Mathematical Model for the Rupture of Cerebral Saccular Aneurysms through Three-dimensional Stress Distribution in the Aneurysm Wall

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CAMS Report 0506-21, Spring 2006
Center for Applied Mathematics and Statistics

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Abstract

A mathematical model for the rupture of cerebral saccular aneurysms is developed through the analysis of three-dimensional stress distribution in the aneurysm wall. We assume in this paper, that a saccular aneurysm resembles a thin spherical shell (a spherical membrane), and then develop a strain energy function valid for finite strain to analyze 3-dimensional stress distribution in the aneurysm wall. We find that rupture occurs when the ratio of the wall thickness to the radius of the aneurysm is 6.1×10^{-3}.

We also conclude from our analysis that rupture can occur when the ratio of thickness to radius of the parent aneurysm equals the ratio of thickness to radius of the daughter aneurysm. These findings may be useful to the neurosurgeon to help predict the rupture potential in patients presenting with unruptured aneurysms.

Key words: cerebral aneurysm, rupture, tensile stress, mathematical model

Abbreviated title for running head: Rupture of Cerebral Aneurysm

Nomenclature and Symbols S.I units

W	Strain energy function	kPa
(r, θ, φ)	Coordinates in the unstrained state	
(R, θ, φ)	Coordinates in the strained state	
$\lambda = \dfrac{R}{r}$	Extension ratio	
C_1, a	Elastic constants	kPa
I_1	Strain invariant	
$\sigma_{\theta\theta}$	Circumferential stress	kPa
$\sigma_{\varphi\varphi}$	Meridional stress	kPa
P_i	Internal pressure	mmHg
P_o	External pressure	mmHg
h	Thickness in the un-deformed state	μm
r	Internal radius in the un-deformed state	mm
H	Thickness in the deformed state	μm
R	Internal radius in the deformed state	mm
T	Tension	N/m

Introduction:

Cerebral aneurysms are focal dilations of cerebral arteries or veins. Very often, aneurysms develop at the point of maximal weakness along a vessel wall, usually corresponding to a congenital absence or incomplete development of the muscular and elastic layers of the vessel. This defect tends to occur at the apex of a bifurcation near the circle of Willis. [1] As the aneurysm grows, its wall stretches, thins and becomes weaker than the rest of the arterial wall, increasing the likelihood of rupture. Rupture of an arterial cerebral aneurysm is the major cause of spontaneous subarachnoid hemorrhage (amounting to approximately 20,000 patients per year in the United States alone) which results in a combined morbidity and mortality of almost 75%.[1] Risk factors are hypertension, heavy alcoholic consumption, and cigarette smoking.[2] It has been suggested that hypertension and atherosclerosis can promote aneurysm growth and rupture. Further evidence suggests that larger aneurysms may rupture earlier than smaller ones and in situations where the size of the aneurysm is the same, a proximally located aneurysm may rupture earlier than a distally located one.[3]

Most studies on the mechanics of saccular aneurysm growth and rupture have primarily focused on the role of blood flow and loading in terms of blood pressure. Since the loads on the inner wall of aneurysm are responsible for expansion and potential subsequent rupture, it is important to study the stress distribution in the wall of aneurysm, especially when it is suggested that these lesions rupture as wall stress exceeds wall strength.[4]. Kyriacou and Humphrey[4] studied the influence of size, shape and mechanical properties on the mechanics of axisymmetric saccular aneurysms, treating such lesions as membranes that exhibit a non-linear behavior under finite strain. They used the converted tension-stretch data from pressure-volume tests on human saccular aneurysm, performed by Scott, et. al[5] and fitted a 2-D Fung-type exponential strain energy function to depict the behavior of the aneurysm wall. Therefore, their results are in terms of two- dimensional stresses and stretches in the aneurysm membrane.

We assume in this paper that a saccular aneurysm resembles a thin spherical shell (a spherical membrane), and thus develop a strain energy function valid for finite strain to analyze three-dimensional stress distribution (circumferential, meridional and radial) in the aneurysm wall, using Scott's data.[5] We use this analysis specifically to determine the conditions under which the aneurysm wall will rupture.

Method:

***Constitutive Equations*:**

Though aneurysms exist in a myriad of sizes and shapes as demonstrated by numerous clinical imaging studies, we shall focus this analysis on axis-symmetric lesions that have a spherical shape. Moreover, according to the findings of Steiger[6], non-spherical aneurysms have a tendency to assume a spherical shape as they enlarge.

Since saccular aneurysms in the stage of their initial formation experience large deformations when subjected to internal pressure, we employ a large deformation theory (see Green and Zerna[9]) for a spherical shape of the saccular aneurysm as assumed by Scott et al.[5], Canham and Fergusson[10], Steiger et al.[11] and Hui Meng, et al,[7] We use the best available tension-stretch data of the human aneurysm[5] to find the elastic parameters involved in the strain-energy function, *W*.

