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Mechanical Properties of Suprarenal and Infrarenal Abdominal Aorta: Implications for Mouse Models of Aneurysms

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Abstract

Multiple mouse models have been developed to increase our understanding of the natural history of abdominal aortic aneurysms. An advantage of such models is that one can quantify the time course of changes in geometry, histology, cell biology, and mechanics as a lesion develops. One of the most commonly used mouse models yields lesions in the suprarenal abdominal aorta whereas most other models target the infrarenal abdominal aorta, consistent with the clinical observation that nearly all abdominal aneurysms in humans occur in the infrarenal aorta. Understanding reasons for similarities and differences between diverse mouse models and human lesions may provide increased insight that would not be possible studying a single situation alone. Toward this end, however, we must first compare directly the native structure and properties of these two portions of the abdominal aorta in the mouse. In this paper, we present the first biaxial mechanical data and nonlinear constitutive descriptors for the suprarenal and infrarenal aorta in mice, which reveals only subtle mechanical differences despite marked morphological and histological differences. Such data promise to increase our ability to understand and model the natural history of these deadly lesions.

Keywords

AAA; stress; strain; stiffness; murine models

INTRODUCTION

Abdominal aortic aneurysms (AAAs) are currently the 13th leading cause of death in the United States. These lesions typically present in older patients and thus are expected to become increasingly problematic in our aging society. AAAs are characterized by a loss or fragmentation of intramural elastin, apoptosis of smooth muscle cells, inflammation, and remodeled collagen, which together allow a localized dilatation of the wall; in most cases,

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AAAs also associate with atherosclerotic development and the enlarged lumen is the site of intramural thrombus. Despite significant advances in our understanding of both the biomechanics^{1,2} and the pathophysiology^{3,4}, much remains unknown regarding the natural history of these deadly lesions. In particular, our lack of understanding stems largely from the difficulty of obtaining longitudinal information from patients. There is, therefore, a pressing need for more data on the evolving geometry, histology, hemodynamics, and mechanical properties as well as the underlying cellular processes that govern these changes. For this reason, mouse models are increasingly used to study the natural history of AAAs.

Three different mouse models have found increased utility in studying the evolution of AAAs. Because of the importance of the loss of elastin, one model relies on the localized removal of intramural elastin via a short term infusion of elastase within the lumen of the infrarenal aorta^{5,6}. This acute loss of elastin allows the wall to dilate slightly, but it also incites a subsequent inflammatory process that leads to the development of an AAA (usually defined by a 1.5 or more fold increase in diameter). Because of the common association of atherosclerosis with AAAs, another model is based on the application of calcium chloride to the adventitial surface of the infrarenal aorta, which initiates an inflammatory process involving atherosclerotic characteristics and results in the development of a dilated wall⁷. Finally, motivated by roles of atherosclerosis, hypertension, and inflammation in the development of AAAs, another model uses a long-term subcutaneous infusion of angiotensin-II (ANG-II), often in the apolipoprotein-E null (ApoE^{-/-}) mouse^{8,9}. Although ANG-II increases blood pressure, it primarily incites an inflammatory response that often leads to AAAs. Interestingly, however, these ANG-II infusion models yield AAAs in the suprarenal rather than the infrarenal aorta, and dissection often precedes dilatation¹⁰. It appears that this site arises in part from the propensity of atherosclerotic lesions to develop in the suprarenal rather than infrarenal aorta in ApoE^{-/-} mice^{11,12}, but also the different hemodynamics¹³ and possibly wall properties in the suprarenal aorta. For a more extensive review of mouse models of AAAs, see Daugherty and Cassis¹⁴.

A complete understanding of processes that lead to the initiation and enlargement of an AAA must include knowledge of the mechanics of the arterial wall from which the lesion arises. In the case of current mouse models of AAAs, there is thus a need to understand the possibly different mechanics of the suprarenal and the infrarenal abdominal aorta. Indeed, understanding reasons for the differential development of lesions in different mouse models and humans may provide insight not possible by analyzing a single situation. In this paper, we present the first direct comparison of the biaxial mechanical behaviors of these two types of vessels in the mouse and quantify the data using a nonlinear constitutive relation that was recently shown to be useful in describing the mechanical behavior of both aging human abdominal aorta and abdominal aortic aneurysms¹⁵.

