

# Poroviscoelastic Modeling of Stress Relaxation of Porcine Liver to Investigate Injury Response

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## ABSTRACT

Highly vascular tissue is a combination of solid and fluid components. The interaction between these two phases during deformation creates a viscoelastic or rate-dependent behavior. To understand how fluid and solid components contribute to the injury response of liver tissue, a constitutive model is needed which reflects the biphasic nature of the material. This study aims to capture the stress relaxation response of porcine liver in unconfined compression using biphasic poroviscoelastic (PVE) modeling. Seventeen fresh porcine liver specimens (19mm diameter, 10mm thick) were compressed to 5% strain at varying strain rates ( $.001s^{-1}$ ,  $.01s^{-1}$ ,  $.1s^{-1}$ ) using a Bose Electroforce Test Instrument. Relaxation response was monitored for 2000 seconds until equilibrium was achieved. Abaqus (v6.8-2, Simulia) SOIL analysis was used to create a PVE axisymmetric finite element model for each strain rate group. Rate dependent and independent responses of the solid phase were modeled with a three-term Prony series and a hyperelastic material model respectively. Best fit parameters were determined using nonlinear least-squares algorithms. Poisson's ratio was selected as 0.49, the initial void ratio 0.2, and material permeability  $3.09 \times 10^{-13} m^4/Ns$ . Compression data showed rate dependence of the peak reaction force. Best fit Prony series parameters were  $g_1=0.5026$ ,  $g_2=.1848$ ,  $g_3=0.1418$ ,  $\tau_1=2.1s$ ,  $\tau_2=47.1s$ ,  $\tau_3=380.1s$  and the initial shear modulus was 795Pa. Linear regression analysis between model and experiment resulted in  $R^2$  values of 0.997, 0.988, and 0.989 for  $0.001s^{-1}$ ,  $0.01s^{-1}$  and  $0.1s^{-1}$  respectively ( $p<0.05$ ). The PVE model accurately predicted the stress relaxation behavior of porcine liver tissue. Advantages of the PVE model include the ability to simulate both the overall mechanical response and the fluid pressure changes in response to loading. Future studies will validate pore fluid pressure model predictions and incorporate higher strain rates to examine interstitial fluid pressure as an injury severity indicator.

## **INTRODUCTION**

Liver injuries account for one-third of all abdominal injuries, with 5% of trauma cases pertaining to liver injury (Moore, 2004). The most common source of blunt liver injury arises from motor vehicle crashes (Moore, 2004). Computational models created from an understanding of the biomechanics of blunt liver injury can aid in evaluating the risk of liver injury. Data from these models may be valuable in progressing vehicle safety.

Previous studies have modeled the mechanical response of liver tissue in high rate loading typical of impact trauma, using phenomenological models such as quasilinear viscoelasticity (QLV) (Miller, 2000; Tamura et al., 2002; Sparks and Dupaix, 2008). In contrast to these studies, the current study adopts a more mechanistic model of liver tissue, basing model design on material structure. The benefit of this approach is the ability to study the interaction between solid and fluid phases of the material.

Vascular tissues such as liver are made up of a combination of solid matrix and fluid from arterial, venous, lymphatic and interstitial sources. This allows the characterization of this tissue as biphasic, or a combination of solid and fluid phases (Mow, 1980). A biphasic poroviscoelastic model allows the rate dependence of the tissue to stem from both intrinsic properties of the solid matrix as well as the interaction between solid and fluid phases. This type of analysis has been used considerably to characterize cartilage and intervertebral discs, and more recently visceral organs (Cheng and Bilston, 2007; Ng et al.; 2005, Ford et al., 1991). An extensive literature search revealed no characterization of liver tissue in this manner.

The objective of this study is to characterize the behavior of porcine liver tissue in unconfined compression through biphasic poroviscoelastic modeling. Strain rates will be varied in order to determine model capability to predict rate-dependence.

## **METHODS**

### **Specimen Preparation**

Porcine livers were acquired from a local abattoir and kept on ice until testing. All testing was conducted within 24 hours post mortem. Seventeen discs, 19mm in diameter and 10mm thick were collected using a scalpel and stencil. The capsule was preserved on the lower surface in order to create parallel loading surfaces.

### **Test Configuration**

Compression testing was conducted using Bose Electroforce (Eden Prairie, MN) equipment and WinTest control software. Samples were tested in a heated (37°C), high humidity environmental chamber designed to prevent sample dehydration. Friction was minimized through a maintained water interface between sample and platens throughout testing.

