ELSEVIER

Journal of Biomechanics 39 (2006) 2521–2525

JOURNAL OF BIOMECHANICS

www.elsevier.com/locate/jbiomech
www.JBiomech.com

Short communication

Material properties of porcine parietal cortex

Brittany Coats, Susan S Margulies*

Department of Bioengineering, University of Pennsylvania, 3320 Smith Walk, 105 Hayden Hall, Philadelphia, PA 19104-6392, USA

Accepted 25 July 2005

Abstract

Computational models of the head can be used to simulate events associated with traumatic brain injury and to design protective equipment and environments. Accurate material property descriptions of biological tissues are crucial to the development of computational models that mimic human responses. Recent finite element models of adult head injury assign distinct homogeneous properties to white and gray matter regions within the brain, based on limited regional data. However, white matter is usually considered homogeneous, despite recent reports of significant mechanical property differences between corpus callosum and corona radiata. In this study, we extend our investigation of homogeneity to gray matter by measuring stiffness of cerebral cortex and comparing it to thalamus from our previous work. Using a parallel plate shear-testing device, we performed a sequence of stress relaxation tests at 2.5%, 5%, 10%, 20%, 30%, 40%, and then 50% strain. Force and displacement were measured and used to determine the stiffness in two different porcine cortical gray matter regions. While no significant difference was found between the two cortical regions, cortical gray matter was significantly less stiff than previously reported values of porcine thalamic gray matter ($p<0.01$) and human cortical gray matter ($p<0.001$). These data indicate that while intraregional gray matter may be considered homogenous, there exists heterogeneity between differing regions of the brain. The assumption of gray matter homogeneity should be carefully considered in future finite element models of the head.
© 2005 Elsevier Ltd. All rights reserved.

Keywords: Gray matter; Material properties; Porcine; Brain

1. Introduction

Each year, 1.5 million Americans suffer traumatic brain injury (TBI), a rate 8 times greater than the annual incidence of breast cancer and 34 times greater than HIV/AIDS (NCIPC, 2001). To gain a better understanding of the mechanisms of TBI, researchers may turn to computational models of the head to investigate internal dynamic responses to multiple loading conditions and to design better protective equipment and environments. Fidelity of these models, however, is highly dependent on the accuracy of the material properties used to describe biological tissues.

Experimental evidence has shown significant difference between the stiffness of gray and white matter (Prange and Margulies, 2002; Shuck and Advani, 1972). Recent computational models have taken into account this difference (Bonovas et al., 2001; Miller et al., 1998; Zhang et al., 2001; Zhou et al., 1995), however, the paucity of regional data has forced them to assume homogeneity within regions of white and gray matter.

Recently, we reported significant material property differences between white matter regions of the corpus callosum and corona radiata, regions that have differing degrees of neural tract alignment (Prange and Margulies, 2002). In this study, we extend our investigation to cerebral cortex and thalamus, two gray matter regions with differing cell organization. We hypothesize that gray matter within the brain may be considered homogeneous.

*Corresponding author. Tel.: +215 898 0882; fax: +215 573 2071.
E-mail address: margulie@seas.upenn.edu (S.S. Margulies).

0021-9290/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jbiomech.2005.07.020

2. Methods

In a protocol approved by the University of Pennsylvania Animal Care and Use Committee, adult porcine brains ($N = 13$) were collected less than 1 h post-mortem from a local slaughterhouse and transported in a chilled saline-based solution used to simulate cerebral spinal fluid. In each brain, rectangular samples (1 mm thick) approximately 5 mm × 10 mm were excised from two parietal cortical locations (Fig. 1) containing predominantly gray matter. Length, width, and depth of any white matter were measured with calipers to estimate the fractional white matter volume of every sample. Specimen location and orientation during testing were consistent to reduce inter-sample variability.

Samples were mounted in a parallel plate shear testing device described previously (Arbogast et al., 1997). Contact area of each sample to the upper plate was measured prior to testing. Samples were tested in a humidified environment using a shear stress relaxation protocol consisting of a rapid ramp of constant duration (60 ms) to 2.5% strain, a 60 s hold period, followed by a return to the unstretched state. The test sequence continued with stress relaxation tests at 5%, 10%, 20%, 30%, 40%, and then 50% strain, allowing 60 s relaxation between each level of strain. Preconditioning was achieved at *each* strain level by performing two stress relaxation tests, at the same magnitude of the strain level investigated, prior to the measured stress relaxation test. Previously we reported that this test sequence was not associated with mechanical tissue damage by determining that the results from a final 5% strain run added after the 50% strain level were not different from the initial 5% stress relaxation test values (Prange and Margulies, 2002). These results are not surprising given our low strain rates of the study (1.1–5.7 s^{-1}) compared to estimated strain rates of 84 s^{-1} for injured football players with concussions and 34 s^{-1} for those without concussions (King et al., 2003).

