Understanding real-world and laboratory traumatic brain injury (TBI) using the computational model with brain functional regions

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A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Mechanical and Materials Engineering
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Abstract

Traumatic brain injury (TBI), including mild traumatic brain injury (mTBI) or concussion, is a severe health concern. Many symptoms, such as headache, dizziness, and working memory deficits, are reported to be related to the dysfunction of brain functional regions, but the underlying mechanism remains unknown. Hence, further developing tools and analyses to understand brain dysfunction for better TBI prevention are important. Additionally, such analyses should be conducted for both real-world TBI cases and laboratory studies, as TBI data can only be collected from the real world, and prevention measures, such as helmets, are developed and evaluated in the lab. Accordingly, this biomechanical study addressed four mTBI-related topics: 1) developing a novel pipeline that can segment the brain finite element (FE) into up to 1000 functional brain regions based on an advanced brain functional atlas; 2) using 39 national football legacy (NFL) kinematic curves (including 13 concussive impacts) which were collected and reconstructed from in-field mTBI impacts, the brain strain responses including strain of each functional region and strain-affected connections among brain functional regions were analyzed; 3) helmet protection mechanism was analyzed by investigating the characteristics of the helmet shell and foam under laboratory impacts; 4) effects of skull thickness change due to repeated mTBI impacts on head kinematics-based and brain strain-based responses were also investigated. This study found that: 1) certain brain functional regions consistently experienced high strain among mTBI impacts under various impacts, indicating their contribution to brain damage; 2) the brain strain could affect the functional connectivity of working memory tasks; 3) among the entire impact events, helmet outer shell absorbed the highest amount of strain energy, while helmet foam played an important role in brain strain responses based on factorial analysis; 4) the increase in skull thickness and the change in skull density had the small effect on head kinematics-based and brain strain responses. In brief, novel brain FE models with detailed function regions were developed. Using the new modeling technique, the potential effects of brain functional region strain under both real-world and laboratory settings, as well as repeated-mTBI-relevant skull changes, were analyzed.
Keywords

TBI, mTBI, concussion, brain functional regions, brain strain responses, brain strain-based connections, helmet, shell, foam, repeated-mTBI, skull thickness, skull density.

Summary for Lay Audience

Traumatic brain injury (TBI) occurs when the head experiences external impacts or inertia effects. Many researchers demonstrated that the TBI symptoms, including working memory deficits, could be related to the dysfunction of brain functional regions or the change in brain functional connections, but the in-depth mechanism remains unclear. Biomechanical researchers found that brain strain could cause neuron cell death, which is related to brain dysfunction, but the brain strain responses of functional regions are still unclear because there lacks a finite element (FE) model with in-detailed brain functional regions. To overcome this challenge, this study developed a pipeline to segment the brain FE model into functional regions and used the FE model with functional regions to investigate the mechanism and prevention guidelines of TBI. By simulating 39 in-field National Football Legacy (NFL) impacts including 13 concussive impacts, the brain functional regions with high strain were identified. Furthermore, the brain strain-affected connection, which refers to more than one brain functional region exceeding the concussive strain threshold per every two brain functional regions, was analyzed, and compared to the healthy brain functional connectivity datasets of working memory. We found that the brain strain could affect the functional connectivity of the brain. The effects of the helmet outer shell and foam stiffness on the brain strain responses were investigated using laboratory impacts of TBI. The helmet outer shell absorbed the highest amount of energy, while the foam played an important role in brain strain responses. Moreover, based on the findings that the skull thickness increased under repeated mTBI impacts, this study investigated the effect of increased skull thickness on brain responses. As a result, the increase in skull thickness and density change played a small role in brain strain responses.
Co-Authorship Statement

Chapter 2 (‘Developing a pipeline to represent MNI-based brain functional regions for FE modeling’) co-authored by Dr. Haojie Mao is approved by Computational Biomechanics for Medicine CBM XVIII for publication.

Chapter 3 (‘Understanding the brain strain effect on working memory among concussion impacts), chapter 4 (‘Temporal characteristics of shell vs foam strain energy and their effects on brain strain reduction’), and chapter 5 (‘Understanding the effect of brain skull change due to repeated mTBI on head responses’) co-authored by Dr. Haojie Mao will be sent for publication.

All chapters are drafted by Kewei Bian and modified by Dr. Haojie Mao.
Acknowledgments

I would like to express my gratitude to Dr. Haojie Mao for his support of my research. I want to thank Dr. Thomas Jenkyn, Dr. Mark Daley, and Dr. Khan for the help with my research. I acknowledge that the Canada Research Chairs program, New Frontiers, and NSERC for support. I also want to thank Dr. Youcai Wu and Dr. Cheng-Tang Wu from LSTC for their help with data analysis.

I acknowledge the Global Human Body Models Consortium (GHBMC) and Elemanence for the support of the finite element model.

This study utilized model(s) licensed from Biomechanics Consulting and Research, LC (Biocore), model(s) derived therefrom, or both. The development of those model(s) was made possible by a grant from Football Research, Inc. (FRI) and the National Football League, with input from the NFLPA. The views expressed are solely those of the authors and do not represent those of Biocore, FRI, or any of its affiliates or funding sources [1].

I acknowledge the NFL head kinematics data from Christopher Withnall from Biokinetics and Associates Ltd.

I acknowledge the available healthy functional connectivity of working memory data online from the work of Dr. Grady’s group [2, 3].
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Acronyms

BrIC: Brain injury criteria

CSDM: Cumulative strain damage measure

DAMAGE: Diffuse Axonal Multi-Axis General Evaluation

GAMBIT: Generalized acceleration model for brain Injury threshold

GSI: Gadd severity index

HIC: Head injury criterion

MPS: Maximum principal strain

MRI: Magnetic resonance imaging

mTBI: Mild Traumatic brain injury

NFL: National Football League

TBI: Traumatic brain injury
Chapter 1

1 Introduction – Brief Overview of the Research Problem

Detailed research background for each specific objective was introduced in the following main chapters. In this chapter, a brief overview of the problem, anatomy of the head, and overall rationale and objectives are described. In brief, the research is focused on the brain through developing advanced brain model and applying such model to understand real-world concussion cases and laboratory helmeted tests.

1.1 The focus on mild traumatic brain injury (mTBI) /concussion

Traumatic brain injury (TBI), including mild TBI (mTBI) or concussion, is a severe and complex health challenge. There were 1.6 to 3.8 million sports-related TBI cases in the US alone [4]. The Centers for Disease Control and Prevention (CDC) reported that there were 60,611 deaths related to TBI in 2019 [5]. The mTBI could cause hospitalizations with 200-300/100,000 per year [6]. In the US, concussion occupied 15% sports-related injuries [7]. In Canada, 1 out of 450 people above 12 years old reported the concussion as the significant injury [8]. Moreover, the repeated mTBI, which could cause chronic brain impairments [9], has also gained the research interests because it could have a serious of health concerns [10, 11].

Researchers actively studied TBI from different perspectives, including biomechanics, TBI symptoms, functional connectivity, the protection realm, and repeated effects of TBI impacts. Though more specific reviews are described in following chapter introductions, brief overview is provided in this paragraph (Figure 1.1). In biomechanics, researchers have tried to collect the head kinematic and brain strain responses, from real-world and laboratory tests, using computational methods including finite element (FE) analysis. Regarding injury symptoms, different concussive symptoms, such as headache, dizziness, and working memory deficits, have been investigated. Studies of functional connectivity have demonstrated that concussion could lead to functional connectivity change, which could cause concussive symptoms. In the protection realm, scientists are focusing on better
protection performance. For repeated mTBI impacts, researchers have tried to understand the effects of repeated mTBI on the brain. However, the interplay between these aspects remains unclear. This includes understanding how biomechanics of brain functional regions influence injury symptoms, the effect of functional regions with strain on functional connectivity, improving helmet design in the perspective of biomechanics to preserve brain health, and the effect of repeated mTBI impacts on head biomechanics. This thesis study addressed these four challenges using the FE model with brain functional regions.

Figure 1.1: Complex realm to study TBI. There are four challenges that need to be addressed: 1) how to get strains of very detailed brain function regions; 2) how do brain functional regions with strain affect functional connectivity; 3) how to improve helmet design to preserve brain health; and 4) how do repeated impacts affect head biomechanics.

1.2 The anatomy of head

The head is considered probably the most vulnerable organ under blunt impacts. The skull and the brain are two main components of the head. The skull, which plays a role in protecting the brain, could be damaged by TBI impacts. Common skull damage includes various skull fractures [12]. The brain is also easily damaged by impacts. The rapid motion
of the head, including the translational and rotational motion, could injure the brain in different mechanisms [13]. The head translation causes the contusion to the brain [14]. The head rotation causes the deformation of the brain tissue [13], which is the main reason to cause diffuse TBI. To understand the head responses under TBI impacts, it’s critical to understand the skull and brain anatomy.

1.2.1 The skull anatomy

As an important part for protecting the brain against the TBI impact, the skull consists of 22 bones (Figure 1.2 [15]) [16]. The main parts of the skull include calvaria and skull base, intracranial fossae, and facial bones [16]. The calvaria and skull base, which mainly support and protect the brain, include frontal bone, parietal bones, temporal bones, and occipital bones [16]. The intracranial fossae contain the anterior cranial fossa, middle cranial fossa, and posterior cranial fossa. There are 14 facial bones including maxilla bones, palatine bones, lacrimal bones, zygomatic bones, the mandible, and vomer [16]. There are three layers of the skull: the outer layer, the diploe, and the inner layer [17, 18].
1.2.2 The brain anatomy

As the most complex organ, the brain, which consists of soft tissues, can be damaged under small deformation. The brain consists of both grey and white matter. The main components of the brain include the cerebral the cortex, the corpus the callosum, the basal ganglia, the thalamus, the cerebellum, and the brain stem (Figure 1.3 [19]).
1.3 Brain functional regions analysis

1.3.1 Brain cortex functional regions

The cerebral cortex consists of $10^{11}$ neurons connected by $10^{15}$ connections [20], and is important to controlling functions such as cognition and emotion processing [21]. The cerebral cortex has attracted significant research interest [22-24]. The auditory cortex was responsible for the language function [25] (Figure 1.4 [26]). The temporal cortex was involved during the eye and mouth movements [27]. The somatomotor cortex was included in the hand movements [28]. The cingulate posterior cortex was reported to be related to cognition [29]. The bilateral dorsolateral prefrontal cortex [30], medial prefrontal cortex [31], left premotor cortex, supplementary motor area, and left superior parietal lobule [32] were reported to be related to the working memory deficits.
The brain functional network includes brain functional regions. The sensorimotor network involves the somatosensory and motor regions [33], and the activation of sensorimotor cortex regions during hand movement was found through the functional MRI method [34]. The dorsal attention network is related to the functions of the sustained attention and memory [35]. Regions in the parietal, temporal, and frontal cortex, which are included in the default mode network, displayed decreased activity during focused tasks and increased activity during complex cognition, which could be related to memory or abstract thought [36]. Furthermore, both the sensory and somatomotor networks are related to the functions of multi-sensory and touch, and the somatomotor and internal mentation networks contain the language-related functions [37].

### 1.3.2 Brain atlas

To further investigate the responses of brain functional regions, scientists have developed brain functional atlases with different functional regions based on Magnetic Resonance Imaging (MRI) data. Collins et al. (1998) from the Montreal Neurological Institute (MNI)
divided the brain into 90 anatomical volumes of interest (AVOI) [38]. Liu et al. (2020) investigated the sex-based human brain organization based on 125 functional regions [39]. Tzourio et al. (1997) divided the brain into 100 AVOI [40]. Heckemann et al. (2006) developed a method to segment the brain into 67 structures [41].

For brain functional atlas (Figure 1.5 [42]), the Atlas of Intrinsic Connectivity of Homotopic Areas (AICHA) includes 192 homotopic region pairs based on functional MRI (fMRI) data from 281 individuals [43]. Craddock et al. (2012) reported a brain functional atlas with up to 1000 regions of interest (ROI) based on 41 subjects [44]. Yeo et al. (2011) demonstrated different regions of the cerebral cortex with the atlas [45]. Schaefer et al. developed the functional atlas with up to 1000 functional regions of the cortex [46].

![Brain functional atlas](http://creativecommons.org/licenses/by/4.0/)

**Figure 1.5: Brain functional atlas [42] (Adapted from Scientific Data with permission of Creative Commons Attribution 4.0 International License [http://creativecommons.org/licenses/by/4.0/]).**

1.3.3 Concussion symptoms and Brain Functional Connectivity

Concussion involves many symptoms like headache, dizziness, cognitive impairments, memory impairments, and language deficits [47-50]. The brain functional regions, which are related to concussion symptoms, have been found to have connections to concussion [51]. The changes in brain functional connectivity (Figure 1.6 [52]) within functional networks, which include specific brain regions, were observed under due to concussion [53]. The brain functional connectivity changes include hyperconnectivity, which refers to
increased connectivity of brain functional regions [54], and hypoconnectivity, which refers to decreased functional connectivity [55]. Researchers have reported both the hyperconnectivity and hypoconnectivity among patients with concussion [56-59].

Figure 1.6: Brain functional connectivity [52] (Adapted from Wikimedia Commons with license (https://creativecommons.org/licenses/by-sa/3.0/legalcode)).

One main challenge in the field is to represent detailed brain function regions in a biomechanical analysis. To address this challenge, new knowledge on how a blunt impact could potentially affect such connections could be analyzed.
1.4 Understanding mTBI in biomechanical view

1.4.1 Brief review of reconstructing mTBI cases

To better understand TBI, scientists have used both in-field and laboratory methods to record the head kinematics under TBI-related impacts (Figure 1.7 [60]). From the in-field impacts, researchers have reconstructed the in-field impacts in the laboratory [60-64] (Figure 1.8 [60]). The wearable sensors, including mouthguard, have also been used to record head motions under TBI impacts [65-67]. These methods have been commonly used, with wearable sensors gaining more popularity, while some classic concussion databases were based on lab reconstruction when sensors were less applied.

Figure 1.7: Video analysis [60] (Adapted from Journal of Neurosurgery with permission).
Figure 1.8: Lab reconstruction [60] (Adapted from Journal of Neurosurgery with permission).

The reconstructed mTBI cases provided an opportunity to analyze overall brain strains and detailed brain functional region responses during impacts. In particular, this study addressed responses of detailed brain functional regions, which were lacking in the literature for these reconstructed cases.

1.4.2 Laboratory tests with dummy and helmets

Laboratory methods were also widely used by researchers to understand and investigate TBI. The helmet performance was evaluated based on the dummy tests in the laboratory [60, 68-70]. Currently, three kinds of laboratory test methods were mainly used to test the helmeted impact: the drop test (Figure 1.10) [71, 72], the pendulum test (Figure 1.11) [61, 73], and the linear impactor test (Figure 1.12) [74, 75]. The effect of the helmet was tested through drop tests and the head kinematic responses were increased by up to 36% when a facemask was included [71]. The drop testes were reported to be able to represent the most severe on-field head impacts among football players [76]. The football helmet, together with the dummy head model, was dropped when the ground surfaces and the temperatures were different, and the result indicated that the ground surfaces and temperature could affect the head kinematic responses [72]. Drop tests, pendulum, and the linear impactor tests were used to validate the FE dummy model with the helmet model [77]. The linear impactor tests were used to test the novel football helmet padding system [75].
Figure 1.9: Drop test.

Figure 1.10: Pendulum test.
1.4.3 Finite element (FE) Human Head Model

The finite element (FE) analysis is widely used to obtain the brain biomechanical responses such as brain strain and brain pressure from the FE model. A detailed overview of several commonly used FE head models can be found in the paper by Ji et al. (2022) [78]. Below are brief descriptions of the human head model. As one of the earliest brain FE models developed in the field, the Wayne State University brain injury model (WSUBIM) version 2001, with 314,500 elements and 281,800 nodes, can simulate the impacts with linear and rotational acceleration of 200 g and 12,000 rad/s², respectively [79]. The Total HUman Model for Safety (THUMS) head model (Figure 1.13b) was developed by researchers of Toyota Central R&D Labs [80, 81]. The recent THMUS head model contains brain components, including cerebrum, corpus callosum, cerebellum, and thalamus, with anisotropic material being applied to the brain [81]. Inspired by the WSU model and other models developed in the field, the Global Human Body Models Consortium (GHBMC) head model (Figure 1.13a) was developed, containing 270,552 elements, 183,795 nodes,
and 62 components including cerebrum, cerebellum, and corpus callosum [82]. The GHBMC model was primarily used in this study.

![GHBMC Head Model](image1.png) ![THMUS Head Model](image2.png)

**Figure 1.12:** (a) GHBMC and (b) THMUS FE model.

### 1.5 Injury Metrics

#### 1.5.1 Head kinematics-based injury metrics

Researchers investigated different kinds of criteria to evaluate concussion. According to head kinematics recorded by in-field and laboratory texts, head injury metrics including peak linear acceleration [83], Head Injury Criterion (HIC) [84], Brain Injury Criterion (BrIC) [85], Gadd Severity Index (GSI) [86], The Generalized Acceleration Model for Brain Injury Threshold (GAMBIT) [87], peak rotational velocity, and Diffuse Axonal Multi-Axis General Evaluation (DAMAGE) [88], and Universal Brain Injury Criterion (UBrIC) [89], have been widely used to investigate concussion.