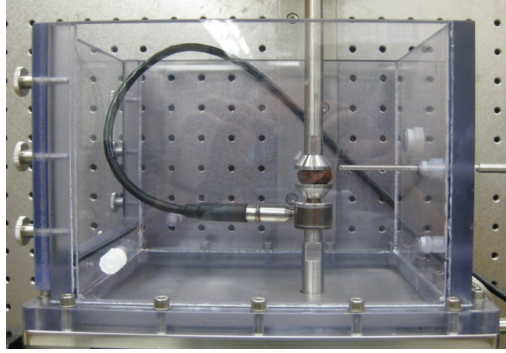


Figure 1: Mechanical testing configuration with environmental chamber (508mm x 381mm x 381mm) for temperature and humidity control.

### **Equilibrium Stress-Strain Experiments**

Equilibrium stress-strain testing was based on work by DiSilvestro on articular cartilage (2001). Successive ramp displacements at rates of  $.01\text{s}^{-1}$  were applied to three tissue samples. Specimens were allowed to equilibrate before the next ramp displacement was applied. Equilibrium was achieved with a relaxation rate of less than  $.01\text{g/s}$  for the final 100 seconds of equilibration. (DiSilvestro et al., 2001). Reaction forces were monitored with a 10N compression load cell (Honeywell Model 31, Bose Electroforce). Strains of 5, 10, 15, 20 and 25% were tested and Lagrangian stress values were recorded at equilibrium.

### **Unconfined Compression Experiments**

Seventeen samples were tested in unconfined compression. A preload of 10% strain was imparted to the samples at a rate of  $.001\text{s}^{-1}$  prior to compression testing. Relaxation was noted for 900 seconds until equilibrium was achieved. A prestrain of 10% was selected in order to create regular loading across the sample surface and achieve repeatable initial stresses.

After prestrain, a ramp displacement was applied to 5% strain at rates of  $.001$ ,  $.01$  or  $.1\text{ s}^{-1}$ . Relaxation was monitored for 2000 seconds until equilibrium was achieved.

### **Finite Element Modeling**

Finite element modeling was conducted using Abaqus (v6.8-2, Simulia Corp.) SOIL analysis. Wu et al. (1998) reported that commercial FEA software based on poroelastic theory provided similar results to FEA codes derived from biphasic theory. Unconfined compression was modeled using three separate axisymmetrical finite element models with geometries based on average sample dimensions per strain rate. Boundary conditions consisted of restraining the lower surface in the vertical direction, symmetry conditions at the symmetry axis and a pore fluid pressure of zero on the lateral surfaces of the model (Cheng and Bilston, 2007). This final boundary condition allowed fluid to freely escape the model during compression. Four-node axisymmetric quadrilateral elements with reduced integration were used (type CAX4RP). The mesh of 168 elements was based on an algorithm from Spilker et al. (1990) for testing of unconfined compression of cartilage. Mesh density was validated with mesh convergence testing.

The liver was modeled as a combination of fluid and solid phases. The solid phase was modeled as a viscoelastic material. A three-term Prony series (Eq. 1) was used to describe the rate dependent response with  $G_0$  representing the instantaneous shear modulus and  $g_k^P$  and  $\tau_k$  as input

parameters governing tissue relaxation.  $Gr(t)$  is the time-dependent shear relaxation modulus characterizing the material response (Abaqus, 2008). Parameters for the Prony series were determined using a nonlinear least-squares error minimizing algorithm, curve fitting mean relaxation data from the fastest strain rate.

$$Gr(t) = G_0 \left( 1 - \sum_{k=1}^N g_k^p (1 - e)^{-\left(\frac{t}{\tau_k}\right)} \right) \quad (1)$$

A hyperelastic material model (Eq. 2) was used to describe the rate independent response of the solid matrix. The model is described by  $U$  (the strain energy per unit reference volume),  $\bar{I}_1$  (the first deviatoric strain invariant),  $J^{el}$  (the elastic volume ratio), and  $N$  (the polynomial order) (Abaqus, 2008). Material parameters ( $C_{i0}$ ,  $D_i$ ) were determined using a least-squares fit to mean equilibrium stress-strain data (Fig. 2).

$$U = \sum_{i=1}^N C_{i0} (\bar{I}_1 - 3)^i + \sum_{i=1}^N \frac{1}{D_i} (J^{el} - 1)^{2i} \quad (2)$$

Poisson's ratio was assumed to be 0.49 (Kim 2003), material permeability ( $k$ )  $3.09 \times 10^{-13} \text{ m}^4/\text{Ns}$  (Swabb, 1974) and initial void ratio ( $e$ ) 0.2 (Cheng and Bilston, 2007; Nagashima et al., 1987).

