Development of a Constitutive Model for Brain Tissue under Multiaxial Loading

Mehdi Shafieian*[,1] , Kaveh Laksari[2], Kurosh Darvish[2] , Jeff Crandall[1]

Abstract Material properties of brain tissue have been characterized under different modes of loading; however it has been shown that a constitutive model developed under one mode of loading (e.g. shear) may not necessarily predict the behavior of the tissue under another mode of loading (e.g. compression). In this study a viscoelastic constitutive model for brain tissue was developed that is capable of predicting the behavior of the tissue under multiaxial loading. Step and hold tests under shear and compression loading were performed on bovine brain samples with a strain rate of 10 s^{-1} to strain levels of 30%. The applicability of quasi-linear viscoelastic assumption was validated for strain levels up to 30% for shear and compression deformation. A generalized Rivlin model with 3 terms was considered and the response of this model to shear and compression was determined. These responses were used to determine the viscoelastic behavior under each mode of loading by fitting to the experimental model simultaneously. The hyperelastic material parameters and parameters of a relaxation function at 4 decay rates were determined. The developed model was compared with previously developed models and it showed a close agreement with them in their corresponding mode of loading, while having the advantage of modeling multiaxial loading as well.

Keywords Brain tissue biomechanics, material properties, finite deformation, shear and compression test, viscoelasticity

I. INTRODUCTION

Traumatic Brain Injury (TBI) caused by direct impact or sudden movement of the head is a contributing factor to one-third of all motor vehicle related deaths in the United States [1]. While Finite Element (FE) simulations can be used to study the mechanisms of TBI and to develop injury prevention techniques, a key element in developing more realistic FE models of the head–brain complex is improving the knowledge of brain tissue material properties.

A large degree of the variability of brain tissue material properties reported in the literature can be associated partly with the differences in experimental methods, i.e., modes of loading and loading rates. Material properties of brain tissue have been mostly characterized under a specific type of loading, e.g., compression [2, 3, 4], tension [5], shear [6, 7, 8], or loading condition, e.g., ramp and hold or oscillation [9]. The derived constitutive equations that represent the tissue material properties under one loading condition do not necessarily predict the behavior of tissue under another mode of loading, e.g. Miller and Chinzei [3] developed a constitutive model for brain tissue under compression and later on showed this model does not predict the brain behavior under tension [5]. Several physical models and FE simulations of brain tissue under loading conditions that relate to TBI have been developed [10, 11, 12] and showed that the brain tissue undergoes a complex combination of loading modes during impact, which signify the need for a comprehensive constitutive model for brain tissue suitable for multiaxial loading.

This study proposes a Quasi-Linear Viscoelastic (QLV) constitutive model for brain tissue consisting of a hyperelastic function and a relaxation function in the form of decaying Prony series to represent the elastic and time-dependent behaviors of the tissue. A three-term generalized Rivlin hyperelastic model was used and characterized based of the response of the tissue under shear and compression tests and the material parameters were found.

* Corresponding author, mehdi@virginia.edu, 001-434-296 7288
[1] University of Virginia, Center for Applied Biomechanics, Charlottesville, VA
[2] Temple University, Department of Mechanical Engineering, Philadelphia, PA

II. METHODS

Experimental Setup

52 cylindrical samples with approximate diameter of 10mm and height of 8mm were acquired from fresh bovine brain tissue from a local slaughterhouse. Bovine brain tissue was chosen due to its availability and similarity in material properties to human brain [8]. In order to maintain the ionic balance and water content, the brains were kept in Phosphate Buffered Saline (PBS) solution immediately after purchase and kept at 0-5°C prior to the experiments, which were conducted 3 to 6 hours post-mortem. The specimens were removed from the PBS solution to perform the experiment which approximately took 2-4 minutes and during this period of time were not hydrated.

Two modes of loading were implemented in the experiments, namely, a group of samples underwent shear (n=30) and the second group were tested under compression (n=22) and previously reported [4]. For a detailed account of the compression tests, the reader is directed to study the report by Laksari et al. [4]. For the shear tests a custom-made testing device that consisted of two parallel plates with the lower plate attached to a high-speed linear actuator (WM60, PT-USA, VA; 95UMB300 and MD-404, Emerson, MO, ±20μm accuracy) and the upper plate attached to a precision load cell (GSO10, Transducer Technique, CA, ±1mN accuracy). For compression tests the configuration setup of the test device was reoriented to apply vertical load. Figures 1 and 2 show the shear and compression test setup. A step-and-hold input was applied and the displacement and resulting shear force were recorded. For the small displacements in this study (less than 2 mm) the actuator provided an approximately constant strain rates in the samples.

