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Mechanical Heterogeneity of Rat Brain Measured Using a Micro-Indentation Technique

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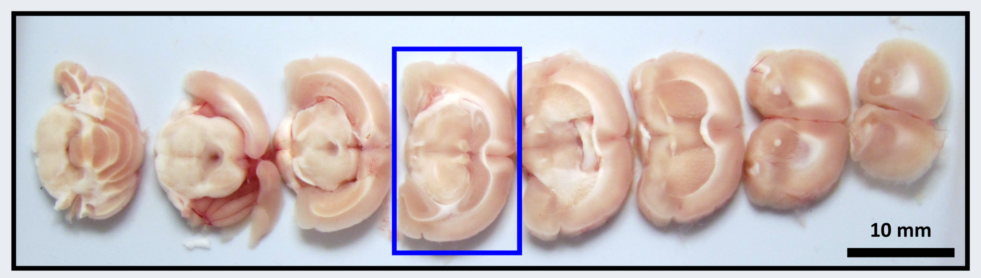
INTRODUCTION

Characterization of the heterogeneity of the mechanical properties of brain tissue is a fundamental step in improving our evaluations of brain deformation and tissue stresses and strains during high rate events that lead to traumatic brain injury (TBI). Recent advances in finite element models of brain tissue with sub-millimeter resolution have brought forth more attention to the heterogeneity of brain material properties. Although rat brain has been frequently used in in vivo neurotrauma studies and its heterogonous injury patterns are well characterized, little is known about its regional viscoelastic material properties. The goal of this study was to investigate the local mechanical behavior of several anatomical regions of rat brain using a custom-designed micro-indentation device.

MATERIALS AND METHODS

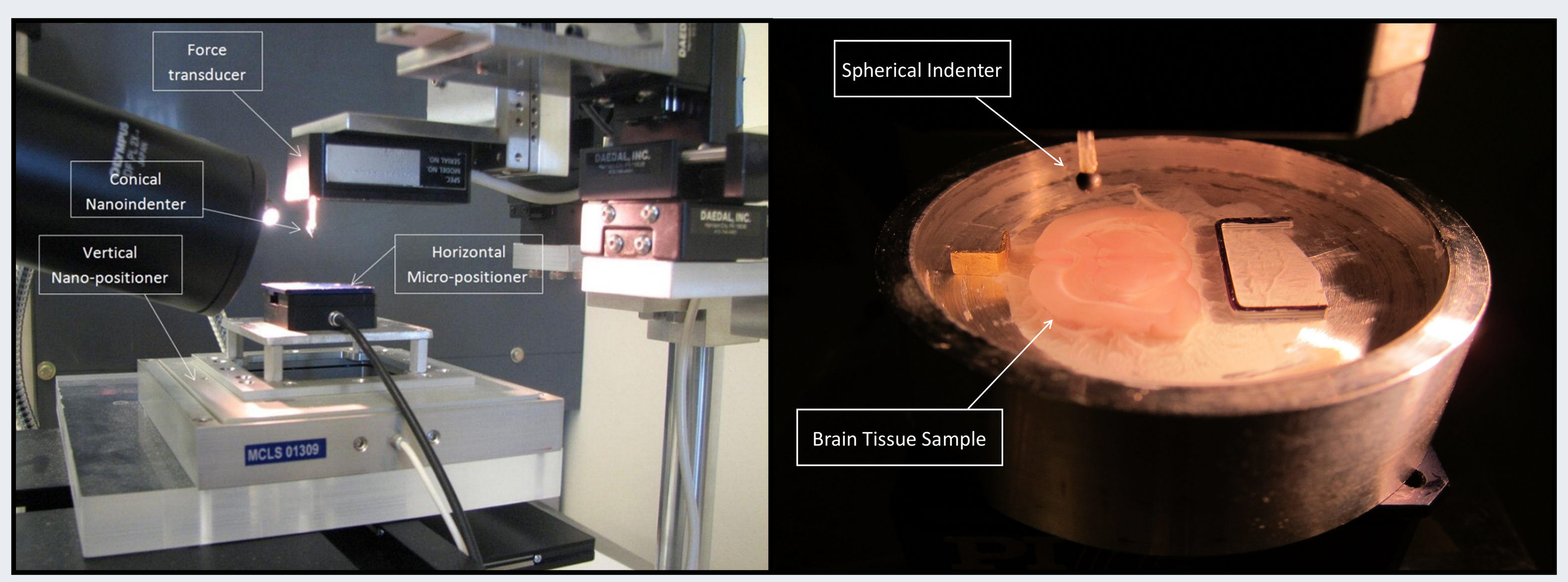
Tissue Preparation:

- Brains of four adult Sprague-Dawley rats were harvested rapidly after euthanasia
- 2-mm coronal slices were cut using a brain matrix
- Slices were kept in artificial cerebrospinal fluid to maintain viability
- One slice including the hippocampus was selected for this study



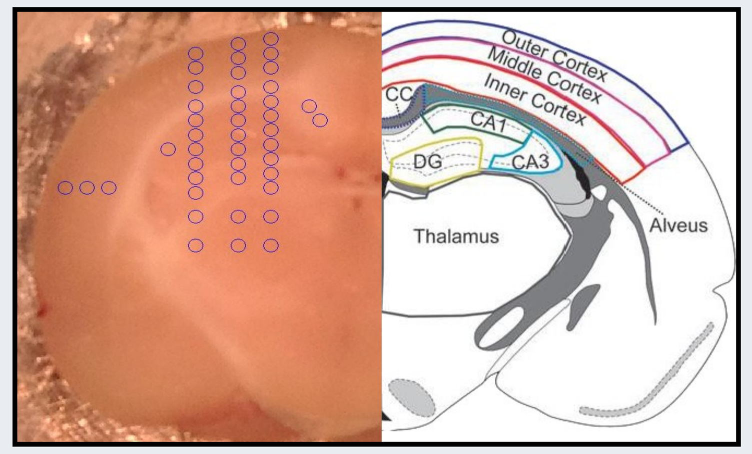
Custom-designed Microindentation Device:

- Z-axis nano-positioner with resolution of 0.2 nm and 100 µm range (Nano-Z100, MCL,WI), and an XY positioner with resolution of 0.02 mm [1]
- Force transducer (Aurora Scientific, Model 406A) with resolution of 10 nN (1 µg) and range of 0.5 mN (50 mg).
- Equipped with a horizontally positioned 300× Stereo Microscope (Olympus SZX7)
- 1.5-mm diameter spherical indenter



Anatomical Regions:

- Gray matter: Inner, Middle and Outer Cortex, Thalamus, Hippocampus (CA1, CA2, CA3, and DG) [2]
- White matter: Corpus Callosum (CC), Alveus (Alv) [2]



Stress Relaxation Indentation Test:

- Ramp and hold displacement was applied with ~10-ms ramp time, 20s hold time, and depth of 40 µm (~200-µm diameter indentation contact area)
- A quasi-linear viscoelastic (QLV) model was fitted to simulate indentation force history in terms of indentation depth:

$$P(t) = \int_0^t G(t-\tau)\frac{\partial P^e(h)}{\partial h}\frac{\partial h}{\partial \tau}d\tau$$

In which $P^e(h)$ is the instantaneous elastic force that is a nonlinear function of h:

$$P^e(h) = \frac{8\mu\sqrt{R}}{3(1-\nu)}h^{3/2}$$

In which μ, R, and υ are shear modulus, indenter radius, and Poisson's ratio which was assumed 0.49.

