High Field MR-Elastography of TBI model

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INTRODUCTION

Traumatic brain injury (TBI) is a devastating disease where at least 1.7 million new cases are diagnosed in the United States each year. The development of novel neuroimaging methodologies could provide valuable insight on the pathophysiology and improve current classification systems; one of these techniques is magnetic resonance elastography (MRE). MRE is a phase contrast-based MR imaging technique capable of acquiring the complex shear modulus in small tissues by visualizing low frequency mechanical shear waves propagating in soft materials [2]. In this paper, the controlled cortical impact (CCI) rodent TBI model is combined with microscopic MRE [3] to measure the mechanical properties of the brain following an injury. The working hypothesis is that TBI alters the mechanical properties of the brain. Possible cause could be the death of neuronal cells and activation of glial cells in response to the injury. Local values of the viscoelastic properties and MR relaxation times (T_1 and T_2) are calculated in different regions of interest (ROIs) of excised rat brains (somatosensory cortex, hippocampus and thalamus) at different time-points following the injury.

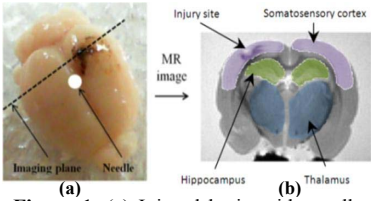

Figure 1. (a) Injured brain with needle location and imaging plane. (b) Corresponding coronal MR magnitude image depicting the ROIs.

MATERIALS AND METHODS

TBI procedures were approved by the University of Nebraska Medical Center (UNMC) Institutional Animal Care and Use Committee (IACUC). A midline incision was performed under anesthesia on adult male Sprague Dawley rats (Charles River Laboratories, MA) and a 6 mm craniotomy was taken to expose the somatosensory cortex of one hemisphere. The animals were then positioned beneath a Precision Systems and Instrumentation TBI-0310 (Fairfax Station, VA) that administered a 2 mm cortical compression. The skull cap was replaced and sealed with dental acrylic and the animals were allowed to recover. Animals were sacrificed by decapitation and brain tissue was extracted and frozen at -80°C at different healing point (immediate, 24 hrs and 7 day). MR experiments were conducted using an 89 mm vertical bore 9.4 T (400 MHz for protons) magnet equipped with a linear triple axis gradient system with a maximum magnetic field strength of 100 G/cm and a 4cm RF Millipede imaging probe (Varian inc., CA). The brains were thawed at room temperature and placed in a 25 mm test tube surrounded by 1% wt agarose gel. A needle attached to a piezoelectric bending element transducer (Piezo system, MA) was then placed between the two hemispheres of the brain. Before MRE imaging, the actuator frequency response was measured using a Laser-Doppler Vibrometer (Polytec, Dexter, MI); this response dictated the actuator operating frequency (~700 Hz with approximate amplitude of 200 μm). Shear wave images were collected using a spin-echo based phase contrast sequence with the following parameters: TR = 1 s, TE = 20 ms, 2 bipolar pairs, bipolar gradient strength = 40 G/cm, and field-of-view = 25 mm^2. The brains were imaged in a coronal view going through the injury, as shown in Fig. 1. Following the acquisition of eight shear wave images evenly distributed over one temporal cycle, the complex shear modulus was calculated using an algorithm performing a local inversion of the differential equations of motion (ratio between the out-of-plane displacement and its Laplacian) [4].

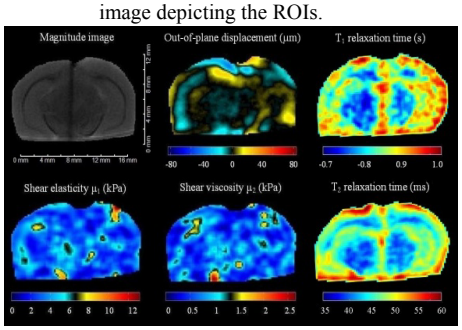

Figure 2. Magnitude image of a sham brain and corresponding shear wave field, viscoelastic properties, and MR relaxation times.

RESULTS

Fig. 2 shows shear waves propagating in a healthy (sham) brain with the corresponding shear elasticity (μ_1), shear viscosity (μ_2) and relaxation maps. Wave propagation with significant amplitude was needed for faithful recovery of the complex shear modulus. The mechanical properties were calculated in both hemispheres for specific ROIs as shown in Table 1. The shear viscosity in the hippocampus, a region responsible for learning and memory, was found to be higher in the injured hemisphere compared to the healthy one as shown in Fig.3.

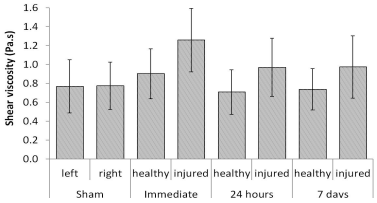

Figure 3. Shear viscosity (Pa.s) in the hippocampus measured around 700 Hz.

