A MATHEMATICAL MODEL TO DESCRIBE AORTIC DISSECTIONS

by

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Abstract

Parameters of simulated aortic dissections in porcine thoracic aortas were measured using a 3-D ultrasound technique, and used to develop a mathematical model to predict the effect of pressure and tear depth on the angle at the longitudinal leading edge of the dissection. Propagation pressure of aortic dissections decreased linearly, from 395 mmHg at 45% tear depth from the lumen, to 215 mmHg at 90%, n=17, p<0.05. By contrast, the propagation pressure of saline-filled blebs increased from 75 mmHg at 20% to 160 mmHg at 90%, n=45, p<0.05. Instron tests on aortic tissue segments revealed a trend in circumferential extensibility, where media > media+intima > media+adventitia. Extensibility, measured using the 3-D ultrasound technique, was used in the model, along with vessel diameter, true and false lumen wall thickness, tear depth, tear length and fraction of circumference dissected. The angle increased with pressure and tear depth, and distensibility was the most important variable.

Keywords: Aortic Dissection, Dissecting Aneurysm, Aorta, Distensibility, Anisotropy, Ultrasound, Mathematical Model.
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## Glossary

- \(a\) = longitudinal length of the intimal flaps [mm]
- \(b\) = maximum height of outer dissected wall from intact [mm]
- \(d_e\) = height of intimal flap from opposing intact wall [mm]
- \(\varepsilon_C\) = circumferential strain
- \(\varepsilon_D\) = circumferential strain in outer wall of false lumen
- \(\varepsilon_L\) = longitudinal strain
- \(E_C\) = Young’s modulus in the circumferential direction [N/mm²]
- \(E_L\) = Young’s modulus in the longitudinal direction [N/mm²]
- \(E_{mD}\) = circumferential modulus for outer wall of dissection, modified for pressures beyond 100 mmHg [N/mm²].
- \(E_R\) = Young’s modulus in the radial direction [N/mm²]
- \(f\) = frequency [cycles/s] or [Hz]
- \(\phi\) = acute angle between intimal flap and intact wall [degrees]
- \(K\) = fraction of circumference dissected
- \(\lambda\) = wavelength of sound [m]
- \(L\) = longitudinal length of dissection [mm]
- \(t\) = longitudinal length [mm],
- \(\nu_{CL}\) = longitudinal to radial Poisson’s ratio
- \(\nu_{CR}\) = circumferential to radial Poisson’s ratio
- \(\nu_{LR}\) = longitudinal to radial Poisson’s ratio
- \(p\) = pressure [N/mm²],
- \(\theta\) = angle outer dissected wall makes with intact wall [degrees]
- \(\rho\) = density [kg/m³]
- \(r\) = radius to middle of wall [mm],
- \(r_{inner}\) = inner radius of cylinder [mm]
- \(r_{outer}\) = outer radius of cylinder [mm]
- \(s\) = maximum circumferential length of outer wall of false lumen [mm]
- \(\sigma_C\) = circumferential stress [N/mm²].
- \(\sigma_D\) = circumferential stress in outer wall of false lumen [N/mm²]
- \(S_{inner}\) = length of the inner wall of the false lumen in circumferential cross-section [mm]
- \(\sigma_L\) = stress in the longitudinal direction [N/mm²]
- \(\sigma_R\) = stress in the radial direction [N/mm²]
- \(t\) = wall thickness [mm],
- \(t_D\) = thickness of outer wall of false lumen [mm]
- \(u\) = length of near zone [m]
- \(v\) = velocity of sound [m/s]
- \(w\) = width of peizoelectric crystal [m]
- \(x\) = maximum width of false lumen [mm]
- \(Z\) = characteristic impedance [kg/(m²*s)]
Chapter 1: Introduction to Aortic Dissections

1.1. Motivation

An aortic dissection is a tear within the media of the aortic wall. Elastic laminae are separated leading to the formation of a false lumen running parallel to the true lumen. The two lumens are connected through an intimal tear (fig. 1.1).

Figure 1.1. Computed Tomography volume image of an aortic dissection in a porcine thoracic aorta (courtesy of Neil MacLean). The perspective is from inside the vessel, so that the intimal side of the lumen is revealed. The diameter of the vessel is approximately 2 cm. Flow would be from top to bottom.
The dissection likely occurs in three stages: 1) formation of an intimal tear, through to the media, 2) propagation of the tear, circumferentially and longitudinally, both antegrade and retrograde to flow and 3) termination, in the form of a final tear, either out through the adventitia leading to exsanguination and death, or back through the intima to the true lumen (Tiessen and Roach, 1993).

The most common type of classification system of aortic dissections is the DeBakey one of Types I, II and III (DeBakey et al., 1982):

Type I: The ascending and descending aorta are involved, extending down to the aorto-iliac bifurcation. The intimal tear is most commonly transverse, in the proximal anterior side of the ascending aorta, but may be found anywhere along the length of the vessel. The incidence of this type of dissection has been reported as 26% (DeBakey et al., 1982) and as 42% (Glower et al., 1991).

Type II: The dissection is limited to the ascending aorta. The intimal tear is usually transverse and located on the anterior side, just above the aortic valves. It usually terminates at the innominate artery. The incidence of Type II has been reported as 11% (DeBakey et al., 1982) and as 14% (Glower et al., 1991).

Type III: This dissection involves the descending thoracic aorta (Type IIIa) and more commonly also involves the abdominal aorta and in some cases the iliac arteries (Type IIIb). The intimal tear is usually transverse just distal to the left subclavian artery. The incidence of Type III
Another classification system that is often used is the Stanford classification. This simply groups those dissections involving the ascending aorta as Type A, and those not involving the ascending aorta as Type B (Panneton and Hollier, 1995). Surgical treatment is necessary for DeBakey Type I or II (Stanford Type A) dissections (Glower et al., 1991), because there is risk of rupture into the pericardium resulting in cardiac tamponade. If blood flows into the pericardium and pressure builds, flow from the veins will be halted and death will follow quickly. However for DeBakey Type III (Stanford Type B) dissections, medical treatment is often preferred (Schor et al., 1996). Surgical treatment is necessary in some cases, if there is branch involvement or if propagation cannot be prevented medically. The mathematical model I have developed applies to the descending thoracic aorta, where medical treatment to lower the blood pressure is relevant. At present, the amount the pressure should be lowered is unknown.

Although the incidence of aortic dissections is less than one in 100 000 population per year in North America, dissection is the most common and most lethal catastrophe of the aorta (Wheat, 1973), (House-Fancher, 1995). The occurrence in men is approximately three times that in women, and aortic dissections are most common in those in their sixth decade of life (Fann et al., 1995). However, because the disease is sometimes associated with a connective tissue disorder such as Marfan's syndrome, which is symptomatic in the young as well as the elderly, the range in age in a 30 year study of 174 patients was 15 to 86 years with an average of 57 ± 14 years s.d. (Fann et al., 1995).

Bickerstaff et al. reported in 1982 that, if left untreated, the one year survival rate of an aortic dissection was 21.6% and the five year survival rate was 7% (1982).
A recent study from New York on patients treated since 1985 has reported that with selective treatment, medical and/or surgical, the one year survival rate for patients with a dissection in the descending thoracic aorta was 92% ± 4% (Schor et al., 1996). However another study from a group in Denmark reported the one year survival rate of patients treated medically, from 1984-1993, for a descending thoracic aortic dissection, was 55% ± 11% (Perko et al., 1995). A third group in California reported that for those treated surgically, from 1962-1992, the one year survival rate was 56% for acute cases (symptoms occurred within 14 days) and 78% for chronic cases (symptoms occurred for longer than 14 days (Fann et al., 1995). Survival rates appear to be highly dependent on the choice of treatment.

If a patient is treated medically, logically the pressure must be lowered enough to prevent propagation, but there have been no studies to define what this pressure should be. This study describes how a change in luminal pressure affects the geometry of a dissection, thereby providing insight into why and how propagation is prevented when the pressure is lowered. With a better understanding of how the tear depth and extent of dissection affect the propagation pressure, perhaps treatment can be improved.

1.2. Objectives

An aortic dissection is a result of mechanical failure of one or more components of the aortic wall. The failure could be due to an extrinsic factor producing abnormally high stress in the wall, or an intrinsic change in the mechanical properties of one or more of the wall components. The distensibility of the wall is a measure of its mechanical properties. A change in the mechanical properties, which changes the overall distensibility of the wall, means that the rupture stress could be reduced. However because of its non-linear elastic
properties, the aortic wall stiffens as blood pressure increases, resulting in a change in distensibility and the propensity for failure associated with high blood pressure in an otherwise healthy artery.

This study deals with the role of distensibility on the pressure required to propagate an aortic dissection. Distensibility is measured in a healthy aorta but the concepts could be applied to one that is diseased. The objectives of the study are as follows:

1) to determine a) the pressure required to propagate a dissection in a healthy aorta, b) whether or not this pressure is in the physiological range, and c) the effect of tear depth (the location of the dissection plane relative to the lumen) on propagation pressure.

2) to determine if the layers within the laminated structure of the wall have qualitatively different mechanical properties, and how such differences may affect the pressure at which a dissection propagates.

3) to use a novel 3-D ultrasound technique to measure some geometric parameters of simulated aortic dissections, tethered to in vivo length, at various pressures and tear depths, in order to determine if any simplifying assumptions can be made prior to the development of a theoretical model.

4) to use the 3-D ultrasound technique to measure the distensibility of the unconstrained vessel wall quantitatively, as a function of pressure, in both the intact wall of a healthy vessel and the outer wall of the false lumen of a dissected vessel, which will be used in the theoretical model.
5) a) To develop a model that predicts the angle at the longitudinal leading edge of a dissection, as a function of tear depth and pressure, as described by the sum of angles $\phi$ and $\theta$ (fig. 1.2), and b) through the development of the model, to gather insight into the mechanical behaviour of an aorta with a dissection.

![Diagram of angles $\phi$ and $\theta$.]

Figure 1.2. A schematic description of the angles $\phi$ and $\theta$ which will be described by the theoretical model. A longitudinal cross-section through the axial centre of the vessel and the false lumen.

Objectives 1-4 are precursors to meeting objective 5. Some hypotheses are stated about this final objective.

1.3. Hypotheses

1) If the plane of dissection of an aortic dissection is close to the adventitia, the high stress in the outer wall of the false lumen will cause it to distend much more than if the plane of dissection is close to the intima.

2) The angles at the leading edges of a dissection will increase with pressure until there is enough stress on the muscle cells for them to fail and propagation to ensue.
To begin the process of meeting the objectives and testing the hypotheses, the aortic wall and its components will be described. The arrangement of the wall components, which is closely related to their distensibility, is important in understanding how tension is maintained in the vessel. Although the process of the formation of a false lumen is still largely unexplained, various findings about the wall structure and changes within it have helped to paint a clearer picture of what factors might eventually lead to a dissection.

1.4. The Aortic Wall

The aorta is an elastic artery, consisting primarily of the fibrous proteins elastin and collagen, and smooth muscle cells. The large proportion of elastin compared to muscle cells and the laminated arrangement of the wall are what distinguish elastic arteries from muscular arteries. The aorta, the large arteries that branch from the aortic arch including the proximal ends of the common carotid and right subclavian, and the common iliac arteries are classified as elastic, while all other arteries in the body are muscular (Ferrans, 1980). Arteries have 3 distinct layers: the intima, the media and the adventitia.

The intima:
The intima is the barrier between the blood and the media. Endothelial cells line the lumen and are attached to the internal elastic lamina (IEL) by connective tissue in the sub-endothelial space. The endothelium is a selectively permeable barrier between the blood and the media, allowing diffusion of oxygen. The endothelial cells are flat and oriented longitudinally which is perpendicular to the orientation of the immediately adjacent medial components. The shear stress acting on the endothelium as blood flows past it causes the cells to respond by arranging themselves in the direction of the stress (Flaherty et al., 1972). The
structures in the sub-endothelial space, namely the microfilament bundles that anchor the endothelial cells along with fine bundles of elastic fibers have also been observed to be aligned longitudinally. Hence, these structures may guide the orientation of the endothelial cells (Buck, 1979). The internal elastic lamina borders the media, and is a thick fenestrated sheet-like layer of elastin (Song and Roach, 1985) differing in structure from the more fibrous layers in the media.

**The media:**
The media is comprised of collagen, elastin, smooth muscle cells and ground substance (fig. 1.3). The elastin is arranged in layers of what appear to be concentric cylinders (Song and Roach, 1985). Smooth muscle cells and collagen fibers are between the elastin layers. The subunits of muscle cell organization consist of so-called musculo-elastic fascicles (Clark and Glagov, 1985). A group of adjacent muscle cells, slightly overlapping and oriented circumferentially, are held in a bundle by a matrix of basal lamina and collagen fibrils. The muscle cells are held together in this way to coordinate cell functions (Clark and Glagov, 1979). The bundles align themselves parallel to the direction of tensile stress acting on them.

Because of the close proximity of the fascicles, the elastin layers appear as concentric sheets. In between the adjacent elastin sheets are wavy collagen bundles and proteoglycans (glycosaminoglycans bound to a protein) associated with collagen fibers or interfibrillar. The proteoglycans are found in greatest abundance in the inner layers of the wall (Eisenstein et al., 1975). Debris accumulates in the intima and media with age, and may be a product of cell death or fragmentation as a result of various cell processes (Joris and Majno, 1974).
Figure 1.3. Movat's stain of a longitudinal section of a porcine thoracic aorta. The elastin is stained black and the muscle cells are pink, with black nuclei. Collagen (yellow) and ground substance (blue or green) are difficult to distinguish. The scale indicates 10 μm increments.

**The adventitia:**

The adventitia consists of dense collagen bundles and a few very thin layers of cells which may be macrophages, serving to remove debris from the artery wall (Joris and Majno, 1974). Also within the adventitia and extending into the media are vasa vasorum (fig. 1.4.). These vessels supply oxygenated blood to the outer portion of the vessel wall. The distance for diffusion through the inner lumen reaches a maximum at approximately 29 lamellar units (Stefanadis et al., 1995), (Wolinsky and Glagov, 1967). If an aortic dissection extends into the vasa vasorum, exsanguination will probably occur.
Figure 1.4. A vasum vasorum entering the media from the adventitia. The colors in the Movat's stain are described in the caption of figure 1.3. The scale in the lower right corner indicates 10 μm increments.

Although all of the structures in the wall may play a role in the initiation and propagation of a dissection, a dissection tears apart the lamellae of the media (fig. 1.5). Thus the structure of the media and the function of its components will be described in further detail, emphasizing the changes that occur with age. Because aortic dissections are most common in the elderly, these changes may be important contributing factors.
1.4.1. Functional Organization of the Media

The functions of the various components of the media provide an explanation for their arrangement within the wall. By considering the response of these components during growth and ageing, the adaptations of the wall to change may be best understood. A change in the structure of the media will alter the mechanical properties, just as a change in the mechanical properties will alter the structure. An understanding of these changes may enable one to predict the onset or propagation of a dissection.

In 1967, Wolinsky and Glagov discovered that the number of elastin and adjacent cell layers is proportional to radius in the thoracic aorta of 10 species of mammals, measured at the midpoint between the left subclavian and celiac
arteries. There is a large difference in aortic wall tension in a mouse as compared to a cow, due to the difference in radius and blood pressure. However they concluded that the average tension per lamellar unit was constant at about 2000 dynes/cm. They termed an individual layer of elastin and smooth muscle cells a medial lamellar unit, or MLU, and suggested this is the primary structural unit in mammals. Within an individual animal, the size of the MLU remains constant regardless of location on the aorta (Berry and Germain, 1973). The number of medial layers in the primate aortas used in the study by Berry and Germain decreased distally but the size of the MLU did not. This is in accordance with the decrease in radius due to taper and the decrease in blood pressure as the distance from the heart increases. However, the authors did not state that the aortas were pressure fixed, so this finding may not apply to an aorta that is in tension.

Because the wall responds to a permanent increase in wall tension by increasing the number of MLU's, some component of the MLU must be capable of withstanding tension. According to Wolff's Law, collagen is laid down along lines of stress, as is seen in bone, scar tissue and tendon (Roach, 1983). Studies on fetal and newborn development in sheep have indicated that elastin may also have this function (Roach, 1983). The number of MLU's increased with age during the last trimester of gestation and continued after birth, coinciding with a marked increase in cardiac output. Elastin production appears to react to the increase in arterial tension during this period of growth. Histologically, elastin and collagen appear within a structured media in the human embryo at about 12 weeks' gestation (Berry et al., 1972). In the third trimester of gestation, the vascular system undergoes development, and the content of both collagen and elastin in the aortic wall continues to increase up to birth. After birth the rate of elastin growth in human aortas is much greater than that of collagen (Berry et al., 1972).
To verify that the increase in pressure associated with the increase in cardiac output triggers elastogenesis, scleroprotein content in the rabbit ascending aorta and the pulmonary trunk were compared at birth and at two months post partum (Leung et al., 1977). The vessels were of equal size, weight and composition at birth, but at two months the ascending aorta had three times as much elastin as the pulmonary trunk and 1.7 times as much collagen. At birth the tension in the two vessels is the same, but after two months the tension in the ascending aorta is approximately six times that in the pulmonary trunk. Because the radii of the two vessels are almost identical during this growth period, the tension is a direct measure of the pressure. The relative proportion of fibrous proteins in the aorta was actually achieved after only two weeks, but the vessel continued to respond to increasing tension by producing both collagen and elastin. The remaining wall components do not respond in the same way to growth. A study done on developing mice aortas after birth indicated that the total thickness of the media increased with age, but the number of lamellae did not (Smith et al., 1951). The increased thickness was due primarily to the thickening of the elastin layers in the media.

The response of fibrous protein content continues with ageing. The gradient of the ratio of elastin to collagen through the wall thickness in both the thoracic aorta and abdominal aorta changes with age (Feldman and Glagov, 1971). In the young human, up to about the age of adolescence, the ratio is greatest near the intima and least near the adventitia. The opposite is true of the elderly, and there is no gradient in those of middle age. During growth, the elastin layers will thicken and additional MLU’s form on the adventitial side. The authors postulate that if the tension in the wall is increasing, each new layer forms under greater tension, and thus there will be a greater amount of collagen in each layer. They also believe that after growth has stopped, the tension in the wall plateaus and the distribution of collagen and elastin equilibrates. As ageing continues, the blood pressure increases. The tension in the wall increases on
the intimal side to a greater extent than on the adventitial side so the gradient will be reversed.

The interaction of the wall components provides the overall mechanical properties of the wall. Thus changes in the individual components change the mechanical function of the entire wall.

1.4.2. Interactive Mechanics of the Wall Components

The response of collagen and elastin to growth indicates that both scleroproteins prevent strain due to tension in the wall, but the difference in their response indicates a difference in their functions. The overall mechanical properties of the wall depend on the interaction of the individual components, each characterized by mechanical properties of its own.

Roy, in 1880, was likely the first to observe that the extensibility of arterial segments decreases as the load increases. It was later found that the total distensibility decreased with age (Hallock and Benson, 1937). The fact that young aortas respond to tension by producing elastin and old aortas respond by producing collagen, suggests that the role of elastin is to maintain tension without the expenditure of energy when the artery is in normal tension and the role of collagen is to support the artery in high tension (Burton, 1954). Elastin provides the high distensibility at low pressures and collagen stiffens the vessel at high pressures (Roach and Burton, 1957).

Thus arterial tissue does not obey Hooke's Law, which states that the relationship between stress, \( \sigma \), (force per unit area) and strain, \( \varepsilon \), (relative extension parallel to the applied stress) is linear, the slope of which is the Young's Modulus, \( E \). In addition to this, the vessel is not purely elastic but is viscoelastic, which will be briefly discussed with regard to hysteresis in Chapter
5. The mechanics of the wall change with pressure, so unlike a homogeneous material, the elasticity cannot be described by a single parameter. Instead, the stress vs. strain curve for the aortic wall can be considered the result of a two-phase material. Although the vessel appears to go through a gradual transition from high to low distensibility, at both extremes the relationship can be approximated as linear. It has been found that the slope of the arterial stress vs. strain curve can be approximately described by the Young's modulus of elastin at low strains, and by that of collagen at high strains (Roach and Burton, 1957). Because the collagen is wavy at low pressures, the elastin will be under increasing tension, while the crimped or wavy collagen is gradually straightened. When the tension is high enough to remove its crimp, the collagen will be under tension and the aorta will be subject to its stiff behaviour. The transition point at which the collagen begins to bear the load has been found to lie somewhere within the physiological pressure range (Bergel, 1961a), (Wolinsky and Glagov, 1964).

Because of the indistinct transition from elastin-like behaviour to collagen-like behaviour, scientists have speculated on the role of muscle cells in wall distensibility. Contractions of the muscle cells enable them to apply 'active' tension as opposed to the passive tension of the elastin and collagen (Burton, 1954). When the muscle cells contract, the vessel radius decreases and the wall thickness increases, which causes an overall decrease in wall distensibility (Dobrin and Rovick, 1969). Further studies that account for the anisotropy, that is the direction dependent extensibility, of the vessel wall have disclaimed this finding (Berry et al., 1975), (Dobrin and Doyle, 1970). Contraction will alter distensibility slightly at low pressures, but there is no significant contribution at physiological pressures. Muscle cell contractions may in fact alter the distensibility in some arteries but not others as was presented in a study on canine arteries (Cox, 1978b). There is a large decrease in circumferential
extensibility, especially at low strains in the iliac, renal and mesenteric arteries, but only slight differences in the thoracic aorta and carotid artery.

A more likely explanation of the departure from the mechanical behaviour of the pure proteins is the recruitment of some collagen fibers at low strain (Cox, 1978a,b) and the distribution of stress in the elastin at high strain. In a study using light and electron microscopy that looked at excised rabbit abdominal aortas tethered to in vivo length at pressures ranging from 0 mmHg to 200 mmHg (Wolinsky and Glagov, 1964), multi-oriented collagen bundles were seen below diastolic pressure, while at pressures beyond diastolic, the bundles disappeared as the fibers became separated and uniformly distributed. These authors suggest that the elastin, which is still under tension serves to distribute the load throughout the wall, so that there is less stress concentration on the individual collagen fibers perhaps giving more strength to the wall. Thus the elastin and collagen are acting in parallel throughout the pressure range. Other authors disagree and conclude that they act sequentially (Newman et al., 1971).

With a knowledge of the structure and function of the aortic wall components, one can understand how changes in the aortic wall could predispose it to dissection.

1.5. Wall Structure and the Aortic Dissection

There are numerous factors that could change the wall structure of the aorta, rendering the aorta more susceptible to a dissection. For instance, connective tissue disorders such as Marfan’s syndrome and Ehlers-Danlos Type IV, which among other abnormalities, are manifested by a weakening of the aortic structures, predispose the wall to dissections (Schlatmann and Becker, 1977a), (Beighton, 1993). Other conditions leading to changes in the wall structure have
been associated with dissections. These include hypertension, atherosclerosis, cystic medial necrosis and ageing. The extent of contribution of these factors is not clear because unless a dissection is associated with a connective tissue disorder or is a result of trauma, the structure of the vessel is not obviously different than that of a normal vessel. Changes in the wall structure associated with these conditions are considered along with how they might contribute to the occurrence of a dissection.

1.5.1. Hypertension

Most investigators agree that hypertension decreases arterial distensibility (Cox and Bagshaw, 1988), (Berry and Greenwald, 1976). Some question whether this is simply due to a shift upwards along the non-linear stress vs. strain curve, or a structural change in the vessel wall. One study found that when brachial-radial arteries of hypertensive subjects were distended at normal blood pressures, the volume distensibility was the same as in normals (Gribbin et al., 1979). They concluded the decrease in distensibility was due only to the shift along the stress vs. strain curve resulting from the increase in pressure, and that there were no irreversible structural changes. However they did not account for wall thickness and did not do a histological study. Their controls (mean age 32) were also considerably younger than their test subjects (mean age 55).

Histological studies of the rat artery have shown that hypertension does affect wall structure, and in fact in the same way as does natural growth. The long-term response of the arterial wall to high tension is an increase in wall thickness due an increase in both elastin and collagen in the middle-aged artery (Wolinsky, 1972), and an increase in elastin in the young artery (Berry and Greenwald, 1976). The increase in tension that causes this change could just as well be due to ageing, characterized by an increase in vessel radius producing an increase in blood pressure, as to hypertension, characterized by
an increase in blood pressure producing an increase in vessel radius. The number of MLU's does not increase but the tension in the wall does (Wolinsky, 1970). An increase in thickness of the elastin lamellae may partly compensate for the increase in tension. A greater proportion of elastin should result in greater distensibility, but the wall in hypertension is actually stiffer. Even with the changes in wall structure, the hypertensive animal has enough stress in the arterial wall to shift it to a higher strain region of the distensibility curve, making it appear stiffer (Berry and Greenwald, 1976).

Most incidences of aortic dissection are associated with hypertension (Fann et al., 1995), (Nakashima et al., 1990). A likely explanation is the increase in stiffness of the intima and inner medial layers due to the high tension. High stress concentration around a defect occurring in this region will result in early structural failure. The indication that long term hypertension leads to thickening of the lamellae suggests a mechanism to withstand high tension. However a hypertensive aorta, especially an ageing one, undergoes further structural changes. The level of elastase increases which reduces the amount of interlamellar elastin fibers (Nakashima and Sueishi, 1992) and may remove the smooth muscle cell basement membrane (Sariola et al., 1986). Such changes weaken the bonds between adjacent elastic lamellae as well as among muscle cells within an MLU, so that less force is required to tear the layers apart. Thus an artery in hypertension might be more susceptible to dissection propagation.

1.5.2. Atherosclerosis

Whether or not atherosclerosis changes the distensibility of the aortic wall is disputed. Newman et al. (1971) showed that thoracic aortas in the cockerel being fed a high cholesterol diet showed an increase in distensibility after the appearance of atherosclerotic lesions. The distensibility was drastically reduced
to below normal when the walls became heavily calcified. Higher distention can cause the same structural changes as described by hypertension, due to the increase in tension associated with an increase in radius. However, in the same year a study was done in Japan on aortas from humans in their eighth decade which concluded that those with more severe atherosclerotic lesions did not have a significantly different distensibility than those without (Nakashima and Tanikawa, 1971).

The correlation of occurrence of dissection with degree of atherosclerosis is just as highly disputed. Some investigators have found such a correlation in an autopsy study (Nakashami et al., 1990) and in an ultrasound study (Fitzgerald et al., 1992) while others have not (Wheat, 1973). However Wheat, who analyzed patients, did not indicate how his conclusion was drawn. Aside from the possibility of an increase in wall stress, atherosclerosis leads to intimal thickening which could impair diffusion to the media, resulting in its degeneration (Braunstein, 1963), (Wilson and Hutchins, 1982). Thus the presence of lesions leads to a decrease in resistance to tearing (Tiessen and Roach, 1993). However, because the resistance is not lowered to such an extent that physiological pressures could initiate a tear (Tiessen and Roach, 1993), atherosclerosis may not be linked to the initiation of a dissection if the blood pressure is normal. However shear forces on a calcified plaque during an angioplasty procedure may indeed be great enough to initiate a tear. The presence of calcium was linked to the size and location of dissections following angioplasty (Fitzgerald et al., 1992). In any case, the decrease in resistance to tearing will likely contribute to a lower propagation pressure.

1.5.3. Medial degeneration

According to the three stages of an aortic dissection, initiation by an intimal tear must precede the formation of a false lumen. However cystic medial necrosis
(CMN) in the region between the inner two thirds and outer third of the wall, could lead to rupture of the vasa vasorum, which are present in this region, and will result in pooling of the blood, creating enough pressure to propagate the false lumen (Hirst and Johns, 1962). However, CMN was found only in 20% of non-Marfan's syndrome cases (Nakashami et al., 1990) so if this mechanism is correct no explanation is offered for the remaining 80% of cases. The role of the vasa vasorum also comes into question if dissections in the aorta are compared to those in the intracranial posterior circulation. Dissections in the intracranial arteries tend to occur between the IEL and the media (Berger and Wilson, 1984). The difference could be associated with structural differences in the arteries, but nevertheless indicates that because vasa vasorum are not present in the intracranial vessels, their involvement is not necessary for the formation of a dissection.

Medial degeneration could be a result of connective tissue disorders such as Marfan's syndrome or Ehlers-Danlos Type IV. Marfan's Syndrome is associated with changes in the aortic structure. The disease is characterized in arterial vessels by a loss and disorganization of elastic fibers, (Ferrans, 1980), (Abraham et al., 1982) reportedly due to a defect in the collagen Type I that serves to support them (Scheck et al., 1979), which leads to the weakening of the aortic wall. Ehlers-Danlos Type IV is characterized by a deficiency in collagen Type III, rendering the vessels abnormally distensible (Beighton, 1993).

Pregnancy can initiate medial degeneration (Nolte et al., 1995) resulting in unusual dissections, occurring in the iliac arteries (Nolte et al., 1995). The role of hemodynamic stresses associated with pregnancy versus the effect of hormones on wall structure alterations has not been distinguished. The fact that hormonal changes should affect all arteries and dissections occur only in the iliacs, suggests that hemodynamic forces may be more important.
1.5.4. Ageing

Because the occurrence of dissection seems to be only partly related to abnormal conditions in the aorta, the normal ageing effects on the aorta should be considered. The ageing aorta is subject to conditions such as cystic medial necrosis, elastin fragmentation and increasing amounts of collagen (Schlatmann and Becker, 1977a). Thus none of these factors can be attributed directly to the onset of a dissection. These same authors propose that a dissection is merely an occurrence associated with the natural ageing of the aorta as it undergoes injury and repair due to normal hemodynamic forces (Schlatmann and Becker, 1977b).

The structure of the wall undergoes expected changes due to growth, as has been discussed earlier. The amount of both collagen and elastin increases, and the relative amount of collagen compared to elastin increases in the outer portion of the media. In ageing aortas, the collagen fibers are recruited at lower pressures (Roach and Burton, 1957). The waviness index of the IEL, which is the lamellar length divided by the straight line distance, as defined by Wolinsky and Glagov (1964), does not change as a function of age (Dunmore and Roach, 1990), but the degree of unfolding does (Samila and Carter, 1981). The latter authors found that the lamellae of the young carotid artery unfolded more before the collagen fibers were recruited. Thus the waviness of the collagen fibers in the young vessels must be greater. They also found a negative correlation between elastic modulus and collagen waviness, resulting in a more distensible vessel.

Natural ageing includes an increase in blood pressure which will distend the wall and decrease its thickness. Thus the pressure gradient through the thickness of the wall increases. If the inner and outer walls are assumed to have the same elastic properties, the inner wall will be at a stiffer location in the stress vs. strain
curve than the outer wall. The stiff inner wall could tear while the outer wall distends, leading to the formation of a false lumen (Robicsek and Thubrikar, 1994). However, the elastic properties of the inner and outer walls may not be the same. The thickness of the elastic laminae in the outer one third of the thoracic rat aorta is considerably thinner than those in the inner two thirds (Berry et al., 1993). More elastin in the inner layers is needed to support the higher stress so that these layers will be more resistant to tearing. A dramatic difference in elastic properties at the junction between the two regions could predispose the artery to dissection in this location. However initiation of the dissection remains unknown.

The description of the aortic wall in this chapter has provided evidence of the non-homogeneous structure of the wall throughout its thickness, even if the vessel is healthy. The next chapter deals with the first two objectives of the study. The mechanical strength and distensibility of the wall as a function of location is investigated, and how these could be related to the pressure required for propagation of a dissection.
CHAPTER 2: Mechanics of the aortic wall

2.1. Introduction: Strength of the media as a function of location

The pressure required to tear apart structures in a normal intact aorta may be used as a measure of medial strength. The lamellae may be torn apart by injecting a fluid such as saline into the media to create a 'bleb'. If the pressure is recorded during injection, a peak value is reached during initiation of the tear (tearing pressure), which will drop dramatically to a reach a plateau pressure associated with the propagation of the tear (propagation pressure). Bleb experiments have produced a variety of results.

The first bleb experiments done on human aortas from autopsy (n = 42, mean age = 54.2 ± 14.2 years s.d.), indicated a considerable variation in individual measurements not only from person to person but also from location to location within one aorta (Robertson and Smith, 1948). Their results also indicated a negative correlation of location along the vessel, from the ascending to descending aorta, with tearing pressure. Only a weak negative correlation with age was reported, and sex did not affect the strength of aortic media. They concluded that normal physiological pressures could not produce the intimal tear as the average tearing pressure was close to 600 mmHg.

A more recent study on human aortas obtained from autopsy (n = 21, mean age = 60 ± 13 years s.d.) reported similar findings in tearing pressure and correlation with location along the vessel. (Tiessen and Roach, 1993). However they found
no correlation with age, and a significant difference in wall strength between the sexes. The resistance to tearing in women was found to be greater than in men, which perhaps explains why the ratio of incidence of men to women is 3:1 (Fann et al., 1995). An earlier study reported no correlation of tear depth with bleb propagation pressure in cut open porcine thoracic aortas (Carson and Roach, 1990). However only tears in the centre of the wall were investigated (tear depths ranged from 15-65% with a mean of 34%), and the maximum volume of saline infused was 0.8 ml. Qualitative observations indicate that a larger volume of saline must be infused before the propagation pressure becomes constant.

When a simulated dissection was subjected to dynamic pressures, tear depth was correlated with propagation rate. The dissection was simulated by creating a bleb, and then using a scalpel to create an intimal tear so that the bleb was open to the true lumen. The tear depth as well as the rate of pressure change \((\text{dP/dt})_{\text{max}}\) affected the propagation rate (van Baardwick and Roach, 1987). The rate increased with the maximum rate of pressure change and with maximum pressure, as might be expected, but decreased with tear depth. Intuitively, one might expect the propagation rate would increase with tear depth, since there would be more stress on the thinner outer wall of the false lumen, and in fact our pilot studies indicate that a dissection created close to the adventitia propagates at a lower pressure than one created close to the intima. However the same trend was found in the bleb study reported in the next section, which suggests a difference in structural properties through the thickness of the wall. Van Baardwick and Roach suggest that the more fibrous sheets near the adventitia (Song and Roach, 1985) could mean more connections between lamellar units and therefore more resistance to tear.
2.2. Propagation Pressure of an Aortic Dissection

Pilot studies were done to determine the effect of tear depth on propagation of an aortic dissection. If the outer wall of the false lumen is very thin, it will be subjected to much higher stress than the thick intact wall. The distention of the wall in high stress should bring on propagation at a lower pressure than a thicker wall that is under less stress. The non-homogeneity of the aortic wall could mean that the difference in structure of the intact wall and the dissected wall may play a role in the onset of propagation. The relationship of tear depth to propagation pressure of simulated dissections in the thoracic aorta was quantified by Amy Tam, a summer student in our laboratory. The results served as a basis for investigating the factors that may contribute to the findings.

2.2.1. Method

Simulated dissections were created in 17 fresh porcine thoracic aortas, obtained from a local abattoir (fig. 2.1.): Excess tissue was removed and the intercostal branches ligated. It was necessary to turn the aortas inside out because a tear had to be created on the intimal side. Approximately 4 ml of 0.9% saline was injected into the media of the wall, on the anterior side, between the 2nd and 3rd intercostal branches. A bleb was thereby created, approximately 30 mm long and 1/3 to 1/2 the circumference wide. A scalpel was used to create a circumferential cut across the bleb in its centre, and the aorta was flipped right side in.
Figure 2.1. Creation of a simulated dissection. a) aorta flipped inside out, saline injected into media to create bleb, b) circumferential cut made through bleb, c) simulated dissection.

Each aorta was cannulated and placed in a 0.9% saline bath. Although the aorta is tethered in vivo at 125-130% of its unpressurized length (Han and Fung, 1995), these aortas were unconstrained. They were pressurized with saline and 1-2 ml of India Ink was added to the saline in the lumen through a 3-way valve immediately proximal to the cannula, to achieve better definition of the false lumen during propagation. The pressure was monitored during pressurization, with a Millar Mikro-Tip® Catheter Pressure Transducer System, consisting of a control unit and a 2.5 F sensor (circumference of 2.5 mm). The sensor was inserted into the 3-way valve proximal to the cannula. The control unit was attached to a voltmeter. The system was calibrated by pressurizing a vessel attached to a mercury manometer, and recording the voltage output at a variety of pressures. A calibration curve of pressure vs. voltage was then used to convert voltage readings back into pressure during the experiments. The
pressure required to initiate propagation was recorded as the *propagation pressure*.

After propagation, the aorta was removed from the apparatus, and fixed, unpressurized, for at least 24 hours in a 10% buffered formalin solution. Histological sections were prepared at the London Health Sciences Centre University Campus Pathology Laboratory. A sample of tissue from the longitudinal leading edge of the dissection was embedded in paraffin wax and longitudinal sections were cut, 4-5 μm in thickness. Two of these sections were prepared with a Movat’s stain, so that the laminated structures of the wall were easily distinguished (fig. 1.5.). A Zeiss Axioskop microscope magnified the section 100x and the layers on both sides of the dissection plane were counted. The layers were counted approximately five times in the same location and the average calculated. The tear depth was expressed as the fraction of total layers that were on the intimal side of the dissection plane.

2.2.2. Results and Discussion:

The propagation pressure decreased significantly with tear depth (fig. 2.2), which supports the first hypothesis. The model described in Chapter 5 will provide a theoretical explanation for this finding.

All of the dissections from which a propagation pressure could be recorded were in the outer half of the aortic wall. Testing the vessels at pressures beyond approximately 450 mmHg resulted in leakage or rupture of the intercostal branches, so pressures required to propagate dissections in the inner half of the wall could not be reached. The range in propagation pressure was between approximately 200 and 400 mmHg. Because longitudinal tethering will cause greater circumferential strain at a given pressure, these pressures might be even lower if the vessel were tethered as it is in vivo. The normal blood pressure of a
pig is 169 (144-185) mmHg systolic and 108 (98-120) diastolic, where the numbers in brackets represent the 95% confidence interval (Spector, 1956). Thus the lowest propagation pressure is very close to normal systolic pressure. The dissections propagated both antegrade and retrograde to the normal direction of flow as well as circumferentially, so pressure rather than flow seems the more likely physical parameter for the propagation. The subsequent studies were designed to determine the contribution of the wall structure to this finding.

Figure 2.2. The pressure needed to propagate a simulated aortic dissection as a function of tear depth measured from the intima. p<0.001. The equation describing the regression line is $y = -4.46x + 617$ mmHg. The error bars are standard deviations of measurement errors from five repeated counts, n = 17.

2.3. Propagation pressure during bleb formation

The purpose of this study was to determine how tear depth affects propagation pressure during formation of a bleb in the media of the aorta. A correlation could indicate structural differences among the layers of the wall. The wall of an unpressurized aorta is 2-2.5 mm thick, and has a diameter of approximately 15 mm. Thus the inner layers must be shorter in circumference than the outer
layers. When the aorta is cut open longitudinally, the cylindrical shape is not maintained. Instead the artery springs open due to release of residual stress (Vaishnav and Vossoughi, 1987), indicating that the inner walls are in compression and the outer walls are in tension when the intact aorta is unpressurized. Propagation pressure during bleb formation was investigated in both cut open and pressurized aortas to determine if the gradient in circumferential stress through the layers of the wall could affect the force required to separate them.

2.3.1. Method

Fifteen fresh porcine thoracic aortas were cleaned of excess tissue and made pressure-tight by ligating the intercostal branches. Each one was cannulated, placed in a 0.9% saline bath and pressurized with saline to 100 mmHg, approximately diastolic pressure in the pig (Spector, 1956) (fig. 2.3.A.). A bleb was created in the media by injecting saline through the adventitial side of the wall through a 1.6 mm long, 25 gauge needle attached to 0.76 mm I.D. polyethylene tubing by way of a 3-way valve. A 20 cc syringe with a 20 gauge needle was attached to the other end of the tubing. The syringe was mounted on a Harvard Apparatus Co. infusion pump which infused the saline at a rate of 1.94 ml/min. A Millar Mikro-Tip® pressure sensor was calibrated as described in section 2.2.1, and connected to the system through the 3-way valve. A second sensor measured luminal pressure via a second 3-way valve in the cannula close to the vessel lumen.

Because only one voltmeter was available, the pressure control units were attached to an analog to digital converter board in a 486 PC. The binary output from the board was converted into a voltage reading through calibration with the voltmeter and a calibration curve like the one described in section 2.2.1 was used to convert the voltage reading into a pressure. The pressure in both the
lumen and in the bleb were recorded during infusion. The pressure sensor which measured pressure during bleb formation was connected immediately proximal to the needle, so the pressure drop through the needle could be measured before creation of the bleb by simply infusing saline through the system and recording the pressure. The propagation pressure was measured by subtracting the pressure drop through the needle and the luminal pressure from the recorded pressure when it had reached a constant value during propagation.

Two histological sections per aorta were prepared as described in section 2.2.1. The layers in both the dissected portion of aorta and the intact portion were counted as described in section 2.2.1., and the number of layers from the intima to the dissection plane was expressed as a percentage of the total number of layers.

Another 10 aortas were cut down their length, so that the tissue could lie flat, and a bleb was created in the wall by inserting the needle into the media through the intima (fig. 2.3.B.). The voltage reading was recorded directly from the voltmeter and converted into a pressure reading using a calibration curve like the one described in section 2.2.1. When the aorta was cut open, the bleb usually grew radially in a hemispherical shape. In the intact aorta the bleb grew radially only until the diameter of the bleb was approximately that of the aorta, after which the bleb grew down the length of the aorta. Once again, longitudinal samples were cut from the edge of the bleb and histological sections were prepared at the London Health Sciences Centre University Hospital Pathology Laboratory as described in section 2.2.1.
Figure 2.3. Setup for the measurement of bleb propagation pressure at various tear depths. A). Vessels were pressurized to 100 mmHg and saline was injected into the media. B). The vessels were cut open and saline injected into the media through the intimal side.
2.3.2. Results and Discussion

The unpressurized state of the aorta does not represent the in vivo state. Some residual stress is present in the wall after excision from the body. Unpublished studies done in our laboratory by Conan McIntyre have shown that if a ring of the inner layers are separated from the outer layers mid-way through the thickness of the wall, and the inner ring is removed, approximately 5% residual compressive circumferential strain is released. If the ring is cut open, another 5% residual strain is released. Strain in the outer ring was not measured because of the difficulty in distinguishing the edge of the adventitia, but by observation the outer ring does not spring open to the extent of the inner ring. Thus even in the unpressurized cut open aorta some residual stress still exists. When the aorta is pressurized, all the layers should be in tension, but a stress gradient may still exist. A comparison of the results for the two states of the vessel should give an indication of the importance of the contribution of a stress gradient in the wall layers to the force required to separate them.

The results are illustrated in figure 2.4. Based on this sample, there is no difference in the relationship of propagation pressure to tear depth in the two experiments. The slope of the relationship for the pressurized aortas is $0.63 \pm 0.19$ mmHg s.e., and the p value is 0.002. The slope of the relationship for the opened up aortas is $2.2 \pm 0.9$ mmHg s.e., and the p value is 0.023. When the two sets of data are combined, the relationship has a slope of $1.0 \pm 0.3$ mmHg s.e., and the p value is <0.001. In all cases propagation pressure correlates with tear depth. Although the slopes of the relationships for the two sets of data look significantly different, comparing the two groups with a Mann-Whitney Rank Sum Test, indicates no statistically significant difference between the medians of the two groups. Thus the difference in the gradient of stress in the wall of a pressurized aorta as compared to that in a cut open aorta is negligible when comparing strength of the medial layers in the experiments described here.
Figure 2.4. The role of tear depth on the propagation pressure in bleb formation in pressurized and cut open aortas. Tear depth is measured from the IEL. The standard deviation of the measurement of tear depth was <5%.

The lower pressure required to propagate an aortic dissection that is close to the adventitia (fig. 2.2.) may not be due to a difference in the failure stress of the muscle cells near the adventitia. In fact a higher pressure was required to propagate a bleb in the outer layers of the wall than in the inner layers (fig. 2.4.). Therefore there must be a difference in the forces acting on the muscle cells as a result of the difference in geometry of the false lumen as a function of tear depth. The geometry is determined by the distensibility of the vessel wall. The thin dissected wall is under a higher stress than the thick intact wall, so will be at a different location in the extensibility curve. However because the structure of the wall is non-homogeneous, the extensibility curve for the outer wall of the false lumen is not necessarily the same as the curve for the intact wall. In the next section, the extensibility curves for the different parts of the wall will be measured.
2.4. Instron tensile tests.

Extensibility curves plotted using the Instron machine were not used to quantify values of the elastic moduli in the circumferential and longitudinal directions, but to determine if in the absence of compressive or tensile forces resulting from the cylindrical shape of the aorta, the various layers of the wall had different elastic properties.

2.4.1. Method

The aortas were cleaned of excess tissue, and cut down their length so that the tissue could be spread open. A bleb was created in the wall between the second and third intercostal branches, to create a dissection plane close to the intima. Two segments of tissue were cut from the intimal side of the bleb, 15 - 20 mm in length and 5 - 10 mm in width, one oriented circumferentially and the other longitudinally. A second bleb was made in the remaining layers, and similar segments of the same dimensions were cut in the medial layer and in the adventitial layer (fig 2.5). The length and width were measured with a ruler, and the thickness of the layers was measured with a Starrett thickness gauge. The thickness gauge has a weighted pad, 9 mm in diameter, that rests on top of the specimen. It measures the distance from the top of the specimen to the resting position on the specimen platform. The amount of saline absorbed in the tissue will therefore affect the measured thickness, as will the amount of collagenous tissue that is part of the adventitia but is not of a constant thickness. A true difference in the thickness of adjacent segments may exist because the thickness of the aortic wall is slightly greater on the anterior side.
Figure 2.5. Locations from which circumferential and longitudinal segments were removed. One segment of each orientation was cut from each of the three layers, for a total of six segments per aorta.

The tissue was mounted on an Instron Universal Testing Instrument (model 1125) with a 500 g load cell. The mounting apparatus is illustrated in figure 2.6. The ends of the tissue samples were held by stainless steel clamps lined with 600 grit sandpaper to reduce slippage. The upper clamp was attached to a stainless steel rod, which hooked onto the Instron machine so that the force applied to the tissue could be measured. The lower clamp was mounted on the moving platform which applies tensile force to the sample. A Pyrex cylinder filled with saline was also attached to the mounting apparatus so that the tissue was suspended in saline throughout testing. The tissue was stretched at a constant rate of 10 mm/min up to a load at which the collagen appeared to be the determining factor in the extensibility curve, but before failure. The time, displacement and load were recorded on a 486 66 MHz PC hooked up to the Instron. The stress and strain were calculated and plotted for each sample.
2.4.2. Results and Discussion

Figure 2.7. shows the results for the extensibility in the circumferential direction, and figure 2.8. the results for the extensibility in the longitudinal direction. A limit of the study is that the tissue was not preconditioned. If the tissue undergoes cyclic straining some hysteresis will be observed due to stress relaxation. However cyclic straining of test segments indicated that the path of stress with strain as the strain is increasing does not change dramatically from one cycle to the next. Although using unconditioned test specimens may result in some quantitative error, the qualitative results will be valid.

To measure the elastic properties of inner vs. middle vs. outer layers of the wall, the wall was separated into three strips of equal thickness. During creation of a bleb the wall is split between adjacent lamellae (fig. 1.5), but there is little control
over the precise location of the dissection plane. Calculation of stress accounts for the thickness (stress = force / area) but because of the non-homogeneous structure of the wall, the inclusion or exclusion of various layers may change the extensibility of a segment. The thickness of the segments is therefore indicated in the figures.

If the thicknesses of the 3 portions of the wall are added together for each artery, it can be seen that there is considerable variation in wall thickness. In most cases the three separated strips were stacked on top of each other before they were separated as indicated in figure 2.5., but if the strip was damaged during the separation process, another strip was cut immediately adjacent to the original location, or some of the layers may have been removed. Thus, in some cases the thickness of the longitudinal test sample was not the same as the circumferential sample that was cut adjacent to it, most notably artery 5 - media, and artery 3 - media + adventitia. The difference in thickness in the rest of the samples was between 0-0.2 mm. This is partly due to measurement error encountered in measuring the macroscopic thickness using the Starrett thickness gauge.

In comparing figures 2.7.A. and C. to 2.8.A. and C., it is apparent that the tissue stiffens at a lower strain in the circumferential direction than in the longitudinal direction. This illustrates the anisotropy of the vessel and is discussed further in the development of the theoretical model in Chapter 5.
Figure 2.7. Stress vs. strain relationships for tissue segments in circumferential direction. A., B. and C. refer to different layers from the intimal side to the adventitial side. The numerals refer to the 5 different arteries. The thickness of the segment is indicated.

Figure 2.8. Stress vs. strain relationships for tissue segments in longitudinal direction. A., B. and C. refer to different layers from the intimal side to the adventitial side. The numerals refer to the 5 different arteries. The thickness of the segment is indicated.
Because the tissue samples were all cut from the same location in the vessel, the difference in elastic properties can be compared from aorta to aorta. In general, some arteries were stiffer than others. For example artery 4 stiffened at a low if not the lowest strain in every case with the exception of figure 2.7.B. In this case the media was much less stiff in the circumferential direction than in the other vessels. Thus there can be a wide variability in stiffness not only from aorta to aorta but also within the wall of a single aorta. Artery 1 in figure 2.7., provides another example of this. The intimal side becomes stiff at a higher strain than the other vessels, but the adventitial side becomes stiff at a lower strain than the other vessels. It is possible that structural differences that make one artery stiffer than another may be localized to a specific region within the thickness of the wall.

There is a notable difference in the mechanical behaviour of the intimal layer in the longitudinal direction (fig. 2.8.A.) vs. the circumferential direction (fig 2.7.A.). In the circumferential direction, the tissue is more extensible at lower strains and stiffer at higher strains than in the longitudinal direction. Because there is no such apparent difference in the medial layers considered alone, the structural components of the intima or the intimal side of the media must be showing this anisotropic behaviour.

If artery 3 is considered in figures 2.7.C. and 2.8.C., the thicker adventitia + media layers appear to stiffen at higher strains. However the range in thickness is not wide enough to support this. Nevertheless, because the components of the media have different properties than the components of the adventitia, as is seen in figure 2.7.B. and C., a thicker dissected wall would be expected to behave differently than a thin one.
These qualitative results have thus provided the following information about the aortic wall:

1) The distensibility of the wall is not the same throughout its thickness
2) The wall is anisotropic, and the extensibility may depend on the radial location within the wall, and
3) There is significant biological variability from aorta to aorta as well as within an individual aorta.

The studies in this chapter have shown that the various layers of the wall do indeed have different mechanical properties. Also, the distention of the outer wall of the false lumen likely accounts for the dependence of propagation pressure on tear depth in an aortic dissection, rather than the difference in medial strength among layers.

Because the tested segments are not continuous with the rest of the tissue in a cylindrical shape, the extensibility results may not be directly applicable to intact vessels under pressure. The results merely serve as a guide in setting up a theoretical model. More applicable stress vs. strain data will be gathered to use in the model, using a novel 3-D ultrasound technique to measure stress and strain in an intact pressurized vessel. First, some experimental observations on the geometry of an aortic dissection using the same 3-D ultrasound technique are presented.
CHAPTER 3
Experimental Observations of Aortic Dissections

Before attempting to develop a model, dissections were simulated in 8 porcine thoracic aortas. The dissections were created randomly at different depths in the aortic wall. The geometry of the vessel wall within the true and false lumens was studied from 3-D ultrasound images through a pressure range of 100-300 mmHg. This is a new technique that uses technology developed by Life Imaging Systems™. Assumptions based on these observations are used in the development of the model. Before the method of obtaining measurements is described, some concepts of ultrasound technology are reviewed, which can be found in basic textbooks on ultrasound, such as the one referenced by Curry et al., 1990.

3.1. Introduction to Ultrasound

Sound travels as a wave through a medium. The range of wave frequency of audible sound is 15 - 20 000 Hz. Ultrasound is defined as having a frequency above 20 000 Hz. If an ultrasonic wave encounters an interface between two media, some of the waves are reflected back to the source. The energy from the reflected wave is transformed into a voltage along a time scale, which provides information about the location of the interface. There are four main types of ultrasound imaging techniques:
1) **A-mode**: or amplitude mode imaging. Spikes originate from a baseline. The height of the spike is proportional to intensity, and the width is proportional to the depth of the interface.

2) **TM-mode**: This is similar to A-mode but is recorded over time so that movement of the interfaces can be recorded.

3) **B-mode**: The signal is displayed as a dot in a two dimensional plane. The intensity of the point represents intensity of the signal and the location in the plane represents the location in the medium, so that a two-dimensional image is produced. A 3-D modification of this mode is used for this study.

4) **Doppler**: This mode utilizes the Doppler effect to determine the velocity profile of a medium. Doppler ultrasound is used in flow studies and will not be discussed further.

The ultrasonic pulse is produced by a piezoelectric crystal. The return time and intensity of the signal depend on the properties of the crystal and the media through which the wave travels.

**The crystal**: A piezoelectric crystal is made up of dipolar molecules. When a voltage is applied across the crystal, the dipoles realign themselves, altering the geometry of the crystal. If the voltage is a pulse, the crystal will vibrate as the molecules realign, producing sound waves. Just as the crystal can transform a voltage into ultrasonic sound waves, it can also transform the energy from the sound waves back into a voltage, thus acting as both a transmitter and a receiver. Mounted behind the crystal is a backing block, which dampens the vibrations after transmission so that the crystal can act as a receiver. Although
some piezoelectric crystals such as quartz, occur in nature, man-made crystals are usually used diagnostically (Curry et al., 1990, p. 328).

The thickness of the crystal determines its natural resonating frequency. Just as a pair of cymbals that have been struck, the surfaces of the crystal vibrate most efficiently if they are at a distance equal to half the wavelength of the sound waves that are produced, so that the vibrations of the surfaces will be synchronized. Therefore a crystal is designed to operate at a required frequency; the higher the frequency, the thinner the crystal.

The medium: The speed at which a wave travels through a medium depends on the characteristic properties of that medium. When an ultrasound source transmits energy at a particular frequency to the molecules in the medium, there is a domino effect. The movement of each molecule affects the surrounding molecules. Thus the rate at which this force is propagated from particle to particle will determine the length of the wave in the medium and thereby the acoustic velocity. The properties of the medium that affect the rate of propagation are density and compressibility.

The speed at which a wave can travel through a solid with large heavy molecules is hindered by the return time of a molecule to its original position after being displaced by the force of the wave. If the molecule is slow to return, the sound waves may obstruct one another and there is a greater loss of energy which decreases the speed of sound. However the close spacing of the molecules allows a higher rate of force propagation than in a gas. In an incompressible medium the molecule travels less distance before coming into contact with another molecule. Thus, in general sound will travel much faster through a solid than through a gas.
Choice of the crystal and the medium: The choice of a crystal depends on the location and types of media interfaces that will be encountered. The waves of an ultrasonic beam will travel in a series of wave fronts over a distance called the near zone. Beyond this distance, in the far zone, the beam will diverge, and there will be attenuation of the signal. The length of the near zone is a function of the width of the crystal and the wavelength of the sound.

\[ u \propto \frac{w^2}{\lambda} \]  \hspace{1cm} (3.1)

where:
- \( u \) = length of near zone [m]
- \( w \) = width of crystal [m]
- \( \lambda \) = wavelength of sound [m]

Since the speed of sound in a medium is constant and is described by:

\[ v = f \cdot \lambda \]  \hspace{1cm} (3.2)

where:
- \( v \) = velocity of sound [m/s]
- \( f \) = frequency [cycles/s] or [Hz]

large, high frequency transmitters will have the best depth resolution. However, depth resolution is not always the best option. With a high frequency beam comes a loss of side to side resolution and greater tissue absorption which attenuates the signal. The decision to sacrifice attenuation for depth resolution is based on the properties of the media.
Each medium has a characteristic impedance based on the speed that sound travels through it. The impedance is defined as:

\[ Z = \rho \cdot v \]  

(3.3)

where:

- \( Z \) = characteristic impedance [kg/(m\(^2\)*s)]
- \( \rho \) = density [kg/m\(^3\)]

The percentage of the wave reflected, depends on the difference in impedance of two media at an interface. The greater the difference in impedance, the greater the reflection. Mineral oil is therefore necessary as an interface between a transmitter and the skin for tissue imaging. The difference in impedance between air and biological tissue causes 99.9% reflection of the signal (Curry et al., 1990, p. 335). Thus if the difference in impedance of two media is small, attenuation can be sacrificed for better depth resolution since there should still be sufficient reflection of the signal for detection.

Since the average value for the speed of sound in human soft tissue is generally accepted to be 1540 m/s (Curry et al., 1990, p. 325), most ultrasound instruments are set to this value (Rickey, 1995, p. 47). However, the speed of sound in various tissues may vary widely. For instance, in fat and muscle sound travels at speeds of 1450 m/s and 1585 m/s respectively (Curry et al., 1990, p. 325). The speed of sound in the bovine aorta, which is likely comparable to that in any mammalian aorta, is slightly higher than the average value having been reported as 1570 m/s (Shung, 1985). To accurately measure the dimensions of a vessel using ultrasonic imaging, the speed of sound traveling through the medium between the transmitter and the tissue should be the same as the setting of the ultrasound instrument. Saline (0.9%) was chosen as the medium, since this will allow the tissue to maintain its physiological properties. At room
temperature, the speed of sound through saline is reported to be 1500 m/s (Wells, 1980, p. 381.). Thus there may be some distortion due to refraction, but the impedances are close enough that a high frequency transmitter can be used (10 MHz). The measurement error due to this difference is in table 3.1.

A solution of 8% glycerol in a 3% agar gel has an acoustic velocity of 1540 m/s (Rickey, 1995, p. 48.), and is thus a suitable transmitting medium for phantoms at Life Imaging Systems™. Thus the dimensional measurement errors when using saline solution as a transmitting medium were compared to those when using the glycerol solution. This was accomplished by imaging a three dimensional wire grid standardized so that the nodes are 1 cm apart along the three co-ordinate axes, and comparing the error in measurements between grids and a standard scale in the two media. If acoustic velocity of a medium differs from that to which the ultrasound machine is set, the error will increase with depth through the medium. Virtually all the measurements in the ultrasound images were between 1-2 cm vertical distance from the transmitter, as were the calibration measurements in table 3.1. The 4% error is assumed negligible, considering straight vertical measurements were avoided.

<table>
<thead>
<tr>
<th>medium</th>
<th>trial 1 [mm]</th>
<th>trial 2 [mm]</th>
<th>trial 3 [mm]</th>
<th>average error</th>
</tr>
</thead>
<tbody>
<tr>
<td>glycerol measured</td>
<td>10.0</td>
<td>10.0</td>
<td>10.1</td>
<td></td>
</tr>
<tr>
<td>standard</td>
<td>9.8</td>
<td>9.8</td>
<td>9.8</td>
<td></td>
</tr>
<tr>
<td>error</td>
<td>2%</td>
<td>2%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>saline measured</td>
<td>10.2</td>
<td>10.1</td>
<td>10.1</td>
<td></td>
</tr>
<tr>
<td>standard</td>
<td>9.8</td>
<td>9.8</td>
<td>9.7</td>
<td></td>
</tr>
<tr>
<td>error</td>
<td>4%</td>
<td>3%</td>
<td>4%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Table 3.1. Results of calibration of saline as a transmitting medium.
Ultrasound has been used clinically in recent years both to evaluate aortic distensibility (Pasierski et al., 1992), (Pearson et al., 1996) and to assess aortic dissections (Vignon et al., 1995). Transesophageal echocardiography (TEE) is used to obtain a B-mode image from the esophagus since the sternum will not allow absorption of the sound waves through to the aorta. The wall thickness is difficult to resolve because of the thick adventitial layer, consisting of loose connective tissue. However with the supplement of TM mode imaging, the medial + intimal thickness can be measured (Pearson et al., 1996) and the extensibility calculated based on these layers. TEE has also been evaluated as the best imaging mode for the evaluation of patients with aortic disruptions because of the accuracy, accessibility and safety of this method (Vignon et al., 1995).

3.2. Method

Simulated dissections were created in eight fresh porcine thoracic aortas as described in section 2.2. The aortas were cannulated, tethered to in vivo length and placed in a saline bath. An ATL™ Ultramark 9 Ultrasound machine, with its probe mounted vertically on a mechanical translator, captured a 3-D image of the region of the aorta with the dissection. A 10 MHz, 38 mm transmitter was used. There were 3 focal depths ranging between 2-3.5 cm. The resolution in the x-y plane of the two dimensional image was 0.1 mm. In the z direction, along which the translator moves, images were captured at 0.3 mm intervals. Linear PC©, an acquisition program designed by Life Imaging Systems™ (LIS) was used to compile the 3-D data. Successive images were captured at pressures of 100, 150, 200, 250 and 300 mmHg.
Various parameters were measured from the images using LIS Slicer® software, to be used for comparison to the model (fig. 3.1). The angles at both proximal and distal ends of the tear should, theoretically, be the same, but measurements were only taken to determine $\theta$ and $\phi$ at the proximal end.

![Diagram](image)

Figure 3.1. Parameters measured from ultrasound volume images. (For an explanation of symbols and equations, see text.) A) longitudinal section through symmetrical centre of dissection, indicating location of cross-sections B. and C.. B) circumferential cross-section proximal to dissection, C) circumferential cross-section at intimal tear of dissection. Intimal stubs at edges of intimal tear are visible.

**Diameter:** The diameter of the aorta, $d$, (fig. 3.1.B.) was measured proximal to the dissection (fig 3.1.A.) at pressures of 100, 200, and 300 mmHg.
- The diameter was measured from circumferential cross-sections of the volume image just proximal to the dissection.
- The measurement was taken horizontally across the diameter, from mid-wall to mid-wall.
- The same measurement was taken from 3 circumferential cross-sections incremented 1 mm apart longitudinally and the average taken.

**Thickness:** The thickness, $t$ (fig. 3.1.B.), of the intact wall proximal to the dissection and of the outer wall of the false lumen of the dissection, $t_0$ (fig. 3.1.C.), were calculated.

- From a circumferential section just proximal to the dissection, the area of the upper half of the wall ($a_1$) and half the circumference ($L$) were measured at pressures of 100, 200 and 300 mmHg.
- The thickness was calculated by dividing the area by the length. At 100 mmHg the thickness was averaged over the 8 aortas.
- From a circumferential section through the centre of the gaping intimal tear, the area ($a_2$) and arc length ($s$) of the outer wall of the false lumen were measured.
- This was repeated for 2 more sections, each approximately 1 mm apart.
- The thickness was calculated by dividing the area by the length and average over the 3 sections.

**Fraction of circumference dissected:** The maximum fraction, $K$ (fig. 3.1.C.), of the total circumference of the aorta that was dissected was measured in each of the 8 aortas with simulated dissections.

- The volume image of the dissection at 100 mmHg was sectioned through the centre of the gaping intimal tear.
- The diameter (d) and length of the intact wall (c) were measured. The length was divided by the diameter and pi.
- This fraction was subtracted from 1 to get K, the fraction dissected.

Angle $\theta$: The angle that the dissected wall makes with the intact wall at the longitudinal leading edge of the dissection, $\theta$ (fig. 3.1.A.), was not measured directly. The height of the dissected wall from the intact wall, b (fig. 3.1.A.), was measured and assumptions were made (section 3.4) to be used to derive the equation to calculate $\theta$ which is described in Chapter 5.

- The volume image was sectioned longitudinally through the axial centre of the dissection.
- The image was imported into Jandel Scientific’s Sigma Scan Pro Image Analysis version 3.00.030. The shape of the dissected segment was digitized.
- The height of the points in the middle of the dissected wall were averaged (seven points, approximately one third of all the points in the digitization), to determine b.
- The equation derived in section 5.1. is used to calculate $\theta$.

Angle $\phi$: The acute angle between the intimal flap and the intact wall, $\phi$ (fig. 3.1.A.), was measured.

- The volume image was sectioned longitudinally through the axial centre of the dissection
- A straight line was drawn in the same orientation as the intimal flap, originating at the proximal point of attachment of the flap to the intact wall. A triangle was made by joining the endpoints of the line to the distal point of attachment. The Slicer© software provides the lengths of the lines.
- The proximal angle was calculated knowing the length of the sides of the triangle using the cosine law.
- The measurement was done in three sections 1 mm apart in the axial centre of the tear.

3.3. Results

Tables 3.2 and 3.3 summarize the results of the measurements taken from ultrasound volume images of dissected aortas. Radius was the variable required for the calculations, and is presented in table 3.2. as half the measured diameter. The diameter was measured rather than the radius to minimize measurement error. Three measurements of diameter were taken proximal to the dissection. Because the taper from the location just proximal to the dissection to the location at the centre of the dissection is approximately 1%, the diameter at the two locations are assumed equal. There was little error in both the measurement of adjacent sections (average of ± 3% s.d.) as well as in measurements from one day to another (average of ± 2% s.d.). Average values for thickness of the intact wall at 100 mmHg and the fraction of circumference dissected were used in the calculations (table 3.3). The standard deviation in measurement from aorta to aorta was greater than the measurement error.
Table 3.2. Radius of intact vessel at various pressures. Diameter was measured proximal to dissection in ultrasound volume images.

<table>
<thead>
<tr>
<th>artery</th>
<th>radius (d/2)</th>
<th>± s.d. [mm]</th>
<th>100 mmHg</th>
<th>200 mmHg</th>
<th>300 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.03 ± 0.06</td>
<td></td>
<td>11.65 ± 0.05</td>
<td>12.15 ± 0.10</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>9.45 ± 0.05</td>
<td></td>
<td>10.52 ± 0.06</td>
<td>10.93 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9.87 ± 0.06</td>
<td></td>
<td>10.83 ± 0.14</td>
<td>11.40 ± 0.09</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>8.78 ± 0.12</td>
<td></td>
<td>9.75 ± 0.10</td>
<td>10.32 ± 0.14</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>9.25 ± 0.05</td>
<td></td>
<td>10.40 ± 0.10</td>
<td>10.88 ± 0.06</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>9.93 ± 0.08</td>
<td></td>
<td>10.20 ± 0.09</td>
<td>11.73 ± 0.06</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>9.07 ± 0.03</td>
<td></td>
<td>10.22 ± 0.03</td>
<td>10.75 ± 0.05</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>9.70 ± 0.10</td>
<td></td>
<td>10.72 ± 0.12</td>
<td>11.43 ± 0.06</td>
<td></td>
</tr>
</tbody>
</table>

Table 3.3. Thickness of intact and dissected wall and fraction of circumference dissected, at 100 mmHg. Intact wall thickness measured proximal to dissection, dissected wall thickness and fraction dissected measured in centre of tear, from ultrasound volume images.

<table>
<thead>
<tr>
<th>artery</th>
<th>thickness at</th>
<th>± s.d.</th>
<th>fraction of circumference dissected</th>
<th>100 mmHg [mm]</th>
<th>± s.d.</th>
<th>dissected</th>
<th>dissected (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>intact (t)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.73</td>
<td>0.69 ± 0.02</td>
<td>0.38</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.66</td>
<td>0.69 ± 0.00</td>
<td>0.40</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.89</td>
<td>0.76 ± 0.03</td>
<td>0.42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.68</td>
<td>0.91 ± 0.02</td>
<td>0.40</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.49</td>
<td>0.96 ± 0.02</td>
<td>0.47</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1.65</td>
<td>1.02 ± 0.00</td>
<td>0.44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.79</td>
<td>1.03 ± 0.01</td>
<td>0.42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1.62</td>
<td>1.07 ± 0.02</td>
<td>0.42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>avg s.d</td>
<td>1.7 ± 0.1</td>
<td></td>
<td>0.42 ± 0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3.4. summarizes the results in measuring the height of the distended outer wall of the false lumen from the intact wall. The value 'b' (fig. 3.1.) is used in calculating the upper angle \( \theta \). Because of the curved nature of the segment of the dissected wall approaching the point of attachment to the intact wall, the angle was very difficult to measure. Instead, the value 'b' was measured and used to calculate the angle. The equation used in the calculation is derived in section 5.1..

Table 3.4. Height of distended dissected wall from intact wall.

<table>
<thead>
<tr>
<th>artery</th>
<th>height 'b' [mm] ± s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 mmHg</td>
</tr>
<tr>
<td>1</td>
<td>2.96 ± 0.07</td>
</tr>
<tr>
<td>2</td>
<td>2.51 ± 0.10</td>
</tr>
<tr>
<td>3</td>
<td>2.27 ± 0.04</td>
</tr>
<tr>
<td>4</td>
<td>1.60 ± 0.03</td>
</tr>
<tr>
<td>5</td>
<td>1.42 ± 0.09</td>
</tr>
<tr>
<td>6</td>
<td>1.55 ± 0.04</td>
</tr>
<tr>
<td>7</td>
<td>1.37 ± 0.01</td>
</tr>
<tr>
<td>8</td>
<td>1.05 ± 0.09</td>
</tr>
</tbody>
</table>

Each of the values in table 3.4. is an average of 7 points in a digitization of the shape of the outer wall. These points were at approximately the maximum height of the wall. They were measured only in one planar cross-section. The plane was at the point in the false lumen where the wall was maximally distended.
Table 3.5. summarizes the measured values for angle $\phi$. Errors in this measurement are possible if the dissection twisted around the circumference of the aorta, so that the measurement was not at the centre of the leading edge. At low pressure (100 mmHg) the intimal flap was not always straight in the axial cross-section. In this case the angle at the point of attachment of the intimal flap to the intact wall was measured.