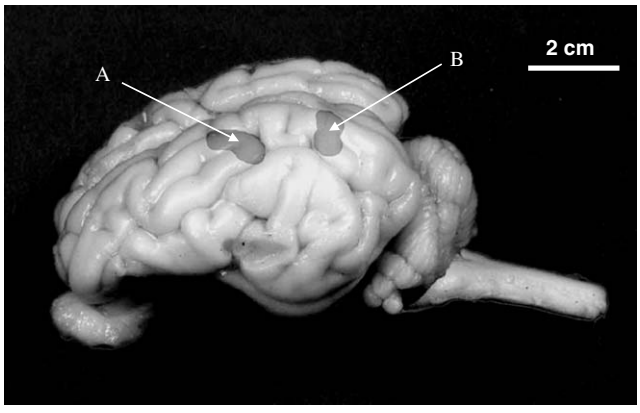

Fig. 1. Adapted photograph of porcine brain to indicate cortical regions used for sample removal.

Load and displacement were measured using a 100 g force transducer (Model BG, Kulite Semiconductor Products Inc., Leonia, NJ) and a LVDT transducer (Model 232, Trans-Tek Inc., Ellington, CT), respectively. All data were collected using a computer data acquisition system (LabView 6.0 National Instruments, Austin, TX) at 1000 samples per second. All tests were completed within 5 h post-mortem.

3. Analysis

All force data were filtered using a lowpass butterworth filter with a cutoff frequency (50 Hz) and stopband frequency (100 Hz) selected from spectrum analyses of the signals to ensure that significant peaks in the power spectrum were retained. Selected representative trace stress responses for a tissue test are illustrated in Fig. 2.

A first order Ogden hyperelastic model (Ogden, 1984) with a strain energy density function, W, was used as the basis for determination of the shear material properties of tissue:

$$W = \frac{2\mu(t)}{\alpha_1^2}(\lambda_1^{\alpha_1} + \lambda_2^{\alpha_1} + \lambda_3^{\alpha_1} - 3), \tag{1}$$

where λ is the principal stretch ratio, α_1 describes the nonlinear strain-magnitude sensitive behavior, and $\mu(t)$ is viscoelastic shear modulus of the tissue. The relationship between the maximum principal stretch ratio, λ, and engineering shear strain, γ, in simple shear ($\lambda_3 = 1$), is given by Eq. (2). The tissue was modeled as incompressible ($\lambda_1\lambda_2\lambda_3 = 1$) and shear stress of the tissue, T_{12} (defined as force divided by contact area) was related to applied strain by Eq. (3). Eq. (3) was normalized to the stress at a specific shear strain ($\lambda_0 = 0.5$, ratio at 25% strain), yielding Eq. (4):

$$\lambda = \frac{\gamma}{2} + \left(1 + \frac{\gamma^2}{4}\right)^{1/2}, \tag{2}$$

$$T_{12} = \frac{2\mu(t)}{\alpha_1}\,\frac{(\lambda^{\alpha_1} - \lambda^{-\alpha_1})}{(\lambda + \lambda^{-1})}, \tag{3}$$

$$T_{12,\mathrm{norm}}(\lambda, t) = \frac{(\lambda^{\alpha_1} - \lambda^{-\alpha_1})(\lambda_0 + \lambda_0^{-1})}{(\lambda_0^{\alpha_1} - \lambda_0^{-\alpha_1})(\lambda + \lambda^{-1})}. \tag{4}$$

To determine, α_1, force data extracted from only the hold period at 5 isochrones (time = 100, 300, 600, 1800 ms, and 60 s) at all strain magnitudes for each sample were fit to Eq. (4) using Igor Pro v. 3.14 (Wavemetrics Inc., Lake Oswega, OR). Measured and calculated values (T_{12}, α_1, λ) were subsequently used in

