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A Mechanical Analysis of Conduit Arteries Accounting for Longitudinal Residual Strains

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Abstract

Identification of an appropriate stress-free reference configuration is critically important in providing a reasonable prediction of the intramural stress distribution when performing biomechanical analyses on arteries. The stress-free state is commonly approximated as a radially cut ring that typically opens into a nearly circular sector, relieving much of the circumferential residual strains that exist in the traction-free configuration. An opening angle is often used to characterize this sector. In this study, we first present experimental results showing significant residual deformations in the longitudinal direction of two commonly studied arteries in the pig: the common carotid artery and the left anterior descending coronary artery. We concluded that a radially cut ring cannot completely describe the stress-free state of the arteries. Instead, we propose the use of a longitudinal opening angle, in conjunction with the traditional circumferential opening angle, to experimentally quantify the stress-free state of an artery. Secondly, we propose a new kinematic model to account for the addition of longitudinal residual strains through employing the longitudinal opening angle and performed a stress analysis. We found that with the inclusion of longitudinal residual strains in the stress analysis, the predicted circumferential stress gradient was decreased by 3-fold and the predicted longitudinal stress gradient was increased by 5.7-fold. Thus, inclusion of longitudinal residual strains has a significant effect on the predicted stress distribution in arteries.

Keywords

Residual stress; Residual strain; Opening angle; Vascular mechanics; Coronary arteries; carotid arteries

INTRODUCTION

Since the classic papers by Choung and Fung¹ and Vaishnav and Vossoughi,¹² the importance of identifying an appropriate stress-free reference configuration when performing stress analyses on blood vessels has been recognized. They showed that residual strains can be revealed by imposing a single radial cut in a traction-free ring, resulting in an open sector, from

which an opening angle can be measured. Incorporation of these residual strains in stress analyses served to reduce the predicted intramural stress gradient. Thus, this prediction suggests that cells living at different locations across the vessel wall experience the same mechanical environment. Although the single radial cut method may not relieve all residual stresses, it is generally accepted that this method is sufficient in approximating the zero-stress state⁸ and therefore commonly used in vascular mechanics.

There has been evidence to suggest that residual strains can also exist along the axis or longitudinal direction of an artery. Vossoughi¹³ first studied these longitudinal residual strains (LRS) in the bovine aorta through the curling of rectangular strips cut from the vessel. He noted that when cut out, these strips curled away from the lumen, signifying compression in the intima and tension in the adventitia in the traction-free state. By calculating the ratio of the arc length of the stress-free intima to the undeformed length of the rectangular strip, he reported an intimal engineering strain of 6%. Recently, Holzapfel *et al.*⁷ investigated three-dimensional residual deformations in strips of intact and mechanically separated intima, media, and adventitia of human aortas with non-atherosclerotic intimal thickening. They noted that in the longitudinal strips, the media curled away from the lumen while the intima and adventitia remained flat; indicating LRS in the media layer. The curling was found to be in the shape of a non-circular sector; therefore they measured local curvatures along the curled strips to quantify the deformations. They concluded that three-dimensional residual deformations in blood vessels cannot be appropriately described by a single opening angle parameter.

In this paper, we present evidence that at certain locations, porcine carotid and coronary arteries contain both circumferential residual strains (CRS) and LRS. We found that the deformations due to LRS are similar to those of previous studies.^{7,13} In addition, if the longitudinal strips were cut into small segments along the length of the artery, nearly circular sectors with varying radii can be achieved. From this, we propose that circumferential opening angle (COA) and longitudinal opening angle (LOA) may be combined to approximate a more appropriate stress-free configuration to use for stress analyses. We analyzed the effect of employing this combined stress-free configuration during parameter estimation and stress analysis. We found that LRS decreased the predicted circumferential stress gradient by 3-fold; however, it increased the axial stress gradient by 5.7-fold. We conclude that a single opening angle parameter is insufficient in characterizing the stress-free configuration of an artery; we submit that an additional LOA is needed to better quantify LRS.