<table>
<thead>
<tr>
<th>artery</th>
<th>angle $\phi$ [degrees] ± s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 mmHg</td>
</tr>
<tr>
<td>1</td>
<td>23 ± 2</td>
</tr>
<tr>
<td>2</td>
<td>23 ± 3</td>
</tr>
<tr>
<td>3</td>
<td>27 ± 3</td>
</tr>
<tr>
<td>4</td>
<td>23 ± 1</td>
</tr>
<tr>
<td>5</td>
<td>28 ± 1</td>
</tr>
<tr>
<td>6</td>
<td>26 ± 1</td>
</tr>
<tr>
<td>7</td>
<td>25 ± 1</td>
</tr>
<tr>
<td>8</td>
<td>26 ± 1</td>
</tr>
</tbody>
</table>

Table 3.5. Measurement of acute angle between the intimal flap and intact wall.

3.4. Discussion

Four important assumptions were made based on the geometry of the dissections in the ultrasound images:

1) The area of the cross-section of the tissue at any location along the length of the aorta is constant with pressure.
Assumption (1) is made based on the fact that the tissue is incompressible (Carew et al., 1968). Because the vessel is tethered longitudinally, the product of the diameter and the wall thickness in a given circumferential cross-section should be equal to a constant area. The average change in area of the cross-section measured immediately proximal to the dissection was $+8\% \pm 5\%$ s.d., indicating that the artery expands with pressure, which is unlikely. As the wall becomes thinner, the measurement error increases due to limits in the resolution. For the most part, considering the average measurement error of thickness and diameter, $4 \pm 1\%$ s.d., the cross-sectional area can be assumed constant and the decrease in cross-sectional area due to tortuosity assumed negligible.

2) The distance between the centre of the edge of the intimal flap and the opposing intact wall, $d_c$, remains constant with pressure (fig. 3.2).

Because the pressure is the same in the true and false lumens, there is no transverse stress on the intimal flap (through the thickness of the segment). The intimal tear releases longitudinal stress by gaping open as the pressure is increased. Although all of the longitudinal stress will not be released, especially near the points of attachment of the intimal flap to the intact wall, at low pressures the edge of the intimal flap is assumed to be at its unpressurized length. The unpressurized length may not be the same as the zero load length of an intact segment of wall. As was mentioned in section 2.3.2, unpublished work done in our laboratory by Conan McIntyre revealed that approximately 5% compressive strain is released in the inner wall, if the plane of dissection is approximately mid-way through the wall.
Figure 3.2. Circumferential sections from ultrasound volume images indicating that distance $d_c$ remains constant with pressure. A) location in dissection sectioned. B) ultrasound images: 2 aortas at 3 different pressures. $d_{c1}$ remains constant in aorta 1 and $d_{c2}$ remains constant in aorta 2.
As the radius of the vessel increases, the radius of curvature of the intimal flap increases, changing the gradient of tensile forces through the flap. Eventually, when the radius of curvature approaches infinity, the entire flap will be in tension. Up to this point, the distance $d_c$ appears to remain constant (fig. 3.2.). When the entire flap is in tension, there will be a large radial stress concentration on the muscle cells at the leading edge and circumferential propagation may ensue.

3) The ends of the dissection have the shape of a spherical segment (fig 3.3. and 3.4.).

In order to accurately determine the upper angle $\theta$, the shape of the dissected wall as it approaches the leading edge has to be approximated. Unpublished studies with casts, by Chang-min He, a former Ph.D. candidate in our laboratory, revealed that when saline is injected into the media, the bleb first grows into a spherical bulge (circumferentially and longitudinally through the media) and then grows longitudinally. In my 3-D ultrasound images, the longitudinal leading edges viewed from above seemed to be semi-circular in shape (fig. 3.3.) because a bleb was made in the media to create the dissections. The edges of the distended wall when considered in longitudinal section through the axial centre, are assumed to be circular in shape (fig. 3.4.). There may be some error in this assumption due to the anisotropy of the aortic wall, however the images appeared to verify the approximation.
Figure 3.3. A longitudinal section of an ultrasound volume image (from above), showing the circular shape of the ends of the false lumen, $p = 100$ mmHg.

Figure 3.4. Longitudinal sections of ultrasound volume images through the centre of the dissection showing the assumed circular shape of the ends. A) pressure = 100 mmHg, B) pressure = 300 mmHg, $d_c$ assumed constant with pressure.
4) The radius of curvature of the intact portion of the wall that is continuous with the dissection is the same as it would be if there were no dissection in the wall.

In figure 3.5. are cross-sections of the aorta through the dissection in the x-y plane, at 7.5 mm increments through this plane. Rather than maintaining its circular shape, the lumen appears more elliptical in the middle of the dissection (fig. 3.5.C.). This geometry is also shown in 3.2 mm increments through the x-y plane (fig. 3.6.). The vessel walls are distended within the false lumen (fig. 3.6.A. and B.) but not in the intact wall (fig 3.6.C.).

Figure 3.5. Circumferential cross-sections through the dissection at 7.5 mm increments. All images are at 100 mmHg. The scale on the right of each image is in cm. A) proximal to the tear, the cross-section is circular, B) after the first increment, the cross-section deviates from circular, C) in the centre of the tear, the cross-section appears elliptical.
Figure 3.6. Longitudinal cross-sections from above, in 3.2 mm increments. All images are at 100 mmHg. The scale on the right is incomplete, but indicates a 1 cm distance. The walls of the false lumen distend from the proximal and distal intact wall (A. and B.), but the intact wall that is circumferentially continuous with the dissected wall does not (C.).

In order for the cylinder to be in equilibrium, there must be uniform tension around the circumference (where tension = pressure * radius). Therefore there must be some other force acting on the wall to prevent it from maintaining a circular shape. The fact that the edges of the intimal tear retract longitudinally in the y-z plane but the centre of the tear does not (fig 3.7.A. and B.) indicates the high longitudinal tension in the flap near the attachment points and the absence of longitudinal tension in the centre. The gradient of longitudinal stress will result in shear forces in the intimal flaps, and a radial component of stress. The magnitude of the radial component has not been quantified, but appears to create enough tension in the edges of the intimal flap to prevent radial expansion of the intact wall. Three millimeters through the y-z plane from the free edges of the intimal flap, the entire intimal flap appears to be in tension, and the walls of the false lumen are distended (fig 3.7.C.). The dissection will likely propagate circumferentially here first.
Figure 3.7. Cross-sections through the x-y and y-z planes indicating the gradient of longitudinal tension in the intimal flap. All images are at 100 mmHg. The sections are in 1.5 mm increments. A) release of longitudinal stress in the centre of the tear, B) buckling of the centre of the intimal flap indicates no longitudinal tension at this point, C) near the longitudinal ends of the tear the intimal flap is in constant tension.

An interesting observation is made, aside from the assumptions, that seems to contradict the second hypothesis. The angle $\theta$ decreases with pressure in some dissections (fig. 3.4). The theoretical model in Chapter 5 and the distensibility measurements in Chapter 4 will explain this finding.

The assumptions outlined here are considered in the development of the model in Chapter 5. However before the model can be developed, quantitative results are needed for the distention of the aortic wall. The same 3-D ultrasound technique is used.
CHAPTER 4: Distensibility Measurements

The change in geometry of the vessel wall is dependent on the change in luminal volume due to a change in pressure, or the distensibility. Distensibility can be described by the directional changes in the length of the vessel with pressure, or the extensibility in various directions. Stress vs. strain data was gathered using a novel 3-D ultrasound technique for both an intact wall and a wall with some of the inner layers peeled or ‘dissected’ away. First, theoretical considerations are described for calculating distensibility.

4.1. Introduction: Distensibility of the aorta

Since Roy’s discovery in 1880 that arteries become less distensible at high pressures, a number of methods have been used to evaluate the elastic properties of an artery. The aortic wall is non-homogeneous and thus the interaction of the various components, which have different elastic properties, will govern the overall distensibility of the aorta. Although the distensibility of arteries can not be described by a simple linear relationship, arteries can be treated as thin-walled cylinders to describe the stress in the walls when subjected to static luminal pressure (Dobrin and Doyle, 1970), (Carew et. al, 1968), (Tickner and Sacks, 1967). Distensibility is an important parameter in the model for an aortic dissection, and thus changes in wall structure that affect distensibility are important to the incidence of dissection propagation.

The derivation for stress in a thin-walled cylinder in the circumferential and longitudinal directions described here can be found in any basic mechanics text.
book, such as Muvdi and McNabb, 1984. The extensibility in the circumferential and longitudinal directions are derived by balancing the forces in each direction. Over a given area, the force due to the luminal pressure must be equal and opposite to the force due to stress in the wall of the vessel (fig. 4.1).

![Diagram of circumferential forces acting on a thin-walled cylinder](image)

Figure 4.1. Circumferential forces acting on a thin-walled cylinder. \( p \) = pressure \([\text{N/mm}^2]\), \( t \) = wall thickness \([\text{mm}]\), \( \ell \) = length \([\text{mm}]\), \( r \) = radius to middle of wall \([\text{mm}]\), \( \sigma_c \) = circumferential stress \([\text{N/mm}^2]\).

Because there is a gradient of pressure in the wall, the average pressure within it is considered to be \( p/2 \). Thus the area over which the force due to pressure is acting is equal to the shaded area in figure 4.1 which is \( 2r\ell \). The balance of forces is described algebraically as:

\[
p \cdot \ell \cdot 2r = \sigma_c \cdot 2 \cdot \ell \cdot t \quad (4.1)
\]

solving for \( \sigma_c \),

\[
\sigma_c = \frac{p \cdot r}{t} \quad (4.2)
\]

Similarly, an equation can be derived for stress in the longitudinal direction. If the forces in the longitudinal direction are balanced (fig. 4.2),
Figure 4.2. Longitudinal forces acting on a thin-walled cylinder. \( p \) = pressure \([\text{N/mm}^2]\), \( t \) = wall thickness [mm], \( r \) = radius to middle of wall [mm], \( \sigma_L \) = longitudinal stress \([\text{N/mm}^2]\).

The algebraic expression is:

\[
p \cdot \pi \cdot r^2 = \sigma_L \cdot 2 \cdot \pi \cdot r \cdot t
\]

Solving for \( \sigma_L \),

\[
\sigma_L = \frac{p \cdot r}{2 \cdot t}
\]

Equations 4.4 and 4.5 will be used to calculate stress in the circumferential and longitudinal directions respectively.
Extensibility is a measure of the extension of a material due to the application of force. The extension is described by strain. In the circumferential direction, the radius is directly proportional to the circumference, so the equation used for circumferential strain is:

\[ \varepsilon_C = \frac{r_i - r_{\text{original}}}{r_{\text{original}}} \]  \hspace{1cm} (4.6)

where:
- \( \varepsilon_C \) = circumferential strain
- \( r_i \) = radius at pressure \( i \) [mm]
- \( r_{\text{original}} \) = radius at starting pressure [mm]

and for longitudinal strain is:

\[ \varepsilon_L = \frac{l_i - l_{\text{original}}}{l_{\text{original}}} \]  \hspace{1cm} (4.7)

where:
- \( \varepsilon_L \) = longitudinal strain
- \( l_i \) = length at pressure \( i \) [mm]
- \( l_{\text{original}} \) = length at starting pressure [mm]

The slope of the stress vs. strain curve describes the elastic properties of the vessel. The elastic modulus for a linearly elastic material is expressed as:

\[ E = \frac{\sigma}{\varepsilon} \]  \hspace{1cm} (4.8.a)

An aortic wall is not linearly elastic as explained in section 1.4. However, the wall is often assumed to be linearly elastic in small increments of strain (Patel et
al., 1969), (Dobrin and Doyle, 1970). Thus for the aortic wall equation 4.8.a can be described for small increments in strain as:

\[ E_{nc} = \frac{\Delta \sigma}{\Delta \varepsilon} \]  

(4.8.b)

To get a more realistic picture of the elastic properties of the vessel wall, the relationship of stress to strain in three dimensions must be determined. When a volumetric unit of tissue is subject to a uniaxial load, the tissue will respond by extending along that axis. The tissue may also extend along the other two coordinate axes, the magnitude of which is determined by the nature of the material. The ratio of strain in one direction to strain in another when the material is subjected to a uniaxial force in the latter direction is referred to as Poisson's ratio. A material that is incompressible and isotropic (the elastic properties are the same in all directions) has a Poisson's ratio of 0.5 in all directions. If the coordinate system of an arterial wall is considered, (circumferential - C, longitudinal - L, and radial - R directions) the strain in the circumferential and longitudinal directions are related to uniaxial strain in the radial direction by the following expressions:

\[ \varepsilon_C = -\nu_{CR} \frac{\sigma_R}{E_R} \]  

(4.9a)

\[ \varepsilon_L = -\nu_{LR} \frac{\sigma_R}{E_R} \]  

(4.9b)

where: \( \varepsilon_C \) = strain in circumferential direction \( \varepsilon_L \) = strain in longitudinal direction \( \nu_{CR} \) = circumferential to radial Poisson's ratio \( \nu_{LR} \) = longitudinal to radial Poisson's ratio
\[ \sigma_R = \text{stress in the radial direction [N/mm}^2\text{]} \]
\[ E_R = \text{Young's modulus in the radial direction [N/mm}^2\text{]} \]

The aortic wall has a multi-component, specifically oriented structure and therefore cannot be considered homogeneous or isotropic. The relationship of stress to strain, or the Young's modulus, is different in every direction, i.e. the tissue is anisotropic. Although it has been reported by at least one group of investigators that the vessel wall is compressible (Tickner and Sacks, 1967), most agree with the studies done by others displaying its incompressibility (Carew et al., 1968). Air was used in the first study as the pressurizing medium, which is likely to dry out the tissue. To simplify computations, some investigators assume isotropic behaviour over incremental strains in the circumferential and radial directions at physiological pressures (Bergel, 1961a), (Tickner and Sacks, 1967), (Peterson et al., 1960), (Weizsacker and Pinto, 1988).

Before any such assumptions are made in this study, a unique equation is derived to determine the strain in a tethered vessel, which is slightly different than those described previously (Tickner and Sacks, 1967), (Patel et al., 1969), (Dobrin and Doyle, 1970).

The porcine aorta is tethered in vivo at 1.2 - 1.6 times its unpressurized length (Han and Fung, 1995). This stretch ratio increases along the length of the aorta from the aortic valve to the aorto-iliac bifurcation. From Han and Fung's results, in the porcine descending aorta the average stretch ratio is approximately 1.3, which is the same as the stretch ratio reported by Carew (Carew et al., 1968) in the canine thoracic aorta. Carew also reported that there was 40% longitudinal strain when the unconstrained vessel was pressurized to 180 mmHg. This is approximately 80 mmHg above diastolic and 30 mmHg above systolic pressure in the dog (Spector, 1956). If the non-linearity of the vessel is considered, it
seems reasonable that, as is assumed in the model in Chapter 5, the aorta is tethered in vivo to a length that is approximately equal to the length to which an unconstrained vessel will extend, if subjected to diastolic pressure.

The true elastic moduli can only be measured in an unconstrained vessel because the longitudinal tethering will impose a longitudinal tensile stress at low pressures and a longitudinal compressive stress at high pressures. The stress in the radial direction can be considered negligible (Dobrin and Doyle, 1970). In the unconstrained vessel, the strain in the circumferential direction will be:

\[
\varepsilon_{C,\text{ uncon}} = \frac{\sigma_C}{E_C} - \nu_{CL} \times \frac{\sigma_L}{E_L}
\]

where:
- \(\nu_{CL}\) = circumferential to longitudinal Poisson’s ratio
- \(\sigma_L\) = stress in the longitudinal direction [N/mm\(^2\)]
- \(E_L\) = Young’s modulus in the longitudinal direction [N/mm\(^2\)]
- \(\sigma_C\) = stress in the circumferential direction [N/mm\(^2\)]
- \(E_C\) = Young’s modulus in the circumferential direction [N/mm\(^2\)]

Both in vivo studies (on the canine thoracic aorta) (Patel et al., 1969) and in vitro studies (on the canine carotid artery) (Dobrin and Doyle, 1970) have provided evidence of some tortuosity in a tethered vessel. However, without the means of measuring the force exerted by tethering in this experiment, tortuosity was considered negligible. To test this assumption the modulus in the tethered vessels is compared to that in the unconstrained vessels. Considering equation 4.5, equation 4.10 can be rewritten in terms of the circumferential stress:
which can be reduced to:

\[ \varepsilon_{C,\text{uncon}} = \frac{\sigma_c}{E_c} - \nu_{cl} \cdot \frac{\sigma_c/2}{E_c} \cdot \frac{E_c}{E_L} \]  \hspace{1cm} (4.11)

If the circumferential strain is considered in a tethered aorta, the strain due to longitudinal stress will be countered by the strain due to tethering. Therefore the equation to describe strain in the tethered aorta is:

\[ \varepsilon_{C,\text{teth}} = \frac{\sigma_c}{E_c} \]  \hspace{1cm} (4.13)

The ratio of the circumferential strain in the tethered aorta (equation 4.13) to circumferential strain in an unconstrained aorta (equation 4.12) at pressure \( i \) can be calculated:

\[ \frac{\varepsilon_{C,\text{teth}}}{\varepsilon_{C,\text{uncon}}} = \frac{1}{1 - \nu_{cl} \cdot \frac{E_c}{2 \cdot E_L}} \]  \hspace{1cm} (4.14)

To solve equation 4.14, only one Poisson’s ratio is needed. In an incompressible material the sum of the Poisson’s ratios in two directions as a result of a force applied in the third, must equal 1, by definition. Poisson’s ratios were calculated in all directions in the canine thoracic aorta in vivo (Patel et al., 1969). These values were based on incremental strains in the range of physiological strain. The Poisson’s ratio needed in equation 4.14 was the same
in all the increments in which it was calculated, with a value of approximately 0.3. This value is probably valid for an intact porcine aorta, however there is no such data for the outer portion of the wall alone (a dissected wall). Because the structure of the adventitia is different than that of the media or intima, the relative proportions of the constituents, specifically the scleroproteins, will be different in the outer wall of a false lumen as compared to an intact wall. The range in Poisson's ratio in all directions in the canine thoracic aorta was 0.3-0.8 with an average of 0.5 in any two directions when force is applied in the third (Patel et al., 1969). Thus Poisson's ratio in equation 4.14, in the outer wall of the false lumen, is approximated as 0.5 for the development of the theoretical model in Chapter 5.