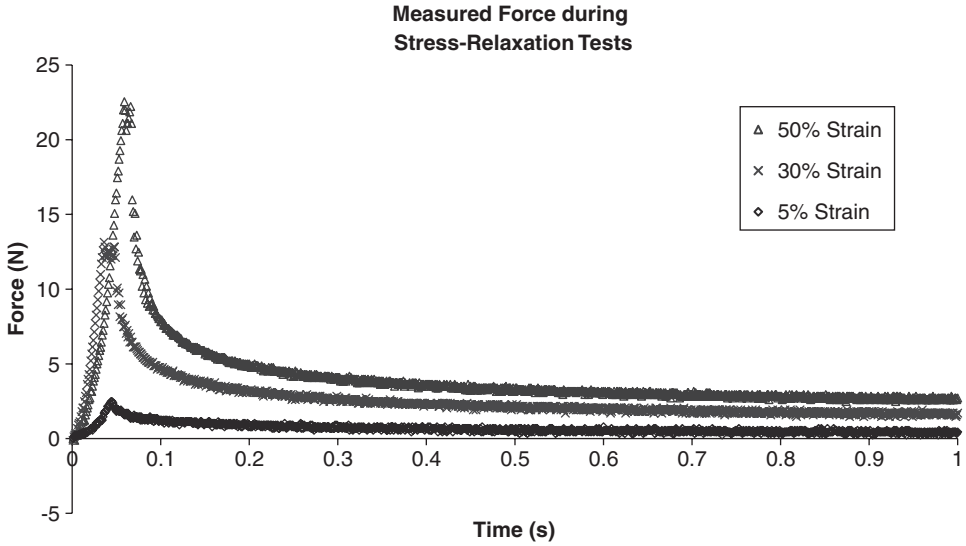

Fig. 2. Representative traces of measured forces during 1 s of testing for one selected series of stress relaxation tests. For figure clarity 10%, 20%, and 40% strain levels are not shown.

Table 1
Ogden material coefficient, α_1, and initial stiffness, $\mu(t=100)_{meas}$, measured from adult porcine cortex

Region	Cortex			Thalamus*	Corpus callosum*	Corona radiata*
Subregion	A	B	Avg	Avg	Avg	Avg
♯ Samples	7	6	13	18	18	12
α_1	.0183	.00810	.0132	.0382	.0614	.0628
μ (100) (Pa)	176.6	159.0	167.5	207.9	140.76	190.99

*From Prange and Margulies (2002).

Eq. (3) to solve for $\mu(t_i)$ at each isochrone, t_i, during the hold period.

Unpaired Student's t-tests with a Type I error of 5% were used to determine significant difference between each region, tissue type, and species at each isochrone.

4. Results

The material parameters, α_1 and $\mu(t)_{meas}$, determined from the above analysis, are reported in Table 1. The coefficient of determination (R^2) was 89.4% for the fit of Eq. (4) to the data (Fig. 3). Previously, an order of magnitude variation of α_1 (0.001–0.8) did not significantly affect the curve fit to Eq. (4) (Prange and Margulies, 2002). All values of α_1 in this study are within this range, we focused our analysis on the average shear moduli ($\mu(t)$). At each isochrone, $\mu(t)$ of the two cortical regions (Fig. 1) were not significantly different and the data were combined for further analysis. The average stiffness of the porcine parietal cortex ($\overline{\mu}_{cortex}$) was found to be significantly lower than thalamic gray matter ($p<0.01$) at every isochrone (Fig. 4). Furthermore, porcine $\overline{\mu}_{cortex}$ was significantly ($p<0.001$) less stiff (38.2–43.9% lower) than fresh (tested within 5 h of excision) adult human temporal cortical gray matter (Prange and Margulies, 2002).

5. Discussion

This study investigates the hypothesis that regions of gray matter within the brain are homogeneous. Previous research reports material property differences between white matter of the corpus callosum and corona radiata in the adult porcine brain, but it does not investigate material property differences among multiple gray matter regions.

The shear moduli of the two cortical regions shown in Fig. 1 were not significantly different at any isochrone, indicating that within close proximity (~1 cm) in the cortex, the tissue appears to be homogeneous. However, the average shear modulus of the cortical region was found to be significantly ($p<0.01$) less stiff (19.4–31.9% lower) than the shear modulus of thalamic gray matter (Prange and Margulies, 2002). Thus, we reject our hypothesis of gray matter homogeneity, and conclude

