Chapter 3
The Stress Relaxation Response of the Porcine Descending Aorta under Combined Normal and Torsional Loadings

Luc Nguyen, Abdelrahman Youssef, Calvin Nguyen, Kirtan Patel, Jack Luce, Benjamin Tijerina, and Chandler C. Benjamin

Abstract Understanding the mechanical properties of aortic tissue is crucial for improving future medical interventions related to cardiovascular diseases. Our group has previously investigated the uni-axial, bi-axial, and shear responses of the porcine thoracic aorta. In this study, we explore the stress relaxation of the porcine aorta under torsional shearing while maintaining a constant normal compressive load. Circular samples, measuring 0.5 inches in diameter, were extracted from the descending section of porcine thoracic aortas. Stress relaxation experiments were conducted at a constant shear strain ranging from 10 to 50% while maintaining a compressive strain ranging from 5 to 25%. We observed that the stress relaxation behavior differs between the normal and torsional shear directions. Results suggest that neither the normal or shear stress relaxation behavior of the porcine aorta is significantly influenced by the degree of compressive strain or shear strain applied.

Keywords Stress relaxation · Creep · Aorta · Viscoelastic · Rheology

Introduction

A better framework for mechanical analysis of aortic tissue is needed to improve medical diagnosis and intervention. Current pathology for aortic diseases (such as aortic aneurysms, dissections, and stenosis) revolve around the determination of other diseases or genes that increase risk [16, 12, 20, 3]. However, the weakening of the tissue seen in aortic aneurysms and the rupture initiation seen in aortic dissections are clear signs that the pathology of aortic diseases needs to address mechanics.

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Observed mechanical properties of the aorta

In 1881, Charles Roy examined the elastic and viscous properties of animal arterial tissue [28]. His experiments demonstrated the first findings of viscoelastic material properties in arterial tissue. In 1969, Patel et al. noticed anisotropy in canine arteries in their inflation experiments. They measured differing mechanical responses in the circumferential and axial directions. They concluded that the thoracic aorta, abdominal aorta, and common carotid artery in canines can all be approximated as an orthotropic cylindrical tube [22]. From such previous work, we see the importance that anisotropy and viscoelasticity have in this material which must be considered in appropriate constitutive modeling for the aorta.

There have been many tests on the porcine aorta focusing on the uni-axial and bi-axial properties [18, 24, 21, 4, 7]. However, it has been observed that the shear strains induced by inflation are not negligible [22]. Coupling of wall shear stress and circumferential shear stress has also been observed in arterial tissue [29]. Torsional shear testing in our lab [26] has shown a nonlinear response between the experienced torsional shear stress and the angle of twist. We have additionally noticed a nonlinear coupling between the experienced torsional shear values and combined normal loadings [19]. In these previous tests in our lab, preconditioning was used to examine the elastic properties of the porcine aorta in its relaxed state. However, the time-dependent viscoelastic properties of the porcine aorta are crucial to proper modeling [17, 25].

Stress relaxation and creep in soft tissue

It has been shown that most basic viscoelastic models, such as Maxwell or Kelvin-Voight, fail to capture the response of biological tissue [10]. In their uniaxial tensile tests, Chen et al. note the stress relaxation measured on strips of porcine aortas at different angles [4]. Samples cut at the same angle with respect to the circumferential axis showed similar relaxation behavior, whereas samples at varying angles showed different stress relaxation behavior. The smallest relaxation occurred in the directions of the tissue fibers. As such, we expect anisotropy to be present even within the viscoelastic properties of the constitutive modeling for the aorta. In their inflation tests on canine carotid arteries, Zatzman et al. postulate the micro-constituents of the tissue to be responsible for the inelastic responses in their data [33]. Anssari-Benam et al. related their experimental stress relaxation data of the aortic valve to a kinematic framework of the fibers [1]. Their framework offers an explanation of the microstructural mechanics resulting in both the relaxation and creep phenomena. Bagshaw and Attinger compare the experienced stress relaxation in various canine arteries to the collagen and smooth muscle content [2]. They found a strong linear correlation between the experienced relaxation and the sum of collagen and smooth muscles content. We see that the phenomena of stress relaxation and creep are strongly tied to the microstructure of the artery. There is, however, a lack of experimental viscoelastic data of arteries under combined loadings.

