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Review

Biomechanics of abdominal aortic aneurysm

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Abstract

Abdominal aortic aneurysm (AAA) is a condition whereby the terminal aorta permanently dilates to dangerous proportions, risking rupture. The biomechanics of AAA has been studied with great interest since aneurysm rupture is a mechanical failure of the degenerated aortic wall and is a significant cause of death in developed countries. In this review article, the importance of considering the biomechanics of AAA is discussed, and then the history and the state-of-the-art of this field is reviewed—including investigations into the biomechanical behavior of AAA tissues, modeling AAA wall stress and factors which influence it, and the potential clinical utility of these estimates in predicting AAA rupture.

Keywords: Abdominal aortic aneurysm; AAA biomechanics; AAA rupture; Aortic wall stress; Intraluminal thrombus; Aortic wall strength; Aneurysm wall weakening

Contents

1. Introduction

Abdominal aortic aneurysm (AAA) is a focal, balloon-like dilation of the terminal aortic segment that occurs gradually over a span of years. This condition is growing in

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prevalence in the elderly population, with approximately 150,000 new cases being diagnosed every year (Ouriel et al., 1992; Bengtsson et al., 1996). An AAA may rupture if it is not treated, and this is ranked as the 13th most common cause of death in the US (Patel et al., 1995). Current AAA repair procedures are expensive and carry significant morbidity and mortality risks (Darling et al., 1977; Wain et al., 1998; Turnipseed et al., 2001; Velazquez et al., 2001; Gabrielli et al., 2004; Ghansah and Murphy, 2004; Blankensteijn et al., 2005; EVAR trial participants, 2005a, b; Goueffic et al., 2005; Schouten et al., 2005; van Marrewijk et al., 2005; Dillavou et al., 2006).

Because most patients with AAA are elderly, and/or have co-morbid conditions, and because current repair techniques are not without complications (Moore and Rutherford, 1996; Blum et al., 1997; Wain et al., 1998; Cuypers et al., 1999; Zarins et al., 2000; Brewster, 2001; Hallin et al., 2001; Sicard et al., 2001), the clinician is faced with a dilemma: deciding when the risk of AAA rupture justifies the risks associated with repair. However, there is no currently accepted technique available to quantify the risk of rupture for individual AAA. The decision to electively repair an AAA is widely based on the "maximum diameter criterion"; i.e., when the aneurysm reaches a certain size (typically 5 or 5.5 cm), it is thought that the risk of rupture warrants repair (Dryjski et al., 1994). However, this criterion is only a general rule-of-thumb and is unreliable (Darling et al., 1977; Geroulakos and Nicolaides, 1992). Autopsy studies have shown that small AAAs can rupture (Choksy et al., 1999; Hall et al., 2000), while some of those considered large will not rupture, given the life expectancy of the patient (Darling et al., 1977). Indeed, intervention based on the "maximum diameter criterion" may be offered too late or not be necessary at all for a particular patient. Therefore, there is a need for a new method that will reliably predict the likelihood of AAA rupture on a patient-specific basis as opposed to a "one-criterion-fits-all" approach.

Through increasingly complex degrees, beginning with the simplified Law of Laplace, biomechanical considerations have been used to consider AAA rupture potential, and these are reviewed below. The basic premise of this consideration is that AAA rupture follows the basic principles of material failure; i.e., an aneurysm ruptures when the mural stresses or deformation meet an appropriate failure criterion.

In this review, the inability of various empirical criteria to accurately assess AAA rupture potential is discussed. Following this, the history and the state-of-the-art of AAA biomechanics are presented, including a summary of investigations into the biomechanical behavior of AAA tissues, modeling AAA wall stress and tensile strength distribution and factors which influence them, and the potential clinical utility of these estimates in predicting AAA rupture. It should be noted that this review will not consider the growing body of literature pertaining to the biomechanics of endovascular aneurysm repair or grafting (Marston et al., 1996; Li and Kleinstreuer, 2005a), but rather will be focused on the native aneurysm itself.

2. Fallacy of empirical criteria to assess AAA rupture potential

Following the pioneering work of DuBost and Vorhees in the middle of the 20th Century (Dubost et al., 1952; Blakemore and Voorhees, 1954), AAA repair became the mainstay of the vascular surgeon's practice. Ever since, clinicians have attempted to develop means to accurately predict the risk of aneurysm rupture. Nearly all of the criteria that have been proposed to date have been based on empirical data as opposed to sound physical principles. The most commonly used criterion is the "maximum diameter criterion", which is based on a statistically derived, cut-off value for the maximum diameter. Other parameters that have been proposed as potential predictors of AAA rupture include the AAA expansion rate (Hatakeyama et al., 2001; Lederle et al., 2002; Brown et al., 2003), wall stiffness (Sonesson et al., 1999), increase in intraluminal thrombus (ILT) thickness (Stenbaek et al., 2000), wall tension (Hall et al., 2000), and peak AAA wall stress (Fillinger et al., 2002, 2003; Venkatasubramaniam et al., 2004). Like all empirical approaches, these have their limitations and could potentially lead to sometimes-fatal errors in decisions pertaining to clinical management of AAA. Described in this section are the most common criteria utilized or proposed to date and the shortcomings associated with their use.

2.1. Maximum AAA diameter

Current widespread clinical thinking is that AAA rupture is best predicted by monitoring its maximum diameter; specifically, that the risk of rupture is highest when the aneurysm reaches 5 or 5.5 cm in diameter (Ashton et al., 2002; Lederle et al., 2002; Powell and Brady, 2004). However, this "maximum diameter criterion" is not reliable, as indicated by careful analysis of autopsy data, and does not have a physically sound theoretical basis.

Darling et al. (1977) studied records from 24,000 consecutive, non-specific autopsies performed over a 23-year period. They found 473 non-resected AAA, of which 118 were ruptured. Nearly 13% of AAA 5 cm in diameter or smaller ruptured, and 60% of the aneurysms greater than 5 cm in diameter (including 54% of those between 7.1 and 10 cm) never ruptured (Table 1). These findings question the "maximum diameter" criterion to assess AAA severity. If this criterion were followed strictly for the 473 subjects with AAA studied by Darling and his associates, 7% (34/473) of them would have succumbed to rupture before surgical repair was offered since their AAA was "too small" (<5 cm). Likewise, 25% (116/473) of them would have undergone major surgery, perhaps unnecessarily since their aneurysm may not have ruptured if left untreated.

Table 1
Relationship of size to rupture in 473 non-resected AAA, adapted from data of Darling et al. (1977)

Size (cm)	Ruptured	Unruptured	Total	% Ruptured
$\leqslant 5.0$	34	231	265	12.8
>5.0	78	116	194	40.0
No size recorded	6	8	14	43.0
Total	118	355	473	24.9

Many point to the Law of Laplace as the theoretical basis for using the "maximum diameter criterion" for AAA rupture potential prediction. This "law" states that the stress in the AAA wall is proportional to its diameter. The use of the Law of Laplace to predict AAA rupture potential is erroneous thinking for two reasons. First, the AAA wall geometry is not a simple cylinder or sphere with a single radius of curvature, for which the Law of Laplace is valid. Rather, the AAA wall is complexly shaped with both major and minor wall curvatures (Elger et al., 1996; Sacks et al., 1999). To use only the maximum diameter to predict wall stresses in AAA, therefore, misses the significant contributions of local complex wall surface shapes. Secondly, consideration of wall stress alone is not sufficient to predict AAA rupture. Material failure, including that accompanying AAA rupture, occurs when the mechanical stress acting on the material exceeds its strength. Therefore, the greater the stress:strength ratio for a particular aneurysm, the greater its likelihood of rupture. AAA diameter is not the only determinant of either wall strength or wall stress (Vorp et al., 1998; Vande Geest et al., 2006a).