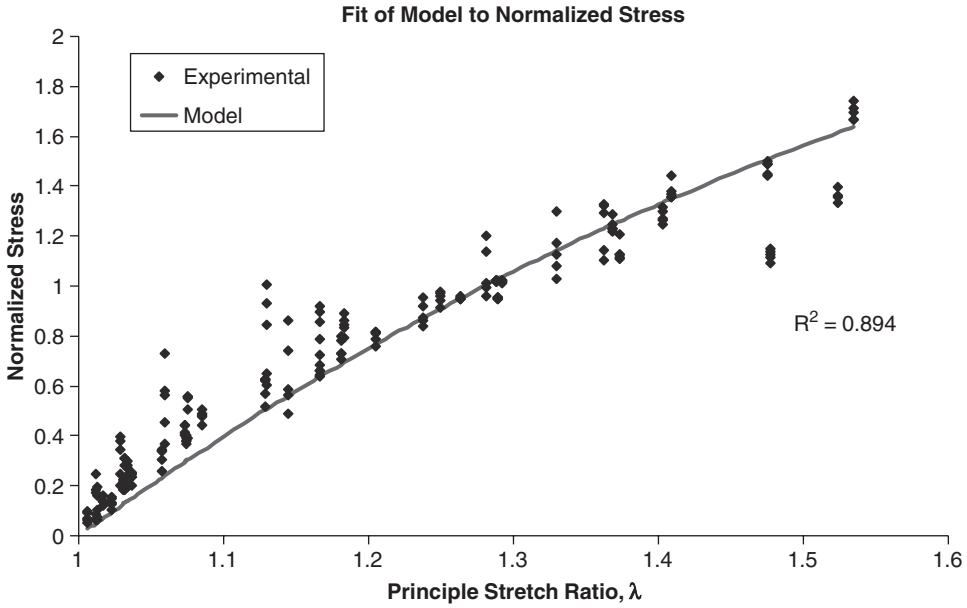

Fig. 3. Fit of the first-order Ogden energy model to all experimental data of porcine cortical tissue. $R^2 = 0.894$.

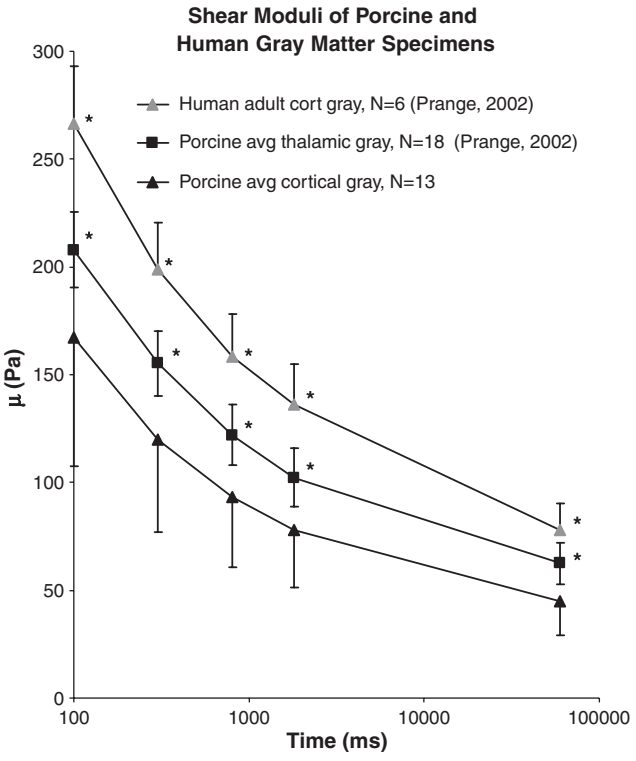

Fig. 4. Shear moduli gathered from Prange and Margulies (2002) compared to the shear moduli of porcine cortical gray matter measured in the present study (mean ± SD). Both human adult cortical gray ($p < 0.001$) and porcine average thalamic gray ($p < 0.01$) were significantly different from porcine average cortical gray (*).

that gray matter within the porcine brain is stiffer in the thalamus than in the cortex.

While the compositions of both thalamic and cortical gray matter regions consist mainly of neurons, the organization is distinctly dissimilar and we hypothesize that this could be a contributing factor in the difference found between the stiffness of the two gray matter regions. While the cortex is composed of 6 layers of varying cell density, the thalamus has a more heterogeneous cellular organization. In this study, the direction of shear testing was parallel to the lamina and we postulate that the outer layers of the cortex could move more freely relative to the denser internal layers than a shear test of a non-laminar structure such as the thalamus.

The shear modulus of the cortical porcine tissue was significantly lower at each isochrone than adult human cortical gray matter values published by Prange and Margulies (2002), underscoring the need for more data from fresh human brain tissue samples.

A summary of the stiffness of gray and white matter regions measured in this investigation and values reported by Prange and Margulies (2002) indicates the stiffest of the four regions studied is the thalamus (Fig. 5). While sub-cortical white matter is stiffer than cortical gray matter, white matter of the corpus callosum was found to be the most compliant of all four regions studied in our laboratory.