Efforts to model aortic tissue

There has been much effort to model aortic tissue, yet each proposed model fails to capture all aspects of the aorta's mechanical properties let alone predict previously unobserved phenomena. Rajagopal and Rajagopal [25] discuss the complexities with modeling such a material. They note that the physical composition of the aorta is the source of many of the complexities as well as it's varying geometry and anisotropy.

Craiem et al. developed a fractional-order relaxation function [6]. They were able to fit uniaxial tensile stress relaxation data using quasilinear viscoelastic theory developed by Fung [11]. Fung et al. discuss the application of an exponential and polynomial strain energy function in fitting experimental data [9]. A given function with enough coefficients can be fit to most experimental data, and Fung et al. do note considerable variation between constants for different sets of data of the same experimental protocol. Tanaka and Fung utilized Fung's form for the reduced relaxation function [11] for canine arteries in cyclic uniaxial extension [31]. They note, however, that "we have no right to expect the quasi-linear relationship to be valid for full range of the inelastic phenomenon in large deformation." This is crucial as the aorta is expected to undergo large deformations.

Cheung and Hsiao developed a nonlinear, viscoelastic, anisotropic constitutive equation [5]. Some of the complexities of the composition of arteries are considered by modeling the material body as a system of micro-elements in equilibrium in their unloaded state. Their integral form of the relaxation function captures the inflation response of the canine carotid artery. Cheung and Hsaio note that only quasi-static conditions are considered and that the inertia term in the equation of motion should be taken into account with future work. Young et al. develop a nonlinear, viscoelastic, orthotropic model [32] where they express the stresses in canine aortas using integrals of four or ten relaxation functions and histories of circumferential and longitudinal strains. A motion comprising of internal inflation and longitudinal extension is examined to ensure no shear forces are present. While this allows for the use of their orthotropic constitutive relation, it greatly simplifies the stresses experienced by arteries. Holzapfel et al. proposed a rate-type constitutive relation based on the additive split of the second Piola–Kirchhoff stress into elastic and viscoelastic components [14]. They developed a finite element formulation modeling the arteries as fiber-reinforced composites. Their model successfully describes the hysteresis that occurs with cyclic loading that is insensitive to strain rate over several decades. Pena et al. used a thermodynamic framework in their constitutive relation to account for the ”pseudo-elastic” behavior that vascular tissues demonstrate after preconditioning [23]. They used a simple neo-Hookean term to model the isotropic response and Holzapfel et al.'s exponential terms [15] to model the anisotropic terms. Pena et al note the following limitations to their constitutive formulation: a need for a large sample size for determination of material constants, omission of permanent set on stress removal due to loading-unloading tests, and the evolution equations of the viscoelastic internal variables are linear. This means that it is not possible to associate such internal variables with any internal micro-structural damage or thermodynamic processes. Haslach proposed a model using a system of evolution differential equations [13]. His model is able to predict both creep and stress relaxation under uniaxial extension. His model operates under the assumption that a unique long-term manifold exists for both creep and relaxation. Zerpa et al. [34] apply fractional viscoelastic models using “high-order spring-pot” to model the ovine ascending aortic wall. They note that the higher-order spring-pots leads to improvement of fitment to experimental data over traditional spring-pots. Zerpa et al. note that future studies should investigate histological interpretations of these higher-order spring-pots.

In general, it is clear that much work is to be done in the way of modeling aortic tissue. More experimental data is needed to further understand the types of mechanical behavior we expect to see from such a complex material. This proceeding focuses on the experimental data set obtained from loading porcine descending aorta in a combination of normal compression and torsional shear.

Experimental Methods

Porcine aortas were obtained from the Texas A&M Department of Animal Sciences. For this experiment, we only used samples from the descending thoracic aorta between the 3rd and the 7th branching arteries. These sections of aorta were longitudinally cut using a surgical scalpel, then circular samples were extracted using a half-inch circular punch. Samples that were visually non-uniform in thickness were discarded. Uniform circular samples were cleaned of excess tissue, placed in a vial filled with Phosphate Buffer Solution (PBS), then stored in a freezer maintained at -20° C. The samples remained frozen for at least 24 hours before testing. It has been previously determined that this method of preservation has no significant impact on the mechanical properties of the porcine aorta [21].