4.2. Ratio of longitudinal to circumferential modulus

The purpose of this part of the study is to compare the longitudinal modulus to the circumferential modulus in intact walls and dissected walls (the intima and part of the media have been removed) at pressures above 100 mmHg, so that equation 4.14. can be solved.

4.2.1. Method

Excess tissue was removed from sixteen fresh porcine aortas and the intercostal branches were ligated. The aortas were flipped inside out, and a bleb was created in the media in the same location as the simulated dissections, between the second and third intercostal branches. This time a cut was made through the intimal side of the bleb in the longitudinal direction. Small circumferential cuts were made at the ends of this tear, so that the inner layers of the dissection could be torn away around the circumference of the aorta (fig. 4.3).
Figure 4.3. A portion of the inner layers torn away around the circumference of the aorta.

The aortas were turned right side out, cannulated and placed in a saline bath. The aortas were not tethered, but were free to extend in the longitudinal direction when pressurized with saline. Two stick pins were placed in the section of the vessel where the layers were removed, 1.5 - 2 cm apart, to serve as reference points. The aortas were scanned with the ultrasound equipment described in section 3.2., at pressures of approximately 100, 150, 200, 250 and 300 mmHg. The diameter and thickness were measured at the insertion point of the distal pin. The distance between the two pins was measured at each pressure using LIS™ Slicer© software.

Three intact aortas were also imaged. The branches served as reference points to measure diameter in the circumferential cross-section, and the distance between the branches in the longitudinal cross section.

4.2.2 Results and Discussion

Because all of the vessels tested were of different thicknesses, they will be at different locations in the stress-strain curve when pressurized to 100 mmHg. Intuitively, stiffness should increase with a decrease in wall thickness. A linear relationship was in fact found, although there was wide variability (fig.4.4).
Figure 4.4. Relationship of wall thickness to the slope of stress vs. strain in the circumferential and longitudinal directions, beyond a pressure of 100 mmHg. n=16. A) circumferential modulus vs. wall thickness, B) circumferential modulus vs. tear depth, C) longitudinal modulus vs. wall thickness, D) longitudinal modulus vs. tear depth.

The relationship does not appear to be linear through all wall thicknesses in figures 4.4.A. and 4.4.B., indicating that if a small number of layers are removed from the intimal side, the modulus is approximated by that of the intact vessel. In figures 4.4.C. and D. the relationship could be considered linear through all wall thicknesses.
The objective was to get a ratio of the longitudinal modulus to circumferential modulus, but the effect of tear depth on this ratio was also considered by plotting the former against the latter. The results are in figure 4.5.

![Graph A](image1.png)  ![Graph B](image2.png)

**Figure 4.5.** The effect of A) wall thickness and B) tear depth, on the ratio of longitudinal to circumferential modulus, n=16.

The results were widely variable (fig. 4.5), with an average value $0.7 \pm 0.3$ s.d.. The use of ultrasound in measuring the longitudinal extensibility of a vessel is not very precise. The longitudinal strain in the range from 100-300 mmHg was between 0.05-0.1, which corresponded to an absolute change in length of 1-2 mm. Because images were captured in the longitudinal direction at 0.3 mm intervals, there is poor precision in the longitudinal measurements. Ultrasound is a useful tool to measure aortic diameter and wall thickness, but the longitudinal extension could be measured more precisely by another method. For instance various equally spaced markers could be placed on the adventitia and the distance between them measured with a ruler as the vessel is pressurized.

A second reason for the wide variability is the method of calculating an incremental modulus over a large increment of strain. It is a broad
approximation to assume that the tissue is linearly elastic between 100 mmHg and 300 mmHg. However, the experimental setup did not allow for measurements of very small strains, especially in the longitudinal direction, because of the low resolution.

If the stress vs strain curves in the Instron tensile tests (figs. 2.7 and 2.8) are compared for the adventitial layers, it appears as if the longitudinal adventitial strip is indeed more extensible than the circumferential adventitial strip. Thus it should be acceptable to use $0.7 \pm 0.3$ s.d. to calculate the correction factor to convert strain in an unconstrained aorta to strain in a tethered aorta (equation 4.14.). The final measurements needed to develop the model are those for plotting circumferential extensibility curves from 0 to 300 mmHg.

4.3. Circumferential extensibility from 0 - 300 mmHg

The stress vs. strain curve was considered to be comprised of two linear relationships between stress and strain, the first for pressures up to 100 mmHg and the second for pressures beyond 100 mmHg. Neither of these relationships is truly linear because the transition from elastin support to collagen support as the vessel undergoes increasing tension is not distinct. However the assumption was made for ease of calculations, and because the errors were considered acceptable due to the large variability in extensibility among aortas.

The stress-strain curve for an intact wall for pressures above 100 mmHg could be plotted from the values for the radius and thickness of the intact wall measured from the aortas with simulated dissections (table 3.2). The slope of the stress vs. strain curve in a longitudinally tethered artery does not represent the true elastic modulus, but is applicable in the model of an aortic dissection tethered to in vivo length. The modulus in a tethered aorta can also be derived
from the stress vs. strain data of an unconstrained aorta if equation 4.14 is applied. The purpose of this part of the study is to plot the relationship of circumferential stress to strain in an unconstrained aorta.

4.3.1. Method

Five fresh aortas were prepared for imaging as described in section 4.2.1. Layers were once again peeled away between the second and third intercostal branches. The same number of layers could not be removed each time because there was little control over the depth of the needle in the media. The aortas were imaged, unconstrained, at pressures of 0, 20, 40, 60, 80, 100, 150, 200, 250 and 300 mmHg.

After the aortas were imaged and removed from the mounting apparatus, more layers were removed from the media of three of them. A second bleb was created in the remaining layers of the dissected portion of the wall, and as before, the bleb was cut open and the inner layers peeled away. The aorta was pressurized and imaged in the same way. Once again, the data were used to plot a stress vs. strain curve. The diameter and thickness were measured in the dissected portion of the aorta as well as proximal to where the layers were removed, where the aorta was still intact. The cross-sectional images used for measurement were similar to those seen in figure 4.6.
Figure 4.6. Circumferential section from volume ultrasound images from which dimensions were measured to determine extensibility in intact and dissected portions of the wall. A) intact portion of wall at pressures of 20, 40 and 60 mmHg, B) dissected portion of wall (inner layers dissected away) of the same vessel, pressures of 20, 40 and 60 mmHg. The resolution in the x-y plane is 0.1 x 0.1 mm.
4.3.2. Results - intact aorta:

Figure 4.7 illustrates the extensibility of a tethered intact aorta above 100 mmHg. The error bars due to measurement error (table 3.2) were not included because the slopes for all aortas was averaged.

The assumption of linearity may lead to an under approximation of radius at lower stresses and an over approximation at higher stresses. The average slope of these aortas was 1.2 ± 0.1 s.d. N/mm². The slope of the most extensible aorta (star symbols in figure 4.7), was 3 standard deviations lower than the average of all slopes. Although it was borderline acceptable, this slope was not included in the average.

Figure 4.8 illustrates the results of the stress vs. strain curves for intact, unconstrained aortas.
Figure 4.8. Extensibility curves for unconstrained intact aortas. n = 5.

This curve is broken down into a linear relationship up to a pressure of 100 mmHg (fig. 4.9.A.) and a linear relationship beyond a pressure of 100 mmHg (fig. 4.9.B.):

Figure 4.9. Linear relationships for extensibility of unconstrained intact aortas. A) from 0 - 100 mmHg, n = 5, B) beyond 100 mmHg, n = 3.
The average slope of the lines in figure 4.9.A. is $0.28 \pm 0.07$ s.d. N/mm$^2$. The large standard deviation reflects the large biological variation in the data. The sample size is only three in figure 4.9.B. because, of the five aortas tested, two developed leaks at pressures beyond 200 mmHg. However the average slope from this figure is not needed for the model, but is useful to compare to the slope of the stress-strain curve in a tethered vessel. The average slope of the lines is $1.6 \pm 0.3$ N/mm$^2$, which is a significantly higher value than the slope of the stress-strain relationship of the tethered aortas ($1.2 \pm 0.1$ s.d. N/mm$^2$) because of the absence of longitudinal compressive stress as a result of the tethering.

Equation 4.14. can be applied to compare these two slopes. Poisson's ratio, which is needed to solve this equation is assumed to 0.3 for an intact wall based on studies described in literature (Patel et al., 1969):

$$\frac{\varepsilon_c, \text{tethered}}{\varepsilon_c, \text{unconstrained}} = \frac{1}{1 - 0.3 \times 1} = 1.25$$

If the standard deviation of the mean of longitudinal modulus / circumferential modulus is considered ($0.7 \pm 0.3$ s.d.), the ratio of tethered circumferential strain to unconstrained circumferential strain will be 1.2-1.6.

If the same stress that was calculated at each pressure in the unconstrained aorta is considered, but each strain is multiplied by the correction factor, 1.25, the moduli can be compared. Considering the error in the correction factor, the converted slope will be between 1.4 - 1.9 N/mm$^2$. Thus the calculated slope of the unconstrained aorta of $1.6 \pm 0.3$ N/mm$^2$ lies in this range.
4.3.3. Results - dissected aorta:

Figure 4.10 illustrates the results of the stress vs. strain curve over the entire range of pressure, between 0 - 300 mmHg for the dissected segments (those having some inner layers removed). These vessels are of a variety of thicknesses according to the number of layers peeled away. Because the thickness of the dissected portion of an aortic dissection will affect the amount of stress to which it is subjected, the thickness will also determine the stiffness. Comparing these curves from a stress corresponding to 100 mmHg as in figures 4.7. and 4.9.B, is not the same as comparing the curve of the outer wall of a false lumen from a stress corresponding to 100 mmHg because the geometries are different. The entire curve has to be considered to determine the extension in the dissected wall.

![Graph showing stress vs. strain for dissected aorta segments](image)

Figure 4.10. Extensibility of wall with a portion of the inner layers removed from 0 - 300 mmHg pressure.
4.3.4. Discussion:

For every point plotted in figures 4.7-4.10, stress was calculated assuming a thin-walled cylinder, which is defined as having a radius to wall thickness ratio of at least 10:1 (Muvdi and McNabb, 1984). An unpressurized aorta does not fit this criterion, as the ratio may be as low as 3.5:1. Nevertheless, the same equation was used in calculating stress in the intact wall. Because only the ratio of stress to strain at 100 mmHg is used in the model in Chapter 5, and not the individual points below 100 mmHg the calculation errors should not be significant. The values of stress used for the dissected wall are at a high enough pressure that the vessel can be assumed a thin-walled cylinder. The stress in an aorta that is assumed to be thick-walled is calculated in Appendix A, and compared to the stress in an aorta assumed to be thin-walled.

Because the distensibility of the vessel wall is dependent on elastin at low strains, the linear relationship in figure 4.9.A. roughly describes the elastic properties of elastin. Similarly, at high strains, the distensibility of the wall is dependent on the collagen, so the linear relationship in figure 4.9.B. roughly describes the elastic properties of the collagen.

If the two slopes were to be separated in figure 4.10 for each series of data points, the strain at which the inflection point occurs varies considerably. A difference in the amount of crimp in the collagen in these samples could cause such a variation. The thickness of the dissected wall did not correlate with the strain of the inflection point when all aortas were considered together, indicating a biological variability from aorta to aorta. However within each aorta, there did appear to be a trend as indicated in figure 4.11.
Figure 4.11. Extensibility data from 3 aortas (A-C) for the intact wall (intact), after first removal of layers (diss 1) and after second removal of layers (diss 2).
For each of the 3 aortas (fig. 4.11.A-C.), the wall became more extensible at low strains after the second removal of layers. Assuming that the elastic properties of the elastin are the same in every aorta, this suggests a later recruitment of collagen. The fact that the modulus of the dissected wall approaches that of the intact wall at high strains also suggests that the properties of the components are the same but there is less overlap in the supporting roles of the elastin and collagen in the dissected aortas. The total distensibility of the different aortas may vary widely, but the change in elastic properties when layers are removed is usually relative to the overall stiffness of the aorta.

The intact artery in 4.11.C. does not follow the same pattern as the other intact arteries. The artery appears to have the same extensibility when it is intact as it does when two sets of layers are removed. There is no apparent explanation for the different pattern in this aorta, except for biological variability among animals.

The aortas were not pre-conditioned prior to pressurization. Because arteries are viscoelastic, they exhibit some hysteresis if subjected to cyclic straining. In 1961, Bergel showed that the incremental circumferential modulus of a canine femoral artery as a function of radius did not change with conditioning (Bergel, 1961a). His second study in the same year showed that the muscle cells are primarily responsible for stress relaxation in arteries. The dynamic and static elastic moduli in the thoracic aorta were almost equal because it is an elastic artery (Bergel, 1961b). Thus hysteresis should have relatively little effect on the results. Predicting the strain at a particular stress, as is needed for the dissected walls, may result in some errors. However because of the large range in this strain (fig. 4.10), the measurement errors should not be significant.

With the quantitative extensibility data presented here, all of the measured variables required for the model are provided. The model can now be derived.
CHAPTER 5
Development of a theoretical model

The model was developed to predict the angles $\theta$ and $\phi$ at the longitudinal leading edge of a dissection (fig. 5.1.) as a function of tear depth (or thickness of the outer wall of the false lumen, assuming an average thickness of the intact wall of all aortas) and pressure.

\[
p_{FL} = p_{TL}
\]

Figure 5.1. A longitudinal section of an aortic dissection indicating the angles $\theta$ and $\phi$ that the model is to describe, based on pressure and the thickness of the outer wall of the false lumen ($t_D$). Under static conditions, the pressure in the false lumen ($P_{FL}$) is equal to the pressure in the true lumen ($P_{TL}$). The thickness of the outer wall of the false lumen is a measure of tear depth if the thickness of the intact wall of every aorta is considered to be the same.

The theoretical model was derived based on the dimensions of the simulated dissections, which are not necessarily of the same dimensions as those that are found clinically. The dissections were simulated by injecting saline into the media to create a bleb. The bleb grew radially outward to a maximum width, limited by the diameter of the wall. At this point the bleb maintained the shape of its circular ends, but grew longitudinally. Because all of the dissections were created in this way, the fraction of wall dissected was less than 50 % and was
relatively constant. Clinically, the fraction of the circumference of the wall dissected can vary, and is often greater than 50% (Williams et al., 1997), which will likely affect the shapes of the ends as well.

The specific equations used in this model are not meant to be directly applied to the clinical situation. Rather the equations can serve to model an early dissection. The model emphasizes the importance of wall distensibility on vessel geometry and so the geometry might be expected to vary with age and hypertension. The equations also provide an explanation for the effect of tear depth on pressure required for propagation. The explanations for the assumptions made in the model could be applied to dissections of other geometries.

Basic geometric and trigonometric principles were used to derive equations to estimate the angle at the longitudinal leading edge of a dissection. The angle that the outer wall of the false lumen makes with the intact wall, $\theta$, was calculated separately from the angle that the inner portion, or intimal flap, makes with the intact wall, $\phi$. Equations describing these angles are also derived separately.
5.1. Calculation of angle $\theta$

The spherical shape of the vessel wall at the ends of the false lumen as seen in the 3-D ultrasound images appeared to verify the approximation based on the shape of a bleb. There may be some error in this assumption, especially in a clinical application. For example a dissection may not necessarily progress as a bleb does during formation. Under such conditions, a similar approach could be used in this part of the model even if the dissection has a slightly different geometry. For instance the ends could be considered elliptical, and the appropriate equations derived. Because of the dependence of the angle at the longitudinal leading edge on $b$ (the height of the outer wall of the false lumen from the intact wall), even if a different geometry is assumed at the ends of the false lumen, pressure and tear depth should affect the angle in a similar way.