EXPERIMENTAL MATERIALS AND METHODS

Specimen Preparation

In this study we measured the COA and LOA in six left anterior descending (LAD) coronary arteries and six common carotid arteries (CCA) of the pig. An additional carotid artery was used for cylindrical biaxial mechanical testing to estimate material parameters and calculate the intramural stresses. Hearts weighing 0.76 ± 0.10 kg (mean $\pm$ SD) and carotid arteries were obtained at a local abattoir (Holifield Farms Inc., Covington, GA) from normal farm pigs 2 to 3 years of age and weighing 150–200 kg. Following the removal of the hearts from the pig, the left coronary branch was flushed with ice-cold Ca^{2+} -free phosphate buffered saline (PBS) by cannulation through the aorta and the CCA were rinsed with PBS to clean away the blood. We harvested the CCA after the removal of the internal organs, as a result we were not able to obtain full-length vessels. The samples were transported back to the laboratory on ice, upon which the LAD were carefully dissected out of the heart and the CCA were cleaned of perivascular tissue. The arteries were then circumferentially sectioned using sets of two single-edge razor blades separated by precision spacers; resulting in 12 LAD sections and 16 CCA sections per vessel, with one shorter CCA resulting in only 12 sections (Fig. 1). The cutting started from the most proximal location for the CCA and from the left coronary bifurcation for

the LAD, these locations therefore served as reference points. The length of these sections alternated between long cylindrical segments (7.2 mm in length for LAD, 9.1 mm for CCA) and short ring segments (3.0 mm in length for both LAD and CCA). Thin longitudinal strips were then cut around each long segment (5–6 strips for LAD and 7–9 strips for CCA). These strips either sprang into a circular sector or remained straight. The lengths of the longitudinal strips were optimized to the dimensions described above so that the strips that become sectors could achieve a nearly circular shape without the ends closing or overlapping. The reported LOA of a section is the mean LOA for all the strips from that section. A total of 226 longitudinal strips and 36 circumferential rings were cut from the six LAD and 367 strips and 46 rings from the six CCA.

Image Capture and Post-Process

The longitudinal strips and circumferential rings were placed in covered Petri dishes containing Ca^{2+} -free PBS and incubated at 37 °C. Images of the rings were collected after 30 min with a CCD camera (Canon PowerShot SD850 IS) to quantify the traction-free configuration. A single radial cut was then imposed on the rings allowing them to spring open into sectors relieving much of the residual stress. These sectors along with the longitudinal strips were further incubated for 4–5 h allowing them to achieve their nearly stress-free configurations, and images were taken thereafter. All images were taken with the Petri dishes placed over a calibration slide (Edmund Optics Ronchi Ruling Slide, 5 lines/mm) to ensure proper dimensional calibration during post-processing. Care was taken to ensure that the camera lens was parallel to the Petri dish for each shot.

In this study, the opening angle is characterized as an angle that increases in response to a stress-relieving cut. In the circumferential direction, the opening angle Φ_0 (COA) is defined as the angle between two lines that bisect the midpoint of the inner sector wall and extend to the inner edges (Fig. 2).¹ In the longitudinal direction, we define a closing angle ψ_0 analogous to the COA. We define it as the longitudinal ‘closing’ angle (LCA) because this angle decreases or closes in response to a stress-relieving cut. The opening angle ξ_0 for the longitudinal direction (LOA) can therefore be defined in terms of the closing angle ψ_0 using the following relationship (in radians)

$$\xi_0 = \pi - \psi_0 \quad (1)$$

Note that the magnitude of the LOA defined in this study can vary depending on the length of the longitudinal section. Although a length-independent measurement, such as curvature, may be calculated, since each longitudinal strip was the same length we present results in terms of LOA.

Image processing and measurements were made using a custom MATLAB program. A reference length in each image was first calibrated by measuring the number of pixels between 5 lines (1 mm) on the calibration slide. Points along the intima and adventitia surfaces were then manually selected. These points were then used to calculate the inner and outer arc length as well as the cross-sectional area of the vessel wall. Calculating the COA and LCA from the bisecting midpoint angle method described previously can be subjected to errors when selecting the midpoint location at the inner wall, particularly in sectors that are not ideally circular. Since the adventitia and intima surfaces are well delineated in the images, we can use instead the arc lengths of these boundaries along with the cross-sectional area to calculate a more consistent COA or LCA that does not depend on selecting a midpoint. The COA and LCA (in radians) along with the thickness (t) calculated from this method are given in the following equations

$$\text{COA, LCA} = \pi - \frac{L_o - L_i}{2t}, t = \frac{2A}{L_o - L_i} \quad (2)$$

where A is the wall cross-sectional area, L_o and L_i are the outer and inner arc lengths, respectively, with L_o being the arc length of the adventitia in circumferential sectors and the intima in longitudinal sectors. The measurement program was validated by measuring the inner and outer diameters of a small metal cylinder with known dimensions.

Cylindrical Biaxial Mechanical Test

To illustrate the role of LRS in parameter estimation and stress analysis, we collected cylindrical biaxial mechanical data on one CCA with the biomechanical testing device reported in Zaucha *et al.*¹⁴ Briefly described, the artery was pressurized quasi-statically (2 mmHg/s) from 0 to 120 mmHg for axial stretches at $\lambda = 1.4, 1.5, 1.6$. At each axial stretch, the artery was preconditioned with four pressurization cycles. Two pressure transducers (Honeywell Sensotec FPG) measured the distal and proximal pressures. Axial force was measured with a force transducer (Delta Metrics XLU68f) and diameter was measured using a video system consisting of a CMOS digital video camera (Allied Marlin F131B IRF). The device and peripheral components were controlled with a computer running a custom LabVIEW program.