The HIC, as described in Equation 1 [84], can be calculated by averaging the integration of resultant linear acceleration curves over the specific time interval. The \( a(t) \) represents the resultant linear acceleration.
\[ HIC = \max_{(t_1, t_2)} \left\{ (t_2 - t_1) \left[ \frac{1}{t_2 - t_1} \int_{t_1}^{t_2} a(t) \, dt \right]^{2.5} \right\} \]  

(1)

The BrIC, as described in Equation 2 [85], \( \omega_x, \omega_y, \) and \( \omega_z \) represents the maximum rotational velocity of x, y, and z axis recorded by the sensors of the dummy, and \( \omega_{xC}, \omega_{yC}, \) and \( \omega_{zC} \) are critical values of three directions. Takhounts et al. (2013) reported the critical values of 66.25 rad/s, 56.45 rad/s, and 48.87 rad/s based on the average of MPS and CSDM [85].

\[ BrIC = \sqrt{\left( \frac{\omega_x}{\omega_{xC}} \right)^2 + \left( \frac{\omega_y}{\omega_{yC}} \right)^2 + \left( \frac{\omega_z}{\omega_{zC}} \right)^2} \]  

(2)

The GSI, as described on Equation 3 [86, 90], can be calculated based on the integration of linear acceleration with the power of 2.5 [90].

\[ GSI = \int a(t)^{2.5} \, dt \]  

(3)

The GAMBIT, as described in Equation 4 [87], can be calculated based on linear acceleration \((a(t))\) and rotational acceleration \((\alpha(t))\). The parameter \(n, m, \) and \(S\) are empirical constants [87].

\[ GAMBIT = \left[ \left( \frac{a_{max}}{a_{cr}} \right)^n + \left( \frac{a_{max}}{a_{cr}} \right)^m \right]^{1/S} \]  

(4)

The DAMAGE, as described in Equation 5 [88], can be calculated based on the direction-dependent rotational acceleration time history and the scale factor that links the maximum resultant displacement to the MPS of the FE model [88].

\[ DAMAGE = \beta_{max} \left[ \left( \delta(t) \right) \right] \]  

(5)

The UBrIC, as described in Equation 6 [89], can be calculated based on the direction-dependent maximum head rotational velocity and rotational acceleration normalized by critical value [89].
$$UBrIC = \left\{ \sum_i \left[ \omega_i^* + (\alpha_i^* - \omega_i^*) e^{-\beta \omega_i^*} \right]^\frac{1}{\gamma} \right\}$$  \hspace{1cm} (6)

Based on 27 reconstruction cases of in-field concussive football impacts, Newman et al. (2005) reported the peak linear acceleration values of 470 m/s\(^2\) (47.91g)-1352 m/s\(^2\) (137.82g) [61]. Among 20 mTBI impacts reconstructed by Sanchez et al. (2019), peak linear acceleration of mTBI ranged from 59g to 138g, peak rotational velocity ranged from 20.6 rad/s to 64.5 rad/s, HIC ranged from 79 to 659, and BrIC ranged from 0.34 to 1.37 [64]. Rowson et al. (2012) reported the rotational velocity of 28.3 rad/s for the 50% risk of concussion among 57 concussive impacts [91].

1.5.2 Brain strain-based injury metrics

The brain strain, which represents the change of brain deformation, was found to be related to the brain neuron cell death which was related to the neurodegenerative diseases [92]. Cater et al. (2006) found the deformed brain tissue caused the cell death under TBI impacts [93]. Morrison III et al. (2006) developed an in vitro model of TBI and found the cell damage was related to strain [94]. Mao et al. (2010) reported the MPS was positively related to the neuron loss [95]. Currently, different kinds of brain strain-based metrics are being studied including 95th percentile MPS [89, 96, 97] which represents the 95th highest MPS value to avoid potential artificial errors, axonal strain [98, 99], Lagrange strain [100, 101], and Cumulative Strain Damage Measure (CSDM)[102, 103].

The CSDM, which represents the ratio of the volume of brain elements above the certain brain strain threshold to the total brain volume, was described in Equation 7.

$$CSDM = \frac{\text{volume of brain elements above strain threshold}}{\text{total brain volume}}$$  \hspace{1cm} (7)

1.6 Effect of Helmet

Wearing a helmet (Figure 1.14 [104]) is an effective way to protect the brain from concussive impacts [105]. The bicycle helmet can decrease the severe head injury risk by up to 40% [106]. The improved football helmet can decrease both head kinematic and strain responses [107, 108]. The hockey helmet with good designs can decrease risk of head
injuries from 8.3/100 games to 3.8/100 games [109]. The number of head injuries had an obvious decrease, from 4.25/100,000 to 0.68/100,000 when National Operating Committee on Standards for Athletic Equipment (NOCSAE) was applied to regulate the use of helmet [110].

Helmets were designed to meet with various helmet safety evaluation methods, which were traditionally about head linear accelerations [111]. More recently, the helmets have been improved by incorporating head rotational accelerations [112]. One further step is to design a helmet based on brain strains, which are directly linked to brain injuries as the stretches of these brain cells or axons cause damage. The brain-strain-based design optimization was conducted in this study.

Figure 1.13: Football helmet [104] (Adapted from Wikimedia with license (https://creativecommons.org/licenses/by-sa/4.0/legalcode)).
1.7 Potential effect of repeated mTBI

Researchers understand the repeated mTBI effects with animal tests [113, 114]. Under the repeated mTBI impacts, the change in skull, which played a role of protecting the brain [115], is topic that researchers are interested in. The repeated mTBI impacts could increase the strength and volume of mice skull [116]. The rat skull thickness and volume were found to have the obvious increase 10 weeks after the repeated mTBI impacts [113].

Repeated mTBI remains a challenging in the field. In this research, the focus was on reported skull changes due to repeated mTBI.

1.8 Brief research rationale and objectives

With extensive mTBI research data being reported in the field, as well as the development of protective helmets, this study intended to provide several novel breakthroughs to advance the understanding of fundamental injury mechanisms and improve prevention. Specifically, this study intended to: 1) develop a novel, detailed functional-region-based brain FE model that allows to analyze strain responses to each of these functions, and hence, brain networks, to understand injury mechanism; 2) understand the effect of strain responses of brain functional regions from FE model using the pipeline on working memory based on the public healthy functional connectivity datasets of working memory; 3) conduct brain-strain-based protective helmet and analysis and examine helmets’ potential effects on brain functional networks; 4) repeated mTBI effects by leveraging reported animal studies.

1.9 Overview of Chapters

Chapter 1 Introduction – Brief Overview of the Research Problem

This chapter describes the background of the research including the introduction of TBI, brain anatomy, the brain functional regions analysis, the biomechanical method to understand TBI, the helmet introduction, and repeated-mTBI impacts.

Chapter 2 Developing a pipeline to represent MNI-based brain functional regions for FE modeling
This chapter describes the pipeline that can segment brain FE models into functional regions based on brain functional atlas. Based on three mTBI NFL impacts, the brain functional regions with high strain were analyzed. The brain strain-affected connections of functional regions and the effect on brain functional connectivity were conceptually investigated. Moreover, the effect of FE model with different mesh sizes on the brain functional regions representation was analyzed.

Chapter 3 Understanding the brain strain effect on working memory among concussion impacts

This chapter describes the brain FE model with 100 functional regions developed in chapter 2 to 39 NFL cases. The common regions with high strain among mTBI impacts were analyzed. Moreover, the common strain-affected connections among mTBI NFL cases were identified and used to investigate the effect of healthy functional connectivity of working memory tasks.

Chapter 4 Temporal characteristics of shell vs foam strain energy and their effects on brain strain reduction during helmeted impacts

This chapter describes the temporal characteristics of helmet impacts. The study analyzed: 1) the brain strain responses under helmet and bare head impacts; 2) strain energy absorbed by helmet components; 3) head kinematics-based responses during the impact to the head with and without helmet; 4) the effect of helmet shell and foam stiffness on brain strain using factorial and main effect analysis; 5) brain strain-affected connections of functional regions under impacts to head with and without helmet based on the model developed in Chapter 2.

Chapter 5 Understanding the effect of brain skull change due to repeated mTBI on head responses

This chapter describes the effect of skull thickness and density change due to repeated mTBI impacts on brain strain and head kinematics-based responses. The brain strain-affected connections of the skull with and without thickness change were analyzed based on the model in chapter 2.
Chapter 6 Conclusions, Limitations and Future Work

This chapter summarizes the main conclusions, limitations, future work, and novelty/impact of this study.
Chapter 2

2 Developing a pipeline to represent Montreal Neurological Institute (MNI)-based brain functional regions for FE modeling

In this study, we developed a pipeline to divide the Global Human Body Model Consortium (GHBMC) FE brain model into functional regions based on the Schaefer atlas in the Montreal Neurological Institute (MNI) template. To evaluate the FE model with functional regions, we subjected it to three typical concussive impacts including frontal, lateral and rear impacts based on the National Football League (NFL) database. Using the cut-off strain threshold of 0.2, brain regions suspected of damage were identified and visualized. Furthermore, we explained conceptual ideas about how the developed detailed functional regions could allow for analyzing strain-based connectivity.

2.1 Introduction

Traumatic brain injury (TBI) is a severe health concern. There are 1.6 to 3.8 million sports-related traumatic brain injuries (TBIs) including concussions in the US alone [4]. Many patients diagnosed with concussions suffered from symptoms like headache, dizziness, and memory impairment [47]. These symptoms could be related to brain anatomy regions including the cerebral cortex [23].

The cerebral cortex, comprised of $10^{11}$ neurons connected by $10^{15}$ connections [20], plays a critical role in controlling functions such as cognition and emotion processing [21] and has garnered significant research interest [22-24]. The cerebral cortex is primarily divided into three types of functional areas: the motor area, sensory area, and association area [117]. Furthermore, the cerebral cortex can be divided into more detailed areas responsible for specific functions such as the primary motor area [118], the primary auditory area [119], and the visual area [120]. In visual perception tasks, Yang et al. (2015) reported the activation of brain regions related to the visual networks [121]. Chenji et al. (2016) reported that the sensorimotor network involved the somatosensory and motor regions [33], and Biswal et al. (1995) found the activation of sensorimotor cortex regions from hand movement through the functional MRI method [34]. The dorsal attention network is related
to the functions of sustained attention and memory [35]. Regions in the parietal, temporal, and frontal cortex, part of the default mode network, showed decreased activity during focused tasks, while increased activity was observed during complex cognition, which could be related to memory or abstract thought [36]. Furthermore, Zhang et al. (2021) reported that both the sensory and somatomotor networks are involved in the functions of multi-sensory and touch, and the somatomotor and internal mentation networks contain language-related functions [37].

The use of functional brain atlases has become increasingly important in studying the brain. These atlases are developed based on the Magnetic Resonance Imaging (MRI) data and allow for the division of the brain into different regions based on their functions. Collins et al. (1998) from the Montreal Neurological Institute (MNI) divided the brain into 90 anatomical volumes of interest (AVOI) [38]. Joliot et al. (2015) reported the Atlas of Intrinsic Connectivity of Homotopic Areas (AICHA) including 192 homotopic region pairs based on functional MRI (fMRI) data from 281 individuals [43]. Craddock et al. (2012) presented a brain functional atlas consisting of up to 1000 regions of interest (ROI) based on 41 subjects [44]. Gordon et al. (2016) used a method to define the parcels of cortical areas [122]. Yeo et al. (2011) studied the different regions of the cerebral cortex with the atlas [45]. Schaefer et al. (2018) developed the functional atlas with up to 1000 functional regions of the cortex area [46], facilitating for a more detailed analysis of functional damage and connectivity within the brain. These functional atlases play an important role in understanding brain function and connectivity.

The brain functional regions have been found to have connections to concussion [51]. Virji-Babul et al. (2014) found that the change in the connectivity of functional brain network occurred due to concussion [53]. Zhu et al. (2015) reported that the disruption of brain networks induced the dysfunction of the whole network [123]. Amir et al. (2021) found increased functional connectivity in the salience network and decreased functional connectivity in part of the default mode network [124]. Iyer et al. (2019) demonstrated the relationship between functional connectivity and post-concussion symptoms, such as poor cognition and sleep, based on 110 resting-state fMRI studies and behavioral assessments of children [125]. Li et al. (2019) reported decreased functional connectivity in the regions
of the left middle frontal gyrus among patients with mTBI [126]. Both hyperconnectivity and hypoconnectivity of functional brain regions were observed [127]. Hyperconnectivity occurs when the connectivity of brain functional regions increases [54], while hypoconnectivity refers to decreased functional connectivity [55]. Mayer et al. (2011) found reduced functional connectivity within DMN and hyperconnectivity between DMN and lateral prefrontal cortex among patients with mTBI [128]. D’Souza et al. (2020) reported decreased functional connectivity in functional networks, including anterior default mode and somato-motor networks, among patients with mTBI [56]. Borich et al. (2015) reported increased functional connectivity in the ventral attention network among adolescents with sports-related concussion [58]. Zhou et al. (2012) reported decreased connectivity in the posterior cingulate cortex and parietal regions, and increased frontal connectivity among the medial prefrontal cortex, which were positively related to the neurocognition dysfunction and negatively related to posttraumatic symptoms [59].

In studying traumatic brain injury (TBI), one main challenge in the engineering field is to investigate neuronal loss and associated brain damage. Using in vitro model, researchers such as Cater et al. (2006) demonstrated that the deformed brain tissue, which leads to the cell death during the head impacts, was the main cause to the TBI [93]. Hence, brain strain, a measure of the change of the brain deformation, has been extensively studied through finite element (FE) simulation to investigate TBI and predict TBI risks, as shown in several recent studies [68, 78, 129]. Moreover, researchers have tried to investigate the effect of strain on the alteration to neuron cells after TBI. Mao et al. (2010) reported that the maximum principal strain was positively correlated with neuron loss [95]. This positive correlation between the brain strain and cell death, stemming from the combination of FE and in vivo studies, was confirmed in vitro findings [93, 94]. The neuron cell death plays a significant role in the neurodegenerative disease [92]. Gabrieli et al. (2020) also reported that the neurodegeneration affected network activities [130]. One noteworthy study by that Wu et al. (2022) combined the study of the brain biomechanics with brain structural and functional networks, finding that the brain damage due to concussion could change the brain functional connectivity [131].
Although there are studies investigating the brain functional connectivity changes due to TBI, the effect of the brain strain on the functional connectivity is still unclear and needs further investigation. In this study, we developed a pipeline that can divide a traditional FE brain model into multiple, various functional regions, based on functional atlas, to get the comprehensive and detailed strain response of these brain functional regions. Then, we calculated and demonstrated brain strain-affected connection characteristics. We further demonstrated the effect of brain strain on functional connectivity with two conceptual ideas.

2.2 Method

2.2.1 Overarching method flow

The FE brain model was divided into functional regions of different partitions according to Schaefer et al.’s study [46]. The group provided detailed information on partitions from 100- to 1000-areas, among which 100-, 200-, 400-, 600-, 800, and 1000-area partitions were referred to develop our models. Based on the Schaefer atlas [46] with a spatial resolution of 2 mm (Figure 2.1a), the voxel point cloud (Figure 2.1b) was extracted by in-house developed code in MATLAB. The point cloud was then morphed to the GHBMC brain model [82] (Figure 2.1c), which was used to divide the conventional FE brain model, including one major cortex component together with the hippocampus and thalamus, into 100, 200, 400, 600, 800, and 1000 functional regions of the cerebral cortex. The GHBMC head model, which was validated against brain pressure and brain motion, contained 183,795 nodes and 270,552 elements including 150,074 hexahedral and 60,828 tetrahedra elements [82]. The brain components information of GHBMC model can be found in Appendix A. The viscoelastic materials were defined and applied to brain components [82]. Then, three concussive impacts reconstructed from NFL events [64] (Figure 2.1e, Figure 2.2) were applied to the GHBMC model to calculate the strain responses of different functional regions (Figure 2.1f). All non-linear explicit FE simulations were solved by Ls-Dyna (R901, double precision, LSTC, Livermore, CA).
For the boundary conditions of the FE simulation, six curves representing time histories of head kinematics were loaded at the center of the gravity of the head model, using LS-DYNA command ‘BOUNDARY_PREScribed_MOTION’ [132].

Figure 2.1: Research method. (a) Schaefer atlas; (b) Morphing voxel point from the Schaefer atlas to GHBMC model; (c) Morphed voxel points; (d) GHBMC model with new functional regions; (e) Kinematic curves; (f) Brain strain responses from simulation.
2.2.2 Getting voxel point cloud that can fit to FE brain model

We developed a pipeline to morph the point cloud from the Schaefer atlas to the GHBMC model (Figure 2.3). A similar morphing method was also used by Wu et al. (2019, 2022) to the brain biomechanics study [131, 133]. In step 1, we obtained the voxel point cloud from Schaefer atlas (Figure 2.3a). In step 2, we scaled the point cloud to fit to the GHBMC model (Figure 2.3b). In step 3, based on the scaled point cloud, we then extracted the surface and inner nodes (Figure 2.3c). In step 4, we applied the iterative closet point (ICP) method [134] to further morph the point cloud to the FE brain model surface (Figure 2.3d). In step 5, we morphed the surface nodes of point cloud to the GHBMC shape (Figure 2.3e), and in step 6, the inner nodes of point cloud were adjusted based on the surface nodes using thin plate spline method [135] (Figure 2.3f).

