Tissue Mechanics as a Predictor for Saccular Aneurysm Rupture

Devin R. Berg

2 May 2011

Abstract

Intracranial saccular aneurysms are highly prevalent in the western world. Although rupture occurs in a only small number of aneurysms, the mortality rate associated with this event is significant. Thus due to the high risk associated with rupture and the risks of rupture repair surgery it is desirable to be able to predict whether a specific aneurysm is likely to rupture or will instead stabilize. Research into aneurysm development has shown that the response can not be quantified with simple mechanical models alone. It is also necessary to consider growth and remodeling of the tissue constituents and complex geometric stress concentrators as well. Through the production of complete aneurysm development models, it may be possible to enable accurate prediction of aneurysm rupture based on clinically observable measures such as aneurysm geometry and growth rates. This would help to minimize the use of risky and unnecessary repair surgeries for aneurysms which would ultimately stabilize naturally.

Introduction

Intracranial saccular aneurysms are sac-like structures that extend from a cerebral artery. These aneurysms typically form at bifurcations (arterial branch locations) located within the Circle of Willis as shown in Figure 1 [1].

Figure 1: Illustration of typical saccular aneurysm location at the apex of a bifurcation [1].

The causes of saccular aneurysms are varied and likely include any mechanism which results in local weakening within the cerebral artery. In particular, cerebral arteries contain less elastin than arteries located elsewhere within the human body [2]. Further, structural irregularities at the bifurcations likely contribute to the weakened structure as well. Ultimately it is the hemodynamic pressure that produces dilation of the artery at the weakened location and thus patients with hypertension due to alcohol consumption, smoking, stress, or a number of related issues may be at greater risk of developing an aneurysm.

It is reported that roughly two to five percent of the western population has at least one intracranial saccular aneurysm [3]. Of this group, roughly 0.2 percent will experience aneurysm rupture; this totals approximately 30,000 aneurysm ruptures per year in the United States alone. Finally, of the cases of aneurysm rupture, approximately 35 to 50 percent (or greater) are fatal and the remaining survivors often experience some level of impairment resulting from the event [2, 3].

These numbers motivate the ongoing effort in developing a better understanding of the methods by which aneurysms grow over time in order to enable a more precise diagnosis and better inform treatment decisions.

Development and Mechanics

As previously mentioned, saccular aneurysms begin the development process at a point of local weakening within the artery and cause the tissue to dilate under hemodynamic loads. As the tissue dilates, the stresses and strains within the arterial wall increase. This increased wall stress within the tissue then induces tissue growth and remodeling. As this process continues, the aneurysm expands until either a stable configuration is reached or the wall stress exceeds the strength of the tissue and rupture occurs. This process is depicted in Figure 2 as described in the literature [2].

Figure 2: Illustration of the development process for a saccular aneurysm [2].

Simple, first approach methods for quantifying the wall stress in an aneurysm model the structure as a pressurized sphere [1, 4]. Using this model, the wall stress is approximated as,

$$\sigma = \frac{Pr}{2t} \quad (1)$$

where P is the hemodynamic pressure, r is the aneurysm radius, and t is the aneurysm wall thickness. Considering this model, it is intuitive that as the wall stress increases, the growth of the aneurysm is an attempt to bring the stress back down to an appropriate level.

These simplified models of stress within an aneurysm have been shown to accurately predict the failure location to be at the aneurysm fundus, in agreement with clinical observations [5]. However, these models also tend to prematurely predict rupture, typically in the size range of 1.2-3.6 mm while rupture is unlikely below 10 mm based on observations [6]. The reasons for this may be that the models incorrectly estimate the wall thickness and/or don't account for curvature variations that may effect the distribution of stresses.

Growth and Remodeling

Another significant consideration that is necessary for accuracy in predicting rupture is the inclusion of growth and remodeling of the tissue. In brief, the growth and remodeling of the aneurysm can be described by elastin degradation, collagen adaptation, and collagen remodeling. Elastin degradation is something that has been observed clinically. The elastin components of the tissue are typically found at significantly reduced levels compared with the surrounding arterial tissue. The remaining components of the aneurysm are composed of a “thin collagenous structure” that is subject to growth and degradation [3]. The details of the collagen remodeling process, as depicted in Figure 3, consists of tissue deformation followed by collagen fiber degradation/replacement [3]. When the collagen fibers are deposited in the deformed tissue, they are deposited at the preferred stretch state and nominal stress condition. By this process the stress in the tissue decreases back towards the preferred stress. The theory behind this process was presented by Humphrey [7] and provided the basis for more sophisticated models of growth and remodeling (for example, [8]).

Figure 3: Flow chart of collagen tissue remodeling process [3].