For shear tests a no-slip boundary condition was achieved by gluing samples to the plates with a thin layer of commercial cyanoacrylate glue and to assure full contact between samples and plates, approximately 10% compression was applied and its effect was included in subsequent analyses. For compression tests to ensure uniaxial compression and maintain the free-sliding boundary condition, vegetable oil was applied to both plates. In order to achieve repeatable results a constant initial compression of 10% was applied before the step-and-hold tests and sufficient time was allowed (2 to 3min) for the samples to relax.

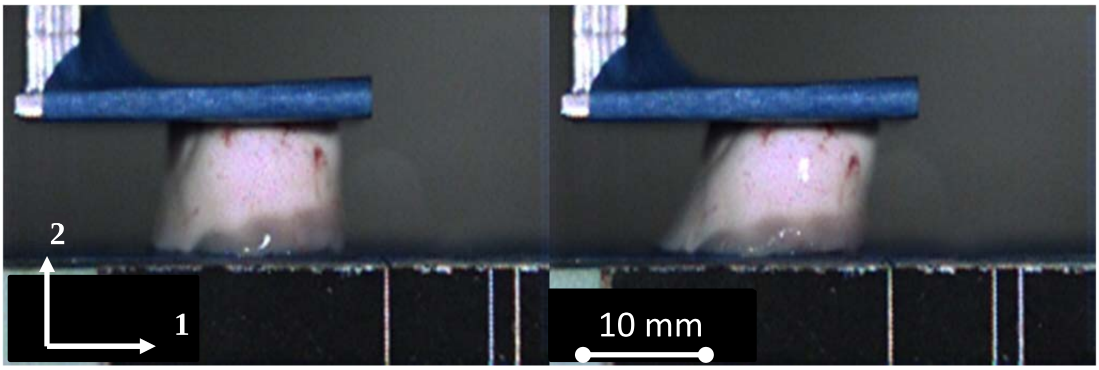


Figure 1. The shear experimental setup before (left) and after (right) deformation

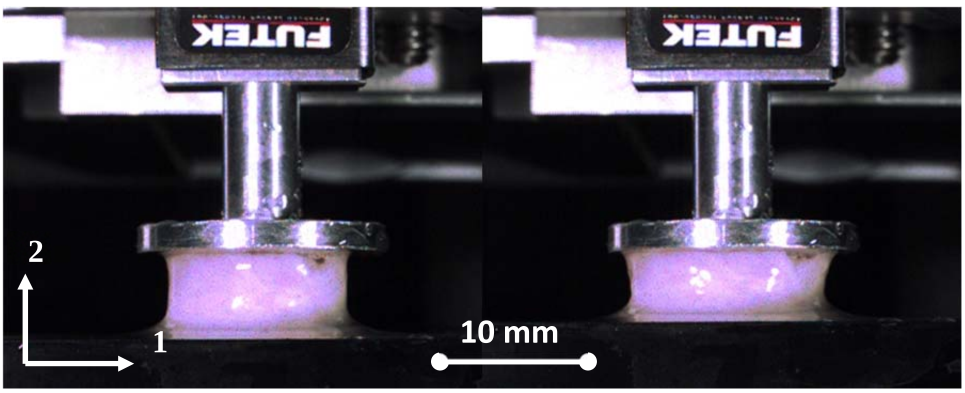


Figure 2. The compression experimental setup before (left) and after (right) deformation (from Laksari et al [4])

Samples in both shear and compression tests were tested at engineering strain levels ranging from 5% to 40% and strain rate of approximately $10s^{-1}$, ramp time of 30ms and hold time of 20s. The average strain rate was calculated based on the sample height, applied displacement and the ramp time. This strain range significantly exceeds the threshold of axonal injury of 18% tensile strain [13].