We assume the *uniform* inflation of a thin spherical shell[9] in which any point (r,θ,ϕ) in the unstrained state moves to (R,θ,ϕ) in the strained state, so that R/r = λ , The strain energy function , W is assumed to be given by

$$W = \frac{C_1(I_1 - 3)}{a - I_1} \tag{1}$$

where $I_1 = \frac{1}{\lambda^4} + 2\lambda^2$ is the strain invariant for the spherical shell (see Green and Zerna[9]), λ is the extension ratio, and C_1 and a are elastic parameters that need to be computed. This is the most suitable form of W, which gives a best fit between the theoretical and experiments values of stress (see Figure 1).

The Tension (Stress Resultant) – Stretch Ratio curve has already been obtained by Kyriacou and Humphrey[4] by photo-enlarging the figure of Scott's data[5] and fitting that data using a 2-D Fung strain-energy function. We use this curve to find the experimentally determined circumferential (tensile) stress $\sigma_{\theta\theta} = \sigma_{\phi\phi}$ (the meridional stress), from the relation, $\sigma_{\theta\theta}$ = T/H, where H is the deformed length and T is the tension. The theoretical or model circumferential stress ($\sigma_{\theta\theta}$) for a thin spherical shell, after some algebraic manipulation, is given by Green and Zerna [9]:

$$\sigma_{\theta\theta} = 2(\lambda^2 - \frac{1}{\lambda^4})\left[\frac{(a-3)C_1}{(a-I_1)^2}\right] - P_i$$

$$= 2(\lambda^2 - \frac{1}{\lambda^4})\left[\frac{(a-3)C_1}{(a-I_1)^2}\right] - \frac{4h}{r}\frac{\left[(\frac{1}{\lambda} - \frac{1}{\lambda^7})(a-3)C_1\right]}{(a-I_1)^2} - P_o \tag{2}$$

Note that *h* (wall thickness) and *r* (the inner radius of the shell) in equation (2) are in the un-deformed state. Expressed in the deformed state, Equation (2) becomes

$$\sigma_{\theta\theta} = 2(\lambda^2 - \frac{1}{\lambda^4})\left[\frac{(a-3)C_1}{(a-I_1)^2}\right] - P_i$$
$$= 2(\lambda^2 - \frac{1}{\lambda^4})\left[\frac{(a-3)C_1}{(a-I_1)^2}\right] - \frac{4H}{R}\lambda^3 \frac{\left[(\frac{1}{\lambda} - \frac{1}{\lambda^7})(a-3)C_1\right]}{(a-I_1)^2} - P_o \quad (3)$$

where P_i and P_o are the internal and external pressures; h, and r are the thickness and radius of the saccular aneurysm in the un-deformed states, respectively.

H and R are the thickness and radius in the deformed state. We have used $H = \lambda_3 h = \frac{h}{\lambda_1 \lambda_2} = \frac{h}{\lambda^2}$ since $\lambda_1 = \lambda_2 = \lambda$ and $R = r\lambda$. Note that $\lambda_1\lambda_2\lambda_3 = 1$ is the condition of incompressibility.

$\sigma_{\theta\theta}$ used here is the stress at the inner surface of the shell, which also is assumed to be the same at the interior of the shell, since the thickness of the shell is extremely small (1% of the radius). We then compute a and C_1 by minimizing the square of the differences of the model (or theoretical) stress and experimental stress values by using non-linear regression. We find the best values to be

$$a = 3.62 \quad \text{and} \quad C_1 = 438.51 \text{ mmHg or } 58.46 \text{ kPa.}$$

The experimental and fitted curves are shown in Figure 1. Various forms for the strain- energy function were then used to obtain the best fit between the experimental and model stress curves. The strain-energy function given by equation (1) is the most suitable form, as can be seen from Figure 1.

The transmural pressure for a thin spherical shell is given by (see for details Green and Zerna[9])

$$P_i - P_o = \frac{4h}{r}\left[\left(\frac{1}{\lambda} - \frac{1}{\lambda^7}\right)\frac{\partial W}{\partial I_1} \right] \quad . \tag{4}$$

Using Equations. (1) and (4), we find

$$P_i - P_o = \frac{4h}{r}\frac{\left[\left(\frac{1}{\lambda} - \frac{1}{\lambda^7}\right)(a-3)C_1 \right]}{(a-I_1)^2} \quad . \tag{5}$$

Results:

We assumed h =27.8 μm, the un-deformed thickness (see Kyriacou and Humphrey[4]), the average radius, *r* ,of the spherical aneurysm as 2.65 mm (see Kyriacou and Humphrey[4] and a = 3.62 and C_1 = 438.51 mmHg or 58.46 kPa. in our calculations for the above equations (1) - (5). The results are reported in Figures 1-6. Figure 1 is a fit of our constitutive relation to the experimental data. By taking the already fitted curve of Kyriacou and Humphrey[4], we determined the values of the elastic parameters, *a* and C_1 in our strain energy function assumed in Equation (1). We plotted the graphs of the circumferential stress, $\sigma_{\theta\theta}$, vs. stretch ratio and the internal pressure P_i , vs. stretch ratio in Figures 2 and 3, respectively for a spherical-shaped aneurysm. The plot of internal pressure versus circumferential stress is given in Figure 4. We see from Figures 2 and 3 that the circumferential stress and transmural pressure increases rapidly with stretch ratio. It is observed from Figure 4 that pressure and stress vary almost linearly, except in the initial stages. We also noted a substantial variation in stress by altering the ratio of thickness and radius. These plots are given in Figure 5. We then plotted the graph of pressure versus stretch ratio beyond the given data values to determine the limit point instability (see Figure 6). As can be further gleaned from Figure 6, pressure increases monotonically with stretch ratio, suggesting a limit point instability, i.e. $dP/d\lambda$ does not exist. This observation confirms previously published finding by Kyriacou. and Humphrey[4] and is appropriately in contradistinction to Akkas[12] who assumed a Neo- Hookean constitutive relation.

In order to find the condition at which the aneurysm ruptures, we assumed that the rupture strength of human lesions is on the order of 1 MPa..[11] .From Figure 5, we find that this corresponds to the ratio of thickness to radius, $k = 6.101387 \text{ X } 10^{-3}$.

We also use the concept given by Hui Meng, et. al [7] to find the conditions for rupture. This concept is based upon the presence of a daughter aneurysm on the dome, which represents the weakest area of the aneurysm. It is speculated that the formation of a daughter aneurysm is the compensatory device to reduce the tensile stress within the parent aneurysm walls that results from the pressure surge in the parent aneurysm. As the daughter aneurysm develops, the stress factor (the ratio of tensile stress in the daughter aneurysm to that in the parent aneurysm) first decreases to protect against rupture. As the daughter aneurysm grows, the stress factor increases, leading to rupture at a stress factor of 1, i.e., when the tensile stress of the daughter aneurysm equals the tensile stress in the parent aneurysm at the tissue's weakest point. Both the daughter and the parent aneurysms are assumed to be of spherical shape in their analysis.

Using this concept in Equation (3) for the tensile (circumferential) stress, we can find the condition at which rupture will occur. Furthermore, denoting $H = h_p; R = R_p$ for the parent aneurysm, and $H = h_d; R = R_d$ for the daughter aneurysm in Equation (3), we find that the rupture stress will occur when the circumferential stress for both the daughter and the parent stress are equal, i.e. when

$$\frac{h_p}{R_p} = \frac{h_d}{R_d} \tag{6}$$

In other words, the rupture will occur when the ratio of thickness to radius of the parent aneurysm equals the ratio of thickness to radius of the daughter aneurysm.

From Figure 5, we conclude that as the ratio of thickness to radius decreases, the stress increases. It means that for a specified radius, *r*, the circumferential stress increases as the thickness, *h* decreases, meaning therefore, that the aneurysm is more likely to burst when the thickness is small compared to the case when thickness is large. Similarly, for a specified thickness, stress will increase if radius increases. Thus, rupture is not dependent solely on the radius (a well known result) but also upon the aneurysm wall's thickness. We find that rupture occurs when the ratio of thickness of the wall to the radius of the aneurysm is $k = 6.101387 \text{ X } 10^{-3}$.

Furthermore**,** with regards to aneurysms with a daughter bleb , we conclude that the rupture will occur when the thickness to radius ratio of the parent aneurysm equals the ratio of thickness to radius of the daughter aneurysm.

We also observe from Figure 6 that pressure increases monotonically with stretch ratio. This means that a limit point instability, i.e., $dP/d\lambda$ does not exist as also observed by Kyriacou. and Humphrey[4] in contrast to Akkas[12] who assumed a Neo Hookean constitutive relation.

Discussion:

We have used the constitutive relations of finite strain for a thin spherical shaped cerebral aneurysm in contrast to constitutive relations for a membrane used by Kyriacou and Humphrey[4]. Although their results show the meridional and circumferential stresses, these are valid only in a plane containing the neck, but not in a bulged out spherical surface in a direction normal to the plane. In contrast, our results are not confined to the plane, but are three-dimensional, although we have assumed that meridional and circumferential stresses to be equal.