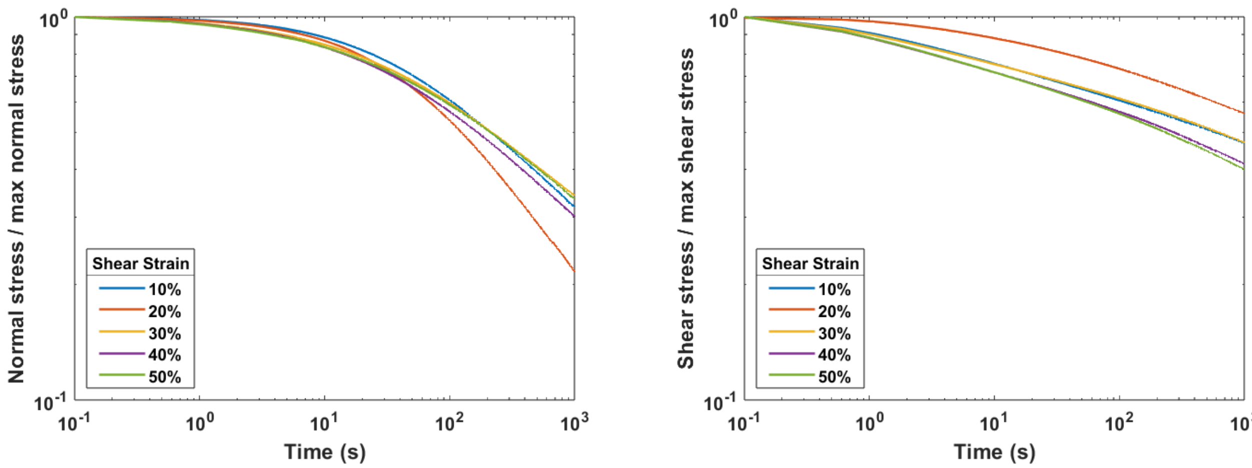
Experimentation was performed on an Anton Parr MCR302 rheometer. The rheometer was set up in a parallel plate configuration. We used a tissue bath for the fixed bottom plate and a 12.5mm diameter top plate. 120-grit sandpaper was attached to both the top and bottom plates to prevent slipping of the test specimen. Before each experiment, the sample was thawed by placing the frozen vial in room temperature water for at least 20 minutes. Measurements of the diameter and thickness of each circular sample were taken using Vernier calipers. Each sample was placed in the rheometer with the intimal side facing up and then visually centered underneath the top plate. The top plate was moved downward until contact with the sample was confirmed. The tissue bath was filled with PBS, and a hood was closed to maintain a temperature of 25° C.

Relaxation testing comprised of an axial normal compression followed by torsional shearing. The initial normal compression of either 5%, 10%, 15%, 20%, or 25% compressive strain was applied to the specimen over the span of 10 seconds. Torsional shearing of either 10%, 20%, 30%, 40%, or 50% was then applied over the span of 1 second. The constant normal strain and torsional shear strain was then maintained for 1000s. Ten samples were experimented on at each combination of normal and torsional shear strain for a total of 250 samples.

Results

Due to microstructural reconfigurations within the tissue, we expect the experienced stress to asymptotically relax to a non-zero value. The rheometer measured the experienced normal stress and shear stress from each sample. For each combination of normal compressive strain and shear strain, the data from the ten samples was averaged together for further analysis.

We normalized the data by plotting the measured stress divided by the maximum experienced stress on the ordinate. From initial observation of our results, we cannot confidently state that varying the normal or shear strain affects the relaxation behavior. For further analysis, we will examine the quasi-linear aspects of the results by averaging the data at varying compressive strains together. The results of this are shown in Figure 1. We notice in Figure 1, that the varying shear strains do not appear to have a significant effect on the relaxation behavior. The plots of each shear strain from Figure 1 were averaged to produce Figure 2. From our results, we see that a quasi-linear model could capture the data reasonably well for the stress relaxation of the porcine aorta in both the normal and shear directions.



(a) Normalized normal stress over time

(b) Normalized shear stress over time

Fig. 1 Normalized (a) normal and (b) shear stress at varying shear strains after averaging all data at the same given normal compressive strain.