2.2. Temporal changes in AAA and ILT dimensions

Limet et al. (1991) first ascribed the risk of rupture of AAAs to expansion rate. Other studies by Lederle et al. (2002) and Brown et al. (2003) have confirmed that the mean expansion rate is significantly higher in ruptured AAAs as compared to non-ruptured AAAs. Although it is intuitive that the growth of an AAA is linked to its eventual rupture, the use of the expansion rate of AAAs for the assessment of likelihood of rupture is only useful for patients who can afford to be "carefully watched" over a period of time. In other words, using the expansion rate criteria alone to predict the rupture risk of an AAA would not serve those patients who initially present with AAAs that are at high risk for rupture to begin with. Stenbaek et al. (2000) investigated the increase of relative ILT volume as a potential rupture risk predictor and concluded that a rapid increase may be a better predictor of AAA rupture than an increase in maximal diameter. Again, however, the use of the rate of increase in ILT area to predict AAA rupture potential would not be able to identify patients who present initially with impending AAA rupture.

2.3. AAA wall stress

Hall et al. (2000) described the relationship between aortic wall stress predicted using the Law of Laplace (i.e., based on maximum AAA diameter) and risk of AAA rupture. In their study of 40 AAA patients, they suggested that there exists a threshold tension of $2.8 \times 10^5\,\mathrm{N/m^2}$ after which rupture was imminent. However, it has been shown by our laboratory (Raghavan, 1998; Vorp et al., 1998; Raghavan et al., 2000; Wang et al., 2002) and others (Stringfellow et al., 1987; Fillinger et al., 2002, 2003; Venkatasubramaniam et al., 2004) that the stresses acting on a AAA are not evenly distributed, and cannot be adequately described by the Law of Laplace. In fact, the stresses acting on the wall of an aneurysm are highly dependent on the shape (e.g., profile, tortuosity and asymmetry) of the specific AAA (Elger et al., 1996; Vorp et al., 1998). Therefore, AAAs with equivalent diameters and pressures (and thus Laplace-predicted wall stress) could have largely different actual stress distributions. It is clear that, like the "maximum diameter criterion", the Law of Laplace cannot effectively describe an aneurysm's risk of rupture on a patient-specific basis.

More recently, the use of peak wall stress as a potential predictor of AAA rupture was explored (Fillinger et al., 2002; Venkatasubramaniam et al., 2004). Fillinger et al. (2002) found that the peak wall stress for AAAs which either ruptured or were symptomatic was significantly greater than that for electively repaired AAAs. In a subsequent study (Fillinger et al., 2003), this same group concluded that peak wall stress is a superior measure than maximum diameter for predicting patients with an unfavorable outcome. A more recent study found similar results, while also showing that the location of AAA rupture correlated with the location of peak wall stress (Venkatasubramaniam et al., 2004). While this is at least a step in the right direction with regards to incorporating biomechanical principles into considering AAA severity, this approach considers only one of the two biomechanical factors that govern AAA rupture. As stated above, AAA rupture occurs when the stresses acting on an AAA exceed its wall strength. That is, the rupture risk of a given AAA would increase with an increase in peak wall stress only if the wall strength is unchanged. Not only is wall strength different from patient-to-patient, but it also varies significantly within the same aneurysm as shown by us (Wang et al., 2002; Vande Geest et al., 2006a) and others (Vallabhaneni et al., 2004). In addition, we have recently shown that the strength of AAA wall from ruptured AAAs is significantly less than that for electively repaired AAAs (DiMartino et al., 2006). Taken alone, much like the peak wall stress correlation to rupture risk, this data might suggest that AAA wall strength on its own is predictive of aneurysm rupture. However, based on the principles of material failure, consideration of neither AAA wall stress nor wall strength alone is sufficient to assess rupture potential, but rather knowledge of both is necessary.

3. Biomechanical behavior of AAA tissues

An AAA is typically comprised of two primary structures—the diseased and dilated aortic wall and an ILT, which is a large, stationary blood clot incorporated with blood cells, platelets, blood proteins, and cellular debris (Adolph et al., 1997). Since ILT is contained in most AAAs (Harter et al., 1982), it is prudent to consider the biomechanical behavior of both this material and the AAA wall, as well as *in vivo* studies that evaluated the biomechanical behavior of the entire AAA structure *in situ*.

3.1. AAA wall

Most early studies on the biomechanical properties of the AAA wall were focused on understanding the effect of the extracellular matrix derangements found in aneurysms on basic properties such as wall stiffness (Sumner et al., 1970; Dobrin, 1989; He and Roach, 1994). An early, hallmark study in this regard was reported by Sumner et al. (1970) in which stiffness measures of aneurysmal and control vessel segments (both obtained post-mortem) were correlated with their collagen and elastin content. They found that aneurysmal portions of a vessel were stiffer and contained less collagen and elastin than the adjacent non-aneurysmal segment. These findings were, in part, corroborated by a later study by He and Roach (1994), who obtained uniaxial sub-failure tensile data from human AAA and non-aneurysmal abdominal aortic specimens (the latter obtained post-mortem). Dobrin (1989) studied *ex vivo* the biomechanical changes associated with experimental enzymatic degradation of structural proteins in arterial segments and suggested that elastolysis leads to aneurysmal-like dilation, while collagen failure was a necessary precursor to rupture.

Our laboratory reported measures of AAA wall stiffness (Vorp et al., 1996b), and formulated both microstructure-based (Raghavan et al., 1996) and hyperelastic, continuum-mechanics based models for the AAA wall (Raghavan and Vorp, 2000). Microstructure-based constitutive models are motivated by the known, fibrous nature of the tissue. For example, the constitutive parameters of our model (Raghavan et al., 1996) are associated with the state of the elastin and collagen within the aortic wall. However, microstructure-based models are difficult to utilize for the estimation of wall stresses in intact, three-dimensional (3D) vessels. For this, it is more appropriate to utilize continuum-based constitutive models which describe gross mechanical behavior. Our continuum-based AAA wall tissue model (Raghavan and Vorp, 2000) is a special case of the generalized neo-Hookean model (Truesdell and Noll, 1992) with the Cauchy stress tensor T taking the form

$$\underline{\mathbf{T}} = -p\,\underline{\mathbf{1}} + 2[\alpha + 2\beta(I_1 - 3)]\,\underline{\mathbf{B}}. \tag{1}$$

Here, p is the hydrostatic pressure within the material, $\underline{\mathbf{1}}$ is the identity tensor, and $\underline{\mathbf{B}}$ is the left Cauchy–Green stretch tensor, $\underline{\mathbf{B}} = \underline{\mathbf{F}}\underline{\mathbf{F}}^{\mathrm{T}}$, where $\underline{\mathbf{F}}$ is the deformation gradient within the material (Truesdell and Noll, 1992). I_1 is the first invariant of $\underline{\mathbf{B}}$ (i.e., $I_1 = \mathrm{tr}\ \underline{\mathbf{B}}$). The model parameters α and β represent the mechanical properties of the AAA wall, which we determined from 69 human AAA specimens to be $\alpha = 17.4 \pm 1.5\,\mathrm{N/cm^2}$ and $\beta = 188.1 \pm 37.2\,\mathrm{N/cm^2}$ (mean ± SEM) (Raghavan and Vorp, 2000). This constitutive model and the mean parameter values have been used extensively for the aneurysm wall in the computational stress analyses of individual AAA (Raghavan et al., 2000; Fillinger et al., 2002, 2003; Wang et al., 2002; Di Martino and Vorp, 2003; Venkatasubramaniam et al., 2004).

While the biomechanical response of normal and pathologic human abdominal aortic tissue to uniaxial loading conditions is useful in many ways, this tissue is simultaneously loaded in multiple directions *in vivo*, so uniaxial loading may be insufficient for the characterization of its multi-axial mechanical response. Biaxial testing allows for more appropriate modeling of aortic tissue as well as the investigation of any apparent anisotropy. While the anisotropy of non-aneurysmal aortic tissue has been demonstrated (Patel et al., 1969; Young et al., 1977; Manak, 1980; Vaishnav and Vossoughi, 1984; Singh and Devi, 1990; Weizsacker and Kampp, 1990; L'Italien et al., 1994; Vorp et al., 1995; Zhou and Fung, 1997; Holzapfel and Weizsacker, 1998; Vande Geest et al., 2004b), very little has been reported on human aortic tissue.