Recently, a mathematical model (see Hui Meng, et al[7]) of the rupture of intracranial saccular aneurysm has been developed through daughter aneurysm formation and growth. Though their model presents quite interesting observations and compelling conclusions, the model is based upon the assumption that the aneurysm wall consists of a constant volume, irrespective of growth of the aneurysm. Observations, however, have suggested that in fact, the aneurysm wall may grow thicker through collagen deposition or other vascular remodeling as observed by MacDonald, et. al. [8]. Further difficulties arise in that their model uses the Law of LaPlace which is based upon the balance of forces only and does not explicitly account for the elastic properties of the aneurysm wall. Further, this law cannot predict relationship of pressure and stress with stretch ratios of the aneurysm wall.

Although we used the rupture strength of human lesions as reported by Steiger, et al.[11], in finding the condition for rupture, this information is based upon one-dimensional tests and not for an *in-vivo* multi-axial state of stress.

The assumptions that have been made in developing this model do not limit the potential usefulness of the mathematical relationships that have been developed. Indeed, such observations may prove useful in the clinical setting since the treatment of unruptured aneurysms does carry a significant risk of stroke and death to the patient who presents with an essentially incidental finding in neurologically normal condition. Understanding the mathematical relationships and the hemodynamic factors predisposing aneurysms to further growth and rupture will enable neurosurgeons to determine which aneurysms have a high likelihood of rupture and should thus be treated. In addition, such knowledge may also help predict which aneurysms will never rupture and thus need not be treated. In making such predictions, only patients with a risk of aneurysmal rupture will thus be exposed to the risk of surgery.

Initial steps in developing this foundation results in the applications of the newly determined elastic constants for the aneurysm wall and applying the finite element analysis method to compute the stresses at the aneurysm wall and the neck for spherical and non-spherical aneurysms.

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Figure Captions:

Figure 1. Fit (solid line) of the Stress Resultant (N/m) as defined by Equation (3) to data (+) of the exponential constitutive relation defined by Kyriacou and Humphrey (1996) (Equation 2., p 1016). Best-fit values are a = 3.615396 and C_1 = 438.4137 mmHg.

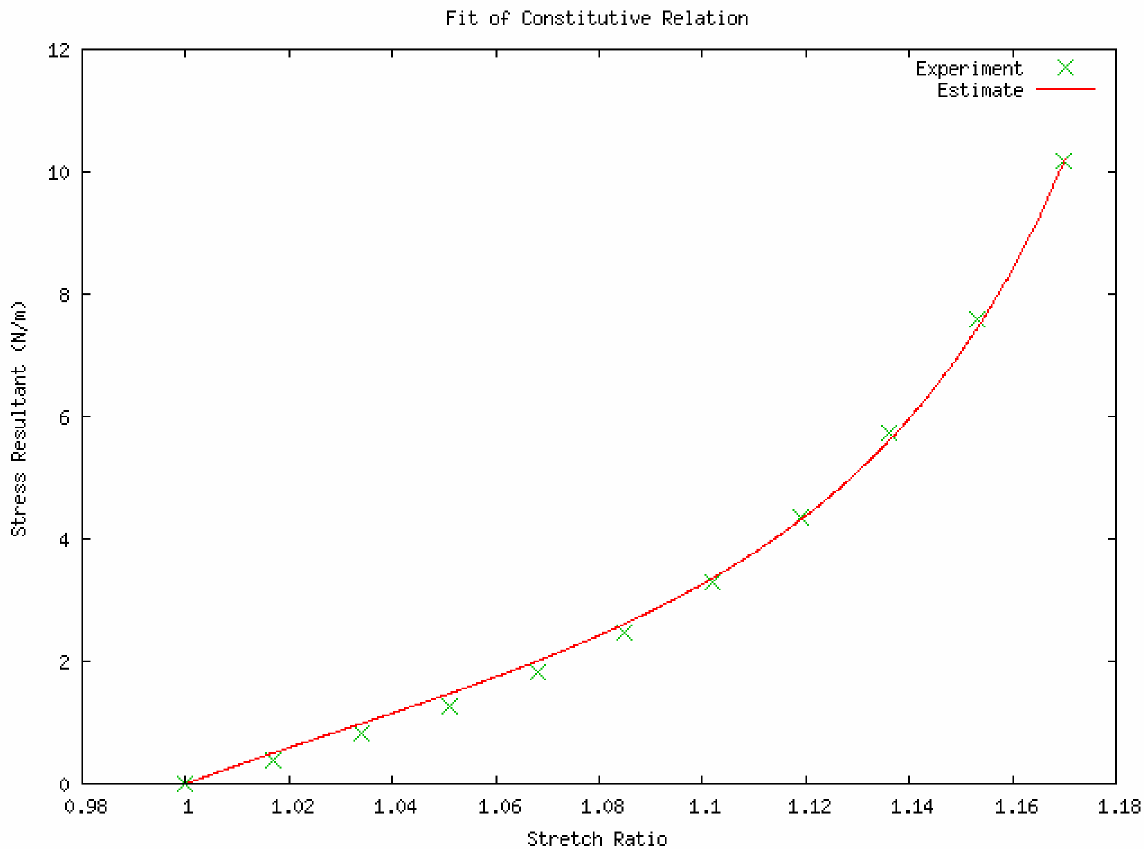
Figure 2. Circumferential stress, $\sigma_{\theta\theta}$, as defined by Equation (3).