Data Analysis

The relationship between the measures of stress $\sigma(t)$ and strain $\varepsilon(t)$ were modeled using the QLV theory [14] which can be written as:

$$\sigma(t) = \int_0^t G(t-\tau)\frac{\partial\sigma^e(\varepsilon)}{\partial\varepsilon}\frac{\partial\varepsilon}{\partial\tau}d\tau \quad (1)$$

where $\sigma^e(\varepsilon)$ is the instantaneous elastic function and $G(t)$ is the reduced relaxation function. A discrete spectrum approximation in the form of Prony series was assumed for $G(t)$:

$$G(t) = G_\infty + \sum_1^4 G_i e^{-\beta_i t} \quad (2)$$

with G_i and β_i representing the amplitudes and decay rates of relaxation respectively. Based on the durations of hold and ramp times, four constant decay rates were chosen to capture any decays that occurred in the time scales of 0.01, 0.1, 1.0 and 10s.

The applicability of QLV theory was validated by forming and comparing two isochronous curves (stress values at different strain levels but at the same time interval after the peak stress) at 0.1 and 10 s after the peak force. The isochronous curve at 0.1 s then was used to characterize the instantaneous elastic response shape as explained by Laksari et al. [4].

The sample deformation for shear tests was assumed to be a combination of simple shear and uniaxial compression with the following deformation gradient:

$$F_s = \begin{bmatrix} \lambda_1 & k\lambda_2 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_1 \end{bmatrix} \quad (3)$$

where k is the engineering shear strain defined as lateral displacement of the sample divided by its height, λ_2 is the stretch ratio corresponding to the constant compression in X_2 direction and λ_1 is the stretch ratio in X_1 and X_3 directions (Figures 1 and 2) and due to incompressibility $\lambda_1^2\lambda_2=1$. The above deformation gradient describes compression deformation when $k=0$ and was used to characterize the compression tests.

Assuming samples to be homogenous and isotropic, a generalized Rivlin model was assumed for the strain energy function [4] as:

$$W = C_{10}(I_1-3) + C_{01}(I_2-3) + C_{11}(I_1-3)(I_2-3) \quad (4)$$

in which I_1 and I_2 are the invariants of the Right Cauchy-Green strain tensor. The Ogden model was also considered, however Rivlin model was preferred because of simplicity and there was no significant advantage in term of number of parameters. In this study, the first Piola-Kirchhoff shear stress P_{12} was used as the measure of stress. For shear tests, the amount of shear k and for compression tests, λ (stretch ratio in the direction of compression) were used as the measure of strain.

Considering the applied 10% compression preload to shear tests, P_{12} was written as:

$$P_{12} = 3.24\,C_{11}k^3 + (1.8C_{10} + 2C_{01} + 0.1267C_{11})k \quad (5)$$

In case of compression the normal stress (P_{22}) was written as:

$$P_{22} = 6\,C_{11}\lambda^2 + (2C_{10} - 6C_{11})\lambda + 2C_{01} - 6C_{11} + \frac{6C_{11} - 2C_{10}}{\lambda^2} + \frac{6C_{11} - 2C_{01}}{\lambda^3} - \frac{6C_{11}}{\lambda^4} \quad (6)$$

By assuming the QLV material model, it can be stated that the instantaneous elastic response is the isochronous curve formed at any time after the peak force multiplied by a constant K. For this study, the calculated P_{12} and P_{22} were fitted to the shear and compression isochrones respectively at 0.1 s after the peak force simultaneously. In this approach, P_{12} and P_{22} were fitted to the data using the same material parameters (C_{10}, C_{01}, C_{11}) by minimizing the sum of squared errors (SSE) and material parameters were determined.

Equations (5) and (6) (for shear and compression tests respectively) were used with equations (1) and (2) to calculate the total stress of the QLV model, and by minimizing (forward newton approach) the SSE of the model results with respect to the experimental ramp and relaxation data, the scale factor K and the reduced relaxation amplitudes G_i were determined for each experiment.

III. RESULTS

The isochronous curves at 0.1 and 10 s after the peak stress for shear and compression tests are shown in Figure 3. The models are based on Equation (5) and (6) and the material parameters are the same at each isochron. Table 1 contains the material parameters at isochrones 0.1 and 10 s.

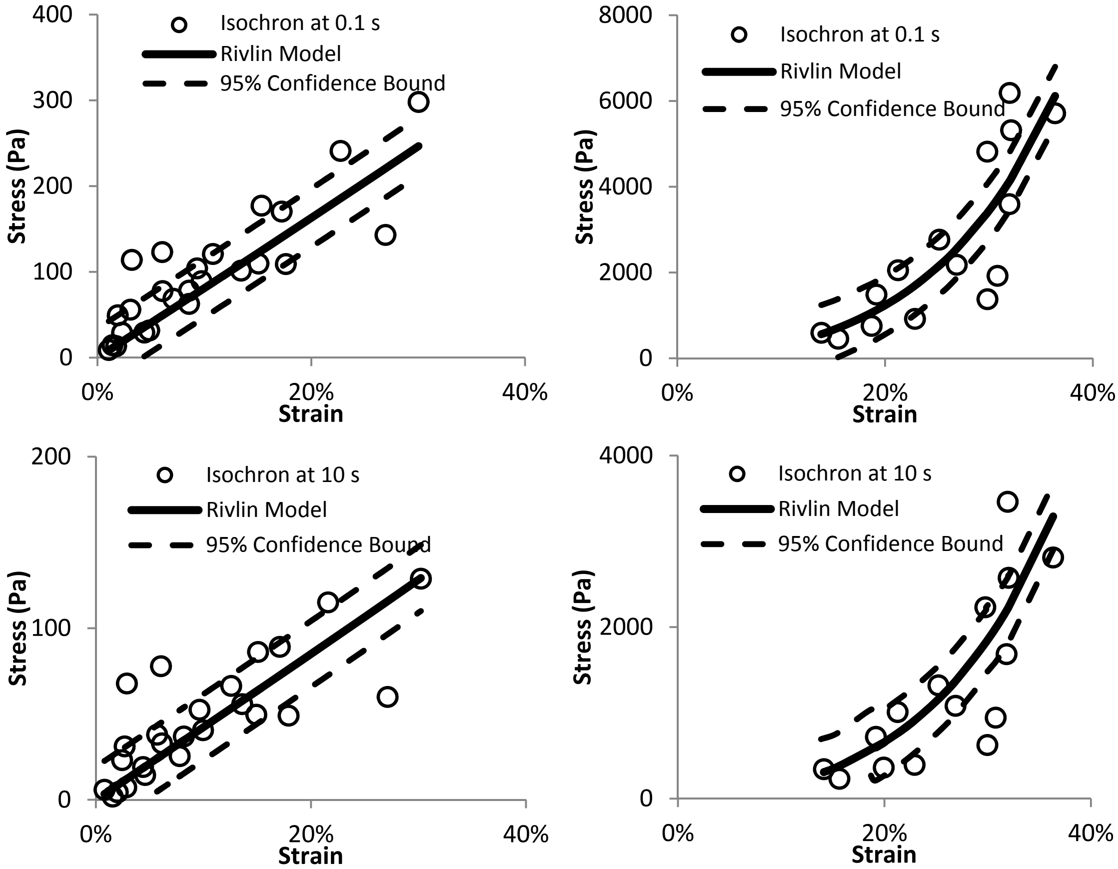


Figure 3. The experimental and Rivlin model fitted to the isochrones at 0.1 and 10 s for shear (left) and compression (right). Note that the Rivlin model fitted to the shear and compression isochrones at 0.1 s (top) have the same material parameters. The isochrones at 10 s (bottom) also have the same material parameters. These material parameters are reported in Table 1.

The validity of QLV assumption was examined by plotting the experimental stresses at isochron 0.1 and 10 versus each other (Figure 4). A straight line with a slope of the average of ratio of model stresses was also plotted as a representative of QLV assumption. As it is shown, the experimental data fall within the error of the QLV model and state the validity of QLV assumption.

The constant ratio between the 2 formed isochronous curves indicates that the 2 curves are different by a constant factor and the instantaneous elastic response can be either of them multiplied by a constant to shift the isochronous curve to the peak when an ideal step is applied. The isochron at 0.1 s was used to determine the scale factor K and the amplitudes of the reduced relaxation function (Table 2). The results showed a slight difference between the K value in shear and compression, 3.24±0.27 and 3.36±0.35 respectively; however a t-test showed there is no significant difference between these two values with p value of 0.798.