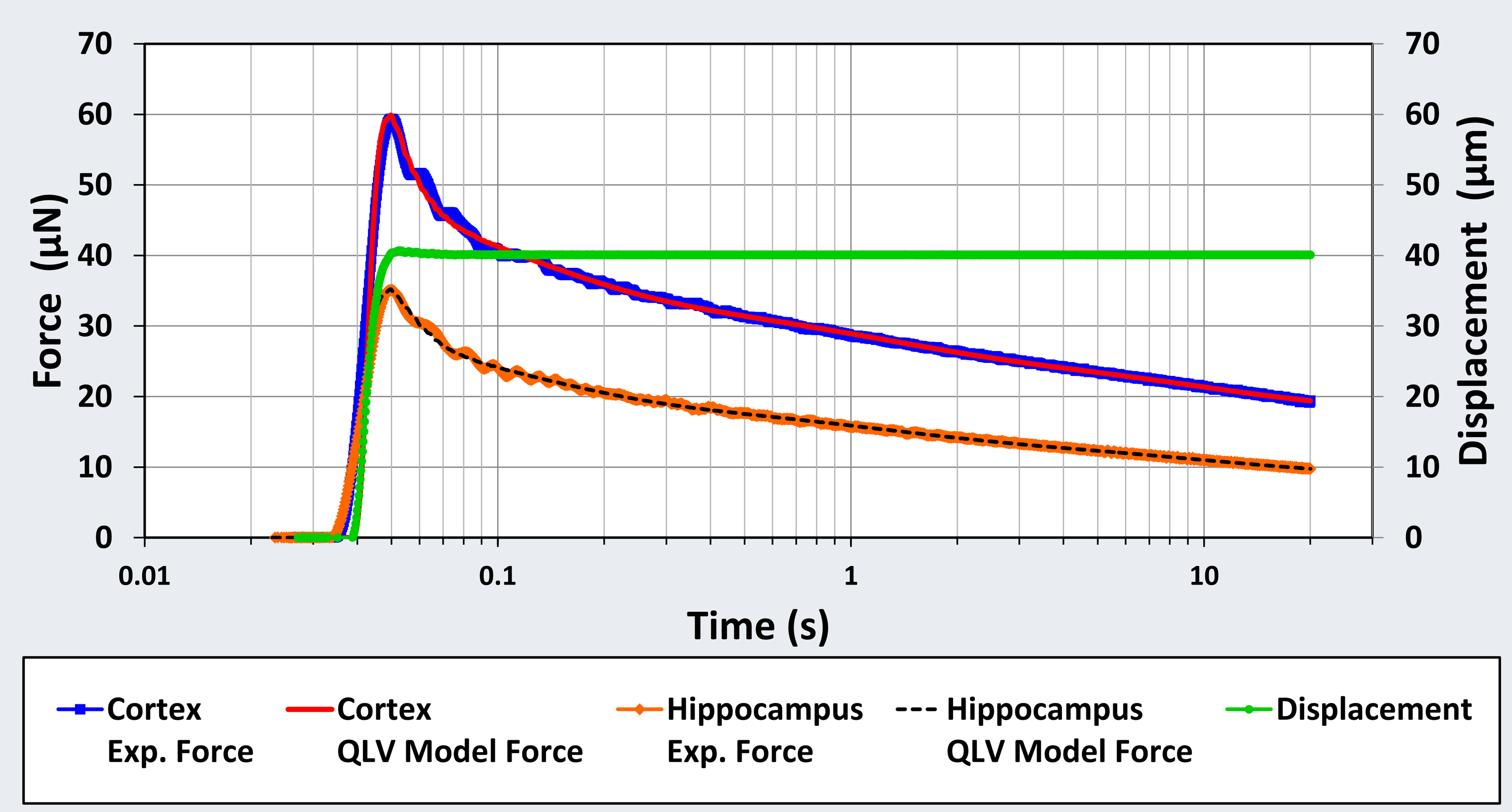
And $G(t)$ is the reduced relaxation function which was assumed to be a Prony series in which G_i and β_i (β_1=100, β_2=10, β_3=1, β_4=0.1 s^{-1}) represent the relaxation amplitudes and decay rates.

