

Finite Element Modelling of Sport Impacts –Brain Strains from Falls Resulting in Concussion in Young Children and Adults

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Abstract

Concussions are injuries that can result in debilitating symptoms, suffered by people of all ages, with children being at elevated risk for injury. Falls account for over 20% of head injuries worldwide, and up to 50% of concussive injuries in children. Following a concussion, children typically take longer for symptoms to resolve compared to adults. It is unknown whether or not children are more, less, or equally susceptible to concussive injury based on the mechanical response, with researchers divided on the subject. There is currently a paucity of published data for concussive injuries in children, with few studies investigating impact biomechanics and strain response in the brain using FE models. Those that exist typically rely on scaled adult models that do not capture age-dependent geometric properties, material properties of tissues, and the developmental stage of the brain reflected by the patterns of grey and white matter within the brain. Newer child models are being developed, however at present they are focused on car crash investigations that do not offer an accurate reflection of sports-related impacts, and those that could be experienced from day-to-day activities since impact characteristics (e.g. magnitude, duration, surface compliance) differ largely between these types of events. Strain magnitudes differ between events causing concussion in adults (falls, collisions, punches, and projectiles), so it follows that the unique impact characteristics of car crash events do not typically coincide with those associated with sports impacts. Car crash events can result in much longer impact durations compared to sporting impacts (100 ms duration in car crashes vs. 5-30 ms in sports impacts). The purpose of this thesis was to assess how the mechanical response of the brain in young children near 6 years old differs from an adult brain in cases resulting in concussive injury for sports impacts.

Study one created a novel FE model of a 6-year-old brain, using medical images to extract an accurate representation of the geometry and tissues inside the head of a 6-year-old child. The developmental stage of the younger brain was captured using a highly-refined mesh to accurately represent the folds of white matter within the cerebrum. With no intracranial data for child cadavers available, published data of adult cadavers was used to validate the brain motion from impacts. Comparisons were made to a scaled adult model to highlight how the different model constructions influence brain motion and resulting strains. The new model showed higher

correlation to the cadaver data compared to the scaled model, and yielded “good biofidelity” measures when assessed using a modified version of the normalized integral square error method. For young children, the new model was proposed to be more appropriate for concussion investigations as it captures age-appropriate geometry, material properties, and developmental stage of the brain, reflected in the patterns and volumes of grey and white matter within the brain.

Study two tested the model for sensitivity across three levels of surface compliance and impact velocity consistent with sport impact events, and compared strain responses to a scaled adult model. The 6-year-old model showed unique strain responses compared to the scaled adult model with peak strains being lower across most impact events. Strain patterns also differed between models, with less strain being transmitted into the white matter in the 6-year-old model. Low compliance impacts yielded highest differences in strains (~30%), moderate compliance impacts yielded more similar strains (~9% lower), with high compliance impacts showing a location dependent response with frontal impacts being 14% lower, and side impacts being 9% higher than the scaled model. The sensitivity study characterized the model responses, allowing for better comparisons between the two different model constructions.

Study three then compared the strain responses of reconstructed real-world concussive events for both children and adults. Forty cases of concussion from falls in children and adults (20 children aged 5-7, 20 adults) were reconstructed using physical models, with the measured impact kinematics used to load the FE models. Concussive cases of children showed lower strains than adults, finding a velocity driven relationship since the child concussions occurred at lower impact velocities compared to the adults. Lower peak strains, as well as cumulative strains in the child cases suggest that children are vulnerable to concussion at lower strain compared to adults. Protective strategies for children should address this vulnerability, no longer relying on product scaling to create head protection for youth.

Preface

This dissertation is organized into four main parts with multiple chapters in each section:

- Part I. Introduction, background, research statement, and objectives of the thesis.
- Part II. Literature review covering the subject area.
- Part III. Three separate studies covering the creation of a novel FE model of a child's brain and its application in sport falls.
- Part IV. Global summaries including points of discussion, limitations and overall conclusions.

The dissertation is comprised of three original research articles, for which I was lead author. I was responsible in creating the study designs, collecting the data, conducting data analysis and interpretations, writing, editing, and submission of the articles for peer review in scholarly journals.

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PART I

1. Introduction

1.1 Statement

Defined by the Mayo Foundation for Medical Education and Research (2014), concussions are the “temporary dysfunction of brain cells resulting from an external mechanical force”. By the age of 6 years old, many children are enrolled in sports programs to promote healthy living and physical activity, and to learn new skills. All sporting and recreational activities increase the risk of accidental injury from falls, collisions with others, and falls after colliding with children or objects. Worldwide, falls account for over 20% of documented head injuries (O’Riordain et al., 2003), and in children, one study reported that falls accounted for over 50% of concussive injuries (Browne and Lam, 2005). The forces experienced by the head from falls are transmitted to the intracranial tissues and the brain, causing strain (a dimensionless unit measuring the deformation of a body). Strain of the brain tissue is reported to be the cause of concussive injuries (Holbourn, 1943; Ommaya and Gennarelli, 1974; King et al., 2003; Kleiven, 2007; Post and Hoshizaki, 2015). Following head impacts, a complex cascade of ionic, metabolic, and physiologic changes have been observed (Giza and Hovda, 2001), leading to symptoms such as impaired coordination, attention, or memory, which are manifestations of the physiologic events (Giza and Hovda, 2001; Hovda 2014). Though symptoms of concussion typically resolve within two weeks, roughly one third of children experience ongoing somatic, cognitive, psychological, or behavioural symptoms in combination or isolation (Barlow et al., 2011; Babcock et al., 2013). Symptoms continuing for more than 10-14 days for adults, and longer than 30 days are referred to as persistent post-concussion symptoms (PPCS) (McCrory et al., 2016) and can have serious consequences. Children with persistent symptoms often experience reduced academic performance, loss of social activities, missed time from school, and mood problems (Choe et al., 2012; Yeates et al., 2012), resulting in a diminished quality of life. It has been suggested that concussive injury in the developing brain can alter the brain’s plasticity (Choe et al., 2012), potentially altering the future cognitive growth of the injured child.

There are an estimated 750 000 annual visits to emergency departments for pediatric concussion in the United States (National Center for Injury Prevention, 2003; Gilchrist et al., 2011), a figure that likely underestimates the true number of concussive injuries since many do not visit the emergency department. For all child head injuries, including traumatic brain injuries and brain bleeds, costs for treatment exceed \$1 billion annually in the United States (Schneier et

al., 2006). The severity of concussive injuries in youth has led to programs and tools being implemented by sporting organizations to help recognize and manage concussions in youth sports, such as the Concussion Toolbox from Hockey Canada, Concussion Guidelines from Soccer Canada, or the guidelines by the Ontario Neurotrauma Foundation (Zemek et al., 2014) for family physicians and health care professionals working with pediatric concussion. While management of concussive injuries is an important contributor to child safety, identifying the cause of brain injuries remains a priority in research so it can inform parents and players how to avoid injuries, inform rule changes, and help develop protective equipment to mitigate risk of injury. Children play sports differently from adults as they are smaller and have not developed their abilities of agility, awareness, or balance, which puts them at risk of head impacts.

Finite element (FE) models have emerged as an important tool for investigating head injuries in youth in car accidents (Cui et al., 2015; Giordano et al., 2017a). Car crash impacts have different impact characteristics (magnitude, duration, surface compliance) when compared to sport impacts. Impacts from car crash events can last over 100 ms (Giordano et al., 2017a), where sport impacts lie in the 5-30 ms impact duration range (Hoshizaki et al., 2016). Because concussions from falls, collisions, punches, and projectile impacts have yielded significantly different strain magnitudes (Kendall, 2016), car crash events published using current child models may not offer a proper comparison. Best results for comparisons between children and adults should be conducted for similar impact events such as falls, which will be the focus of this thesis. Finite element models allow for investigations of the tissue response from these impacts, incorporating important material characteristics of the intracranial tissues. The versatility of FE models to be loaded using physical reconstructions allows assessments of impacts parameters, and their influence on the brain's response to impacts.

1.2 Research Question

Concussive injuries in young children can be highly detrimental to their development, resulting in cognitive deficits that can persist long after the initial injury event (Adelson and Kochanek, 1998; Giza and Hovda, 2001; Choe et al., 2012). Neuroplasticity of the brain has been suggested to be affected by the ionic changes following concussive injury (Choe et al., 2012; Hovda 2014). Following injury, young children and adolescents have been documented to require longer recovery times than adults (McClincy et al., 2006; Gilchrist et al., 2011; Choe et

al., 2012; McCrory et al., 2013; Lax et al., 2015). Evidence supports the developing brain is more sensitive to a concussive injury, requiring more time to recover, however it is unknown whether or not the brain is more sensitive to the mechanical insult causing said injury.

There are documented changes that occur in the grey and white matter between youth and adults, changing the distribution of the grey and white matter within the brain as development and myelination occurs (Reiss et al., 1996; Lenroot and Giedd, 2006). The grey and white matter in the brain are mechanically different, with several studies documenting the white matter in the brain to be 1.2-2.6 times stiffer than the grey matter (Bayly et al., 2012; Chatelin et al., 2010; Clayton et al., 2012). As a youth's brain remodels during learning and life experiences, there are mechanical reinforcements, or deteriorations occurring within different regions of the brain as the grey and white matter remodel themselves. Additionally, there are geometric differences between a young child's and an adult's brain, with the head and skull having not quite reached full size. A 6-year-old child's brain has only reached roughly 90% of an adult's brain size (Giedd, 2004; National Academy of Sciences, 2014).

This thesis will focus on children aged 5-7 years old, an age group that is documented to have longer recovery times following injury than adults (Gilchrist et al., 2011; McCrory et al., 2013). They are also engaging in various sports leagues where the play environment creates potential for head impacts and concussive injury. It has been reported that male children over the age of 5 sustain 2-4 times more head injuries than younger children (Adelson and Kochanek, 1998). There could be differences in the mechanical properties of young brain tissue compared to adult brain tissue that could elicit a different mechanical response under impact conditions. Differences in the relative volumes of grey and white matter within the brain of a young child and an adult could also change the mechanical response of the brain to impact. The purpose of this thesis is to assess how the mechanical response of the brain in young children around 6 years old differs from an adult brain in cases resulting in concussive injury, with the following research question, *based on the strain response within the brain resulting from finite element model impact simulations of falls, are concussions in young children mechanically similar to concussions in adults*. This question will be addressed in three studies:

1. A 3D finite element model of a 6-year-old child for simulating brain response from physical reconstructions of head impacts

2. Sensitivity of a 6-year old child finite element model to simulated fall events for three levels of surface compliance
3. Differences in brain strain between young children and adults for head impacts from falls resulting in concussion

1.3 Background and Rationale

Brain tissue mechanical tests and the use of FE models in adult concussion and brain injury research have yielded many important results, identifying sensitivity to impact direction (Zhang et al., 2001b; Kleiven 2003; Kleiven 2006), the effect of an anisotropic brain tissue response (Giordano and Kleiven, 2014; Sahoo et al., 2014), and the influence of viscoelastic properties of the brain over a time window consistent with sport impacts (Zhao et al., 2018). These studies and many others are helpful in addressing concussive injury in adults, however there is little research into the impact biomechanics of concussion in young children as well as few FE models.

Two FE models of young children have been developed to date (Cui et al., 2015; Giordano and Kleiven, 2016a). Both youth models have published data relating to car crash events, which differ largely from sports impacts. In a study by Giordano et al. (2017a), acceleration pulses were shown lasting over 100 ms, whereas sports collisions exist mainly in the 5-30 ms impact duration range (Hoshizaki et al., 2016). In addition to distinct impact characteristics, survivability is the main concern for car crash events due to the high energy events resulting from high velocity collisions. Sport impacts exist within a relatively narrow range of impact characteristics. For young children, addressing this subset of impacts specifically can benefit understanding of concussive injuries as a whole, as well as inform future protection strategies to best reduce risk of concussive injury from sports.

Young children are at higher risk for prolonged symptoms following concussion (Gilchrist et al., 2011), but it is unknown how tolerant children are to head impacts compared to adults. They are at an age where playful activities involve risk of head impacts, but they do not necessarily have the physical ability to protect themselves from accidental falls and head injuries, resulting in higher risk of sustaining head impacts. These head impacts differ in several ways from those experienced by adults as children are smaller and are at a different stage in their

overall development, including their brain. By age 6, the brain is roughly 90% of an adults size, but there are differences in the relative volumes of grey and white matter (National Academy of Sciences, 2014), as well as the development of the neural pathways (Maxwell, 2012). White matter has been reported to be between 1.2-2.6 times stiffer than grey matter (Bayly et al., 2012; Chatelin et al., 2010; Clayton et al., 2012), meaning that subtle differences in grey and white matter may structurally influence the response to impact. Additionally, the mechanical properties of the brain could be different between young children and adults. Studies have examined the influence of age on the mechanical response of brain tissue with varied results. There are reports that young children have stiffer brain tissue (Gefen et al., 2003), more compliant brain tissue (Thibault and Margulies, 1998), or stiffer tissue once exposed to over 2.5% strain (Prange and Margulies, 2002). Some authors suggest that rapid changes in brain material properties exist up to roughly 2 years old with no significant change thereafter (Chatelin et al., 2012). In general, different testing conditions, testing methods, and different species being tested are all contributors in the variance of published data (Forte et al., 2017), resulting in published shear moduli spanning over 3 orders of magnitude (Chatelin et al., 2012). In this light, it is not yet established whether or not youth tissue is stiffer, more compliant, similar, or if a significant variance in mechanical properties exists for human brain tissue. Using FE models, these anatomical and mechanical differences can be tested under impact events. With a youth specific FE model, sporting impacts can be better understood in pursuit of better understanding concussive injuries to inform effective protective strategies for sporting events.

1.4 Objectives

The objective of this dissertation was to assess how the mechanical response of the brain in young children around 6 years old differs from an adult brain in cases resulting in concussive injury. The dissertation is divided into three separate studies designed to facilitate this comparison with FE models. The specific aims of the three studies are:

1. To develop, and partially validate a new FE model of a 6-year-old child against experimental data, creating a new tool with age-appropriate parameters for use in concussive research of young children, with results compared to a scaled adult FE model.

2. To test the sensitivity of the new FE model of a 6-year-old child for fall impacts in sports compared to a scaled adult FE model, identifying unique brain response characteristics of the new 6-year-old model.
3. Compare the brain strain response for real-world reconstructions of falls resulting in concussion in young children (ages 5-7), and adults.

PART II

2. The Biomechanics of Head Injuries in Sporting Type Impacts

2.1 Mechanisms of brain injury

Over the many years of brain injury research, theories of how the brain is injured have evolved. Understanding the cause of brain injuries is important in the pursuit of creating protective technologies that can prevent or reduce risk of injuries in sports, as well as recreational activities. In a review on mechanisms of brain injury, King et al. (2003) suggests that it is brain deformation or strain as a principal cause of injury. Due to the inability of directly observing how the brain is injured, different methods have been employed to understand the surrounding mechanics of brain injuries. Animal models as well as numerical modelling techniques have been employed, each with their own advantages and limitations. The following sections will discuss the theories surrounding the mechanisms of brain injury. First, traumatic brain injury mechanisms will be discussed, followed by the mechanisms of concussive injury, which will be the focus of this thesis, highlighting where differences between children and adults are important for risk of injury.

2.1.1 Mechanisms of traumatic brain injury

There are several review articles detailing the theories regarding the mechanisms of brain injury (Viano et al., 1989; King et al., 2003). In summary, the mechanisms of brain injury have been described as follows: brain contusion from skull deformation at point of contact, brain contusion from movements of the brain against rough and irregular interior skull surfaces or from the side opposite the impact, brain deformation in response to pressure gradients and motions relative to the skull, intracerebral hematoma from movement of the brain relative to its dural envelope (Viano et al., 1989).

Contusions

Contusions are a bruise of the brain tissue. The bruising can be caused by skull deformation at the site of an impact, with the skull “slapping” the brain tissue resulting in a contusion (Gurdjian et al., 1964). In addition to the skull “slapping” the brain tissue, contusions can be formed from brain motion against the surface of the skull (Gurdjian, 1972). Because the brain has its own inertia and is loosely coupled to the skull, when the head is impacted the brain will continue to move even when the skull is stopped. The interior surface of the skull is rough

and irregular, so the resulting relative movement of the brain can cause damaging contact (Gurdjian, 1975).

Pressure gradients

When the head is impacted, the brain will move towards the impact site due to its inertia. This causes an area of high pressure at the impact site, and a corresponding lower pressure opposite the impact site (Gurdjian et al., 1964). The human tolerance to impact forces is related to the duration of the impact event. Humans can withstand higher impact forces and accelerations for short duration events compared to long duration events (Gurdjian et al., 1954; Gurdjian et al., 1955). During the impact, intracranial pressure waves are formed with steep gradients (Gurdjian and Webster, 1947; Gurdjian et al., 1955). The steep pressure gradients and subsequent brain motion as a result of the impact can cause brain deformation, putting stresses and strains on the brain tissue (King et al., 2003). The highest shear strain will likely be located in the brain stem above the foramen magnum as its movement is more limited compared to the cerebrum (Gurdjian et al., 1964). The resulting stresses and strains in the brain tissue from increased intracranial pressure and brain motion are a possible source of brain injury from head impacts, however brain motion can also cause other types of injuries in the surrounding tissues as well, as mentioned above.