Statistical Analysis

All experimental data are reported individually as well as their mean $\pm$ SD for each section number. Experimental results were first analyzed with one-way analysis of variance (ANOVA) between groups. The results being statistically significant if $p < 0.05$. In conjunction with ANOVA, we utilized Tukey's test to determine specifically which means were statistically different. Pairs of statistically significant groups were then analyzed with Student's t -test to calculate their p -value.

ANALYTICAL METHODS

Kinematic Modeling

Consider a local neighborhood k_i about a point with position $\mathbf{x}(r, \theta, z)$ in the loaded configuration β_i . Let this neighborhood be denoted k_n in the locally stress-free (or natural) configuration β_n , which has position $\mathbf{X}_n(R_n, \Theta_n, Z_n)$ (Fig. 3). Let the gradient of the map $\mathbf{X}_n(R_n, \Theta_n, Z_n) \mapsto \mathbf{x}(r, \theta, z)$ be denoted $\mathbf{F}$. The natural configuration β_n is defined such that the local neighborhood about every point in the body is stress-free; in general, this configuration may be thought of as a set of discontinuous elements. Note, β_n is not experimentally tractable. It is often convenient to decompose the map $\mathbf{X}_n(R_n, \Theta_n, Z_n) \mapsto \mathbf{x}(r, \theta, z)$ into a map from $\mathbf{X}_n(R_n, \Theta_n, Z_n) \mapsto \mathbf{p}(\rho, \vartheta, \zeta)$ and a map from $\mathbf{p}(\rho, \vartheta, \zeta) \mapsto \mathbf{x}(r, \theta, z)$, where $\mathbf{p}(\rho, \vartheta, \zeta)$ is the location of this material point in the traction-free (unloaded) configuration β_u ; let the gradient of these maps be $\mathbf{F}_1$ and $\mathbf{F}_2$, respectively, where

$$\mathbf{F} = \mathbf{F}_2 \cdot \mathbf{F}_1. \quad (3)$$

For the inflation and extension of a long, straight, axisymmetric tube, neglecting variations along axial direction the gradient of map from $\mathbf{p}(\rho, \vartheta, \zeta) \mapsto \mathbf{x}(r, \theta, z)$ is

$$[\mathbf{F}_2] = \text{diag} \left\{ \frac{\partial r}{\partial \rho}, \frac{r}{\rho}, \lambda_z \right\}, \quad (4)$$

where $\lambda_z = \ell/L_u$ is the axial stretch ratio, ℓ is the loaded length of the vessel, and L_u is the unloaded length of the vessel in the traction-free configuration.

For a straight, axisymmetric tube, neglecting variations along axial direction, since each material point at a given radius r has the same deformation gradient, β_n may be thought of as a set of discontinuous cylinders with radius R_n , axial length L_n , and infinitesimal thickness dR_n (Fig. 3). Since each ring is infinitesimally thin, they cannot support a residual stress; thus, each cylinder is stress-free. The map from $\mathbf{X}_n(R_n, \Theta_n, Z_n) \mapsto \mathbf{p}(\rho, \vartheta, \zeta)$ serves to ‘assemble’ the discontinuous stress-free cylinders into a continuous, albeit residually stressed, tube; the gradient of this map may be defined as

$$\mathbf{F}_1 = \text{diag}\{\Lambda_r(\rho), \Lambda_\theta(\rho), \Lambda_z(\rho)\}, \quad (5)$$

where $\Lambda_r(\rho)$, $\Lambda_\theta(\rho)$, and $\Lambda_z(\rho)$ are the stretch ratios of the infinitesimally thin cylinder that passes through point ρ in β_u . If the stress-free configuration is known, then these stretch ratios may be calculated as

$$\Lambda_\theta(\rho) = \frac{\rho}{R_n(\rho)}, \Lambda_z(\rho) = \frac{L_u}{L_n(\rho)}, \text{ and } \Lambda_r(\rho) = \frac{\partial \rho}{\partial R_n} = \frac{R_n(\rho)L_n(\rho)}{\rho L_u}, \quad (6)$$

where $R_n(\rho)$ and $L_n(\rho)$ are the radius and axial length of the stress-free cylinder in β_n that passes through radial location ρ in β_u ; incompressibility was assumed in Eq. (6)₃. Since $R_n(\rho)$ and $L_n(\rho)$ are not measurable, experimentalists are forced to approximate the components of $\Lambda_r(\rho)$, $\Lambda_\theta(\rho)$, and $\Lambda_z(\rho)$ from experimentally tractable quantities.