$$G(t) = G_\infty + \sum_{i=1}^{4} G_i e^{\beta_i t}$$

RESULTS AND DISCUSSSION

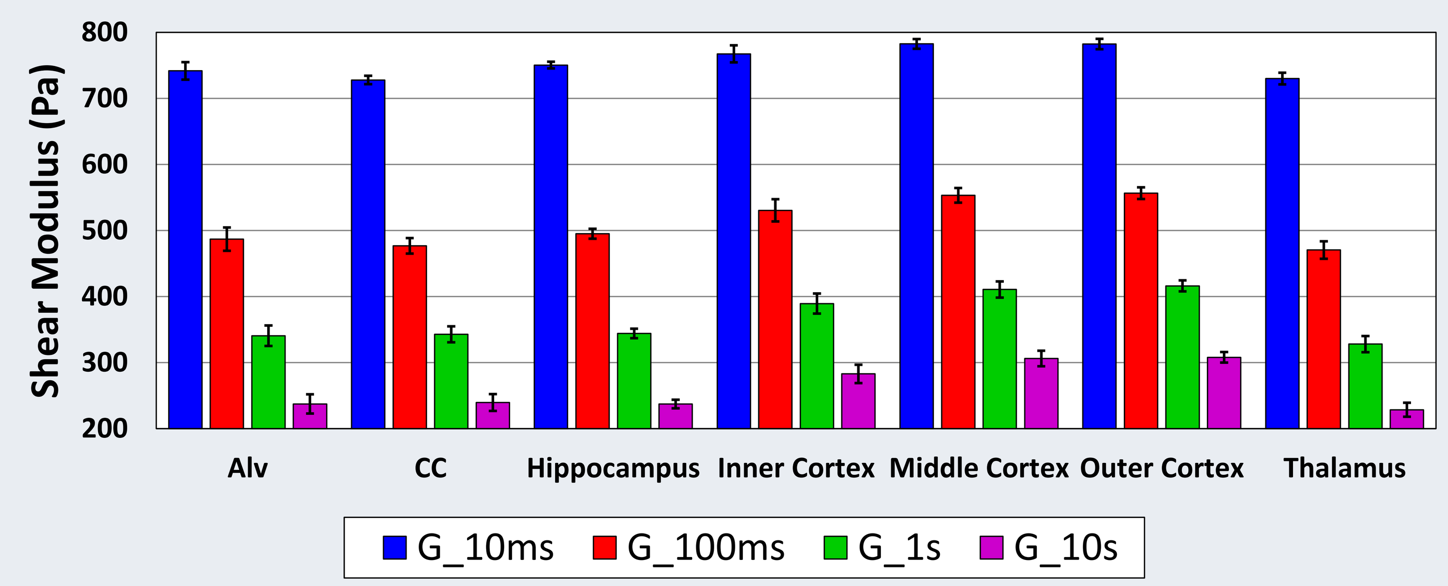
A Representative Force–Displacement Curve

- All R^2 values were greater than 0.9



Heterogeneity in Shear Modulus:

- Generally the brain tissue showed more compliant behavior moving from Cortex (surface) toward Thalamus (core) and therefore more susceptible to injury due to higher strain levels under uniform loading



- More difference was observed in longer term shear modulus between anatomical regions which should be considered in modeling neurosurgery, hydrocephalus, or tumor growth applications.

Overall Range of Shear Modulus (Pa)

	G_{10ms}		G_{100ms}		G_{1s}		G_{10s}	
Min	CC	728±6	Thalamus	470±13	Thalamus	328±12	Thalamus	229±11
Max	Outer Cortex	783±8	Outer Cortex	556±9	Outer Cortex	416±8	Outer Cortex	308±8
Diff		8%		18%		27%		35%

- Gray matter showed generally stiffer behavior than the white matter which is in agreement with results reported by Elkin et al [2].

Average Shear Modulus in White & Gray Matter (Pa)

	G_{10ms}	G_{100ms}	G_{1s}	G_{10s}
White Matter	735±10	482±15	342±14	239±14
Gray Matter	763±8	521±11	378±11	273±10
Difference	4%	8%	11%	14%

- Shear modulus reported in our study is a little more compliant than the results reported by Elkin et al [2], which could be due to the higher strain level in their experiments due to use of flat indenter.

REFERENCES

[1] Hemmasizadeh, Ali, Michael Autieri, and Kurosh Darvish. "Multilayer material properties of aorta determined from nanoindentation tests." Journal of the mechanical behavior of bio-medical materials 15 (2012): 199-207.

[2] Elkin, Benjamin S., Ashok I. Ilankovan, and Barclay Morrison III. "A detailed viscoelastic characterization of the P17 and adult rat brain." Journal of neurotrauma 28.11 (2011): 2235-2244.