Brain motion

Brain motion relative to the dural envelope will result in strains of the surrounding supporting tissues. If the brain motion is sufficient, there can be tearing of arteries or veins within the cranium, causing intracerebral hematomas (Gurdjian, 1975). The bleeds represent several different types of injuries: epidural hematoma, subdural hematoma, and subarachnoid hemorrhage. These bleeds can result in an increase in intracranial pressure from the accumulation of blood. All intracranial bleeds are severe, with acute subdural hematomas shown to occur in 30% of patients with severe head injuries and have an associated mortality rate of 60% (Gennarelli and Thibault, 1982).

Traumatic brain injuries are the most frequent cause of children's disability and death in the US (Parker, Rolland, 2012). Impacts leading to traumatic brain injuries are typically high energy events with high magnitude responses, resulting in severe injury. With traumatic brain

injuries and intracranial bleeds comprising high severity brain injuries, Hoshizaki et al. (2013) discussed a continuum of injury based on impact response magnitude. Using reconstructions and finite element methods, the continuum of injury by order of severity from lowest to highest magnitude is listed as follows: sub-concussive impacts (no symptoms), concussion with transient symptoms, concussion with persistent symptoms, subdural hematoma, contusion, subarachnoid hemorrhage, epidural hematoma (Hoshizaki et al., 2013). The previous section highlighted the high severity injuries. The following section will discuss the theories of the mechanism of concussive injury, which is on the opposite end of the spectrum of severity and will be the focus of this thesis.

2.1.2 Mechanisms of concussion

Since concussion symptoms typically resolve within two weeks for most children (Zemek et al., 2016), concussive injuries are deemed lower severity compared to brain bleeds. Concussions show no visible signs of damage when using any medical imaging (Halstead et al., 2010), meaning there is no significant mechanical damage to the tissue at the resolution visible by typical medical images. Defined by the Mayo Foundation for Medical Education and Research (2014), concussions are “temporary dysfunction of brain cells resulting from an external mechanical force”. The mechanical forces that are transferred to the brain then cause ionic, metabolic, and physiological cascades (Giza and Hovda, 2001), leading to symptoms such as impaired coordination, attention, memory, which are manifestations of the physiologic events (Giza and Hovda, 2001; Hovda 2014). The following section discusses theories of what specific biomechanical forces cause concussive injuries.

Cavitation theory

When the head is struck, there is an area of positive pressure at the impact site (coup site) with a lower pressure opposite the impact site (contrecoup). When the contrecoup site pressure reaches negative levels, Gross (1958) theorized there would be cavitation of the cerebrospinal fluid (CSF), causing damage to the surrounding brain tissue resulting in a concussion. This theory was included in a list of mechanisms of brain injury by Gurdjian et al. (1964), along with tissue deformation in compression, tension and shear. Gurdjian (1975) reported cavitation is simple to reproduce in a lab setting with flasks, water, and a hammer, however there is great difficulty in reproducing this phenomenon outside of isolated, ideal lab settings. An example of

this was published by Ommaya et al. (1971), citing that the lesions which should be associated with cavitation (extreme lacerations or shear stresses) have not been observed experimentally with monkeys, so their data did not support the cavitation theory of brain injury. Current research does not discuss cavitation as a cause of concussion or other brain injuries, with more focus given to brain deformation metrics of stress, strain, or rate dependent metrics such as strain rate.

Brain deformation resulting from head motion

On impact, the skull is accelerated, causing motion of the head and brain. The brain motion loosely follows the motion of the skull. Due to the high resistance to changes in volume, but low resistance to changes in shape, the brain deforms predominantly in shear from the rotational motion (Holbourn, 1943). Ommaya et al. (1967) stated that shear strains were likely the mechanical cause for concussion, supporting Holbourn's hypothesis that concussive injury is created from shear strains. While both linear and rotational motion can cause brain motion and deformation, Holbourn (1943) stated that shear resulting from linear accelerations is small and suggested rotational motion is more likely responsible for causing concussion.

Linear acceleration is a metric commonly used by standards associations to measure helmet performance (Rueda et al., 2011). Its use in standards has resulted in helmets effectively reducing risk of traumatic brain injuries, but reducing forces to levels more closely associated with concussion (Hoshizaki et al., 2013). In studies of head injury, peak linear acceleration was reported to be associated with skull fracture, brain bleeds, and contusions with skull fracture (Gurdjian et al., 1961; Kleiven, 2013). For these severe injuries, peak linear acceleration is an indication of the impact energy, with higher energy required to fracture the skull or damage the underlying tissues. For concussive injury, peak linear acceleration contributes little to intracranial distortional strains (Kleiven, 2007). Since concussive injuries do not mechanically damage the brain tissue, linear acceleration is less influential in predicting these injuries in sports. In cadaveric tests, linear acceleration was shown to be responsible for ± 1 mm of brain motion, five times lower than rotational acceleration (Hardy et al., 2001). Every impact will impart some measure of linear and rotational acceleration so both can play a part in causing concussive injury.

Rotational acceleration has been strongly supported as more influential than linear acceleration in causing concussion (Gennarelli et al., 1971; Holbourn, 1943; Holbourn, 1945; Ommaya et al., 1967). Cadaveric data supports this hypothesis, with five times more brain motion associated with rotational motion (Hardy et al., 2001). Hardy et al. (2001) used neutral density targets inserted into cadaver heads and tracked the motion during impacts using high-speed biplanar X-rays. Impact locations were selected to result in both linearly and rotationally dominant motions. The study is used for validation of finite element models, confirming that the model's brain motion is consistent with cadaver tests. The results showed that rotationally dominant impacts show the neutral density targets moving ± 5 mm compared to linearly dominant impacts which showed only ± 1 mm of motion (Hardy et al., 2001), supporting that rotational acceleration is more influential in causing shear of the brain than linear acceleration, as it causes more brain tissue motion. While linear acceleration will translate the brain as a whole inside the skull, the rotational motion causes shearing of the brain tissue (Gilchrist, 2003). Rotational forces cause shear waves to form, traveling back and forth during impact, in addition to the brain translating inside the skull, causing higher brain motion. While concussion does not cause mechanical damage to the brain tissue, diffuse axonal injury is caused by widespread shearing of the brain tissue causing damage (Gennarelli et al., 1982; Adams et al., 1989; Kleiven, 2013; Moenninghoff et al., 2015). It has been suggested that post-concussive syndrome could be micro-bleeds unable to be detected on 1.5T or 3T MRI machines, with higher magnet strength MRI machines able to detect these injuries (Moenninghoff et al., 2015).

2.1.3 Summary

Both linear and rotational motions are important in the brain response to impact, though rotational motion causes more tissue strain. Continued research is required to fully understand the mechanisms causing concussions, so as to better create protective strategies to reduce risk of injury, especially in youth. This thesis will measure both linear and rotational motion from impacts, however the analysis will focus on the resulting strains from the FE models because concussive injury from sport related impacts are the results of a mechanical force on the brain tissue, not a global acceleration experienced by the head. This thesis aims to challenge the assumption that brain deformation for events causing concussion are similar in adults and

children, creating a finite element model of a 6-year-old child to investigate concussive injury in youth.

2.2 Age effects on brain injury

Many physical changes happen as we grow and develop from infants, to children, to adults. In addition to the height difference between children and adults, there are dynamic changes going on inside the brain as myelination occurs (Lenroot and Giedd, 2006). Some differences may have little or no effect on the mechanical response of the brain during impacts, while some may play an instrumental role, influencing impact characteristics. Contained in this section are key anatomical and structural differences between young children and adults that can influence impact characteristics, how forces are transmitted to the brain, as well as differences within the brain.

2.2.1 Size differences in children and adults

The size differences between young children and adults are important, as significant growth occurs during puberty and young children have not yet reached this stage in development. In this thesis, the focus is on children aged 5-7 years old, well before puberty. As children grow, there are substantial changes in height and mass, including changes to head size and mass. A summary of the changes in height and body mass is shown in Table 1, with changes in head circumference shown in Table 2.

Table 1 - Height and weight percentiles for boys ages 6 – 20 years old (CDC, 2014)

Percentile	6-year-old			12-year-old			20-year-old		
	5th	50th	95th	5th	50th	95th	5th	50th	95th
Height (cm)	107	116	124	137	149	162	165	177	189
Mass (kg)	17	21	27	30	40	59	56	71	96

The head grows at a much different rate than the rest of the body, showing much more development between 0-24 months, accounting for roughly two thirds of total growth (Nellhaus, 1968). The final third of growth occurs after two years old. The increases in head circumference lead to a larger intracranial space and larger brain. As the head grows and skull thickens, so do

other structures such as the ventricles, meaning larger intracranial space does not directly translate into a larger brain volume.

Table 2 - Head circumference changes for ages 2 - 18 years old (Nellhaus, 1968)

Percentile	6-year-old			12-year-old			18-year-old		
	2nd	50th	98th	2nd	50th	98th	2nd	50th	98th
Head circumference (cm)	48.5	51.5	54.0	50.5	53.5	56.5	53.0	56.0	58.5

2.2.2 Size effects on impact characteristics

Based on height, free falls from 116 cm and 177 cm would result in impact velocities of roughly 4.8 m/s and 5.9 m/s respectively without accounting for any outside influences on the head kinematics (body motion, air resistance, bracing). These velocities are worst-case scenarios for falls from standing, but highlight that stature alone will create meaningful differences in impact velocities between age groups. Also, though physical models are not perfect in representing the heads of humans, the Hybrid III 6-year-old head form is 3.47 kg, compared to the 50th percentile adult, which is 4.54 kg (Humanetics Innovative Solutions, 2017). Impact mass is influential in the impact characteristics as it contributes to the overall impact energy. Kartan et al., (2014) showed incremental increases in peak linear acceleration from increasing impact mass as well as resulting strains in the brain. During a fall, there is an almost complete energy transfer to the head. For equal impact forces, a smaller mass head will accelerate more than a heavier counterpart. Children could experience higher impact accelerations due to lower head mass, a result found by Gimbel and Hoshizaki (2008) when testing helmets with different sized head forms. Though children could experience higher accelerations, they typically would fall from lower heights resulting in lower impact velocities, possibly mitigating some risk they would experience.

2.2.3 Brain size

Increases in brain size occur mostly during the first 5-6 years of life, with several authors reporting that the brain reaches up to 90-95% of its final volume by ages 5-6, showing very little change after this point (Lenroot and Giedd, 2006; Reiss et al, 1996). Shown in Figure 1, total cerebral volume actually decreases after roughly age 14.5 for males and 11.5 for females

(Lenroot and Giedd, 2006). Even with a slightly smaller brain, using the scaling law proposed by Ommaya et al. (1967) designed to scale head accelerations between humans and different species of animals, there will be a measurable difference in the proposed acceleration to cause injury in children compared to adults. Ommaya et al. (1967) scaled test results from rhesus monkeys to a human adult equivalent using Equation 2.1:

$$\alpha_h/\alpha_r = (m_r/m_h)^{2/3} \quad (2.1)$$

where α_h is the human head acceleration, α_r is the rhesus monkey head acceleration, m_h is the human brain mass, and m_r is the rhesus monkey brain mass. If a child's brain mass is substituted into the equation instead of a rhesus monkey with a brain mass of 90-95% of that of an adult, the predicted acceleration required to injure a child would be 3.5-7.3% higher than an adult, suggesting children are slightly less susceptible to brain injuries based solely on brain size. Mass alone does not account for the differences in children and adult brain injuries.

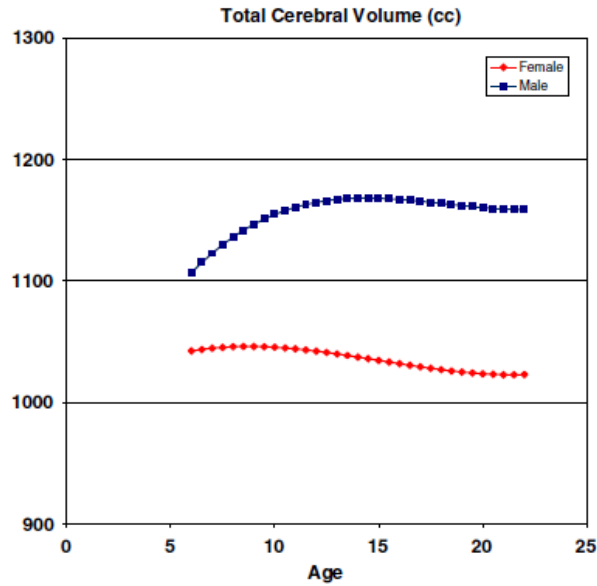


Figure 1. Total cerebral volume by age for both males and females (Figure taken from Lenroot and Giedd, 2006)

Though there are minimal changes in overall brain volume, changes in the grey and white matter continue with age; with significant remodelling occurring into the 3rd decade of life (Lenroot and Giedd, 2006; Reiss et al., 1996). The remodelling of the brain, in addition to size differences, could influence the strain fields in the brain. Danelson et al. (2008) showed that the proper

representation of the young brain and skull changes the resulting strain distribution in the brain from impacts, but not the magnitude. This effect on the distribution of strain may be further influenced by different mechanical differences between grey and white matter, discussed further in the following section, Material Properties.

2.2.4 Developmental differences of brain structures

During development, there are dynamic changes occurring inside the brain with remodelling of the pathways in the brain (Lenroot and Giedd, 2006; Reiss et al., 1996) (See Figure 2). This remodelling causes changes in the organization of grey and white matter within the brain that continue for many years (See Figure 3). The differences amount to different sizes of individual structures and different organization of grey and white matter within the brain. Giedd et al. (1996) showed a high degree of variability with age when examining various structures of the brain (cerebrum, ventricles, cerebellum, caudate, thalamus etc.).

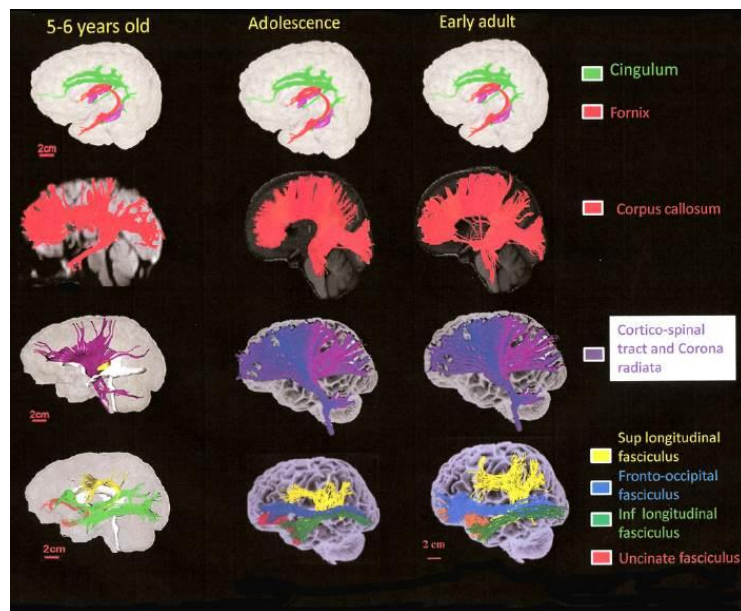


Figure 2. Development of white matter tracts from 5-6 years old, through adolescence, into early adulthood, (Figure taken from Maxwell (2012))

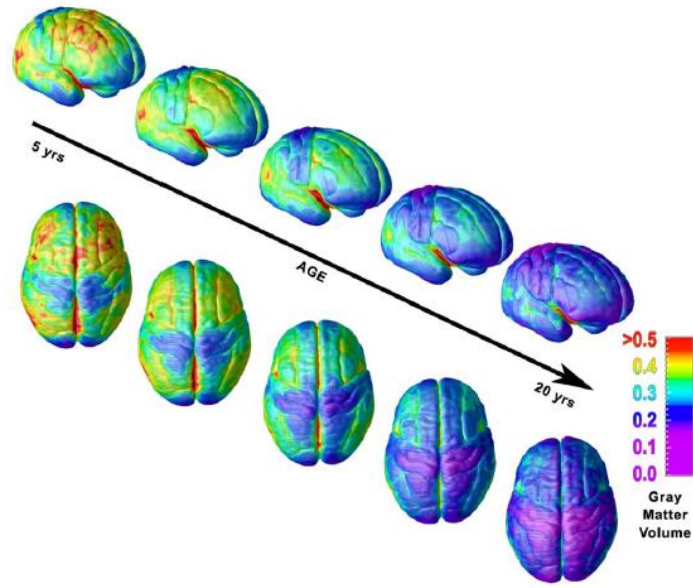


Figure 3. Right lateral and top views of the dynamic sequence of grey matter maturation over the cortical surface (Figure taken from Lenroot and Giedd (2006))

Figure 4 shows the increase in white matter volume with age for males and females, demonstrating that although total cerebral volume may decrease through the teenage years, white matter volume continues to increase. The increase in white matter volume in association with total cerebral volume decrease has been noted in an earlier study by Reiss et al. (1996), finding a loss in overall cerebral grey matter as further myelination occurs.