In traditional vascular mechanics, one typically considers an experimentally measurable (nearly) stress-free configuration β_0^c taken as an excised arterial ring that springs open when cut radially to relieve a large part of the residual stress (Fig. 2; see Chuong and Fung¹). The mapping of points $\mathbf{X}_0^c(R, \theta, Z) \mapsto \mathbf{p}(\rho, \vartheta, \zeta)$ from β_0^c to β_u is defined as $\rho = \rho(R)$, $\vartheta = (\pi/\Theta_0)\Theta$, and $\zeta = \Lambda Z$. Given this map, the deformation gradient $\mathbf{F}_1^c$, has the components

$$\mathbf{F}_1^c = \text{diag}\left\{\frac{\partial \rho}{\partial R}, \frac{\pi \rho}{\Theta_0 R}, \bar{\Lambda}_z\right\}. \quad (7)$$

The mean axial stretch ratio $\bar{\Lambda}_z$ is assumed to be constant. That is, the changes in axial stretch with radial location are ignored in this configuration and the configuration β_0^c is assumed to be a cylindrical sector (with straight side walls). The incompressibility constraint requires that

$$R(\rho) = \sqrt{\frac{\pi \bar{\Lambda}_z}{\Theta_0}(\rho^2 - \rho_i^2) + R_i^2}. \quad (8)$$

It is clear, however, that when thin longitudinal strips are cut from arteries, these strips often bend to relieve LRS. The mapping of points $\mathbf{X}_0^\ell(R, \Theta, S) \mapsto \mathbf{p}(\rho, \vartheta, \zeta)$ from β_0^ℓ to β_u is defined as $\rho = \rho(S)$, $\vartheta = \bar{\Lambda}_\Theta \Theta$ and $\zeta = 2\alpha_0 S$ (Fig. 2). Given this map, the deformation gradient $\mathbf{F}_1^\ell$, has the components

$$\mathbf{F}_1^\ell = \text{diag} \left\{ \frac{\partial \rho}{\partial S}, \bar{\Lambda}_\Theta, \frac{L_u}{2\alpha_0 S} \right\}. \quad (9)$$

where α_0 is the arc angle, S the radius of curvature for the axial strip after bending, and variations in the ‘circumferential’ stretch ratio are neglected; thus, the local circumferential stretch ratio is taken as the mean circumferential stretch $\bar{\Lambda}_\Theta$. The incompressibility constraint requires that

$$S(\rho) = \sqrt{\frac{\bar{\Lambda}_\Theta L_u}{\alpha_0} (\rho - \rho_i) + S_i^2}. \quad (10)$$

Our experimental data presented in the results section show that when thin longitudinal strips are cut from arteries, these strips often bend to relieve LRS and when a radial cut is imposed on thin rings, even from a location adjacent to the axial strips, these rings spring open to relieve CRS. Thus, vessels at many locations along the vascular tree contain both CRS and LRS in the traction-free configuration. One consequence of this observation is that neither a cylindrical sector (β_0^c) representing a radially cut ring nor a cylindrical sector representing a curved longitudinal strip (β_0^ℓ) accurately represents a truly stress-free configuration. Indeed, when both CRS and LRS are present, an experimentally tractable stress-free configuration does not exist. Rather, a traction-free sector deforms into a saddle shape (Fig. 4), which contain residual stresses.

Nevertheless, when the ratio of circumferential arc length to axial arc length is small (e.g., for a thin axial strip) the axial bending is only negligibly affected by CRS. Thus, a thin axial strip may be used to quantify the axial stretch $\Lambda_z(\rho)$ from Eq. (6)₂. Similarly, as this aspect ratio becomes large (e.g., for a thin radially cut ring), circumferential bending is only negligibly affected by LRS. Thus, a thin radially cut ring may be used to quantify the circumferential stretch $\Lambda_\Theta(\rho)$ (as done by Chuong and Fung¹). Taken together, we may approximate the components of $\mathbf{F}_1$ as

$$\Lambda_\theta = \frac{\pi \rho}{\Theta_0 R(\rho)}, \Lambda_z = \frac{L_u}{2\alpha_0 S(\rho)}, \text{ and } \Lambda_r = \frac{\partial \rho}{\partial R_n} = \frac{(\Theta_0 R(\rho))(2\alpha_0 S(\rho))}{\pi \rho L_u} \quad (11)$$

where $R(\rho)$ and $S(\rho)$ are given via Eqs. (8) and (10), respectively. The radial component is calculated assuming incompressibility, with $\Lambda_r \Lambda_\theta \Lambda_z = 1$. The incompressibility constraint also requires that

$$\int_{\rho_i}^{\rho} \frac{\rho}{R(\rho)S(\rho)} d\rho = \frac{2\Theta_0 \alpha_0}{\pi L_u} \int_{R_i}^R dR_n \quad (12)$$

which may be evaluated with numerical integration techniques.

