A previous approach based on the analysis of bidimensional dynamic tomographic angiography had been designed to investigate those correlations, but its main limitation was that wall motion was measured in a selected plane. In this work a high time and spatial resolution four-dimensional computerized tomographic angiography image of an anterior communicating artery aneurysm was acquired and analyzed to identify and characterize wall motion and intra-aneurysmal hemodynamics. All three-dimensional images were filtered and segmented and wall displacement was estimated within the aneurysm sac and compared to wall shear stress distributions from patient-specific unsteady finite element blood flow simulations. Regions were high wall motion was detected are in close agreement with regions were high wall shear stress values were obtained from the numerical blood flow simulations.

1 To whom any correspondence should be addressed.
Introduction

Stroke is the leading cause of long-term disability and the third cause of death in the Western World. Subarachnoid hemorrhage is one of the most severe types of stroke, which usually occurs when an intracranial aneurysm ruptures [1]. This kind of aneurysms tends to initiate at or near arterial bifurcation, mostly in the circle of Willis. The optimal management of unruptured aneurysms is controversial and current decision making is mainly based on aneurysm size and location, as derived from the International Study of Unruptured Intracranial Aneurysms (ISUIA) [2]. However, it is widely accepted that hemodynamics, particularly the wall shear stress (WSS), plays an important role on the development, growth and rupture of cerebral aneurysms. Previous studies have shown that ruptured aneurysms tended to have small impaction zones and complex or unstable flow patterns [3]. An association between concentrated jets, high WSS and high rupture rate was found in two previous studies where two cohorts of patients with cerebrovascular networks harboring aneurysms were analyzed using an image-based patient-specific computational fluid dynamics (CFD) methodology in the anterior communicating artery [4] and a set of terminal aneurysms [5]. Other authors analyzed twenty middle cerebral artery aneurysms and also found high WSS values in the group of ruptured aneurysms accompanied with low WSS in their domes, which would suggest that low WSS values may be responsible for aneurysm rupture [6]. However, in that study CFD models were truncated close to the aneurysm neck resulting in a simplified flow lacking of secondary flows. The effect of parent artery on intra aneurysmal hemodynamics was previously studied and higher WSS in the aneurysm domes was found to be systematically related to those secondary flows [7,8]. Another study showed that more than 80% of bleb formation occurs in regions of high WSS [9]. Recently, independent works showed that aneurysms tend to initiate in regions of moderate and elevated WSS [10] and regions of high WSS or high WSS spatial gradient [11]. Those findings have encouraged researchers to explore possible connections between hemodynamics, wall motion, wall weakness and aneurysm rupture. Many of the quantitative results of pulsation measurement reported in the literature correspond to experiments with phantoms, simulated images or experimental models [12-15]. A Methodology to estimate wall motion from X-ray dynamic imaging and impose the time-dependent deformation on the vascular CFD models reconstructed from 3D angiographic images was presented [16]. The blood flow characterization obtained from numerical integration of the Navier-Stokes equations in a rigid wall model did not significantly differ from that in compliant models where the deformation field was extrapolated from the bidimensional measurements [17,18]. The purpose of this work is to present a methodology to both estimate regions of high wall motion and reconstruct CFD vascular models from 4D computerized tomographic angiography (CTA) data sets.

Materials and methods

1.1. Images and modeling

A patient with a cerebral aneurysm in the anterior communicating artery was selected from our data base. A four dimensional computerized tomographic angiography image containing nineteen time points along the cardiac cycle was acquired using a Philips Integris System (Philips Medical Systems, Best, The Netherlands). Each three dimensional volume consisted of 512 x 512 x 205 pixels with a spatial resolution of 0.3125 x 0.3125 x 0.6125 mm covering a field of view of 16.0 x 16.0 x 12.81 cm. The imaging protocol was approved by the institutional review board and informed consent was obtained from the subjects. The data was exported into a PC for mathematic vascular modeling using a previously presented methodology [3,4,19]. Figure 1 shows three axial slices for the first time point. Images were cropped (Nx x Ny x Nz) and averaged in order to reduce the noise and the computational cost. In lower regions masks were applied to all images in order to differentiate internal carotid arteries from extravascular structures and properly reconstruct parent arteries, which is needed for a realistic blood flow simulation [7,8]. The vascular model was reconstructed from the reduced noise image obtained after averaging the nineteen three dimensional volumes. A high-quality volumetric finite element grid composed of tetrahedral elements with an advancing front technique was generated.
[20-22]. Element size was adjusted in order to approximately maintain the same number of elements in both large and small arteries (see Figure 2).