METHODS

Specimen Preparation

All animal protocols were approved by the Texas A&M University Institutional Animal Care and Use Committee and followed methods used previously in our laboratory^{16,17}. Briefly, following an overdose of sodium pentobarbital, the abdominal aorta was harvested by gentle dissection from 8 to 12 week old male mice using a dissection microscope. The suprarenal aorta was excised from the diaphragm to between the left and right renal arteries; the infrarenal aorta was similarly excised from between the left and right renal arteries to immediately proximal to the aortic trifurcation. All vessels were trimmed of excess adventitial tissue, cannulated using custom drawn glass pipettes, and secured to the cannulae using 6-0 suture. Branches were ligated with suture to enable the specimen to be pressurized when mounted in a modified version of our computer-controlled biaxial testing device¹⁸.

The testing chamber was filled with a standard phosphate buffered saline solution and maintained at 37°C.

Testing Protocols

The original unloaded outer diameter and axial length of the mounted specimen (i.e., at zero pressure and zero axial force) were measured interactively using a video-microscope and custom LabView software, with each measurement repeated for verification. Following a subsequent acclimation period of 15 minutes at a luminal pressure of 80 mmHg and an axial stretch of 1.5 (i.e., at the mean in vivo stretch determined in pilot studies), the artery was preconditioned at this stretch via 3 cycles of pressurization from 10 to 140 mmHg at ~2 mmHg/sec. This loading rate is consistent with that used in most studies of arterial mechanics and is motivated by the relative strain-rate insensitivity exhibited by most arteries¹⁹. The nearly unloaded outer diameter and axial length were measured again, this time at a pressure of 5 mmHg to prevent the vessel from collapsing; there were typically minimal increases in dimensions relative to measurements taken prior to acclimation and preconditioning. Biaxial data were then collected during cyclic pressurization tests from 10 to 140 mmHg at the same rate and mean in vivo stretch as well as at ~5% above and below this stretch. Finally, biaxial data were collected during cyclic extension tests at different constant pressures of 60, 100, and 140 mmHg. These tests were performed such that the axial force ranged from 0 to 24.5 mN for the suprarenal aorta and from 0 to 6 mN for the infrarenal aorta. These values were selected based on findings during pilot tests, which accounted for the much larger cross-sectional area of the suprarenal aorta. Luminal pressure, axial force, outer diameter, and overall axial length were measured online using a custom LabView program and recorded continually during testing. Finally, note that the unloaded inner diameter, and thus thickness, was measured using a calibrated dissection microscope to image intact rings cut from each end of the specimen prior to cannulation; 2 to 3 measurements around the circumference of each ring were averaged to yield mean values for each specimen.

Data Analysis

The biaxial data were converted to mean circumferential and axial Cauchy stresses using standard formulae¹⁹

$$t_{\theta\theta}^{\text{exp}} = \frac{P^{\text{exp}} a}{h}, \quad t_{zz}^{\text{exp}} = \frac{f^{\text{exp}}}{\pi h(2a+h)}, \quad (1)$$

where a is the inner radius in any loaded state and h is the associated thickness of the wall.

The axial force applied to the artery is given by $f^{\text{exp}} = f_r^{\text{exp}} + \pi a^2 P^{\text{exp}}$, where f_r^{exp} is measured by the force transducer and P^{exp} is measured by the pressure transducer.

We employed a “four fiber family” hyperelastic constitutive model¹⁵ to quantify the measured passive biaxial mechanical behaviors. This model has proven useful in capturing biaxial mechanical responses of diverse mouse carotid arteries^{17,20,21}. The specific form of the strain energy function is

$$W(\mathbf{C}, \mathbf{M}^i) = \frac{c}{2}(I_c - 3) + \sum_{i=1}^4 \frac{c_1^i}{4c_2^i} \left\{ \exp \left[c_2^i (I_4^i - 1)^2 \right] - 1 \right\}, \quad (2)$$

where c, c_1^i are material parameters having units of stress and c_2^i are dimensionless, $I_c = \text{tr} \mathbf{C}$ is the first invariant of the right Cauchy-Green tensor, and $I_4^i = \mathbf{M}^i \cdot \mathbf{C} \mathbf{M}^i$ is the square of the stretch of the i -th collagen fiber family (i.e., $(\lambda^i)^2$). Fiber orientations are defined in the reference configuration by unit vectors $\mathbf{M}^i$, which depend on angles α_o^i defined between fiber and axial directions. Axial and circumferential fibers were thus defined at $\alpha_o^1=0$ and $\alpha_o^2=90$ degrees, respectively, while symmetrically oriented diagonal fibers were accounted for via a single parameter, $\alpha_o^3 = -\alpha_o^4 = \alpha_o$. Note that