Stress Analysis

We modeled the artery to be a thick-walled cylindrical tube composed of an incompressible, orthotropic, homogeneous material undergoing an elastic deformation of inflation and axial extension. We described the elastic property of the artery using a seven-parameter exponential-type strain energy density function of Chuong and Fung¹ given as

$$W(\mathbf{E}) = \frac{c_0}{2}(e^{Q(\mathbf{E})} - 1), \quad (13)$$

where $\mathbf{E} = \frac{1}{2}(\mathbf{F}^T \mathbf{F} - \mathbf{I})$ is the Green strain tensor, $\mathbf{I}$ is the identity tensor, and the exponential factor is given by

$$Q = c_1 E_{rr}^2 + c_2 E_{\theta\theta}^2 + c_3 E_{zz}^2 + 2c_4 E_{\theta\theta} E_{rr} + 2c_5 E_{\theta\theta} E_{zz} + 2c_6 E_{zz} E_{rr}.$$

The Cauchy stress $\mathbf{t}$ is

$$\mathbf{t} = -p\mathbf{I} + \mathbf{F} \cdot \frac{\partial W(\mathbf{E})}{\partial \mathbf{E}} \cdot \mathbf{F}^T, \quad (14)$$

where p is a Lagrange multiplier that arises due to the incompressibility constraint. From equilibrium, pressure and axial force are

$$P_i = \int_{r_i}^{r_a} (t_{\theta\theta} + t_{rr}) \frac{1}{r} dr \quad \text{and} \quad f = \pi \int_{r_i}^{r_a} (2t_{zz} - t_{rr} - t_{\theta\theta}) r dr, \quad (15)$$

A nonlinear least-square fitting algorithm was implemented in MATLAB to solve for the material constants by fitting the theoretical pressure and force values over the loading curves at the three stretches to the experimental data. The unloaded length of the vessel measured from suture to suture was 26 mm. The *in situ* stretch was considered to be the stretch in which the axial force is constant for increasing pressures. This was found to be 1.5; in agreement with published literature value on porcine CCA.⁶

RESULTS

LAD Opening Angle Results

LRS was present throughout the six sections of the LAD as indicated by the presence of LOA (Fig. 5a). The LOA increased with increasing section number (ANOVA $p < 0.05$); statistical significance was observed between sections 1 and 6 (Fig. 6b). In one vessel (denoted with the plus symbol) we observed a negative LOA at section 1 indicating that the sectors curled into the lumen; all other vessels and locations curled away from the lumen. Trends in COA of the LAD are less apparent (Fig. 6a). When examining data from each vessel separately, there appeared to be large variability with the COA to section number. Due to the large variability, when averaging the data across groups no statistical significance was observed between the COA and section number.

CCA Opening Angle Results

CCA exhibited significant release of LRS upon cutting into axial strips (Fig. 5b). The LOA were nearly zero in the first two sections but increased with the section number thereafter, achieving a maximum LOA of approximately 90° at section 8 (ANOVA $p < 0.0001$); statistical significance was observed between the higher and lower section numbers (Fig. 7b). For COA, the data were more scattered. When examining the data from each vessel separately, the COA decreased, then increased across the sections. Because the minimum COA appeared at different

locations from one vessel to the next, when averaging the data across groups no statistical significance was observed between COA and section number (Fig. 7a).

Thickness Results

The LAD and CCA wall thicknesses were measured from the traction-free rings (Fig. 8). For both vessels the thicknesses decreased with section number (ANOVA $p < 0.005$ for LAD) and (ANOVA $p < 0.0005$ for CCA), with higher section numbers statistically thinner than lower ones.

Stress Analysis Results

The inner and outer radii of the CCA in the traction-free configuration were $\rho_i = 2.18$ mm and $\rho_a = 3.46$ mm, respectively. The segment length was $L_u = 10.1$ mm. The inner radius of the circumferential stress-free sector was $R_i = 4.43$ mm and the inner radius of the longitudinal stress-free sector was $S_i = 5.34$ mm. COA and LCA were measured to be $\Theta_o = 79.4^\circ$ and $\psi_o = 117.9^\circ$ respectively, corresponding to approximately sections 6–7 (see Fig. 7). The thickness of this segment was larger than the nominal CCA thickness shown in Fig. 8b. The mean circumferential ($\bar{\Lambda}_\theta$) and axial ($\bar{\Lambda}_z$) stretch ratios were assumed to be 1. The traction-free and circumferential stress-free measurements were made on a ring cut from the location where diameter was being measured during the biaxial mechanical test. The longitudinal stress-free measurements were taken on strips cut distal to the ring. All stress-free configuration measurements were taken after mechanical testing.