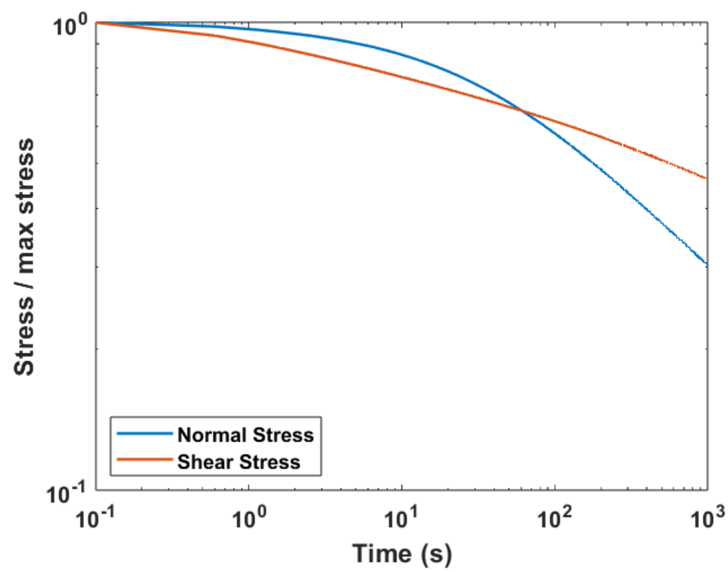


Fig. 2 Normalized normal and shear stress after averaging all data from Figure 1 at the same given shear strain.

Analysis

The normal relaxation modulus and the shear relaxation modulus are given by,

$$E(t) = \frac{\sigma(t)}{\epsilon_0} \tag{1}$$

$$G(t) = \frac{\tau(t)}{\gamma_0}, \tag{2}$$

where ϵ_0 and τ_0 denote the applied normal strain and shear strain, respectively. We normalized the data by

$$f(t;\vec{p}) = \frac{\sigma(t)}{\sigma_0} \qquad , \qquad g(t;\vec{p}) = \frac{\tau(t)}{\tau_0}. \tag{3}$$

Here, *f(t)* represents the normalized normal stress and *g(t)* represents the normalized shear stress. σ_0 denotes the initial normal stress at (the normal stress at $t = 0^+$), and τ_0 denotes the initial shear stress. We will model the normalized experimental data using a least-squares regression analysis. We will choose to model the data with

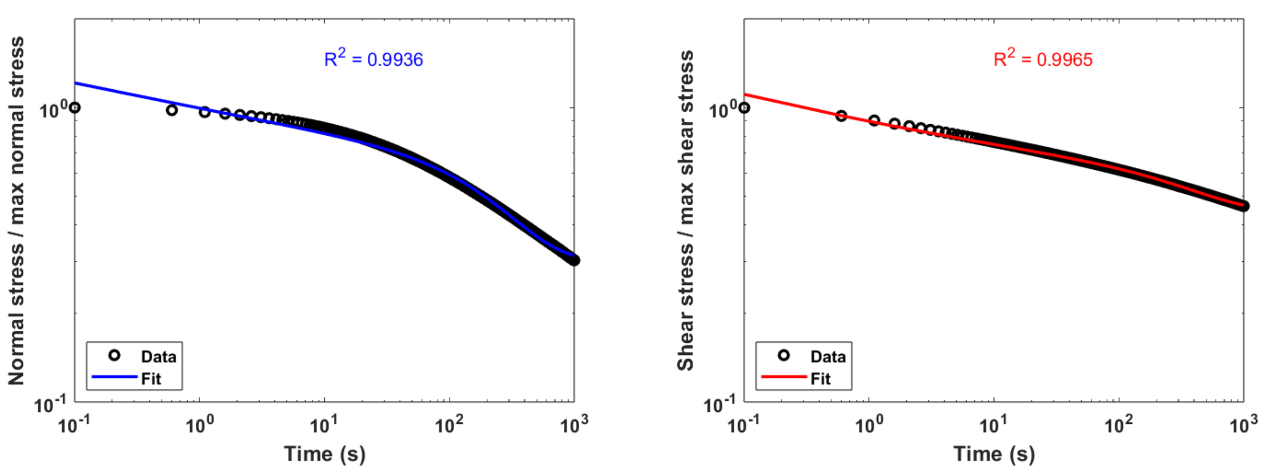
$$f(t;\vec{p}) = A + B\exp\left(\frac{-t}{\lambda}\right)\left(\frac{t}{\lambda}\right)^n. \tag{4}$$

Equation 4 is a modified version of the Weibull distribution [30]. Other variations of the Weibull distribution have been used to measure the creep and stress relaxation in polymeric materials [8]. In such models, we liken the viscoelastic, microstructural elements to a population of time-dependent mechanical latches, each with their own time to failure. The parameters n and λ are the shape and characteristic time parameters, respectively. A and B are coefficients. We seek to model the normalized data given in figure 2. We chose the modified Weibull distribution (equation 4) based on the shape of the relaxation data seen in figure 2. We expect an equation of exponential form to fit the data reasonably well. For an initial study, we are seeking to find a nonlinear equation that can be curve fit to the data with a reasonably good coefficient of determination (R-squared value).