Figure 2.2: Kinematic curves used to apply to the GHBMC head model.
2.2.3 Strain analysis of functional region

Based on the numerical simulations of NFL concussive impacts, we then analyzed detailed strain responses. First, we developed the python code to obtain the maximum principal strain (MPS) time history of each brain element. Then, the maximum peak MPS of each functional region was collected. In this study, we used 95th percentile MPS as the maximum strain to avoid potential artificial error of some elements. The functional regions with the strain above the pre-set threshold were identified based on the MPS of each functional region. The brain strain-affected connections were then calculated based on the strain difference between two functional regions. The nilearn package of Python (https://nilearn.github.io/stable/index.html) was used to display these strain-relevant connections.
2.3 Results

2.3.1 GHBMC brain model with functional regions

Based on the morphed point cloud, which was extracted from the Schaefer atlas representing different functional regions, the GHBMC model was divided into 100 (Figure 2.4a), 200 (Figure 2.4b), 400 (Figure 2.4c), 600 (Figure 2.4d), 800 (Figure 2.4e), and 1000 (Figure 2.4f) functional regions. These regions represent cortical gray matter areas made with neurons. White matter regions such as the corpus callosum were not changed.

Figure 2.4: GHBMC model updated to represent different functional regions.
GHBMC model with (a) 100, (b) 200, (c) 400, (d) 600, (e) 800, and (f) 1000 functional regions.

The functional regions of GHBMC brain model are essential in forming different functional networks. Taking the GHBMC brain model with 100 functional regions (Figure 2.5a) as an example, this model includes the functional regions of peripheral visual network (Figure 2.5b), somatomotor networks (Figure 2.5c, d), dorsal attention networks (Figure 2.5e, f), salience networks (Figure 2.5g, h), limbic networks (Figure 2.5i, j), control
networks (Figure 2.5k-m), default networks (Figure 2.5n-p), temporal parietal network (Figure 2.5q), and central visual network (Figure 2.5r).

![Image of brain functional networks and included functional regions.](image)

**Figure 2.5: Brain functional networks and included functional regions.**

### 2.3.2 Common functional regions with high strain across NFL impacts

Among three NFL concussive impacts, there were 35 out of 100 functional regions showing 95th MPS above the strain threshold of 0.2 (Figure 2.6a), 10 out of 100 regions showing 95th MPS above 0.25 (Figure 2.6b), and two regions showing 95th MPS above 0.3 (Figure 2.6c). Taking the strain threshold of 0.2 as an example, the regions experiencing strains above the threshold include the somatomotor cortex, auditory cortex, temporal occipital cortex, post central cortex, frontal eye fields, insula cortex, parietal medial cortex, temporal pole, lateral prefrontal cortex, cingulate posterior cortex, dorsal prefrontal cortex, precuneus posterior cingulate cortex, and S2 cortex (Table 2.1). Accordingly, the peripheral somatomotor network, dorsal attention network, salience network, limbic network, control network, and default mode network were affected (Table 2.1).
Figure 2.6: Common functional regions above high strain across NFL impacts.

Table 2.1: Functional regions experiencing strain above 0.2 among three concussive impacts.

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<th>Network Name</th>
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<td>salience / ventral attention A</td>
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<tr>
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<td>temporal</td>
<td>control B</td>
</tr>
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</tr>
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<td>86</td>
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<tr>
<td>90</td>
<td>dorsal prefrontal cortex</td>
<td>default A</td>
</tr>
<tr>
<td>95</td>
<td>dorsal prefrontal cortex</td>
<td>default B</td>
</tr>
</tbody>
</table>
2.3.3 Brain strain-affected connections

The brain strain-affected connections of three concussive impacts are displayed in Figure 2.7. These strain-affected connections described the connections between multiple function regions that have experienced strain values above a preset threshold of 0.2. As all these regions experienced high strain level above a preset threshold, which is 0.2 here. These regions could fire simultaneously whether they are intrinsically linked in a neurological function or not. In one of concussive cases, case 113, some strain-affected connections were between the functional regions of left and right hemisphere (Figure 2.7a), with a total of 63 strain-affected connections. In case 148, strain-affected connections were observed at two hemispheres (Figure 2.7b), with a total of 164 strain-affected connections. In case 162, functional regions of both the left and right hemispheres had strain-affected connections (Figure 2.7c), with 82 strain-affected connections in total.

Figure 2.7: Brain strain-affected connections. (a) 63, (b) 164, and (c) 82 strain-affected connections were produced under three NFL cases with concussion respectively.
2.4 Discussion

2.4.1 Suspectedly damaged brain regions across impacts

Across concussive impacts, brain functional regions could be damaged. In this preliminary study with three concussive NFL impacts, we found that the brain functional regions from somatomotor, dorsal attention, salience, default, and temporal parietal networks were damaged based on a strain threshold of 0.2. During the laboratory tests, Xiong et al. (2016) reported that cognitive function in terms of working memory index and processing speed index were decreased due to mTBI [136]. Iraji et al. (2015) reported the alterations to the default mode network functional connections, which could affect cognitive functions [137]. Banks et al. (2021) reported that the speech rate of the athletes could be slowed due to concussion [138], which may be related to the damage to the auditory cortex related to the functions of speech and music [139]. McCrory and Johnston (2002) reported that the memory loss was one of the concussion symptoms [140], which could be the result of the damage to the dorsal attention network responsible for the functions of attention and memory [35]. Prigatano (2005) reported that the patients with moderately severe to severe TBI could face the symptoms of impaired self-awareness [141]. The insula cortex, which was one part of ventral attention network based on Schaefer atlas [46], was reported to be related to functions including self-awareness, risk forecasting, and emotion [142]. Leddy et al. (2017) reported that concussion may cause the vision problems [143], and we found the temporal pole, responsible for processing the complicated objects visually [144], was affected during the impacts. Witt et al. (2010) reported the reduced activity of the lateral prefrontal cortex, which is related to the functions including executive behavioral control due to mTBI [145, 146]. Leech and Sharp (2014) reported that after TBI, there were impairments to the attention due to disfunction of posterior cingulate cortex in three impacts [147]. We found the dorsal lateral prefrontal cortex experienced strain above the threshold of 0.2. Similarly, Cho et al. (2022) reported that the deficit in short-term memory was related to dorsal lateral prefrontal cortex due to mTBI [148]. The pipeline developed in this study allows for a comprehensive examination of the responses of each functional region during impacts.
Concussions are believed to be induced, at least partly, due to head impacts that strain various functional regions, as well as axons. Meanwhile, unravelling the relations between these strained regions and observed symptoms requires extensive data collection of head kinematics, finite element simulations and clinical observations. Zimmerman et al. (2023) reported that the loss of consciousness resulted from head impacts producing large brain tissue deformation in brainstem and cerebellum parts, and dystonic posturing was observed in cases producing high brain deformation in cortical regions including motor cortex, based on extensive effort that collected kinematics, brain strain, and injury data over years [149].

2.4.2  Potential applications in combination with brain functional connections

We found that several functional regions experienced similar peak strain under concussion impacts (Figure 2.6 and Table 2.1). We proposed two conceptual explanations regarding the effect of strain in functional regions on the connectivity change: 1) the damaged brain functional regions due to high strain could terminate the connectivity that goes through these regions; 2) the functional hyperconnectivity and hypoconnectivity of the brain may be affected by the strain connection.

2.4.2.1  Damaged brain regions could disrupt functional connections

Our results showed that several brain functional regions experienced strain above a strain threshold during impacts. Hence, the functional connections to the damaged functional regions could be disrupted due to the high strain of these regions. Figure 2.8 explains this conceptual idea. The healthy brain functional network is displayed in Figure 2.8 (a). After the concussive impact, some functional regions, which were labelled grey, were damaged and the functional connections to these regions could be terminated (Figure 2.8b).
2.4.2.2 Strain-based connections could affect functional connections analysis

Another conceptual idea is that the strain-affected connection could be related to the hyperconnectivity and hypoconnectivity observed in mTBI cases. Figure 2.9 (a) displays the connectivity network of a healthy brain when performing a task. Due to a concussive impact, regions 2 and 3, 2 and 4, 3 and 6, and 4 and 6 become strain-affected connected (Figure 2.9b). The strain-affected connection could either increase functional connectivity (Figure 2.9c, d) or decrease functional connectivity (Figure 2.9e, f).
Figure 2.9: Brain strain-affected connections could cause hyperconnectivity and hypoconnectivity. (a) Healthy brain functional connections; (b) Brain strain-affected connections; (c) Hyperconnectivity; (d) Hypoconnectivity; (e) Increased connectivity; (f) Decreased connectivity.

We postulated that strain-affected connections could result in hypoconnectivity, as indicated by the literature showing that high strains induce neuronal cell loss through in vitro [93, 94] and combined in vivo and FE brain simulations [95]. Hence, this may demand less of blood flow, which is observed in fMRI.

2.4.3 Brain mesh density effect and limitations

In this study, the functional regions were segmented based on the GHBMC model with the average element size of 2 mm [82]. However, we found the current model was limited in representing detailed functional regions. For example, in Figure 2.10 (a), the labelled part (Figure 2.10a, d) of the model with the original size included three elements. When the mesh size reduced to half of its original length, thus increasing element number to 8 times,
the functional regions were better represented (Figure 2.10b, e). When the mesh size was further reduced to quarter of the original length, thus increasing the element number to 64 times, the functional regions were better represented (Figure 2.10c, f).

The element size played a more important role in the brain region representation when the brain model was divided into a larger number of functional regions. When the brain model was divided into 1000 functional regions, one part included 33 elements of the model with original mesh size (Figure 2.10g, j). When the mesh size reduced to the half and then quarter size, the part representation improved (Figure 2.10h, k, i, l).

**Figure 2.10:** Functional regions in the model with different element sizes. Different numbers of elements of GHBMC model with 100 (a-c) and 1000 (g-i) functional regions.
2.4.4 Limitations

In this study, an MNI template was used to develop brain functional regions on an average adult head model. Meanwhile, it should be highlighted that individual variances contributed brain biomechanical responses [150]. This study was limited to investigating cortical functional regions, which consist of gray matter materials. Meanwhile, white matter could be damaged during impacts especially impacts with large head rotations, and such damage contributes to diffuse brain injury. It is postulated that damage to both the gray-matter functional regions and white-matter axons contribute to concussions. Hence, a comprehensive investigation of concussion needs to consider both functional regions as reported in this study, and white matter tracts [131, 133, 151].

2.5 Conclusions

In this study, we developed a pipeline that can convert a conventional FE brain model into detailed functional regions based on functional atlas and demonstrated the development of six detailed brain models. With these FE brain models representing detailed functional regions, the suspected damaged functional regions and networks were investigated under three concussive impacts. Further analysis could be conducted on more real-world concussive impacts and can then be combined with helmet research to study how to optimize head protection methods in preserving critical functional regions. We also conceptually investigated the effect of the brain strain-affected connections on functional connectivity, including identifying damaged regions that could disrupt brain networks and potential hyperconnectivity and hypoconnectivity as being triggered by high strains. In brief, the pipeline could be used to efficiently convert an existing FE brain model into detailed functional regions, thus enabling a bridge between detailed brain biomechanics and brain functional damage to better understand the fundamental mechanisms causing concussion/mTBI.
Chapter 3

3 Understanding the brain strain effect on working memory among concussion impacts

In chapter 2, the responses of brain functional regions and conceptual effect of strain-affected connections of functional regions were analyzed based on the three NFL cases. In this study, 39 real-world NFL cases were applied to further investigate the brain strain responses and the effect of brain strain on working memory. Based on 35 brain functional regions that were commonly above concussive strain threshold of 0.2, 149 potentially working-memory-related connections were identified as susceptible to damage despite impact scenarios.

3.1 Introduction

Traumatic brain injury (TBI) has become a severe health challenge. According to the Centers for Disease Control and Prevention (CDC), TBI caused 60,611 deaths in 2019 [5]. Moreover, 15% of US high-school sports-related injuries were concussions [7]. In Canada, 1 out of 450 of 12 years and older reported brain injuries, including sported-related concussion, as the most significant injury [8]. Concussion can induce cognitive impairments, including the alteration of working memory performance [152-155]. Working memory is short-term and refers to remembering the small amount of information for tasks [155, 156]. Working memory deficits caused by concussion could become prolonged and needed long time to recover [155].

Functional magnetic resonance imaging (fMRI) measures the blood-oxygenation-level-dependent (BOLD) signals to identify regional responses of the brain to specific tasks and conditions [157, 158]. The working memory can be tested using N-back task, which aims to test the ability of the participants to judge whether the stimulus matches the one that occurred n times previously [159, 160]. To investigate the working memory deficits due to concussion, fMRI datasets are scanned among patients with concussion when they perform the N-back tasks [161-163].
The brain consists of different regions related to different functions. Forseth et al. (2020) revealed that the auditory cortex was related to the language function [25]. Salmelin et al. (1995) reported that the somatomotor cortex was involved in the hand movements [28]. Puce et al. (1998) found that the temporal cortex was activated during the eye and mouth movements [27]. Malach et al. (1995) found the object-related activation in object recognition cortex [164]. Robinson and Fuchs (1969) reported that the frontal eye fields were related to the eye movements [165]. De Pisapia et al. (2007) Herlin et al. (2021) summarized that the temporal pole was related to some cognitive processes, including face recognition, word-object labelling, and processing complicated objects visually [144, 166]. Leeth and Smallwood (2019) reported that the cingulate posterior cortex played a role in cognition [29]. Seminowicz and Massieh (2017) reported that the dorsal prefrontal cortex may be related to the acute and chronic pain [167]. Researchers (2018) reported that the lateral prefrontal cortex played a role in executive behavioral control [145], integration of emotion and cognition [168], making decisions [169], and working memory [170].

Some brain regions were found to be related to working memory deficits due to concussion. Dettwiler et al. (2014) found increased activation in bilateral dorsolateral prefrontal cortex among concussed athletes [30]. Kightley et al. (2014) reported the decreased activity in the brain regions including bilateral dorsolateral prefrontal cortex, left premotor cortex, supplementary motor area, and left superior parietal lobule among youth with sports-related concussion [32]. Van der Horn et al. (2016) reported the patients with mTBI experienced reduced activation in the medial prefrontal cortex [31]. Shah-Basak et al. (2018) reported the abnormal responses in frontoparietal, ventral occipitotemporal, temporal, and subcortical areas among patients with concussion [171].

The change of brain functional connections among brain functional networks consisting of brain functional regions was related to concussion [53]. Currently, the main brain functional networks include the default mode network [172], sensorimotor network (also called the somatomotor network) [173], dorsal attention network [174], ventral attention network [175], limbic network [176], and control network [45]. Zhu et al. (2015) reported the sports-related concussion changed the functional connectivity with default mode
network [123]. Hocke et al. (2018) reported the reduced functional connectivity among adults with persistent post-concussion symptoms [177].

From empirical studies, it’s difficult to obtain the image dataset right after mTBI. In the perspective of brain biomechanics, the stretch of brain tissue due to head motion could induce brain injury [93, 95, 101]. Mao et al. (2010) found that the brain strain, which can be obtained from finite element (FE) analysis [78, 129], was positively correlated with the injury risk of different brain parts [95]. However, how damaged brain functional regions affect the brain functional connectivity is unknown.

The objective of this study is to understand how strain affects the brain functions and working memory. Based on the FE model with 100 functional regions, we analyzed in-field football cases, including both concussive and non-concussive impacts, and obtained the brain strain responses of each region. We then identified the common regions experiencing the strain above concussive threshold across concussive cases. The strain-affected connection, which refers to the connection between two brain functional regions with at least one region above the concussive strain threshold, was found across concussive, non-concussive and all cases. The effect of common high-strain regions among concussive cases on the working memory tasks was also analyzed.

3.2 Method

3.2.1 Overall method flow

The GHBMC brain model was divided into 100 functional regions (Figure 3.1a) using the method mentioned in Chapter 2. A total of 39 National Football Legacy (NFL) cases [64], including 13 concussive and 26 non-concussive cases (Figure 3.1b), were simulated using finite element analysis. Brain strain responses (Figure 3.1c) in terms of 95th percentile maximum principal strain (MPS) were collected. With the 95th percentile MPS of each functional region, the common regions experiencing high strain above concussive threshold among 13 concussive cases were analyzed (Figure 3.1d). We further identified the strain-affected connections as the connection of two brain regions with at least one region above the concussive strain threshold. The circular plot (Figure 3.1e)[178] and 3D plot (Figure 3.1f) (https://nilearn.github.io/stable/index.html) were used to display strain-
affected connections among 13 concussive cases, 26 non-concussive cases, and a total of 39 cases including both concussive and non-concussive cases. Moreover, with 144 1-back healthy working memory datasets obtained from Rieck et al. (2021)[2, 3], we analyzed the effect of strain on working memory due to concussion.

![Figure 3.1: Analysis method; (a) GHBMC model with 100 functional regions; (b) Kinematic curves from NFL impacts; (c) Brain strain responses from FE simulation; (d) Common functional regions experiencing high strain across concussive impacts; (e) Circular plot to display strain-affected connections; (f) 3D plot of strain-affected connections.]