1.2. Numerical simulations
Finite element blood flow numerical simulations were performed. Blood was modelled as an incompressible fluid with density $1.0 \text{ g/cm}^3$ and viscosity $0.04 \text{ Poise}$. The governing equations were the unsteady Navier-Stokes equations in 3D [23]. Vessel walls were assumed rigid, and no slip boundary conditions were applied at the walls. Pulsatile flow conditions derived from phase-contrast magnetic resonance measurement in a healthy subject were imposed at the inlet of the model. Flow waveforms were scaled with the inlet area to achieve a mean WSS of $15 \text{ dyne/cm}^2$ at the inflows of the model according to a typical mean WSS value, and Murray’s and Poiseuille’s laws [24,25]. Fully developed pulsatile velocity profiles were prescribed with use of the Womersley solution [26,27]. Assuming that all distal vascular beds have similar total resistance to flow, traction-free boundary conditions with the same pressure level were applied at outlet boundaries. Both Newtonian and non-Newtonian rheologies were considered. For the non-Newtonian case, the Casson model was incorporated into the simulations by considering a velocity dependent apparent viscosity. The Navier-Stokes equations were numerically integrated by using a fully implicit finite-element formulation [28]. Our methodology is based on a projection scheme which arises from the hyperbolic character of the advection operator and the elliptic character of the pressure-Poisson equation. A fully implicit finite element formulation that yields to stable solutions for arbitrary time steps was utilized. The discretized momentum equation is solved using a generalized minimal residual (GMRES) algorithm, while the pressure equation, which is obtained by taking the divergence of the momentum and considering the incompressibility constraint, is solved using an incomplete lower-upper (ILU) preconditioned conjugate gradient solver. The algorithm is iterated until convergence is achieved at each time step. Two cardiac cycles using 100 time-steps per cycle were computed, and all of the results reported correspond to the second cardiac cycle.

Figure 1: Axial slices for the first time point. The following vascular structures are circled in red. Left: both internal carotid arteries along with the basilar artery. Middle: both A1 segments of the anterior cerebral arteries, the anterior communicating artery and the lower portion of the aneurysm. Right: both A2 segments of the anterior cerebral arteries along with the upper portion of the aneurysm. See Figure 2 for A1 and A2 segments.

1.3. Wall motion and wall shear stress
In order to detect those regions where wall motion is not negligible the time evolution of segmented clusters at every slice within the volume of interest was analyzed. For each of the $N=19$ three dimensional images ($N \times Ny \times Nz$) the same selected number of $NS$ slices covering the whole aneurysm was chosen for the analysis. A set of $NS$ images $N x Ny x N$ was created to analyze the time evolution of pixel intensity in all $NS$ slices. Four classes were identified, two of which corresponded to the background ($C1$ and $C2$), and the other two are associated to the border of the vascular domain ($C3$) and the vasculature ($C4$). A four-class fuzzy c-means algorithm was utilized to create the four
images corresponding to the membership probability associated to each of the NS images, where the pixel intensity \(I(0<I<1)\) represents the probability of that pixel to belong to the corresponding class. Particularly, for the image associated to \(C4\), the pixel intensity represents the probability of that pixel to belong to the vasculature. It is expected that those probabilities should significantly change for pixels close to a moving boundary. Consequently, the maximum difference of the probability along the \(N\) time slices was computed for each of the \(NxNy\) pixels for each of the NS images. This information was used to reconstruct a \(NxNy\) image where the pixel intensity represents the maximum difference in time of the probability to belong to class \(C4\). Since \(C1\) and \(C2\) clusters correspond to the lowest intensities and \(C4\) to the highest ones, pixels that change from vasculature to background due to wall motion are expected to have significant different probability to belong to class \(C4\). That image was segmented using different thresholds. Regions that are likely to change from vasculature to background were isolated and compared to shear stress distribution over the wall.