We recently reported a population-wide biaxial constitutive relation for human AAA and non-aneurysmal abdominal aortic (AA) tissue (Vande Geest et al., 2004c). In brief, 26 AAA tissue samples and eight age-matched (>60 years of age) AA tissue samples were obtained and tested within a well-validated biaxial tensile testing system (Sacks, 2000). Both types of tissue exhibited an anisotropic exponential response, warranting the use of the well-known anisotropic exponential strain energy function first described by Tong and Fung (1976):

$$W = \frac{c}{2}(\mathrm{e}^{Q} - 1) \text{ where } Q = A_{ijkl}E_{ij}E_{kl}. \tag{2}$$

Here, W is the strain energy function, E_{ij} are the components of the Green strain tensor, c and the A_{ijkl} are material parameters, and each of the indices (i, j, k and l) can take on values of θ, L, or R. Neglecting all shear terms, the expression for the exponent in Eq. (2) becomes

$$Q = A_1E_{\theta\theta}^2 + A_2E_{LL}^2 + 2A_3E_{\theta\theta}E_{LL}. \tag{3}$$

Individual specimen material parameters as well as an averaged set of material parameters were derived for both AA and AAA (Table 2). The mean peak Green strains $E_{\theta\theta\,\max}$ and $E_{LL,\max}$ for the equibiaxial tension ($T_{\theta\theta} = T_{\mathrm{LL}} = 120\,\mathrm{N/m}$) protocol for the AA specimens were 0.13 ± 0.03 and 0.12 ± 0.03, respectively ($p = 0.77$; Fig. 1A). $E_{\theta\theta\,\max}$ and $E_{\mathrm{LL},\max}$ under equibiaxial tension for the AAA specimens were 0.07 ± 0.01 and 0.09 ± 0.01, respectively ($p = 0.047$; Fig. 1A). There was no significant difference in $E_{\mathrm{LL},\max}$ between the AA and AAA groups

Table 2
Averaged constitutive parameters for AAA and age-matched AA tissue as related to Eqs. (2) and (3)

	Averaged model fits				
	c (kPa)	A_1	A_2	A_3	R_2
AA	1.61	32.3	32.4	20.9	0.95
AAA	0.61	104.9	101.9	63.2	0.92

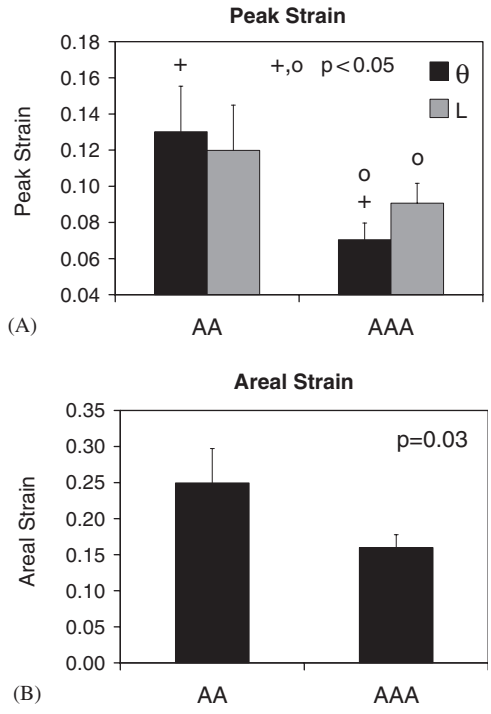

Fig. 1. Peak strain and aerial strain for the equibiaxial tension protocol for AA and AAA tissue. From Vande Geest et al. (2004c).

($p = 0.24$). However, $E_{\theta\theta,\max}$ was found to be significantly smaller for AAA as compared to AA ($p = 0.01$). The average values of $E_{LL,\max}/E_{\theta\theta,\max}$ for the AA and AAA groups were 0.96 ± 0.09 and 1.62 ± 0.01, respectively ($p = 0.1$). The mean areal strain for AA (0.25 ± 0.05) was significantly larger ($p = 0.03$) than that of the AAA (0.16 ± 0.02), suggesting that AA tissue is more distensible than AAA tissue (Fig. 1B). The results of this work suggest that aneurysmal degeneration of the abdominal aorta is associated with an overall decrease in tissue extensibility (stiffness) as well as significant changes in its biaxial biomechanical behavior.

In order to demonstrate the differences in the isotropic relation derived from uniaxial testing (Raghavan and Vorp, 2000) with the anisotropic relation derived from biaxial testing (Vande Geest et al., 2004c), the strain energies for both models were calculated and plotted for an equibiaxial strain state up to 12% strain (Fig. 2). Note that the isotropic model displays significantly larger strain energy at lower strains as compared to that for the anisotropic model. The marked difference in mechanical

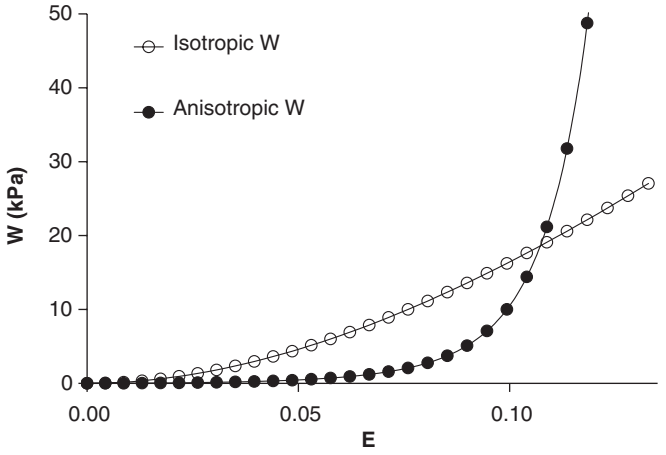

Fig. 2. The strain energy of the averaged isotropic relation from Eq. (1) (Raghavan and Vorp, 2000) and the averaged anisotropic constitutive relation for AAA (Eqs. (2) and (3) and Table 2) versus equibiaxial strain (E). From Vande Geest et al. (2004c).

response of the tissue between the two models demonstrates the importance of correct model choice in biomechanical simulations.

3.2. Intraluminal thrombus

Using non-invasive, ultrasound-based measures of ILT, we determined that the ILT undergoes non-linear strains *in vivo* and is incompressible (Vorp et al., 1996a). This work supported the idea that the ILT may be "mechanically protective", providing a stress shielding or cushioning effect for the AAA wall (Inzoli et al., 1993). In order to fully investigate the role of ILT on the biomechanics of AAA, it was important to first establish the biomechanical behavior of the ILT. DiMartino et al. (1998) evaluated the linearly elastic behavior of ILT, suggesting that it behaves as a Hookean material. More recently, uniaxial tensile testing suggested that ILT is non-linearly elastic, inhomogeneous, and isotropic (Wang et al., 2001). In that work, three layers of the ILT were identified: a well-formed inner (luminal) layer, a slightly degraded medial layer, and an amorphous, highly degenerated outer layer. Pairs of ILT specimens (i.e., one in the longitudinal direction and one in the circumferential direction) were cut from the luminal and medial layers of ILT obtained freshly at AAA resection and used for tensile testing. The outer layer was too fragile to be tested. We found, for the case of uniaxial tension, the ILT behaved according to:

$$T = 2\left[c_1 + 2c_2\left(2\lambda + \frac{1}{\lambda^2} - 3\right)\right]\left(\lambda - \frac{1}{\lambda^2}\right), \tag{4}$$

where λ is the applied axial stretch, T is the resulting Cauchy stress component acting in the axial direction, and c_1 and c_2 are the constitutive properties of the material. The values of c_1 and c_2 within each of the tested layers were found to be statistically equivalent between the circumferential and longitudinal specimens, suggesting isotropy

(Table 3). However, the luminal layer was found to be stiffer and stronger than the medial layer, demonstrating the inhomogeneity of the ILT (Fig. 3).

To further investigate the possibility that the ILT is an isotropic material, we recently evaluated the biaxial behavior of this material (Vande Geest et al., 2006b). For this work, the medial and abluminal layers were too fragile to be procured and tested, so data were collected for only the luminal layer. The peak stretch values under equibiaxial tension for the luminal layer of the ILT were 1.18 ± 0.02 and 1.13 ± 0.02 in the θ and L directions, respectively ($p = 0.14$). The maximum tangential modulus values were 20 ± 2 and $23 \pm 3\,\mathrm{N/cm^2}$ in the θ and L directions, respectively ($p = 0.37$). These results were consistent with the conclusions drawn from the previous uniaxial study (Wang et al., 2001) in that the ILT appears to behave in an isotropic manner.