### 3.2.2 Finite element model

The GHBMC brain model [82] was used in this study. Based on the Schaefer atlas [46], which identified 100 functional regions, the GHBMC brain model was segmented into these 100 functional regions (Figure 1a). The morphing methods were applied during the segmentation process to fit the voxel point clouds of the Schaefer atlas to GHBMC model. The 100 functional regions were categorized into 17 functional networks, including central visual network, peripheral visual network, somatomotor networks, dorsal attention...

The kinematic curves of 39 NFL cases were loaded at center of the gravity of the head using the LS-DYNA command ‘BOUNDARY_PREScribed_MOTION’ [132]. The brain components information of GHBMC model can be found in Appendix A.

3.2.3 Strain responses

The brain strain responses of NFL simulations were collected and analyzed. The 95th percentile MPS of each functional region was analyzed. The common functional regions with 95th percentile MPS above 0.2 in 13 mTBI impacts were identified using self-developed MATLAB codes (The MathWorks Inc., Natick, MA).

Here, we defined the strain-affected connection as the connection between two regions, with at least one region above the 95th MPS of threshold. In this study, we analyzed the strain-affected connections where at least one out of two regions above 95th MPS of 0.2. The strain threshold values could be conveniently adjusted in codes based on new studies reported in the literature. The common strain-affected connections of 13 mTBI cases, 26 non-mTBI cases, and a total of 39 cases were analyzed. In-house MATLAB codes (The MathWorks Inc., Natick, MA) were developed to calculate the strain connections of functional region. The strain connections were further plotted with Python (https://nilearn.github.io/stable/index.html).

3.2.4 Healthy brain functional connectivity of working memory

We obtained healthy brain functional connectivity datasets for working memory tasks. Based on 144 healthy functional connectivity datasets of working memory task obtained from Rieck et al (2021) [2, 3], the average connectivity data was calculated. We then plotted the significant functional connectivity, with the threshold above 0.5. With common strain-affected connections of NFL impacts, we then analyzed the potential effects of strain effect on the working memory.
3.3 Results

3.3.1 Common brain functional regions among concussive impacts with high strain

Among 13 mTBI NFL cases, we found that there were 35 common regions with the 95th percentile MPS above 0.2 (Figure 3.2a), 10 common regions with 95th percentile MPS above 0.25 (Figure 3.2b), and 2 common regions with 95th percentile MPS above 0.3 (Figure 3.2c). 35 common regions above 95th percentile MPS of 0.2 included the somatomotor A cortex, auditory cortex, temporal occipital cortex, post central cortex, frontal eye fields cortex, insula cortex, parietal medial cortex, temporal pole cortex, lateral prefrontal cortex, cingulate posterior cortex, dorsal prefrontal cortex, precuneus posterior cingulate cortex, post central cortex, frontal medial cortex, medial posterior prefrontal cortex, lateral dorsal prefrontal cortex, inferior parietal lobule cortex, and dorsal prefrontal cortex (Table 3.1). The networks with brain functional regions above 95th percentile MPS of 0.2 included the somatomotor network, dorsal attention network, salience network, limbic network, control network, and default network (Table 3.1). 10 common regions with 95th percentile MPS above 0.25 included the somatomotor A cortex, post central cortex, lateral prefrontal cortex, auditory cortex, frontal eye fields cortex, parietal medial cortex, frontal medial cortex, and temporal cortex (Appendix Table 1). The functional networks including regions above 95th percentile MPS of 0.25 were the somatomotor network, dorsal attention network, control network, and salience network (Appendix Table 2). Two common regions with 95th percentile MPS above 0.35 were the somatomotor A cortex and parietal medial cortex, from somatomotor and salience network, respectively (Appendix Table 3).
Figure 3.2: Common brain functional regions among NFL impacts. (a) 35 common functional regions with strain above 0.2; (b) 10 common functional regions with strain above 0.25; (c) 2 common functional regions with strain above 0.3.

Table 3.1: Common brain functional regions with 95th percentile MPS above 0.2.

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<th>Network Name</th>
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</thead>
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<tr>
<td>18</td>
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<tr>
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</tr>
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<td>salience / ventral attention A</td>
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</tr>
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3.3.2 Common brain strain-affected connections

We plotted common brain strain connections among 13 mTBI impacts, 26 non-mTBI impacts, resulting in a total of 39 NFL impacts. Among 13 mTBI impacts, there were 3331 common strain-affected connections, each included at least one brain region with 95th percentile MPS above 0.2 (Figure 3.3).

Figure 3.3: 3331 common strain-affected connections of regions above 0.2 with 17 functional networks among mTBI impacts. (a) Circular plot of strain-affected connections; (b) 3D plot of strain-affected connections.
Among the 26 non-concussion impacts, there were 105 common strain-affected connections (Figure 3.4a). 99 strain-affected connections originated from the somatomotor A cortex, which was part of somatomotor network, extending to other 99 regions. Two strain-affected connections started from lateral prefrontal cortex, one extending to parietal medial cortex and the other extending to somatomotor A cortex (Figure 3.4a). These two strain-affected connections connected control networks to salience and somatomotor network, respectively (Appendix Figure B). Two strain-affected connections originated from somatomotor A cortex, one extending to parietal medial cortex and the other extending to somatomotor A cortex (Figure 3.4). These two strain-affected connections connected somatomotor networks to salience and somatomotor cortex individually (Appendix Figure B). The S2 cortex, part of somatomotor B network, was connected to parietal medial cortex (from somatomotor B network) and somatomotor A cortex (somatomotor A network) (Figure 3.4, Appendix Figure B).
Among 39 impacts, including both concussive and non-concussive cases, there were 105 common strain-affected connections (Figure 3.5). 99 strain-affected connections originated from the somatomotor A cortex, which was part from somatomotor network, extending to other 99 regions. Two connections started from lateral prefrontal cortex, one extending to parietal medial cortex, and the other to somatomotor A cortex (Figure 3.5a). These two
strain-affected connections connected control networks to salience and somatomotor network, respectively (Appendix Figure C). Two strain-affected connections originated from somatomotor A cortex, one extending to parietal medial cortex, and the other to somatomotor A cortex (Figure 3.5a). These two strain-affected connections connected somatomotor networks to salience and somatomotor cortex individually (Appendix Figure C). The S2 cortex of somatomotor B network connected to parietal medial cortex (from somatomotor B network) and somatomotor A cortex (somatomotor A network) (Figure 3.5a, Appendix Figure C).
Figure 3.5: 105 common strain-affected connections of regions above 0.2 with 100 functional regions among total 39 NFL Impacts. (a) Circular plot of strain-affected connections; (b) 3D plot of strain-affected connections

3.3.3 Compare strain-affected connections of concussion cases to the healthy functional connectivity of working memory task

There were 325 healthy functional connections with the strength above 0.5 among 144 datasets of 1-back working memory tasks (Figure 3.6a, Figure 3.7). All 100 functional regions were involved. There were 149 working memory connections of 35 common regions with strain above 0.2 (Figure 3.6b, Figure 3.8), which were also regarded as
damaged brain functional regions. The functional connections of these 35 regions with high strain were mainly located in cortex including prefrontal cortices. There were 176 connections when excluding connections from 35 damaged functional regions (Figure 3.6c, Figure 3.9).

Figure 3.6: Applying concussive brain functional regions to healthy functional connections of 1-back working memory tests. (a) Healthy functional connections; (b) Functional connections affected by functional regions with high strain; (c) Functional connections excluding damaged functional regions caused by high strain.
Figure 3.7: 325 functional connections among healthy working memory datasets with 1-back task. (a) Circular plot of strain-affected connections; (b) 3D plot of strain-affected connections.
Figure 3.8: 149 connections of common concussed functional brain regions. (a) Circular plot of strain-affected connections; (b) 3D plot of strain-affected connections
Figure 3.9: 176 connections excluding damaged brain regions. (a) Circular plot of strain-affected connections; (b) 3D plot of strain-affected connections

3.4 Discussion

3.4.1 High strain regions of concussive impacts

We found that 35 functional regions commonly experienced 95th percentile MPS above 0.2. The common regions included the cingulate posterior cortex, auditory cortex, frontal eye fields, insula, lateral dorsal prefrontal cortex, lateral prefrontal cortex, posterior
cingulate cortex, and lateral dorsal prefrontal cortex. Leech and Sharp (2014) reported that the posterior cingulate cortex could be damaged, which may cause impairments of attention [147]. Patel et al. (2023) reported that the rate of speech errors increased due to concussion [50], which may be related to the damage in the auditory cortex related to the language function [25]. Ventura et al. (2016) demonstrated that concussion changed the brain pathways of eye movements [179], which may involve the frontal eye fields responsible for eye movements [27]. Churchill et al. (2021) reported that insula, which was related to the cognition [180], had connectivity changes after concussion [181]. Witt et al. (2010) found the activity in the right dorsolateral prefrontal cortex was obviously reduced among patients with concussion during the target stimulus detection tests [146]. Fogleman et al. (2017) reported that the volume of lateral prefrontal cortex was reduced due to mTBI [182]. The memory deficit is one of the reported concussion symptoms [153, 183]. We found posterior cingulate cortex, which was important for memory retrieval [184], was one of the common high-strain regions among mTBI impacts. Chen et al. (2008) found the reduced activation in the dorsolateral prefrontal cortex among concussive athletes with depression symptom [185]. This region also experienced high strain in our study.

### 3.4.2 Common strain-affected connections among NFL impacts

In this study, we considered two functional regions to have strain-affected connections if at least one region experiencing 95th percentile MPS above the threshold. Based on the strain threshold of 0.2, we found there were 3331 common strain-affected connections among 13 mTBI impacts, 105 common strain-affected connections among non-mTBI impacts, and a total of 39 impacts including mTBI and non-mTBI cases. There was a large amount of common strain-affected connections across mTBI impact because the brain regions experienced high strain. Among NFL impacts, Sanchez et al. (2019) reported that 95th percentile MPS values were generally higher under mTBI impacts, being compared with non-mTBI cases [64].

We also found 105 common strain-affected connections among total NFL cases. There were 99 strain-affected connections that originated from the somatomotor A cortex, which was part from somatomotor network, extending to other 99 regions belonging to the functional networks including the default network, dorsal attention network, ventral
attention network, control network and limbic network. D’Souza et al. (2020) reported that mTBI reduced connectivity within default mode network, somoto-motor network, auditory network, and central executive network [56]. Li et al. (2020) found the disconnections between the sensorimotor network and visual network due to mTBI [186]. Zhu et al. (2015) found reduced functional connectivity within the default mode network among patients from day 1 to day 7 following sports-related concussion [123]. Hocke et al. (2018) reported that reduced functional connectivity could associate with severe post-concussion symptoms [177].

3.4.3 Compare strain-affected connections of concussive cases to the healthy functional connectivity of working memory task

From the plot of healthy functional connectivity for 1-back working memory task, we found all 100 functional regions were involved and played a role. The common functional regions with high strain contained prefrontal cortices including the dorsolateral prefrontal cortex, lateral prefrontal cortex, and dorsal prefrontal cortex. Kennerley and Wallis (2009) reported that the lateral prefrontal cortex played a role in spatial working memory [187]. Owen et al. (1999) found that the mid-dorsolateral prefrontal cortex was related to processing the information with the working memory [170]. Curtis and D’Esposito (2003) reported that the dorsolateral prefrontal cortex played a role in working memory and assisted the information maintenance [188]. Barch et al. (1997) found the increased activity in dorsolateral prefrontal cortex during working memory tasks [189].

We also demonstrated that due to high strain, the brain functional regions could be damaged, hence disrupting the functional connections of the brain. Stevens et al. (2012) reported abnormal brain functional connections among mTBI patients [190]. In our study, we found connections originating from the dorsolateral prefrontal cortex, which experienced high strain. These connections may be easily deactivated due to the damaged dorsolateral prefrontal cortex caused by high strain. Khetani et al. (2019) reported that children with post-concussion symptoms exhibited hypoactivation in the dorsolateral prefrontal cortex during working memory tasks [191]. We also found connections from high-strain regions of the default network. Van der Horn et al. (2016) found deactivation of default mode network among patients with mTBI [31]. Moreover, they reported that
mTBI could cause hypoactivation of the medial prefrontal cortex [31], we also found the connections originating from medial posterior prefrontal cortex, which was one of common regions experiencing high strain among concussive impacts.

3.5 Conclusions

In this study, we obtained the strain responses of 100 functional regions among NFL impacts, including both concussive and non-concussive cases. We found common functional regions with strain values above concussive threshold among concussive cases. We then investigated the brain strain-affected connections, defined as connections between two brain functional regions with at least one region above the threshold. There were 105 common strain-affected connections among 39 NFL impacts, which indicates that these connections may be disrupted due to the damaged brain functional regions caused by high strain. We further analyzed the effect of strain on healthy functional connectivity of working memory 1-back tasks. We found that the common high strain region among concussive impacts could affect 149 functional connections of working memory tasks, which could affect the working memory performance.
Chapter 4

4 Temporal characteristics of shell vs foam strain energy and their effects on brain strain reduction during helmeted impacts

By absorbing the energy during the impact, helmets play an important role in head protection. Different kinds of helmets were tested in laboratories to optimize the designs. To further optimize the helmet performance effectively, it is critical to understand the effect of helmet outer shell and foam on strain energy absorption and brain strain responses. Moreover, the way helmets affect the brain strain-affected connections of functional regions remains unclear in the field and needs to be quantified.

4.1 Introduction

Traumatic brain injury (TBI) remains a severe health concern, with 1.6 to 3.8 million sports related TBI cases annually [4]. Helmet has been reported as an effective way to prevent head injury from external impacts [105]. Bailey et al. (2020) demonstrated that the helmet with good laboratory performance exhibited reduced concussion rate on-field [192]. McNally and Whitehead (2013) reported that a helmet can reduce the severe head injury risk by up to 40% among adult cyclists [106]. Collins et al. (2006) reported that the wearing the helmet with new technology can reduce the risk of concussion [193]. Viano et al. (2012) reported the improved football helmets reduced the head peak linear and rotational acceleration by up to 14% and 15.9%, respectively [107].

Helmet performance has gained the research interest from different groups, especially in terms of reducing brain strain, which is main culprit causing mild TBI [93]. The helmet performance was usually evaluated by investigating whether the brain injury risk was reduced when using a helmet [194]. Currently, the head kinematics-based brain injury metrics including peak linear acceleration [195], Head Injury Criterion (HIC) [84], Brain Injury Criterion (BrIC) [85], and Diffuse Axonal Multi-Axis General Evaluation (DAMAGE) [88], along with brain strain-based injury metrics including maximum principal strain (MPS) [196] and Cumulative Strain Damage Measure (CSDM) [102], are widely used to evaluate and investigate helmet performance. Corrales et al. (2020)
observed a positive correlation between helmet component strain energy and HIC, while the correlation to BrIC was not substantial [197]. Ghazi et al. (2022) evaluated helmet performance using MPS and CSDM through convolutional neural network (CNN) method, indicating that current helmets have the room to improve [198]. It is important to understand the strain energy distribution of helmet parts and evaluate the helmet performance based on both the head kinematics-based metrics and brain strain responses.

Helmet structural designs have been optimized to improve helmet performance. Bailey et al. (2021) reported two helmet shell add-on products, the Guardian Cap NXT and the ProTech Helmet Cap, decreased impact severities by reducing head acceleration response metric results [199]. Mills et al. (2021) found that head linear acceleration did not change obviously when applying different material properties to helmet foam during the linear impactor tests [200]. Giudice et al. (2020) found that the effect of outer shell and column stiffness on head translational kinematic response was more than the effect on rotational kinematic responses based on Vicis Zero1 (VZ1) football helmet with the structure of buckling columns [77]. Alizadeh et al. (2019) demonstrated that the helmet with fluid shock absorber decreased strain by 27.6% ± 9%, being compared with existing helmet designs [108]. Moreover, Cecchi et al. (2023) reported that the design of liquid shock absorbers improved the football helmet performance with the average Head Acceleration Response Metric (HARM) reduction of 33% under sub-concussive and 32% under concussive impacts, respectively [201]. However, the effect of helmet shell and foam on brain strain responses remains unknown.

With a validated FE helmet model, and its integration with a human head model, it is now possible to analyze detailed temporal characteristics of energy absorption of various helmet parts, the reduction in head responses due to helmet, and the effect of helmet shell and foam on brain strain responses. Such knowledge can help to further improve helmet designs that are effective in reducing brain strains.
4.2 Method

4.2.1 Finite element model

The Global Human Body Model Consortium (GHBMC) head-neck model (Figure 4.1a) [202] and the open-source Riddell Speed Classic helmet FE model (model R41179) (Figure 4.1b) [203] (https://biocorellc.com/#biocore) were combined to investigate the brain strain responses. The well-defined head-neck model contained 526,635 elements, 501,961 nodes, and 297 parts [202]. The brain components information of GHBMC model can be found in Appendix A. The head parts included the brain parts such as corpus callosum, thalamus, and brain stem [82]. The head model was validated against brain pressure [204, 205] and brain motion [206, 207]. The neck model contained the parts including the spinal cord, cervical bones, discs and facet joints. The GHBMC neck model was validated in extension and flexion loading at the segmental level [202, 208]. The whole head & neck model was validated in frontal and lateral impact [209]. The Riddell helmet FE model contained 147,445 elements, 141,015 nodes and 57 components including outer shell, foams, and facemask [203]. Elastic material [132] was applied to the helmet shell. The Fu Chang material [132] was applied to helmet foams. The facemask consisted of beam elements with elastic material.

