INTRODUCTION

With the increase in the number of soldiers sustaining traumatic brain injury from military incidents and the recent attention on sports related traumatic brain injury, there has been a focused effort to develop preventative and treatment methods for traumatic brain injury (TBI). Traumatic brain injury is caused by mechanical loading to the head, such as from impacts, sudden accelerations, or blast loading, and the pathology can range from focal damage in the brain to widespread diffuse injury [1]. In this study, we investigate the injury mechanisms of diffuse axonal injury (DAI), which accounts for the second largest percentage of deaths due to brain trauma [2]. DAI is caused by sudden inertial loads to the head, and it is characterized by damage to neural axons. Despite the extensive research on DAI, the coupling between the mechanical loading to the head and the damage at the cellular level is still poorly understood. Unlike previous computational models that use macroscopic stress and strain measures to determine injury, a cellular injury criterion is used in this work as numerous studies have shown that cellular strain can be related to the functional damage of neurons. The effectiveness of using this cellular injury criterion to predict damage in a finite element model of DAI is investigated.

BACKGROUND

When neural axons are stretched beyond a critical threshold, normal biological processes in the cell are disrupted, which can lead to the functional impairment of neurons or even cell death. Experimental studies on nerve fibers, neural cell cultures, and organotypic brain slice cultures have shown that cellular stretch is directly related to the functional and morphological damage of neurons [1,3-6]. In a study by Bain and Meaney, the optic nerve tract of a guinea pig was stretched in vivo at strain rates of 30-60/s, and an optimal strain threshold of 0.18 was determined for the onset of electrophysiological impairment [2]. Since the neural axons in the optic tract were highly aligned along the direction of stretch, this strain is proportional to the cellular strain of the neural axons; therefore, in this study, an axonal strain threshold of 0.18 is used to indicate the onset of neural damage.

Although experimental studies have shown that the stretching of neural axons can be directly related to the damage of neural cells, current computational models of traumatic brain injury do not use axonal strain as a measure of injury. In recent years, intracranial injury criteria such as the von Mises stress, maximum shear stress and strain, and the maximum principal strain have commonly been used to measure the degree of axonal injury in a computational simulation [7-10]; however, these parameters do not have a direct physiological basis. The use of axonal strain offers the advantage that it is a physiologically relevant parameter that can be obtained directly from experimental studies on neural axons. To apply this injury criterion in a finite element model, microstructural information about the arrangement of neural axons must be incorporated into the model, and the white matter must be modeled as an anisotropic material. This is achieved through the use of diffusion tensor imaging data and through the application of a transversely isotropic model for the white matter.

ANISOTROPIC MATERIAL MODEL

The white matter is approximated as a nearly incompressible, transversely isotropic material. The transversely isotropic assumption is reasonable for white matter regions with highly aligned axons, such as the corpus callosum, or for small representative volumes of white matter. The constitutive model of a transversely isotropic material is defined in terms of a strain energy function [11]. A quadratic reinforcing strain energy function is chosen to model the white matter.
Using the axonal strain injury criterion of 0.18 and a von Mises stress injury criterion of 26 kPa from the literature [13], the predicted regions of axonal damage are plotted for the 4000 Pa applied shear load (Figure 3). The regions shown in red exceed the injury threshold, and therefore, represent tissue that would exhibit axonal injury. The blue regions represent undamaged tissue. There is a significant difference in the locations of axonal damage between the two measures of injury. In particular, a region of the corpus callosum (circled in black) is indicated as damaged with the axonal strain injury criterion, but this damage is not predicted with the von Mises stress injury criterion.

**CONCLUSION**

Measures of injury, such as maximum principal strain and von Mises stress, are commonly used as injury tolerance criteria in computational models of DAI. When using an injury criterion that has a direct physiological relevance, such as axonal strain, the locations of predicted axonal damage differ significantly from other intracranial measures of injury. This study demonstrates the importance of choosing an appropriate measure of injury in a DAI model. In addition, the inclusion of anisotropy into a model of white matter can have large effects on the stress and strain distributions in brain tissue, which can also affect injury predictions.

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**REFERENCES**