The stretch ratios without LRS (i.e., diagonal components of the deformation gradient $\mathbf{F}_i^c$) agree with results by Choung and Fung,¹ where the axial stretch ratio is $\Lambda = 1$. In their Fig. 2a the circumferential stretch ratio changes from a compressive state to a tensile state at the mid-wall (see our Fig. 9a). Inclusion of LRS dramatically altered the stretch ratios as calculated via Eq. (5) with Eqs. (6) and (11) (Fig. 9b). Most notably, the longitudinal stretch ratio changes from a constant to a varying distribution in which the inner-wall is in compressive stretch and the outer-wall in tensile stretch. This agrees intuitively with the observed bending of a longitudinal sector into a straight beam, which would require that the top of the beam (adventitia) be under tension and the bottom (intima) be under compression.

Material parameters solved by our regression analysis without including LRS (–LRS) and with LRS (+LRS) are presented in Table 1. The stress gradients $\Delta t_{\theta\theta}$ and Δt_{zz} (the maximum stress minus the minimum stress) were calculated for each analysis. For the circumferential direction without LRS $\Delta t_{\theta\theta} = 73.58$ kPa (Fig. 10a dotted line) and inclusion of LRS resulted in $\Delta t_{\theta\theta} = 23.88$ kPa (Fig. 10b dotted line), reducing the gradient by 3-fold. In the longitudinal direction, analysis without LRS resulted in $\Delta t_{zz} = 28.82$ kPa (Fig. 10a dashed line) and analysis with LRS resulted in $\Delta t_{zz} = 163.27$ kPa (Fig. 10b dashed line), increasing the gradient approximately 5.7-fold.

DISCUSSION

Numerous studies have demonstrated well that vascular cells possess the remarkable ability to sense and respond to changes in their local mechanical environment (e.g., Davies² and Dzau and Gibbons³). These mechano-biological mechanisms play a key role in many physiological and pathophysiological processes, as well as the success (or failure) of many clinical interventions. Fundamental to quantifying mechanically mediated biological mechanisms is the quantification of the local mechanical environment within tissues and how this mechanical environment evolves as the tissue grows and remodels. Whereas universal solutions (e.g., Laplace's law) may be used to determine the mean stresses within a tissue, stress analysis is required to predict the local stresses within a tissue under applied loads.

The experimental results of this study clearly show the existence of LRS in porcine coronary and carotid arteries. We have characterized the LRS through measuring the LOA of thin strips cut around the artery. We have also investigated the change in the LOA along the artery. For the LAD, LRS was found along all the sections that we excised as indicated by the presence of LOA in those sections. Statistical analyses show that the LOA is dependent on the section number or location along the vessel, increasing with increasing section number. The LAD exhibited more complex residual deformations apart from the longitudinal and circumferential bending. As seen in certain longitudinal sectors in Fig. 5a, although these sectors are nearly circular, some possess a twist. Twists were also observed in the circumferential sectors. This indicates a residual shear deformation in some LAD sections. The variability in the COA was too large to observe any statistical significance. As a result, we were not able to extract any relationship between the LOA and COA.

In the carotid arteries, the LOA increased with the section number. We were not able to see any statistically significance for the COA. Observed individually, we realized each vessel had a point of lowest COA that was significantly different from the surrounding segments. The location of the lowest COA varied between the vessels. However, we observed two main groups; one which the lowest COA appeared at lower section numbers (2–3) and one at higher section numbers (6–7). From previous studies that recorded the COA with vessel location in rat aortas, there always appeared to be a point of lowest COA.^{4,5} In these studies, the COA was given as a function of the percentage of aortic length; as a result the location of the lowest COA was consistent. In our study, since we could not harvest the entire CCA, we were unable to normalize the COA to the percentage of the vessel length.