By incorporating a growth/remodeling model into the aneurysm model it is possible to more accurately predict the response of the aneurysm with time. In the work of Kroon and Holzapfel, a theoretical model for saccular aneurysm growth was developed based on the principles of collagen fiber remodeling [6]. The model presented there shows how the aneurysm grows with time normalized against the life cycle of the collagen fibers (Figure 4). In this figure, t_{cl} is the life cycle of the collagen which can range between 6 and 180 days and thus the longest period presented is at a time between 300 days and 25 years.

Figure 4: Predicted growth of a saccular aneurysm [6].

Additionally, the model presented by Kroon and Holzapfel in Figure 5 estimates the change in thickness of (left) and stress in (right) the aneurysm wall. In this figure, the value S/R_0 represents the circumferential surface position on the aneurysm where $S/R_0 = 0$ is the point at the fundus and $S/R_0 = 1$ is the point at the base of the neck where the aneurysm connects with the healthy arterial tissue. What the model tells us is that the wall thickness of the aneurysm thickens over the entire surface with time but at a greater rate near the neck than at the fundus. Further, with time the stress in the aneurysm wall increases significantly at the fundus and to a lesser extent near the neck. Predicting the highest stresses at the fundus is consistent with clinical observation of rupture location, as previously mentioned.

Figure 5: Model estimated wall thickness and stress distribution within an aneurysm [6].

One consideration that remains unaccounted for in the model presented by Kroon and Holzapfel is possible effects due to variations in surface curvature since the model is assumed to be axisymmetric and thus possibly over simplifies the problem [6]. Recently, a more sophisticated computational model has been presented by Watton and Ventikos [3]. The model makes the assumptions that the aneurysm grows according to the growth and remodeling of the collagen constituents and that the elastin constituents degrade locally at the site of the aneurysm. The model then predicts both the elastin degradation and collagen adaption with time. First, Figure 6 shows that the elastin very quickly degrades at the location of the aneurysm and goes to zero at the fundus within six years.

Figure 6: Model prediction for elastin concentration within an aneurysm from 0 to 10 years [3].

Figure 7 shows the prediction for the collagen fiber concentration within the aneurysm. It can be seen

that the collagen fibers concentration largely mirrors the degradation of the elastin in order to compensate for the loss of material and add additional material for the growth of the aneurysm and increase in thickness.

Figure 7: Model prediction for collagen fiber concentration within an aneurysm from 0 to 10 years [3].

Lastly, in Figure 8 the collagen fiber strains are analyzed. The model predicts that at 10 years the strains are the greatest at the fundus of the aneurysm. Following an additional 6 years of growth, the strain has begun to decrease at the fundus but remains elevated at the neck, as seen in (b). Also, if the growth is increased by a factor of ten between years 10 and 12, the aneurysm has mostly stabilized with only slightly elevated strains at the neck region.

Figure 8: Model prediction for collagen fiber strain at (a) 10 years, (b) 16 years, and (c) 16 years after a 10 fold increase in the growth parameter [3].

Watton et al. has recently published a revised version of their model that takes into account the effects

of shear stress from hemodynamic flow on the stress profile in the aneurysm wall and how the aneurysm responds to this shear stress [9]. This model thus provides a more complete picture of the conditions within the developing saccular aneurysm as shown in Figure 9 where the geometry of the aneurysm is predicted under both systolic and diastolic pressures. The inclusion of wall shear stress in the model is interesting because it is something that may be a significant contributor to the total state of stress within the wall and provides an extra layer of completeness (and possibly accuracy) to the model predictions. While the model presented by Watton et al. does not currently include mechanisms for predicting and modeling rupture, it is likely that the work of others in that area could be applied to this model and allow for a model that fully predicts aneurysm growth and rupture.

Figure 9: Model prediction for developed aneurysm geometry at 17 years and at systolic and diastolic pressures [9].

Rupture Prediction

Ultimately, the goal of the work presented here is to fully understand aneurysm development and be able to accurately predict whether a patient specific aneurysm is likely to stabilize or rupture. Since the majority of aneurysms ultimately do not rupture, it is desirable to use rupture prediction to avoid risky repair surgery if a particular aneurysm will stabilize on its own. Typically, aneurysm size is used as the primary means for assessing rupture risk; however, several alternative measures have been suggested in the literature to have to have greater prediction accuracy [10].

One such predictor is the aneurysm aspect ratio as suggested by Ujiie et al. [10]. As shown in Figure 10, the aspect ratio is a measure of the size of the aneurysm to the diameter of the neck. By examining the records of a number of patients Ujiie et al. found that for aspect ratios greater than 1.6, the rupture rate was 80% and the successful prediction of rupture versus stabilization was statistically significant at this aspect ratio. Therefore, with enough data behind it, the aneurysm aspect ratio may be able to accurately predict rupture.