The vector $\vec{p}$ denotes the material parameters which, in equation 4, are

$$\vec{p} = \begin{bmatrix} A \\ B \\ \lambda \\ n \end{bmatrix}.$$

We will model both the normal and shear relaxation data using equation 4. A nonlinear least squares regression produces the best-fit parameters for $\vec{p}$ given in Table 1. The experimental data, the modeled equation and the R-squared values are shown in Figure 3.



(a) Normalized normal stress over time

(b) Normalized shear stress over time

Fig. 3 The data and fit using a least-squares regression analysis of the experimental data and equation 4 for the normalized (a) normal and (b) shear stress.

We notice the characteristic time parameter, λ, differs between the normal and shear directions. We also note that, even with a nonlinear least-squares regression analysis, the model fails to perfectly capture the data at $t = 0.1$s. Because Figure 3 is on a log-log scale, the difference between the model and data becomes exaggerated compared to a linear scale. Next, we examine the results using linear-log axes to determine the effects of varying the magnitude of compressive strain and shear strain on the relaxation response.

Table 1 Solved material parameter values

Direction	**A**	**B**	$\lambda(\mathrm{s})$	**n**
Normal	0.305	0.356	293	−0.117
Shear	0.448	0.162	488	−0.166

Figure 4 shows all raw data plotted on a semi-log scale. From the data, we do not observe any clear effect of the shear strain amplitude on the stress relaxation response in either the normal or shear directions. The characteristic time generally appears to remain the same regardless of the input shear strain chosen. Considering the effect of the compressive strain amplitude, we observe a generally positive correlation between the nominal stress values and the given compressive strain. However, after normalization (Figure 1), we cannot state a clear significant effect that varying compressive strain has on the relaxation behavior.

Discussion

Implications of Experimental Data

From our normalized data, we notice there is not a significant difference in stress relaxation behavior due to varying the input normal strain nor the input shear strain. With ten samples at each combination of control variables, we believe this experiment sufficiently demonstrates that the viscoelastic response of the porcine aorta can be approximated using a quasi-linear viscoelastic model. We also note the difference in the shape of the trend lines between the normal and shear stress response. This demonstrates the anisotropy of the material.

In our analysis, we see that both data sets in the normal and shear directions can be fitted using a model of the form of equation 4. At the time of this publishing, we have not proved uniqueness to this model. In fact, we do not expect uniqueness from this model. Further study is required for the viscoelastic constitutive modeling of the porcine aorta. The purpose of this paper is to provide an experimental data set in which future modeling can be validated with.

From this data set, we see the magnitude of the time-dependence of the material in combined normal and shear loading. Within the time frame of the experiment (1000 seconds), we can further examine the viscoelastic behavior of aortic tissue. From Figure 3, we can see that neither the normal or the shear stress plateau to a finite stress value. From longer experiments, we can determine whether the material behaves as a viscoelastic solid or viscoelastic fluid.