Based on the assumption that the geometry is spherical, the angle, $\theta$, that the dissected wall makes with the intact wall, can be derived from geometrical principles described in figure 5.2.
Figure 5.2. The shape of the leading edge of the false lumen. A) the semi-circular shape of the false lumen when viewed from above (fig. 3.3), $x =$ maximum width of false lumen, $d =$ diameter of intact vessel. B) the circular shape of the distended wall in longitudinal section through its axial centre (fig. 3.4.), $R =$ radius of curvature of segment, $b =$ height of dissected wall from intact. C) labeling of points of dimensions to be used in the derivation.

As seen in figures 5.2.B. and 5.2.C., line ‘no’ is a tangent to the curve of radius ‘$R$’. Angle $\theta$ is equal to $90^\circ - \angle \text{mli}$. Angle ‘mli’ is equal to $90^\circ - \angle \text{mil}$. Because $\angle \text{ki}j = \angle \text{ml}k$, (equivalent triangles), and $\angle \text{mil} = 2 \times \angle \text{ki}j$, it follows that $\angle \theta = 2 \times \angle \text{kl}m$. Therefore the equation used to calculate the angle $\theta$ is:
where:
- \( \theta \) = angle outer dissected wall makes with intact wall [degrees]
- \( b_i \) = maximum height of outer dissected wall from intact wall at pressure \( i \) [mm]
- \( x_i \) = maximum width of false lumen at pressure \( i \) [mm]

Both parameters \( b \) and \( x \) depend on the distensibility of the aortic wall. Equations will be derived to predict these values at various pressures.

5.1.1. Calculation of width of false lumen, \( x \)

The parameter \( x \) is a function of the radius, \( r_i \). The radius at 100 mmHg was measured and the thickness of the wall at 100 mmHg was the average value of 1.7±0.1 s.d. mm, from table 3.3. The radii at pressures of 200 and 300 mmHg were predicted assuming that the aorta is a thin-walled cylinder. The circumferential stress can then be calculated using equation 4.2.

The longitudinal strain is considered minimal beyond diastolic pressure because the vessel is tethered. Most of the vessels had some curvature and so at high pressures they could become tortuous. However the amount of longitudinal strain that resulted from tortuosity was considered negligible relative to the radial and circumferential strain. Thus knowing that the tissue is incompressible, the thickness at pressure \( i \) when the radius is \( r_i \) can be evaluated:

\[
t_i = t_{100} \frac{r_{100}}{r_i} \tag{5.2}
\]
Considering strain beyond 100 mmHg:

\[ \varepsilon = \frac{r_i - r_{100}}{r_{100}} \]  \hspace{1cm} (5.3)

and the relationship:

\[ E_m = \frac{(\sigma_i - \sigma_{100})}{\varepsilon_i} \]  \hspace{1cm} (5.4)

where \( E_m \) [N/mm²] is the circumferential modulus for the intact wall, modified for pressures beyond 100 mmHg where the relationship is assumed roughly linear. The value was calculated in section 4.3.2. The radius at pressure \( i \) can then be approximated by:

\[ r_i = r_{100} \sqrt{1 + \frac{t_i}{E_m t_{100}} \frac{r_{100}}{r_{i}}} \]  \hspace{1cm} (5.5)

To calculate \( x \), the maximum distance between circumferential leading edges through the cross-section, \( r_i \) and \( K \), the fraction of wall dissected (table 3.3.) are needed:

\[ x_i = 2r_i \sin(K \pi) \]  \hspace{1cm} (5.6)

In every case, \( r_i > x_i/2 \).
5.1.2. Calculation of height of dissected wall, \( b \)

The equation for \( b \) is formulated based on assumption 4 in section 3.4., which states that the radius of curvature of the intact portion of the wall that is continuous with the dissection is the same as if there was no dissection in the wall. Thus, the overall equation to calculate \( b \) is:

\[
b_i = \frac{s_i - \pi \cdot \frac{x_l}{2} + \sqrt{r_i^2 - \left(\frac{x_l}{2}\right)^2} \cdot \frac{x_l}{2} - r_i}{2}
\]  

(5.7)

where:
- \( s_i \) = max. circumferential length of dissected wall at pressure \( i \) [mm]
- \( x_l \) = max. width of the false lumen at pressure \( i \), a function of \( r_i \) [mm]
- \( r_i \) = radius of intact portion of wall at pressure \( i \) [mm].

Figure 5.3. schematically breaks down the 4 components of this equation.
Figure 5.3. Schematic description of equation 5.7. A) $A = \frac{s_i - \pi \times x_i/2}{2}$. This value can be either positive or negative. B) $B = \sqrt{r_i^2 - (x_i/2)^2}$. C) Dimensions of the 4 components of equation 5.7., $b = A + B + x_i/2 - r_i$.

The equation used to calculate distance $A$, is actually describing a very small arc length. Because the length of the arc is very small compared to its radius of curvature, the equation can be used to approximate the straight line distance $A$. 
The parameter $s$ is the only unknown in this equation. A different method is required to calculate $s_i$ when $i = 100$ mmHg than when $i > 100$ mmHg. The method to determine $s_{100}$ is described first.

- $s_{100}$ (maximum arc length of outer wall of false lumen in circumferential cross-section at 100 mmHg):

The general equation describing $s_{100}$ is:

$$s_{100} = \varepsilon_{D100} \cdot s_o + s_o$$  \hspace{1cm} (5.8)

where:
- $\varepsilon_{D100} = $ circumferential strain in outer wall of dissection between 0-100 mmHg.
- $s_o = $ arc length of dissected wall in unpressurized aorta [mm]

Both of these parameters have to be determined.

- $s_o$ (maximum arc length of outer wall of false lumen in circumferential cross-section at 0 mmHg):

The general equation to solve for $s_o$ is:

$$s_o = \left( r_o + \left( t_o - \frac{t_{D100}}{t_{100}} \cdot \left[ \frac{t_{D0} \cdot t_{100} }{t_o \cdot t_{D100} } \right] \right) \right) \cdot \frac{1}{2} \cdot 2 \cdot \pi \cdot K$$  \hspace{1cm} (5.9)

where:
- $t_{Di} = $ thickness of dissected portion of the wall at $i$ mmHg [mm]
- $t_i = $ thickness of intact wall at $i$ mmHg [mm]
- $r_o = $ radius of intact vessel at 0 mmHg [mm]
\[ K = \text{fraction of circumference dissected} \]

The value in square brackets is a correction factor, which is needed because the thickness of the dissected wall expressed as a fraction of total wall thickness is different at 0 mmHg and 100 mmHg. The thickness of the dissected wall can be measured at 100 mmHg, but must be calculated at 0 mmHg using the correction factor, the average thickness of the intact wall at 0 mmHg and the average thickness of the intact wall at 100 mmHg. The average unpressurized thickness of the intact wall \( t_0 \) of the five aortas used in section 4.3 was 2.3 ± 0.3 s.d. mm, the average thickness of an intact aorta pressurized to 100 mmHg \( (t_{100}) \) is 1.7±0.1 s.d. mm (table 3.3), and the correction factor averaged over the 5 dissected aortas used in section 4.3 was 1.14 ± 0.08 s.d. The value in round brackets in equation 5.9 is the difference in diameter of an unpressurized intact artery and an unpressurized dissected artery.

All thicknesses were measured in the upper half of the circumference of the vessels to eliminate errors due to the difference in acoustic velocity in the tissue and the saline. However because the ultrasound images indicated the aorta is slightly thinner on the posterior side, the thickness may be slightly over approximated.

The parameter K from table 3.3. can be used in equation 5.9., but the radius \( r_0 \) must be calculated.

\[ r_0 \quad \text{(radius of the unpressurized intact aorta):} \]

The radius of the unpressurized aorta is calculated assuming a linear relationship between stress and strain below a pressure of 100 mmHg (fig. 4.9.A.). The average slope of the curves in figure
4.9.A. is $0.28 \pm 0.07 \text{ s.d. [N/mm}^2\text{]}. \text{ Therefore the unpressurized radius is:}

$$r_0 = \frac{r_{100}}{1 + \frac{\rho_{100} \cdot r_{100}}{t_{100} \cdot 0.28}}$$

(5.10)

All the variables in equation 5.9 are now known, so $s_a$ can be calculated. The second parameter to calculate in equation 5.8 is $\varepsilon_{D100}$.

- $\varepsilon_{D100}$ (circumferential strain in the outer wall of the dissection between 0-100 mmHg):

The strain $\varepsilon_{D100}$, which is also needed to solve equation 5.8, is a function of the stress acting on the wall, $\sigma_0$. The relationship between stress and strain in the range of stress of interest is assumed linear. The stress varies according to the thickness of the dissected wall. Thus the general equation to describe the strain in the dissected wall at 100 mmHg is:

$$\varepsilon_{D100} = \frac{\sigma_{D100} + \text{intercept}}{\text{slope}}$$

(5.11)

where:

$$\sigma_{D100} = \text{stress in outer wall of dissection at 100 mmHg [N/mm}^2\text{].}$$

An equation must be derived to determine this stress as a function of radius and wall thickness.
- \( \sigma_{D100} \) (stress in outer wall of dissection at 100 mmHg):

The images indicated that the radius of curvature of the dissected portion can be approximated by the radius of the intact vessel. Therefore \( \sigma_0 \) can be calculated when \( i = 100 \) mmHg:

\[
\sigma_{D100} = \frac{P_{100} \cdot r_{100}}{t_{D100}} \tag{5.12}
\]

The average stress in the eight aortas with dissections was 0.15 \( \pm \) 0.03 s.d. N/mm\(^2\) with a range between approximately 0.1-0.2 N/mm\(^2\). The extensibility data for a wall with a portion of the inner layers removed, in figure 4.10, can be used to approximate the strain in this range of stress (fig. 5.4.). For each aorta tested, the slope of the relationship was determined, from which the strain at a stress of 0.1 N/mm\(^2\) could be calculated. The average of the slopes was 1.46 \( \pm \) 0.62 s.d. N/mm\(^2\) and the average strain at 0.1 N/mm\(^2\) was 0.32 \( \pm \) 0.08 s.d.. From the strain and the slope, the intercept was calculated to be 0.37 N/mm\(^2\) with a minimum value of 0.10 N/mm\(^2\) and a maximum of 0.74 N/mm\(^2\).
Figure 5.4. Extensibility of the aortic wall with a portion of the inner layers removed in the range of stress corresponding to the stress on the outer wall of an aortic dissection at 100 mmHg.

Knowing the intercept and slope, $\sigma_{D100}$ in equation 5.12 can be solved. Knowing $\sigma_{D100}$, $\varepsilon_{D100}$ in equation 5.11 can be solved.

Now that $s_0$ and $\varepsilon_{D100}$ have been calculated, the values can be substituted into equation 5.8 to solve for $s_{100}$. $x_{100}$ from equation 5.6 and $s_{100}$ can be substituted into equation 5.7 along with the measured value for $r_{100}$ to solve for $b_{100}$.

The values for $b_{200}$ and $b_{300}$ are calculated in a similar way. A modification of equation 5.8 is used to determine $s$ at pressures beyond 100 mmHg.

$\text{s}_i$ (maximum arc length of outer wall of false lumen in circumferential cross-section at $i$ mmHg, if $i > 100$):

The general equation required to calculate the length of the dissected wall at pressure $i$ is:
\[ S_i = \varepsilon_{Di} \cdot s_{100} + s_{100} \]  \hspace{1cm} (5.13)

where:
- \( \varepsilon_{Di} \) = circumferential strain in outer wall of dissection if original radius is \( r_{100} \).
- \( s_{100} \) = circumferential length of outer wall of dissected wall at 100 mmHg [mm].

The length of the dissected segment at 100 mmHg has already been calculated. The strain \( \varepsilon_{Di} \) has to be calculated.

- \( \varepsilon_{Di} \) (circumferential strain in the outer wall of the dissection if the original radius is \( r_{100} \)).

The general equation used to calculate \( \varepsilon_{Di} \) is:

\[ \varepsilon_{Di} = \frac{(\sigma_{Di} - \sigma_{D100})}{E_{mD}} \]  \hspace{1cm} (5.14)

where:
- \( \sigma_{Di} \) = stress in the dissected wall at pressure \( i \) [N/mm²]
- \( E_{mD} \) = circumferential modulus for outer wall of dissection, modified for pressures beyond 100 mmHg [N/mm²].

The radius of curvature of the dissected portion of the wall was once again considered to be the same as that in the intact wall, so equation 5.11 could be applied to find the stress at pressure \( i \). The modified circumferential modulus, \( E_{mD} \), must be determined.
- $E_{mD}$ (circumferential modulus for outer wall of dissection, modified for pressures beyond 100 mmHg):

The modulus $E_{mD}$, is the slope of the circumferential stress-strain curve of a dissected wall, such as those used to plot the points in figure 4.10, beyond the strain and stress in the outer wall of an aortic dissection at a pressure of 100 mmHg. The stress at 100 mmHg, as stated above, is approximately 0.15 N/mm$^2$. The points in figure 4.10 that corresponded to stresses approximately equal to and above this value were considered. The strain was recalculated for each point assuming an initial radius equal to the radius corresponding to the first point, and the points were re-plotted (fig. 5.5.). The slope of these lines could be correlated with wall thickness as is apparent in figure 5.6. This is an important finding as it has not been reported previously. The equation relating this modified modulus, $E_{mD}$, to wall thickness is then:

$$E_{mD} = -7.6 \cdot t_{D,100} + 12.8 \quad (5.15)$$
Figure 5.5. Relationship of stress to strain above a pressure of 100 mmHg in an unconstrained vessel.

Figure 5.6. Relationship of modulus above 100 mmHg to fractional tear depth from intima, where $y = -7.6x + 12.8$, $p = 0.024$.

The slope in figure 5.6 is less than the slope in figure 4.4.A. because the moduli in 4.4.A. were calculated from an initial strain and stress of the wall at 100 mmHg if the layers are dissected around the entire circumference, while the moduli in figure 5.6. are
calculated from an initial strain and stress at 100 mmHg of the outer wall the false lumen in an aortic dissection. The radius of curvature is smaller in the latter case.

The strain at pressure $i$, $\varepsilon_{Di}$, can now be calculated knowing the stress and modulus. This is the strain in an unconstrained aorta, but the aortas with the simulated dissections are tethered longitudinally. Therefore equation 4.14. can be applied, remembering the ratio $E_D/E_L = 0.7 \pm 0.3$ s.d., and assuming an average value of Poisson's ratio of 0.5:

$$\frac{\varepsilon_{D,tethered}}{\varepsilon_{D,unconstrained}} = \frac{1}{1 - 0.5 \times \frac{1}{2 \times 0.7}} = 1.54$$

Thus strain in the dissected portion of the vessel can be calculated with equation 5.14., and multiplied by the constant 1.54 to convert circumferential strain in an unconstrained vessel to that in a tethered vessel. The circumferential length of the outer wall of the dissection, $s_i$, can be calculated for pressures greater than 100 mmHg using equation 5.13:

Substituting $s_i$ and $x_i$ into equation 5.7, $b_i$ can be calculated for $i > 100$ mmHg. Finally $\theta$ can be calculated by substituting $x_i$ and $b_i$ into equation 5.1.

5.2. Calculation of angle $\phi$

The overall equation used to describe the lower angle $\phi$ (fig. 5.7.), is:

$$\phi = \tan^{-1}\left(\frac{2 \cdot r_i - d_i}{a}\right)$$

(5.16)

where:
- $\phi$ = acute angle between intimal flap and intact wall [degrees]
- $d_c$ = height of intimal flap from opposing intact wall [mm] (fig. 3.3)
- $a$ = a function of the length of the dissection [mm]

![Diagram of parameters](image)

**Figure 5.7.** Parameters needed to calculate angle $\phi$.

The theoretical value for $r_i$ can be calculated using equations 5.5. The parameters $d_c$ and $a$ must be calculated.

### 5.2.1. Calculation of height of intimal flap from intact wall, $d_c$

In the simulated dissections, the height $d_c$ remained relatively constant, so the change in $d_c$ with pressure was assumed negligible. The theoretical basis for the negligible change in $d_c$ is in Appendix B. Although the equation that describes the height $b$ assumes a radial component of tension in the intimal flap (section 3.4.), figure 3.8.B. also demonstrated the lack of tension in the middle of the flap. The strain in this segment as seen in the $x$-$y$ plane close to the intimal tear is therefore assumed negligible. Thus as the aortic radius increases, the segment $s_{inner}$ will straighten out (fig. 5.8.). Eventually when the segment has straightened, the entire segment will be subject to tensile forces. $d_c$ can be
calculated when the vessel has distended to this radius, if the length of the inner dissected segment, $s_{\text{inner}}$, is known.