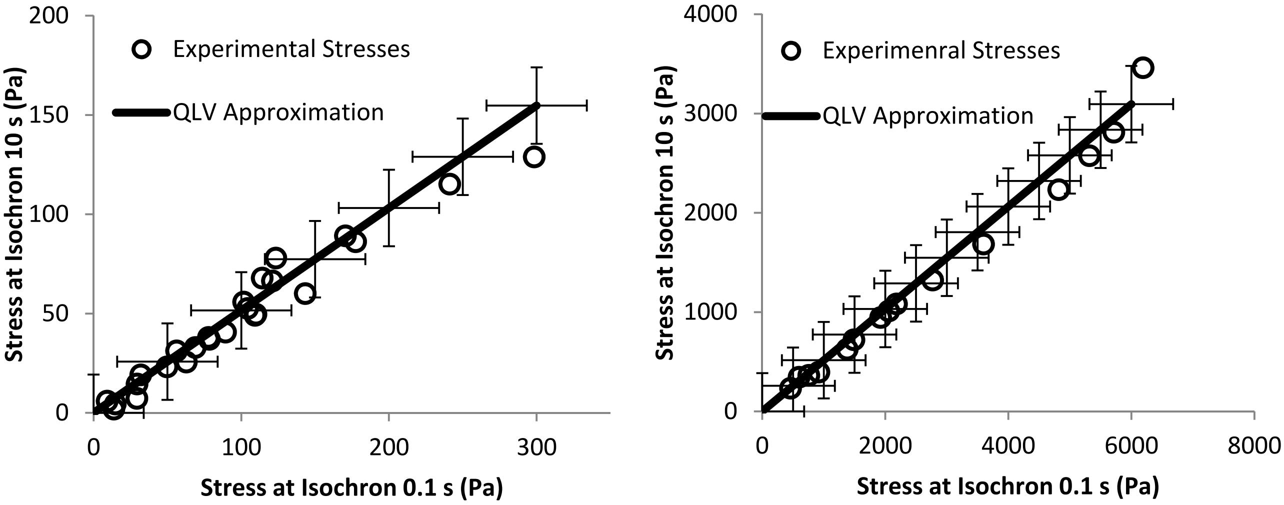


Figure 4. Experimental stress at 0.1 and 10 s for shear (left) and compression (right). A constant ratio between the isochrones states the validity of QLV theory. As it is illustrates, the experimental data fall within the variability of the model.

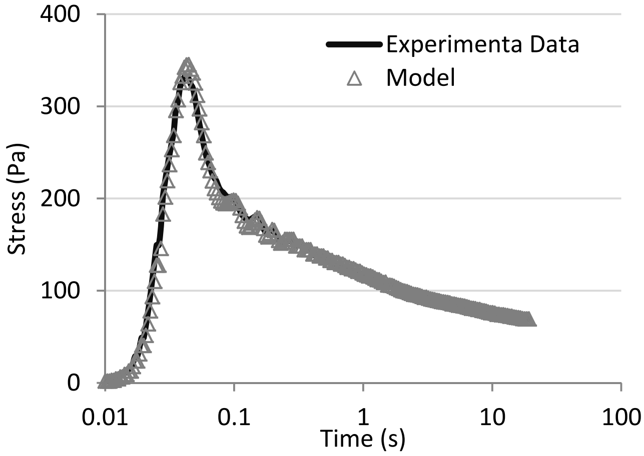
Table 1. The material parameters found by fitting to isochron at 0.1 s and 10 s

	Isochron at 0.1 s	Isochron at 10 s
C_{10} (Pa)	-2346.177	-1306.533
C_{01} (Pa)	2513.613	1386.002
C_{11} (Pa)	40.475	17.669

Table 2. The parameters of instantaneous elastic response and reduced relaxation function for brain tissue. All material parameters were statistically significant.

Instantaneous Elastic Response				Reduced Relaxation Function			
C_{10}	-2346.177		Pa	G_∞	0.143	±	0.049
C_{01}	2513.613		Pa	$G_1(\beta_1$=0.1/s)	0.116	±	0.090
C_{11}	40.475		Pa	$G_2(\beta_2$=1/s)	0.103	±	0.085
				$G_3(\beta_3$=10/s)	0.187	±	0.078
K	3.292	±	0.213	$G_4(\beta_4$=100/s)	0.451	±	0.066

Figure 5 shows a representative of experimental data and model fitted in shear and compression under 20% strain. The shown models both resulted from the same sets of material parameters (Table 2) and successfully captured the experimental data. The slight difference between model and experimental data at peak stress is due to the inertial effect.