Novelty of our experiment

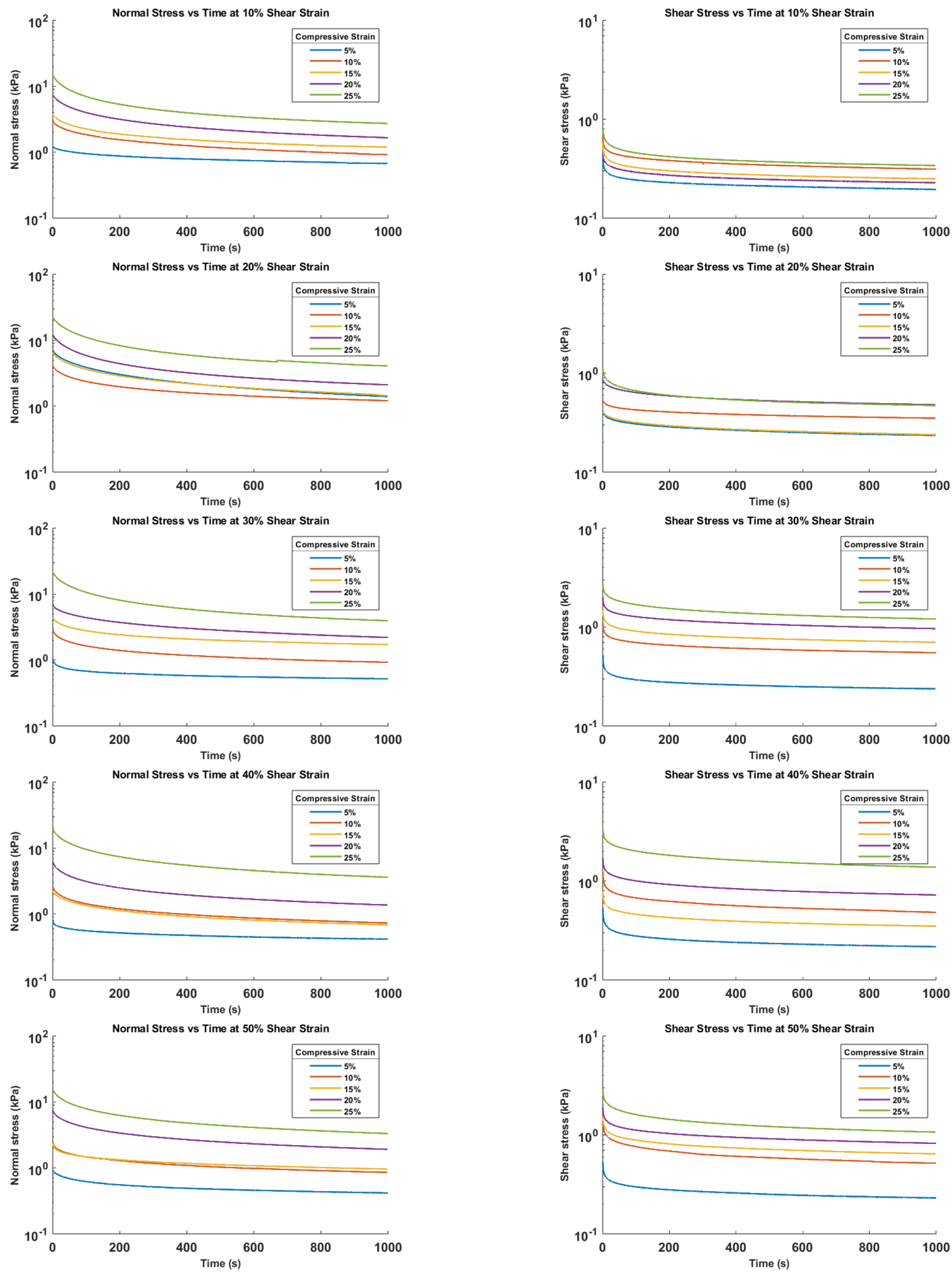
The novelty of this experiment comes from both the loading configuration and the combination of normal and shear forces onto the test samples. We did not test samples of porcine aortas in their natural, exhumed configuration. In fact, we do not expect normal physiological loadings in the configuration in which we are testing. Additionally, with the way the samples are prepared, we expect residual stresses to exist within the body. Thus, the nominal values of our experiments will not correlate to the stress values we expect to see in vivo. However, the purpose of this experiment is to gather an understanding of the viscoelastic response the porcine aorta shows under combined loading. Our methods allow us to take multiple samples from each aorta. This allows for a wider range of loading conditions and a larger number of samples at each combination. As a biological material, we expect each sample of porcine aorta to show large variance, and testing at least 10 samples at each loading condition is necessary for characterizing the material. While statistical accuracy is expected to be low for a biological material, we can minimize this by taking many samples out of each aorta retrieved.

Implication on future modeling

We discovered a clear anisotropic relaxation response within the porcine aorta. From the relaxation experiment, we determine if the material behaves as a viscoelastic solid or fluid. This will impact the choice between a Gibbs or Helmholtz free energy [27]. From our findings, we determine that future modeling of the porcine aorta must include anisotropic relaxation behavior. The rate of dissipation will need to vary in the normal and shear directions.