The inner layer of the helmet model was pre-deformed to fit to the head model tightly, with the maximum gap of 0.4 mm. The head shape model was moved towards the helmet inner foams to fit to the helmet model by deforming the helmet foams. For the deformed helmet model, 99.98% elements had Jacobian above 0.4, with minimum above 0.22. The simulations were calculated through Ls-Dyna R901 (R901, double precision, LSTC, Livermore, CA).

The GHBMC head-neck model and pre-deformed helmet model were combined. The LS_DYNA contact command [132] was applied to the helmet foam components and the skin of head and neck model to avoid penetration during the simulation. The LS-DYNA contact command [132] was also applied to the impactor and outer shell, facemask, and chinstraps of the helmet model to prevent penetration. The bottom of the head-neck model was constrained.
4.2.2 Impact Conditions

To quantify the effect of the helmet to protect the brain, the impactor [1, 210] under the velocity of 6 m/s based on the NOCSAE standard [211] was used to impact the frontal site (Figure 4.1c), frontal boss site (Figure 4.1d), lateral site (Figure 4.1e), rear boss site (Figure...
4.1f), and rear site (Figure 4.1g). The impactor with the same speed was applied to impact the same sites to the bare head model (Figure 4.1h-l). The total impact duration was 40 ms. The LS-DYNA command ‘INITIAL_VELOCITY’ [132] was used to define the motion of the impactor based on the local coordinates created in the impactor.

4.2.3 Helmet and head responses

In this study, both helmet and head responses were analyzed. The strain energy of different helmet components was collected based on the FE simulation. We analyzed the peak strain energy of different helmet components and the time histories.

The head kinematic curves, including the time history of linear acceleration, rotational velocity, and rotational acceleration, were exported under the local coordinates with the center node of center of gravity of the head, using the interpolation command of Ls-Dyna.

The 95th percentile maximum principal strain (MPS) was selected to represent the peak strain to avoid potential artificial high strain. The average MPS, and cumulative strain damage measure (CSDM) with the threshold of 15%, which represents the ratio of the brain elements experiencing the peak strain above 15% to the whole brain element volume, were also included.

4.2.4 Design of Experiment

To investigate the effect of helmet shell and foam on brain strain, the design of experiment method was adopted. Two levels of impact velocity (3 m/s and 6 m/s), roughly representing minor and moderate impacts, respectively, were included. To identify the main effect of the shell and foam material, we increased helmet shell stiffness to 0.5, 1, and 1.5 times, and changed helmet foam stiffness to 1, 2, 3, 4, 5, 6, and 7 times. Based on the main effect results, we further increased the shell stiffness to 5 levels (0.5, 0.75, 1, 1.25, and 1.5 times) and foam stiffness increased to six levels (0.5, 1, 1.5, 2, 2.5x, and 3 times) to investigate the factorial effect. Minitab was applied to the factorial and ANOVA main effect analysis (https://www.minitab.com).
Without design optimization, we would need 60 cases (2 levels of impact velocity x 5 levels of shell stiffness and x 6 levels of foam stiffness) to obtain the factorial effect. In this study, the D-Optimal method, based on R language (https://www.r-project.org/) was used to reduce the number of simulations to 40 (20 cases for each impact velocity level).

4.2.5 Brain strain-affected connections of functional regions

Using the brain FE model segmented into 100 functional regions, based on the pipeline developed in Chapter 2, we investigated the brain strain-affected connection. This connection connected two brain functional regions, with at least one functional region above the strain threshold. The brain strain-affected connections resulting from the impact to bare head and impact to helmeted head with shell and foam material optimized by main effect analysis were analyzed.

4.3 Results

We investigated the peak strain energy absorbed by helmet components. Under the frontal impact (Figure 4.2a), the helmet shell absorbed the highest amount of energy (46.66%), followed by the frontal foam (36.73%), the foams on the top (2.13% and 1.95%, respectively) and the foams on the side (1.76% and 1.15%, respectively). These foams were close to the sites that the impactor touched the helmet. Under the frontal boss impact (Figure 4.2b), shell element absorbed 58.44% strain energy, followed by the frontal foam (36.60%), and other foams closed to the impact sites (2.47%, 2.03%, and 1.88%, respectively). Under the lateral impact (Figure 4.2c), shell components absorbed 53.49% energy. The foams close to the impact site absorbed the strain energy of 17.23%, 12.14%, 2.72% and 1.24%, respectively. Under the rear boss impact (Figure 4.2d), shell absorbed 54.50% of energy, followed by foams closed to the impact site (25.97%, 3.67%, and 3.02%, respectively). Under the rear impact (Figure 4.2e), shell absorbed 44.89% of energy, followed by the foams closed to the impact site (16.04%, 13.04%, 3.33%, 3.31%, 2.89%, 2.86%, 2.77%, 2.58%, and 2.48%, respectively).
Figure 4.2: Helmet strain energy distribution. Helmet strain energy distribution under (a) frontal impact, (b) frontal boss impact, (c) lateral impact, (d) rear boss impact, and (e) rear impact.

4.3.1 Brain strain responses of different impact conditions

We demonstrated the brain strain responses, including CSDM15, 95th percentile MPS, and the average MPS, from FE simulations. Under the frontal impact (Figure 4.3a), CSDM15, 95th percentile MPS, and average MPS of the head without the helmet were 0.28, 0.21 and 0.12, respectively. When the helmet was included, such results decreased to 0.11, 0.17 and 0.09, respectively, with the reduction of 60.97%, 21.47%, and 23.63%, respectively. Under the frontal boss impact (Figure 4.3b), CSDM15, 95th percentile MPS, and average MPS of the head without the helmet were 0.56, 0.31 and 0.17, respectively, while it reduced to 0.32, 0.23, and 0.13 when helmet was applied, with the reduction of 43.57%, 27.43%, and 25.57%, respectively. Under the lateral impact (Figure 4.3c), when helmet was included, CSDM15 reduced from 0.73 (without helmet) to 0.24 by 66.89%, 95th percentile MPS decreased from 0.43 (without helmet) to 0.22 by 48.68%, and average MPS reduced from 0.23 (without helmet) to 0.12 by 49.05%. Under the rear boss impact (Figure 4.3d), CSDM15, 95th percentile MPS, and average MPS of the head without the helmet were 0.63, 0.34 and 0.18, respectively, while it reduced to 0.42, 0.27, and 0.14 when helmet was
considered, with the reduction of 33.22%, 18.87%, and 22.78%, respectively. Under the rear impact (Figure 4.3e), helmet reduced the CSDM15, 95th percentile MPS, and average MPS from 0.41 to 0.09 (77.82%), 0.26 to 0.16 (36.55%), and 0.14 to 0.08 (39.96%), respectively.

Figure 4.3: Brain strain response. Strain responses under (a) frontal impact, (b) frontal boss impact, (c) lateral impact, (d) rear boss impact, and (e) rear impact.

4.3.2 Head kinematics-based responses

The head kinematics-based injury metrics results were presented in Table 4.1. Under the frontal impact, being compared with the bare head impact, the helmet reduced peak linear
acceleration from 106.1 g to 99.24g, with the reduction of 6.51%. The helmet reduced HIC15 values from 186.31 to 152.44 by 18.18%. The BrIC and Damage values were reduced from 0.51 to 0.49, with the reduction of 3.03%, and 0.24 to 0.17, with the reduction of 30.79%, respectively. Under the front boss impact, helmet reduced peak linear acceleration from 132.56g to 76.63g by 42%, HIC15 from 208.10 to 124.50 by 40.17%, and Damage from 0.25 50 0.18 by 26.67%, while it slightly increased BrIC from 0.63 to 0.67 by 6.57%. Under the lateral impact, helmet reduced peak linear acceleration from 113.13g to 96.40g by 14.79%, HIC15 from 217.49 to 139.69 by 35.77%, BrIC from 0.72 to 0.58 by 18.85%, and Damage from 0.35 to 0.31 by 8.76%. Under the rear boss impact, helmet reduced peak linear acceleration from 120.59g to 77.07g by 36.09%, HIC15 from 198.35 to 141.64 by 28.59%, BrIC from 0.66 to 0.60 by 9.09%, and Damage from 0.28 to 0.25 by 10.71%. Under the rear impact, helmet reduced peak linear acceleration from 130.13g to 78.45g by 39.71%, HIC15 from 229.67 to 166.55 by 27.48%, and BrIC from 0.56 to 0.48 by 15.69%. Helmet increased Damage from 0.27 to 0.33 by 21.52%.

Table 4.1: Head injury metrics under impacts.

<table>
<thead>
<tr>
<th>Impacts</th>
<th>Head Injury Criteria</th>
<th>With Helmet</th>
<th>Without Helmet</th>
<th>Reduction by Helmet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal Impact</td>
<td>Peak linear Acceleration(g)</td>
<td>99.24</td>
<td>106.14</td>
<td>6.51%</td>
</tr>
<tr>
<td></td>
<td>HIC15</td>
<td>152.44</td>
<td>186.31</td>
<td>18.18%</td>
</tr>
<tr>
<td></td>
<td>BrIC</td>
<td>0.49</td>
<td>0.51</td>
<td>3.03%</td>
</tr>
<tr>
<td></td>
<td>Damage</td>
<td>0.17</td>
<td>0.24</td>
<td>30.79%</td>
</tr>
<tr>
<td>Frontal Boss Impact</td>
<td>Peak linear Acceleration(g)</td>
<td>76.63</td>
<td>132.56</td>
<td>42.19%</td>
</tr>
<tr>
<td></td>
<td>HIC15</td>
<td>124.50</td>
<td>208.10</td>
<td>40.17%</td>
</tr>
<tr>
<td></td>
<td>BrIC</td>
<td>0.67</td>
<td>0.63</td>
<td>-6.57%</td>
</tr>
<tr>
<td></td>
<td>Damage</td>
<td>0.18</td>
<td>0.25</td>
<td>26.67%</td>
</tr>
<tr>
<td>Lateral Impact</td>
<td>Peak linear Acceleration(g)</td>
<td>96.40</td>
<td>113.13</td>
<td>14.79%</td>
</tr>
<tr>
<td></td>
<td>HIC15</td>
<td>139.69</td>
<td>217.49</td>
<td>35.77%</td>
</tr>
<tr>
<td></td>
<td>BrIC</td>
<td>0.58</td>
<td>0.72</td>
<td>18.85%</td>
</tr>
<tr>
<td></td>
<td>Damage</td>
<td>0.31</td>
<td>0.34</td>
<td>8.76%</td>
</tr>
<tr>
<td>Rear Boss Impact</td>
<td>Peak linear Acceleration(g)</td>
<td>77.07</td>
<td>120.59</td>
<td>36.09%</td>
</tr>
<tr>
<td></td>
<td>HIC15</td>
<td>141.64</td>
<td>198.35</td>
<td>28.59%</td>
</tr>
<tr>
<td></td>
<td>BrIC</td>
<td>0.60</td>
<td>0.66</td>
<td>9.09%</td>
</tr>
<tr>
<td></td>
<td>Damage</td>
<td>0.25</td>
<td>0.28</td>
<td>10.71%</td>
</tr>
</tbody>
</table>
Rear Impact | Peak linear Acceleration(g) | 78.45 | 130.13 | 39.71%
| HIC15 | 166.55 | 229.67 | 27.48%
| BrIC | 0.48 | 0.56 | 15.69%
| Damage | 0.33 | 0.27 | -21.52%

### 4.3.3 Helmet shell and foam material effect range for optimization

The effect of helmet shell and foam on CSDM, 95th percentile MPS, average MPS and peak linear acceleration was initially investigated using the shell and foam material properties that increased to 0.5, 1, and 1.5 times (Figure 4.4).
Figure 4.4: Helmet shell material effect. (a) CSDM 10 under impact velocity of 3 m/s; (b) CSDM 15 under impact velocity of 6 m/s; (c) 95th percentile MPS under impact velocity of 3 m/s; (e) 95th percentile MPS under impact velocity of 6 m/s; (f) Average MPS under impact velocity of 3 m/s; (f) Average MPS under impact velocity of 6 m/s; (g) Peak linear acceleration under impact velocity of 3 m/s; (h) Peak linear acceleration under impact velocity of 6 m/s.
In general, the brain strain responses both experienced increasing and decreasing trend when shell stiffness increased to 0.5 to 1.5 times under the velocity of 3 m/s and 6 m/s. Under the impact velocity of 3 m/s, CSDM10 (Figure 4.4a), 95th percentile MPS (Figure 4.4c) and average MPS (Figure 4.4e) increased when helmet shell stiffness increased from 0.5 to 1 times. The results reduced slightly when shell stiffness increase to 1.5 times (Figure 4.4a, c, and e). Peak linear acceleration increased when shell stiffness increased from 0. to 1.5 times (Figure 4.4g). Under the impact velocity of 6 m/s, CSDM15 (Figure 4.4b), 95th percentile MPS (Figure 4.4d) and average MPS (Figure 4.4f) decreased when shell stiffness increased from 0.5 to 1 times. The results increased slightly when shell stiffness changed from 1 to 1.5 times. Peak linear acceleration increased as shell stiffness increased (Figure 4.4h).

The brain strain responses reached to the lowest when helmet foam stiffness was increased to 3 and 4 times under the impact velocity of 3 m/s (Figure 4.5a, c, and e) and 6 m/s (Figure 4.5b, d, and f). Under the impact velocity of 3 m/s, CSDM10 (Figure 4.5a), 95th percentile MPS (Figure 4.5c), and average MPS (Figure 4.5e) decreased significantly when foam stiffness increased from 0.5 to 2 times and reached to the lowest when stiffness increased to 3 times. The strain results then rebound with foam stiffness increased from 4 to 7 times. Peak linear acceleration increased when helmet foam stiffness increased from 1 to 7 times (Figure 4.5g). Under the impact velocity of 6 m/s, CSDM15 (Figure 4.5b), 95th percentile MPS (Figure 4.5d), and average MPS (Figure 4.5f) significantly decreased when foam stiffness increased from 0.5 to 2 times and reached to the lowest when stiffness increased to 5 times. The strain results then rebound when foam stiffness increased from 6 to 7 times. Peak linear acceleration increased when helmet foam stiffness increased from 1 to 7 times (Figure 4.5h).
Figure 4.5: Helmet foam effect. (a) CSDM 10 under impact velocity of 3 m/s; (b) CSDM 15 under impact velocity of 6 m/s; (c) 95th percentile MPS under impact velocity of 3 m/s; (e) 95th percentile MPS under impact velocity of 6 m/s; (f) Average MPS under impact velocity of 3 m/s; (f) Average MPS under impact velocity of 6 m/s; (g) Peak linear acceleration under impact velocity of 3 m/s; (h) Peak linear acceleration under impact velocity of 6 m/s.
4.3.4 Helmet foam and shell factorial and main effect analysis

From factorial analysis, the helmet foam stiffness played the most important role in CSDM results, 95th percentile MPS, and average MPS under the impact velocity of 3 m/s and 6 m/s (Figure 4.6, Figure 4.7, and Figure 4.8). Under the impact velocity of 3 m/s, the helmet foam stiffness played the most important role in CSDM10 (Figure 4.6a), 95th percentile MPS (Figure 4.7a), and average MPS (Figure 4.8a), followed by the interaction effect of helmet foam and shell stiffness, and helmet shell stiffness. Under the impact velocity of 6 m/s, the helmet foam stiffness played the most important role in CSDM15 (Figure 4.6b), 95th percentile MPS (Figure 4.7b), and average MPS (Figure 4.8b), followed by helmet shell stiffness and the interaction effect of helmet foam and shell stiffness.

Figure 4.6: Factorial analysis based on CSDM. Factorial analysis based on CSDM under (a) impact velocity of 3 m/s; (b) impact velocity of 6 m/s.
Figure 4.7: Factorial analysis based on 95th percentile MPS. Factorial analysis based on 95th MPS under (a) impact velocity of 3 m/s; (b) impact velocity of 6 m/s.

Figure 4.8: Factorial analysis based on average MPS. Factorial analysis based on average MPS under (a) impact velocity of 3 m/s; (b) impact velocity of 6 m/s.

In the ANOVA main effect analysis, the helmet shell stiffness was increased to five levels (0.5, 0.75, 1, 1.25, and 1.5 times) and helmet foam stiffness was increased to six levels.
(0.5, 1, 1.5, 2, 2.5, and 3 times). Under the impact velocity of 3 m/s, the helmet shell stiffness increased to 1.25 times had the highest CSDM10 mean (0.134) (Figure 4.9a). The shell stiffness increased to 0.75 times had the highest 95th percentile MPS mean (0.121) (Figure 4.10a) and average MPS mean (0.06) (Figure 4.11a). The shell stiffness increased to 1.5 times had the lowest CSDM10 mean (0.099) (Figure 4.9a), 95th percentile MPS mean (0.113) (Figure 4.10a), and average MPS mean (0.06) (Figure 4.11a). The helmet foam stiffness increased to 0.5 times had the highest CSDM10 mean (0.196) (Figure 4.9a), 95th percentile MPS mean (0.135) (Figure 4.10a), and average MPS mean (0.070) (Figure 4.11a). The helmet foam stiffness increased to 2.5 times had the lowest CSDM10 mean (0.070) (Figure 4.9a) and lowest 95th percentile MPS mean (0.106) (Figure 4.10a). The helmet foam stiffness increased to 3 times had the lowest average MPS mean (0.058) (Figure 4.11a).

Under the impact velocity of 6 m/s, the shell stiffness stiffness increased to 0.75 times has the highest CSDM15 mean (0.305) (Figure 4.9b) and average MPS mean (0.128) (Figure 4.11b). The helmet shell stiffness increased to 0.5 times stiffer had the highest 95th percentile mean (0.230) (Figure 4.10b). The shell stiffness increased to 1.25 times had the lowest CSDM15 mean (0.252) (Figure 4.9b), 95th percentile MPS mean (0.211) (Figure 4.10b), and average MPS mean (0.122) (Figure 4.11b). The helmet foam stiffness increased to 0.5 times had the highest CSDM15 mean (0.357) (Figure 4.9b), 95th percentile MPS mean (0.247) (Figure 4.10b), and average MPS mean (0.135) (Figure 4.11b). The helmet foam stiffness increased to 3 times had the lowest CSDM15 mean (0.216) (Figure 4.9b) and lowest 95th percentile MPS mean (0.200) (Figure 7b), and average MPS mean (0.0118) (Figure 4.11b).
Figure 4.9: Main effect analysis based on CSDM. Main effect analysis based on CSDM under (a) impact velocity of 3 m/s; (b) impact velocity of 6 m/s.

Figure 4.10: Main effect analysis based on 95th percentile MPS. Main effect analysis based on 95th percentile MPS under (a) impact velocity of 3 m/s; (b) impact velocity of 6 m/s.
4.3.5 The brain strain-affected connections affected by helmet

The brain strain-affected connections were investigated based on the brain model segmented into 100 functional regions (Figure 4.12). Under the impact velocity of 3 m/s, there were 4830 connections linking the brain functional regions above 95th percentile MPS above 0.12 under the impact to the bare head. When the helmet with shell stiffness increased to 1.5 times and foam stiffness increased to 3 times based on the main effect analysis was applied, the number of strain-affected connections reduced to 1122. Under the impact velocity of 6 m/s, there were 4872 strain-affected connections under the impact to the bare head above the 95th percentile MPS threshold of 0.22, when helmet with shell stiffness increased to 1.25 times and foam stiffness increased to 3 times, the number of strain connections reduced to 1869. Overall, optimized helmets demonstrated significant benefit in reducing strain-affected connections, hence reducing the risk of brain damage such as working memory damage.
Figure 4.12: Brain strain-affected connections. (a) Strain-affected connections of bare head under impact velocity of 3 m/s; (b) Strain-affected connections of head with helmet optimized by increasing shell stiffness to 1.25 times and foam stiffness to 3 times head under impact velocity of 3 m/s; (c) Strain-affected connections of bare head under impact velocity of 6 m/s; (d) Strain-affected connections of head with helmet optimized by increasing shell stiffness to 1.25 times and foam stiffness to 3 times head under impact velocity of 6 m/s;

4.4 Discussion

4.4.1 Strain energy absorbed by helmet components

Across frontal impacts, frontal boss impact, lateral impact, rear boss impact, and rear impact, we found that helmet outer shell absorbed highest amount of energy, around half of the total energy absorbed by helmet, followed by helmet foams close to the impact site (Figure 4.1). Based on the Xenith X2E helmet model, Corrales et al. (2020) also reported that helmet shell absorbed highest amount of strain energy [197]. Since elastic material was used in the helmet outer shell and Fu-Chang foam material was in the foams of the
helmet model, the strain energy absorption was related to the relative deformation. From
time history of helmet dimension and thickness of foams close impact site, deformation of
helmet shell and foams were observed among five impacts. For example, under the frontal
boss impact, the helmet length (Figure 4.13a) experienced the largest compression of 1.9
mm within first 10 ms, the time slot when the impactor touched the helmet. However, the
helmet width (Figure 4.13b) did not have obvious deformation initially, which indicates
that the helmet shell tried to hold the impactor and absorbed impact energy. The largest
compression percentages of the foams close to the impact site were 31.25% (Figure 4.13c),
21.72% (Figure 4.13d), 18.73% (Figure 4.13e), and 17.89 (Figure 4.13f), respectively,
falling under the energy absorption area defined by Fu-Chang material.
Figure 4.13: Helmet dimension and foam thickness time history under frontal boss impact. Time history of (a) helmet shell length; (b) helmet shell width; (c) foam 1 thickness; (d) foam 5 thickness; (e) foam 6 thickness; (f) foam 7 thickness.

4.4.2 Brain strain and head kinematics-based responses

Helmet reduced both brain strain and head injury criteria values. We found that the effectiveness of helmet in strain reduction varied by different impacts due to different strain values of different impact locations. Researchers also reported that the strain responses varied with different impact locations [68, 212]. Under the frontal and rear impact, we found that the helmet reduced 95th percentile MPS values from 0.21 to 0.17 by 21.47% and 0.26 to 0.16 by 36.55%, respectively. Bruneau and Cronin (2021) reported the 95th percentile MPS of 0.32 and 0.37 under the frontal and rear impacts, respectively, with the
impact speed of 5.5 m/s [213]. The strain difference could be attributed to the helmet difference, as Ghazi et al. (2022) reported that the effectiveness of different helmets were different [198]. We also found the peak linear acceleration of 99.24g under frontal impact, 76.63g under frontal boss impact, 96.40g under lateral impact, 77.07g under rear boss impact, and 78.45g under rear impact (Table 1). Newman et al. reconstructed the football impacts with concussion and reported the lowest peak linear acceleration of 52.09g (511m/s²) under the impact velocity of 5.5 m/s and highest peak linear acceleration of 134.25 g (1317m/s²) under the impact velocity of 10.3 m/s [61]. Campolettano et al. (2020) reported the concussive threshold of 102.5 ± 32.7 g for adults [214]. Greenwald et al. (2008) reported the peak linear acceleration of 98.9 g for 75% possibility of concussion [215]. In our study, helmet decreased peak linear acceleration by 36.09% and 39.71% under rear boss and rear impact, respectively (Table 1). Lewis et al. (2001) reported the head peak linear acceleration reduction of above 30% by football helmet [216]. The HIC15 value of five impacts with helmet in this study ranged from 124.5 to 166.55 (Table 1). Zhang et al. (2004) reported HIC15 values for 25%, 50%, and 80% of probability of mTBI were 151, 240, and 369, respectively [217]. Among helmeted impacts, we found BrIC values of 0.58 under lateral impact and 0.60 under rear boss impact, and 0.48 under rear impact (Table 1). Elkin et al. tested the Riddell Revolution Speed helmets under the impact velocity of 5.5 m/s and reported the BrIC values of 0.44 under side impact and 0.47 under rear impact [68].

We plotted the time history of helmet energy absorption, shell energy absorption, resultant rotational velocity, resultant linear acceleration, resultant rotational acceleration, and strain among five impacts. For example, under the frontal boss impact, helmet energy absorption process mainly occurred within the first 10ms (Figure 4.14a, b). The peak value of head linear acceleration and acceleration decreased (Figure 4.14d, e) within first 10ms, which corresponds to the time when helmet absorbed the impact energy. From the helmet strain
time history (Figure 4.14f), helmet reduced the brain strain. The head energy absorption and kinematics time histories of other impacts can be found in Appendix B.

Figure 4.14: Helmet energy absorption and head kinematics time history under frontal boss impact. Time history of (a) strain energy absorbed by helmet, (b) strain energy absorbed by helmet, (c) resultant rotational velocity, (d) resultant linear acceleration, (e) resultant rotational acceleration, and (f) brain average MPS.
4.4.3 Helmet shell and foam factorial and main effect analysis

From factorial and main effect analysis, we found the helmet foam was the most important factor that affected brain strain responses under the impact velocity of 3 m/s and 6 m/s, followed by the interaction effect of shell and foam stiffness and shell stiffness under impact velocity of 3 m/s, and by shell stiffness and the interaction effect of shell and foam stiffness under the impact velocity of 6 m/s. Although peak energy absorbed by helmet outer shell occupied nearly 50%, the role of foam cannot be ignored. Foster et al. (2018) found that auxetic foam could reduce the head response by up to 44% [218]. Vanden Bosche et al. (2017) reported that using anisotropic polyethersulfone foam for bicycle helmet can have the reductions in peak rotational acceleration and peak linear acceleration of 40% and 37%, respectively [219].

Under impact velocity of 3 m/s, we found the peak linear acceleration has a large increased of 17.17% when foam stiffness was increased from 1 to 3 times (Figure 4.5g). Slight increase of 9.28% was found when foam was increased from 3 to 7 times. Under the impact velocity of 6 m/s, we found large increase when foam stiffness was increased from 1 to 3 times, by 16.53%, and slight increase by 8.22% when foam stiffness was increased from 3 to 7 times (Figure 4.5h). Millers et al. (2021) found that different magnitudes of helmet foam material properties didn’t change the peak linear acceleration obviously, while the impact speed affected the peak linear acceleration dominantly [200]. We also found that under the same foam stiffness, impact velocity changed peak linear acceleration obviously. For example, the peak linear acceleration was 64.06g and 97.32g under the impact velocity of 3m/s and 6m/s, respectively when foam stiffness was increased to 7 times (Figure 4.5g, h).

With ANOVA main effect analysis, we found that the effects of different helmet shell and foam stiffness on brain strain responses were different. Under the impact velocity of 3 m/s, we found the shell stiffness increased to 1.5 times and foam stiffness increased to the 2.5-3 times induced lowest strain, respectively. Under the impact velocity of 6 m/s, We found shell stiffness increased to 1.25 times and foam stiffness increased to 3 times produced
lowest strain responses individually. Using the statistical analysis, we can have the better understanding about the helmet optimization.

4.4.4 The brain strain-affected connections affected by helmet

The brain strain-affected connections, which link brain functional regions above the strain threshold, were largely reduced by helmet with the foam and shell material optimized by main effect analysis. Under the impact velocity of 3 m/s and 6 m/s, being compared to the impact to the bare head, the number of strain-affected connections were largely reduced from 4830 to 1122 and 4872 to 1869 respectively (Figure 4.14). This results indicated that the helmet could reduce number of brain functional regions with high strain.

4.5 Conclusions

This study comprehensively investigated the effect of the helmet on the head kinematic and brain strain responses. We found that peak head linear acceleration, HIC15, BrIC, DAMAGE, and brain strain responses were largely reduced by helmet. The helmet outer shell absorbed the highest amount of peak energy, approximately 50%, followed by foams close to the impact site. By using the statistical analysis, we found that the helmet foam played an important role in brain strain responses. Through ANOVA main effect analysis, we found that the helmet shell stiffness increased to 1.25-1.5 times and foam stiffness increased to 3 times produced the lowest strain responses. The helmet also reduced the brain strain-affected connections.
Chapter 5

5  Understanding the effect of brain skull change due to repeated mTBI on head responses

The rat skull thickness change was observed during the repeated mTBI experiments in the laboratory. However, how the change of skull thickness affected the brain strain responses, head kinematics, and functional connections were unknown. In this study, we investigated the effect of skull thickness on brain strain responses, head kinematics, and brain strain-affected connections. We found that the increased skull thickness could slightly change the brain strain responses and head kinematic responses, but the change was very small. Moreover, the slight effect of skull thickness on brain strain-affected functional connection was observed.

5.1 Introduction

Traumatic brain injury (TBI) occurs when the external force impacts the head [220]. Mild traumatic brain injury (mTBI), which causes 200-300/100,000 hospitalizations per year [6], can cause many symptoms including headache, dizziness, and cognitive difficulties [221]. Although the brain deficits from a single mTBI impact may be transient [222], the brain impairments from repeated mTBI may be chronic [9]. Pearce et al. (2018) reported the retired professional rugby athletes with the history of repeated concussions had longer dexterity and visuomotor reaction time and worse cognitive performance, compared with players with no concussions [11]. Oyegbile et al. (2020) found that the history of concussion could cause longer concussion duration and higher levels of sleep disturbance [10]. Moreover, based on animal studies, researchers found that mTBI could cause ultrastructural changes to the mice brain [223] and deficits in the brain functions [224].

In addition to the effect of repeated mTBI on the brain, researchers are also interested in the skull, which protects the brain under the external impact [115]. McColl et al. (2018) found that mTBI could change the skull’s material properties of adolescent mice by increasing both the skull volume and strength [116]. Dill et al. (2022) found the obvious increase of volume and thickness of interparietal bone 10 weeks after the rats being exposed to repeated mTBI impacts, [113]. Zvejniece et al. reported that the skull fracture
due to TBI could damage the brain and decrease the brain functional outcomes [225]. Ruan and Prasad (2001) demonstrated that the skull deformation was decreased when skull thickness increased because less impact energy would be absorbed by the skull [226]. Lillie et al. (2016) reported that the cortical thickness of skull was influenced by age [227]. Jones et al. (2017) reported that the skull deflection was positively correlated with the brain strain [228].

Understanding the brain and skull responses under mTBI impacts also gained interest in the biomechanical field. Based on head kinematics, head injury metrics including head peak linear acceleration [83, 229], head injury criteria (HIC) [84, 230], peak rotational acceleration [91, 231], and brain injury criteria (BrIC) [85, 232], were analyzed to understand the head injury risk. Using in vitro model, researchers found that the brain strain, which refers to the change of brain tissue deformation, was positively correlated with the brain cell death [93]. Hence, the brain strain, which can be analyzed from finite element (FE) simulations, is widely used to TBI prediction [78, 129, 233, 234]. From the FE analysis, the skull von Mises stresses have also been analyzed by researchers [235].

Although changes in skull thickness and volume due to repeated mTBI were reported by researchers, the biomechanical effects of the changes in skull thickness and density on the head responses remain unknown. This study investigated the effects of skull thickness and density changes on the brain strain and head kinematic responses.

5.2 Method

5.2.1 Skull thickness change

Based on the obvious skull thickness increase of 2*mTBI impacts after 10 weeks reported by Dill et al. (2022) [113], The skull thickness of GHBMC head model was adjusted accordingly. The total area measuring 54.26 mm by 64.62 mm, aligned with the lambda of the skull, was selected for the skull thickness increase. To fill the gap between the head and helmet, the skull thickness was increased by up to 16.57% (Figure 5.1a) based on the skull thickness time history reported by Dill et al. (2022) [113].
Figure 5.1: Skull thickness increase and impact to the helmet. (a) Increased skull thickness; (b) Impact to the head with helmet.

5.2.2 Finite element simulations

A total of eight simulations with two impact speed levels including 3 m/s and 6 m/s were involved in this study (Figure 5.1b). Under each impact speed level, four scenarios were included: the case with no change in skull thickness and density, the case with increased skull thickness but no change in skull density, the case with increased skull thickness and the increase of 10% in skull density, and the case with increased skull thickness but the decrease of 10% in skull density (Table 5.1). The initial velocity of 3 m/s and 6 m/s were applied to the impacter, using LS_DYNA command ‘INITIAL_VELOCITY’ [132] based on the local coordinates created in the impacter. The contact command of LS_DYNA [132] was applied to the impacter and the head model to avoid penetration during the simulation. The total simulation duration of 40 ms was defined. The brain components information of GHBMC model can be found in Appendix A.

<table>
<thead>
<tr>
<th>Impact Conditions</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>No change in skull thickness and density</td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>Only increasing the skull thickness.</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>Increasing skull thickness and increasing skull density by 10%.</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>Increasing skull thickness but decrease skull density by 10%.</td>
</tr>
</tbody>
</table>
5.2.3 Brain strain responses

The 95th percentile MPS and average MPS were obtained from each simulation. The strain response differences were calculated between the baseline case and other three cases, including the case with increased skull thickness but no change in skull density, the case with increased skull thickness and the increase of 10% in skull density, and the case with increased skull thickness but the decrease of 10% in skull density.

5.2.4 Head kinematics-based responses

The head kinematics-based responses, including peak linear acceleration, HIC15, BrIC, DAMAGE, and peak rotational velocity, were calculated from each simulation. The kinematics-based responses differences were calculated between the baseline case and other three cases, including the case with skull thickness increase but no change in skull density, the case with skull thickness increase and skull density increase by 10%, and the case with skull thickness increase but skull density decrease by 10%.

5.2.5 Brain strain-affected connections

Using the brain FE model segmented into 100 functional regions based on the pipeline developed in Chapter 2, the brain strain-affected connections, which connected two brain functional regions where at least one functional region exceeding the strain threshold, were investigated in this study. We analyzed the brain strain-affected connections of the impact to model with unchanged skull thickness and increased thickness.

5.3 Results

5.3.1 Brain strain responses

The 95th percentile MPS and average MPS results were obtained under the impact velocity of 3 m/s and 6 m/s (Table 5.2). Under the impact velocity of 3 m/s, the 95th percentile MPS was 0.1061 when skull thickness and density were not changed. When skull thickness increased without the change in density, 95th percentile MPS decreased to 0.0997, by 6.06%. When skull thickness was increased, and density increased by 10%, 95th percentile MPS decreased to 0.1018, by 4.08%. When skull thickness was increased, but the density was decreased by 10%, 95th percentile MPS decreased to 0.1019, by 3.96%. Under the
impact velocity of 6 m/s, 95th percentile MPS was 0.2531 when both the skull thickness and density were not changed. When skull thickness was increased without the change in density, 95th percentile MPS decreased to 0.2504, by 1.05%. When skull thickness was increased, and density was increased by 10%, 95th percentile MPS increased to 0.2571, by 1.61%. When skull thickness was increased, but the density decreased by 10%, 95th percentile MPS decreased to 0.2490, by 1.62%.

Table 5.2: 95th percentile MPS of the brain during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>95th Percentile MPS</th>
<th>Difference</th>
<th>95th Percentile MPS</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 m/s</td>
<td>6 m/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.1061</td>
<td>0.2531</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>0.0997</td>
<td>-6.06%</td>
<td>0.2504</td>
<td>-1.05%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>0.1018</td>
<td>-4.08%</td>
<td>0.2571</td>
<td>1.61%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>0.1019</td>
<td>-3.96%</td>
<td>0.2490</td>
<td>-1.62%</td>
</tr>
</tbody>
</table>

Under the impact velocity of 3 m/s (Table 5.3), the average MPS was 0.0531 when both the skull thickness and density were unchanged. When skull thickness was increased without the change in density, average MPS decreased to 0.0501, by 5.66%. When skull thickness was increased, and density was increased by 10%, average MPS decreased to 0.0509, by 4.16%. When skull thickness was increased, but the density decreased by 10%, average MPS decreased to 0.0510, by 3.97%. Under the impact velocity of 6 m/s (Table 5.3), average MPS was 0.1320 when both the skull thickness and density were unchanged. When skull thickness was increased without the change in density change, average MPS
decreased to 0.1309, by 0.86%. When skull thickness was increased, and density was increased by 10%, average MPS increased to 0.1344, by 1.81%. When skull thickness was increased, but the density was decreased by 10%, 95th percentile MPS decreased to 0.1301, by 1.47%.

Table 5.3: Average MPS of the brain during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>Average MPS</th>
<th>Difference</th>
<th>Average MPS</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 m/s</td>
<td>6 m/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.0531</td>
<td>0.1320</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>0.0501</td>
<td>-5.66%</td>
<td>0.1309</td>
<td>-0.86%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>0.0509</td>
<td>-4.16%</td>
<td>0.1344</td>
<td>1.81%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>0.0510</td>
<td>-3.97%</td>
<td>0.1301</td>
<td>-1.47%</td>
</tr>
</tbody>
</table>

5.3.2 Head kinematics-based responses

Under the impact velocity of 3 m/s (Table 5.4), the head peak linear acceleration was 37.676g when both the skull thickness and density were unchanged. Head peak linear acceleration reduced to 37.391g, by 0.76%, when skull thickness increased, but without the change in density. Peak linear acceleration decreased to 36.876g, by 2.12%, when skull thickness was increased, and density was increased by 10%. Peak linear acceleration increased to 38.199g, by 1.39%, when skull thickness was increased, but density was reduced by 10%. Under the impact velocity of 6 m/s (Table 5.4), peak linear acceleration was 82.501g when both the skull thickness and density were unchanged. When skull thickness was increased, but without the change in density, peak linear acceleration decreased to 82.317g, by 0.22%. When skull thickness was increased, and density was increased by 10%, peak linear acceleration increased to 83.758g, by 1.52%. When skull
thickness was increased, but the density was decreased by 10%, peak linear acceleration decreased to 81.769g, by 0.89%.

Table 5.4: Peak linear acceleration of the head during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>Peak Linear Acceleration (g)</th>
<th>Difference</th>
<th>Peak Linear Acceleration (g)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 m/s</td>
<td>6 m/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>37.676</td>
<td>82.501</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>37.391</td>
<td>-0.76%</td>
<td>82.317</td>
<td>-0.22%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>36.876</td>
<td>-2.12%</td>
<td>83.758</td>
<td>1.52%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>38.199</td>
<td>1.39%</td>
<td>81.769</td>
<td>-0.89%</td>
</tr>
</tbody>
</table>

Under the impact velocity of 3 m/s (Table 5.5), HIC15 was 30.156 when both the skull thickness and density were unchanged. HIC15 increased to 30.235, by 0.26%, when skull thickness increased but without the change in density. HIC15 decreased to 29.670, by 1.61%, when skull thickness was increased, and density was increased by 10%. HIC15 increased to 30.661, by 1.39%, when skull thickness was increased but density was reduced by 10%. Under the impact velocity of 6 m/s (Table 5.5), HIC15 was 152.318 when both the skull thickness and density were unchanged. When skull thickness was increased without the change in density, HIC15 decreased to 152.216, by 0.07%. When skull thickness was increased, and density was increased by 10%, HIC15 was increased to 154.864, by 1.67%. When skull thickness was increased, but density was decreased by 10%, HIC15 decreased to 150.409, by 1.25%.
Table 5.5: HIC15 of the brain during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>HIC15 3 m/s</th>
<th>Difference</th>
<th>HIC15 6 m/s</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>30.156</td>
<td></td>
<td>152.318</td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>30.235</td>
<td>0.26%</td>
<td>152.216</td>
<td>-0.07%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>29.670</td>
<td>-1.61%</td>
<td>154.864</td>
<td>1.67%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>30.661</td>
<td>1.67%</td>
<td>150.409</td>
<td>-1.25%</td>
</tr>
</tbody>
</table>

Under the impact velocity of 3 m/s (Table 5.6), peak rotational velocity was 18.32 rad/s when both the skull thickness and density were unchanged. Peak rotational velocity decreased to 17.72 rad/s, by 3.26% when skull thickness was increased without the change in density. Peak rotational velocity decreased to 17.92 rad/s, by 2.17%, when skull thickness was increased, and density was increased by 10%. Peak rotational velocity decreased to 18.12 rad/s, by 1.08%, when skull thickness was increased, but density was reduced by 10%. Under the impact velocity of 6 m/s (Table 5.6), peak rotational velocity was 37.34 rad/s when both the skull thickness and density were unchanged. When skull thickness was increased without the change in density, peak rotational velocity decreased to 37.04 rad/s, by 0.80%. When skull thickness was increased, and density was increased by 10%, peak rotational velocity increased to 37.86 rad/s, by 1.39%. When skull thickness was increased, but the density was decreased by 10%, peak rotational velocity decreased to 37.05 rad/s, by 0.78%.
Table 5.6: Peak rotational velocity of the brain during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>Peak Rotational Velocity (rad/s)</th>
<th>Difference</th>
<th>Peak Rotational Velocity (rad/s)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3m/s</td>
<td>6 m/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>18.32</td>
<td>37.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>17.72</td>
<td>-3.26%</td>
<td>37.04</td>
<td>-0.80%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>17.92</td>
<td>-2.17%</td>
<td>37.86</td>
<td>1.39%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>18.12</td>
<td>-1.08%</td>
<td>37.05</td>
<td>-0.78%</td>
</tr>
</tbody>
</table>

Under the impact velocity of 3 m/s (Table 5.7), BrIC was 0.325 when both the skull thickness and density were unchanged. BrIC decreased to 0.314, by 3.26%, when skull thickness was increased without the change in density. BrIC decreased to 0.318, by 2.16%, when skull thickness was increased, and density was increased by 10%. BrIC decreased to 0.321 by 1.08% when skull thickness was increased but density was reduced by 10%. Under the impact velocity of 6 m/s (Table 5.7), BrIC was 0.663 when both the skull thickness and density were unchanged. When skull thickness was increased without the change in density, BrIC decreased to 0.658, by 0.78%. When skull thickness was increased, and density was increased by 10%, BrIC increased to 0.671, by 1.32%. When skull thickness was increased, but the density was decreased by 10%, BrIC decreased to 0.657, by 0.79%.
Table 5.7: BrIC of the brain during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>BrIC 3 m/s</th>
<th>Difference 3 m/s</th>
<th>BrIC 6 m/s</th>
<th>Difference 6 m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.325</td>
<td></td>
<td>0.663</td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>0.314</td>
<td>-3.26%</td>
<td>0.658</td>
<td>-0.78%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>0.318</td>
<td>-2.16%</td>
<td>0.671</td>
<td>1.32%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>0.321</td>
<td>-1.08%</td>
<td>0.657</td>
<td>-0.79%</td>
</tr>
</tbody>
</table>

Under the impact velocity of 3 m/s (Table 5.8), DAMAGE was 0.1082 when both the skull thickness and density were not changed. DAMAGE decreased to 0.1010, by 6.65% when skull thickness was increased without the change in density. DAMAGE decreased to 0.1031, by 4.71%, when skull thickness was increased, and density increased by 10%. DAMAGE decreased to 0.1025, by 5.27%, when skull thickness was increased but density reduced by 10%. Under the impact velocity of 6 m/s (Table 5.8), DAMAGE was 0.2801 when both the skull thickness and density were unchanged. When skull thickness was increased without the change in density, DAMAGE decreased to 0.2770, by 1.10%. When skull thickness was increased, and density was increased by 10%, DAMAGE increased to 0.2870, by 2.46%. When skull thickness was increased, but the density decreased by 10%, DAMAGE decreased to 0.2743, by 2.08%.
Table 5.8: DAMAGE of the brain during impacts to the head with helmet.

<table>
<thead>
<tr>
<th>Case</th>
<th>DAMAGE 3 m/s</th>
<th>Difference 3 m/s</th>
<th>DAMAGE 6 m/s</th>
<th>Difference 6 m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.1082</td>
<td></td>
<td>0.2801</td>
<td></td>
</tr>
<tr>
<td>Increased Skull Thickness + No Change in Skull Density</td>
<td>0.1010</td>
<td>-6.65%</td>
<td>0.2770</td>
<td>-1.10%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Increase of 10% in Skull Density</td>
<td>0.1031</td>
<td>-4.71%</td>
<td>0.2870</td>
<td>2.46%</td>
</tr>
<tr>
<td>Increased Skull Thickness + Decrease of 10% in Skull Density</td>
<td>0.1025</td>
<td>-5.27%</td>
<td>0.2743</td>
<td>-2.08%</td>
</tr>
</tbody>
</table>

5.3.3 Brain strain-affected connections

The brain strain-affected connections were investigated based on the brain model segmented into 100 functional regions (Figure 5.2). Under the impact velocity of 3 m/s, there were 4797 strain-affected connections linking the brain functional regions above 95\textsuperscript{th} percentile MPS above 0.1 of the baseline case that the skull thickness and density were unchanged (Figure 5.2a). When skull thickness was increased, there were 4779 brain strain-affected connections (Figure 5.2b). Under the impact velocity of 6 m/s, there were 4209 strain-affected connections above the 95\textsuperscript{th} percentile MPS threshold of 0.2 under the impact to the model that the skull thickness and density were not changed (Figure 5.2c). When skull thickness was increased, there were 3744 strain-affected connections (Figure 5.2d).
Figure 5.2: Brain strain-affected connections of skull thickness change. (a) Strain-affected connections of head with no change in skull under impact velocity of 3 m/s; (b) Strain-affected connections of head with increase in skull thickness but no change in skull density under impact velocity of 6 m/s; (c) Strain-affected connections of head with no change in skull under impact velocity of 6 m/s; (d) Strain-affected connections of head with increase in skull thickness but no change in skull density under impact velocity of 6 m/s;

5.4 Discussion

5.4.1 Effect of skull change due to repeated mTBI on brain strain responses

In general, the effect of skull thickness and density on the brain strain responses existed but was very small. Increasing the skull thickness decreased the 95th percentile MPS by
6.06% and average MPS by 5.66% under the impact velocity of 3 m/s, and 95th percentile MPS by 1.05% and average MPS by 0.86% under the impact velocity of 6 m/s, respectively. Although being compared with the strain difference under impact velocity of 6 m/s, increased skull thickness caused larger strain difference under the impact velocity of 3 m/s, the strain values under the impact velocity of 3 m/s were low (95th percentile MPS around 0.1 and average MPS around 0.05), hence, the change of low strain values could be high. Jones et al. (2017) reported that the skull deflection due to TBI impact was positively correlated with the brain strain [228].

By changing the skull density together with the increase in skull thickness, the brain strain responses were slightly changed. For example, decreasing the skull density by 10% along with the increase in skull thickness decreased 95th percentile MPS by 3.96% and 1.62% under impact velocity of 3 m/s and 6 m/s, respectively, and average MPS by 3.97% and 1.47% under impact velocity of 3 m/s and 6 m/s, respectively.

5.4.2 Effect of skull change due to repeated mTBI on head kinematics-based responses

The effect of skull thickness and density on head kinematics-based responses was slight. Increasing the skull thickness decreased head linear acceleration by within 1%. For example, the increase in skull thickness reduced head peak linear acceleration by 0.76% under the impact velocity of 3 m/s and 0.22% under the impact velocity of 6 m/s. The HIC15, which was calculated based on linear acceleration time history, also decreased by 0.26% and 0.07% due to increased skull thickness under impact velocity of 3 m/s and 6 m/s, respectively. The peak rotational velocity, BrIC, and DAMAGE experienced larger reduction compared with the linear acceleration due to increase in skull thickness. Increased skull thickness reduced peak rotational velocity by 3.26% and 0.8% under impact velocity of 3 m/s and 6 m/s, respectively. The BrIC values, calculated by peak rotational velocities along x, y, and z axis, were reduced by 3.26% and 0.78% due to increased skull thickness under the impact velocity of 3 m/s and 6 m/s, respectively. The DAMAGE values, which were calculated by rotational acceleration, were decreased by 6.65% and 1.10% due to increased skull thickness under the impact velocity of 3 m/s and 6 m/s,
respectively. Ruan and Prasad reported the increase of the skull thickness affected the head kinematics-based responses [226].

When the change of skull density was applied together with the increased skull thickness, the change in head kinematics-based responses was present but very small. The increased skull thickness together with increased skull density up to 10% reduced the peak linear acceleration by 2.12%, HIC15 by 1.61%, peak rotational velocity by 2.17%, BrIC by 2.16%, and DAMAGE by 4.71% under the impact velocity of 3 m/s. However, a slight increase was found in peak linear acceleration by 1.52%, HIC15 by 1.67%, peak rotational velocity by 1.39%, BrIC by 1.32%, and DAMAGE by 2.46% under the impact velocity of 6 m/s. When increased skull thickness was applied together with decreased skull density up to 10%, the slight increase of 1.39% and 1.67% were found in peak linear acceleration and HIC15 under the impact velocity of 3 m/s, respectively. The small reduction of 1.08%, 1.08%, and 5.27% were found in peak rotational velocity, BrIC, and DAMAGE under the impact velocity of 3 m/s. Under the impact velocity of 6 m/s, the reduction of 0.89%, 1.25%, 0.78%, 0.79%, and 2.08% in peak linear acceleration, HIC15, peak rotational velocity, BrIC, and DAMAGE.

5.4.3 Brain strain-affected connections affected by increased skull thickness

The effect of increased skull on brain strain-affected connection was velocity-dependent. Under the impact velocity of 3 m/s, the brain strain-affected connections were not affected by increased skull thickness, with brain strain-affected 4797 connections in the baseline case and 4779 strain-affected connections in the model with increased skull thickness. However, under the velocity of 6 m/s, the brain strain-affected connections were more notably affected by increased skull thickness, with brain strain-affected 4209 connections in the baseline case and 3774 strain-affected connections in the model with increased skull thickness. Such change may be related to the high strain under the impact speed of 6m/s, as one functional region with high strain may cause strain-affected connections to other 99 regions.
5.5 Conclusions

This study investigated the biomechanical effect of changed skull thickness and skull density due to repeated mTBI impacts. Specifically, variances of brain strain and head kinematics-based responses due to such local skull changes were studied. The effect of repeated-mTBI-related skull changes on head linear accelerations was small with 2%-and-less reduction. The effect of repeated-mTBI-related skull changes on brain rotational kinematics was also small with 7%-and-less reduction. However, the absolute rotational kinematics-based responses changes were less than 0.01. The effect of skull changes on brain strain was impact velocity-dependent, with less than 3% reduction under 6 m/s impact, while reaching up to 6% reduction under 3 m/s impact. However, the absolute changes in brain strain were less than 0.01. The data demonstrated that increased vulnerability of the brain after repeated mTBI was not, at least primarily, due to skull changes, as these changes had small effects on brain strains and in generally reduced brain strains compared with baseline case. Meanwhile, with the number of strain-affected connections reducing from 4209 to 3774, the potential effect on brain functions given small overall brain strain changes could be further investigated.

6 Conclusions, Limitations, Future Work, and Novelty

The conclusions, limitations, future work, and the novelty and impact of the thesis part are described in this chapter.

6.1 Conclusions

Understanding brain dysfunction following a blunt impact remains challenging. This has led to several unique techniques and findings regarding brain functional regions. Using the new model, real-world reconstructed head impact cases, laboratory helmeted impacts, and potential repeated mTBI effects were analyzed.
6.1.1 Developing a pipeline to represent MNI-based brain functional regions for FE modeling

We developed a novel pipeline that can efficiently convert a conventional FE brain model into detailed functional regions based on functional atlas, and demonstrated the development of six detailed brain models. With these brain FE models representing detailed functional regions, the suspectedly damaged functional regions and networks were investigated under three concussive impacts. We also conceptually investigated the effect of the brain strain-affected connections on functional connectivity, including identifying damaged regions that could disrupt brain networks and potential hyperconnectivity and hypoconnectivity as being triggered by high strains. In brief, the pipeline can be used to efficiently convert an existing FE brain model into detailed functional regions, thereby enabling a linkage detailed brain biomechanics to brain functional damage to better understand the fundamental mechanisms causing concussion/mTBI.

