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A mechanistic model on the role of “radially-running” collagen fibers on dissection properties of human ascending thoracic aorta

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Abstract

Aortic dissection (AoD) is a common condition that often leads to life-threatening cardiovascular emergency. From a biomechanics viewpoint, AoD involves failure of load-bearing microstructural components of the aortic wall, mainly elastin and collagen fibers. Delamination strength of the aortic wall depends on the load-bearing capacity and local micro-architecture of these fibers, which may vary with age, disease and aortic location. Therefore, quantifying the role of fiber micro-architecture on the delamination strength of the aortic wall may lead to improved understanding of AoD. We present an experimentally-driven modeling paradigm towards this goal. Specifically, we utilize collagen fiber microarchitecture, obtained in a parallel study from multi-photon microcopy, in a predictive mechanistic framework to characterize the delamination strength. We then validate our model against peel test experiments on human aortic strips and utilize the model to predict the delamination strength of separate aortic strips and compare with experimental findings. We observe that the number density and failure energy of the radially-running collagen fibers control the peel strength. Furthermore, our model suggests that the lower

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Appendix. Supporting information: Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.jbiomech.2014.01.005>.

delamination strength previously found for the circumferential direction in human aorta is related to a lower number density of radially-running collagen fibers in that direction. Our model sets the stage for an expanded future study that could predict AoD propagation in patient-specific aortic geometries and better understand factors that may influence propensity for occurrence.

Keywords

Peel force; Aorta; Dissection; Collagen fibers; Fiber bridge failure model

1. Introduction

Aortic dissection, characterized by delamination of the aortic wall layers, is one of the most common forms of aortic disease (Jondeau and Boileau, 2012; Lu et al., 2012; Matsushita et al., 2012; Takigawa et al., 2012). It usually begins with a tear of the intimal layer in the ascending thoracic aorta (ATA), which permits blood to enter the wall, split the media, and create a false lumen that can reenter the true lumen anywhere along the course of the aorta or exit through the adventitia causing frank rupture. The occurrence of aortic dissection is typically 5–30 cases per million of the population annually, while the mortality rate during first 24–48 h in patients not treated surgically is 74% (Davies et al., 2002; Knipp et al., 2007).

A possible mechanism for aortic dissection is the occurrence of mechanical wall stresses in excess of the delamination strength between the aortic wall layers. This strength most likely primarily depends on the transmural content and arrangement of elastin and collagen fibers, which are the principal load-bearing elements of the aortic wall. Several studies have been carried out to gain insight into the dissection propagation in aortic tissue. Peeling experiments have been performed on human abdominal aorta (Sommer et al., 2008) and human carotid artery (Tong et al., 2011) to quantify fracture energy required for dissection. Gasser and Holzapfel (2006) developed a nonlinear continuum framework to investigate the dissection failure in the arterial wall during a peeling experiment. However, these studies do not attempt to relate the fracture energy with the load bearing components of the artery wall. Recently, Pasta et al. (2012) quantified the delamination strength (S_d) of non-aneurysmal and aneurysmal human ATA by conducting peel tests on tissue samples that were artificially dissected across the medial plane. The induced peel tension reached a plateau when the dissection started propagating and the average mean value of this plateau was taken as S_d . Scanning electron microscopy images of the dissected planes revealed the presence of broken and disrupted elastin and collagen fibers. Moreover, the experimental delamination curves exhibited considerable oscillations leading to the conclusion that these fibers may have acted as “bridges” between the delaminating layers of ATA, resisting dissection and contributing towards S_d .

The aim of the current study is to present a theoretical framework that will relate S_d as obtained from the previously reported peel tests by Pasta et al. (2012) to the biomechanical properties of collagen fiber bridges. We will also make use of state-of-the-art multi-photon microscopy analysis in the longitudinal–radial (LONG–RAD) and circumferential–radial (CIRC–RAD) planes of human ATA wall tissue that exhibits the presence of “radially-

running” collagen fibers that may act as fiber bridges (Tsamis et al., 2013). We have formulated a fiber bridge failure model that incorporates the biomechanical properties of collagen, and have calibrated the model parameters using peel experiments on LONG-oriented ATA specimens from two patients. Finally, we have predicted the S_d of the CIRC-oriented ATA for the same patients using these model parameters and compared our results with experimental findings. In the future, our validated fiber bridge failure model can be used to seek associations between resistance to delamination of dissected aortic tissue and failure energy of collagen fiber bridges. This analysis will be further advanced towards identification and measurement of biological markers associated with potential decrease in the failure energy of collagen fiber bridges in presence of aneurysm and subsequent propensity of the tissue to dissect.