Figure 3. Internal Pressure, P_i, as defined by Equation (4) assuming external pressure P_0 to be zero.

Figure 4. Circumferential Stress, $\sigma_{\theta\theta}$ as defined by Equation (3) as a function of Internal Pressure, P_i, as defined by Equation (4).

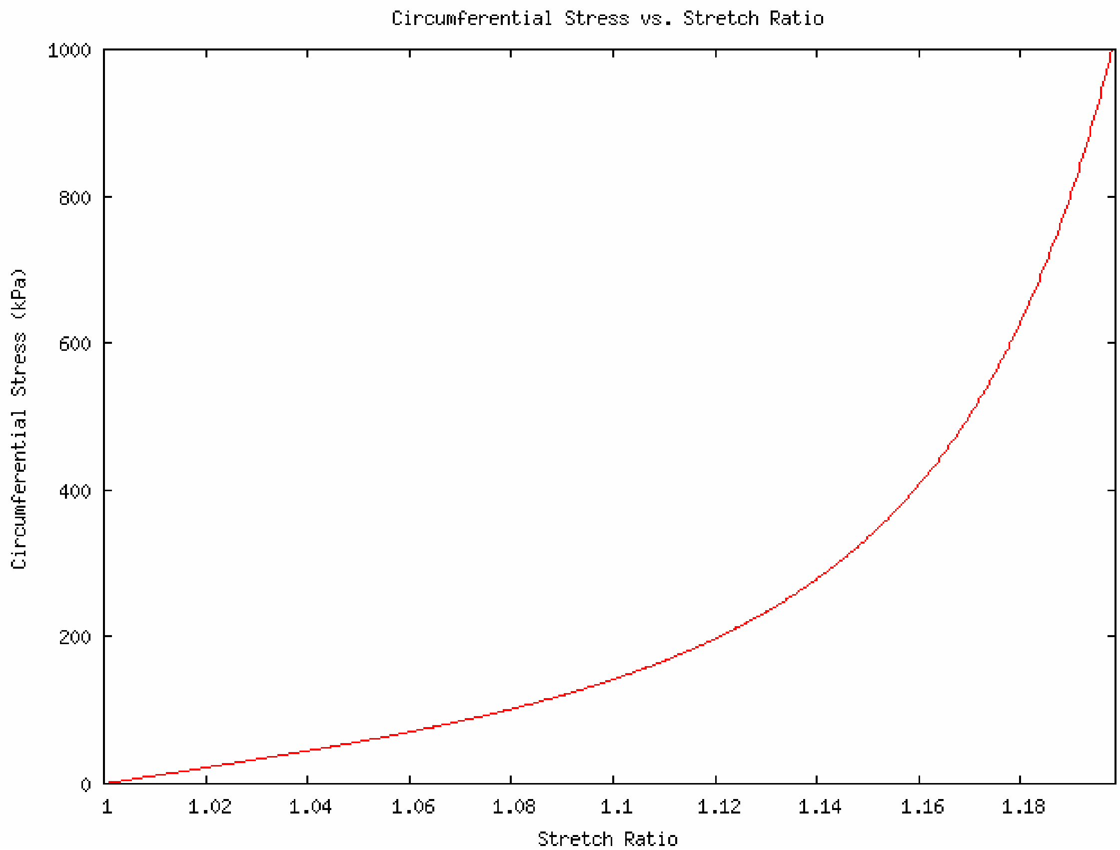
Figure 5. Circumferential stress, $\sigma_{\theta\theta}$, as defined by Equation (3) for varying $k = H/R$. Note that the values of stress decrease as k increases. The value of k for breaking stress of 1000 kPa is k = 6.101387 X 10^{-3}.

Figure 6. Internal Pressure, Pi, as defined by Equation (3). Note that P_i = 325 mmHg at λ = 1.233 and P_i = 1000 mmHg at λ = 1.249.