3.3. In vivo AAA

The mechanical behavior of *in situ* AAA has been reported based on non-invasive measurements using ultrasonography (Länne et al., 1992; MacSweeney et al., 1992; Vorp et al., 1996a; Sonesson et al., 1999; Wilson et al., 2001; Long et al., 2005). The beta stiffness (Hayashi, 1993) and/or pressure–strain elastic modulus (E_p) or compliance is typically used in such studies. A general and consistent observation has been that compliance is reduced in segments of the aorta due to aneurysm. Our laboratory reported that the mean compliance was lower for the AAA wall alone than for the luminal surface enclosed by ILT, and that ILT area was nearly constant over the cardiac cycle, suggesting that this material is virtually incompressible (Vorp et al., 1996a). Wilson et al. (2001) demonstrated a positive correlation between blood serum levels of elastolytic markers and AAA compliance in patients with aneurysms. Sonesson et al. (1999) measured the beta stiffness of ruptured and non-ruptured AAAs and found there to be no correlation between this property and eventual fate of the aneurysm. However, others found that those AAA whose E_p decreased over time had a shorter time to rupture (Wilson et al., 2003), and a significant positive correlation between AAA compliance and size; i.e., larger AAA are more compliant than smaller AAA (Long et al., 2005).

Table 3
Constitutive parameters for ILT from AAA as related to Eq. (4)

Region	Orientation	c_1 (N/cm^2)		c_2 (N/cm^2)	
		Specimen	Group	Specimen	Group
Luminal layer	Longitudinal ($n = 14$)	2.89 ± 0.39	3.12	3.10 ± 0.45	3.39
	Circumferential ($n = 14$)	3.19 ± 0.45	3.62	2.93 ± 0.36	3.55
Medial layer	Longitudinal ($n = 11$)	2.06 ± 0.33	2.77	1.77 ± 0.28	2.11
	Circumferential ($n = 11$)	2.21 ± 0.48	1.80	2.57 ± 0.43	2.38

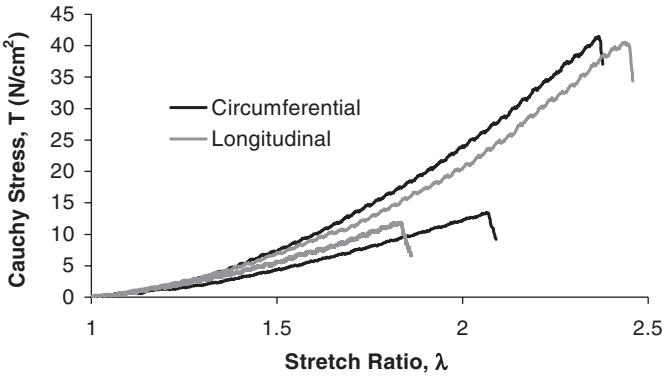

Fig. 3. Typical set of stress–stretch curves for ILT samples taken from the luminal region (upper set of curves) and the medial region (lower set of curves). All data were obtained from the same ILT (same patient). From Wang et al. (2001).

4. AAA wall stress

Given that the Law of Laplace suggests that the wall tension in AAA is elevated compared to the undilated aorta, the earliest investigations of AAA biomechanics were focused on estimating AAA wall stress. In 1986, Stringfellow et al. (1987) used the Law of Laplace to determine the wall stresses in a hypothetical AAA by idealizing its geometry as cylindrical or spherical. A simplified two-dimensional (2D) stress analysis was also performed to evaluate the effect of aorta-aneurysm geometry. Subsequently, others performed similar, but more complex 2D analyses (Inzoli et al., 1993; Mower et al., 1993; Elger et al., 1996). For example, Inzoli et al. (1993) used axisymmetric 2D geometries and finite element (FE) analysis to introduce an important, though controversial concept: that ILT may act to reduce the peak stress acting on the AAA wall. Similar conclusions have been made recently by two other groups using hypothetical geometries (Mower et al., 1997; DiMartino et al., 1998). Mower et al. (1993) also used FE methods to observe the effect of AAA size on wall stresses. Elger et al. (1996) demonstrated using 2D, hypothetical, axisymmetric models that the shape of the AAA profile is an important determinant of the magnitude and location of the maximum wall stress.

Each of these early mechanical wall stress models for AAA, while providing useful information on the general factors influencing AAA wall stress, did not provide realistic stress distributions in patient-specific AAA. First, the use of linearized elasticity theory or other inappropriate tissue constitutive models (Stringfellow et al., 1987; Inzoli et al., 1993; Mower et al., 1993; Elger et al., 1996; Mower et al., 1997; DiMartino et al., 1998; Vorp et al., 1998) can lead to erroneous stress distribution predictions (Raghavan and Vorp, 2000) (Fig. 4). Secondly, the use of simplified

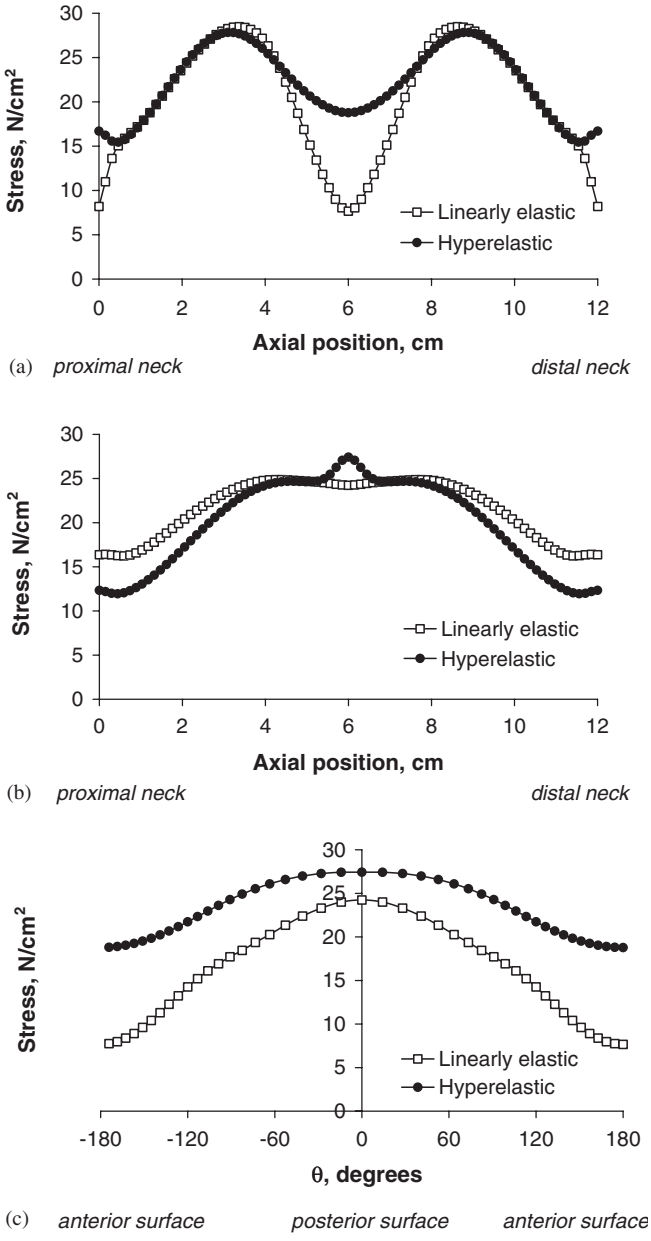

Fig. 4. Comparison of stresses computed for a 3D asymmetric AAA model using the hyperelastic constitutive model given by Eq. (1) (Raghavan and Vorp, 2000) with those using a linearized elasticity model along anterior surface (A), along posterior surface (B), and around mid-section (C). Note the substantial error involved with using the theory of linearized elasticity. From Vorp et al. (1998).

geometries to model real AAA fails to demonstrate the importance of abrupt, local changes in surface curvature and diameter on the distribution of stresses, which are likely very important (Sacks et al., 1999).