2. Methods

We have developed a predictive mechanistic framework to characterize the delamination strength of human non-aneurysmal (control, CTRL) ATA tissues from the experimentally determined micro-architecture and biomechanical properties of radially-running collagen fibers. The specimens were collected from organ donor/recipient subjects with tricuspid aortic valve according to guidelines of our Institutional Review Board and Center for Organ Recovery and Education. We used results from a separate multi-photon microcopy analysis of the fiber microarchitecture in the LONG–RAD and CIRC–RAD planes of these tissues (Tsamis et al., 2013). As depicted in the schematic flowchart of Fig. 1, the developed model was first calibrated using peel experiments of LONG-oriented ATA specimens from two patients (Pasta et al., 2012) and the number of radially-running collagen fibers in the LONG–RAD plane (N_{LR}). Finally, we used the model and the radially-running collagen fibers in the CIRC–RAD plane (N_{CR}) to predict the delamination strength of the CIRC-oriented ATA for the same patients. Here, we describe the method to count the number of radially-running fibers and the theoretical model development as well as the finite element implementation.

2.1. Characterization of radially-running collagen fibers using multi-photon microcopy

Tsamis et al. (2013) recently used state-of-the-art multi-photon microcopy (Cahalan et al., 2002; Jiang et al., 2011; Konig et al., 2005) to observe the elastin and collagen fiber arrangements in the LONG–RAD and CIRC–RAD planes of human CTRL ATA tissue specimens that were artificially dissected along the medial plane in the previous study by Pasta et al. (2012). Their analysis of these images provided quantitative fiber micro-architectural characteristics in the LONG–RAD and CIRC–RAD planes of aortic tissue near the plane of artificial dissection (Tsamis et al., 2013). From these images, we extracted the number density of radially-running fiber bridges (Fig. 2) for two separate specimens from two patients, see Table 1. A radially-running fiber bridge is defined as either a radially-oriented fiber component or a radially-oriented segment of a fiber owing to its undulation about LONG or CIRC axis. In short, this data was obtained by manually counting the number of fiber bridges within a distance of 100 μm (1/5 of the image height) from the delaminated plane for all specimens of ATA for both adventitial–medial and medial–intimal delaminated halves in the LONG–RAD and CIRC–RAD planes, and by converting the

number of fiber bridges into a number density (number of radially-running components/mm), see Table 1.

2.2. Theoretical model for peel test of ATA tissue

Propagation of delamination or dissection in an elastic solid requires an expenditure of energy supplied by its potential energy, a combination of energy due to applied loads, and strain energy arising from deformation of the body (Fig. 3). Using this concept, we can quantify the peel tension T_{peel} as

$$T_{peel} = \frac{w}{2(\lambda - \cos\theta)} \left[G_c + h \int_1^\lambda d\Psi \right], \quad (1)$$

where λ is the stretch of the peeling arms, θ denotes the angle between the delamination plane and direction of applied tension, and w and h stand for the width and thickness of the peeling arm, respectively. ψ is the strain energy function that embodies the constitutive behavior of the material and G_c is the fracture toughness of the material, or the energy required for a dissection to propagate by a unit distance. G_c depends on the structural features of the material, i.e., on different microstructural components present in the vicinity of the dissection, such as collagen and elastin, as well as their mechanical properties.

When a dissection propagates, it will cause failure in the radially-running fibers bridging the delamination plane. While a continuum description suffices to deribe the matrix failure, the fiber bridges fail sequentially with the propagation of dissection. Denoting the energy required for a fiber bridge to fail as U_f , the fracture toughness can thus be written as

$$G_c = G_{matrix} + nU_f, \quad (2)$$

where G_{matrix} is the fracture toughness of the matrix material and n is the number density of the fiber bridges ($\#/m^2$). As the external loading increases, individual fibers can stretch to a maximum fiber force F_{max} where they either break or debond from the surrounding soft matrix ultimately resulting in zero fiber force. This occurrence denotes failure of the bridge and complete separation of the delaminating planes (Fig. 3(d)) (Dantluri et al., 2007). The area under the load–displacement curve is equivalent to U_f . In absence of direct experimental observations, we present a phenomenological model of fiber bridge failure embodying these events.