$$I_4^d = (\lambda^{i=3,4})^2 = \lambda_z^2 \cos^2 \alpha_o + \lambda_\theta^2 \sin^2 \alpha_o, \quad (3)$$

where the superscript d denotes “diagonal.” These two families of collagen are typically regarded as mechanically equivalent, hence $c_1^3 = c_1^4 \equiv c_1^{3,4}$, $c_2^3 = c_2^4 \equiv c_2^{3,4}$. This overall model thus requires estimation of eight unknown parameters ($c, c_1^1, c_2^1, c_1^2, c_2^2, c_1^{3,4}, c_2^{3,4}, \alpha_o$) that describe the passive mechanical behavior. Pilot studies suggested that there was little active response in the phosphate buffered saline, hence we used a passive constitutive model alone.

Assuming a 2-D state of stress within the central region of thin-walled biaxially tested arteries, the deformation gradient tensor has the form $\mathbf{F} = \text{diag}(\lambda_r, \lambda_\theta, \lambda_z)$. Circumferential and axial stretch ratios during finite inflation and extension testing were calculated via

$$\lambda_\theta = \frac{r_{mid}}{R_{mid}}, \quad \lambda_z = \frac{l}{L}, \quad (4)$$

where $r_{mid} = (a + b)/2$ and $R_{mid} = (A + B)/2$ represent loaded and unloaded mid-wall radii and, similarly, l and L represent loaded and unloaded axial length; here a and b denote loaded inner and outer radii whereas A and B denote associated unloaded radii. Assuming incompressibility during transient loading, the inner deformed radius was computed from

experimentally measurable quantities via $a = \sqrt{b^2 - \bar{V}/\pi l}$, where $\bar{V}$ denotes mean wall volume with $V = \pi (B^2 - A^2)L$. Incompressibility also requires that $\lambda_r = 1/(\lambda_z \lambda_\theta)$.

For a plane state of stress ($t_{rr} \approx 0$), equation (2) yields theoretically calculated Cauchy stresses of the form

$$\begin{aligned} t_{\theta\theta}^{th} &= c \left(\lambda_\theta^2 - \frac{1}{\lambda_z^2 \lambda_z^2} \right) + c_1^2 (\lambda_\theta^2 - 1) \exp \left[c_2^2 (\lambda_\theta^2 - 1)^2 \right] \lambda_\theta^2 + 2c_1^{3,4} (I_4^d - 1) \exp \left[c_2^{3,4} (I_4^d - 1)^2 \right] \lambda_\theta^2 \sin^2 \alpha_o, \\ t_{zz}^{th} &= c \left(\lambda_z^2 - \frac{1}{\lambda_\theta^2 \lambda_z^2} \right) + c_1^1 (\lambda_z^2 - 1) \exp \left[c_2^1 (\lambda_z^2 - 1)^2 \right] \lambda_z^2 + 2c_1^{3,4} (I_4^d - 1) \exp \left[c_2^{3,4} (I_4^d - 1)^2 \right] \lambda_z^2 \cos^2 \alpha_o. \end{aligned} \quad (5)$$

Best-fit values of the unknown parameters in equation (2) were determined using a nonlinear least squares minimization of the error e between normalized theoretically predicted (th) and experimentally inferred (exp) applied loads, namely

$$e = \sum_{i=1}^N \left[\left(\frac{P^{th} - P^{exp}}{P^{avg}} \right)_i^2 + \left(\frac{f^{th} - f^{exp}}{f^{avg}} \right)_i^2 \right], \quad (6)$$

where N is the total number of data points (i.e., equilibrium configurations) for all experimental protocols combined for each specimen and avg denotes the overall average value. The error e was minimized using the built-in function *lsqnonlin* in MATLAB, subject to physical constraints that $c, c_1^i, c_2^i \geq 0$ and $0 \leq \alpha_0 \leq \pi/2$ due to the symmetry of the diagonal fibers.

Histology

At the completion of mechanical testing, all vessels were fixed in 4% formalin in an unloaded state for 1 hour, immersed in a cryoprotectant (30% sucrose) overnight, and placed in optimum cutting temperature medium in 2-methylbutane cooled with liquid nitrogen and stored at -80°C . Frozen samples were sectioned at 5 microns and stained with either Verhoeff van Gieson (VVG) to identify elastin or hematoxylin and eosin (H&E) to identify cell nuclei and overall morphology. Elastin area fractions were determined using a method of thresholding described previously¹⁷ and were based on one cross-section per sample.