Maps of WSS magnitude were created to visualize the distribution of shear forces on the aneurysm wall at the systolic peak where the maximum values are expected. Regions of elevated, mild and low WSS were investigated. Additionally, WSS computed using Newtonian and Casson rheologies were compared. Although in this preliminary study the model walls were rigid, it is expected that flow pattern should remain roughly unchanged for moderate wall displacements [16,17]. This hypothesis will be further tested in large aneurysms with high deformations using dynamic tomographic angiography images. Streamlines were created and the velocity field was imaged in order to investigate the relation between the location of the impaction zone, the maximum wall motion and the elevated WSS values and the flow characterization.

Figure 2: a) Vascular model containing both internal carotid arteries, anterior cerebral arteries and middle cerebral arteries (anterior view); b) Grid of triangles (posterior view). A1 segments are proximal to the AComA, while A2 segments are distal to the AComA.

Results
This first paragraph explains the results of the clustering algorithm used to detect regions of high wall displacements. Figure 3a corresponds to a selected axial slice and a given time were the brightest spots correspond to both A2 segments of the anterior cerebral arteries (upper left corner) and the upper region of the anterior communicating artery aneurysm (brightest and largest spot). Visual inspection of that image revealed a background (extravascular structures) with a large range of pixel intensities, while the highest intensities corresponded to the vasculature. A transition takes place in the boundary between the vasculature and the background. Figures 3b through 3e correspond to the probability maps for classes \(C1\) through \(C4\), respectively. Darker regions correspond to pixels that unlikely belong to a particular class. Figure 4a and 4b correspond to the same selected slice but at different times. Slightly changes in the aneurysm morphology can be observed. Figure 4c shows the maximum difference in the probability that a given pixel belongs to class \(C4\) at that slice. Pixels with higher
intensities have significant different probability of belonging to class $C4$ along the cardiac cycle. Those pixels are mainly located at the aneurysm wall. Additionally, non-zero values are observed in other regions, which is due to the typical noise observed in these images. It is expected that higher threshold should discriminate between changes produced by noise and those that arise from the wall displacement.

Figure 3: a) Selected axial slice at a given time; b) Membership probability for class $C1$; c) Membership probability for class $C2$; d) Membership probability for class $C3$; e) Membership probability map for class $C4$.

Figure 4: a,b) Selected axial slice at two different times; c) Maximum difference in the probability of those pixels to belong to class $C4$ (Vasculature).

The image that represents the maximum change along the cardiac cycle in the probability of a given pixel to belong to class $C4$ (Figure 4c) can be segmented in order to identify those pixels that experiment the highest changes. Changes due to noise are not extremely high and are observed in small disconnected regions. On the other hand, changes due to wall motion are associated to higher values and are observed in larger areas. Therefore, an intensity-based segmentation for different thresholds ($T1=0.325$, $T2=0.400$) was performed in order to investigate the location where the highest displacements take place. The segmented pixels are shown along with the WSS distribution at the systolic peak for the Newtonian rheology (Figure 5a) and the Casson rheology (Figure 5b). As it was expected, the lower the threshold, the larger the segmented region. The grey regions in Figure 5c and Figure 5d correspond to pixels that experiment a change in the probability of belonging to class $C4$ higher than 0.325 and 0.400, respectively, displayed over the Newtonian WSS distribution. For example, in Figure 5d, if any of those grey pixels belongs to class $C4$ with a probability of 0.80 at a given time, there exists another time when that probability drops below 0.40. Figure 6 compares WSS distribution, the velocity field and the region where the largest wall displacement is more likely to occur, for the Newtonian case. That region is located close to WSS peak slightly displaced in the flow direction in region of elevated WSS (see Figures 6b).

Streamlines were computed in order to study whether or not the aneurysm behaves as a bilateral aneurysm (e.g., it receives blood from two differences sources). Blue streamlines are originated in the right internal carotid artery and red ones do in the left carotid artery (see Figure 6d). Complex velocity field observed in Figure 6d is due to the collision of both jets. However, intraneurysmal flow pattern is mostly dominated by the left inflow while high WSS values occur where both jets collide.