The initial loading response of a fiber is modeled using a nonlinear exponential force–separation law, which is typical for collagen fibers (Gutsmann et al., 2004), while the post-peak behavior is assumed to be linear. We have assumed that the visco-elastic effect in the force–displacement behavior of collagen fiber is negligible. The fiber force F depends on the separation between the ends of the fiber Δ_f through the following relationship

$$F = \begin{cases} A[\exp(B\Delta_f) - 1] & \text{if } \Delta_f \leq \Delta_p \\ F_{max} \left(\frac{\Delta_{max} - \Delta_f}{\Delta_{max} - \Delta_p} \right) & \text{if } \Delta_f > \Delta_p \end{cases}, \quad (3)$$

with A and B denoting two shape parameters that control the nonlinear rising response of the fiber. The linear drop is controlled by Δ_{max} , the maximum separation at which bridging force becomes zero, and the separation at the maximum force, Δ_p . The energy required for complete fiber bridge failure is given by the area under force–separation curve, i.e.

$$U_f = \frac{F_{max}}{B} \frac{(\exp(B\Delta_p) - B\Delta_p)}{(\exp(B\Delta_p) - 1)} + \frac{1}{2} F_{max} (\Delta_{max} - \Delta_p), \quad (5)$$

where F_{max} denotes the maximum force a fiber bridge can sustain. Shape of our bridge failure model thus depends on four parameters: A , B , F_{max} (or Δ_p), and Δ_{max} .

2.3. Finite element implementation and simulation procedure

A custom nonlinear finite element code incorporating energetic contribution from a propagating dissection was developed in house. Numerical simulations of a peel test on ATA strips were performed on a 2D model with $\theta = 90^\circ$, non-dissected length $L_0 = 20 \text{ mm}$, and applied displacement $\delta = 20 \text{ mm}$ on each arm (Fig. S1), as reported in experiments (Pasta et al., 2012). Resulting finite element model was discretized with 11,000 four-noded quadrilateral elements resulting in 12,122 nodes. The constitutive model proposed by Raghavan and Vorp (2000) was adopted for the tissue. Material parameters for the constitutive model were taken as $\alpha = 11 \text{ N cm}^{-2}$ and $\beta = 9 \text{ N cm}^{-2}$ for LONG ATA specimen and $\alpha = 15 \text{ N cm}^{-2}$ and $\beta = 4 \text{ N cm}^{-2}$ for CIRC ATA specimen (Vorp et al., 2003). We considered the mid-plane in-between two arms to be the potential plane of peeling. Accordingly, fiber bridges were explicitly placed on this plane with a uniform spacing, and modeled utilizing the constitutive behavior described by bridge failure model (see the inset of Fig. S1). Also, contribution of matrix towards failure response of the ATA tissue was taken to be negligible, hence $G_{matrix} = 0$. As the dissection spanned the entire width w of the specimen, the fiber bridges were reported in terms of numbers N per unit length in the dissection propagation direction, where $N = nw$.

Delamination strength S_d in LONG and CIRC directions were obtained from experimental results reported by Pasta et al. (2012). U_f was treated as the free parameter in our model, and we estimated it from experimentally obtained peel tension curves in the LONG direction (Pasta et al., 2012) using appropriate N_{LR} from Table 1. Least-squares curve fitting technique was utilized for this purpose. We hypothesized that U_f , being the energy required for a fiber bridge to fail, would be independent of dissection direction. Consequently, we used these estimated values of U_f in conjunction with appropriate N_{CR} from Table 1 to predict peel tension in CIRC direction.

3. Results

Fig. 4(a) shows representative delamination curves from simulated tests for three cases with different numbers of fiber bridges per unit length, N . The initial rising part of the curve corresponded to the stretching of peel arms. Once the dissection started propagating, the average peel tension P remained essentially constant and corresponded to the delamination strength S_d of the specimen. The nature of the simulated curves agreed qualitatively with

those determined experimentally (Pasta et al., 2012). Fig. 4(b) shows the delamination curves for different fiber failure energy U_f . These two figures revealed that S_d depends strongly on both N and U_f . Although these curves appeared smooth, a zoomed-in view in Fig. 4(a) (inset) shows the presence of fine oscillations arising.

The effect of fiber bridge model parameter F_{max} on S_d keeping N and U_f constants is shown in Fig. 4(c). Note that S_d remained essentially unchanged, and the curves differed only at the initiation region of the plateau. The effect of other fiber bridge model parameters was studied in detail, and is presented in the Supplementary information (SI).