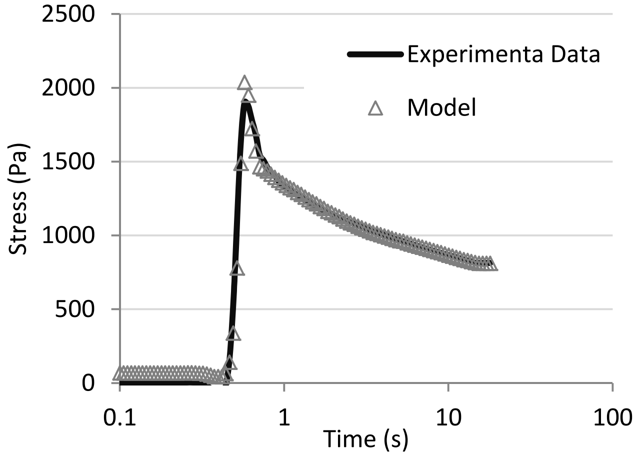
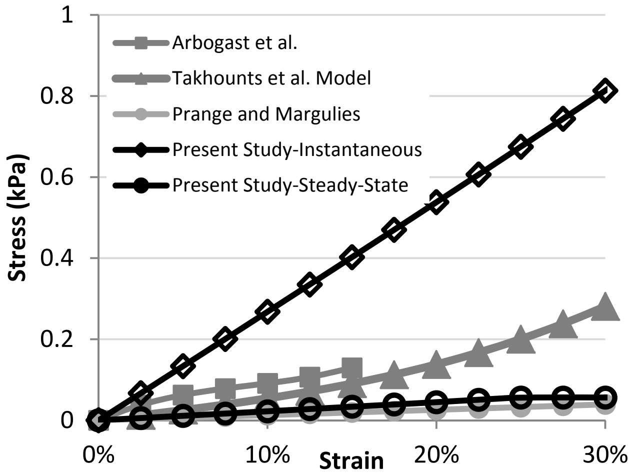


Figure 5. A representative of experimental data and fitted QLV model to shear (left) and compression (right). The models are the results of the same sets of material parameters presented in equation (5) and (6).



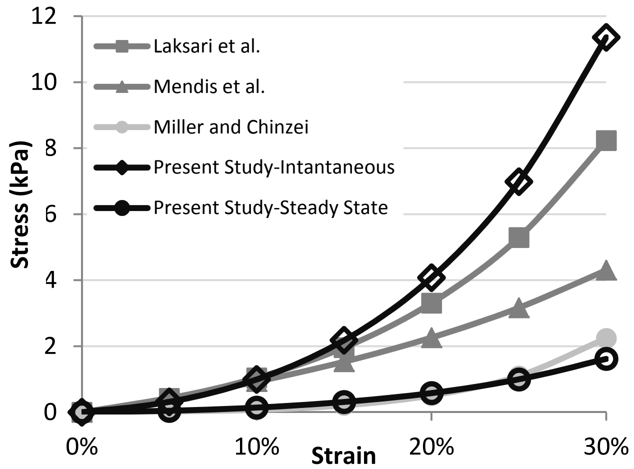


Figure 6. The instantaneous elastic response and steady state response found in this study in comparison with previous studies for shear (Left) and Compression (Right)

IV. Discussion

This study validated the applicability of the theory of QLV to characterize the behavior of the brain tissue and proposed a QLV constitutive model is capable of predicting the behavior of the tissue under a combined mode of loading of shear and compression up to 30% strain.

The proposed generalized Rivlin model with 3-terms (Eq. 4) to capture the elastic behavior of the tissue predicts the behavior of the tissue under shear and compression loading condition and is in agreement with the most recent reported studies [4, 15]. Combining the results of this study with the available results of the brain tissue in tension will be a significant expansion of the present model in all modes of loading.