Table 1. Averaged properties of excised rat brains around 700 Hz averaged over different regions.

		Sham (n=4)		Immediate (n=4)		24h (n=3)		7d (n=1)	
		Left hemisphere	*Right hemisphere*	*Healthy hemisphere*	*Injured hemisphere*	*Healthy hemisphere*	*Injured hemisphere*	*Healthy hemisphere*	*Injured hemisphere*
Stiffness (kPa)	*Cortex*	6.4 ±2.6	6.5 ±2.8	5.9 ±2.4	6.2 ±2.4	6.2 ±2.4	6.9 ±2.7	4.8 ±1.5	4.3 ±1.1
	Hippocampus	7.1 ±2.6	6.5 ±2.4	7.4 ±3.0	8.4 ±2.7	6.6 ±2.1	7.1 ±2.6	4.7 ±1.8	5.1 ±2.3
	Thalamus	6.7 ±2.1	6.2 ±2.0	7.6 ±2.2	8.5 ±2.9	6.2 ±2.0	6.9 ±2.9	8.8 ±2.9	6.4 ±2.8
Shear elasticity μ1 (kPa)	*Cortex*	3.8 ±1.5	3.9 ±1.6	3.5 ±1.6	3.7 ±1.4	3.5 ±1.4	3.8 ±1.4	2.6 ±0.7	2.6 ±1.0
	Hippocampus	4.6 ±1.4	3.6 ±1.1	4.6 ±2.5	4.6 ±1.7	4.1 ±1.3	4.0 ±1.8	2.5 ±1.1	2.9 ±1.6
	Thalamus	3.9 ±1.2	3.6 ±1.1	4.7 ±1.4	5.0 ±1.9	3.7 ±1.2	4.2 ±1.9	4.4 ±1.5	3.2 ±1.7
Shear viscosity μ2 (Pa.s)	*Cortex*	0.71 ±0.4	0.74 ±0.4	0.76 ±0.4	0.79 ±0.4	0.80 ±0.4	0.88 ±0.4	0.73 ±0.3	0.62 ±0.2
	Hippocampus	0.77 ±0.3	0.77 ±0.3	0.90 ±0.3	1.3 ±0.3	0.71 ±0.2	0.97 ±0.3	0.74 ±0.2	1.0 ±0.3
	Thalamus	0.80 ±0.3	0.75 ±0.3	0.93 ±0.4	1.1 ±0.4	0.73 ±0.3	0.78 ±0.2	1.4 ±0.5	1.0 ±0.5
T_1 relaxation time (s)	*Cortex*	1.2 ±0.1	1.2 ±0.1	1.5 ±0.1	1.5 ±0.1	1.1 ±0.1	1.2 ±0.3	1.2 ±0.1	1.2 ±0.1
	Hippocampus	1.1 ±0.1	1.1 ±0.1	1.4 ±0.1	1.4 ±0.1	1.1 ±0.1	1.2 ±0.1	1.2 ±0.1	1.2 ±0.1
	Thalamus	1.1 ±0.1	1.1 ±0.1	1.4 ±0.1	1.3 ±0.1	1.1 ±0.1	1.1 ±0.1	1.1 ±0.1	1.1 ±0.1
T_2 relaxation time (ms)	*Cortex*	50 ±7	49 ±6	50 ±8	51 ±6	47 ±10	59 ±7	49 ±9	48 ±6
	Hippocampus	46 ±2	45 ±3	46 ±3	48 ±3	45 ±4	51 ±4	46 ±4	46 ±6
	Thalamus	43 ±3	43 ±3	45 ±3	45 ±3	43 ±3	44 ±3	43 ±3	42 ±4

CONCLUSION AND FUTURE WORK

This work represents our initial proof-of-principle attempts at using MRE to detect change in the mechanical properties of traumatically injured rodent brains. *In vivo* work on traumatically injured mice is planned and has recently been approved by IACUC at the University of Nebraska-Lincoln. Shear viscosity in the hippocampus trended higher in the injured hemisphere compared to the healthy one which may be related to injury-induced cognitive deficits (statistically insignificant, possibly due to insufficient sample size). Because of the complex shape and large attenuation in the brain, special attention has to be given to the wave propagation in order to obtain faithful estimations of the viscoelastic properties. The design of an efficient mechanical transducer is crucial when attempting to study brain with MRE. Current studies emphasize on increasing statistical power of this study and extending measurements to *in vivo* TBI model.

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REFERENCES

[1] Faul et al. *TBI in the United States: Emergency Department Visits, Hospitalizations and Deaths 2002-2006*. CDC, Atlanta, GA, 2010. [2] Muthupillai et al., *Science*, 1995; 269:1854-1857. [3] Othman et al., *Mag. Resonance in Medicine*, 2005; 54(3):605-615. [4] Oliphant et al., *Mag. Resonance in Medicine*, 2001; 45:299–310.