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Protection of cortex by overlying meninges tissue during dynamic indentation of the adolescent brain

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ABSTRACT

Traumatic brain injury (TBI) has become a recent focus of biomedical research with a growing international effort targeting material characterization of brain tissue and simulations of trauma using computer models of the head and brain to try to elucidate the mechanisms and pathogenesis of TBI. The meninges, a collagenous protective tri-layer, which encloses the entire brain and spinal cord has been largely overlooked in these material characterization studies. This has resulted in a lack of accurate constitutive data for the cranial meninges, particularly under dynamic conditions such as those experienced during head impacts. The work presented here addresses this lack of data by providing for the first time, *in situ* large deformation material properties of the porcine *dura-arachnoid mater* composite under dynamic indentation. It is demonstrated that this tissue is substantially stiffer (shear modulus, $\mu = 19.10 \pm 8.55$ kPa) and relaxes at a slower rate ($\tau_1 = 0.034 \pm 0.008$ s, $\tau_2 = 0.336 \pm 0.077$ s) than the underlying brain tissue ($\mu = 6.97 \pm 2.26$ kPa, $\tau_1 = 0.021 \pm 0.007$ s, $\tau_2 = 0.199 \pm 0.036$ s), reducing the magnitudes of stress by 250% and 65% for strains that arise during indentation-type deformations in adolescent brains.

Statement of Significance

We present the first mechanical analysis of the protective capacity of the cranial meninges using *in situ* micro-indentation techniques. Force-relaxation tests are performed on *in situ* meninges and cortex tissue, under large strain dynamic micro-indentation. A quasi-linear viscoelastic model is used subsequently, providing time-dependent mechanical properties of these neural tissues under loading conditions comparable to what is experienced in TBI. The reported data highlights the large differences in mechanical properties between these two tissues. Finite element simulations of the indentation experiments are also performed to investigate the protective capacity of the meninges. These simulations show that the meninges protect the underlying brain tissue by reducing the overall magnitude of stress by 250% and up to 65% for strains.

1. Introduction

Traumatic brain injury (TBI) is a major cause of death and disability worldwide, accounting for 1.7 million injuries, 275,000 hospitalizations, and 50,000 deaths in the United States each year [1]. The high occurrence of TBI has rendered it a significant public health and socioeconomic problem [2]. It is estimated that 5.3 million people in the United States and 7.7 million people in the European Union are living with a TBI related disability. Traumatic brain injuries typically lead to neurocognitive deficits, psychological health issues, increased impulsivity, poor decision making, and impulsive-aggressive behavior [2]. In Toronto, Canada, it was found that 45% of homeless men had a positive screening for TBI. Of these, 87% experienced their first TBI before they became homeless, and 73% before the age of 18 [3].

Traumatic brain injuries are the result of a rapid acceleration or impact of the head that can occur from motor vehicle impacts, falls, assault, head collisions in sports and other recreational activities. Rotational accelerations of the head and brain can cause shearing

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of the brain cells, known as neurons, leading to traumatic axonal injury (TAI), whereas linear accelerations cause the brain to impact against the inside of the skull wall creating coup (impact region) contusions and cavitation at the contre-coup (opposite side of impact region) site [4]. Brain injuries can also result in increased intracranial pressure (ICP), rupture of vasculature, brain swelling (edema), chronic traumatic encephalopathy (CTE), and concussion.

To better understand the mechanisms, pathogenesis, and prevention of TBIs, many laboratories have created detailed 3D finite element (FE) models of the head and brain [5–8]. These models are used to investigate the stress and strain distribution within neural tissue, with particular attention given to the regions in which stress and strain maxima occur. However, the accuracy and reliability of these models are affected by the fact that the brain is a complex organ made up of many different functional and structural regions consisting of different types of cells such as neurons and glia, as well as the surrounding protective layers known as the meninges [9].

The meninges are a tri-layer protective membrane that encloses the brain and spinal cord. The outermost layer is called the *dura mater* and it adheres directly to the inner surface of the skull. The inner layer, known as the *pia mater*, is in direct contact with the neural tissue and the *arachnoid mater* is found between the *dura mater* and *pia mater*. These layers have a protective function, enclosing the brain and anchoring it against sudden movements. They also enclose the cerebrospinal fluid (CSF) which acts as a shock absorber to help protect the brain against trauma [9].