Non-invasive assessment of the surface geometry of AAA may be beneficial for a number of reasons. For example, knowledge of the spatial variations in wall curvature would identify regions of high wall tension based on the generalized Law of Laplace, which states that wall tension is proportional to the inverse of mean curvature. Moreover, it would allow the detailed analysis

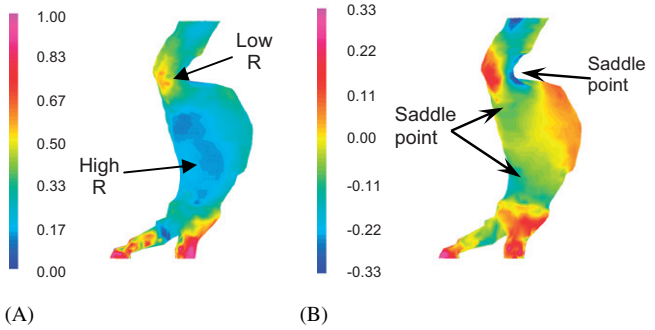

Fig. 5. Surface curvature analysis of a representative AAA. Shown are the mean (A) and Gaussian (B) curvature distributions. The mean curvature is equal to the inverse of mean radius of curvature of the surface. The Gaussian curvature indicates local surface shape. Adapted from Sacks et al. (1999).

of AAA geometry and determination of localized blebs in the aneurysm wall (Hunter et al., 1989). We previously performed non-invasive assessment of the curvature of *in vivo* AAA (Sacks et al., 1999). Our results revealed the complex geometry of AAA (Fig. 5), and demonstrate that local mean curvature (and hence wall tension) is highly variable across the AAA surface (Fig. 5A). Gaussian curvature (Fig. 5B) provided an indication of the presence of "saddle-shaped" regions (a negative Gaussian curvature indicates that the surface is saddle shaped, or convex in one aspect and concave in the other).

We have previously performed stress analyses on hypothetical models of AAA in order to determine the different effects of aneurysm size and shape on the wall stress distribution (Vorp et al., 1998), and to evaluate the constitutive models that we previously derived for the AAA wall (Raghavan and Vorp, 2000) and ILT (Di Martino and Vorp, 2003). From the first study, we concluded that the stress magnitude and distribution within the AAA wall are dependent on both the shape of the AAA bulge as well as its diameter (Fig. 6) (Vorp et al., 1998). This was an important observation since the "maximum diameter criterion" is often used to assess severity of an AAA, when in reality aneurysms with the same diameter may not necessarily have the same propensity for rupture.

To perform stress analysis on individual AAA, the material parameters specific to each aneurysmal wall and ILT (i.e., α and β in Eq. (1), and c_1 and c_2 in Eq. (4), respectively) should be employed. However, the only way to accurately determine these parameters is to perform *ex vivo*, destructive mechanical testing, which of course is not possible for a presurgical situation. Instead, the group mean values of the material parameters as assessed for a large number of AAA and ILT specimens (Raghavan and Vorp, 2000; Wang et al., 2001) have typically been used (Raghavan et al., 2000; Wang et al., 2002; Fillinger et al., 2002, 2003; Di Martino and Vorp, 2003; Venkatasubramaniam et al., 2004). We evaluated this approach by performing parametric analyses to demonstrate that

"biologically reasonable" deviations in the actual values of the material parameters for an individual AAA and ILT from the mean values determined for a large AAA population will not significantly affect the estimated wall stress distribution (Raghavan and Vorp, 2000; Di Martino and Vorp, 2003). This was accomplished by repeated FE stress analysis on a hypothetical, 3D, asymmetric AAA model. Each of the two material parameters in each of the constitutive models (Eqs. (1) and (4)) were individually varied from their minimum "biologically reasonable value" to their maximum "biologically reasonable value" (i.e., [mean]±[95% confidence interval] from our experimental data), while the other parameter remained constant. We found that these large variations in the material parameters led to a maximum of less than 5% error in predicted wall stresses (Raghavan and Vorp, 2000; Di Martino and Vorp, 2003). This suggests that the differences in AAA wall stresses from patient to patient are driven more by the differences in surface geometry than in material properties. Importantly, these results suggest that the population mean values for the parameters of the constitutive model for AAA wall and ILT are sufficient for reasonably accurate patient-specific computations.

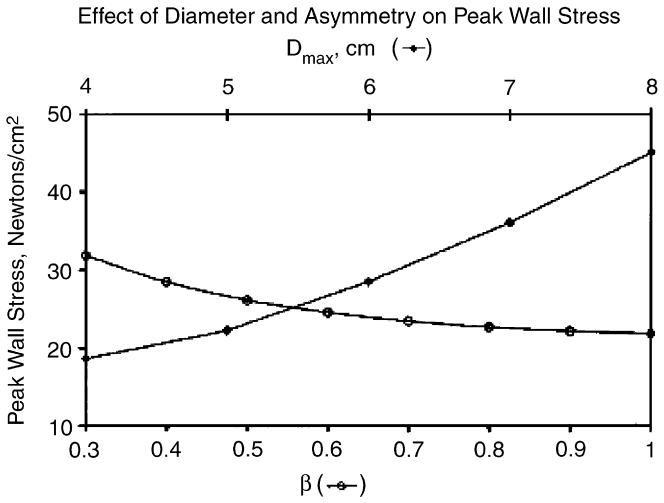

Fig. 6. Effect of asymmetry parameter β (bottom axis) and maximum diameter (top axis) on magnitude of peak stress within a patient-specific AAA. Both increasing diameter and increasing asymmetry (decreasing b) cause a non-linear increase in peak stress. From Vorp et al. (1998).

While the stress analyses using 3D, hypothetical AAA were useful for their intended purposes, the wall stress distribution in real, *in vivo* AAA is even more complex. Our laboratory has developed (Raghavan and Vorp, 2000) and subsequently modified (Wang et al., 2002) techniques for the non-invasive assessment of the *in vivo* wall stress distribution in patient-specific AAA. In our earlier approach, which did not include the presence of ILT in the 3D reconstructed models, we noted that the stress distribution in AAA is very complex, demonstrating regions of low and comparatively high wall stress. In the AAA shown in Fig. 7, *top left*, wall stress varied from a minimum of about 9 N/cm^2 on the proximal neck, to over 40 N/cm^2 on the posterolateral surface. For the AAA shown in Fig. 7, *top right*, wall stress varied from a minimum of about 6 N/cm^2 on the proximal neck, to over 40 N/cm^2 on the posterolateral surface. It is interesting to