## RESULTS

### Equilibrium Stress-Strain Relationship

The average equilibrium stress-strain response showed a nonlinear relationship over the strains tested (Fig. 2). Variation increased with added strain as demonstrated by the 95% confidence interval bars. This variation pattern was similar to that observed by DiSilvestro et al. for articular cartilage (2001).

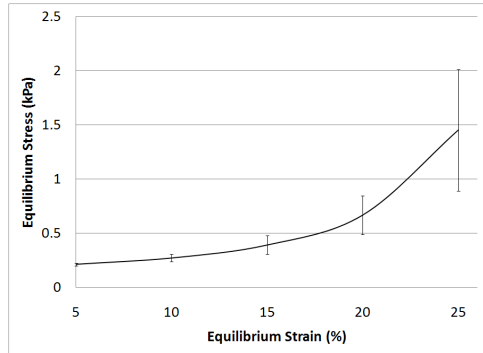


Figure 2: Steady state stress compared to various tissue strain shown with 95% confidence intervals.

### Unconfined Compression Response for Varying Strain Rates

Reaction forces are reported in this study because sample diameter was not monitored throughout testing. A rate dependent response is clearly shown (Fig. 3), with peak reaction forces varying with strain rate. However, equilibrium reaction force was consistent across strain rates, demonstrating no rate dependence for that portion of the tissue response. Maximum coefficients of variation (standard deviation divided by mean) for the loading rate were 0.42, 0.35 and 0.22 for the  $.001\text{s}^{-1}$ ,  $.01\text{s}^{-1}$  and  $.1\text{s}^{-1}$  loading rates respectively. The unloading coefficients of variation

had similar values with 0.41, 0.35 and 0.31 for the  $.001s^{-1}$ ,  $.01s^{-1}$  and  $.1s^{-1}$  loading rates. These coefficients of variation demonstrate acceptable repeatability, and are comparable to numbers from Cheng and Bilston (2007) for unconfined compression of white matter.

### Model Fitting

Prony series parameters were determined from the mean relaxation data from the  $.1s^{-1}$  strain rate. They were determined to be  $g_1 = 0.5$ ,  $g_2 = 0.19$ ,  $g_3 = 0.14$ ,  $\tau_1 = 2.1s$ ,  $\tau_2 = 47s$  and  $\tau_3 = 380s$ . Hyperelastic material parameters were determined from average equilibrium stress-strain data to be  $D_1 = 5.063 \times 10^{-5}$ ,  $D_2 = 0$ ,  $C_{10} = 397.69$  Pa and  $C_{20} = 208.55$  Pa. Initial shear modulus was calculated as  $\mu_0 = 2C_{10} = 795.38$  Pa, and bulk modulus was determined to be  $K_0 = \frac{2}{D_1} = 39502.27$  Pa.

Table 1: Poroviscoelastic model parameter values.

Model Type	Solid Phase										Fluid Phase	
	Rate-Dependent Response						Rate-Independent Response					
	$g_1$	$g_2$	$g_3$	$\tau_1$ (s)	$\tau_2$ (s)	$\tau_3$ (s)	$D_1$	$D_2$	$C_{10}$ (Pa)	$C_{20}$ (Pa)	$k$ ( $m^3/Ns$ )	$e$
PVE	.5	.19	.14	2.1	47	380	5.1E-05	0	397.7	208.6	3.1E-13	.2

These parameters (Table 1) were used to predict the mechanical response of the two slower strain rates ( $.01s^{-1}$  and  $.001s^{-1}$ ) (Fig. 3). Linear regression analysis was conducted comparing experimental data against the PVE models. A high goodness-of-fit was indicated for the comparison between PVE and experimental data ( $R^2 = .988$  to  $.997$ ). A slope near unity indicates a one to one correlation between model and experiments (slope = 0.799 to 1.038,  $p < .05$ )