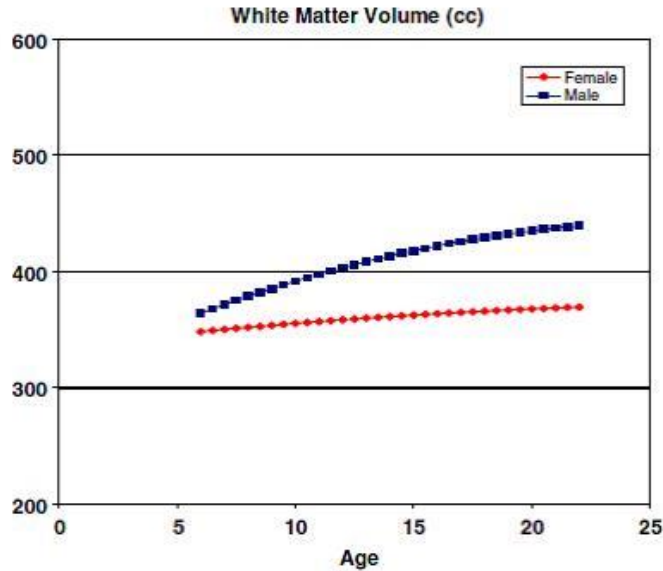


Figure 4 - Total white matter volume with age for males and females (Figure taken from Lenroot and Giedd, 2006)

The differences in structure and arrangement of grey and white matter can lead to differences in different mechanical response since the unmyelinated grey matter is softer (Coats and Margulies, 2006; Parker, Rolland, 2012; Jin et al., 2013). Also, white matter will show a more directional material response than grey matter due to the higher degree of axonal alignment (the differences in mechanical response will be discussed in the next chapter). Shear strain of brain tissue has been theorized to be the mechanical cause of concussion (Ommaya et al., 1967), so differences in shear properties of the brain will influence the strain response in the brain.

2.3 Summary

There are a number of anatomical differences between young children and adults. Not only are children shorter and smaller than adults, dynamic remodeling of the grey and white matter occurs throughout their development (Reiss et al., 1996). The differences in height will influence fall velocity since children have shorter distances to fall, with differences in mass resulting in different responses from impacts. The lower impact velocities and structural differences in the brain should be recognized when investigating brain injury, as authors have theorized that there is a significant age-dependent response of brain tissue to impacts (Thibault and Margulies, 1998; Gefen et al., 2003; Prange and Margulies, 2002; Kirkwood et al., 2006).

Differences in arrangement of tissues and tissue mechanics should be considered when using FE modelling for brain injury in children. The following section will discuss general material models, and how brain tissue is currently being employed in FE models for children and adults with summaries of published material properties.

3. Material Properties of the Brain

Material properties are arguably the most important part of an FE model, governing the stress and strain response based on the input parameters. Different material models with varying levels of complexity have been employed to capture the response of brain tissue under load. The following section describes brain tissue testing methods, results, and gives a description of influential factors that affect the precision of published mechanical properties of brain tissue.

3.1 Mechanical testing of brain tissue

Modelling the mechanical response of brain tissue is a complicated task. This is reflected by the large number of authors who have endeavoured to characterize brain tissue over the last 50 years shown in Figure 5 (Chatelin et al., 2010). There are several factors which contribute to the difficulty in accurately modelling brain tissue including heterogeneity, anisotropy, inter-species variation, age-dependence, and post-mortem time (for *in vitro* studies).

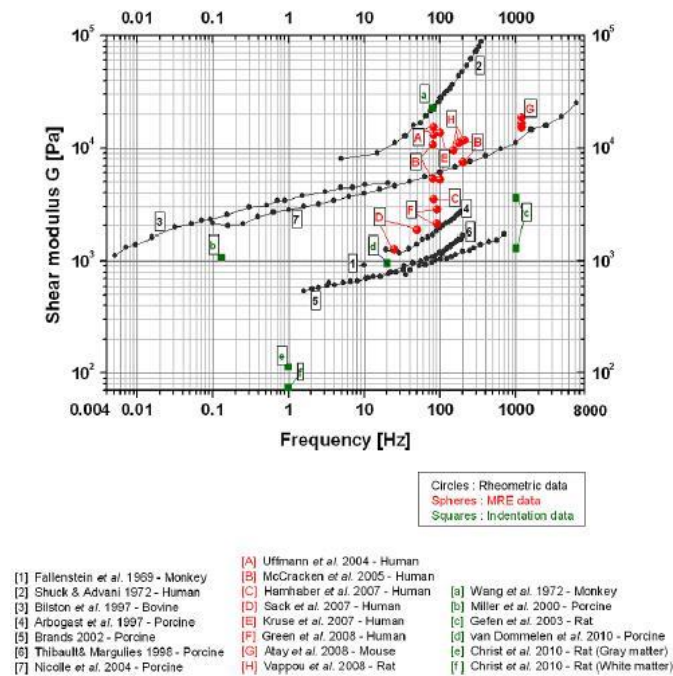


Figure 5. Comparison of shear modulus values showing the variance from *in vitro* tests by dynamical mechanical analysis, and *in vivo* values from indentation and magnetic resonance elastography (Figure taken from Chatelin et al. 2010)

Brain tissue response is highly complex, exhibiting a nonlinear mechanical response with hystereses during cyclic loading, as well as significant softening during repeated loading cycles (Budday et al. 2017c). Figure 6 illustrates the nonlinear response of brain tissue to repeated loading compression loading cycles.

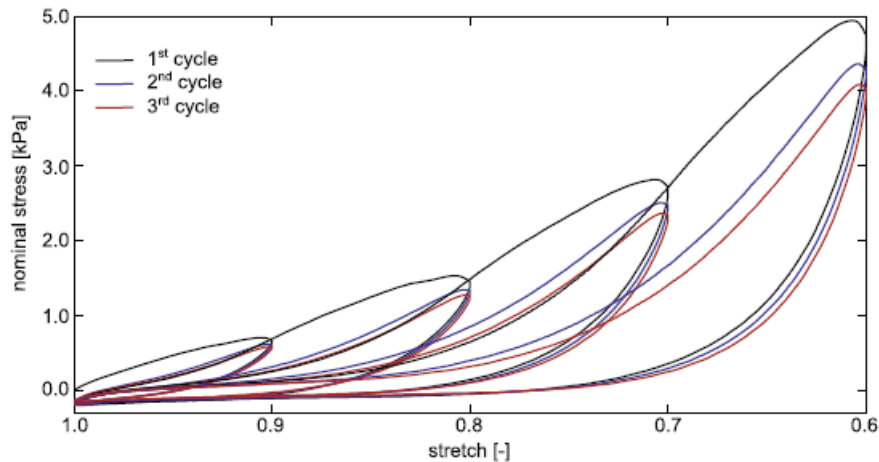


Figure 6. Stress-stretch results from one sample of corona radiata presented by Budday et al. (2017c), showing the effect of preconditioning of brain tissue for four compressions of brain tissue (Figure taken from Budday et al. (2017c))

3.1.1 Tissue heterogeneity

Brain tissue is heterogeneous given that it is made up of grey and white matter (Prange and Margulies, 2002; Rashid et al., 2013; Coats and Margulies, 2006). Grey and white matter differ in structure, with white matter having a highly directional orientation of fibres with a myelin sheath. Isolating the mechanical response for grey and white matter can be difficult as it can be difficult to section exclusively grey or white matters samples when conducting tissue testing. Many studies have tested mixed samples of both grey and white matter. Nicolle et al. (2004) documented that grey and white matter react similarly at small strains, whereas the opposite has been demonstrated by other authors (Fallenstein et al., 1969; Ommaya, 1968; Prange and Margulies, 2002; Kruse et al., 2008). In addition to potential differences in grey and white matter as a whole, differences within the same tissue have been observed, with changes in their mechanical behaviours at different locations (Prange and Margulies, 2002; Coats and Margulies, 2006; Johnson et al., 2013). There is little agreement in brain tissue studies, though

many have worked to characterize the response under different conditions. Local differences could be attributed in part to the vasculature, with blood vessels being more resistant to damage than brain tissue (Besenski, 2002), though Ho and Kleiven (2007) found small to negligible effects on the strain in the brain tissue when including vasculature in FE models. It is possible that blood vessels offer some level of strain shielding by acting as structural members within the brain, but this is not well documented. Budday et al. (2017c) suggests that the capillary density significantly contributes to overall mechanical strength of the tissue, however it was not tested in their study. Blood flow can also change the mechanical response; the effect of blood flow in brain tissue was modelled by Bilston (2002), finding that increased blood pressure can stiffen the surrounding tissue, with increasing effects with higher pressure. At lower pressures, the difference in results was minimal but at higher pressures the tissue stiffened considerably, an idea supported by Gefen and Margulies (2004). In areas of the brain with larger blood vessels, the pressure may help stiffen the surrounding tissue, and in areas with significant capillary density the vessels may add some mechanical strength due to the vessels having higher stiffness. When testing sectioned samples of brain tissue, *in vitro* samples will likely include some capillaries as the sections of brain tissue will include vasculature, but larger vessels will not be pressurized to stiffen the response. Capillary stiffness will then be present in the tissue tests, but not the stiffness associated with pressurized vessels. The effect of vasculature is not likely to be obvious and it has been suggested that vasculature inclusion in FE models is not necessary for brain tissue injury investigations, but more necessary for investigations of acute subdural hematoma (Ho and Kleiven, 2007). The model created in this thesis follows this recommendation, and does not include vasculature, though it is recognized it could create some local differences in material response of the brain.

3.1.2 Tissue anisotropy

Another concern for FE models is the level of anisotropy, which is tied to the structure of grey and white matter. White matter is highly oriented compared to grey matter. The assumption that grey matter can be treated as isotropic has been supported by many authors (Prange and Margulies, 2002; Gefen and Margulies, 2004; Hrapko et al., 2008). White matter has been shown to be transversely isotropic, with increases in stiffness reported to be 10-20% (Arbogast and Margulies, 1998), or between 25-54% (Hrapko et al., 2008) in the transverse direction. A

limitation for properly modelling white matter is that the fibre orientation is difficult to determine; diffuse tensor imaging techniques need to be used as demonstrated by Sahoo et al. (2014), and Giordano and Kleiven (2014). Additionally, a recent study found no significant anisotropy in any brain tissue (Budday et al., 2017c), conflicting with previous studies. Anisotropic modelling enables simulations of a more complex brain response, but it is not possible to exactly replicate the complexity of the white matter tract orientations in the finite element model and the process is labour intensive. Additionally, Giordano and Kleiven (2014) did not find significant differences in cerebral brain motion after adding the axonal tracts. This FE model did not employ anisotropic models, since sufficient data has not established anisotropic models offer improved accuracy of the brains response to impact.

3.1.3 Inter-species variation

Another factor affecting published mechanical properties of brain tissue is inter-species variation. Many studies opt to use brain tissue from other species, due to the increased availability as well as the ability to test with limited post-mortem time. Studies have tested human, porcine, monkey, bovine, rat, and mouse brain tissues (Fallenstein et al., 1969; Darvish and Crandall, 2001; Prange and Margulies, 2002; Gefen et al., 2003; Nicolle et al., 2004; Urbanczyk et al., 2015; MacManus et al., 2016; Budday et al., 2017a; MacManus et al., 2017a). Differences in the mechanical response of brain tissue between species has been listed as an influencing factor which helps to partially explain the disparity in published data (Ommaya, 1968; Prange and Margulies, 2002; Gefen and Margulies 2004; Hrapko et al., 2006; Hrapko et al., 2008). Inter-species variation may influence the results, but has also been cited as a minor issue in comparison to other issues such as post-mortem time (Gefen and Margulies, 2004; Prange and Margulies, 2002), meaning all *in vitro* human brain tissue studies have a significant limitation. The advantages of using animal tissue for brain tissue testing can often outweigh the disadvantages as there can be more control on the treatment of the samples since there are fewer ethical considerations which need to be met, and post-mortem time can be much more easily reduced in animal studies.

3.1.4 Post-mortem time

Post-mortem time is an important factor as tissue degradation will alter the results from testing. For all *in vitro* tests, limiting post-mortem time should be prioritized as it has been

shown to have a greater effect compared to inter-species differences (Prange and Margulies, 2002). For this reason, non-human brain tissue was used for assigning material properties in this thesis. Human tissue is often unavailable until several days post-mortem. Though human tissue offers the best opportunity for accurately modelling the mechanical response, it is hard to determine whether brain tissue from a different species tested *in situ*, *in vivo*, or obtained only a few hours post-mortem might serve better than human brain tissue obtained after several days. Authors testing human tissue have often frozen samples or kept them refrigerated in saline solution in order to preserve the tissue and prevent degradation. Rashid et al. (2013) showed this to be good practice, finding that storage at room or body temperature accelerates tissue degradation. This degradation resulted in lower stresses in the tissue, with the frozen samples showing 1.5 times higher stresses than the samples stored at higher temperatures. Although freezing reduces tissue degradation, Brossolet and Vito (1997) found venous tissue stiffness increases shortly following thawing of frozen samples. The tests were conducted on veins rather than brain tissue, but it highlights that storage techniques can significantly alter mechanical response. Post-mortem time is highly significant when assessing material properties of the brain for use in modelling as it can cause considerable variability.

Ideally, properties would be obtained from human participants with *in vivo* testing. For many years, there were no suitable *in vivo* testing methods available for human tissue and so *in vitro* tests were done instead. Magnetic resonance elastography (MRE) has emerged as a solution to this problem with many studies using this technique (Kruse et al., 2008; Vappou et al., 2008; Zhang et al., 2011; Clayton et al., 2012; Mousavi et al., 2014; Johnson et al., 2013; Urbanczyk et al., 2015; Pong et al., 2016). One limitation of this method is that the head is vibrated to elicit a mechanical response; a different event from a head impact such as a fall. In addition, the material must be assumed to be isotropic and homogenous (Zhang et al., 2011; Clayton et al., 2012). This assumption may be adequate for grey matter; however several authors challenge this assumption stating that white matter should be treated as anisotropic (Ueno et al., 1995; Prange and Margulies, 2002; Hrapko et al., 2008). Though there are limitations, the method has shown some promising results similar to other testing methods. In a review of the mechanical testing of brain tissue over the last 50 years, Chatelin et al. (2010) found large variations in MRE results similar to previous studies, however there was some agreement between different testing methods, both *in vivo* and *in vitro* studies. As explained by Chatelin et al. (2010), there is moderate agreement

between the different methods with the MRE results lying around the “mean” *in vitro* tests (see Figure 5). Despite the agreement, every testing method yields differences between studies extending over an order of magnitude. This serves to highlight the difficulties with accurately characterizing the complex response of brain tissue.

3.1.5 Age-dependence

Age-dependence has been investigated with several studies, mostly using rat or porcine subjects and scaling the development states to humans (Gefen et al., 2003; Thibault and Margulies, 1998; Prange and Margulies, 2002; Pong et al., 2016). These studies have all found mechanical differences which occur with age. These changes could be due to several anatomical influences, such as changes in brain composition. An increase in myelin with a simultaneous decrease in brain water content is cited as a possible explanation for age-dependency of brain tissue by Gefen et al. (2003). The water content of the brain is an important factor in the mechanical response of brain tissue, with Budday et al. (2017b) finding that the fluid phase of brain tissue provides resistance to loading. Composition of brain tissue as well as cerebral blood volume have been cited by Kirkwood et al. (2006) as being in part responsible for an age-dependent mechanical response. Chatelin et al. (2010) also conducted tests and concluded that young brain tissue does not differ significantly from adult tissue after roughly two years old. Overall, age-dependency of brain tissue response could be due to a change in tissue composition or from changes in the structure of the brain because as myelination occurs, nerve pathways are reinforced functionally as well as mechanically. This thesis will employ different mechanical properties for the child model, following results of authors finding differences in youth and adult brain tissue. If further studies are conducted that confirm that brain tissue does not change after ~2 years old, parameters could be changed accordingly. It is acknowledged that the scalable PIPER model (Giordano and Kleiven, 2016a) uses adult material properties, so the present model and PIPER model will differ in material characterization.

In general, brain tissue has been tested mostly for differences in grey and white matter, however some tests have identified differences between structures of the brain. Many models treat brain tissue as either homogeneous (Ruan et al., 1994; Gilchrist et al., 2001; Kleiven, 2007; Giordano and Kleiven, 2016a) or distinguish between grey and white matter properties (Zhang et al., 2001a; Horgan and Gilchrist, 2003; Mao et al., 2013). Most models use the mechanical

properties of grey matter for the cerebellum, and do not include different material properties for any smaller structures such as the thalamus, though they may be identified as a distinct brain region as done by Mao et al., (2013). The brainstem is typically modelled using a stiffer shear modulus, since it has been reported to be 2-3 times stiffer than both grey matter from the thalamus, and white matter from the corona radiata (Chatelin et al., 2012). Results from Arbogast and Margulies (1998) show similar behaviour, with the brain stem showing an increase in stiffness of 80-100% as opposed to 2-3 times. Again, due to the large variance in published data these values do not necessarily reflect the exact mechanical response of the different structures, however there is reasonable evidence to support further characterization studies as well as different modelling techniques for the different structures. The cerebellum has been reported to be more compliant than the cerebrum using MRE (Zhang et al., 2011), however it is normally modelled with similar properties to the grey matter in the brain. Overall, there is still no consensus of brain tissue material properties, and references can be found to support most choices of material parameters.

3.2 Modelling brain tissue and intracranial contents

Modelling brain tissue and the intracranial contents is a complex task. The tissues of the brain are heterogeneous, there are several membranes that lend support to the soft brain tissue, and the brain can translate within CSF, which is a difficult behaviour to approximate. The most relevant physical properties of the brain according to Holbourn (1943) are the relatively uniform density, high incompressibility, and low modulus of rigidity, which means there is a small resistance to change in shape compared to the high resistance to changes in size. As a whole, the intracranial contents are generally treated as incompressible due to high water content. The consistency of the brain however is more similar to a gel-like material composed of roughly 77-78% water (Ommaya, 1968). Though the CSF and the tissues in the brain are assumed to be mostly incompressible, to help model the motion of the brain inside the skull, a minimal degree of compressibility of the intracranial contents is added with a Poisson's ratio for the brain in the range of 0.48-0.499 (Ruan et al., 1991; Ruan et al., 1994). The CSF has been modelled as an elastic solid with a low shear modulus (Horgan and Gilchrist, 2003; 2004) to allow for movement between the brain and skull, since the brain motion can lag behind that of the skull during impacts (Horgan, 2005).

3.2.1 Brain tissue modelling

Most studies on the mechanical behaviour of brain tissue have shown that the brain exhibits viscoelastic behaviour (Fallenstein et al., 1969; Shuck and Advani, 1972; Arbogast and Margulies, 1998; Thibault and Margulies, 1998; Gefen et al., 2003; Hrapko et al., 2008; Kruse et al., 2008; Shafieian et al., 2009; Rashid et al., 2013). Linear viscoelastic models have been employed by several FE models of the brain, with shear characteristics following Equation 3.1:

$$G(t) = G_{\infty} + (G_0 - G_{\infty})e^{-\beta t} \quad (3.1)$$

where G_{∞} is the long-term shear modulus, G_0 is the short-term shear modulus, and β is the decay factor. Studies using finite element models have incorporated different levels of sophistication and modelled brain tissue differently, with a selection of different studies' material properties summarized in Table 3. Earlier models used purely linear elastic material models (Shugar and Katona, 1975; Hosey and Liu, 1982; Ward, 1982). As more brain tissue characterization studies were completed, material models progressed as well. Linear elastic models gave way to linear viscoelastic models, to linear viscoelastic combined with large deformation theory (Ruan et al., 1994; DiMasi et al., 1991; Turquier et al., 1996). Presently, hyperelastic viscoelastic models are being employed with anisotropic properties (Giordano and Kleiven, 2014; Chatelin et al., 2013). Recent FE models of the brain have primarily used two different hyperelastic models, the Mooney-Rivlin, and the Ogden model. In Abaqus (Dassault Systèmes, 2014), the Mooney-Rivlin model follows the strain energy potential shown in Equation 3.2,

$$U = C_{10}(\bar{I}_1 - 3) + C_{01}(\bar{I}_2 - 3) + \frac{1}{D_1}(J^{el} - 1)^2 \quad (3.2)$$

where C_{10} , C_{01} , and D_1 are material parameters, $\bar{I}_1$ and $\bar{I}_2$ are the first and second deviatoric strain invariants, and J^{el} is the elastic volume ratio. The Ogden hyperelastic model differs from many hyperelastic models in that it is based on the principal stretch ratios, rather than strain invariants and follows the strain energy potential shown in Equation 3.3,

$$U \stackrel{\text{def}}{=} \sum_{i=1}^N \frac{2\mu_i}{\alpha_i^2} (\bar{\lambda}_1^{\alpha_i} + \bar{\lambda}_2^{\alpha_i} + \bar{\lambda}_3^{\alpha_i} - 3) + \sum_{i=1}^N \frac{1}{D_i} (J_{el})^{2i} \quad (3.3)$$

$$\bar{\lambda} = J^{-\frac{1}{3}} \lambda_i \rightarrow \bar{\lambda}_1 \bar{\lambda}_2 \bar{\lambda}_3 = 1$$

In Abaqus (Dassault Systèmes, 2014), the viscoelastic response is characterized by an N-term Prony series shown in Equation 3.4,

$$\mu(t) = \mu_0 \times \left(1 - \sum_{i=1}^N g_i (1 - e^{-t/\tau_i})\right) \quad (3.4)$$

A short summary of mechanical properties applied to FE models of the brain is presented in Table 3.

Table 3 - Material properties of brain tissue used in finite element model studies

Authors	Viscoelastic parameters			Linear Elastic parameters		
	Short Term Shear Modulus (kPa)	Long Term Shear Modulus (kPa)	Bulk modulus (GPa)	Decay Factor (s-1)	Young's Modulus (kPa)	Poisson's Ratio
Ruan et al. (1991)					66.7	0.48
Ruan et al. (1994)			2.19			0.4996
Bandak and Eppinger (1994)	5.0 psi	2.5 psi	1.86			
Zhang et al. (2001a)	White – 41 Grey – 34	7.8 6.4	2.19 2.19	700 700		
Kleiven and von Holst (2002)	Mooney-Rivlin hyperelastic/viscoelastic $C_{10}(t) = 0.9C_{01}(t)$ $= 620.5 + 1930e^{-t/0.008} + 1103e^{-t/0.15} (Pa)$					0.49999635
Horgan and Gilchrist (2003)	Same as above					
Horgan and Gilchrist (2003)	White – 12.5 Grey – 10 Brainstem – 22.5	2.0 2.5 4.5		80		0.499995
Willinger and Baumgartner (2003)	49	16.2		145		
Zhang et al. (2004)	White – 41 Grey – 34 Brainstem – 58	7.8 6.4 7.8	2.19 2.19 2.19	400 400 400		
Ishikawa et al. (2006)					17000	0.49

Kleiven (2007)	Ogden hyperelastic/viscoelastic $\mu_1=26.9 - 107.6$ Pa, $\mu_2= (-60.2) - (-240.8)$ Pa, $\alpha_1=10.1$, $\alpha_2=-12.9$ $G_1=0.16-0.64$ MPa, $G_2=39-156$ kPa, $G_3=3.1-12.4$ kPa, $G_4=4-16$ kPa, $G_5=0.05-0.20$ kPa, $G_6=1.5-6.0$ kPa, $\beta_1- \beta_6 = 106, 105\dots, 101$ (1/s)			
Takhounts (2008)	1.66	0.928	0.55847	16.95
McAllister et al. (2012)	Same as Kleiven (2007)			
Mao et al. (2013)	White – 7.5 Grey – 6.0	1.5 1.2	2.19 2.19	80 80
Giordano and Kleiven (2014)	Gasser-Ogden-Holzapfel model $G=1214$ Pa, $K=50$ MPa, fiber alignment values $k_1= 11590$ Pa, $k_2 = 0$ Pa Viscoelastic parameters $g_1-g_6= 0.7685, 0.1856, 0.0148, 0.0190, 0.0026, 0.0070$ with time constants $\tau_1- \tau_6=10^{-6}, 10^{-5} \dots, 10^{-1}$ s Anisotropic viscous hyperelastic model			
Sahoo et al. (2014)	Mooney-Rivlin parameters $C_{10}= -1.034$ kPa, $C_{01}=7.809$ kPa, $K=1125$ MPa Fiber reinforcement parameters $C_3=13.646$ kPa, $C_4=4.64$, Long-term shear moduli $S_1=4.5$ kPa $S_2= 9.11$ kPa Time constants $T_1=1.1-9$ s, $T_2=0.1450$ s			

Shear moduli employed in the models above vary by over an order of magnitude, and the viscoelastic constants also span a wide range, meaning there is little consistency in application of mechanical properties of brain tissue between models. It is difficult to interpret the response variables from different models since the stress and strain response is highly dependent on the mechanical properties applied to each particular model. The same issue is present with pediatric and child FE models. Recent efforts to create pediatric models and those of young children have yielded many combinations of material properties and viscoelastic constants. Each model has employed different material properties, with a summary shown in Table 4.

Table 4 - Material properties of brain tissue used in finite element model studies involving infants and children

Authors	Age	Mechanical properties			
		Short Term Shear Modulus (kPa)	Long Term Shear Modulus (kPa)	Decay Factor (s ⁻¹)	Bulk modulus (GPa)
Roth et al., (2007)	6 months	5.99	2.32	0.09248	2.11
Roth et al., (2009)	3 years	49	16.2	145	1.125
		9.884	3.725	920	1.125
Li et al., (2011)	8 days	6	2.32	35	2.11
	45 days	27.5	10.65	477.5	2.11
	90 days	49	18.98	920	2.11
Roth et al., (2010)	17 days	5.99	2.32	0.09248	2.11
Li et al., (2013)	6 months	10	2	80	2.19
Cui et al., (2015)	6 years old	4.9-490	1.62-162	1.45-1450	0.0219-2.19
Giordano and Kleiven, (2016a)	Scalable from 1.5 – 6 years old	Ogden hyperelastic/viscoelastic $\mu_1=53.8$ Pa, $\mu_2= -120.4$ Pa, $\alpha_1=10.1$, $\alpha_2=-12.9$ $G_1=0.32$ MPa, $G_2=78$ kPa, $G_3=6.2$ kPa, $G_4=8.0$ kPa, $G_5=0.10$ kPa, $G_6=3.0$ kPa, $\beta_1- \beta_6 = 10^6, 10^5 \dots, 10^1$ (1/s)			

3.2.2 Skull and membrane modelling

The last structural components to be modelled are the skull and meninges. The skull has mostly been modelled as a linear elastic solid (Zhang et al., 2001a; Kleiven and Hardy, 2002; Kleiven, 2006; Sahoo et al., 2014), with some authors using a 3 layer skull representing the inner and outer table as well as the diploë. Many authors have cited the importance of skull deformation when modelling head impacts (Gefen et al., 2003; Horgan and Gilchrist, 2003; Horgan and Gilchrist, 2004; Li et al., 2013), though skull deformation is not always represented in the model. Models can also use acceleration loads rather than simulating impacts, requiring a rigid skull. Skull deformation is an important aspect of simulations for youth models used in car crash investigations (Cui et al., 2015; Giordano et al., 2017a), so the skull was discretized and meshed. For pediatric modelling, treating the skull as rigid may prove a poor assumption since the stiffness of bone increases with age (Margulies and Thibault, 2000; Coats and Margulies, 2006). Additionally, in infants the cranial sutures are softer than the cranial bone (Coats and Margulies, 2006), adding compliance to impacts. Neglecting skull deformation is a limitation in

FE modelling, however when used with physical reconstruction methods, the compliance of the skull and scalp is represented by the head form, a vinyl skin in the case of the Hybrid III head form. Moreover, in investigations of sports, there are often helmets being worn, adding significant compliance to the system, which would reduce skull deformation.

The supporting membranes of the cranium help to limit the motion of the brain within the cranium (Ruan et al., 1991; Kumaresan and Radhakrishnan, 1996; Martini, 2006; Marieb and Hoehn, 2007). Though the membranes are a complex biological tissue, they can be represented by a simple elastic model, as shown by McElhaney et al. (1973) who tested samples of dura mater. There is a paucity of published mechanical testing data describing the intracranial membranes so most models have used the data from McElhaney et al. (1973). Though these tests showed evidence of viscoelastic behaviour under different strain rates, many models continue to use an elastic material model for the intracranial membranes. Further, Giordano and Kleiven (2016a) have employed a Mooney-Rivlin hyperelastic model for the dura mater in the scalable PIPER child model.

3.3 Summary

This chapter has summarized brain tissue tests, material models, and the mechanical parameters employed in FE models highlighting the large variance in testing results, as well as application of material properties in FE models. Head impacts are serious events that can cause large deformation of brain tissue, so accurate material modelling for tissues experiencing large strains is important to obtain valid results from finite element models of the brain. Overall, there have been many approaches to characterize brain tissue for adults as well as differences in the way pediatric tissues are treated compared to adult tissues. Current application of FE models of young children have been limited to car crashes, which are unique events when compared to sporting impacts. This project aims to develop a young child model to be loaded with impact parameters typical of sporting-type impacts. In this thesis, physical reconstructions will be used to load the FE model, so a rigid skull will be employed rather than using a deformable skull and simulating the impact events fully.

The material properties for the child model this study were chosen based on three criteria, the strain the tissue underwent, the strain rate tested such that it relates to a viscoelastic response

relevant to concussive injury, and the age-equivalent of the tissue being tested. The tests must have been conducted to a minimum strain value of 0.14, representing 25% risk of concussion of adult American Football Players (Zhang et al., 2004). Tests must also have tested sufficient strain rates to elicit a viscoelastic response relevant to concussive and sub-concussive injury, which lies in a range of 5-40 ms (Zhao et al., 2018). Finally, the tests must have been conducted on subjects near a 6-year-old human age equivalent, provided they satisfied the previous two conditions. A full description of the decision process is presented in Study 1.

4. Finite element modelling of head injuries

Before an FE model is used for brain injury research, it must first be validated with experimental data. With brain models overall, there is relatively little data available for validation, with available metrics of intracranial pressure (Nahum et al., 1977; Trosseille et al., 1992), relative brain skull motion (Hardy et al., 2001; Hardy 2007, Hardy et al., 2007), and skull deformation (Nyquist et al., 1986; Allsop et al., 1988; Yoganandan, 1995). Pressure is related to linear acceleration (Kleiven, 2013), but is not often reported in concussion studies as it contributes little to tissue strain. The strain caused by pressure gradients is smaller than that caused by rotational acceleration (Meaney and Smith, 2011) meaning relative brain skull motion is likely more important to validate FE models with, compared to the pressure response, as the brain motion is related to the tissue strain.

Once validated, brain models can be used for investigations with various loading scenarios such as a simulated environment using FE software such as Abaqus or LS-DYNA (Mao et al., 2013), using kinematic simulation programs such as MADYMO (TASS International) to generate rigid body kinematics of the head from impacts (Post et al., 2014a), or generating head impact velocities to be used for physical reconstructions (Koncan et al., 2017). Pure simulations offer the advantage of full control over all variables, however they require more characterization of materials and surface interactions. Using MADYMO to generate the rigid body kinematics of the head from impacts has a similar limitation to pure simulations, as the response of the body models are driven by the validation data used in their development, shown to have lower impact kinematics compared to physical models (Post et al., 2014a). Using physical reconstructions to generate impact kinematics to drive FE models offers the advantage of matching the impact event in a lab setting, using a head form, matching impacting surface, helmets if required, and not needing to simulate the material interactions. Physical models have limitations as well, as they were designed to withstand many impacts and while the response is reliable, it may not be biofidelic (Post et al., 2012). In sporting impacts, physical reconstructions are used to more accurately represent the impact characteristics than simulations as there are complex material interactions between the head and helmet padding, shell and helmet padding, and shell-shell interactions if the shells are made of multiple parts fitted together as is the case for ice hockey helmets. These interactions are not easily replicated by FE software requiring friction coefficients for each surface pair. Physical reconstructions offer the simplicity of using real-world equipment with a reliable head form to measuring impact kinematics.

4.1 Validation of finite element models of the brain

Validation data for FE models of the brain for intracranial pressure can be done using cadaveric results provided by Nahum et al. (1977) and Trosseille et al. (1992), as well as some impacts from Hardy et al. (2001). The authors used pressure transducers located around the skull so that measures would be available in the coup, and contrecoup regions. Trosseille et al. (1992) also implanted pressure transducers into the ventricles of the cadaver. FE models typically match pressure data well in validation studies (Deck and Willinger, 2009).

For relative brain-skull motion, data from Hardy et al. (2001; 2007) are used for all FE models of the brain. The data were collected using high-speed X-ray systems tracking neutral density targets implanted into the cadaver brains in either a columnar array, or a cluster. The tests done by Hardy et al. (2001; 2007) all involved cadaveric specimens over the age of 52, and were typically low velocity (<4 m/s), as to not risk fracturing the skull given several impacts were collected on each specimen and set-up time was extensive. Due to the difficulties in conducting cadaver research, many impacts showed significant noise in the recorded kinematic signals, and some targets were not visible throughout all impacts. Despite the limitations, the data set represents the largest and most important validation data set for FE models of the brain.

For FE models of the brain that include deformable skulls, skull impacts and deformation data are important steps to validate the models. Yoganandan (1995) collected force-deflection and rupture data for cadaver impacts, Nyquist et al., (1986) conducted facial impacts with a 32 and 64 kg cylindrical impactor, and Allsop et al. (1988) also conducted facial impacts to the frontal, zygomatic, and maxillary regions. Both Nyquist et al. (1986), and Allsop et al. (1988) found that dummy models like the Hybrid III (vinyl skin over aluminum skull) require alterations to obtain accurate force and acceleration data, and also provided cadaveric skull deformation data for FE models. Skull stiffness is an important parameter, and physical models have attempted to mimic the response but end up too stiff, likely to prevent damage and the need for reliable responses. The stiffness of physical models, such as the Hybrid III, is a limitation when conducting physical reconstructions of short impact duration events, however as more compliance is added to the system the differences between a human and the physical model will diminish.