Fit of Constitutive Relation
Experiment
Estimate
Stress Resultant (N/m)
Stretch Ratio
0
2
4
6
8
10
12
0.98
1
1.02
1.04
1.06
1.08
1.1
1.12
1.14
1.16
1.18

Figure 1



Circumferential Stress vs. Stretch Ratio
Circumferential Stress (kPa)
Stretch Ratio
0
200
400
600
800
1000
1
1.02
1.04
1.06
1.08
1.1
1.12
1.14
1.16
1.18

Figure 2

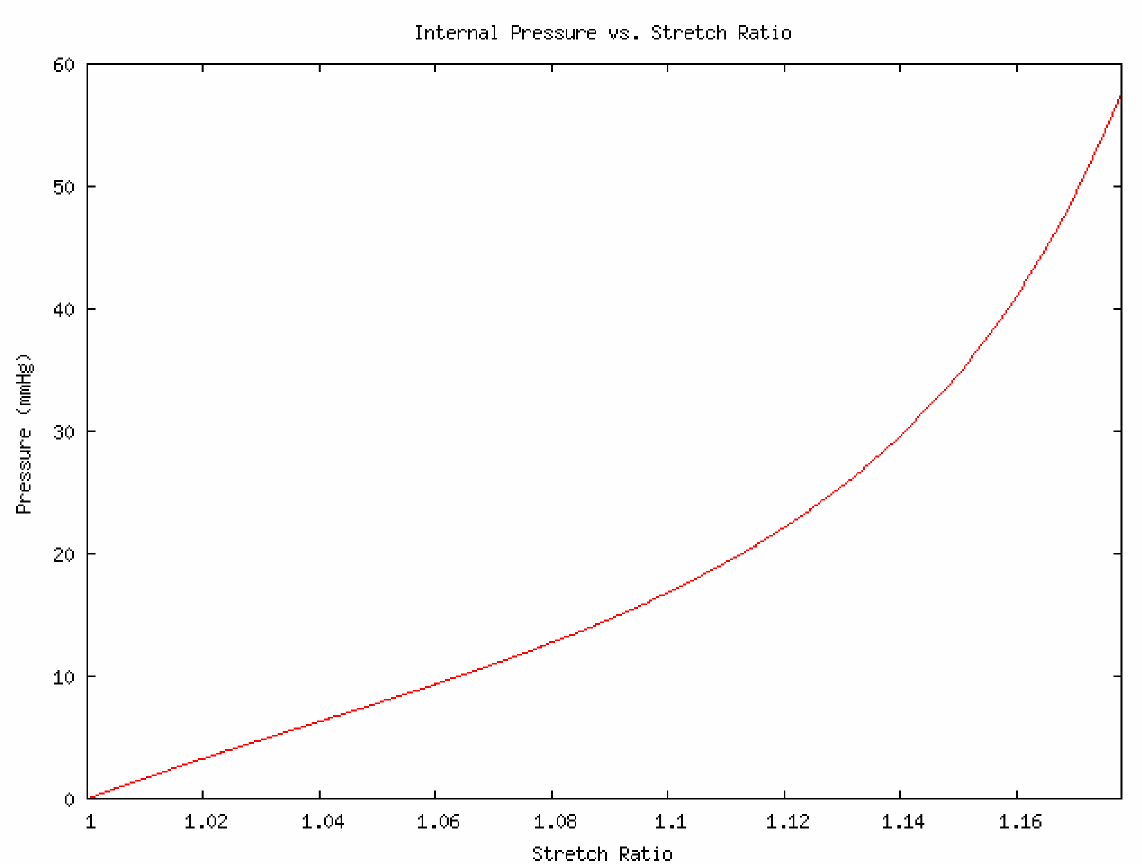
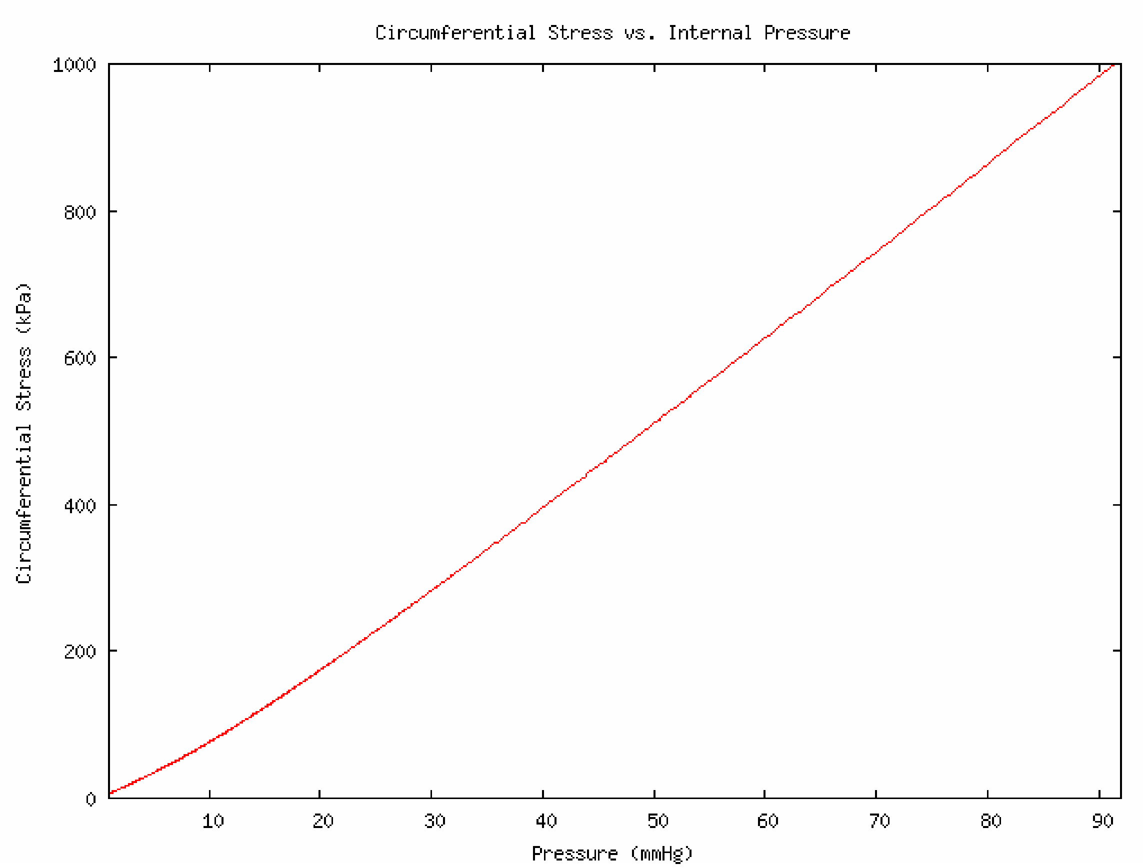