Questions our data pose

From figure 4, we see that the averaged data of the different compressive strains do not behave entirely as expected. In some cases, such as the data set run at 20% shear strain, we see that 10% compressive strain experiences less normal stress than

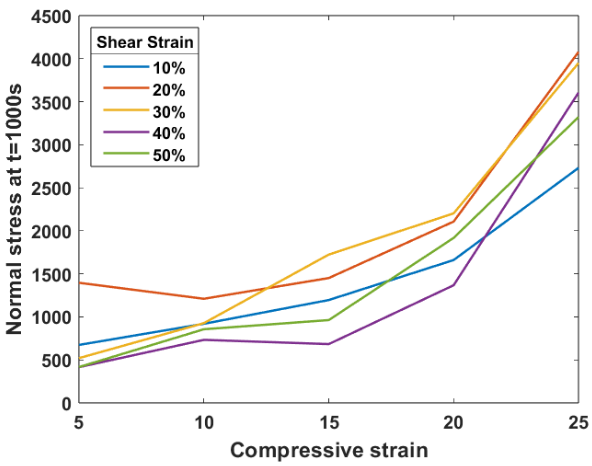


(a) Normal stress over time

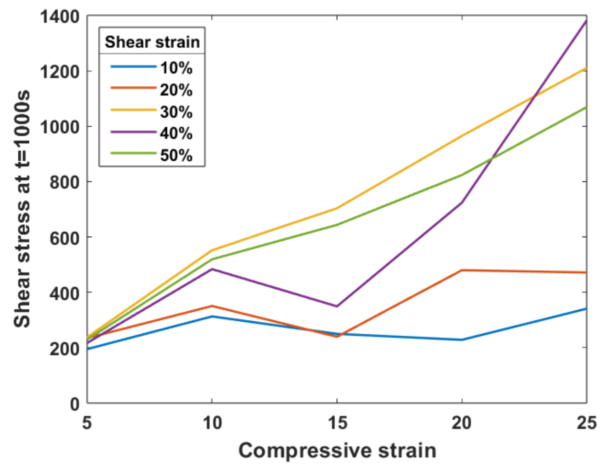
(b) shear stress over time

Fig. 4 Semilog plots of (a) normal stress and (b) shear stress as a function time at varying shear strain and varying compressive strain.

5% compressive strain. If we examine the final stress (the stress value at the end of the test) in relation to the changes in compressive strain, shown in figure 5, we do not see any definitive correlation. We expect there to be a high variance within the different biological samples, so the question arises as to whether this peculiarity in the data is a result of the large spread in experimental data or if there is something within the microstructure of the porcine aorta that leads to such a phenomenon.



(a) Final normal stress vs applied compressive strain



(b) Final shear stress vs applied compressive strain

Fig. 5 The (a) normal and (b) shear stress at time t = 1000s as a function of the applied compressive strain. The varying shear strains are plotted on the same figures.

Conclusions

We noticed the relaxation behavior is different in the normal and shear directions. The amplitude of compressive strain appears to have a larger impact on the quantitative experienced stress compared to the amplitude of the applied shear strain. There appears to be some nonlinear correlation between the normal and shear stress responses of the porcine descending aorta. Further investigation is required to better characterize this correlation.

Future work

Future work for this project will include a creep experiment to examine if the creep behavior can be predicted using this relaxation data. This creep experiment will be conducted using similar testing conditions as those found in this paper. We expect the porcine aorta to behave as a nonlinear material, so the creep behavior should not be able to be directly predicted from the relaxation data. Creep experimental data will be needed to confirm such hypotheses. An analysis on the kinematics and force balances will also be done for the problem given by this experimental set up. With the creep and relaxation data and the mechanics analysis, further improvements on constitutive modeling can be made.

The purpose of this study is to provide a robust set of experimental data on the relaxation response of the porcine aorta. As such, testing time was limited to 1000 seconds per sample. In the future, we seek to test samples until the value of the stress plateau in both the normal and shear directions. This will help to determine with certainty if the porcine aorta acts as a viscoelastic solid or viscoelastic fluid. We also seek to perform histology analysis on samples used in these relaxation experiments. This will further examine how the relaxation response of the porcine aorta relates to the permanent damage to the tissue.

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