Low grade head motions have been conducted on human participants by Bayly et al. (2005), using a system originally designed to measure cardiac deformation. High-speed MRI methods were used, with accelerations from occipital impacts ranging from ~2-3 g, with an estimated strain response of 0.02-0.05. These present a good low-severity impact comparison, but cadavers remain the only comparison for higher severity impacts.

Intracranial measures are still lacking in youth, however Loyd (2011) conducted drop tests and quasi-static skull compressions on cadavers ranging from 20 weeks gestation to 16 years old, in addition to tests on adult cadavers and different dummy head forms. The study found that skull stiffness changes with age, assessing age groups of neonate (< 1 month), toddlers (5-11 months), youth (9-16 years), and adults (18+ years). While the study adds a lot of valuable data for validation purposes of FE models, there are still no intracranial measures to compare against, which is a limitation of pediatric brain modelling.

4.2 Reconstruction methods to drive FE models

In general, there are three main ways to load models: pure simulations conducted entirely in the FE software environment, simulations using other programs such as MADYMO to obtain the rigid body kinematics from impacts, and physical reconstructions with instrumented head forms. These methods will be discussed in the following sections.

4.2.1 Simulation reconstruction methods

With the ever-growing computational power of personal computers, not only are simulation study numbers increasing, they are also increasing in complexity. Full kinematics and brain response to impacts can be simulated in much less time than previously, with highly complex interactions and material models. To run a brain model to obtain a strain response, two methods can be used to simulate the event: an impact simulation can be conducted assigning the head or object an initial velocity and simulating contact between the two appropriately characterized bodies, or the three dimensional head impact kinematics can be simulated, and then assigned to the skull of the brain model as a second simulation.

Head impacts can be fully simulated in a single software environment such as Abaqus (Dassault Systèmes) or LS-DYNA (Livermore Software Technology Corporation)

demonstrated by Mao et al. (2013). So long as all materials are properly characterized, and interactions and frictional properties are well defined, the events can be reconstructed virtually. Many physical tests are normally required to properly characterize materials and interactions. Car crash investigations have used full simulation environments to assess probability of injury (Cui et al., 2015; Giordano et al., 2017a), and offer flexibility of determining occupant safety in different situations without prototyping or crash testing. Many different aspects of vehicle safety can then be tested for flaws prior to physical tests that are required to pass safety standards.

Head kinematics from impacts can be simulated using MADYMO (TASS International). The program uses pedestrian models that can be assigned initial and boundary conditions specific to a fall or impact event to simulate the fall or impact kinematics. These simulations can be used to reconstruct the event as described by witnesses or video data (McIntosh et al., 2014), or to obtain head impact kinematics that can then be evaluated and further processed by inputting them into an FE model of the brain (Patton et al., 2015). MADYMO simulations can also provide metrics such as head impact velocity, to be further used in physical reconstructions to generate impact kinematics to load the brain model (Koncan et al., 2016; Koncan et al., 2017; Post et al., 2017a; Post et al., 2017b). Simulation reconstructions are a popular alternative to physical reconstructions, although care must be taken on their interpretation as the simulation can only be as accurate as the validation and input data that supports it. Full simulation reconstructions will not be conducted in this thesis, instead the studies will rely on kinematic simulations to establish head impact velocity which will then be used to conduct physical reconstructions.

4.2.2 Physical reconstruction methods

In general, sporting impacts can be characterized into four main groups: falls, collisions, projectile impacts, and punches, each with unique impact characteristics (Kendall, 2016). Falls can be simple to reconstruct since the main parameters required are the height of the fall, impact location, and the impacting surface. Collisions require accurate representation of the impact mass, which depends on the colliding body segments (elbow, shoulder, knee, hip etc.), in addition to correct velocity and location. Projectiles are normally low mass but have large ranges of possible velocity and it must be measured accurately to properly reconstruct impact events. Punches are normally illegal in sports, with the exception of boxing and mixed martial arts, and

require an accurate impact mass, velocity, and location. To reconstruct the four main impact events of falls, collisions, projectiles, and punches requires different equipment. This thesis will only include fall data, and so a description of fall reconstruction equipment and methods follows. Equipment for other impact events will not be described.

A monorail drop rig is commonly used to conduct physical reconstructions of falls. The head form is connected to a carriage which is then attached to the monorail, which guides the head form to hit the anvil at the bottom. With the monorail, a neck form can be attached to the head form, or a free drop can be conducted. A monorail drop set up using a Hybrid III 50th percentile male head and neck form impacting a 1" MEP anvil is shown in Figure 7. The monorail drop rig allows the head form to be positioned to hit the appropriate impact site, at a specified velocity, onto the specified impact surface. Worldwide, falls account for over 20% of documented head injuries (O'Riordain et al., 2003), and in children, one study reported that falls accounted for over 50% of concussive injuries (Browne and Lam, 2005). The monorail drop rig has been used in numerous helmet investigations and head injury studies of sports impacts in adults (Willinger and Baumgartner, 2003; Kendall et al., 2012; Post, 2013; Post et al., 2014b; Bonin et al., 2016), as well as some for youth (Koncan et al., 2016; Koncan et al., 2017). This thesis will focus on fall events, since it is a common event that causes head injury. The monorail drop rig will be used for all impacts and data collection for this thesis.

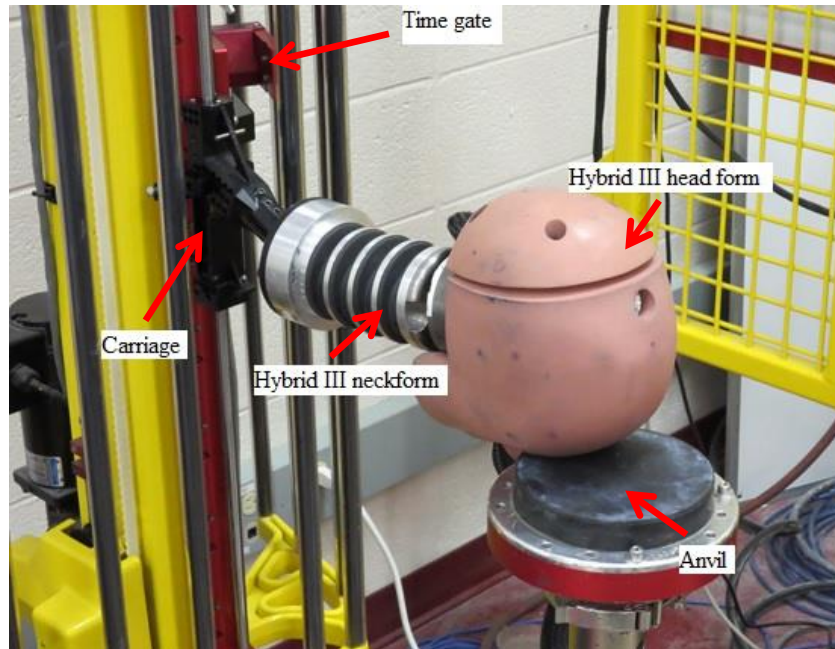


Figure 7. Example of a monorail drop test set-up using a Hybrid III headform and neckform, impacting an MEP anvil

4.3 Finite element modelling of adult brain injury

Adult brain FE models have been in use for over 20 years, starting with 2-dimensional brain models (Ruan et al., 1991; Gilchrist et al., 2001), giving way to 3-dimensional models (Willinger et al., 1999; Zhang et al., 2001a; Kleiven and von Holst, 2002; Horgan and Gilchrist, 2003), leading to more recent models with higher mesh density, directional response of white matter, hyperelastic viscoelastic material models, or combinations thereof (Kimpura et al., 2006; Takhoumts et al., 2008; McAllister et al., 2012; Mao et al., 2013; Sahoo et al., 2014; Giordano et al., 2017b). Using these models, there are many published reconstructions of adult head impacts resulting in no injury, concussive injuries, diffuse axonal injury (DAI), as well as traumatic brain injuries. These have been done using physical reconstructions as well as simulations using MADYMO.

When studies include cases resulting in no head injury, they are used to calculate logistic regression curves to estimate risk of specific injuries based on metrics from an FE model. The most common metrics used for calculating risk are maximum principal strain, and the cumulative strain damage measure (CSDM), though rate dependent metrics of strain rate or the product of strain and strain rate are also presented in some studies. Maximum principal strain has been used

to calculate risk of concussive injury (Kleiven, 2007; Kimpapa and Iwamoto, 2012; Patton et al., 2012) and DAI (Takhounts et al., 2003; Deck and Willinger, 2009). The CSDM measure can be calculated at various strains, as it is the volume fraction of brain tissue experiencing strain over a set threshold (e.g. 0.05, 0.10, 0.15, and 0.20) during the impact simulation. The cumulative strain damage measure has been used at differing levels for predicting risk of head injuries such as CSDM10 for concussion (Kleiven, 2007; Kimpapa and Iwamoto, 2012), CSDM15 and CSDM25 for DAI (Takhounts et al., 2003; Takhounts et al., 2008). Strain rate and the product of strain and strain rate have been used in several studies (King et al., 2003; Zhang et al., 2004; Ji et al., 2014; Patton et al., 2015), but are not as widely presented. A summary of concussion reconstruction data and risk of concussive injury in adults is presented below in Table 5.

Several studies have conducted reconstructions of concussive or other brain injuries associated with various strain metrics (Takhounts et al., 2003; Zhang et al., 2004; Viano et al., 2005; Kleiven, 2007; Deck and Willinger, 2008; McAllister et al., 2012; Kimpapa and Iwamoto, 2012; Patton et al., 2012; Oeur et al., 2015; Post et al., 2015). A summary of FE responses relating to concussive risk from injury reconstructions is shown below in Table 5. Much of the data that has been used to investigate concussion in adults comes from a study of the NFL conducted by Pellman et al. (2003), who reconstructed both concussive and non-injurious impacts, that were then shared with other research groups, and further analyzed in another study by Viano et al. (2005) where FE modelling was conducted as well. Professional contact sports typically offer a high-quality data source for investigating concussion, as there is good video data to draw on, and published injury reports. Similar to the study by Pellman et al. (2003), video analysis of professional sports was conducted by Patton et al. (2012), instead investigating unhelmeted head impacts from Australian rules football, rugby union, and rugby league.

Table 5. Summary of finite element model metrics associated with risk of concussive injury from reconstructions of injury events

Brain Region	Value	Strain variable	Author(s)
Grey matter	0.26 (50% risk)	MPS	Kleiven (2007)
Grey matter	0.48 (average)	MPS	Post et al. (2013)
White matter	0.26 (50% risk)	MPS	Patton et al. (2015)
White matter	0.38 (average)	MPS	Post et al. (2013)
Corpus callosum	0.15 (50% risk)	MPS	Patton et al. (2015)
Corpus callosum	0.21 (50% risk)	MPS	Kleiven (2007)
Corpus callosum	0.28 (average)	MPS	McAllister et al. (2012)
Midbrain	0.15 (50% risk)	MPS	Patton et al. (2015)
Midbrain	0.34 (average)	MPS	Viano et al. (2005)
Cerebrum	0.32 (average)	MPS	Viano et al. (2005)
-	0.44 (average)	MPS	Oeur et al. (2015)
-	0.32 (50% risk)	MPS	Kimpara and Iwamoto (2012)
-	0.31 (50% risk mild DAI)	MPS	Deck and Willinger (2008)
Midbrain	0.19 (50% risk)	Shear strain	Zhang et al. (2004)
-	0.32 (50% risk)	Shear strain	Kimpara and Iwamoto (2012)
-	0.60 (50% risk)	CSDM10	Kleiven (2007)
-	0.18 (50% risk)	CSDM10	Kimpara and Iwamoto (2012)
-	0.55 (50% risk of DAI)	CSDM15	Takhounts et al. (2003)

MPS: Maximum principal strain

CSDM: Cumulative strain damage measure

From the published data in the Table 5, maximum principal strains in the cerebrum representing 50% risk of concussion in adults ranged from 0.15-0.32, with average values from concussive cases ranging from 0.32-0.48. These strains are lower than previously published literature involving traumatic brain injuries by Doorly (2007), where cases averaged maximum principal strains of 0.60, or those by Post (2013), where cases averaged maximum principal strains of 0.81. Since several models were used in the studies listed above, results should not be directly compared (Ji et al., 2014). Care should be taken in interpreting values from different models because differences in material models, as well as discretization differences, influence the final result. Despite these differences, there is some general agreement regarding strains associated with concussive injury when using different FE models, with strains of ~0.25-0.35 encompassing many average values or values representing 50% risk of concussive injury.

In addition to the studies summarized above, other investigations of head injury have been conducted that did not present strain values. Kang et al. (1997) reconstructed a motorcycle crash simulation and found von Mises stress to correlate well with locations of neurological

lesions. The study was expanded on by Willinger and Baumgartner (2003), adding pedestrian falls as well as concussions from American football, and calculated a 50% risk of concussion associated with 18 kPa von Mises stress. Results from Patton et al. (2015) are similar, with 15.1 kPa associated with 50% risk of concussion from reconstructions of unhelmeted head impacts. Compared to two other studies by Kleiven (2007) and Zhang et al. (2004) where 50% risk of concussion was associated with von Mises stresses of 8.4 kPa and 7.8 kPa respectively, the impacts from Patton et al. (2015) and Willinger and Baumgartner (2003) were much higher, likely because they included higher energy impacts (motorcycle crash), or were unhelmeted impacts. As documented by Kendall (2016), non-compliant impacts resulting in concussions yielded higher strains than compliant impacts, offering an explanation as to why the results from Patton et al. (2003) and Willinger and Baumgartner (2003) are larger than those from strictly helmeted American football impacts by Kleiven (2007) and Zhang et al. (2004).

4.3.1 Tissue models of concussion

Finite element studies offer the advantage of being able to analyze representations of local deformations of brain tissue under loading, which is the cause of concussive injury (King et al., 2003). Finite element models of the brain allow for tissue level investigations, which complement real nervous system tissue tests, to draw parallels in strains that cause injury in real tissue compared to simulated strain values. Researchers have tested nervous tissue to find thresholds to functional injury (Bain and Meaney, 2000), mechanical failure (Hrapko et al., 2006), effects of strain and strain rate on cell damage and death (Morrison et al., 2003), and thresholds causing cell death (Cater et al., 2006). Neural tissue studies examining the function of neurons under mechanical loading have yielded similar results for what strain levels brain tissue can handle before losing functional capability, or sustaining irreparable damage. Bain and Meaney (2000) found no injury for 0.14 strain of the optic nerves of guinea pigs, and calculated an “optimal” threshold for functional impairment at 0.18 strain. Maxwell et al. (1997), reported strains of 0.15 causing disruption of the axon, with strains over 0.20 capable of causing membrane fragmentation and damage. Morrison et al. (2003) found no injury for 0.10 strain at varying strain rates relevant to head impacts, but strains above 0.20 showed cell injury, with more cell death at increasing strain rates. This study showed similar results to tests on squid axons by Galbraith et al. (1993), where strains over 0.20 caused irreversible injury. Neural tissue

tests suggest that near 0.20 strain, functional impairment of nervous tissue will occur, with further strains more likely to cause damage that is increased at higher strain rates, possibly causing cell death. Stress of the brain tissue was not investigated in the animal models of concussion.

The values from tissue tests are valuable to establish a tissue level injury threshold, however there are more influential factors that can limit some comparisons between FE responses and tissue tests. First, the validation of the model and the material properties are highly influential in the resulting strain response. Secondly, Kendall (2016) showed that the event that causes the concussive injury affects resulting strains. With variance in strains causing concussive injury from an FE model from different events (collisions, helmeted falls, unhelmeted falls, punches), it is difficult to establish a single value associated with concussive risk.

4.4 Finite element modelling of pediatric brain injury

Investigations involving children and adolescents can be quite difficult because descriptions of the events are not always available. Roth et al., (2009) excluded cases where the event description was only provided by the child's caretaker due to their stressed behaviour possibly creating a likelihood for misrepresentation of the accident event. Additionally, when impacts occur the event is not always witnessed by another person, or recollections of the event are insufficiently detailed to do a proper event reconstruction. Unlike adult professional sports, for children there is rarely quality video footage to confirm details such as impact velocity or impact location more accurately than a general sense of front, side, or rear of the head for collision events. Falls can be simpler to reconstruct since in many cases, people faint or lose their balance and fall a total distance equal to their height, an easily obtainable parameter. The location of impact can also be identified from the swelling or abrasion caused by the impact, not always apparent from collisions, especially if helmets and padding are involved. Despite the difficulties with studying the pediatric population, finite element modelling of pediatrics has grown in the last decade, attempting to overcome the limitations of studying this age group.

4.4.1 Finite element modelling of infants and toddlers

In older studies, authors have investigated different age-related effects regarding brain tissue properties, cranial sutures, and cranial bone properties (Thibault and Margulies, 1998;

Gefen et al., 2003; Margulies and Thibault, 2000; Prange and Margulies, 2002; Coats and Margulies, 2006), that led to the capability of building FE models of the head. In addition to these material tests, two studies have published skull compression data (Prange et al., 2004; Loyd, 2011), allowing authors to partially validate their models with pediatric data. The skull compression tests do allow for a limited level of validation for simulated impact environments that is crucial for many modelling efforts. Currently there are no studies of children that have investigated brain displacement and relative brain-skull motion as reported by Hardy et al. (2001) on adult cadavers.

The first 3D pediatric model of an infant was developed by Lapeer and Prager (2001), assessing skull deformations during birth. This model did not include the brain as it was designed only for skull deformations when subjected to intra-uterine pressures. Following this study, Klinich et al. (2002) created a 3D model and conducted a parametric study to assess the influence of material properties on stress and strain in the infant skull for car impacts. The model by Klinich et al. (2002) simulated a 6 month old child and combined both human adult material properties as well as pediatric porcine material properties reported in the literature. There have since been more models developed, covering a larger age range from infants to a 3-year-old child. Two models cover an age range of 8-90 days old (Roth et al, 2010; Li et al., 2011), two models cover 6 month old infants (Roth et al., 2007; Li et al., 2013), and one model covers 3 year-olds (Roth et al., 2009). The investigations of each of the models have varied in purpose with comparisons between shaking and impacts (Roth et al., 2007), and influential parameters such as surface stiffness and drop height on head dynamic response (Li et al., 2013), to analyses on skull fracture from real world head trauma (Roth et al., 2010). For infants, many investigations are focused on abuse related cases.

4.4.2 Finite element modelling of young children

Two studies employed MADYMO to simulate head impact kinematics to load FE models for fall events (Doorly and Gilchrist, 2006; Roth et al., 2009). A series of 25 falls were simulated by Roth et al. (2009), for both injury and non-injury cases of 3-year-old children. These simulations found that von Mises stress was the best predictor of injury, though the study included moderate neurological injuries (2 AIS scale), as well as severe neurological injuries (>3 AIS scale), which are more severe injuries than those investigated in this thesis. Doorly and

Gilchrist (2006) analyzed a single case of an 11-year-old boy fainting. The study used a scaled version of the UCDBTM to match the proper head size and weight, rather than developing a new model. More recently, efforts in pediatric modelling have advanced, with a published FE model of a 6-year-old child (Cui et al., 2015), and a continuously scalable model from 1.5-6-years-old (Giordano and Kleiven, 2016a). These models have been used for car crash investigations (Cui et al., 2015; Giordano et al., 2017a), simulating the entire crash environment. Car crash events differ significantly from sporting type impacts, with acceleration traces from Giordano et al. (2017a) lasting over 100 ms. In sporting type impacts, the majority of impact duration lies within 5-30 ms (Hoshizaki et al., 2016). Given the viscoelastic nature of the brain, the different time scales are important when assessing the strain response of the brain (Zhao et al., 2018).

While the use of scaled adult FE models to study youth has its drawbacks and limitations, it is one method to study concussion in young children. In a study of youth ice hockey, Koncan et al. (2017) found that despite the lower impact velocities experienced in a game, all impacts to the ice and boards showed high enough brain strain values from a scaled model to suggest reasonable risk of concussive injury based on adult risk data. For concussive events in children, there was a Canada-wide data collection, drawing from pediatric emergency departments for children presenting with concussion between the ages of 5-18 years old with aims to find predictors of persistent post-concussive symptoms (Zemek et al., 2016). A subset of cases that had sufficient case descriptions were then reconstructed in the laboratory using different size head forms to represent the different ages, and were then modelled using a scaled FE model of the brain (Post et al., 2017a; Post et al., 2017b). The aim of the later studies was to investigate whether biomechanical variables predicted persistence of symptoms (Post et al., 2017a), or if they can distinguish between those with or without a history of previous concussions (Post et al., 2017b). These studies presented a large number of cases of concussive injuries for a population without many data sets for comparison. A smaller subset of the data was previously used by Dawson (2016) to analyze biomechanical metrics for young children, adolescents, and compared to adults from a subset of previously published cases of concussion with persistent symptoms by Post et al. (2015). The results showed that young children were experiencing concussive injury at lower levels of all metrics examined, though not all differences were statistically significant. The results from the brain model however should be interpreted with care, as a scaled model was used without modification to address specific age-dependent characteristics of geometry, grey

and white matter development, and material properties. This thesis will build on the results from Dawson (2016), to assess how influential these parameters are for concussive injuries in young children with a newly developed FE model of a 6-year-old child.

4.5 Summary

Finite element modelling continues to grow as a method for studying brain injury, and as more data for validating models is published their validity should improve. A lack of validation data is still the most prominent limitation for FE models, with minimal published adult data, and no intracranial data for children and adolescents. Finite element models are an important tool for investigating brain injury and concussions as they provide a representation of local tissue responses. Though the results require interpretation to be placed within the literature, they remain a valuable tool, capable of investigating many different metrics for correlation and injury prediction. At the current level of development, FE model responses typically show strains that are higher than tissue models of concussion would suggest.

This thesis aims to assess how the mechanical response of the brain in young children near 6 years old differs from an adult brain in cases resulting in concussive injury. To answer this question, this work will cover the creation of a valid FE model to answer how age affects the strain response in the brain from concussive events, with impact parameters characteristic of sport impacts.

PART III - STUDIES

Study 1 - A 3D finite element model of a 6-year-old child for simulating brain response from physical reconstructions of head impacts

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Abstract

Despite young children being a high-risk population for sustaining concussive injuries in sport, there are few studies investigating head impact biomechanics from sporting impacts using physical models and finite element models of the brain. Physical reconstructions are often used in concussive research, using the recorded kinematics to load finite element models of the brain to obtain better information of real-life head injuries. For children, scaling adult models is a common method used to study the youth population, however this does not capture age-dependent material properties, or the unique geometry of the developing brain. To address this, a novel 3D finite element model of a 6-year-old child was developed and compared against a scaled adult model, for use with physical reconstructions. With the lack of intracranial validation data for the youth population, adult cadaveric data for brain motion was used for comparison. The new brain model showed unique responses in motion and strain compared to the scaled adult model. Using the Normalized Integral Square Error method, the new model was classified to have “fair” to “excellent” biofidelity. The new model is proposed as more appropriate for conducting concussion and brain injury research in young children near 6 years of age.

Introduction

Children are particularly vulnerable to concussive injuries compared to adults,¹ as well as at risk for persistent symptoms long after the initial injury.^{1,2} General and localized trauma or strain in the brain has been reported as the cause of concussive injury.³⁻⁷ Finite element (FE) models of the brain provide a means to measure the brain response to head impacts, enabling investigations of the tissue response rather than solely relying on impact kinematics of the head. Mainly two methods are used to obtain tissue responses, pure impact simulations, and physical reconstructions paired with FE models using recorded impact kinematics to load the FE models. Physical reconstructions require accurate parameters of impact mass, velocity, location, as well as the surface compliance, where FE models require fully characterized material responses, geometric interactions, contact definitions, and impactor stiffness interactions. Physical reconstructions and FE models have been used extensively in investigations of adult concussive events, as well as the parameters that influence.⁶⁻¹⁵ Hundreds of published impact reconstructions have been undertaken with the University College Dublin Brain Trauma Model (UCDBTM),^{16,17} encompassing injury and non-injury events for helmeted and un-helmeted falls, motorcycle

accidents, body-to-head collisions, head-to-head collisions, and mixed martial arts punches.¹⁸ Studies have also included individual and multiple impact parameters (mass, velocity, location, compliance) together and in isolation,¹⁹⁻²¹ providing an extensive reference database for the Dublin model for sport impact events. In children, research involving concussions, impact parameters, and FE modelling is limited, even though children are at increased risk for concussion, prolonged recovery, and repeat concussive injury when compared to adults.¹

While FE models of infants up to the age of 3 years old have been developed,²²⁻²⁷ there are fewer models of children over the age of 3 years old. Two FE models have been developed for use for young children, the PIPER model,²⁸ which is a scalable model for ages 1.5- to 6-years-old and another by Cui et al.,²⁹ of a 6-year-old child. Both of these models have been developed and used to simulate car crash scenarios.^{29,30} Head impacts from car crashes are unique when compared to those experienced in sports settings (falls, collisions with people, collisions with objects), crashes and primarily involve high velocity impacts to the padded interior of the car or air bags. Hoshizaki et al. described impact kinematics from different events in the literature, reporting that most sporting impacts lie within 5-30 ms in impact duration.¹⁸ Car crash simulations have showed acceleration curves for the head longer than 100 ms in duration,³⁰ differing greatly from sports and recreational events. FE models are dependent on reference data from real-life events in order to accurately interpret the values obtained by that specific model. While there are two published, sophisticated 6-year-old models, the large reference data for sports impacts available using the UCDBTM provides an important advantage when interpreting the meaning of the results. Unique characteristics of the models and dynamic differences in sports impacts and car crashes limit the value in using one reference set to interpret results from the other. Usefulness of FE models is increased by having a large reference data set for the specific head impacts under study, allowing for better interpretation of data.

Though there is a wealth of published data from the UCDBTM for sports impacts in adults, there is limited data for youth, where an FE model was scaled to better represent the age groups.³¹⁻³⁵ While size is influential on the brain's response,³⁶ how the brain deforms in a child is age-dependent, based on characteristics such as the mechanical properties of the brain,^{37,38} and the distribution of grey and white matter in the brain.^{39,40} The different mechanical properties create a unique response in the brain specific to young children, with different patterns and

magnitudes of strain. FE models can be used to assess these characteristics and their influence on brain response. With an estimated 750,000 annual visits to emergency departments for pediatric concussion in the United States,^{1,41} brain injuries remain a cause for concern in children. At the age of 6, children are starting to engage in organized sports programs, where participants experience head impacts from falls and collisions with other players. The forces that are transmitted to the brain from these head impacts result in strain on the underlying tissues.

To create a FE model for studying sporting impacts and concussion in young children, the model requires age-appropriate material properties, as well as distributions of grey and white matter, which have been documented to remodel well into the 3rd decade of life.^{39,40} As a result, medical images are required since the mechanical response could differ as different neural pathways develop. It is unknown if children are more susceptible to brain injuries such as concussion. A more specific FE model will help understand how tissue trauma is created and allow further understanding into whether children are more or less susceptible to strain based brain injuries. Using an established model with large and wide ranging published reference data sets for interpretation will provide a means of demonstrating how responses of a new model for youth differs from scaled models, and the importance of these differences.

This study presents a novel FE model developed specifically for children around 6 years of age to be used alongside physical models to investigate concussive injuries. This study compares the newly created FE model of a 6-year-old child with a scaled version of the UCDBTM, using adult experimental data to partially validate the model response.

Methods

Model creation/geometry

A 6-year-old FE model was developed by extracting geometric information from magnetic resonance images of a 6-year-old child. Multiplanar MRI of the head was obtained using a 3.0 tesla magnet and the sliced images had a spacing of 0.8 mm in each axis. Segmentation of the MRI was done using Mimics software (Materialise, USA), based on automatic grayscale thresholding methods, creating masks representing the grey matter, white matter, ventricles, brainstem and cerebellum, cerebrospinal fluid, and skull. The masks were manually edited to ensure accuracy of contours to a 3-pixel level of accuracy for contours

between different tissues (2.4 mm deviation maximum). The intracranial membranes were thinner than the resolution of the MRI, so exact masks were not completed. Instead, regions of CSF near these membranes were expanded from the representation shown on the MRI to accommodate a consistent 3 mm layer of CSF (expanded from 1.5-2.5 mm), which is consistent with the size used in previous FE models of the brain.^{16,42} The lack of MR data in the facial region precluded discretizing the facial bones in the model, therefore the inner surface of the skull is represented as well as the occipital condyles, used for centre of gravity (COG) translation described later.

The masks were then exported into Hypermesh 2017 (Altair, USA) to create the FE model mesh. The masks were used to define the boundaries of each type of tissue, creating a surface mesh with full nodal connectivity. The intracranial membranes were then defined using a mid-surface operation between the two cerebral hemispheres, and between the cerebellum and the cerebral hemispheres following points where the membranes were visible to create surfaces representing the tentorium and falx. Each surface was then meshed with a target size ranging between 4-6 mm using triangle elements. The target element size was smaller in thin sections (near the tentorium and falx or thin folds of the white matter) to facilitate creating a quality volume mesh, and a highly accurate representation of the complex contours of the white matter in the brain, which is a difficulty when using quad and brick elements. The maximum target element size of 6 mm maintained geometric complexity but reduced the overall number of elements. The new 6-year-old model is shown in Figure S1- 1 beside a scaled adult model, the UCDBTM, highlighting differences in the number of elements and white matter representation.

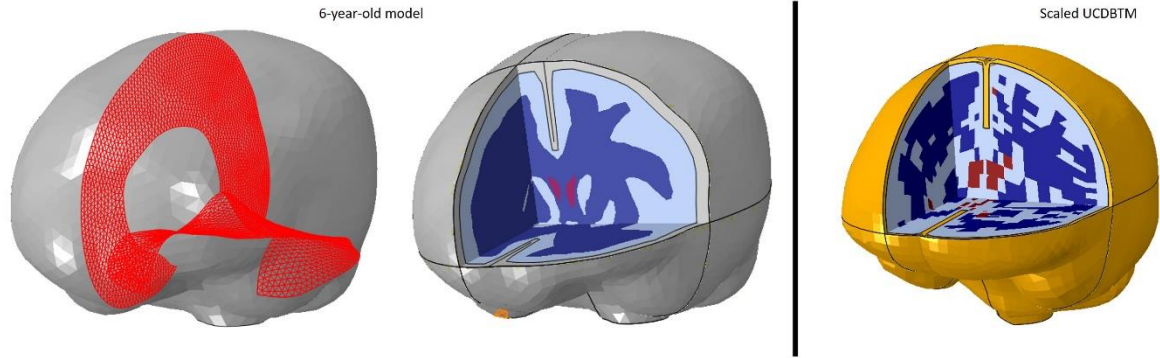


Figure S1- 1. Views of the new 6-year-old model (top), showing from left to right, the whole model, the brain matter with tentorium and falx highlighted, a coronal section of the white matter. On the bottom, the scaled UCDBTM, showing the whole model on the left, and a coronal section of the white matter on the right.

The surface mesh was then assessed for quality measures of aspect ratio and length, with limits of 5.0 and 1.2 mm respectively. A tetrahedral volume mesh was then constructed from the surface meshes, creating element sets representing each region of the head (skull, CSF, brainstem, cerebellum, grey matter, white matter, ventricles, tentorium, falx, and pia). The mesh contained a total of 148,562 nodes making 169,849 elements, with all structures tied together in a continuous mesh, including the brain-CSF interface. The model employed 1st order shell elements (skull), 1st order membrane elements (pia, falx, tentorium), and 2nd order tetrahedral elements (brain tissue, CSF). 2nd order tetrahedral elements were used to reduce the required mesh density as 1st order tetrahedral meshes can require a high mesh density to produce an accurate response and can also suffer from volumetric locking in near incompressible cases (Dassault Systèmes, 2014). Simulations were run using Abaqus 6.14 software, using an explicit-dynamic solver (Dassault Systèmes, 2014).

The use of a single MRI image to create a FE model of the brain has been published previously in the development of FE models.^{6,16,42} The limitation of this approach involves the model may not represent all individuals of the age-group and is an acknowledged limitation of FE brain models.

Because there was no data in the facial region of the MRI, an accurate COG of the child head could not be discerned. As a result, the COG was assigned following published average

inertial properties of pediatric heads from a CT imaging study.⁴³ The study determined the COG location of pediatric heads with respect to the occipital condyles. Using the measurements from the occipital condyles of the pediatric heads, the model COG was calculated from average properties of 6-year-old children. The difference between the model COG (brain and interior skull surface only) and the calculated COG using measurements from Loyd et al.⁴³ amounted to 1.47 mm anterior, 3.75 mm laterally, and 14.51 mm inferior to the model COG. The difference in COG location is attributable to the inclusion of the facial structure in the CT study, as well as individual variation. It was reasoned that the calculated COG using data from Loyd et al.⁴³ is more representative for running the model. The new 6-year-old model is 179 mm long, and 145 mm wide, and is within 1 standard deviation of average length (185 mm), and is equal to the average width of 6-year-old children (145mm).⁴³

Tissue properties

There is little agreement on the mechanical behaviour of brain tissue, as studies have been conducted over several decades, with results spanning several orders of magnitude.^{44,45} Brain tissue studies are divided in results and have reported the youth brain being stiffer,³⁸ more compliant,⁴⁶ as well as stiffer only once strain exceeds 2.5%.³⁷ Rapid changes in brain material properties have also been reported to exist up to roughly 2-years of age but no significant change occurs after.⁴⁷ In a magnetic resonance elastography (MRE) study of adults aged 18-88, Sack et al.⁴⁸ reported a decrease in shear moduli of the brain tissue with increasing age. If one extrapolated this relationship to youth brain tissue, it would be stiffer than adult tissue. Following this trend, this study will employ stiffer material properties than adults, following Gefen et al.³⁸ who found youth to have stiffer brain tissue, and Prange and Margulies³⁷, with stiffer tissue after exceeding 2.5% strain. In general, different testing conditions, testing methods, and different species being tested are all contributors in the variance of published data.⁴⁵ It is undefined what material properties are most suitable for use in a 6-year-old brain model for use in sports impact research, and is a limitation of the field of research.

The material properties in this study were chosen based on three criteria, the strain the tissue underwent, the strain rate tested such that it relates to a viscoelastic response relevant to concussive injury, and the age-equivalent of the tissue being tested. Tissue must have underwent a strain of 0.13, the lowest strain value associated with 50% risk of concussion from

reconstructions of adult Australian football and rugby leagues, which showed concussive risk at strains of 0.13-0.26 in different regions of the brain.⁴⁹ Previous impact reconstructions of concussive injury in children aged 5-17 averaged strains over 0.30,³⁵ so it should be expected that large strains will result from the sports impact modelling of children. Also, a sufficient strain rate is required to elicit a viscoelastic response relevant to concussive and sub-concussive injury, which lies in a range of 5-40 ms.⁵⁰ To address age-appropriate material properties, a study that tested subjects near a 6-year-old human age equivalent was chosen.

Shear properties were applied from MacManus et al.,⁵¹ a set of indentation tests conducted on porcine brain tissue equivalent to an adolescent human age that tested up to 65% strain, yielding a shear modulus of 6.97 ± 2.26 kPa. Two different sets of material properties were run for the model, the published average shear modulus of 6.97 kPa (hereafter termed the average model), and a shear modulus increased by two standard deviations, to a value of 11.49 kPa (hereafter termed the stiff model). The stiff model was run in support of the argument that youth have stiffer brain tissue compared to adults. Additionally, running these two material models will show the influence of the shear modulus within the range of values similar to adult models. With the UCDBTM being the comparable model in this study, 11.49 kPa is ~15% stiffer than the 10 kPa shear modulus of grey matter in the brain used by the UCDBTM and other models.^{16,42} Shear moduli were adapted from the grey matter value similarly to the UCDBTM and Wayne State University Brain Trauma Model, using a 25% higher shear modulus for the white matter, and 80% stiffer shear modulus for the brainstem. The 25% higher shear modulus for white matter was to account for the fibrous nature of the white matter.⁴² This assumption is supported by MRE studies, finding white matter to be 1.2-2.6 times stiffer than grey matter.^{44,52,53} Using an 80% stiffer shear modulus for the brainstem is from Arbogast and Margulies,⁵⁴ where tests of a porcine brain revealed the brainstem to be 80-100% stiffer than the cerebral white matter. Material properties are shown for the models below in Table S1- 1, Table S1- 2, and Table S1- 3, with material properties of the brain for the UCDBTM shown in the appendix in Table S1- 8, which were not altered.

The Ogden form of the hyperelastic strain energy function was used to model the brain tissue in this model as it has been suggested for use in higher strain applications.^{51,55} In Abaqus,

the Ogden strain energy potential is expressed in terms of principal stretches, with the formulation below in Eq. (1):

$$U \stackrel{\text{def}}{=} \sum_{i=1}^N \frac{2\mu_i}{\alpha_i^2} (\bar{\lambda}_1^{\alpha_i} + \bar{\lambda}_2^{\alpha_i} + \bar{\lambda}_3^{\alpha_i} - 3) + \sum_{i=1}^N \frac{1}{D_i} (J_{el})^{2i} \quad (1)$$

where

$$\bar{\lambda} = J^{-\frac{1}{3}} \lambda_i \rightarrow \bar{\lambda}_1 \bar{\lambda}_2 \bar{\lambda}_3 = 1$$

The viscoelastic response is characterized by an N-term Prony series:

$$\mu(t) = \mu_0 \times \left(1 - \sum_{i=1}^N g_i (1 - e^{-t/\tau_i}) \right)$$

where μ_0 is the initial shear modulus, and g_i , τ_i , and α_i are material constants. The Ogden material constant α was taken from MacManus et al.⁵⁶ for *in situ* measurements of the cortex of the mouse brain at the highest strain rate tested (4.28 mm/s indentation velocity, equating to a strain rate over 10/s), and viscoelastic parameters were taken from MacManus et al.,⁵⁷ from indentations of the porcine cortex. Two viscoelastic time constants were calculated from MacManus et al.,⁵⁷ one short and long term, with the short term constant being 21 ms, in the middle of durations relevant to sports impacts and concussion.^{18,50} The Ogden hyperelastic model has been reported to accurately predict the response of brain tissue,^{55,58-61} and used in other brain models,^{6,28} and so was used in this study.

Table S1- 1. Proposed material properties for tissues in the new 6-year-old model

Material	Young's modulus (MPa)	Poisson's ratio	Density (kg/m ³)
Skull	Rigid		2000
Pia	11.5	0.45	1130
Falx and Tentorium	31.5	0.45	1130
Brain	Hyperelastic	~0.5	1060
CSF	0.015	~0.5	1000

Table S1- 2. Material properties of the brain for the stiff model, with increases in shear moduli from properties published by MacManus et al.^{51,56,57}

	Initial shear modulus (kPa)	Ogden material constant α	Viscoelastic parameters				
			g_1	τ_1 (s)	g_2	τ_2 (s)	g_∞
Grey matter	11.5						
White matter	14.4	0.59	0.451	0.021	0.301	0.199	0.249
Brain stem	25.9						
Cerebellum	11.5						

Table S1- 3. Material properties of the brain for the average model, with shear moduli from properties published by MacManus et al.^{51,56,57}

	Initial shear modulus (kPa)	Ogden material constant α	Viscoelastic parameters				
			g_1	τ_1 (s)	g_2	τ_2 (s)	g_∞
Grey matter	6.97						
White matter	8.71	0.59	0.451	0.021	0.301	0.199	0.249
Brain stem	15.68						
Cerebellum	6.97						

The bulk modulus of the brain tissue was assumed to be $10000 \times \mu$, which assumes slight compressibility with a Poisson's ratio roughly equivalent to 0.49995. The proposed material properties for this model lie within the range of properties employed by isotropic FE models of infants and toddlers (5.99-49 kPa).²⁵⁻²⁷ While directionality of the brain matter response has been established by several studies,^{37,54,58} Budday et al.⁶⁰ found no statistically significant dependencies on nerve fiber orientation, though the tests were conducted at low strain rates and results may not translate to strain rates relevant to high-speed impacts. Creating an isotropic model is a first step in the development of an FE model of a child's brain for sporting impacts. Material properties of the intracranial membranes will not be altered from those of adult models, following previous models of infants and children that did not alter properties for the intracranial membranes.^{24,25,27,28}

The assumption of a rigid skull was used as the model was designed to be used in conjunction with physical models and reconstruction techniques. Physical reconstructions allow for accurate replication of impact velocity, location, surface compliance, and uses materials that are designed to approximate a response that is close to humans. The Hybrid III head form uses a

vinyl skin to approximate the compliance of the skin and skull. The FE model uses a rigid skull since the model is to be paired with physical reconstructions, which account for the compliance of the skull.

Model response confirmation

Response confirmation of the 6-year-old model was conducted against intracranial measures from adult cadaveric impacts.^{63,64} With no published intracranial cadaveric data for children or adolescents, comparisons within the correct age-group were not possible, a major limitation of studying the youth population. The scalable PIPER model conducted validation using published youth data of head acceleration from drop tests and stiffness from head compression tests,²⁸ but no intracranial measures were validated. The 6-year-old model developed in this study is designed for use in sports impacts using physical reconstructions and employs a rigid skull, with impact kinematics being used for the simulation loading. Comparisons of model response were made to a scaled version of the UCDBTM,^{16,17} used previously in concussion research in youth,^{31,34,35} to assess the influence of material properties, geometry, and brain tissue arrangement. Since the UCDBTM and scaled UCDBTM have been used extensively in previous research of concussions in sports events, it was used to assess how the new model is unique and how the construction affects the strain response. The scaled UCDBTM is 179 mm long and 143 mm wide.

The cadaveric impacts were chosen based on cadaver head length and width. The 6-year-old model is 179 mm long, and 145 mm wide, compared to the cadaveric specimens C064 and C241 from Hardy,⁶² reported to be 177 mm long and 145 mm wide, and 181 mm long and 145 mm wide respectively. Three impacts were used to validate the model. Impacts C064-T1 and C064-T4 were used, two occipital impacts aligned with the COG, and C241-T3, an offset occipital impact. Other impacts to cadavers C064 and C241 were excluded due to noise in the acceleration signals or a lack of results for NDT excursions. Pressure traces were not compared for C241-T3 due to both the coup and contrecoup pressure readings being positive.

Validation comparisons were made against intracranial pressure and neutral density target tracking. The neutral density target tracking measured the relative brain skull motion during the cadaveric impacts. Nodes from the models that were closest to the specified locations set by Hardy et al.⁶⁴ were selected to compare to the cadaver data, with all nodes being less than 1.5

mm away from the specified location. Model assessment was conducted using the Normalized Integral Square Error (NISE) method,⁶⁵ employed by Giordano and Kleiven⁶⁶ when assessing the PIPER scalable model for responses of head acceleration for drops, and compression tests. The NISE outputs error measures and uses these to calculate a correlation score for amplitude, phase, and curve shape. The NISE method and equations are shown in the Appendix. To assess the biofidelity of the model, the correlation scores (CS) estimated by the NISE method were averaged to calculate an overall biofidelity rating,⁶⁶ with levels as follows: unacceptable biofidelity ($0.0 \leq CS < 26$), marginal biofidelity ($26 \leq CS < 44$), fair biofidelity ($44 \leq CS < 65$), good biofidelity ($65 \leq CS < 86$), and excellent biofidelity ($86 \leq CS < 100$). Giordano and Kleiven⁶⁶ suggested that models perform at a minimum level of “fair” biofidelity in order to be used in brain injury work, corresponding to a minimum B value of 4.4. Additionally, a scaled version of the UCDBTM¹⁷ was also assessed for biofidelity and compared to the new 6-year-old model. The UCDBTM was scaled globally to 90% of its original size, as has been used in previous investigations involving concussions in children.^{34,35} This size was chosen based on MRI brain size data from Uchiyama et al.,⁶⁸ an average for the 6-year-old children involved in the study (n=9). Fit was determined in the anterior-posterior and inferior-superior axes (within one standard deviation).

Results

Intracranial pressure data validation

The first set of experimental data that was used for validation of the new 6-year-old model was the intracranial pressure data from two occipital impacts (C064-T1, C064-T4).^{63,64} Simulated pressure traces showed agreement with experimental data for the first 10ms, with simulated results trending towards zero where experimental values remained below zero for impact C064-T1, and slightly elevated for impact C064-T4 shown in Figure S1- 2.

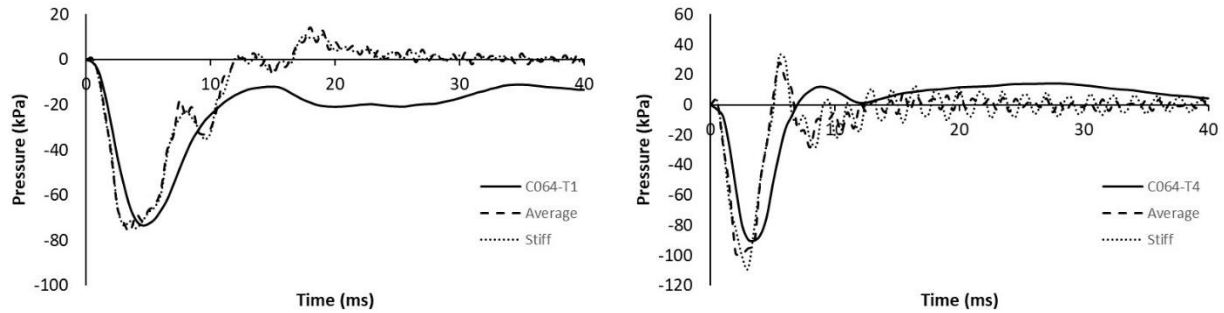


Figure S1- 2. Comparison of intracranial pressure between the new 6-year-old model versions and experimental data by Hardy (2007): Left - C064-T1; right - C064-T4

Oscillations in pressure were present in both simulated tests, with largest amplitude oscillations for the stiff model in the C064-T4 test. Both experimental traces show elevated pressures lasting over the 40 ms that were assessed, with simulated values trending towards zero after 15 ms. Good agreement in both magnitude and phase was observed between the average model, stiff model, and experimental data for the initial pressure pulse.

Brain motion data validation

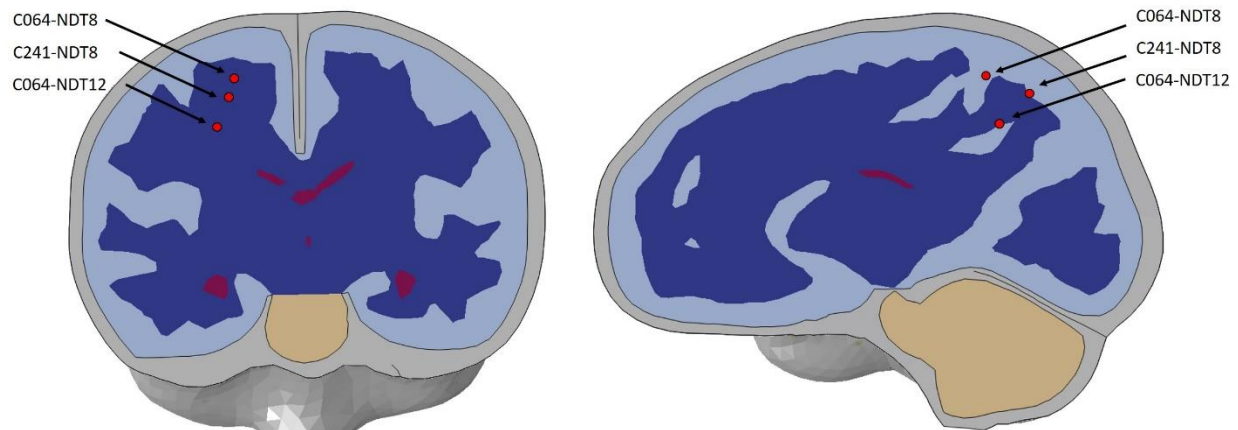


Figure S1- 3. Target locations within the brain for NDT-8 in specimens C064 and C241 and NDT-12 for specimen C064.

NDT locations in the brain are shown in Figure S1- 3. Simulated target excursions are shown in

Figure S1- 4,

Figure S1- 5, and

Figure S1- 6. The average and stiff models showed similar motion and peak excursions to the scaled UCDBTM, with the scaled UCDBTM showing more oscillation in the x-axis for impact C064-T4. Differences in phase were observed in all models compared to the experimental data for NDT-8. Less motion overall was observed in the z-axis for both impacts compared to the x-axis. Peak excursions for all targets are summarized in Table S1- 7 in the appendix.

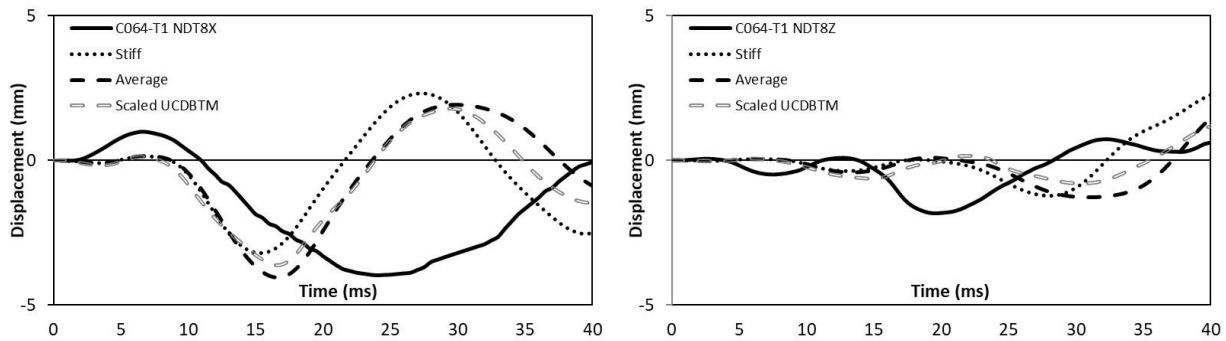


Figure S1- 4. Comparison of brain motion data between the new 6-year-old model versions, scaled UCDBTM, and experimental data (impact C064-T1) by Hardy (2007): Left - x-axis; right - z-axis

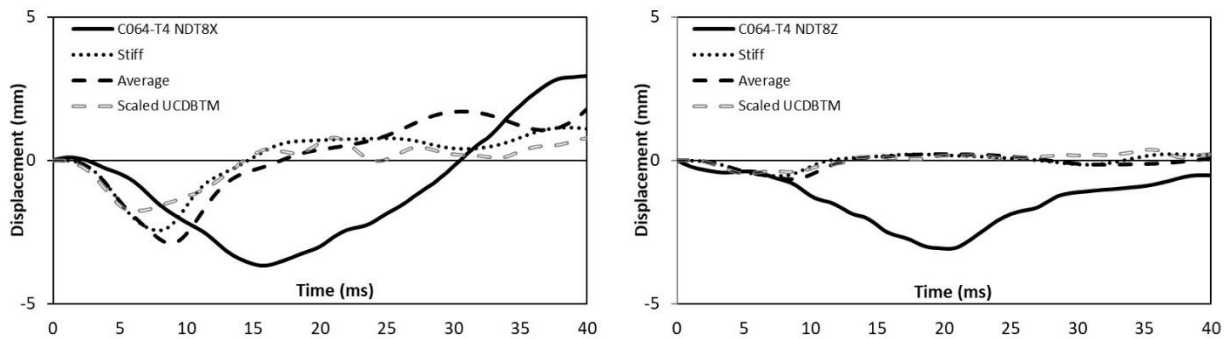


Figure S1- 5. Comparison of brain motion data between the new 6-year-old model versions, scaled UCDBTM, and experimental data (impact C064-T4) by Hardy (2007): Left - x-axis; right - z-axis

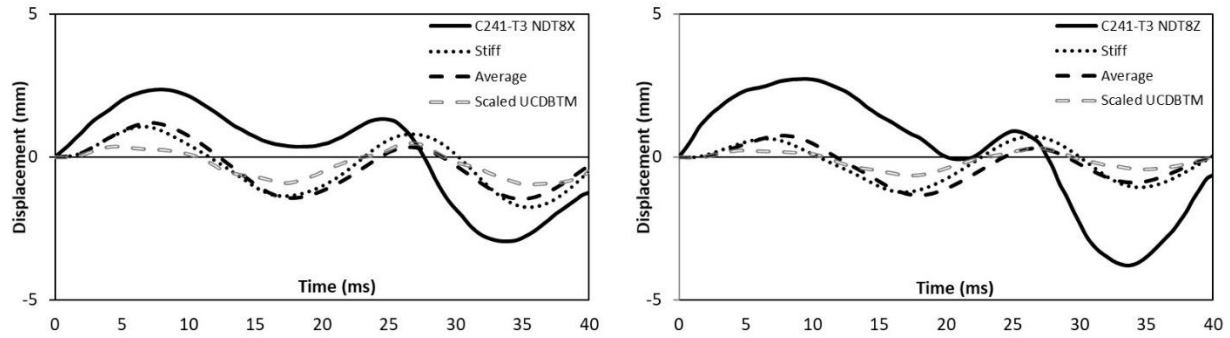


Figure S1- 6. Comparison of brain motion data between the new 6-year-old model, scaled UCDBTM, and experimental data (impact C241-T3) by Hardy (2007): Left - x-axis; right - z-axis

NISE correlation scores

The results of the Normalized Integral Square Error assessment for the average model, stiff model, and the scaled UCDBTM are shown in Table S1- 4, Table S1- 5, and Table S1- 6 respectively.