Statistics

Statistical significance was evaluated using either an unpaired Student's t-test or an Analysis of Variance (with $n = 6$ for suprarenal and $n = 6$ for infrarenal specimens taken from separate animals), with significance taken at a level $p < 0.05$.

RESULTS

Biaxial data (i.e., pressure – diameter and axial force – pressure responses at multiple fixed axial stretches) revealed slightly different characteristic behaviors for the suprarenal and the infrarenal aorta (Figures 1 and 2, respectively). For increased clarity, a reduced number of data (symbols) are shown in these figures; note, too, that the theoretical fits to data achieved using equations 1, 5, and 6 are also shown (solid curves), with associated best-fit values of the model parameters listed in Table 1 for all 12 specimens. Two conspicuous differences in behavior are the more sigmoidal pressure – diameter response exhibited by the suprarenal aorta and the larger value of axial force needed to extend the suprarenal aorta over comparable axial stretches. The former is sometimes ascribed to a higher elastin-to-collagen ratio; the latter appeared to be due simply to the greater cross-sectional area of the suprarenal aorta (which can be computed via $\pi h(2a + h)$). The best-fit value of the parameter c , which is thought to model the elastin-dominated portion of the wall¹⁵, was statistically higher for the suprarenal than the infrarenal aorta (26.09 versus 14.97 kPa, respectively; Table 1), also consistent with a greater contribution of elastin to the overall behavior. Indeed, VVG images (Figure 3, left) suggested that the suprarenal aorta tended to have an additional musculo-elastic fascicle (i.e., layer of smooth muscle bounded by elastic lamellae), though not in all cases. Moreover, the elastic lamellae appeared to be thicker in the suprarenal aorta. Hence, although wall thickness at in vivo conditions differed by only 15% (43.7 and 37.9 microns, respectively; Table 2), the percentage of the wall occupied by elastin was 36% higher in the suprarenal aorta (38 and 28%, respectively, which was statistically different based on VVG images). The deformed luminal radius was also significantly larger in the suprarenal aorta than in the infrarenal aorta, as, for example, $a = 488$ microns versus $a = 305$ microns at a common pressure of 80 mmHg and the individual in vivo axial stretches. Interestingly, despite differences in cross-sectional area and percent

elastin, the in vivo stretches (Figure 4) were remarkably similar for the two types of vessels: mean values were 1.50 and 1.49 for suprarenal and infrarenal aorta, respectively (Figure 4 and Table 2), which were not statistically different. Other information, such as animal age and weight and unloaded geometry, is also listed in Table 2.

When the biaxial data were plotted as Cauchy stress – stretch, the behaviors of both portions of the abdominal aorta appeared to be characteristically nonlinear, perhaps exponential (Figure 5). In these plots, the symbols again represent culled data, but the solid curves now represent predictions rather than fits because pressure/force data were used in the nonlinear regressions. Indeed, with the exception of the parameter c , the best-fit parameters were comparable for the two types of vessels as well (Table 1). Because it is difficult to compare overall behaviors based on values of multiple parameters in a nonlinear model, consider the strain energy predicted to be stored, per unit reference volume, at the same levels of pressure (from 60 to 120 mmHg) and the individual in vivo axial stretch (Figure 6a). As it can be seen, the overall stiffness of the suprarenal aorta tended to be higher than that of the infrarenal aorta, especially at higher pressures. This conclusion was supported by a direct comparison of circumferential stress – stretch behaviors at the in vivo stretch (Figure 6b). These differences were not statistically significant, however, at a $p < 0.05$ (ANOVA).

DISCUSSION

Aneurysms arise in the human abdominal aorta due to dramatic localized changes in the microstructure of the wall, which in turn alter biomechanical properties significantly^{1,15,22}. Despite the plethora of papers investigating the biology, and implicating the mechanics, of AAAs in the mouse^{5,6,7,8,9,10,14}, there has been almost no attention heretofore to the biaxial mechanical properties of the aortic wall, including possible differences between the suprarenal and infrarenal abdominal aorta that may help explain the different types of aneurysms that occur in common mouse models.