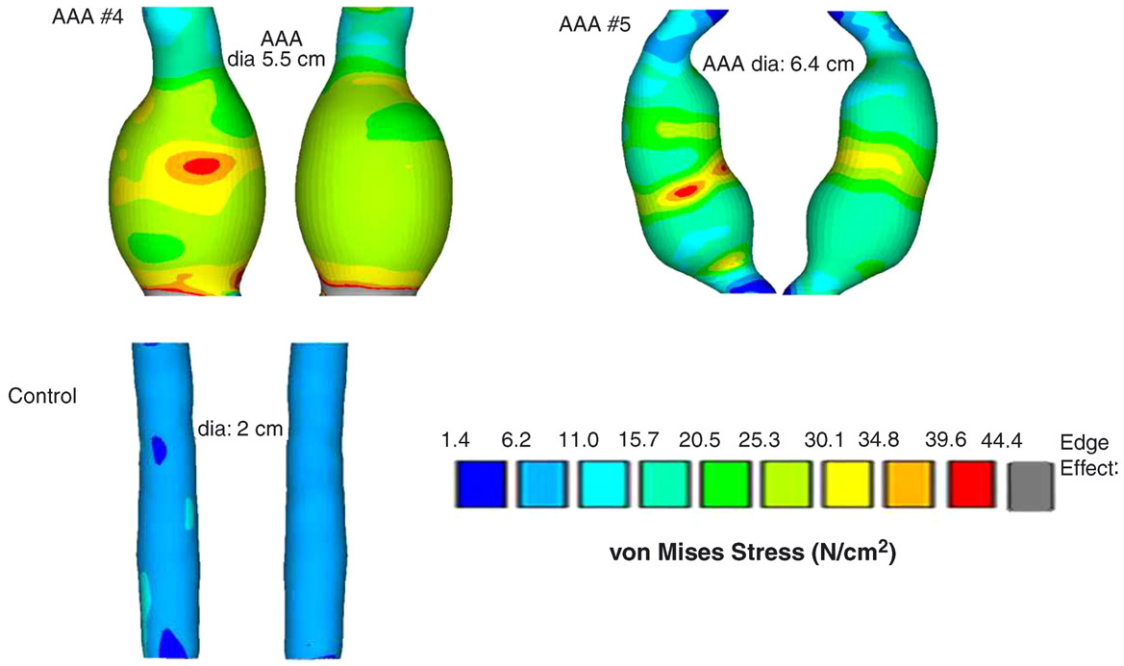

Fig. 7. Wall stress distributions for two AAA (top) and one non-aneurysmal aorta (bottom). Two views are shown for each aorta. The left view is the posterior surface, the right view is the anterior surface. Images are not to scale. The maximum diameter of the AAA at top, left is 5.5 cm, while that at top, right is 6.4 cm. All subjects had normal blood pressure. Note that, despite one AAA being smaller in diameter than the other, the peak wall stress is essentially equal, underscoring the need for a patient-specific technique to evaluate AAA. Adapted from Raghavan et al. (2000).

compare the stress distribution in AAA to the stresses in an undilated aorta. For that case (Fig. 7, *bottom*), our analysis shows a more uniformly distributed stress of about 9 N/cm^2 (range 5–12 N/cm^2).

Because of the observations that suggest that the ILT within AAA may have a significant influence on AAA wall stresses (Inzoli et al., 1993; Vorp et al., 1996a; Mower et al., 1997), we modified our techniques to incorporate this structure (Wang et al., 2002). Subsequent FE analyses demonstrated that incorporation of the ILT to the 3D stress analysis models of AAA has a profound influence on the magnitude and distribution of stresses acting on the AAA wall (Fig. 8) (Wang et al., 2002). These results underscore the importance of incorporating ILT into computational stress analysis models for accurate wall stress estimations for actual AAA.

Li and Kleinstreuer (2005b) recently proposed a semi-empirical equation for the peak AAA-wall stress based on clinical observations and numerical analyses. They argued that their equation suitably predicted peak wall stress (σ_{max}) without the need for complex analyses such as FE or other computational approaches. The equation was an adaptation of the Law of Laplace, empirically taking into account the area ratio of AAA sac to ILT (α), the asymmetry parameter (β)(Vorp et al., 1998), maximum transverse diameter (D_{max}) and wall thickness (t) of the AAA wall, and the systolic blood pressure (p_{sys}):

$$\sigma_{max} = 0.006 \frac{(1 - 0.68\alpha)e^{0.0123(0.85p_{sys} + 19.5d_{AAA,max})}}{t^{0.63}\beta^{0.125}}. \quad (5)$$

These authors applied their equation to 10 different AAA published in the literature and compared their estimated peak wall stress with those previously reported, as well as with that predicted from the Law of Laplace. Eq. (5) was able to estimate the peak wall stress to within an error of up to 9.5% compared to the full FE analyses, whereas the Laplace estimation resulted in an error of up to 86%. While Eq. (5) appears to provide reasonable estimates for more simply shaped AAA geometries, its accuracy reduces greatly with geometric complexities. Unfortunately, most end-stage AAA in need of consideration of repair are quite complex and therefore use of the more rigorous full 3D reconstruction and FE analyses would be prudent. Moreover, the empirical analysis represented by Eq. (5) is unable to pinpoint the location of maximum stress, which would be important when comparing to estimates of wall strength distribution

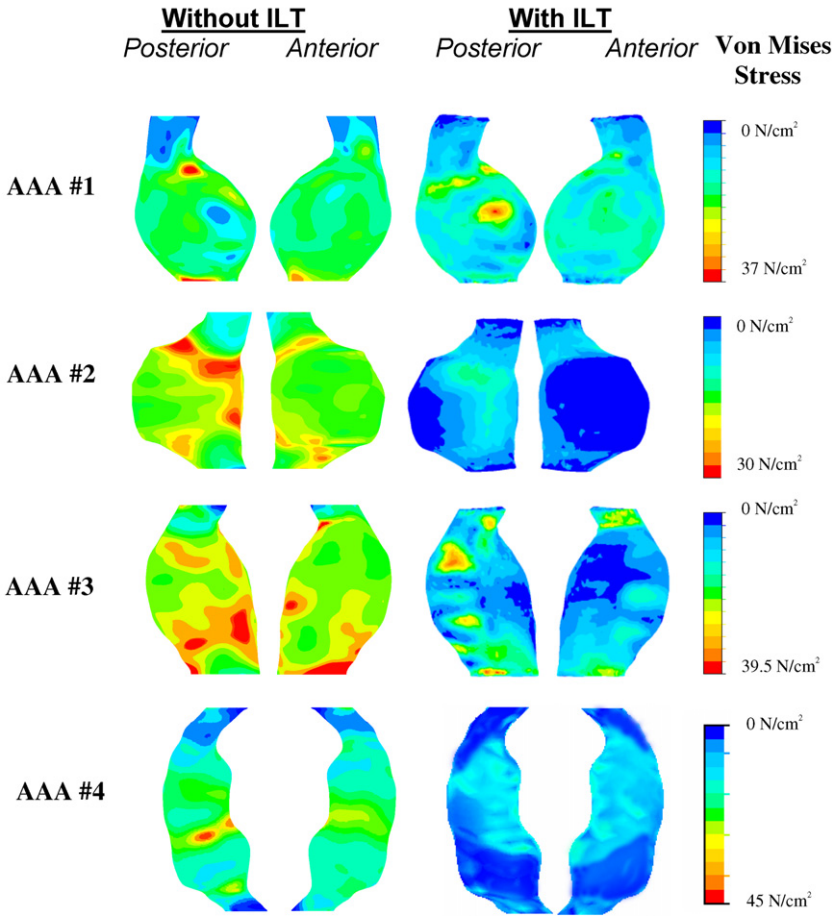

Fig. 8. Comparison of 3D wall stress distribution between AAA models with and without ILT. Individual color scales (right) indicate von Mises stress for each AAA. Both posterior and anterior views are shown for each case. From Wang et al. (2002).

and hence estimating rupture potential of a particular aneurysm.

We recently demonstrated that utilization of the anisotropic material model described by Eqs. (2) and (3) may lead to an improved prediction of the stress distribution in the AAA (Fig. 9) (Vande Geest et al., 2004a; Vande Geest, 2005). Two non-ruptured and one ruptured AAA were reconstructed and subjected to two FE simulations each: one using our previous isotropic wall constitutive relation (i.e., Eq. (1)) (Raghavan and Vorp, 2000), and the other using the averaged AAA anisotropic biomechanical relation (i.e., Eqs. (2) and (3), and Table 2) (Vande Geest et al., 2004c). A paired *t*-test was used to compare the peak maximum principal stresses (S_{max}) and strains (E_{max}) between the two simulations. To evaluate the stress distributions, not just the peak stresses, a Wilcoxon signed rank test was used to compare all of the nodal stresses using the isotropic material model to those using the anisotropic model. The maximum principal stress contours for the isotropic and anisotropic simulations for all three aneurysms display similar shapes, but the anisotropic simulations consistently displayed larger stress values over larger areas of the aneurysm (Fig. 9). The peak maximum principal stresses for the anisotropic simulations were also larger than their isotropic counterparts ($p<0.001$), but no difference was noted in peak maximum principal strains (Table 4).