Figs. 5 and 6 demonstrate representative collagen fiber arrangement in CIRC–RAD and LONG–RAD planes, respectively, as obtained by multi-photon microscopy (Tsamis et al., 2013). These images clearly showed the presence of undulating radially-running fiber components. Simulated peel force curves for the LONG direction are depicted in Fig. 7(a and b) along with experimentally observed ones (Pasta et al., 2012) from two representative ATA specimens. A least-squares-based parameter estimation technique yielded the values of U_f as $0.0281 \pm 0.0072 \text{ J/m}$ and $0.0096 \pm 0.0022 \text{ J/m}$, for two ATA specimens. Fig. 8(a and b) presents our model-predicted delamination curves using these values of U_f , along with the experimental data for CIRC direction. We observed that our predictions agree favorably with the experimentally evaluated S_d for each patient in CIRC direction, demonstrating the model's excellent predictive capability.

4. Discussion

Earlier biomechanical studies on dissection of arterial wall (Gasser and Holzapfel, 2006; Pasta et al., 2012; Sommer et al., 2008; Tong et al., 2011) based on peel tests and mathematical models focused on the delamination strength and failure energy required for the dissection to propagate. However, the role of fiber bridges and their arrangement on the emergent behavior in tissue dissection has never been quantified. To fill this gap our model takes into account the number distribution and failure properties of radially running collagen fibers as obtained from multiphoton image analysis of ATA wall tissue specimens.

Our analytical model for the peel test experiments performed by Pasta et al. (2012) revealed that peel tension depends on the geometry and mechanical properties of the radially-running fiber within the peel test specimen. Considering a peel test with $\theta = 90^\circ$, and $\lambda \approx 1$ which implies negligible elastic contribution to the peel force during dissection propagation, Eq. (1) provides an estimate for S_d as

$$S_d \approx \frac{wG_c}{2} \quad (6)$$

Denoting $N = nw$ as the number of fiber bridges per unit length in the dissection direction and utilizing the expression for G_c from Eq. (2), we obtain

$$S_d \approx \frac{1}{2}(wG_{matrix} + NU_f) \quad (7)$$

We consider that $wG_{matrix} \ll NU_f$, i.e., matrix contribution to the delamination strength is negligible compared to fibers. Therefore, delamination strength can be expressed only in terms of the number density of the fiber bridges N and the energy required for each fiber bridge to fail U_f

$$S_d \approx \frac{1}{2}NU_f \quad (8)$$

Multi-photon microscopy enabled us to estimate N from the distribution of radially-running collagen fibers bridging the separating surfaces of dissection and providing resistance against dissection. On the other hand, failure energy of each bridge could be enumerated from biomechanical experiments on single fiber bridges, for example see (Yang, 2008). Thus our model links the delamination strength of ATA tissue to the image-based evaluation of structural features of radially-running collagen fibers and its mechanical properties. In the current paper, we did not evaluate U_f experimentally; instead we related it with a phenomenological force–separation curve mimicking fiber bridge pull out behavior (Eq. (5)). We considered it as a free parameter to be estimated from experimentally obtained N and S_d using Eq. (8). As revealed by this equation, plateau value of the peel tension, i.e., S_d , varied almost linearly with N , arising from local fiber micro-architecture, and U_f , characterized by mechanical properties of fiber bridge (Fig. 4(a and b)).

While N can be obtained directly from image analysis, U_f depends on the shape of fiber bridge model (Fig. 4(c)) through four shape parameters. For a given value of U_f , many combinations of these parameters are possible. We have studied in detail the sensitivity of these parameters on the predicted delamination curves (see SI and Figs. S2 and S3 therein), and have found that their effect on computed S_d is minimal. However, they may affect the finer details of the peel force profile. For example, we observed from Fig. 4(b) that the parameter F_{max} affected only the region of the delamination curves where the plateau starts, leaving the rest unaltered.

A zoomed view of the delamination curve in Fig. 4 revealed an oscillatory behavior with alternate peaks and troughs. This is due to a discrete failure event of the fiber bridges that bear load and then break sequentially in the direction of dissection propagation. Randomness in the model inputs amplified these peaks and troughs and gave rise to highly oscillatory behavior as evidenced in experiments. Figs. S4 and S5 demonstrate this fact where a normal distribution of F_{max} and distance within consecutive bridges respectively, have been considered. We observed that the simulated curves exhibited amplified oscillatory behavior as the standard deviation was increased. However, the mean value of S_d remained unchanged for all these simulations. Thus, we conclude that the variability in ATA wall microstructural parameters manifested itself through oscillations in the delamination curve, keeping the mean response unaltered.