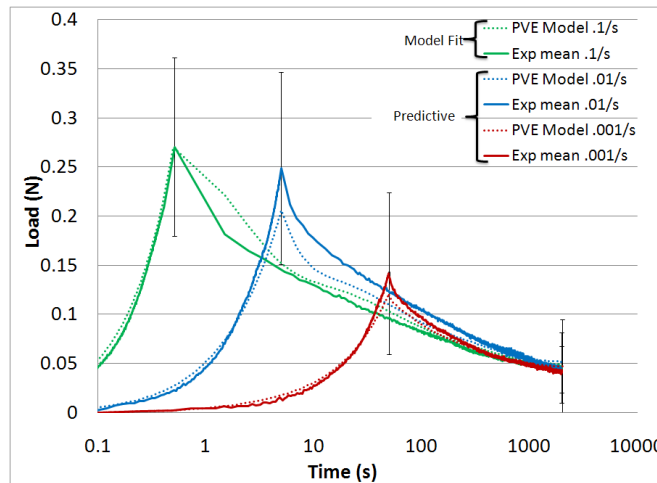


Figure 3: Experimental data (shown with 95% confidence intervals) compared to PVE model on a log time scale. Highest confidence intervals occurred at peak loading.

### CONCLUSIONS

PVE models correlated well to experimental data ( $R^2 > .988$ , slope  $> .8$ ). A significant advantage of the PVE model is the ability to calculate pore fluid pressure (Fig. 4). Pressure has been shown to correlate to whole organ injury severity (Sparks et al., 2007; Foster et al., 2006), but the

magnitude of contribution from solid or fluid components is unknown. A model demonstrating the individual pressure contributors will aid in determining which plays a greater role in injury causation.

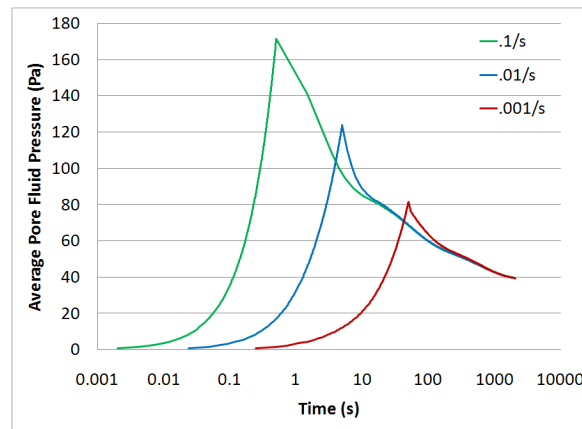


Figure 4: Pore fluid pressure time history for  $.001s^{-1}$ ,  $.01s^{-1}$  and  $.1s^{-1}$ .

Pore fluid pressure (Fig. 4) has the same shape as force-time data, demonstrating a rate dependence of peak values, but rate-independence for equilibrium values. Under physiological conditions, interstitial fluid pressures (IFP) is 133-400 Pa (1-3 mmHg) relative to atmospheric pressure (Guyton, 2006). All testing for this study was conducted at atmospheric pressure; therefore, it is reasonable to expect pore fluid pressure (Fig. 4) to fall within this range considering the low strains and strain rates imparted to tissue during testing. Future work will validate model IFP predictions experimentally.

Frictionless boundary conditions for specimen-platen interface were assumed for model creation. This was considered a reasonable assumption based on the preserved fluid boundary between sample and platen, maintained by the humid testing environment. The near-frictionless condition allowed the free expansion of the tissue in response to loading. However, previous studies have shown that overestimated model reaction forces may result from unaccounted friction (Wu et. al 2004a). Complete elimination of friction may not be possible with the current experimental setup. Therefore, a technique proposed by Wu et al. (2004b) to integrate residual friction into model will be investigated for use in future work.

In order to maintain sample diameter and parallel loading surfaces, the liver capsule was retained on the lower surface of the specimen. Due to the fibrous nature of the capsule, free expansion of tissue near the capsule surface may have been somewhat limited. However, these interactions are inherent to the total response of liver tissue, which is applicable when considering injury. Future work will investigate methods for complete capsule removal and study the effect of the capsule on liver response.

A single set of parameters was able to model liver response to three different strain rates using a mechanistic PVE model created in Abaqus. In the context of injury prediction, PVE models offer the additional benefit of calculating pore fluid pressure, which may be helpful in further understanding injury causation from fluid or solid pressure components. For strain rates on the order of  $.01s^{-1}$ , peak reaction forces have been shown to depend strongly on interstitial fluid pressurization (Cheng and Bilston, 2007). Future work will investigate this effect at strain rates typical of impact trauma (Tamura 2002; Melvin 1973).

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