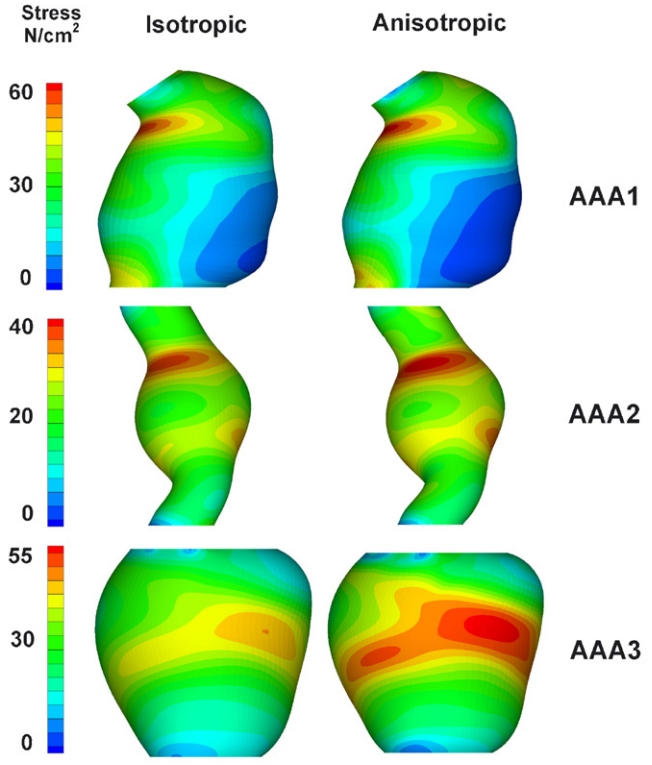

Fig. 9. Maximum principal stresses for finite element simulations utilizing isotropic (Eq. (1)) and anisotropic (Eqs. (2) and (3)) constitutive relations. From Vande Geest (2005).

Table 4
Peak maximum principal stresses (S_{max}) and strains (E_{max}) for the three AAA simulations shown in Fig. 9

	AAA1		AAA2		AAA3	
	Biaxial	Uniaxial	Biaxial	Uniaxial	Biaxial	Uniaxial
S_{max} (N/cm^2)	63.80	59.30	42.60	39.40	57.50	53.20
E_{max}	0.23	0.20	0.20	0.16	0.19	0.19

It should be noted that there have been several studies that have inspected the flow and pressure fields as well as shear stress patterns in AAA, both in hypothetical and patient-specific models (Perktold, 1987; Budwig et al., 1993; Taylor and Yamaguchi, 1993; Asbury et al., 1995; Peattie et al., 1996, 2004; DiMartino et al., 2001; Finol and Amon, 2002). While these studies have been important to demonstrate that the pressure field in AAA is relatively constant (Asbury et al., 1995; Peattie et al., 1996, 2004), a common assumption in stress analyses of AAA, this author believes that shear stresses do not influence AAA that are already formed for at least three reasons. First, as has been mentioned, most AAA contain ILT which would shield the AAA wall from the effects of shear stresses. Moreover, many studies have neglected to include the ILT in their flow simulations, and this would produce an inaccurate estimate of the actual shear stresses acting on the AAA wall. Secondly, clinically presented AAA are largely devoid of a recognizable intimal layer (Holmes et al., 1995), so the highly shear-sensitive endothelial layer is likely not functionally present in the AAA wall. Finally, the flow-induced shear stresses acting on the AAA wall is orders of magnitude smaller than the pressure/stretch-induced, in-plane wall stresses. For example, Peattie et al. (2004) found that shear stresses acting on the AAA lumen were less than 2×10^{-4} N/cm^2, while peak in-plane AAA wall stresses are five or six orders of magnitude higher than this (Fig. 7).

5. AAA wall strength

Our 1996 reports on the uniaxial tensile testing of freshly excised specimens appears to be the first to provide measures of AAA wall strength (Raghavan et al., 1996; Vorp et al., 1996b). We found that AAA wall tissue was approximately 50% weaker than control (non-aneurysmal) abdominal aorta. We also noted in this work that there were no significant differences in strength between circumferentially-oriented and longitudinally-oriented AAA tissue specimens. We have since performed tensile testing on specimens from hundreds of AAA and control aorta, and these trends have held. Subsequent work, described below, suggests that tissue from ruptured AAA is weaker than that from electively repaired AAA, that the wall of infected AAA is weaker than in non-infected AAA, and that AAA wall strength is variable within a single AAA, possibly due to the presence of hypoxic regions. The potential

mechanisms behind AAA wall degeneration are discussed in a recent review (Vorp and Vande Geest, 2005).

Several studies have reported the important observation that the biomechanical properties of a given AAA varies spatially (Thubrikar et al., 2001; Vorp et al., 2001; Vallabhaneni et al., 2004; Vande Geest et al., 2006a). Work performed in our laboratory suggested that the presence of ILT tends to decrease local wall strength in an ILT-thickness-dependent manner (Vorp et al., 2001; Vande Geest et al., 2006a), and that this inverse relationship is due to ILT serving as a barrier to oxygen flux from the lumen to the inner layers of the aortic wall thereby inducing hypoxic conditions and wall degeneration (Vorp et al., 2001). Vallabhaneni et al. (2004) suggested that the spatial variation in wall strength was linked to variations in matrix metalloproteinase production. These observations underscore the premise that evaluation of AAA wall stress distribution alone is insufficient to predict rupture since the wall strength is not the same from point-to-point in the aneurysm wall. That is, the point of peak wall stress could possibly coincide with a greater wall strength compared to regions with lower stresses.

In order to investigate the association of aortic wall weakening with AAA rupture, we recently performed *ex vivo* tensile tests on freshly excised wall tissue specimens from patients who suffered AAA rupture prior to surgery and compared them to specimens from electively repaired, asymptomatic AAA (DiMartino et al., 2006). In this study, 13 AAA wall specimens were obtained from nine patients (age 72 ± 3 years) during repair of their ruptured AAA (diameter $= 7.8\,\text{cm}\pm0.5$). For comparison, 26 AAA wall specimens were obtained from 16 patients (age 73 ± 3 years, $p =$ NS) undergoing elective repair of their AAA (diameter $7.0\pm0.5\,\text{cm}$, $p =$ NS). A significant difference was noted in wall thickness between electively repaired and ruptured AAA: 2.5 ± 0.1 vs. $3.6\pm0.3\,\text{mm}$, respectively ($p<0.01$). The tensile strength of the ruptured AAA tissue was found to be significantly lower than that for the elective AAA tissue (see Fig. 10: 54 ± 6 vs. $82\pm9\,\text{N/cm}^2$; $p<0.05$). These data

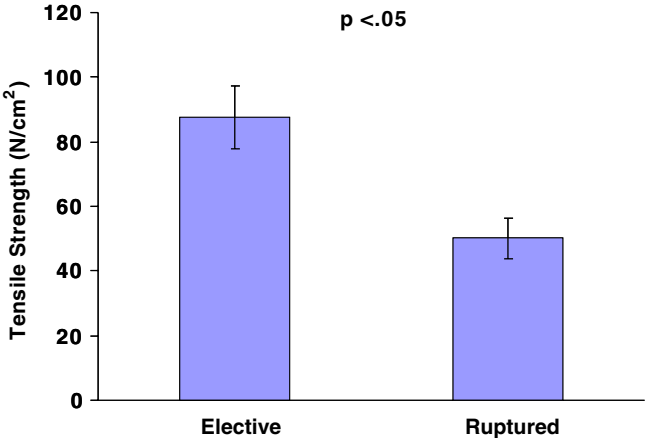

Fig. 10. Difference in tensile strength of ruptured and electively repaired AAA wall specimens. From DiMartino et al. (2006).

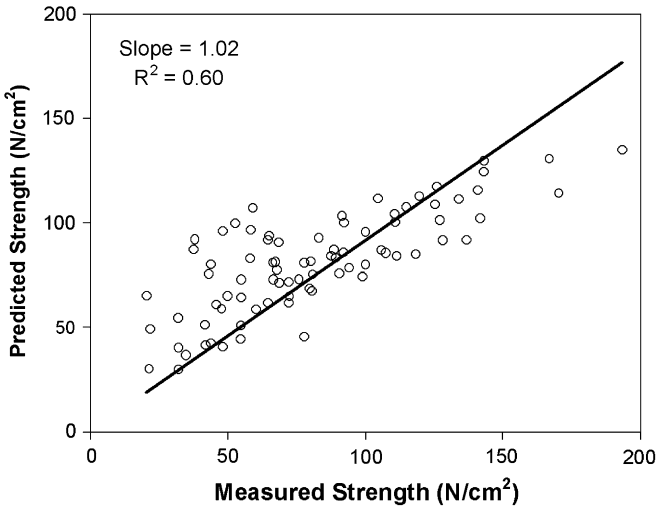

Fig. 11. Predicted versus measured strength for one statistical model of wall strength. The solid line represents the line of unity. From Vande Geest et al. (2006a).

suggest that AAA rupture is associated with significant aneurysm wall weakening, and this supports the argument that wall strength needs to be carefully considered on a patient-specific basis in order to accurately predict rupture potential of individual aneurysms.