Amirbekian et al.¹³ reported an important comparison of hemodynamic conditions in the mouse suprarenal and infrarenal aorta, the latter of which was contrasted qualitatively to conditions in the human. Despite similar mean blood velocities in the suprarenal and infrarenal aortas, both the mean (15.3 versus 7.5 ml/min) and the maximum (49.3 versus 21.6 ml/min) volumetric flowrate was much lower in the latter because of the high flow to the kidneys. More importantly, however, they found that the infrarenal aorta in the mouse does not experience the flow reversal that is seen in the human infrarenal aorta, which in turn is thought to yield oscillatory shear stresses that may contribute to the development of aneurysms. Given that the suprarenal aorta in the mouse similarly did not experience flow reversal, it was suggested that further studies were needed to determine its susceptibility to aneurysms in the ANG-II infusion model, including fluid-solid interaction (FSI) computations. Such studies obviously require detailed information on multiaxial wall properties, which the present paper provides for the first time. In contrast, with regard to wall properties, Amirbekian and colleagues merely compared percent distensibility over the cardiac cycle in these two segments of the aorta ($72 \pm 26\%$ and $63 \pm 18\%$ in the suprarenal and infrarenal aorta, respectively, which were not significantly different). Goergen et al.⁶ similarly reported maximum cyclic Green strains during the cardiac cycle of $20.8 \pm 4.2\%$ and $19.4 \pm 2.5\%$ in the mouse suprarenal and infrarenal aorta, respectively. Together, these reports suggest that suprarenal and infrarenal aortas have a similar structural stiffness in the mouse, which was suggested to be significantly less than that in the human¹³.

In vivo structural stiffness depends on the material stiffness, thickness of the wall, axial prestretch, and perivascular support. Of these, only perivascular support was not measured herein. As revealed by Figure 4, the axial prestretch was similar in the suprarenal and

infrarenal aorta (about 1.5). This finding is similar to the report by Guo and Kassab²³ that the proximal and distal abdominal aorta have similar axial prestretches (~1.6). These investigators also reported that the circumferential “modulus” was similar at these two sites, but the numerical values must be viewed cautiously because the data were inappropriately reduced assuming linear elastic behavior. Our findings are nonetheless similar, in that the suprarenal aorta tended to be slightly stiffer overall, but not significantly so. Wagenseil et al.²⁴ also reported axial prestretches and biaxial stress-stretch data for the abdominal aorta from the mouse, but they did not document which portion of the aorta was used in their study. Their reported value for axial prestretch was also ~1.6. Whereas our value was inferred from cross-over points in axial force – extension tests at multiple pressures (Figure 4), both Guo and Kassab and Wagenseil and colleagues measured this value based on the degree of retraction at excision. Given that the cross-over point is generally regarded as a useful estimate of in vivo stretch²⁵, it is not clear whether our results near 1.5 differ from these two reports because of our different experimental approach, the gentle removal of loose perivascular tissue prior to our in vitro testing, the anesthetics used, the different strains of mice, or so forth. Nevertheless, it is clear that the in vivo axial prestretch does not differ significantly from the suprarenal to the infrarenal aorta. Wagenseil and colleagues did not attempt to quantify the measured aortic mechanical behavior, hence it is not possible to compare results directly. Their circumferential Cauchy stress – stretch plots appear to be comparable to the present results, however, with stresses on the order of 200 kPa at circumferential stretches about 1.6 (cf. Figure 6).

Data that compare the suprarenal and infrarenal abdominal aorta histologically also appear to be scant. A notable example is the work by Bunce²⁶, who compared most large arteries in the dog. Notwithstanding expected differences in the number of musculo-elastic fascicles in the thicker walled dog aorta, a conspicuous difference between the abdominal aorta in the mouse and the dog is the more regular musculo-elastic fascicles in the mouse. That is, the infrarenal aorta, and to a lesser extent the suprarenal aorta, in the dog has a greater density of elastin in the outer one-third of the media, similar to that seen in the dog left common carotid artery. This single example of species-to-species differences reminds us of the need for caution in extrapolating results from mice to men, though a detailed understanding of the reasons for such differences may provide yet increased insight that can be helpful in understanding the human condition. As seen in Figure 3, VVG staining suggested that the suprarenal mouse aorta typically had ~4 musculo-elastic fascicles whereas the infrarenal aorta typically had ~3 fascicles. These findings are consistent with the report by Goergen et al.²⁷, who noted that the suprarenal aorta contains about 50% more elastin than does the infrarenal aorta. Our data (38% versus 28%, or 36% different) are comparable with their findings. Indeed, the higher best-fit value of the model parameter c (Table 1) is similarly consistent with this finding.