Figure 7 compares WSS distributions for the Newtonian and Casson rheologies. Figures 7a and 7c show the Newtonian WSS distribution at the systolic peak from the front and back view, respectively. Analogously, Figures 7b and 7d show the difference between both rheologies. No significant difference in the absolute value of the WSS is observed in black regions (higher velocities). Magenta represents regions where the Casson WSS is as much as twice as the Newtonian WSS. It is
observed that Cason WSS is larger in regions of low WSS, which are located far from the impaction zone and where the wall exhibit larger amplitudes of motion. On the other hand, blue represents regions where the Newtonian WSS is as much as twice the Casson WSS. The region where the highest WSS values are observed at the systolic peak has an average of 68.6 dyn/cm$^2$ and 69.2 dyn/cm$^2$ for Casson and Newtonian rheologies, respectively. Therefore, Newtonian WSS is 0.87% higher than Casson WSS. On the other hand, in the region where the lowest WSS values are observed, the average WSS values are 1.22 dyn/cm$^2$ and 0.51 dyn/cm$^2$, for Casson and Newtonian rheologies, respectively. Therefore, Newtonian WSS is 42.8% lower than Casson WSS, in agreement with the theory [18].

Figure 5: WSS distribution at the systolic peak for Newtonian rheology (a) and Casson rheology (b). Newtonian WSS distribution at the systolic peak along with the segmented region where higher wall displacements are expected for T1=0.325 (c) and T2=0.400 (d).

Figure 6: a) WSS distribution at the systolic peak; b) WSS distribution at the systolic peak along with the segmented region where higher wall displacements are expected (T1=0.325); c) Velocity field; d) Streamlines coloured according to the source of inflow. Blue streamlines are originated at the right internal carotid artery, and red to the left internal carotid artery.

Figure 7: a) Newtonian WSS distribution at the systolic peak (front view); b) Difference between WSS distributions at the systolic peak (front view); c) Newtonian WSS distribution at the systolic peak (back view); b) Difference between WSS distributions at the systolic peak (back view). In Figures (b) and (d), magenta represents regions where the Casson WSS is as much as twice the Newtonian WSS, while blue represents regions where the Newtonian WSS is as much as twice the Casson WSS. No significant difference in the absolute value of the WSS is observed in black regions.
Discussion
The purpose of this work was to design and test a methodology to estimate both the aneurysm wall shear stress, and aneurysm wall motion from 4D computerized tomographic angiography images. A test case was randomly selected from our data base. The patient had a large aneurysm with multiple blebs in the anterior communicating artery. The high temporal and spatial resolution set of images consisted of nineteen three dimensional images along the cardiac cycle. Images were averaged to reduce the impact of noise on the reconstruction of the vascular model used to generate the finite element unstructured volumetric grid for the blood flow simulation and wall shear stress estimation. In order to estimate the localization of regions that exhibit an important wall displacement, the time evolution of individual slices across the aneurysm was analyzed and a fuzzy c-means clustering algorithm was applied to simultaneously segment all time points in four different classes for each slice. The probability maps for each class were recorded. Pixels within the vascular domain but close to a moving boundary exhibited a change in that probability. That difference was segmented using different thresholds. The regions exhibiting important displacements were overlapped with the WSS distribution. Maximum WSS values at the systolic peak occurred close to the region where important displacements took place. Particularly, this anterior communicating artery aneurysm behaved as a bilateral aneurysm, which means that received blood from both A1 segments of the anterior cerebral arteries [4], and high wall motion occurred close to where both jets collided. This strategy estimates the wall motion from a 3D analysis and overcomes some of the limitations from a previous methodology where the motion was measured in a plane and extrapolated to the aneurysm [16]. WSS distributions remain unchanged when different rheologies are used. However, absolute values in specific regions are observed. Vascular regions under high velocities have high WSS values associated in the wall therefore, Casson effect is almost negligible. On the other hand, in regions under extremely low WSS, non-Newtonian effects are more important. However, that does not occur in regions where the wall exhibit large amplitudes of motion.