The predicted elastic response in this study for a complex mode of loading is in close agreement with previous studies. The previously reported instantaneous elastic responses [6, 8] fall between the instantaneous and steady state elastic response determined in this study (Figure 6); however, reported response by Prange and Margulies [7] is softer and that can be due to small sample thickness and possible mechanical damage. The almost linear response in shear (due to the small C_{11} constant) is in agreement with reported response by Prange and Margulies [7] (Figure 6) and Takhounts et al. [8] that has stated that brain tissue illustrates linear behavior under shear for strain levels up to 20% shear strain. In compression, the previously reported elastic responses in the literature lie between the instantaneous and steady state responses of this study and follow the same nonlinear pattern. The stiffer response in this study can be attributed to the significantly higher rate of the applied ramp in this study (10 s^{-1} versus 0.5-4 s^{-1}) comparing to the previous studies.

V. CONCLUSIONS

The brain tissue under impact experiences a complex mode of loading. This complex mode of loading needs to be addressed and considered in the process of determining the material properties since it has been shown that constitutive models developed under a specific mode of loading do not necessarily predict the behavior of the tissue under another mode of loading. This study developed a constitutive model based on the experimental results of shear and compression deformation that predicts the tissue behavior under complex loading conditions. Also, the validity of QLV assumption under shear and compression in high deformation rates was validated.

VI. ACKNOWLEDGEMENT

The work reported herein was partially supported by the Southern Consortium for Injury Biomechanics under Grant no. DTNH22- 01-H-07551 and Temple University College of Engineering.

VII. REFERENCES

[1] CDC, National Center for Injury Prevention and Control, "Traumatic Brain Injury Facts", http://www.cdc.gov/ncipc/factsheets/tbi.htm, 2011.

[2] Mendis K.K., Stalnaker R.L., Advani S.H., A constitutive relationship for large deformation finite element modeling of brain tissue, *Journal of Biomechanical Engineering*, 117, 279–285, 1995.

[3] Miller K., Chinzei K., Constitutive Modeling of Brain Tissue: Experiment and Theory, *Journal of Biomechanics,* 30, 1115-1121, 1997.

[4] Laksari K., Shafieian M., Darvish K., Constitutive model for brain tissue under finite compression, *Journal of Biomechanics,* 45, 4, 642-646, 2012

[5] Miller K.,Chinzei K., Mechanical properties of brain tissue in tension, *Journal of Biomechanics*, 35, 483–490, 2002.

[6] Arbogast K. B., Meaney D. F., and Thibault L. E., Biomechanical Characterization of the Constitutive Relationship for the Brainstem, *Proceedings of the 39th Stapp Car Crash Conference*, 153-159, 1995.

[7] Prange M.T., Margulies S.S., Regional, directional and age dependent properties of the brain undergoing large deformations, *Journal of Biomechanical Engineering* 124, 244–252, 2002.

[8] Takhounts E.G., Crandall J.R., and Darvish K., On the importance of nonlinearity of brain tissue under large deformations. *Stapp Car Crash Journal*, 47,79–92, 2003.

[9] Darvish K., Crandall J. R., Nonlinear Viscoelastic Effects in Oscillatory Shear Deformation of Brain Tissue, *Journal of Medical Engineering & Physics*, 23, 633-645, 2001.

[10] Thibault L. E., Margulies S.S, Gennarelli T. A., The Temporal and Spatial Deformation Response of a Brain Model in Inertial Loading, *Proceedings of the 32th Stapp Car Crash Conference*, 267-272, 1987

[11] Viano D., Aldman B., Pape K., van Hoof J., von Holst H., Brain kinematics in physical model tests with translational and rotational acceleration, *International Journal of Crashworthiness*, 2, 2, 191-206, 1997.

[12] Zhang L., Yang K. H., King A. I., Comparison of Brain Responses Between Frontal and Lateral Impacts by Finite Element Modeling, *Journal of Neurotrauma*, 18, 21-30, 2001.

[13] Bain A. C., Meaney D. F., Tissue-level thresholds for axonal damage in an 6 experimental model of central nervous system white matter injury. *Journal of Biomechanical Engineering,* 6, 615-622, 2000.

[14] Fung Y. C., Biomechanics: Mechanical properties of living tissues. *Springer,* New York, 1993.

[15] Shafieian M., Toward a universal Constitutive Equation for Brain Tissue, PhD Dissertation, 2012.