To estimate the free parameter U_f , we chose two sets of data from two different LONG peel-tests for ATA tissue from two different patients. As this parameter represents the mechanical energy required to fail a single fiber bridge, it should not depend on the direction of the dissection propagation hypothesizing identical failure properties of single collagen fibers in CIRC–RAD and LONG–RAD planes. To verify this hypothesis, we performed simulations on test specimens in the CIRC direction using the above-estimated values of U_f and corresponding N_{CR} from Table 1 as model input. Estimated errors in mean S_d for CIRC direction are 0.373% and 0.285%, respectively, for the two specimens in consideration.

Note from Figs. 7 and 8(a) that the delamination strength for the CTRL ATA specimens is highly anisotropic: S_d in the CIRC direction is significantly lower than in the LONG direction. While the undulation of the collagen fibers provides us with the number of bridges in the LONG direction ($N_{LR} = 11$ bridges/mm and 9.5 bridges/mm for two separate specimens), these numbers in the CIRC direction were 8:6 bridges/mm and 6:4 bridges/mm, respectively. With the fiber bridge failure energy U_f considered direction-independent, it is evident from Eq. (8) that this anisotropy may be an outcome of different local fiber microarchitecture.

Previous studies have been successful in characterizing the planar material response of ascending thoracic aortic tissue with or without aneurysm. Tensile tests in the CIRC and LONG directions demonstrated that both aneurysmal and non-aneurysmal ATA were stiffer and stronger in the CIRC compared to LONG direction (Sokolis et al., 2012a). Layer-specific tensile tests revealed that CIRC and LONG stiffness exhibited the highest values in the adventitia or intima and the smallest in the media, with CIRC stiffness being higher than LONG stiffness in every layer but the intima. Iliopoulos et al. (2013) reported that aging had a deleterious influence on the tensile strength of the aneurysmal sinus tissue, causing also stiffening and reduced extensibility that was consistent with deficient elastin and collagen contents. Recently, Pichamuthu et al. (2013) showed that both the CIRC and LONG tensile strengths were higher in ATA aneurysms from patients with bicuspid aortic valve (BAV) when compared with tricuspid aortic valve (TAV).

Findings from the above tensile test experiments of ATA tissue are essential in supporting various hypotheses about mechanisms mediating dilatation characteristics of ATA aneurysms. However, this information is not sufficient to characterize the inter-laminar failure mechanisms that affect the dissection behavior. In this case, one needs an experimental setup to measure the inter-laminar strength of the material, such as the peel test experiments (Gasser and Holzapfel, 2006; Pasta et al., 2012; Sommer et al., 2008; Tong et al., 2011). Presented analysis attempts to provide a mechanistic understanding of the role of fiber micro-architecture, specifically the “radially-running” components, on the delamination strength of human ATA as measured by Pasta et al. (2012). In specific, our model relates two structural characteristics – the local microarchitecture of the radially-running collagen fibers and the energy required to fail a fiber bridge – to the delamination strength of the tissue. Our study however has following limitations. Pasta et al. (2012) evaluated delamination strength by artificially dissecting tissue samples, while physiologically dissected samples may have an altered biomechanical state in the vicinity of the delamination. Moreover, the model is validated only against non-aneurysmal ATA tissue

specimens, which may not actually dissect. However, biomechanical failure events occurring at the fiber bridges are expected to be qualitatively similar in all these cases. Thus our analysis of the role of radially running collagen fibers on the delamination strength of ATA wall is still valid. Further studies are under way to validate the presented model for aneurysmal patients.

It has been reported in the literature that both the overall architecture of collagen fibers and the architecture of inter-laminar (including radially-running) fibers in the ATA wall can be affected by aging, disease, and CIRC location. For example, it was shown that collagen content increased significantly with age in human ATA (Andreotti et al., 1985; Halme et al., 1985). Further, the content of collagen was found to be decreased in the right lateral region of ATA aneurysm (Sokolis et al., 2012b). With respect to specific types of collagen, in ATA aneurysm with bicuspid aortic valve and aortic valve regurgitation (co-morbid conditions), the content of collagen type IV was found to be increased, whereas the contents of collagen types I and III were found to be decreased, compared with CTRL ATA, and the decrease was more in the convexity than in the concavity of the ATA wall (Cotrufo et al., 2005; Della Corte et al., 2006). In another report, the content of inter-laminar collagen types I and III was found to be increased in ATA dissection with cystic medial degeneration and medionecrosis, and in ATA dissection with mild or moderate atherosclerosis (Sariola et al., 1986). Also, the amount of collagen cross-links was found to be increased in the wall of ATA aneurysm of Marfan patients compared with CTRL ATA (Lindeman et al., 2010; Recchia et al., 1995).

