Determination of Wall Tension in Cerebral Artery Aneurysms by Numerical Simulation

Jørgen Gjernes Isaksen, MD; Yuri Bazilevs, PhD; Trond Kvamsdal, PhD; Yongjie Zhang, PhD; Jon H. Kaspersen, PhD; Knut Waterloo, PhD; Bertil Romner, PhD; Tor Ingebrigtsen, PhD

Background and Purpose—Cerebral artery aneurysms rupture when wall tension exceeds the strength of the wall tissue. At present, risk-assessment of unruptured aneurysms does not include evaluation of the lesions shape, yet clinical experience suggests that this is of importance. We aimed to develop a computational model for simulation of fluid-structure interaction in cerebral aneurysms based on patient specific lesion geometry, with special emphasis on wall tension.

Methods—An advanced isogeometric fluid-structure analysis model incorporating flexible aneurysm wall based on patient specific computed tomography angiogram images was developed. Variables used in the simulation model were retrieved from a literature review.

Results—The simulation results exposed areas of high wall tension and wall displacement located where aneurysms usually rupture.

Conclusion—We suggest that analyzing wall tension and wall displacement in cerebral aneurysms by numeric simulation could be developed into a novel method for individualized prediction of rupture risk. (Stroke. 2008;39:3172-3178.)

Key Words: computer assisted numerical analysis ■ intracranial aneurysm ■ risk ■ rupture ■ tension

Modern neuroimaging techniques often detect unruptured cerebral artery aneurysms, which are estimated to be prevalent in 3% to 6% of the population.1 Prophylactic treatment is then an option, but may cause morbidity.2 The specific risk for rupture is unknown, and advice to patients is therefore based on general knowledge on risk factors for subarachnoid hemorrhage (SAH), derived from epidemiological studies. The most important are hypertension, smoking, and family history of SAH.3 Further, aneurysms of large size, proximal location, and small neck/fundus ratio are associated with increased risk for rupture, but this knowledge is not sufficiently specific for risk assessment in individuals.2,4

Biomechanically, rupture of an aneurysm occurs when wall tension exceeds the strength of the wall tissue. The ideal approach to risk assessment would therefore be to determine tension and material strength of the tissue in the aneurismal wall. Individual aneurismal material strength is impossible to measure noninvasively, but wall tension can be estimated using numeric simulation. Recently, we showed that numeric simulations based on patient-specific image data may be used to simulate wall shear stress (WSS) and pressure in the circle of Willis.5 Others have attempted the same approach to analysis of cerebral aneurysms, with focus on WSS, which is thought to be associated with aneurysm formation.5–7 Studies of abdominal aortic aneurysms suggest that patient specific computational modeling of maximum wall tension (MWT) may predict rupture.8,9 MWT in the aneurysm wall is therefore the quantity of interest in the present computational simulations.

The aim of this study was to develop a computational procedure for determining wall tension in cerebral aneurysms for individual patients. The ultimate goal is to provide the surgeon with a methodology that indicates low or high rupture risk based on noninvasive patient specific imaging data.

Methods

Source of Imaging Data
Image-data from a 68-year-old female patient with an unruptured middle cerebral artery aneurysm treated at our department was used for analysis. Three dimensional (3D) imaging of the aneurysm was obtained by CT angiography (CTA) on a 16 multi-detector row spiral computed tomography (CT) scanner (Somatom Sensation 16, Siemens). Using an intravenous cannula in the antecubital fossa, 90 mL of contrast agent (Omnipaque, Schering AG) diluted with 40 mL NaCl 0,9% were injected with a powered injector at the rate of 4.0 mL/s. The computed tomography images were reconstructed using a slice thickness of 1 mm, and a reconstruction interval of 0.5 mm. The reformatted images were performed in the plane of the external carotid artery (ECA).
mL/s. An automatic bolus-tracking system was used, which started the data acquisition when the reference point (the intracranial left internal carotid artery) reached 100 Hounsfield units (HU) according to the following protocol: spiral mode, 0.5 rotation/s, 16-detector rows at 1.0 mm intervals with 0.5 mm increment, table speed 10 mm/rotation at Kernel H10 and acquisition parameters 120 KVP/260 mAs.