Internal Pressure vs. Stretch Ratio
Pressure (mmHg)
0
10
20
30
40
50
60
1
1.02
1.04
1.06
1.08
1.1
1.12
1.14
1.16
Stretch Ratio

Figure 3



Circumferential Stress vs. Internal Pressure
Circumferential Stress (kPa)
Pressure (mmHg)
0
200
400
600
800
1000
10
20
30
40
50
60
70
80
90

Figure 4

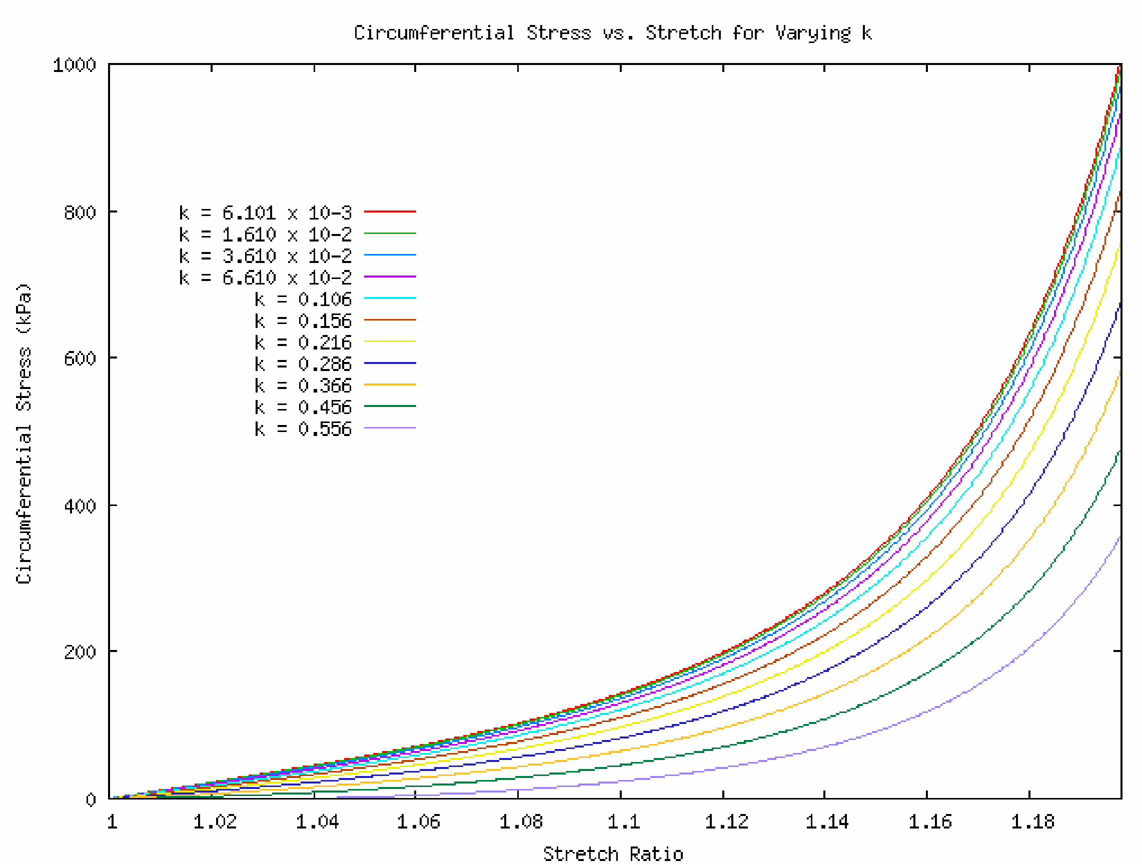

Circumferential Stress vs. Stretch for Varying k
Circumferential Stress (kPa)