Because it was difficult to obtain a cortical sample that contained only gray matter, a volume fraction approach was used to determine the effect white matter had on the measured shear modulus. Using white matter fractional volumes measured in all cortical samples and shear moduli values for corona radiata (Prange and Margulies, 2002), we calculated an adjusted shear modulus for the cortical gray matter. After repeating all statistical analyses, there were no changes in findings and we conclude that this small amount of white matter

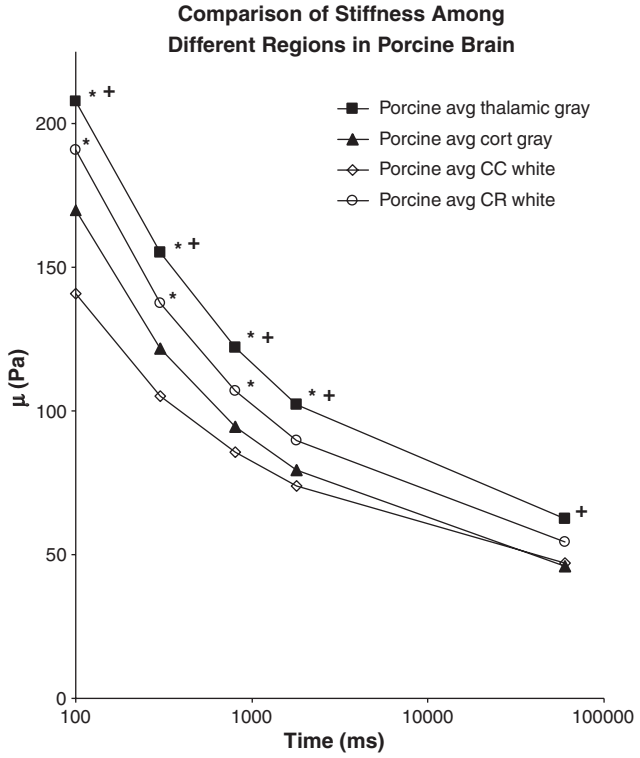

Fig. 5. Shear moduli of porcine gray and white matter regions from Prange and Margulies (2002) compared to shear moduli of porcine cortical gray matter measured in the present study. Average corpus colosum was significantly different from both thalamus ($p<0.002$) and corona radiata ($p<0.005$) at the isochrones indicated (*). Cortex was significantly different than the thalamus ($p<0.006$) at all isochrones (+). SD bars not shown for clarity.

(0–20%) in each cortical sample does not significantly affect any conclusions.

While most current head injury models assume homogeneity of brain tissue, the regional differences in the shear modulus of gray matter reported in this work further confirms the presence of tissue heterogeneity within the brain. The assumption of homogeneity should be carefully evaluated in future computational models of the head.

Acknowledgements

We are grateful to Michael Prange for his technical guidance. Support was provided by NIH-NINDS R01/NS39679, CDC–NCIPC R49-CCR312712, and USDOT-NHTSA DTNH22-01-H07551.

References

Arbogast, K.B., Thibault, K.L., Pinheiro, B.S., Winey, K.I., Margulies, S.S., 1997. A high-frequency shear device for testing soft biological tissues. Journal of Biomechanics 30, 757–759.

Bonovas, P., Kyriacou, G., Sahalos, J., 2001. A realistic three dimensional FEM of a human head. Physiological Measurement 22, 65–76.

King, A.I., Yang, K.H., Zhang, L., Hardy, W., Viano, D.C., 2003. Is head injury caused by linear or angular acceleration? In: International Conference on the Biomechanics of Impact, pp. 1–12.

Miller, R., Margulies, S., Leoni, M., Nonaka, M., Chen, X., Smith, D., Meaney, D., 1998. Finite element modeling approaches for predicting injury in an experimental model of severe diffuse axonal injury. In: Proceedings of 42nd Stapp Car Crash Conference, Tempe, AZ, SAE.

NCIPC, 2001. Injury Fact Book 2001-2002. Centers for Disease Control and Prevention, Atlanta, GA.

Ogden, R., 1984. Non-linear Elastic Deformations. Ellis Harwood Ltd., Chichester, England (reprinted by Dover Publications Inc, Mineola, New York, 1997).

Prange, M., Margulies, S., 2002. Regional, directional, and age-dependent properties of brain undergoing large deformation. Journal of Biomechanical Engineering 124, 244–252.

Shuck, L., Advani, S., 1972. Rheological response of human brain tissue in shear. Journal of Basic Engineering, 905–911.

Zhang, L., Yang, K., King, A., 2001. Comparison of brain responses between frontal and lateral impacts by finite element modeling. Journal of Neurotrauma 18, 21–30.

Zhou, C., Khalil, T., King, A., 1995. A new model comparing impact responses of the homogeneous and inhomogeneous human brain. In: Proceedings of 39th Stapp Car Crash Conference, San Diego, California.