Based on the above reports and assuming that the density of fiber bridges N depends on the content and organization of collagen fibers, one would expect that N would be increased with aging, and decreased in the right lateral region of ATA aneurysm. Further, one might need to assign different N to different collagen types such as I and III. In this case, the respective N_I and N_{III} would be decreased more in the convexity than in the concavity of ATA aneurysm (with co-morbid conditions), and would be increased in ATA dissection (with co-morbid conditions). On the other hand, assuming that the energy U_f required to break a fiber bridge depends on the amount of collagen cross-links, higher energy U_f would be required in the wall of ATA aneurysm of Marfan syndrome patients. Thus, although the present model is implemented using non-aneurysmal ATA data, in the future, it may provide a further classification of the effect of aging, disease, and location on the delamination properties of ATA tissue using two separate parameters, which are based on the variation of microarchitectural properties of collagen fibers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

A flowchart for the model calibration and model prediction procedure as discussed in the text. Quantities in red denote input to the model, while green quantities are output. T_{peel} , peel tension; U_f , energy required to fail a single fiber bridge; N , number of fiber bridges per unit length in the direction of the peel test propagation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 2.

(a) Example multi-photon microscopy image ($0.5 \times 0.5 \text{ mm}^2$) of collagen fibers in the adventitial–medial half of ATA in the LONG–RAD plane. The border of dissected medial surface is on the bottom. (b) Processed image with small arrows in blue that follow the direction of the fibers. (c) Processed image with the radially-running fiber segments overlaid in red color. (d) A higher magnification of a small area of Fig. 2b that displays the blue arrows which have an orientation between 0° and 180° . (e) A higher magnification of a small area of Fig. 2c that displays only the radially-running fiber components (bridges) in red. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 3. Schematic representation of (a) artificial dissection of human ATA, (b) arrangement of collagen fibers along the dissection/fracture plane, (c) fiber bridge on the fracture plane, and (d) force-separation law for a collagen fiber bridge with nonlinear loading and linear post peak behaviors. The modes of fiber deformation and failure are depicted in the insets. The shaded region represents the energy required for failure of the fiber bridge.

Fig. 4.

Force vs. separation response for (a) different number of fiber bridges N along the fracture plane while fiber bridge parameters remain constant (inset shows the zoomed view of the plateau of the response), (b) different fiber failure energies U_f while number of fiber bridges N along fracture plane remains constant, and (c) different failure strength F_{max} while number of fiber bridges N along the delamination plane and fiber bridge failure energy U_f are constant.

Fig. 5. Multi-photon microscopy images ($0.5 \times 0.5 \text{ mm}^2$) displaying collagen fibers in the CIRC–RAD plane of ATA. The magnification is 25 X. (a and b) adventitial–medial delaminated half, (c and d) medial–intimal delaminated half, (a and c) collagen channel in red, (b and d) radially-running collagen fiber components displayed as red arrows overlaid onto the collagen channel displayed in gray. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 6. Multi-photon microscopy images ($0.5 \times 0.5 \text{ mm}^2$) displaying collagen fibers in the LONG–RAD plane of ATA. The magnification is 25 X. (a and b) adventitial–medial delaminated half, (c and d) medial–intimal delaminated half, (a and c) collagen channel in red, (b and d) radially-running collagen fiber components displayed as red arrows overlaid onto the collagen channel displayed in gray. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 7.

Comparison of simulated peel force vs. separation response with experimentally observed delamination curves for (a) LONG dissection in one representative ATA specimen, and for (b) LONG dissection in another representative ATA specimen.

Fig. 8. Predicted peel force vs. separation response compared with experimentally observed delamination curves for (a) CIRC dissection in one representative ATA specimen, and for (b) CIRC dissection in another representative ATA specimen.

Table 1

Number count of radially-running fibers along the delamination plane.

Type of dissection/strip	Number of radially-running fibers/mm
LONG (patient 1)	11
CIRC (patient 1)	8.6
LONG (patient 2)	9.5
CIRC (patient 2)	6.4