Stretch Ratio
0
200
400
600
800
1000
1
1.02
1.04
1.06
1.08
1.1
1.12
1.14
1.16
1.18
k = 6.101 x 10-3
k = 1.610 x 10-2
k = 3.610 x 10-2
k = 6.610 x 10-2
k = 0.106
k = 0.156
k = 0.216
k = 0.286
k = 0.366
k = 0.456
k = 0.556

Figure 5

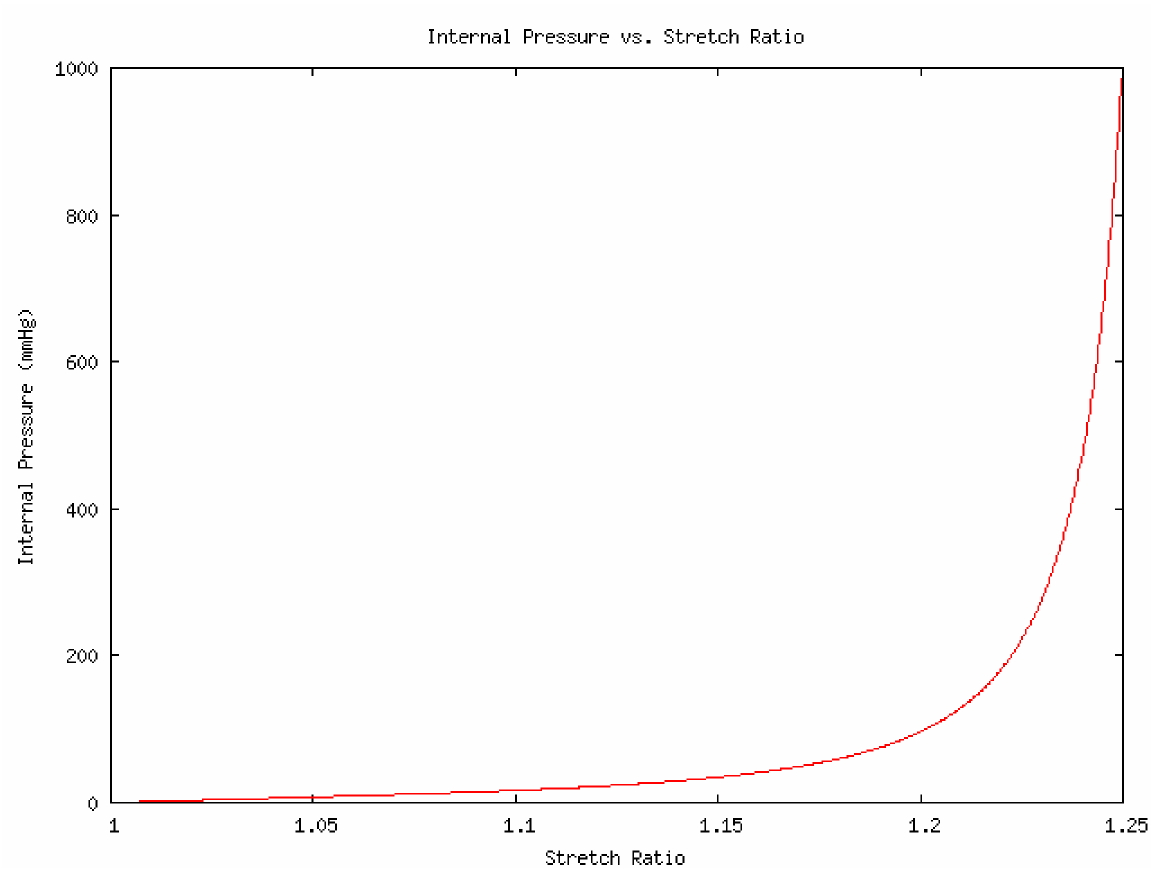

Internal Pressure vs. Stretch Ratio
Internal Pressure (mmHg)
Stretch Ratio
0
200
400
600
800
1000
1
1.05
1.1
1.15
1.2
1.25

Figure 6