Another recent study suggests that the wall degeneration noted in AAA compared to non-aneurysmal aorta is exacerbated in those aneurysms infected by *Chlamydia pneumoniae* (Witkewicz et al., 2005). In contrast to earlier findings which found no difference (Raghavan et al., 1996; Vorp et al., 1996b), this study reported that AAA tissue is stronger in the longitudinal direction than in the circumferential direction.

In order to accurately predict the risk of rupture of AAA, a means is necessary to predict AAA wall strength distribution non-invasively, much like that for AAA wall stress distribution (Figs. 7 and 8). Only then can a pointwise relative comparison of wall stress to wall strength be performed, and a biomechanically sound prediction of AAA rupture be made. Our laboratory has developed (Vande Geest, 2005; Vande Geest et al., 2006a) mathematical models for the prediction of AAA wall strength based on non-invasively measurable parameters, including local AAA diameter, local ILT thickness, patient age, patient gender and patient's family history of AAA disease. The predictability and example applications of such a model are shown in Figs. 11 and 12, respectively.

6. Clinical application of AAA biomechanics

There have been only a few reported studies where a biomechanical approach was applied to clinical data to determine whether a correlation exists between biomechanical parameters and AAA rupture. Sonesson et al. (1999) investigated the beta stiffness of ruptured and non-ruptured aneurysms and concluded that this parameter

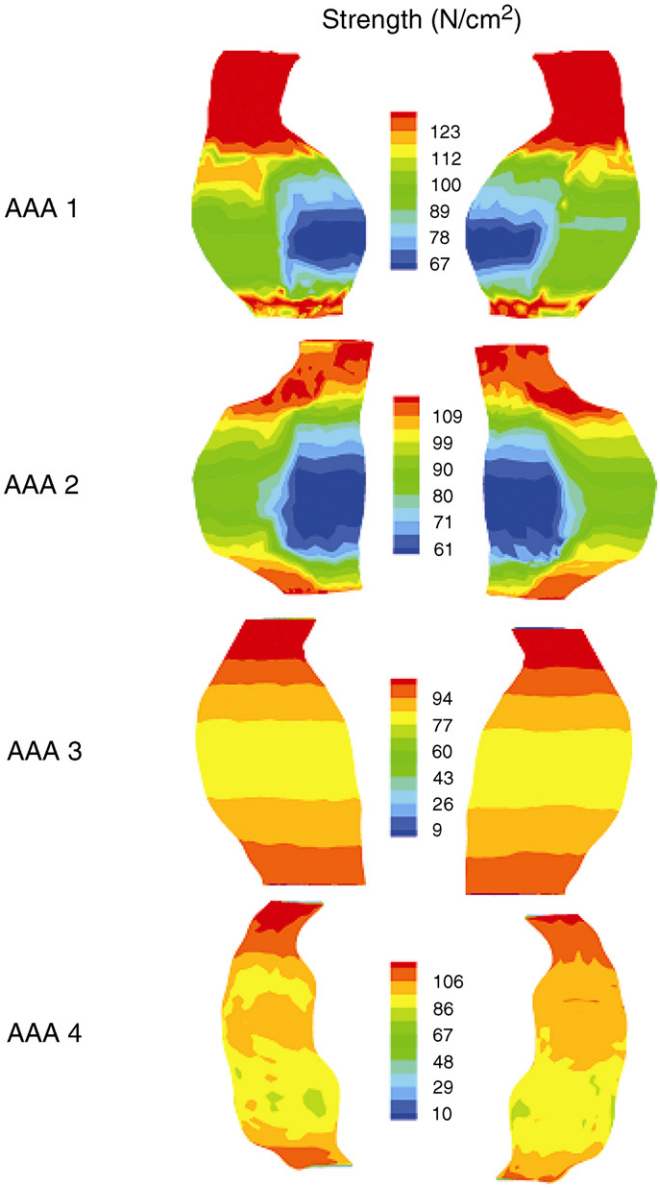

Fig. 12. Demonstrative application of the statistical model of wall strength for four representative AAAs. Both posterior (left) and anterior (right) aspects are shown for each AAA. From Vande Geest et al. (2006a).

could not be used as an indicator of eventual AAA rupture. Hall et al. (2000) described the relationship between AAA wall stress derived from the Law of Laplace (i.e., based on maximum AAA diameter) and risk of AAA rupture. They suggested from their study of 40 patients that there exists a threshold stress of 28 N/cm^2 above which rupture was imminent. However, it has been shown by our laboratory (Raghavan, 1998; Vorp et al., 1998; Wang et al., 2002) and others (Fillinger et al., 2002, 2003; Venkatasubramaniam et al., 2004) that the stress distribution acting on an AAA cannot be adequately described by the Law of Laplace.

More recently, patient-specific FE simulations were performed to compare the peak wall stress between ruptured or symptomatic and non-ruptured AAAs (Fillinger et al., 2002, 2003). Despite utilizing an isotropic tissue constitutive model (Raghavan and Vorp, 2000), and neglecting to include the presence of the ILT-each of which has been shown to influence AAA wall stress (Wang et al., 2002; Vande Geest et al., 2004a; Vande Geest, 2005)—this study found a significant difference between the groups, even when matched for equivalent maximum diameters. The peak stress for ruptured/symptomatic AAAs was 46.8 ± 4.5 N/cm^2 versus 38.1 ± 1.3 N/cm^2 for the electively repaired group ($p = 0.05$).

Kleinstreuer and Li (2006a) recently proposed a patient-specific "severity parameter" to estimate the risk of AAA rupture and provide a threshold value when surgical intervention becomes necessary. This time-dependent severity parameter takes into account the AAA geometry (including size, shape, expansion rate, and amount of ILT), the patient's diastolic pressure, peak AAA wall stress, and stiffness change. The authors calculated the severity parameter for three different AAA, and found the highest value for the one AAA that ruptured and found values for the other two AAA that were electively repaired. While this approach is intriguing, like Eq. (5) for peak stress prediction, its utility would likely break down with more complexly shaped AAA. However, more work is encouraged to fully explore the utility of this approach.

Clearly, the ability to reliably evaluate the susceptibility of a particular AAA to rupture could vastly improve the clinical management of these patients. Though the application of biomechanics in this regard is in its infancy, it is clear from the above studies that it holds much promise. However, validation of biomechanics-based rupture prediction will require carefully-planned retrospective and prospective studies, preferably with synthetic phantoms with know shape and material strength distributions.

7. Conclusion

Current clinical assessment methods to evaluate AAA rupture potential are unreliable. In general, an enlarging AAA is accompanied by both an increase in wall stress and a decrease in wall strength, and both of these parameters are critical and need to taken into account as the instant of AAA rupture occurs when the former exceeds the latter. For these reasons, much attention has been focused over the years on the biomechanics of AAA, particularly with regards to wall stress assessment. The Law of Laplace has been erroneously applied and is not reliable for the analyses of the complexly shaped AAA. Rather, more established and accurate methods such as FE analysis are required. The ILT is an important structure that requires consideration when estimating wall stress or strength of AAA. Constitutive models for AAA wall and ILT continue to be developed. These efforts, along with the advent of more accurate imaging techniques will lead to improved estimates of AAA wall stress and strength distributions *in vivo*. In this author's opinion, the current state-of-the-art is not quite ready for clinical application and patient

management. However, it is believed that reasonable, focused clinical trials could begin within several years, after the continued improvements to constitutive modeling, imaging, segmentation and 3D reconstruction techniques are completed, and rigorous retrospective and prospective validation trials are successfully completed. Once this point is reached, we will reap the benefits of the decades of work detailed here and beyond that will lead to greatly improved diagnosis and management of patients with AAA.

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