There is greater variability of farm pigs in size and weight compared to laboratory rats; as a result we expect the vessel geometry and properties to be more varied. This is a possible explanation for the discrepancy between the locations of the lowest COA that we observed. To reduce this variability we normalized the COA and LOA based on the lowest COA for each vessel, shifting the COA data in each vessel to match the lowest COA for each vessel to one section (Fig. 11a). The LOA was shifted by the same amount (Fig. 11b). The consequence of this normalization was that a more apparent trend in the COA and LOA was revealed. This shows that COA does indeed decrease to a lowest value (normalized section 7), surprisingly consistent between all six vessels and very small in magnitude. ANOVA of the non-normalized COA did not reveal any statistical significance; however, significance was observed when the normalized COA was analyzed ($p < 0.0005$). Tukey's test revealed all sections were statistically significant from normalized section 7. Keeping in mind that this normalization scheme reduced the amount of data points for the lower and higher normalized sections, as a result section 12 was not included in the analysis because it only had a sample size of 1. Normalizing the LOA revealed that the higher sections starting from section 6 were statistically significant from the lower sections. The most important relationship to observe is that as the COA nears the lowest value (between normalized sections 6–7), the LOA begins to increase. Our thickness measurements indicate that the wall is thinner at higher section numbers (Fig. 8b), therefore a decrease in COA along with a decrease in thickness, would result in lower magnitudes of circumferential residual stress in those sections. We speculate that this exchange between the COA and LOA could indicate a compensation mechanism that attempts to preserve the circumferential stress gradient. Our stress analysis does indeed show that the circumferential stress gradient is reduced if the LRS is taken into account, but at the expense of increasing the axial stress gradient.

Limitations of the current study lie in the underlying assumptions of the kinematics and stress analysis. First, we modeled the arteries as a homogeneous material; clearly, however, these arteries are heterogeneous. One possible extension of this study would be to dissect the medial and adventitial layers apart (see Holzapfel *et al.*⁷) and test each layer individually for

mechanical properties and COA and LOA. In healthy porcine LAD and CCA, the mechanical contribution of the intima may be neglected. In several additional porcine CCA, we removed the adventitial layer and measured the COA and LOA. Both the COA and LOA were comparable to the experimental findings of vessels with the adventitia intact; this finding is comparable to reports elsewhere for the COA.^{5,9,10} Thus, it appears that both COA and LOA exist in the media (which may be nearly homogeneous) and are not solely a function of kinematic and material differences between the media and adventitia. In addition, the experimental and computational approaches presented herein could easily be extended to multi-layered vessels.

The existence of residual strains in the traction-free state is a consequence of tissue development, growth, and remodeling which occur in the physiologically loaded state. It has been argued that cells grow and remodel to restore the mechanical environment in the local neighborhood in which they live.¹¹ The consequence of this hypothesis is that the stresses (or perhaps the strains) in the physiologically loaded configuration would be uniform throughout the tissue. Indeed, our findings suggest that the circumferential stress is nearly uniform across the vessel wall under physiological loading. The axial stress, however, is highly non-uniform across the wall. Limitations of the assumption that the material is homogeneous aside, these results suggest that the smooth muscle cells, which are oriented in the circumferential direction, preferentially restore tractions in the circumferential direction, compared to the axial direction. The non-uniform axial stress results in high tension in the adventitia layer. For the carotids, which do not have much perivascular support, a tensile adventitia in the axial direction may be favorable in stabilizing the artery from buckling during physiological loading. This, however, does not explain why the coronary arteries, which are sufficiently embedded in perivascular support, also possess LRS. We believe that the residual deformations of the coronary arteries have additional complexities due to the twisting of the longitudinal strips observed experimentally. These speculations, however, warrant further investigation.

In conclusion, we present evidence that circumferential and longitudinal residual strains coexist at many locations in porcine carotid and coronary arteries and that incorporation of these residual strains in stress analysis significantly affects the predicted stress distribution across the wall. We hope this study provides a deeper breadth of understanding for the residual stress states of an artery.

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FIGURE 1.

Schema of the sectioning method used in this study. Each main section, labeled with a section number 1, 2, 3, ..., N , consists of longitudinal strips of length L_u ($N = 6$, $L_u = 7.2$ mm for LAD and $N = 8$, $L_u = 9.1$ mm for CCA) cut around the artery and one circumferential ring approximately 3 mm wide. The number of longitudinal strips per section varied between 5 to 6 for LAD and 7 to 9 for CCA. Section numbers increase distal to the ascending aorta.

FIGURE 2.

Mapping from experimentally tractable, nearly stress-free configurations β_o^c and β_o^ℓ to traction-free configurations is accomplished by the deformation gradient tensor. The stress-free configurations consist of a circumferential sector described by radius R , opening angle Θ_0 or arc angle Φ_0 and a longitudinal sector described by radius $S(R)$, closing angle ψ_0 , opening angle ξ_0 , or arc angle α_0 . The traction-free configurations consist of a circumferential ring of radius ρ and a longitudinal strip of length L_u . The adventitia (*adv*) and intima (*int*) surfaces for the stress-free configurations are labeled accordingly.