6.1.2 Understanding the brain strain effect on working memory among concussion impacts

We investigated the strain responses of 100 functional regions among NFL impacts including both concussive and non-concussive cases. We found common functional regions exceeding concussive threshold among concussive cases. We then investigated the brain strain-affected connections, which we defined as connections between two brain functional regions where at least one region was above the threshold. There were 105 common strain-affected connections among 39 NFL impacts, which means that the connectivity of these connections may be disrupted due to the damaged brain functional regions caused by high strain. We further analyzed the effect of strain on healthy functional connectivity of working memory 1-back tasks. We found that the common high strain regions among concussive impacts could influence 149 functional connections of working memory tasks, which could affect the working memory performance.

6.1.3 Temporal characteristics of shell vs foam strain energy and their effects on brain strain reduction

This study comprehensively investigated the effect of the helmet on the head kinematics and brain strain responses. We found that peak head linear acceleration, HIC15, BrIC,
DAMAGE, and brain strain responses were largely reduced by helmet. The helmet’s outer shell absorbed the highest amount of peak energy, approximately 50%, followed by the foams close to the impact site. Through statistical analysis, we found that the helmet foam played an important role in brain strain responses. Using ANOVA main effect analysis, we can find that the helmet shell stiffness increased to 1.25-1.5 times and foam stiffness increased to 3 times resulted in the lowest strain responses. The helmet also reduced the number of the brain strain-affected connections.

6.1.4 Understanding the effect of brain skull change due to repeated mTBI on head kinematics-based responses

This study investigated the biomechanical effect of changed skull thickness and skull density due to repeated mTBI impacts. Specifically, variances of brain strain and head kinematics-based responses due to such local skull changes were studied. The effect of repeated-mTBI-related skull changes on head linear accelerations was small with 2%-and-less reduction. The effect of repeated-mTBI-related skull changes on brain rotational kinematics was also small with 7%-and-less reduction. However, the absolute rotational kinematics-based responses changes were less than 0.01. The effect of skull changes on brain strain was impact velocity-dependent, with less than 3% reduction under 6 m/s impact, while reaching up to 6% reduction under 3 m/s impact. However, the absolute changes of brain strain was less than 0.01. The data demonstrated that increased vulnerability of the brain after repeated mTBI was not due to skull changes, as these changes had small effects on brain strains and in generally reduced brain strains compared with baseline case. The effect of the change in skull thickness on brain functions was small overall.

6.2 Limitations

6.2.1 Developing a pipeline to efficiently represent MNI-based brain functional regions for FE modeling

Although a pipeline was developed to represent the brain functional regions for the FE model, it lacks a comprehensive, code-based validation process. With a couple of morphing methods, although the shape of the point cloud from the atlas can match the FE model, the
quantitative differences between the brain functional regions of FE model and the atlas were unknown. Therefore, a comprehensive, code-based validation of the geometry, the volume, and the location of each functional region will be helpful. In this study, visual comparison was performed, and randomly selected brain function regions were used to confirm that developed FE brain regions corresponded with imaging data.

In this study, the strain effect in terms of hyperconnectivity and hypoconnectivity was conceptually discussed, but there is a lack of data to further identify the idea. The data should include the functional connectivity datasets of the sample before and after the concussive impact, the concussive symptoms, and the head kinematics of the concussive impact.

In this study, the brain functional regions of brain models with brain elements 8 times and 64 times smaller were demonstrated. However, the brain models with 8 times and 64 times smaller elements (over 1 million brain elements) need long computational time. Therefore, a brain model that can balance the small brain element size and the affordable computational time is needed.

6.2.2 Understanding the brain strain effect on working memory among concussion impacts

Other brain atlases should be included. In this study, the brain FE model was segmented into 100 functional regions, based on the Schaefer atlas, to analyze the strain responses. Ideally, the Schaefer atlas with different number of functional regions, for example, the Schaefer atlas with 400 functional regions, should be included too. Moreover, according to the literature, other brain atlases that were widely used by scientists, like Brodmann atlas and Harvard-Oxford atlas, should be used to segment the brain FE model into functional regions in the future.

Experimental data should be included. While this study analyzed the common brain functional regions with high strain across concussive impacts and their conceptual effect on the functional connectivity of working memory, experimental datasets including the kinematic curves of the concussive cases with working memory deficits are needed.
6.2.3 Temporal characteristics of shell vs foam strain energy and their effects on brain strain reduction

Different helmet models should be included. This study focused on the shell and foam effect based on the Riddell helmet model, which followed the traditional helmet structural design with hard outer shell and softer inner foam. Recently, there were different helmet designs including softer outer shell and more effective energy absorbers, which were not included in this study.

The impact speed of severe mTBI should be included. This study investigated the brain strain responses of helmet impact under speed of 6m/s and the effect of foam and shell on the brain strain responses under the speed of 3m/s. More analysis on high speed, such as 9 m/s, will help to better understand helmet performance and optimization.

6.2.4 Understanding the effect of brain skull change due to repeated mTBI on kinematics-based head responses

The effect of skull density change due to repeated mTBI impacts needs to be further identified. In this study, ±10% of the density was applied to the skull to initially demonstrate the skull density change effect. However, the skull density change should be identified based on the CT scans.

The skull thickness effect is being investigated based on rat FE model. In this study, the skull thickness time history was obtained from the rat study, and skull change in percentage was applied to the human head FE model. To further finalize the skull thickness effect on the brain strain response, demonstrating the skull thickness effect on the rat FE model is necessary.

6.3 Future work

6.3.1 Validation of the brain FE model with functional regions

A comprehensive, coding-based validation process will be applied to the entire brain FE model with functional regions developed by the pipeline. The entire geometry, volume, and the location of each brain function region from FE model will be validated against the atlas developed by the imaging method through in-house developed codes.
6.3.2 Experimental data of concussive impacts

The experimental data of the real-world mTB impacts, including the functional connectivity of the brain before and after the diagnosis of mTBI, the head kinematics of the mTBI impacts, and the mTBI symptoms, will be collected in the future. This data will help to further identify the effect of high strain of brain functional regions associated with specific symptoms, and the hyperconnectivity or the hypoconnectivity caused by high strain. The model developed in this study makes the study of functional brain region responses possible and is expected to be largely applied.

6.3.3 Using the pipeline to represent brain functional regions based on more atlases

The pipeline will be used to represent the brain functional regions of more atlases based on more brain models. Other detailed and widely used atlases, including the Schaefer atlas ith 400 regions, Brodmann atlas, and Hard-Oxford atlas will be applied for the functional region segmentation with the pipeline. Moreover, other brain FE models, like THMUS FE model, will be used for the segmentation process.

6.3.4 Developing a new brain FE model with finer meshes

This study initially found that the brain FE model with smaller meshes could represent the brain functional regions better. Therefore, developing a new brain FE model with smaller meshes but can also balance the computational time, and output results is highly recommended.

6.3.5 Involve more impact cases

In this study, in-field impacts, especially the NFL impacts, were simulated and analyzed. In the future, a border range of impacts, including hockey impacts, soccer impacts, and impacts with loss of consciousness due to TBI, will be simulated. Through a combined experimental and computational approach, a large database linking brain functional region strains to actual brain dysfunctions will be established.
6.3.6 Validation of helmet & head-neck model

The validation of the helmet & head-neck model against head kinematics and brain strain responses will be included. The currently used head-neck model was validated against cadaver data. Validating the head-neck model against volunteer data, including muscle activation, can better help to understand neck effects.

6.3.7 Understand helmet shell & foam effect on brain strain with more helmet models under mTBI impact

Other helmet models, including Vicis helmet model, will be included to investigate the effect of helmet shell and foam effect on the brain strain. Moreover, besides the impact speed of 3 m/s and 6 m/s, the 9 m/s, which may cause severe mTBI, will be applied to the study. Lastly, novel helmet designs will be explored, focusing not just reducing head kinematics, but, more importantly, on preserving brain functional regions.

6.3.8 Identify skull density change under repeated mTBI impacts based on CT scans

The change in skull density under repeated mTBI impacts will be identified based on the CT scans. This will be helpful to further investigate the effect of skull density change due to repeated mTBI impacts on the brain strain. Current data on rodents regarding skull changes after repeated mTBI indicate potential role of the skull, and more experimental data, especially regarding skull density, will be needed.

6.3.9 Understand the skull effect on the brain strain responses based on animal (rat) FE model

In this study, the skull thickness change (in percentage) time history was applied to the human skull. In the future, the skull thickness change data can also be applied to the rat FE model to identify the brain strain change.

6.4 Novelty and impact

This thesis research has provided several novel methods, analyses, and data to advance the active mTBI research field. The brain strain responses under both the in-field and laboratory tests were investigated using a variety of methods including the morphing
method, FE analysis, statistical analysis, brain functional connectivity analysis, MATLAB,
Python, and R programming.

First, a novel pipeline, which can segment the brain FE model into functional regions based
on brain functional atlas up to 1000 functional regions, builds the bridge to understand the
biomechanical responses of brain functional regions. As neuroimaging technology, such as
fMRI method, improves, the brain functional atlas with more detailed brain functional
regions will be developed. This pipeline can be used to investigate the brain biomechanical
responses of such detailed functional regions.

Second, the brain FE models with functional regions enable identifying the dangerous brain
functional regions, which experience high strain, under any type of mTBI impact such as
football impact, hockey impacts, and car crush impacts. Identifying the dangerous brain
functional regions will be helpful to mTBI diagnosis and protection such as helmet
optimization.

Third, this study conceptually explored the effect of brain strain on the brain functional
connectivity changes. Literature studies indicated that change of brain functional
connectivity due to mTBI may be related to mTBI symptoms. However, why brain
functional connectivity changes due to mTBI is unknown because current technologies
cannot get the rapid responses of brain functional regions when mTBI impacts occur.
Under in-vitro experiments, brain strain was found to cause the dysfunction of brain
functional regions due to the neuron cell death. Therefore, we have the assumption that
brain strain could affect functional connectivity of the brain. By identifying the brain strain-
affected connectivity, which refers to damaged connections of every two brain functional
regions caused by high strain, we found that there is the overlap between the brain strain-
affected connections and functional connectivity, indicating the effect of brain strain on
functional connectivity.

Fourth, the circular plot, which is widely used to display functional connectivity, was
applied to the display the brain strain-affected connections. This helps to understand
functional brain regions that are simultaneously affected by physical impacts, while these
regions could be picked up in a fMRI analysis as related. With the circular plot, there is an
opportunity to distinguish brain functional regions that are indeed functionally connected, or just affected together by biomechanical strains during impacts.

Fifth, this study delved into the connection of impacts to potential working memory dysfunction by conducting brain network analysis. Although extensive data will be needed, this study provided a model that makes such an analysis possible and is expected to garner further data, especially with active data collection in the field using wearable sensors and brain dysfunction measures.

Sixth, this study identified the temporal characteristics of brain strain, helmet energy absorption and head kinematics under both helmet and bare head impacts. This will be helpful to helmet design optimization, such as understanding early-stage hard shell energy absorption and later-stage foam energy absorption.

Seventh, this study used factorial and main effect analysis to investigate the effect of helmet outer shell and foam stiffness on the brain strain responses. This will be helpful to helmet design optimization to reduce brain strains.

Eighth, the D-optimum method was applied to reduce the total number of FE simulations from 60 to 40 to investigate the effect of helmet outer shell and foam stiffness on brain strain. This saved approximately 1440 computational hours and is recommended for improving product design efficiency.

Ninth, the brain strain-affected connections of bare head and helmet impacts were analyzed in this study. This method further demonstrated that helmet reduced not only head kinematics, such as peak linear acceleration, but also the number of functional regions and strain connections.

Tenth, this study investigated the effect of skull thickness change due to repeated-mTBI impacts on the brain strain responses. The brain strain-affected connections were also analyzed. This will be helpful to understand the effect of repeated mTBI impacts on the brain.
In brief, these above novel methods and findings not only help readers to develop critical understanding of brain function regions during real-world and laboratory impacts, helmet protective effects and potential repeated-mTBI-relevant skull change effects, but also provide novel and important tools to be combined with extensive data collections in the field to better understand what happens inside the brain during impacts.
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Appendices

Appendix A: Material property of main components of GHBMC model

Appendix Table 1 Material and element types of GHBMC model components [82]

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<thead>
<tr>
<th>Component</th>
<th>Material Type</th>
<th>Element Type</th>
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<tbody>
<tr>
<td>Cerebrum</td>
<td>Viscoelastic</td>
<td>Solid</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>Viscoelastic</td>
<td>Solid</td>
</tr>
<tr>
<td>Thalamus</td>
<td>Viscoelastic</td>
<td>Solid</td>
</tr>
<tr>
<td>Brain Stem</td>
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<td>Solid</td>
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<td>Basal Ganglia</td>
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<tr>
<td>CSF</td>
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<td>Solid</td>
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<td>3rd Ventricle</td>
<td>Viscoelastic</td>
<td>Solid</td>
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<tr>
<td>Corpus Callosum</td>
<td>Viscoelastic</td>
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<tr>
<td>Dura</td>
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<td>Shell</td>
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<td>Shell</td>
</tr>
<tr>
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<td>Shell</td>
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<td>Arachnoid</td>
<td>Elastic</td>
<td>Shell</td>
</tr>
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<td>Inner skull</td>
<td>Linear Elastic Plasticity</td>
<td>Solid</td>
</tr>
<tr>
<td>Outer Skull</td>
<td>Linear Elastic Plasticity</td>
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<tr>
<td>Diploe</td>
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<tr>
<td>Bridging Vein</td>
<td>Elastic</td>
<td>Beam</td>
</tr>
<tr>
<td>Facial Tissue</td>
<td>Viscoelastic</td>
<td>Solid</td>
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<tr>
<td>Scalp</td>
<td>Viscoelastic</td>
<td>Solid</td>
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Appendix B: Supplementary data for Chapter 3

Appendix Table 2: Common regions above 95th percentile MPS of 0.25

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<th>ROI Label</th>
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<td>somatomotor A</td>
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<tr>
<td>9</td>
<td>somatomotor A</td>
<td>somatomotor A</td>
</tr>
<tr>
<td>18</td>
<td>post central</td>
<td>dorsal attention B</td>
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<tr>
<td>32</td>
<td>lateral prefrontal cortex</td>
<td>control A</td>
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<tr>
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<td>somatomotor A</td>
<td>somatomotor A</td>
</tr>
<tr>
<td>61</td>
<td>auditory</td>
<td>somatomotor B</td>
</tr>
<tr>
<td>70</td>
<td>frontal eye fields</td>
<td>dorsal attention B</td>
</tr>
<tr>
<td>73</td>
<td>parietal medial</td>
<td>salience / ventral attention A</td>
</tr>
</tbody>
</table>
Appendix Table 3: Common regions above 95th percentile MPS of 0.3.

<table>
<thead>
<tr>
<th>ROI Label</th>
<th>Full Component Name</th>
<th>Network Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>somatomotor A</td>
<td>somatomotor A</td>
</tr>
<tr>
<td>73</td>
<td>parietal medial</td>
<td>salience / ventral attention A</td>
</tr>
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</table>

Appendix Figure A: Common strain-affected connections of regions above 0.2 with 17 functional networks among mTBI impacts with labels of network names.
Appendix Figure B: Common strain-affected connections of regions above 0.2 with 17 functional networks among non-mTBI impacts with labels of network names.
Appendix Figure C: Common strain-affected connections of regions above 0.2 with 17 functional networks among total 39 impacts with labels of network names.
Appendix Figure D: Healthy brain functional connections with threshold of 0.5 among datasets with 1-back working memory tasks with labels of network names.
Appendix Figure E: Connections of common concussed functional brain regions with labels of network names.
Appendix Figure F: Working memory connections excluding concussed brain regions with labels of network names.
Appendix Figure G: Head responses time history under frontal impact. Time history of (a) strain energy absorbed by helmet, (b) strain energy absorbed by helmet, (c) resultant rotational velocity, (d) resultant linear acceleration, (e)
resultant rotational acceleration, and (f) brain average MPS.

Appendix Figure H: Head responses time history under lateral impact. Time history of (a) strain energy absorbed by helmet, (b) strain energy absorbed by helmet, (c) resultant rotational velocity, (d) resultant linear acceleration, (e) resultant rotational acceleration, and (f) brain average MPS.
Appendix Figure I: Head responses time history under rear boss impact. Time history of (a) strain energy absorbed by helmet, (b) strain energy absorbed by helmet, (c) resultant rotational velocity, (d) resultant linear acceleration, (e) resultant rotational acceleration, and (f) brain average MPS.
resultant rotational acceleration, and (f) brain average MPS.

Appendix Figure J: Head responses time history under rear impact. Time history of (a) strain energy absorbed by helmet, (b) strain energy absorbed by helmet, (c) resultant rotational velocity, (d) resultant linear acceleration, (e) resultant rotational acceleration, and (f) brain average MPS.
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