![Diagram of vessel dimensions](image)

Figure 5.8. Definition of distance $d_c$ and vessel dimensions on which it is dependent

As was stated in section 2.3., the inner portion of an unpressurized dissected wall has a residual strain of approximately -5%, i.e. before the dissection is made this portion of the wall is under compression. Therefore to calculate the length of the inner segment $s_{\text{inner}}$, the residual strain has to be considered. Therefore the equation describing the length of the inner wall when it is under neither tension nor compression is:

$$ s_{\text{inner}} = 2 \cdot \pi \cdot K \cdot r_0 \cdot 1.05 \quad (5.17) $$

The segment $s_{\text{inner}}$ is in tension when it becomes straight. Therefore the radius of the intact aorta that is required to apply tension to the segment, $r_t$, can be calculated:
Finally, $d_c$ can be calculated when $r = r_1$:

$$d_c = r_1 + \sqrt{r_1^2 - (s_{inner}/2)^2} \quad (5.19)$$

5.2.2. Calculation of longitudinal length of the intimal flaps, $a$

The constant $a$ is a function of the length of the dissection. The length of the intimal flaps at the axial centre of the tear are calculated knowing that the aorta is tethered at approximately 130% of the unpressurized length (Han and Fung, 1995). At a pressure of 100 mmHg, the intimal flaps are assumed to retract to their original length with the creation of an intimal tear. The validity of this assumption depends on the width of the intimal tear. In the simulated dissections, the intimal tear always extended across the width of the dissection, and in most cases the ends of the intimal tear buckled indicating an absence of longitudinal tension (fig. 3.8.). If a dissection with a shorter intimal tear is pressurized, the tear usually continues across to the width of the dissection before propagation, so it is appropriate to design the simulated dissections with an intimal tear that extends across the width of the dissection, and the axial centre of the intimal flaps should not be stressed longitudinally.

Considering figure 5.7., at a pressure of 100 mmHg, parameter $a$ can be calculated:

$$a = \sqrt{\left(\frac{1}{2} \cdot \frac{L}{1.30}\right)^2 - \left(2 \cdot r_{100} - d_c\right)^2} \quad (5.20)$$
where:
- $L$ = longitudinal length of dissection [mm]
- the first term in the square root is the average length of the intimal flaps assuming the intimal tear is in the middle of its longitudinal length.

5.3. Comparison of measured to theoretical values.

The success of the model was assessed by comparing the theoretical angles to the measured ones. Application of the model served to describe trends in the change in geometry of a dissected vessel with pressure.

5.3.1. Angle $\theta$: Results and Discussion

The theoretical value of $\theta$ was calculated using equation (5.1), substituting in the calculated values for $x$ and $b$. For comparison, a 'measured' angle $\theta$ is determined by substituting the measured values for $r$ (table 3.2) and $b$ (table 3.5) into equation 5.1. First the measured and theoretical values of the radius are compared (fig. 5.9). Labeled on the x-axis is the thickness of the dissected wall at 100 mmHg. The tear depth has no bearing on the radius of the intact wall, but is indicated for consistency with the presentation of the rest of the results.

The relationship between stress and strain is assumed linear in calculating $r_i$ knowing $r_{100}$. Therefore the radius will be under-estimated at lower pressures (fig. 5.9.A.) and over-estimated at higher pressures (fig. 5.9.B.). The theoretical and measured values are relatively close since the slope of the stress-strain curve was based on dimensions measured from the dissected aortas themselves.
The comparison of measured to theoretical values of b are in figure 5.10. The large error bars in the theoretical values at a pressure of 100 mmHg are due to the variation in the slope of the stress strain curve from 0 to 100 mmHg. The error bars at 200 and 300 mmHg are due to the variation in strain in the dissected wall at a pressure of 100 mmHg. This error increases with pressure.

As was expected, there was an obvious trend in distention of the dissected wall with dissected wall thickness, which supports the first hypothesis. There was
also a general trend of a decrease in $b$ with pressure which appears to contradict the second hypothesis, which states that the angle at the leading edge of the dissection will increase with pressure. In some instances the value $b$ increased at 200 mmHg and then decreased at 300 mmHg. This is because of the non-linear nature of the stress-strain curve. The intact wall may be at a high enough strain that the collagen is determining the extensibility, while in the dissected wall the collagen may still be crimped. Because the stress-strain relationship was assumed linear, the model predicted a decrease in $b$ with pressure for each dissection. Nevertheless, in most cases the measured value fell within the error of the predicted value. The value for $b$ in artery 1 is poorly predicted because the dissection in this artery started to propagate at 200 mmHg. The model only describes the false lumen before propagation ensues.

The fact that the parameter $b$ usually decreases with pressure could be an important finding, indicating that the tear depth of the dissection may be a more important factor in the incidence of propagation than high pressure in the lumen.

Figure 5.11. shows the results of the angle $\theta$ based on the measured $r$ and $b$ compared to the theoretically calculated $r$ and $b$. The measured values are not direct measurements of the angle from the ultrasound image, but are based on measured dimensions that were used to calculate the angle assuming the shape was spherical. If the dissection does not remain between adjacent layers, non-uniform distention of the outer wall could cause deviation from a spherical shape as could the anisotropy of the tissue, which could lead to errors. The trends in figure 5.11. are very similar to those seen in figure 5.10., since there is little error in the calculation of radius.
Figure 5.10. Effect of pressure and wall thickness on height $b$. The calculated error bars are a result of the standard deviation based on the measurement error of the circumferential modulus, and the standard deviation of the ratio of longitudinal modulus to circumferential modulus. The measured error bars are standard deviations. There is no significant difference between the measured and calculated values, with the exception of artery 1.
Figure 5.11. Results for prediction of angle $\theta$. The error bars are a result of the errors in figures 5.9. and 5.10. There is no significant difference between the measured and calculated values.
5.3.2. Angle $\phi$: Results and Discussion

The measured values for the angle $\phi$ were compared to the theoretical values which were calculated with equation 5.16 (fig. 5.12). The results indicate that there is no trend in the angle $\phi$ with the thickness of the dissected segment. In fact, the predicted values are almost the same for every aorta. Differences are associated with differences in aortic diameter and tear length, indicating the angle $\phi$ can likely be predicted by assuming an average radius and tear length.

The theoretical model does not effectively predict the angle at 300 mmHg because the model assumes that the segment $S_{\text{inner}}$ will eventually straighten. This segment may not straighten completely before propagation because of the tension in the muscle cells at the points of attachment. The muscle cells could fail in tension before the segment completely straightens, leading to propagation.

In most cases, the angle $\phi$ increased as the pressure increases to a greater extent than angle $\theta$ decreased (fig. 5.10), which is why although the angle $\theta$ is usually greatest at 100 or 200 mmHg, propagation does not occur until the luminal pressure is increased beyond this. Considering this finding, the second hypothesis is actually proven correct.

Conclusion: The model presented appears to predict the change in geometry of the false lumen with pressure. The applicability of this model to the clinical situation is described in the conclusions in the next chapter.
Figure 5.12. Results for prediction of angle $\phi$. The error bars of the calculated values are a result of the error in predicting the initial radius of the unpressurized aorta (fig. 4.9.A.), and in predicting the radius at pressure $i$ (fig. 5.9.). There is no significant difference between the measured and calculated values with the exception of artery 4 at $p = 300$ mmHg.
CHAPTER 6
Conclusions and Direction for Further Study

If the results of the two angles $\phi$ and $\theta$ are considered together, the overall error in the prediction of the angle at the leading edge is in the range of $\pm 17$ degrees. This will not allow for precise predictions of the false lumen geometry, however this is to be expected due to biological variability. The error due to biological variability combined with the variability in the shape of a false lumen makes it difficult to predict the response of every aortic dissection to pressure. However my model served to supply some important information about the propagation of a dissection.

6.1. Conclusions

1) The change in angle $\phi$ with pressure was the same for all simulated dissections.

The independence of angle $\phi$ is an important finding, because if $\phi$ is predictable, only the distention of the outer wall need be measured. The angle $\phi$ is dependent on the fraction of the circumference that is torn and the equations used to calculate $\phi$ assume the fraction is less than 0.5. The equations would have to modified if the fraction was greater than 0.5.

2) The change in the angle $\theta$ illustrates the non-linearity of the distention of the vessel wall.
The fact that $\theta$ decreases with pressure was not an expected result, but is a good indicator of the non-linearity of the vessel distensibility. The distended wall is under higher stress than the intact wall and is therefore stiffer. Because the strain of the intact wall will be greater than that of the dissected wall, the distance that the dissected wall distends from the intact wall should decrease with pressure. If the tear were to extend more than 50% of the way around the circumference, perhaps there would no longer be tension in the intimal flap. The outer wall of the false lumen could then be free to extend circumferentially so that there is uniform tension around the circumference. However a dissection that is torn less than 50% of the way around the circumference is more representative of an early dissection.

3) The slope of the stress-strain relationship above 100 mmHg in the dissected portion of the wall is proportional to tear depth.

If the same luminal pressure is considered for a thin wall and a thick wall, the thin wall would be expected to be at steeper location in the stress strain curve, and therefore should be stiffer. However in figures 5.9. and 5.10. there is a significant difference in the stiffness of the vessel, even if the arteries are at the same point along the stress strain curve, suggesting that perhaps even at high stress elastin is still supporting the wall. The adventitia has a greater proportion of collagen as compared to elastin, so this wall will be stiffer.

4) The intimal flap plays an important role in the onset of propagation.
The description of the behaviour of the inner wall of the false lumen is important in the understanding of dissection propagation. Tension in the intimal flap will provide tensile and shear forces to the muscle cells in both the longitudinal and circumferential directions. In the static pressure model, the intimal flap is not subjected to transverse stress (between the true and false lumens). This means that at the edge of the intimal tear the flap will be close to a zero stress state at low pressures, if the longitudinal stress at the points of attachment is not considered. The pressure required to increase the radius to a point at which the intimal flap is in tension is a good indication of the pressure that is required for propagation.

6.2. Directions for Further Study

The results of this study suggest a number of interesting questions:

1) What are the elastic properties of the inner part of the media, including the intima?

Surprisingly, in the Instron study, the strip of tissue that was removed from the middle of the media exhibited different elastic properties in the circumferential direction than the media + intima strip. The media did not stiffen to the extent of either the strip that included the intima nor the strip that included the adventitia. Also the strip that had media + intima stiffened at a much at higher strain in the circumferential direction than in the longitudinal direction. These are interesting findings that to my knowledge have not been described in literature.

2) What are Poisson's ratios in a dissected wall and how do they differ from those in an intact wall?
Poisson's ratio that describes strain in the circumferential direction when subjected to stress in the longitudinal direction was approximated as 0.5. This was an average value that was chosen since the vessel is assumed to be incompressible and the ratio must lie between 0-1. A value of 0.5 fit the data rather well, so it would be interesting to determine what the actual value for this ratio is.

3) Clinically, what geometries might an aortic dissection exhibit prior to propagation?

This shape of the false lumen was controlled by bleb propagation. The model was developed based on this shape. Models could be developed for false lumens of different shapes.

4) Now that the effects of static pressure have been investigated, how will the false lumen geometry be affected by pulsatile pressure?

The most obvious next step in studying aortic dissections would be to apply pulsatile pressure. Obviously static pressure alone can cause a dissection to propagate, but the propagation pressure could be lowered if the pressure is pulsatile. The fraction of wall dissected will be an important factor if pulsatile pressure is considered. A long intimal flap could occlude the vessel and cause a proximal pressure increase, leading to propagation.

This study is merely a beginning in the understanding of the mechanics of an aortic dissection. There are still many questions to be answered, but this study was successful in outlining some of the important factors to consider.
Appendix A

Stress in a Thick-Walled Cylinder

A thin-walled cylinder is defined as one in which the ratio of radius to wall thickness is at least 10:1. This is not the case for the aorta at low pressure. Table A.1 indicates this ratio as a function of pressure for an intact wall and a dissected wall:

<table>
<thead>
<tr>
<th>pressure [mmHg]</th>
<th>t/r intact</th>
<th>t/r dissected 1</th>
<th>t/r dissected 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>0.33</td>
<td>0.23</td>
<td>0.18</td>
</tr>
<tr>
<td>21</td>
<td>0.33</td>
<td>0.18</td>
<td>0.13</td>
</tr>
<tr>
<td>43</td>
<td>0.31</td>
<td>0.17</td>
<td>0.08</td>
</tr>
<tr>
<td>64</td>
<td>0.25</td>
<td>0.13</td>
<td>0.07</td>
</tr>
<tr>
<td>107</td>
<td>0.20</td>
<td>0.12</td>
<td>0.07</td>
</tr>
<tr>
<td>161</td>
<td>0.16</td>
<td>0.10</td>
<td>0.06</td>
</tr>
<tr>
<td>214</td>
<td>0.14</td>
<td>0.09</td>
<td>0.06</td>
</tr>
<tr>
<td>268</td>
<td>0.14</td>
<td>0.10</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table A.1. The wall thickness (t) to radius (r) ratio for an intact wall, after the first removal of layers, and after the second removal of layers.

The intact wall does not fit the requirements of a thin-walled cylinder up to a pressure of 270 mmHg. If the wall is dissected, the ratio will approach the thin-walled assumption at much lower pressures, however that pressure depends on the thickness of the wall. The stress and strain values were plotted using the equation for stress for a thick-walled cylinder (Muvdi and McNabb, 1984):

\[
\sigma_c = \frac{p \cdot r_{\text{inner}}^2}{r_{\text{outer}}^2 - r_{\text{inner}}^2} \left(1 + \frac{r_{\text{outer}}^2}{r^2}\right)
\]  

(A.1)

where:

- \( \sigma_c \) = stress in circumferential direction [N/mm²]
- \( p \) = pressure [N/mm²]
The stress was calculated at each pressure in table A.1, for 5 values of radius:

\[
\begin{align*}
\ r_1 & = r_{inner} \\
\ r_2 & = r_{inner} + \frac{1}{4} (r_{inner} - r_{outer}) \\
\ r_3 & = r_{inner} + \frac{1}{2} (r_{inner} - r_{outer}) \\
\ r_4 & = r_{inner} + \frac{3}{4} (r_{inner} - r_{outer}) \\
\ r_5 & = r_{outer}
\end{align*}
\]

where \( r_{inner} \) and \( r_{outer} \) are measured at each pressure.

Figure A.1 shows the results. In figure A.1.C, the slopes of the curves for the inner radius and the outer radius are very similar because this vessel becomes a thin-walled cylinder at approximately 40 mmHg. The wall thickness of the dissected vessel in figure A.1.B is greater than in A.1.C., and thus there is a slight difference in the slope of the inner vs. outer wall. In the case of the intact wall, figure A.1.A., there is a large discrepancy in the slope of the curve at any given stress in the outside of the wall compared to the inside of the wall. When the vessel is unpressurized, the inner layers are in compression. Therefore, they must extend much more to reach the same degree of tension as the outer walls. If the inner layers are dissected off, the average extension of the wall will no longer be affected by the inner walls, and thus the average stiffness of the dissected vessel will be greater than the intact vessel at the same stress.
Figure A.1. Circumferential extensibility using stress for a thick-walled cylinder. a) intact wall, b) first section of inner layers removed, c) second section of inner layers removed.
Appendix B

The Position of the Intimal Flap (dc) as a Function of Radius

The distance dc was assumed constant with pressure based on qualitative observations of the ultrasound images. The height dc is actually a function of the radius r. A model for the relationship of dc to r is derived from figure B.1.

Figure B.1. Parameters defined for derivation of dc as a function of r.

We know that:

\[ x = 2 \cdot r \cdot \sin(K \cdot \pi) \]  \hspace{1cm} (B.1)

and:

\[ dc = c + r + \sqrt{r^2 - (x/2)^2} \]  \hspace{1cm} (B.2)
so if we know how \( c \) varies as a function of \( x \), we will know how \( d_c \) varies as a function of \( r \). Since:

\[
g = R - c
\]

it follows that:

\[
R^2 = (R - c)^2 + (x/2)^2
\]

R must be solved in terms of \( x \) and \( e \). We know:

\[
R = 2 \cdot s_{\text{inner}} \cdot \varphi
\]

and:

\[
\varphi = 2 \cdot \tan^{-1}\left(\frac{2 \cdot c}{x}\right)
\]

so solving equations (B.5) and (B.6) we have:

\[
R = 4 \cdot s_{\text{inner}} \cdot \tan^{-1}\left(\frac{2 \cdot c}{x}\right)
\]

Substituting (B.7) into (B.4) we have:

\[
4 \cdot s_{\text{inner}} \cdot \tan^{-1}\left(\frac{2 \cdot c}{x}\right) = \left[ 4 \cdot s_{\text{inner}} \cdot \tan^{-1}\left(\frac{2 \cdot c}{x} - c\right) \right]^2 + \left(\frac{x}{2}\right)^2
\]

solving for \( c \) as a function of \( x \):
\[ c = 4 \cdot s_{\text{inner}} \cdot \tan^{-1}\left(\frac{2 \cdot c}{x}\right) - \sqrt{4 \cdot s_{\text{inner}} \cdot \tan^{-1}\left(\frac{2 \cdot c}{x}\right)^2 - \left(\frac{x}{2}\right)^2} \]  

(B.9)

This equation can be solved by iteration. The results are presented for \( s = 20 \) mm, and a range of \( x \) from 14 to 19 mm (fig. B.2).

<table>
<thead>
<tr>
<th>( x/2 ) [mm]</th>
<th>( r ) [mm]</th>
<th>( dc ) [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.00</td>
<td>7.23</td>
<td>14.98</td>
</tr>
<tr>
<td>7.50</td>
<td>7.74</td>
<td>15.23</td>
</tr>
<tr>
<td>8.00</td>
<td>8.26</td>
<td>15.39</td>
</tr>
<tr>
<td>8.50</td>
<td>8.78</td>
<td>15.45</td>
</tr>
<tr>
<td>9.00</td>
<td>9.29</td>
<td>15.33</td>
</tr>
<tr>
<td>9.50</td>
<td>9.81</td>
<td>14.94</td>
</tr>
</tbody>
</table>

There is in fact very little change in \( d_c \). Furthermore it is not a linear relationship, but has a maximum. Due to the small variation in \( d_c \) with radius, the assumption that it remains constant with pressure appears valid.
References