The methodology has some limitations. First, the computational fluid dynamics simulation was performed under the assumption of rigid walls. Although this assumption is not accurate, it was observed in a previous work that moderate wall displacements along the cardiac cycle do not significantly change the WSS distribution over the wall of the aneurysm sac [17]. However, in future works wall motion will be also included in the CFD blood flow simulations. Second, bilateral anterior communicating artery aneurysms have flow patterns that depend on inflow conditions. We imposed the same waveform at both internal carotid arteries, but scaled according to their cross-sectional areas based on a typical wall shear stress value, and both Murray’s and Poiseuille’s laws [23]. However, it was previously observed that differences in either those mean flow rates at the inflow segments or waveform phases may relocate the region where the maximum wall shear stress appeared. In this particular case, a sensitivity study should be carried out to determine whether or not the location of that maximum may be affected. Finally, in order to estimate the probability to belong to a given class, images were not pre-processed. Consequently, pixels in the background that changed from one class to another due to the noise were also detected as possible candidates. However, those regions were isolated and the change in the probability was not as large as that observed in boundary pixels. It was observed that higher thresholds kept the large regions where displacements occurred due to wall motion, and discarded those small regions due to the noise.

Conclusions
The present work shows that four dimensional computerized tomographic angiography images can be used to estimate the location of regions with both important wall motion and high wall shear stress by means of a combination of image segmentation algorithms and image-based computational fluid dynamics blood flow simulations. The results suggest that aneurysm wall tends to exhibit higher displacements along the cardiac cycle in regions with elevated wall shear stress and complex flow pattern.
Acknowledgements
Marcelo Castro wants to acknowledge CONICET (Consejo Nacional de Investigaciones Científicas y Técnicas), MINCyT (Ministerio de Ciencia y Tecnología – Project PICT Bicentenario # 984), UTN (Universidad Tecnológica Nacional, Project PID # 1579), and Fundación Florencio Fiorini, Buenos Aires, Argentina, for financial support.