FIGURE 3.

The theoretical stress-free state consists of concentric cylindrical shells. Each shell is infinitesimally thin and therefore stress-free. Circumferential and longitudinal residual strains develop as a result of radial and length incompatibility of the cylindrical shells as they are mapped to the traction-free state.

FIGURE 4.

A saddle-like shape is created in a segment of a CCA. Although not residually stress-free, this shape shows the combined effect of longitudinal and circumferential residual stresses. The shorter side aligns in the longitudinal direction, while the longer side is in the circumferential direction.

Panel (a) **Panel (b)** **FIGURE 5.**

Longitudinal stress-free sectors from a LAD segment (panel a) from section 6 and a CCA segment (panel b) from section 7. The nearly circular sectors from the CCA allow for the measurement of opening angles and the use of conventional deformation mapping. The residual deformations in the LAD show additional complexity due the possible presence of residual shear strain in some of the sectors. Note that the sectors bend away from the lumen; the intima is the smooth side. The picture was taken over a calibration slide after 4 h incubating in PBS at 37 °C.

FIGURE 6.

COA (panel a) and LOA (panel b) of the LAD shown against the section number as individual data points and the mean $\pm$ SD (dashed line with error bars). The mean of the COA appears to have a parabolic trend, but no significance when statistically analyzed. Analysis of the LOA reveals one significant section, number 6, compared to section 1. The mean LOA appears to have an increasing trend. * $p \leq 0.05$ compared to section 1.

FIGURE 7.

COA (panel a) and LOA (panel b) in the CCA shown against the section number. Figures show individual data points along with the mean $\pm$ SD (*dashed line with error bars*). The COA appears to have a parabolic trend, but no significance when analyzed statistically. Individual data points reveal a minimum COA for each vessel that is significantly different from the surrounding sections. However, the section number of the minimum value varies between vessels. ANOVA reveals statistically significant relationship between LOA and section number. Further analyses using Tukey's and *t*-test show that the LOA of higher section numbers are statistically greater than lower ones. * $p \leq 0.05$ compared to sections 1, 2, and 3. ** $p \leq 0.001$ compared to sections 1, 2, 3, and 4.

FIGURE 8.

Changes in wall thickness for LAD (panel a) and CCA (panel b) shown against the section number. Individual data points are presented as well as the mean $\pm$ SD (*dashed line with error bars*). ANOVA reveals that the thicknesses from both vessels are statistically significant to the section number ($p < 0.005$ for LAD) and ($p < 0.0005$ for CCA). Further analyses show statistically thinner sections with higher section numbers. For LAD, * $p \leq 0.05$ and ** $p \leq 0.001$ compared to section 1. For CCA, * $p \leq 0.05$ compared to section 1.

FIGURE 9.

Distributions of stretch ratios through the arterial wall in the unloaded state without (panel a) and with (panel b) LRS plotted against normalized radius. Accounting for LRS dramatically changes the axial stretch ratio by altering the inner portion of the wall to be under compressive stretch and outer wall to be under tensile stretch.

FIGURE 10.

Carotid intramural stress distributions calculated without (panel a) and with (panel b) LRS at physiological pressure (120 mmHg) and stretch ($\lambda = 1.5$) shown against normalized radius. Circumferential stress is nearly homogeneous through the wall, but the axial stress gradient is increased with inclusion of LRS.

FIGURE 11.

Normalizing the section number based on the smallest COA for the each CCA reveals a more apparent trend between the COA and LOA to the location. ANOVA reveals statistical significance for COA and LOA between normalized sections 1–11 ($p \leq 0.0005$). Further analysis on the COA data shows that normalized sections 1–5 and 6–11 are statistically greater than section 7, $*p \leq 0.05$. Normalized sections 1–5 are statistically greater than normalized section 6, $\star p \leq 0.05$. Analysis on the LOA shows that higher sections (starting from normalized section 7) are statistically greater than lower sections, $*p \leq 0.05$. This appears to show that as the COA decrease towards the lowest point, the LOA increase simultaneously; possibly as a

compensation mechanism to maintain the circumferential stress gradient. Figure shows individual data points along with the mean $\pm$ SD (*dashed line with error bars*). Section 12 was not included in the analysis since it has only a sample size of 1.

TABLE 1

Material parameters calculated through regression analysis.

	c (kPa)	c_1	c_2	c_3	c_4	c_5	c_6	% Error
-LRS	93.367	1.075	0.452	0.612	0.491	0.248	0.416	3.27
+LRS	137.930	1.019	0.350	0.518	0.463	0.232	0.438	3.49