Figure 10: Illustration showing measure of aneurysm aspect ratio [10].

Another method for analyzing the rupture risk of an aneurysm is through examining the size of daughter aneurysm formations. Daughter aneurysms develop on aneurysms that are approaching rupture as a temporary way to relieve wall stress [11]. It was found through their mathematical model that minimal stress was found for a daughter aneurysm aspect ratio of $\lambda = 0.577$ regardless of the ratio of the size of the daughter aneurysm orifice to the parent aneurysm radius, μ . As depicted in Figure 11, this value of λ represents a possible stable configuration; however, any further growth eventually leads to rupture [11]. It can also be seen from Figure 11 that as the orifice of the daughter aneurysm gets larger the stress concentration increases. This study concludes that the formation of a daughter aneurysm is informative to the physician regarding impending rupture; however, it would seem that it would be desirable to predict aneurysm rupture at a much earlier stage than the formation of daughter aneurysms.

Figure 11: Stress concentration for various daughter aneurysm geometries [11].

Summary

The models for saccular aneurysm growth have evolved over the years to include an increasing number of influencing characteristics. These range from a mechanical understanding of the wall stresses and strains to time sensitive growth and remodeling of the tissue constituents. With each advancement in the models, predictions for aneurysm growth and development become more comprehensive.

It has been suggested that the aneurysm growth rate may be a more suitable predictor of rupture [6]. Further, it is likely a combination of growth rate and geometry that will motivate the most accurate rupture predictions. For this to be possible, it is necessary for continued development of an accurate aneurysm growth model. This would then allow physicians to examine a specific patient's aneurysm (possibly at two separate occasions) and use the growth rate and geometry to arrive at a reasonable prediction of stabilization or rupture, possibly avoiding unnecessary and risky repair surgery.

References

- [1] G. Ferguson, "Physical factors in the initiation, growth, and rupture of human intracranial saccular aneurysms," *Journal of Neurosurgery*, vol. 37, no. 6, pp. 666–677, 1972.
- [2] J. Humphrey, *Cardiovascular solid mechanics: Cells, tissues, and organs*. Springer Verlag, 2002.
- [3] P. Watton and Y. Ventikos, "Modelling evolution of saccular cerebral aneurysms," *The Journal of Strain Analysis for Engineering Design*, vol. 44, no. 5, pp. 375–389, 2009.
- [4] S. Baek, K. Rajagopal, and J. Humphrey, "Competition between radial expansion and thickening in the enlargement of an intracranial saccular aneurysm," *Journal of Elasticity*, vol. 80, no. 1, pp. 13–31, 2005.
- [5] P. Canham, R. Korol, H. Finlay, R. Hammond, D. Holdsworth, G. Ferguson, and A. Lucas, "Collagen organization and biomechanics of the arteries and aneurysms of the human brain," in *Mechanics of Biological Tissue* (G. Holzapfel and R. Ogden, eds.), pp. 307–322, Springer, 2006.
- [6] M. Kroon and G. Holzapfel, "A theoretical model for fibroblast-controlled growth of saccular cerebral aneurysms," *Journal of Theoretical Biology*, vol. 257, no. 1, pp. 73–83, 2009.
- [7] J. Humphrey, "Remodeling of a collagenous tissue at fixed lengths," *Journal of Biomechanical Engineering*, vol. 121, p. 591, 1999.
- [8] P. Alford, J. Humphrey, and L. Taber, "Growth and remodeling in a thick-walled artery model: effects of spatial variations in wall constituents," *Biomechanics and Modeling in Mechanobiology*, vol. 7, no. 4, pp. 245–262, 2008.
- [9] P. Watton, A. Selimovic, N. Raberger, P. Huang, G. Holzapfel, and Y. Ventikos, "Modelling evolution and the evolving mechanical environment of saccular cerebral aneurysms," *Biomechanics and Modeling in Mechanobiology*, vol. 10, pp. 109–132, 2010.
- [10] H. Ujiie, Y. Tamano, K. Sasaki, and T. Hori, "Is the aspect ratio a reliable index for predicting the rupture of a saccular aneurysm?," *Neurosurgery*, vol. 48, no. 3, p. 495, 2001.
- [11] H. Meng, Y. Feng, S. Woodward, B. Bendok, R. Hanel, L. Guterman, and L. Hopkins, "Mathematical model of the rupture mechanism of intracranial saccular aneurysms through daughter aneurysm formation and growth," *Neurological Research*, vol. 27, no. 5, pp. 459–465, 2005.