BED-Vol. 50, 2001 Bioengineering Conference
ASME 2001

ABDOMINAL AORTIC ANEURYSMS
A NEW MATHEMATICAL MODEL

Paul N. Watton, N. A. Hill

Department of Applied Mathematics
University of Leeds
Leeds
U.K.

INTRODUCTION

An aneurysm is characterized as a localized dilation of the arterial wall. They mainly occur in the abdominal aorta and the cerebral vasculature, can be saccular or fusiform in shape and be classified into several different types according to their etiology. This paper is concerned with abdominal aortic aneurysms of the atherosclerotic type, which will affect approximately 0.5% of the population at some point in their life. The growth of the aneurysm is associated with a weakening of the wall and the possibility of rupture. At least 50% of ruptured aneurysms will result in death. Surgery to remove the aneurysm is an option, but it is a high-risk procedure with a 5% mortality rate. When the probability of rupture exceeds 5% an operation to remove the aneurysm would be deemed appropriate. The criterion used for predicting rupture only takes into account the diameter of the aneurysm. It is calculated from the population as a whole rather than being patient specific. Consequently, the problem encountered is that some small aneurysms burst, whilst other larger ones do not. Improved mathematical models of aneurysms may lead to a greater understanding of the pathogenesis of the disease and hopefully lead to improved criteria for rupture.

THE MODEL

The pathogenesis of the disease is still not fully understood. What is clear is that the elastin, one of the primary load bearers in the arterial wall degrades and consequently the wall weakens. Hence the first requirement of a model is that the loss of elastin can be suitably represented. Models of the artery are often phenomenological in nature and describe the gross mechanical properties of the arterial wall rather than considering the contributions of the elastin and collagen separately. Although it may be the case that there is some interaction between the two materials, it is of primary importance to able to identify parameters that explicitly relate to either the collagen or elastin. For this reason, the mechanical response of the wall will be modelled as the sum of responses from each material.

It is widely accepted that the artery remodels in order to maintain certain characteristics due to changes in its environment. Hence, the question arises, which remodelling process is of importance in the development of aneurysms. In [1], Humprey proposes a cell mediated mechanism for the remodelling of collagen which effectively restores the strain in the fibres to some normotensive value. This idea can be applied to aneurysms. In the normal healthy artery it can be assumed that there is a normotensive strain in the collagen fibres at which no remodelling occurs. If the strain in the collagen fibres deviates from this value then they will remodel in order to try to maintain the strain. Clearly the degradation of elastin will increase strains in the collagen fibres as they have to support a greater load and subsequently they will remodel.

An important feature of this model is to be able to relate the strains in the collagen fibres to those in the elastin. In [2] a 1-D model is proposed which takes into account the waviness of the collagen fibres. Effectively beyond a certain strain as measured relative to the elastin the collagen fibres begin to be recruited, see Fig. 1. Given a length L of unstrained elastin, which is subsequently stretched, the collagen fibres become straight when the elastin has been stretched to a length rL. The collagen fibre will now begin to bear load and is said to be 'recruited'.

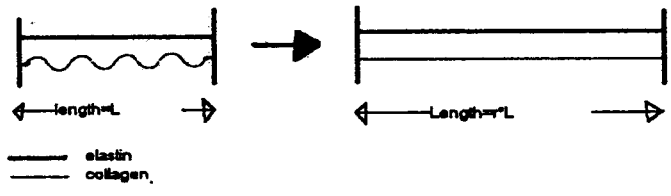

Figure 1. The parameter r

The collagen fibres will in fact have a range of waviness but it is assumed here that there is a minimum strain for recruitment of the collagen fibres and beyond this strain the stress-strain response can be suitably modelled. Before any collagen fibres are recruited their contribution to load bearing is assumed to be zero; once recruitment begins, the subsequent stress-strain relationship can be represented, see [3]. Now [2,3] did not consider the remodeling of collagen, and have not explicitly stated a parameter which defines the minimum factor the elastin must be stretched by in order for the collagen to be recruited. The importance of this parameter is clear when the remodelling of the collagen is taken into account.

The assumption in this paper follows on from that of [1] and a current view held in the medical field, namely that there is an equilibrium level of strain, ε_H, in normotensive conditions for the collagen fibres. If the strain in the collagen fibres deviates from this value, a remodelling process will occur to restore their strain to ε_H. In order to maintain strain in the fibres there are essentially two processes that can happen:

1. The parameter r can increase in value.
2. More collagen fibres can be laid down 'in parallel' - in effect a thickening of the collagen - this would decrease the load on each fibre and thus act to restore strain.

1-D MODEL

From a simple mathematical analysis, see Fig. 2, the strains in the elastin, ε_E, and collagen, ε_C, are related by

$$\varepsilon = \frac{y}{rl} = \frac{x+l-rl}{rl} = \frac{\varepsilon_E + 1 - r}{r} \qquad (1)$$

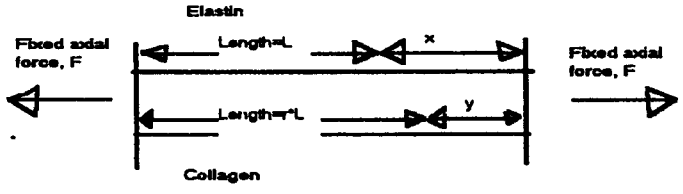

Figure 2. The uni-axial model

The governing equation for this system is

$$F = k_E A_E(t)\sigma_E(\varepsilon_E) + k_C A_C(t)\sigma_C(t) \qquad (2)$$

here F is the fixed axial force, $\sigma_E(\varepsilon_E)$ and $\sigma_C(\varepsilon_C)$ are stress functions, $A_E(t)$ and $A_C(t)$ the cross sectional areas of the elastin and collagen respectively. k_E, k_C are constants chosen such that at $t=0$, $A_E(0)=A_C(0)=1$. The parameters are determined from the assumption that at $t=0$ the normotensive strain in the collagen, ε_H, is given and the system is in equilibrium along with suitable physiological assumptions for the relative contributions to load bearing of the collagen and elastin. The depreciation of elastin drives the system and was modelled using exponential functions and data from [4]. As the elastin depreciates the collagen remodels to restore its strain to ε_H.

$$\frac{\partial r}{\partial t} = G(\varepsilon_C - \varepsilon_H), \quad \frac{\partial A_C}{\partial t} = H(\varepsilon_C - \varepsilon_H), \qquad (3)$$

for some monotonically increasing functions G,H with $G(0)=H(0)=0$. The simplest such functions are linear,

$$G = \alpha(\varepsilon_C - \varepsilon_H), \quad H = \beta(\varepsilon_C - \varepsilon_H). \qquad (4)$$

These satisfy the necessary requirements and the constants α, β can be adjusted to simulate differing rates of the remodelling for the two processes. Using physiological data and reasonable assumptions for the timescale of remodelling, in accordance with processes detailed in [1], ranges of values for the remodelling constants were determined.

The elastin was represented by a linear Hookean relationship, the non-linearity of the collagen by an exponential function. The system was solved numerically. Results obtained over the relevant timescales were found to agree with those observed *in vivo*, i.e. decreasing compliance, increasing diameter and collagen thickening.

3-D MODEL

Using suitable strain energy representations for the collagen and elastin, and considering the artery to be a cylindrical shell, remodelling features of the uni-axial case can be incorporated into a 3 dimensional model of the artery. In [5], the collagen is described as forming low-pitch helical paths around the artery. Hence, the strain field for the elastin can be resolved in the direction of the pitch to enable an r field to be defined which describes the relationship between the strain in the collagen and elastin over the shell. As the elastin depreciates the strain field will change and hence remodelling equations can be proposed for the thickening of the collagen and lengthening of the fibres. Large displacement shell theory, with the Kirchoff-Love assumption simplifies this to a 2 dimensional problem. The Principal of Virtual Displacements is used to determine the subsequent deformations. The theoretical framework has been formulated and a numerical code is currently underway.

DISCUSSION

The model proposed captures two essential features of the development of the aortic aneurysm, the degradation of the elastin and the remodelling of the collagen fibres. Under the assumption that the collagen remodels in order to maintain an equilibrium level of strain, two parameters, which relate to thickening and lengthening of the collagen, are seen to be important. Also, it is shown that the increasing diameter of the aneurysm is a consequence of both the remodelling of the collagen and the depreciation of the elastin.

Obviously other constituents of the wall may play a part in the load bearing, such as the smooth muscle, or the presence of an intramural thrombus. These would reduce the required load bearing and subsequent remodelling of the collagen. Such features may be built in to future developments of the model.

Further experimental research is needed to verify the assumptions and equations for the remodelling of collagen and provide more data for the spatial and temporal evolution of the degradation of the elastin.

REFERENCES

1. Humphrey, J. D., 1999, "Remodeling of a Collagenous Tissue at Fixed Lengths", Journal of Biomechanical Engineering, Vol. 121, pp. 591-597
2. Vorp, D., Raghavan, M. & Webster, M., 1996, "Ex-vivo bio-mechanical behavior of AAA: Assessment using a new mathematical model", Annals of Biomedical Engineering, Vol. 24, pp. 573-582
3. Armentano, R. , Barra, J., Leveson, J., Simon, A., Pichel, R. 1995, "Arterial Wall Mechanics in Conscious Dogs", Circulation Research, Vol. 76, No 3 pp.468-478
4. Chang, M., Roach, M., 1993, "The composition and mechanical properties of abdominal aortic aneurysms", Journal of Vascular Surgery, Vol.20, No.1, pp. 6-13
5. Shadwick, R., 1999, "Mechanical Design in Arteries, The Journal of Experimental Biology", Vol. 202, pp. 3305-3313