References
[1] Hwang S, Kim K, Nam T. “A pseudoaneurysm appeared after rebleeding,” Journal of Korean Neurosurgical Society, 41, 134-136 (2007)
[2] Wiebers DO, et al. “International study of unruptured intracranial aneurysms investigators. Unruptured intra-cranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment,” Lancet, 362, 103–110 (2003)
[3] Cebral JR, Castro MA, Burgess JE, Pergolizi RS, Sheridan MJ, Putman CM. “Characterization of cerebral aneurysms for assessing risk of rupture using patient-specific computational hemodynamics models,” Am J Neuroradiol, 26, 2550 –2559 (2005)
[4] Castro MA, Putman CM, Cebral JR. “Hemodynamic Patterns of Anterior Communicating Artery Aneurysms: A Possible Association with Rupture,” Am J Neuroradiol, 30(2), 297-302 (2009)
[5] Castro MA, Putman CM, Radaelli A, Frangi AF, Cebral JR. “Hemodynamics and rupture of terminal cerebral aneurysms,” Acad Radiol, 16(19), 1201-1207 (2009)
[6] Shojima M, Oshima M, Takagi K, Torii R, Hayakawa M, Katada K, Morita A, Kirino T. “Magnitude and role of wall shear stress on cerebral aneurysm: computational fluid dynamic study of 20 middle cerebral artery aneurysms,” Stroke, 35, 2500-2505 (2004)
[7] Castro MA, Putman CM, Cebral JR. “Computational fluid dynamics modeling of intracranial aneurysms: effects of parent artery segmentation on intra-aneurysmal hemodynamics,” Am J Neuroradiol, 27, 1703-1709 (2006)
[8] Castro MA, Putman CM, Cebral JR. “Effects of Parent Vessel Geometry on Intraaneurysmal Flow Pattern,” Proc. SPIE Medical Imaging 2006: Physics of Medical Imaging Image Reconstruction, 6143, 123-131 (2006)
[9] Cebral JR, Sheridan MJ, Putman CM. “Hemodynamics and Bleb Formation in Intracranial Aneurysms,” Am J Neuroradiol, 31, 304-310 (2010)
[10] Castro MA, Putman CM, Cebral JR. “Computational analysis of anterior communicating artery aneurysm shear stress before and after aneurysm formation,” Journal of Physics C.S., 32, 1-7 (2011)
[11] Kulcsár Z, Ugron A, Marosfo M, Berentei Z, Paal G, Szikora I. “Hemodynamics of Cerebral Aneurysm Initiation: The Role of Wall Shear Stress and Spatial Wall Shear Stress Gradient,” Am J Neuroradiol, 32(3), 587-594 (2011)
[12] Yaghmai V, Rohany M, Shaibani A, Huber M, Soud H, Russell EJ, Walker MT. “Pulsatility imaging of saccular aneurysm model by 64-slice CT with dynamic multiscan technique,” J Vasc Intervent Radiol, 18, 785–788 (2007)
[13] Boecher-Schwarz HG, Ringel K, Kopacz L, Heimann A, Kempski O. “Ex vivo study of the physical effect of coils on pressure and flow dynamics in experimental aneurysms,” Am J Neuroradiol, 21, 1532–1536 (2000)
[14] Ueno J, Matsuo T, Sugiyama K, Okeda R. “Mechanism underlying the prevention of aneurismal rupture by coil embolization,” J Med Dental Sci., 49, 135–141 (2002)
[15] Zhang C, Villa Uriol MC, De Craene M, Pozo JM, Frangi AF. “Time-resolved 3D rotational angiography reconstruction: Towards cerebral aneurysm pulsatile analysis,” Int J Comput Assist Radiol Surg, 3, S44–46 (2008)
[16] Oubel E, Cebral JR, De Craene M, Blanc R, Blasco R, Macho J, Putman CM, Frangi AF. “Wall motion setimation in Intracranial aneurysms,” Physiol Meas, 31, 1119-1135 (2010)
[17] Dempere-Maro L, Oubel E, Castro MA, Putman CM, Frangi AF, Cebral JR. “Estimation of wall motion in intracranial aneurysms and its effects on hemodynamic patterns,” Lecture Notes in Computer Science, 4191, 438-445 (2006)  
[18] Castro MA, Putman CM, Cebral JR. “Computational hemodynamics of cerebral aneurysms: Assessing the risk of rupture,” VDM Verlag (2008)  
[19] Yim P, Vasbinder GB, Ho VB, Choyke PL. “Isosurfaces as deformable models for magnetic resonance angiography,” IEEE – Trans Med Imag, 22(7), 875-881 (2003)  
[20] Löhner R. “Extensions and improvements of the advancing front grid generation technique,” Comp Meth App Mech Eng, 5, 119–132 (1996).  
[21] Löhner R. “Regridding surface triangulations,” J Comput Phys, 126, 1–10 (1996)  
[22] Löhner R. “Automatic unstructured grid generators,” Finite Elements Analysis Design, 25, 111–134 (1997)  
[23] Mazumdar JN. “Biofluid Mechanics,” World Scientific, Singapore (1992)  
[24] Cebral JR, Castro MA, Putman CM, Alperin N. “Flow-area relationship in internal carotid and vertebral arteries,” Physiol Meas, 29(10), 585–594 (2008)  
[25] Sherman TF, “On connecting large vessels to small. The meaning of Murray’s law,” J Gen Physiol, 78, 431–453 (1981)  
[26] Womersley JR, “Method for the calculation of velocity, rate of flow and viscous drag in arteries when the pressure gradient is known,” J Physiol, 127, 553–563 (1955)  
[27] Taylor CA, Hughes TJR, Zarins CK. “Finite element modeling of blood flow in arteries,” Comp Meth Appl Mech Engin, 158, 155–196 (1998)  
[28] Cebral JR, Castro MA, Appanaboyina S, Putman C, Millán D, Frangi A. “Efficient Pipeline for Image-Based Patient-Specific Analysis of Cerebral Aneurysms Hemodynamics: Technique and Sensitivity,” IEEE - Trans Med Imag - Special Issue on Vascular Imaging, 24(4), 457-467 (2005)