In summary, the present study quantified, for the first time, the mean biaxial mechanical behavior of the suprarenal and infrarenal abdominal aorta in young mature male mice. The same constitutive relation that has proven useful in describing the behavior of the human infrarenal abdominal aorta and human AAAs was found to fit data from mice as well (cf. Figures 1 and 2). Indeed, even most of the best-fit parameters reported herein (Table 1) are comparable to results for young humans (mean values of which are¹⁵

$\{c, c_1^1, c_2^1, c_1^2, c_2^2, c_1^{3,4}, c_2^{3,4}, \alpha_o\} = \{19.34 \text{ kPa}, 2.37 \text{ kPa}, 1.48, 4.70 \text{ kPa}, 0.59, 11.87 \text{ kPa}, 0.87, 41.8 \text{ deg}\}$). Nevertheless, it was found that, in comparison to the suprarenal aorta, the infrarenal aorta had a slightly lower material stiffness, which when combined with its lower thickness and similar axial prestretch might suggest a lower structural stiffness. Yet, such a conclusion would be in contrast to the aforementioned in vivo measurements of distensibility and cyclic strain^{6,13}, thus suggesting possible differences in perivascular tethering above and below the

level of the renal arteries, which was not evaluated herein. Albeit often not considered in most biomechanical models, there is clearly a need to understand better and then account for aortic perivascular tethering (which is not axisymmetric) in future models of the aorta and the subsequent development of aneurysms. Indeed, our results necessarily yielded mean properties since diameters were measured anterior to posterior, which does not allow one to delineate possible circumferential differences due to possible perivascular support on the posterior aspect. Similarly, we focused on responses within the central region of each specimen, away from branches. There is also a need to understand possible regional heterogeneities associated with branch sites. Finally, we focused on young male mice. There is a need to quantify the effects of aging, which could differ in these two regions of the abdominal aorta, and to quantify possible gender related differences, particularly because AAAs tend to occur more often in males than females. Regardless, it is hoped that the present novel results on aortic material behaviors will provide a foundation for and stimulate much needed modeling of aneurysmal progression in diverse mouse models of AAAs.

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References

1. Vorp DA. Biomechanics of abdominal aortic aneurysm. *J Biomech.* 2007; 40:1887–1902. [PubMed: 17254589]
2. Duo MM, Dalman RL. Hemodynamic influences on abdominal aortic aneurysm disease: Application of biomechanics to aneurysm pathophysiology. *Vasc Pharmacol.* 2010; 53:11–21.
3. Shimizu K, Mitchell RN, Libby P. Inflammation and cellular immune responses in abdominal aortic aneurysms. *Arterioscler Thromb Vasc Biol.* 2006; 26:987–994. [PubMed: 16497993]
4. Thompson RW, Curci JA, Ennis TL, Mao D, Pagano MB, Pham CTN. Pathophysiology of abdominal aortic aneurysms: Insights from the elastase-induced model in mice with different genetic background. *Ann NY Acad Sci.* 2006; 1085:59–73. [PubMed: 17182923]
5. Ailawadi G, Moehle CW, Pei H, Walton SP, Yang Z, Kron IL, Lau CL, Owens GK. Smooth muscle phenotypic modulation is an early event in aortic aneurysms. *J Thorac Cardiovasc Surg.* 2009; 138:1392–1399. [PubMed: 19931668]
6. Goergen CJ, Azuma J, Barr KN, Magdefessel L, Kallop DY, Gogineni A, Grewall A, Weimer RM, Connolly AJ, Dalman RL, Taylor CA, Tsao PS, Greve JM. Influences of aortic motion and curvature on vessel expansion in murine experimental aneurysms. *Arterioscler Thromb Vasc Biol.* 2011; 31:270–279. [PubMed: 21071686]
7. Sheth RA, Maricevich M, Mahmood U. In vivo optical molecular imaging of matrix metalloproteinase activity in abdominal aortic aneurysms correlates with treatment effects on growth rate. *Atherosclerosis.* 2010; 212:181–187. [PubMed: 20542274]
8. Cassis LA, Gupta M, Thayer S, Zhang Z, Charnigo R, Howatt DA, Rateri DL, Daugherty A. Ang II infusion promotes abdominal aortic aneurysms independent of increased blood pressure in hypercholesterolemic mice. *Am J Path.* 2009; 296:H1660–1665.
9. Deguchi JO, Huang H, Libby P, Aikawa E, Whittaker P, Sylvan J, Lee RT, Aikawa M. Genetically engineered resistance for MMP collagenases promotes abdominal aortic aneurysm formation in mice infused with angiotensin-II. *Lab Invest.* 2009; 89:315–326. [PubMed: 19153555]
10. Saraff K, Babamusta F, Cassis LA, Daugherty A. Aortic dissection precedes formation of aneurysms and atherosclerosis in angiotensin-II infused, apolipoprotein E-deficient mice. *Arterioscler Thromb Vasc Biol.* 2003; 23:1621–1626. [PubMed: 12855482]
11. Nakashima Y, Plump AS, Raines EW, Breslow JL, Ross R. ApoE deficient mice develop lesions of all phases of atherosclerosis throughout the arterial tree. *Arterioscler Thromb.* 1994; 14:133–140. [PubMed: 8274468]

12. Hayenga HN, Trache A, Trzeciakowski J, Humphrey JD. Regional atherosclerotic plaque properties in ApoE^{-/-} mice measured by atomic force, immunofluorescence, and light microscopy. *J Vasc Res.* 2011 (in press).
13. Amirbekian S, Long RC, Consolini MA, Suo J, Willett NJ, Fielden SW, Giddens DP, Taylor WR, Oshinski JN. In vivo assessment of blood flow patterns in abdominal aorta of mice with MRI: implications for AAA localization. *Am J Physiol.* 2009; 297:H1290–1295.
14. Daugherty A, Cassis LA. Mouse models of abdominal aortic aneurysms. *Arterioscler Thromb Vasc Biol.* 2004; 24:429–434. [PubMed: 14739119]
15. Ferruzzi J, Vorp DA, Humphrey JD. A structurally-motivated constitutive relation for the biaxial mechanical behavior of human aorta and abdominal aortic aneurysms. *J Roy Soc Interface.* 2011; 8:435–450. [PubMed: 20659928]
16. Dye WW, Gleason RL, Wilson E, Humphrey JD. Biaxial biomechanical behavior of carotid arteries in two knockout models of muscular dystrophy. *J Appl Physiol.* 2007; 103:664–672. [PubMed: 17525297]
17. Eberth JF, Taucer AI, Wilson E, Humphrey JD. Mechanics of carotid arteries from a mouse model of Marfan Syndrome. *Annls Biomed Engr.* 2009; 37:1093–1104.
18. Gleason RL, Grey S, Wilson E, Humphrey JD. A multiaxial computer-controlled organ culture and biomechanical device for mouse carotid arteries. *ASME J Biomech Engr.* 2004; 126:787–795.
19. Humphrey, JD. *Cardiovascular Solid Mechanics: Cells, Tissues, and Organs.* Springer; NY: 2002.
20. Gleason RL, Dye WW, Wilson E, Humphrey JD. Quantification of the mechanical behavior of carotid arteries from wild-type, dystrophin-deficient, and sarcoglycan-delta knockout mice. *J Biomech.* 2008; 41:3213–3218. [PubMed: 18842267]
21. Wan W, Yanagisawa H, Gleason RL. Biomechanical and microstructural properties of common carotid arteries from fibulin-5 null mice. *Annl Biomed Engr.* 2010; 38:3605–3617.
22. Humphrey JD, Taylor CA. Intracranial and abdominal aortic aneurysms: Similarities, differences, and need for a new class of computational models. *Ann Rev Biomed Engr.* 2008; 10:221–246.
23. Guo X, Kassab GS. Variation of mechanical properties along the length of the aorta in C57bl/6 mice. *Am J Physiol.* 2003; 285:H2614–2622.
24. Wagenseil JE, Nerurkar NL, Knutsen RH, Okamoto RJ, Li DY, Mecham RP. Effects of elastin haploinsufficiency on the mechanical behavior of mouse arteries. *Am J Physiol.* 2005; 289:H1209–1217.
25. Humphrey JD, Eberth JF, Dye WW, Gleason RL. Fundamental role of axial stress in compensatory adaptations by arteries. *J Biomech.* 2009; 42:1–8. [PubMed: 19070860]
26. Bunce, DFM. *Atlas of Arterial Histology.* Warren H. Green, Inc; St. Louis, MO: 1974.
27. Goergen CJ, Barr KN, Huynh DT, Eastham-Anderson JR, Choi G, Hedehus M, Dalman RL, Connolly AJ, Taylor CA, Tsao PS, Greve JM. In vivo quantification of murine aortic cyclic strain, motion, and curvature: Implications for abdominal aortic aneurysms. *J Mag Res Imag.* 2010; 32:847–858.

Figure 1. Representative results from pressure – diameter tests at three different fixed axial stretches for the suprarenal abdominal aorta. A reduced number of data points (symbols) are shown for clarity; also shown are fits to data (solid lines) using equation 5.

Figure 2. Representative results from pressure – diameter tests at three different fixed axial stretches for the infrarenal abdominal aorta. A reduced number of data points (symbols) are shown for clarity; also shown are fits to data (solid lines) using equation 5.

Figure 3. Histological images from representative suprarenal (top) and infrarenal (bottom) abdominal aorta from the mouse. Specimens stained with VVG (which reveals elastin as black) are shown on the left and those stained with H&E (which reveals cell nuclei in blue and overall tissue morphology in pink) are shown on the right.

Figure 4.

Results from axial force – extension tests at three different fixed luminal pressures for the suprarenal (top) and infrarenal (bottom) aorta. The “cross-over” points (vertical lines) estimate the in vivo axial stretch, mean values of which were 1.51 and 1.49 for the suprarenal and infrarenal aorta, respectively, which were not statistically different.

Figure 5. Experimentally inferred (symbols) and theoretically predicted (solid curves) circumferential Cauchy stress – stretch responses for the supracranial (top) and infrarenal (bottom) aorta during cyclic pressurization tests at three different fixed axial stretches.

Figure 6.

Top: Computed values (mean $\pm$ standard deviation) of the strain energy stored in supracranial (circles) and infrarenal (triangles) aorta at multiple values of luminal pressure and the individual in vivo axial stretch. An ANOVA revealed no significant differences despite a trend for the supracranial aorta to store more energy at the same pressure. Bottom: Also shown are mean predicted Cauchy stress – stretch responses at the in vivo stretch for both the supracranial (circles) and the infrarenal (triangles) aorta.

Table 1

Best-fit values of model parameters (equation 2) for all 6 suprarenal and 6 infrarenal aortic specimens, with mean values $\pm$ standard deviations

Vessel #	AXIAL		CIRCUMFERENTIAL		DIAGONAL	
	c (kPa)	c_1(kPa)	c_2	c_1(kPa)	c_2	Angle(deg)
SUPRA						
1	35.47	0.02	1.32	4.02	0.51	3.44
2	17.56	13.40	1.23E-08	4.68	0.45	10.98
3	42.64	13.64	0.17	3.37	0.64	0.84
4	16.04	1.60	1.06	1.53	2.47	13.64
5	20.12	14.12	0.41	2.99	0.48	8.12
6	24.72	24.56	0.06	4.18	0.32	0.59
INFRA						
1	13.65	6.18	0.19	7.91	0.16	1.68
2	9.14	4.65	0.25	8.14	0.47	0.67
3	6.89	15.13	0.01	1.54	0.32	1.63
4	10.56	2.04	0.97	2.36	0.40	2.45
5	26.67	11.96	0.29	4.70	1.33	0.65
6	22.90	9.21	0.77	3.35	0.64	1.13
Mean Supra	26.09 $\pm$ 10.71	11.22 $\pm$ 9.11	0.50 $\pm$ 0.55	3.46 $\pm$ 1.12	0.81 $\pm$ 0.82	6.27 $\pm$ 5.47
Mean Infra	14.97 $\pm$ 8.00	8.19 $\pm$ 4.86	0.41 $\pm$ 0.37	4.67 $\pm$ 2.81	0.55 $\pm$ 0.41	1.37 $\pm$ 0.69
						1.74 $\pm$ 1.06
						40.02 $\pm$ 5.69
						38.62 $\pm$ 1.95

Table 2

Mean values $\pm$ standard deviations of relevant data on age, weight, and geometry of the suprarenal ($n = 6$) and infrarenal ($n = 6$) aorta

Vessel	Age* (wks)	Weight(g)	Axial Stretch(--)	Length* (mm)	Outer Diameter* (μ m)	Wall Thickness* (μ m)	a* (μ m)@80 mmHg	h* (μ m)@80 mmHg
Supra	8.9 $\pm$ 0.9	22.4 $\pm$ 1.9	1.51 $\pm$ 0.10	4.50 $\pm$ 0.80	787 $\pm$ 43	100.1 $\pm$ 11.5	488 $\pm$ 21	43.7 $\pm$ 3.6
Infra	9.7 $\pm$ 0.8	21.8 $\pm$ 2.5	1.49 $\pm$ 0.16	3.35 $\pm$ 0.65	523 $\pm$ 46	88.7 $\pm$ 9.1	305 $\pm$ 34	37.9 $\pm$ 5.1

Note that the length, outer diameter, and thickness are given in the unloaded configuration whereas inner radius a and wall thickness h are given at the near in vivo condition.

An * indicates statistically different values for the suprarenal and infrarenal aortas at a level $p < 0.05$.