Computational model can predict aneurysm growth

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Linking changes in arterial microstructure with fluid dynamics of blood flow provides a detailed account of how aneurysms develop.

Aneurysms are local dilations of the wall of an artery. They primarily form in the aorta where it passes through the chest or abdomen and in arteries that feed the brain. Abdominal aortic aneurysms are found in approximately 2% of elderly people, while cerebral aneurysms are present in 2–5% of adults. Although the causes and geometries of abdominal and cerebral aneurysm formation differ, both may rupture. The resulting hemorrhage can lead to death. Rupture of cerebral and abdominal aneurysms results in morbidity rates of 35–50 and 80%, respectively.

An operation may be performed to remove an aneurysm or repair the arterial wall, but the surgery is risky. Thus, the accepted protocol is to monitor a patient until the chance of rupture exceeds the risk of an operation. However, the estimated risk of rupture is based on crude measures: maximum diameter of the swelling and growth rates. These criteria fail to identify small aneurysms that are likely to rupture. They also may miscalculate the risk from large aneurysms that are unlikely to rupture for which dangerous (and expensive) surgery could safely be avoided. Computational models that can predict 3D stress fields and future growth of aneurysms may provide effective diagnostic tools. To address this issue, we are developing novel models of cerebral aneurysm growth. Our effort is part of the @neurist program, a European initiative to integrate biomedical informatics in the management of cerebral aneurysms.

Aneurysm formation

The physiology and microstructure of the artery are intimately linked to its hemodynamic environment. For example, when blood pressure is chronically elevated, the arterial wall thickens in response to the increased load. Persistently altered rates of blood flow may cause the artery to change its diameter. Such remodeling usually maintains the artery and the cells within it in an optimum homeostatic state. However, pathological remodeling can occur, as in the development of an aneurysm.

The formation of an aneurysm is a complex physiological process that is not yet clearly understood. The mechanisms that give rise to an aneurysm involve the interplay between local mechanical forces acting on the arterial wall and biological processes occurring at the cellular level.

Cells within the arterial wall continually maintain the structure of the artery. The inner surface of the arterial wall is

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Figure 2. Green–Lagrange strains in elastin (left) and collagen (right) as an aneurysm develops. Note that the elastin strains continue to increase, while the collagen strains return to equilibrium values as the size of the aneurysm stabilizes.

Figure 3. Solution of the 3D blood flow within a computational model of a developing aneurysm.

Figure 4. Wall shear stress distributions within a developing aneurysm.

composed of endothelial cells (see Figure 1), which have mechanoreceptors that respond to shear stress on the vessel wall by sending chemical signals. These messages activate signaling pathways within the cell that control the expression of genes and proteins, which can alter the microstructure of the artery.

To develop a model of aneurysm growth, it is desirable to use a constitutive model of the healthy arterial wall that explicitly accounts for the individual structural components. The model developed by Holzapfel, Gasser, and Ogden (HGO model) is ideal for this purpose. It accounts for the mechanical response of the individual layers of the arterial wall and the predominant load-bearing constituents of each layer, i.e., elastin and collagen (see Figure 1). Elastin allows the artery to stretch, while collagen prevents excessive distortion.

Watton et al. developed the HGO model to incorporate microstructural variables that relate to the density of elastinous and collagenous constituents. Their model also simulates the remodeling of the configuration of the collagen fibers as the aneurysm develops. Previous models of aneurysm growth have not related this tissue remodeling to hemodynamic stimuli. The revised model accounts for such changes in arterial microstructure during aneurysm development.

We use the 3D aneurysm growth model developed by Watton et al. to describe the formation of a type of cerebral aneurysm in the internal carotid artery, one of the main vessels that sends blood to the brain. The solid model is now combined with detailed 3D hemodynamics solutions (computed using ANSYS CFX fluid flow analysis software). This approach enables us to link the remodeling of the arterial microstructure to local hemodynamic stimuli as the aneurysm evolves. We explore simple hypotheses that relate the degradation of elastinous constituents and the rate of collagen turnover to changes in hemodynamics.

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Figure 5. Degradation of arterial elastin is explicitly linked to low levels of shear stress where the arterial wall has swelled. Arrows denote increasing time. (top left) Geometry of evolving aneurysm. (top right) Elastin concentration. (bottom left) Collagen density. (bottom right) Elastin concentration for final geometry.

Computational model

The internal carotid artery is modeled as a cylindrical membrane subject to a constant systolic pressure of 16KPa. In the reference configuration, i.e., the unloaded geometry of the artery, the radius is 1.6mm and the wall thickness is 0.375mm. In the initial systolic configuration, the artery has an axial prestretch of 1.3 and a circumferential stretch of 1.25. The systolic radius is 2mm and the domain is 16mm long. Elastinous constituents are assumed to bear 80% of the load.

Development of the aneurysm arises as the material constituents reform while it is subject to a constant internal systolic pressure and fixed boundaries of the axial domain. First we consider the development of the aneurysm without the influence of hemodynamic factors. In this case, the elastinous constituents are degraded completely in a localized circular patch (radius 1mm) over a period of 8 years and the collagen half-life is 1 month. The aneurysm enlarges and stabilizes in size as the collagen fibers change to compensate for the loss of elastinous material (see Figure 2).

The evolution of the blood flow within the aneurysm (Figure 3) determines the evolution of the distribution of wall shear stresses acting on the inner layer of the aneurysm (see Figure 4). Analysis of the evolving shear stress distributions guides suitable hypotheses to link tissue remodeling to hemodynamic parameters.\(^6\)\(^,\)\(^7\) Figure 5 illustrates an example of an aneurysm developing with elastin degradation linked to low levels of wall shear stress.

Conclusion

This is the first 3D model of cerebral aneurysm growth to explicitly link remodeling of arterial tissue to the local hemodynamic environment. Our approach provides the foundation for future studies that will yield insight into how aneurysms form and rupture.

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