**Segmentation and the Vascular Pipeline**

The vascular pipeline (supplemental Figure I, available online at http://stroke.ahajournals.org) is a sequence of procedures that allow one to go from patient-specific imaging data to simulation in four main stages: (1) preprocessing stage with quality improvement of the imaging data and segmentation, (2) surface model construction and arterial paths extraction, (3) analysis-suitable Non-Uniform Rational B-splines (NURBS) solid construction stage, (4) fluid-structure interaction analysis stage that uses isogeometric analysis.\(^{10,11}\) First, the 16 bit CTA data sets were imported into ImageJ (open-source software, http://rsb.info.nih.gov/ij/) and resampled to an 8-bit RAW image data volume with a size of 256\(^\times\)256\(^\times\)N. N represents the number of images in the DICOM series, which in this case equals the number of images acquired in the axial direction. The RAW image data volume was then loaded into CustusX and visualized using a volume rendering procedure. CustusX is developed by SINTEF Health Research as a planning and navigation system for imaged data volume with a size of 256\(^\times\)256\(^\times\)N. It includes a segmentation module based on the Visualization Toolkit (open-source software, http://public.kitware.com/VTK/). Based on the Visualization Toolkit (open-source software, http://public.kitware.com/VTK/).

The aneurysm was identified, and a seed point for the segmentation was set in the middle. Then an upper and lower threshold for the region grow algorithm was specified, and the connecting vessels identified and kept. This area of interest included the aneurismal structure with its connecting vessels. The 3D surface of the segmented structure was defined by passing the segmented volume through a marching cubes procedure. The surface of the aneurismal structure was saved in STL format, which is the input data for the construction of the analysis-suitable geometric model. Analysis-suitable NURBS solid construction used skeleton-based sweeping of the vessel cross-section template, application of intersection templates for constructing branching configurations, and projection onto the true geometry.

**Literature Review of Geometric and Material Parameters and Boundary Conditions**

Geometric parameters (aneurysm wall thickness), material parameters (aneurysm and arterial wall properties, blood viscosity, and fluid and tissue density), and boundary conditions (flow characteristics at inflow arteries, resistance in outflow arteries, and inlet and outlet arteries relation to environment) were retrieved from the literature. We performed a PubMed search using the words “aneurysm, cerebral, flow, pressure, wall, properties, blood, intracranial, FEM, and finite element” in different combinations. With regard to measurable properties such as aneurysm wall thickness, blood flow, blood viscosity, etc, only results from articles reporting original

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MCA indicates middle cerebral artery.
measurements were used. Aneurysm wall properties are not possible to evaluate exact in vivo studies, so results from articles reporting computational modeling and in vitro tests were also accepted.

Studies consistently report variations in wall thickness between aneurysms and within single aneurysms, and most report that the wall is thinnest in the dome.13-15 Histological studies of aneurysms resected during surgery,12,15 and autopsy-studies of unruptured aneurysms13,14 were identified, and the reported thicknesses varied between 16 and 400 μm. In summary, the reviewed studies indicate that most aneurysms have a wall thickness between 30 and 200 μm.

The aneurysm wall is not rigid but is less distensible than arteries.13 In vitro studies of aneurysms from autopsy material, resected aneurysms, and model aneurysms from connective tissues have measured different wall properties, such as elastance and breaking strength.13,14,16 Based on these directly measured properties, different equations describing aneurysm wall properties have been developed. The most accepted model is the nonlinear isotropic material, described by Fung-Type strain energy function and isotropic nonlinear hyperelastic material.17-20

For computational purposes, blood is generally accepted as a noncompressible Newtonian fluid with a density slightly higher than water (1000 to 1055 Kg/m³).20-22 This may be inaccurate in the smallest vessels, where the size of blood cells approximates the vessel diameter, and in low-flow vessels like veins, where blood starts to deviate from Newtonian properties.23-25 In these settings, simulations with the non-Newtonian Casson stress model show the same spatial distribution of WSS with only slightly higher values than the Newtonian model.26

The viscosity of blood varies according to measurement technique, initial or late phase of fluid movement, hematocrit, and temperature.23,24 Different models and different units are reported. Both dynamic and static viscosities are used and may differ, depending on the flow system studied. For computational purposes incorporating blood as a Newtonian fluid, the viscosity is generally accepted to be approximately 4.0×10⁻¹ N s/m².23,27

Measurements of cerebral blood flow velocities and flow rates show variations among patients, but reference values based on a reasonable number of measurements have been reported.26-30 Generally, internal carotid artery (ICA) and middle cerebral artery (MCA) flow velocities are approximately 40 cm/s and 60 cm/s, respectively. Flow rates are more difficult to obtain because of the need for invasive measurements. Therefore, values calculated from other measurements such as pulsatility and flow velocities are used in computed simulation work. The Womersley formulation is generally the most accepted method in recent numeric simulation work.20 A summary of all parameters of interest, values from the literature, and values used in our model is given in the Table.

Geometric and Material Parameters and Boundary Conditions Used in the Patient-Specific Computation

We formulated the fluid-structure interaction problem as follows: Blood was governed by the Navier-Stokes equations of incompressible flow using constant viscosity. The arterial and aneurismal wall was treated as an isotropic nonlinear hyperelastic solid. At the interface between the blood and the walls, the following 2 conditions were assumed to hold: (1) fluid and solid velocities coincide, and (2) fluid and solid traction forces are in equilibrium. Both the solid and the fluid equations were posed over a moving domain. The domain motion was prescribed as follows: In the solid region, Lagrangian description was used, that is, the motion of the solid subdomain coincides with the particle motion of the solid. However, the motion of the fluid domain is not coincident with the motion of fluid particles, except at the fluid-solid boundary. To prescribe the motion of the fluid domain, we solved an auxiliary linear elastic boundary value problem. The following boundary conditions were used: At the inlet we specified a pulsatile flow with a period of 1 s. The flow rate was set to a pulsatile velocity profile described by the Womersley formulation.27 All outlets were assigned a resistance boundary condition of the form p = CrQ + p₀, where p is the pressure, Q is the flow rate, C is the resistance constant, and p₀ is the base pressure. The p₀ is responsible for setting the physiological pressure level in the system. The solid was fixed at all the inlets and outlets and zero stress boundary condition was specified at the outer arterial wall.

The following material parameters were used in the simulation: The density of the solid was 1 g/cm³, equivalent reference configuration Young’s modulus and Poisson’s ratio were 10⁹ dyn/cm² and 0.45, respectively. The density of the fluid was also 1 g/cm³, and its viscosity was 0.04 g/cm s. In the computations, p₀ was set to 113350.5 dyn/cm², which corresponds to 85 mm Hg, and C, was set to 37500 dyn s/cm² at all outflow boundaries. We assumed the aneurismal wall to be uniform and equal to 0.015 cm.

Computational Procedures

We used NURBS-based isogeometric analysis31 to discretize the coupled fluid-structure system in space. Vascular blood flow is a time-dependent phenomenon, and we used the generalized-alpha method to discretize the equations in time.32 The fluid-structure system was advanced in time for several heart beats before the data were collected. Figure 1 shows the computational model with the associated geometry and boundary conditions.

Results

Figure 2 shows relative arterial wall displacement during peak systole and diastole in a part of the aneurysm model, illustrating the fact that wall displacements may not be ignored during the dynamic analysis. In Figure 3, contours of the magnitude of wall tension plotted on the moving domain are visualized. Wall tension was unevenly distributed, and one spot of high wall tension appeared at the aneurysm dome at peak systole. Figure 4 shows the distribution and magnitude of wall displacement during the heart cycle. The maximum displacement occurred at peak systole in 3 distinct spots at the aneurysm dome. The magnitude of wall displacement was equal to approximately three times the wall thickness. The location of maximum displacement during the dynamic simulation remained unchanged, and corresponded to the regions with highest wall tension, located directly above the inflow plane. Notably, the spot with highest wall displacement had the same localization as the spot of highest wall tension.
tension, corresponding to the region where aneurysms are empirically most likely to rupture. Finally, blood velocity streamlines at different times during the heart cycle are visualized in Figure 5. Blood flow velocities were highest near the aneurysm neck and, inside the aneurysm, along the wall. Recirculation was present inside the aneurysm dome. Reynolds number of the flow was not sufficiently high for turbulence to occur, but the flow was unsteady and fairly complex.

**Discussion**

This study report the development of a patient-specific computational model with flexible walls for numeric simulation of interaction of blood flow and vessel walls in cerebral artery aneurysms. Specifically, the simulations exposed areas of high wall tension and wall displacement located where aneurysms usually rupture. This approach may be developed to a method for better prediction of risk for aneurysm rupture in each individual patient.

Early research on computation of vascular blood flow used simplified model geometries, reduced fluid models, and rigid arterial walls. Taylor and co workers introduced patient-specific vascular modeling, wherein the finite element Navier-Stokes solver was used to compute blood flow in arteries. Subsequent research showed that the rigid wall assumption precludes pressure wave propagation, overestimates WSS, and is incapable of predicting the time delay between the peaks of inflow and outflow flow rates. Accordingly, flexible walls should be incorporated in the computations. Introduction of flexible walls require more advanced methods for fluid-structure interaction, because two moving subdomains (blood and the arterial wall) are included in the simulations. Various computational procedures have successfully been applied to this problem. Isogeometric analysis was recently introduced in as a new computational approach.
methodology. This approach generalizes and improves the standard finite element method in geometric modeling, mesh refinement, and discrete solution representation. Isogeometric analysis based on NURBS has recently been successfully applied to simulation of arterial fluid-structure interaction. NURBS are accurate and efficient for geometric modeling, and exhibit convergence properties superior to low order finite elements, and are especially suited for simulations that involve complex geometry of the cerebral vasculature and abnormalities such as aneurysms.

Few have attempted to apply numeric simulation to patient specific analysis of cerebral artery aneurysms, and previous studies have been restricted by the assumption of rigid arterial and aneurismal walls. Therefore, these studies could not analyze wall tension or wall displacement, but were limited to simulations of WSS. The results generally suggest that WSS is highest near the neck of the aneurysm, and conclude that WSS probably contributes to the formation of aneurysms. Recently, the first simulations of cerebral aneurysms including elastic walls were reported. Maximum wall displacement was found at the tip of the aneurysm, and impingement forces on the aneurismal wall were found to be greatest in the neck. The present study is the first to report simulations of cerebral aneurysms using isogeometric fluid-structure interaction analysis with flexible walls, focusing on wall tension. We show that the areas of maximum wall tension and displacement correspond, and that they are located where aneurysms are known to be most vulnerable to rupture. Based on the present study and results from similar work, we hypothesize that WSS and impingement forces on the aneurismal wall are involved in formation and growth of the aneurysm, while rupture is dependent on wall tension.

The need for more precise evaluation of individual aneurysm rupture risk is desirable but challenging. With current management-guidelines, some patients still bleed from their aneurysm which was decided not to treat, and many patients are probably given treatment causing morbidity for aneurysms with very low rupture risk. Another clinical dilemma is when a patient presenting with SAH has multiple aneurysms (about 10%), and the aneurysm responsible for the hemorrhage cannot be identified. The possibility evaluate the aneurysms with the method presented in this study might improve decision making in the management of patients in both of these settings.

Numeric simulations must be based on reliable material properties and boundary conditions. Most of the parameters cannot be measured in the individual patient, and the simulations must therefore be based on data retrieved from experimental studies. This generalization will influence the simulation results, but are unavoidable with current technology. The present study is based on a comprehensive overview of such parameters, to make the simulations as robust as possibly (Table). The assumption of a uniform and average wall thickness and wall property represent the most challenging inaccuracies in the simulation. This will cause the absolute values of the simulation results to be inaccurate and ignore the effect of local areas of thin wall and weak material properties. The spatial distribution of simulation results will be less affected, and the observed variations will be caused by the shape of the aneurysm and, to a lesser degree, the anatomy.
of the connected arteries. Also, the assumption of a uniform and average blood viscosity is inaccurate, as the viscosity is influenced by patient-specific parameters like hematocrit, osmolality, and temperature. Because of the assumptions and generalizations used in the simulations, interpretation of the results should focus on the spatial distributions and differences of stress and pressures, and not absolute values. The possibility to use patient specific parameters in the model constitutes the strength of the methodology. To further improve and individualize the simulation results, additional patient specific data, such as blood pressure and blood flow velocities measured by Doppler ultrasonography, can easily be included. To test the predictive value of the method, two follow up studies are in progress: One where ruptured and unruptured aneurysms are compared and one study where we analyze aneurysms which were not treated and eventually ruptured with comparable untreated aneurysms that did not rupture.

Conclusion
We report a patient-specific numeric simulation model of cerebral artery aneurysms with flexible walls. Because rupture of an aneurysm occurs when the wall tension exceeds the wall tissue strength, our simulation model focuses on wall tension, which is highly dependent on the three dimensional conformation of the lesion. The reported results, where areas with high wall tension corresponded to the usual rupture sites, support clinical experience suggesting that the shape of the aneurysm is an important factor with regard to its rupture risk. We believe that the model has a potential to be developed into a novel method for individualized prediction of risk for aneurysm rupture. Two ongoing follow-up studies compare simulation results between ruptured and nonruptured aneurysms and untreated aneurysms that ruptured with untreated aneurysms that did not. This work illustrates how recent progress in computational modeling may be applied to analysis of common problems in daily clinical decision making.

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None.

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