Current FE models lack accurate constitutive data for the cranial meninges at dynamic strain-rates comparable to those experienced during traumatic events. These data are required to correctly predict the stresses and strains produced in the brain during these events, and how the mechanical properties of the meninges can influence injury. Current constitutive data available for meninges are typically obtained from spinal cord *dura mater* [10–12]. A previous study by Maikos et al., characterized the mechanical properties of rodent spine and cranial *dura mater* tissue under tension and found cranial *dura mater* to be less stiff and to have a faster relaxation response than spinal cord *dura mater* [13]. Polarized light microscopy was also performed on both tissues and it was found that spinal cord *dura mater* exhibited a preferential collagen fiber alignment; however, cranial *dura mater* did not present with any preferential fiber direction. Another study by Hamman et al. found similar results with some regions of the *dura mater* having no preferential fiber direction and other regions to be highly aligned [14].

The work presented here addresses this dearth of data by providing for the first time, *in situ* large deformation material properties of the porcine *dura-arachnoid mater* (DAM) tissue under dynamic indentation. Large and dynamic deformation conditions are confirmed with finite element simulations showing strains in the range of 5–65% and 4–50% in the immediate vicinity of the indenter for the brain tissue and DAM tissue, respectively. With indentation duration at approximately 16.5 ms, the resulting strain-rate range is 3–42/s and 2–30/s for brain and DAM tissues, respectively. It is demonstrated that DAM is substantially stiffer and relaxes at a slower rate than the underlying brain-*pia mater* tissue, agreeing with previous reports of the mechanical properties of collagen [15–17] and brain tissue [18–21], and reducing the magnitudes of stress and strain that occur during indentation-type deformations in brain tissue. Obtaining the mechanical properties of DAM tissue *in situ* (post-mortem) is important due to the presence of *in vivo* residual strains in the tissue which are released upon excision. Performing micro-indentation measurements on *in situ* meninges that still encloses the brain allows one to preserve the *in vivo* residual strains in its material characterization. The work presented here is the first report on *in situ* porcine cranial DAM tissue under dynamic, large-deformation micro-indentation.

2. Theory

2.1. Neo-Hookean hyperelastic model

Brain tissue is initially assumed here to be both incompressible, due to its high water content, and non-linearly hyperelastic. A versatile and elegant model of such a mechanical response was proposed by Rivlin (1948), generalizing the corresponding linear theory in a natural way. This so-called neo-Hookean model has the following strain-energy function:

$$W = \frac{\mu}{2}(I_1 - 3) \tag{1}$$

where μ is the infinitesimal shear modulus and, if C is the right Cauchy-Green strain tensor, $I_1 = \mathrm{tr}(C)$. The numerical difficulties associated with locally enforcing the incompressibility constraint in the displacement formulation of the finite element method means that a slightly compressible version of the neo-Hookean model is often assumed when simulating soft tissue, with the following form typically used:

$$W = \frac{\mu}{2}(\bar{I}_1 - 3) + \frac{\kappa}{2}(J-1)^2 \tag{2}$$

where $J \overset{def}{=} \det(C), \bar{I}_1 \overset{def}{=} J^{-2/3} I_1$ and κ is the infinitesimal bulk modulus, assumed to be $4.7 \times \mu$ for the DAM tissue and $10{,}000 \times \mu$ for the underlying brain tissue. This value for bulk modulus assumes slight compressibility of the DAM tissue and brain tissue with Poisson's ratios of 0.4 and 0.49995, respectively [22,23].

2.2. Neo-Hookean-based viscoelastic framework

To accurately describe the viscoelastic response of neural tissue, a quasi-linear viscoelastic (QLV) framework is assumed. The QLV theory assumes that the force $P(t)$ exerted by an indenter on a viscoelastic material can be written as the convolution of a reduced relaxation function $g(t)$ with an elastic force response function $P^e(t)$ as follows:

$$P(t) = \int_{-\infty}^{t} g(t-s)\frac{dP^e(s)}{ds}ds \tag{3}$$

In this implementation of the QLV framework, $P^e(t)$ is the instantaneous elastic force determined from pre-computed neo-Hookean responses, over a range of shear moduli values, using the inverse finite element method [19,20]. Following Puso & Weiss it is assumed that the reduced relaxation function has the standard Prony series form [24,25], i.e.,

$$g(t) = g_l + \sum_{i=1}^{N} g_i \exp\left(-\frac{t}{\tau_i}\right) \tag{4}$$

where g_i is the ith relaxation modulus, τ_i is the ith time constant, and g_l is the long term relaxation modulus. In order to ensure that the purely elastic response is recoverable from the viscoelastic model on letting $\tau_i \to \infty$, it will be required that:

$$g(0) = 1 \tag{5}$$

and so therefore

$$g_l = 1 - \sum_{i=1}^{N} g_i \tag{6}$$

Substitution of Eq. (4) into Eq. (3) gives the following viscoelastic response: