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Research Paper

Development and validation of an advanced anisotropic visco-hyperelastic human brain FE model

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ABSTRACT

This paper proposes the implementation of fractional anisotropy and axonal fiber orientation from diffusion tensor imaging (DTI) of 12 healthy patients into an existing human FE head model to develop a more realistic brain model with advanced constitutive laws. Further, the brain behavior was validated in terms of brain strain against experimental data published by Hardy et al. (2001, 2007) and for brain pressure against Nahum et al. (1977) experimental impacts. A reasonable agreement was observed between the simulation and experimental data. Results showed the feasibility of integrating axonal direction information into FE analysis and established the context of computation of axonal elongation in case of head trauma.

1. Introduction

Traumatic brain injury (TBI) is the preeminent cause for abridgment of public safety, vulnerable to complex injury and leading to permanent impairment and fatalities over last decades. Around 1.7 million people have suffered of TBI annually in the US (Faul et al., 2010; Langlois et al., 2004). Among the most European nations, the estimated incident rate of TBI is 235 for every 100,000 patients hospitalized (Tagliaferri et al., 2006). In both severe and mild TBI, diffuse axonal injury (DAI) is the most common pathology, in which rapid tensile elongation of axonal fibers leads to fiber rupture yielding retraction balls of 30 μm in diameter (Arfanakis et al., 2002). This process results in a decrease of brain tissue elasticity and leads to axonal degeneration (Smith and Meaney, 2000; Smith et al., 2003). Addressing axonal elongation within the brain during head impact can allow a better understanding of DAI mechanism.

In the prospect of excrescent growth of TBI, computational modeling of brain is an efficient and very promising tool to study the head fatalities. FE models can be used to describe the complex geometry of brain in detail and multiple material composition of brain. Also there are limitations in conducting studies on post-mortem human subjects (PMHS). Hence, FE head models (FEHM) are proved to be very effective in understanding the damage at macroscopic level and to compute stress and strain at all locations. Since 1970s, FE human head models have been a focus of research and explicated as tools to predict head injury risk and eventually injury location. The first FE head model was proposed by Ward and Thompson (1975). After that several FE head models have been reported in the literature in the last decades (Kang et al., 1997; Zhang et al., 2001; Horgan and Gilchrist, 2003; Kleiven, 2007; Iwamoto et al., 2007; Takhounts et al., 2008). The FEHM developed by Kang et al. (1997) was equivalent to a 50th percentile adult head and used 13,208 elements. The brain was modeled as linear viscoelastic and the other parts were made of elastic material. This model was validated for intracranial pressure. Zhang et al. (2001)

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developed a 50th percentile male FEHM having 314,500 elements and a mass of 4.5 kg. The brain was modeled with a linear viscoelastic material. The model was validated for intracranial pressure and brain skull relative motions. However, the model was computationally costly. The University College Dublin Brain Trauma Model (UCDBTM) by Horgan and Gilchrist (2003, 2004) was developed from CT images and having element densities varying from 9000 to 50,000. Linear viscoelastic material was used for brain and validated for intracranial pressure. The FEHM developed by Kleiven (2007) used isotropic hyper viscoelastic material for brain and validated for intracranial pressure and brain skull relative motions. Iwamoto et al. (2007) and Takhounts et al. (2008) used isotropic viscoelastic material for their brain FE model. Most of these models are composed of homogeneous and isotropic material properties for brain. Very few of them have non-linear visco-elastic and hyperelastic brain material behavior because brain mechanical properties are typically derived from experiments conducted on post-mortem brain samples. These hypotheses were acceptable from a mechanical point of view as there were no advanced *in vivo* data available. But nowadays, advanced imaging techniques give new insight into brain mechanics and provide appropriate *in vivo* data to go further than the classical FE computation (Colgan et al. 2010; Chatelin et al., 2011, in press).

The bio-fidelity of FE head model primarily depends upon appropriate incorporation of anatomical detail, material model, accurate injury measures and experimental data for validation. With the progress of innovative imaging technique called diffusion tensor imaging (DTI), Brownian motion of water molecules has been tracked in three dimensions to reveal the microscopic properties and anatomy of nerve fiber inside the human brain. It was found that, the water diffusion is anisotropic in brain white matter in which water tends to diffuse predominantly along the long axis of the fibers (Beaulieu ,2002). This indicates that the hypothesis to model the brain with isotropic material is not adequate. The main deterrent in water diffusion perpendicular to fibers is the longitudinal oriented tissue structure, the densely packed axons. It is possible to extract the information concerning to the trajectory of axonal fibers within the brain by performing DTI. The very first attempt of axonal strain computation based on the DTI data was proposed by Chatelin et al. (2011) but this study considered an isotropic brain model. With the help of DTI, successive anisotropic diffusion experiments were carried out on human brain to construct the three dimensional map of axonal fiber orientation by accurately tracking the water molecule diffusion in several major white matter pathways in a voxel-by-voxel manner. The anisotropy of diffusion called fractional anisotropy (FA) and direction of fiber orientation were obtained from DTI to get a thorough understanding of structural detail of human brain in a non-invasive manner. According to Cloots et al. (2011), the individual axons oriented away from the main axonal direction have logarithmic strain of about 2.5 times the maximum logarithmic strain of the axons in main axonal direction. This study is based on the simulation of plane strain FE models to investigate the relation between mechanical loading of brain tissue and axonal stretching. The result indicates the influence of heterogeneity at cellular level on axonal strain, sensitivity of the tissue to the orientation and location of axonal fibers in various mechanical loadings. Hence, anisotropy at microscopic level should be taken into account for a better injury assessment in FE head model. Wright and Ramesh (2011) conducted two dimensional plane strain FE analysis for the different regions of interest by implementing anisotropy into the constitutive hyperelastic material model for white matter. The result of the study showed a strong influence of the inclusion of anisotropy in FE model for predicting the DAI. Colgan et al. (2010) also incorporated anisotropic orientations of axonal fibers into a hyperelastic material of a brain FE model to predict the mechanical response and effect of anisotropy in case of high rotational TBI. All these studies are maneuvering towards the importance of the implementation of anisotropy data (FA and fiber orientation) in FE brain model to compute axonal elongation during head impact simulations.

The state of the art FE head model is validated by comparing and correlating the simulation results against the experimental data to better predict the accuracy and fidelity of the model. Most of the previous models have been validated against the pressure data provided by Nahum et al. (1977) and Trosseille et al. (1992). However, it is not adequate to validate FE models for pressure only and then use them for injury prediction (Bradshaw and Morfey, 2001). Brain strain due to relative motion between brain and skull during different impact scenarios is of great importance over the last few years to investigate the brain injury mechanism. Motion of the brain relative to the skull occurs during normal activity. However, if the head undergoes intolerable level of energy by high acceleration during impact, the induced large deformation of neuronal and axonal tissues can lead to severe TBI and long term disabilities (Bain and Meaney, 2000). Very few studies are reported in the literature which measure the relative motion between brain and skull by conducting low energy impact tests with PMHS (Hodgson et al., 1966; Hardy et al., 2001, 2007; Zou et al., 2007). Though PMHS do not predict the DAI but the mechanical response can be determined. However, strong limitation exists as the intracranial medium is not pressurized as it is for human being *in vivo*.

In the present study, DTI has been used to implement anisotropy and heterogeneity into an existing brain FEM. The brain behavior has been validated in terms of brain strain against Hardy et al. (2001, 2007) and against Nahum et al. (1977) experiments to ensure that this new model is capable of predicting reasonable pressures. One of the principal objectives of this work is to enhance the existing isotropic FE head model by considering new constitutive laws. The new constitutive law includes fractional anisotropy and axonal fiber orientation from DTI to provide more accurate model and to enable it to compute axonal elongation in case head impact. Therefore, this study contributes to consider axonal tensile elongation as directly linked with DAI mechanism.

2. Materials and methods

This section exposes the head FEM on which the study is based on the presentation of DTI data and how these data are