Table S1- 4. NISE correlation scores for the average model for three impacts, assessing relative brain-skull motion in the x- and z-axis, and pressure values.

Average 6-year-old model Measure	Correlation scores			Average	Biofidelity
	CS Shape	CS Magnitude	CS Phase		
C064-T1 NDT-8 X	40.3	83.9	47.10	57.1	Fair
C064-T1 NDT-8 Z	83.1	98.9	53.6	78.5	Good
C064-T1 Pressure	76.7	99.1	97.0	90.9	Excellent
C064-T4 NDT-8 X	31.0	96.8	97.1	75.0	Good
C064-T4 NDT-8 Z	52.2	55.6	88.5	65.5	Good
C064-T4 Pressure	58.0	99.9	85.2	81.1	Good
C241-T3 NDT-8 X	62.8	88.9	98.9	83.6	Good
C241-T3 NDT-8 Z	42.2	82.1	99.2	74.5	Good

Table S1- 5. NISE correlation scores for the stiff model for three impacts, assessing relative brain-skull motion in the x- and z-axis, and pressure values.

Stiff 6-year-old model		Correlation scores			Biofidelity
Measure	CS Shape	CS Magnitude	CS Phase	Average	
C064-T1 NDT-8 X	46.9	99.9	25.7	57.5	Fair
C064-T1 NDT-8 Z	88.1	99.9	85.9	91.3	Excellent
C064-T1 Pressure	77.6	99.2	97.2	91.3	Excellent
C064-T4 NDT-8 X	15.7	96.3	97.5	69.8	Good
C064-T4 NDT-8 Z		No correlation			Unacceptable
C064-T4 Pressure	56.7	99.9	85.6	80.8	Good
C241-T3 NDT-8 X	64.4	90.1	95.9	83.5	Good
C241-T3 NDT-8 Z	39.1	83.6	99.8	74.2	Good

Table S1- 6. NISE correlation scores for the scaled UCDBTM for three impacts, assessing relative brain-skull motion in the x- and z-axis.

Scaled UCDBTM		Correlation scores			Biofidelity
Measure	CS Shape	CS Magnitude	CS Phase	Average	
C064-T1 NDT-8 X	35.0	99.9	84.6	73.2	Good
C064-T1 NDT-8 Z	99.9	90.2	1.9	64.0	Fair
C064-T1 Pressure		N/A			-
C064-T4 NDT-8 X	18.0	93.1	98.3	69.8	Good
C064-T4 NDT-8 Z		No correlation			Unacceptable
C064-T4 Pressure		N/A			-
C241-T3 NDT-8 X	52.1	77.7	97.7	75.8	Good
C241-T3 NDT-8 Z	31.9	77.3	99.8	69.7	Good

Individual correlation scores varied for all models, ranging from 31.020 to 99.990 for the average model, 15.675 to 99.999 for stiff model, and 1.930 to 99.973 for the scaled UCDBTM. For z-axis motion in impact code C064-T4, no correlation was calculated in the responses of the stiff 6-year-old model and the scaled UCDBTM, visible from the negligible motion shown in Figure 4. The average model calculated a rating of 65.456, and the trace was very similar to both the stiff 6-year-old model and the scaled UCDBTM, so the rating was an overassessment by the NISE method. Scores for the average 6-year-old model came to 75.762 overall, corresponding to good biofidelity, the stiff 6-year-old model scored 78.340 overall, corresponding to good biofidelity, and the scaled UCDBTM scored 70.497, also corresponding to good biofidelity.

Strain results

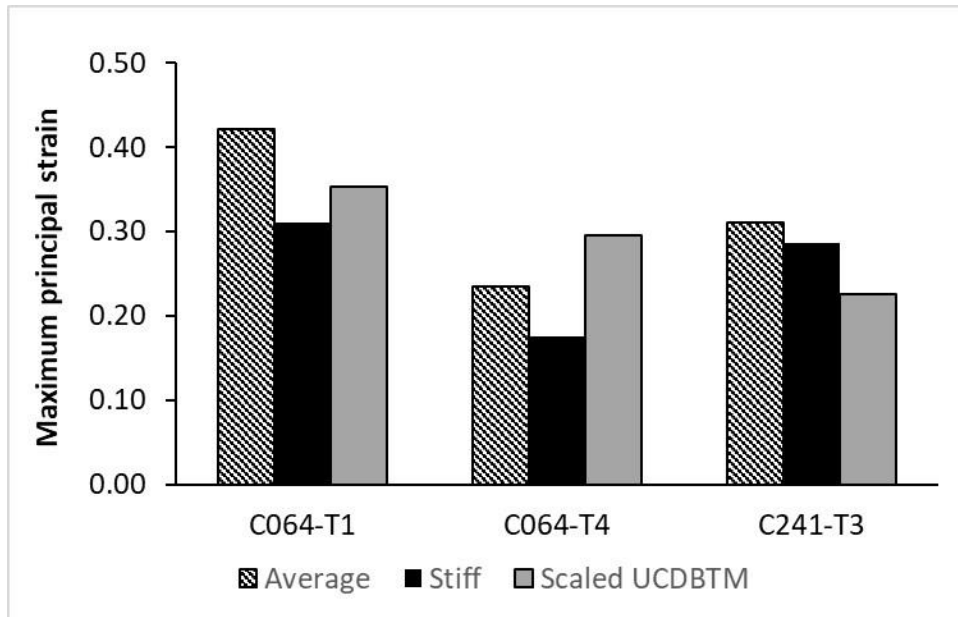


Figure S1- 7. Maximum principal strains resulting from impact codes C064-T1, C064-T4, C241-T3 from Hardy⁶³ for the average, stiff, and scaled UCDBTM models

From highest to lowest severity based on strain for the average and stiff models, impact codes were ordered C064-T1, C241-T3, and C064-T4. The scaled UCDBTM showed different trends in response, showing C064-T4 as higher severity than C241-T3. Maximum principal strain results for the average model were 0.422, 0.235, and 0.311, compared to the stiff model that had strains of 0.310, 0.175, and 0.287 for impacts C064-T1, C064-T4, and C241-T3 respectively. The scaled UCDBTM showed strains of 0.353, 0.296, and 0.226 for impacts C064-T1, C064-T4, and C241-T3 respectively. The stiff model had the lowest strains for impacts C064-T1, and C064-T4, but the scaled UCDBTM had the lowest strains for impact C241-T3.

Discussion

The 6-year-old model developed in this study is an anatomically accurate representation of the brain of a 6-year-old, run using both more compliant, and less compliant material characteristics compared to what is used in a scaled adult model, the UCDBTM. The average and stiff models show the influence of changes in shear modulus over a range of values consistent with those employed by other adult and child FE models of the brain.^{6,25-29,42} The NISE scores from three cadaveric impacts corresponded to levels of biofidelity from “fair” to “excellent”

based on pressure responses and time histories for NDT 8. Time histories for other NDTs were not available for comparison, but would add value to the assessment of biofidelity of the models. The stiff model scored the highest overall of the three models, excluding impact C064-T4 z-axis excursions. The z-axis nodal excursions were influenced by the proximity of the node to the surface of the brain. Because of the tied interface and incompressibility of the CSF, very little z-axis motion is possible near the surface of the brain as the brain cannot translate through the CSF. Deeper in the brain, larger displacements were observed for NDT 12. For impact C064-T4, both the average and stiff 6-year-old models showed over double the magnitude of nodal excursions in the z-axis for NDT 12 compared to NDT 8. Despite poor agreement for all models for C064-T4 z-axis excursions, both the average and stiff 6-year-old models showed larger relative brain skull motion than the scaled UCDBTM over the 40 ms that were analyzed and had higher NISE scores compared to the scaled UCDBTM. The difference in shear moduli between the average and stiff models resulted in changes to the measured NDT excursions, but negligible changes were observed in pressure traces, similar to results by Cui et al.²⁹ For the NDT excursions, the average model showed peak responses roughly 2-4 ms after those from the stiff model, and with larger amplitudes of motion, consistent with use of a more compliant material model.

The average model showed more brain motion than the scaled UCDBTM and the stiff model, however it did not result in the highest strains in all cases. For impact C064-T4, the scaled UCDBTM showed higher strains than the average and stiff models. Geometric differences, boundary conditions, as well as viscoelastic characteristics likely interacted to create this effect. Geometric differences are likely to influence strains as brain motion is restricted by a different shape skull, allowing or limiting different motions. The boundary conditions, mainly the brain-CSF interface will also influence the strains as the scaled UCDBTM uses a contact interface that allows for sliding between the brain and CSF, however the 6-year-old model uses a tied interface. The contact interface may increase strains locally, whereas the tied interface would distribute forces better leading to less strain concentrations. The viscoelasticity is also important, since the scaled UCDBTM has a higher shear modulus initially, but transitions to a lower shear modulus than the average model after roughly 11 ms based on the different viscoelastic parameters. The viscoelastic time constants are highly influential in the strain response of a model, but not necessarily in the NDT excursions.⁵⁰ Differing impact durations will

influence how much strain is experienced based on the viscoelastic time constants. The effect of viscoelastic properties of the new 6-year-old model is important for future use in sporting impacts, where durations range from ~5-30 ms.¹⁸ The viscoelastic properties used in this study show measurable change in shear modulus over 5-40 ms, an important time window for studying concussion and sub-concussive events.⁵⁰

As discussed above for the NDT8 z-axis excursions, nodal positions were influential in the resulting nodal excursions. Since the COG and shape of the 6-year-old model, as well as the cadaver tests were different, differences in nodal positions were unavoidable, and could not be quantified. Locally (~2 mm), nodal positions do not show any meaningful differences in the resulting motion,⁶⁹ however as noted with NDT 12 compared to NDT8, double the magnitude of z-axis excursions resulted for NDT 12, which is located is ~1.6 cm deeper in the brain compared to NDT8. While the nodes being tracked in the average and stiff models were within 1.5 mm of the location specified by Hardy,⁶³ the different COG location means that the nodes being tracked are likely at different depths in the brain tissue compared to the cadaver and may have different responses due to the tied cortical surface boundary condition.

The pressure traces of both the average and stiff models showed good agreement for the initial pressure pulse but deviated afterwards as the simulation values trended towards zero with some oscillations, and the cadaver tests remained elevated. Modelling the CSF as a solid with low shear modulus could cause the pressure to trend to zero, a result previously noted with the WSUBIM.⁴² The oscillations in pressure could be a result of the tied interface between the CSF and pia, as well as the fixed boundary condition at the foramen magnum, with rebounding of the pressure waves continuing inside the skull.

The strain results from the average, stiff, and scaled UCBDTM highlight that geometric differences and viscoelastic effects are the highly influential over the 40 ms that were analyzed. With the stiff model showing lower strains than the scaled UCBDTM for impacts C064-T1 and C064-T4, but higher strains than C241-T3, the model response is not clearly stiffer in all cases and there are influences from the shape of the skull, the loading curve shapes, and the viscoelastic parameters of the brain tissue.

The NISE offered a quantitative assessment of the agreement in time histories for the two FE models compared to the available experimental data. This method may overestimate the correlation between two curves in some circumstances, as evidenced in the C064-T4 z-axis traces for the average model, where agreement was observed for the first 10 ms but deviated thereafter and still calculated “good” biofidelity. Despite the drawbacks of the NISE method, the biofidelity measures suggest that the average and stiff models are suitable for use in brain injury research of sporting impacts.

The average and stiff models showed different responses compared to the scaled UCDBTM, evidenced by brain motion and strain measures, supporting that the newly constructed model will yield different responses for sporting impact reconstructions compared to a scaled adult model. Due to the severity of brain injuries in youth,¹ more investigations involving sporting impacts and concussion in this vulnerable population should be conducted. The 6-year-old model presented in this study offers a tool to investigate sporting impacts in children around the age of 6 years old, conducting analyses on strain responses in both the grey and white matter of the brain.

Limitations

One limitation in the field of brain modelling research remains validation data. Since there are no published intracranial measures for brain displacement, strain, or pressure for the youth population, there is no direct way to validate intracranial responses for brain models for this age group. Adult data must be used and interpreted accordingly. While head acceleration and stiffness comparisons can be made to child cadaver data from Loyd,⁷⁰ these do not offer any insight into the brain response. Despite the lack of intracranial validation data, it should not prevent biomechanics investigations involving sporting impacts and concussions in the youth population. There is value in the pursuit of improving knowledge and safety for young children. Additionally, published material properties for brain tissue vary by several orders of magnitude. With no agreement in the literature on the mechanical response of brain tissue, assumptions are required for the material model and parameters that are used in models. When comparing outputs to other models, it should be done in light of the difference in material parameters, including viscoelastic constants, which are influential in the brain’s response to impacts.⁵⁰ This study presented both an average and stiff model response, covering a shear modulus range both above

and below the UCDBTM. The use of both material models allows for interpretations of brain response whether the brain is stiffer, softer, or similar to adults based on FE model response. Until the material properties of brain tissue overall are better defined, sensitivity studies will be required to help define a corridor of response.

Despite these limitations, there are several published FE models of young brains which were validated to skull response data,^{23,25,26,28} a first but valuable step in modelling the youth population. This study aims to take a step further to cover children near the age of 6 years old, with the focus on sporting impacts rather than car crash, which has been studied by Giordano and Kleiven³⁰ with the PIPER model. Sporting impacts in children vary from those in adults based on their ability level, mass, and speed, so investigations in youth need to address these properties in physical reconstruction methods, as well as with appropriate brain model. While it is acknowledged that the new model of a 6-year-old child is based on a single individual and not necessarily representative of the entire population, the model characteristics will allow investigations to determine how tissue arrangement and brain material properties influence brain response to impacts.

The NISE method has been documented to overestimate correlation in some cases,⁶⁶ which occurred in this study for the average 6-year-old model on impact code C064-T4 z-axis excursion. The NISE method was used to partially validate the new 6-year-old model with experimental data and compare how differences in model construction influence simulation results. With no validation data available for intracranial measures for children, comparisons to adult cadaver data are presently the only means to assess the model's intracranial response for this age group. While size was approximated between the child model and the cadaver specimen, this addresses only some geometric differences, whereas any tissue level differences as well as COG location were not accounted for.

Several studies have assessed the influence of age on brain tissue properties,^{37,38,46,71,72} with no consensus in findings. Brain tissue mechanics have been studied extensively over the past decades with a review by Chatelin et al.⁴⁴ showing shear modulus values spanning over 2 orders of magnitude. Studies have shown that youth brain tissue is equivalent to adult tissue after ~2-3 years of age, however shear moduli for brain tissue continue to be published both above and below infant values, leaving an unclear picture of brain tissue response. Having accurate

modulus values for youth continues to be a limitation for research in this field. This study makes an argument for using stiffer material properties for the brain in youth, though validation data for the youth brain covering more impact sites and locations within the brain would be beneficial. A more compliant material model is also presented for reference as the authors realize brain tissue is not adequately defined in the literature given the large variance.

Conclusions

This study presents a new FE model of a 6-year-old child for use in sporting impact research of young children. The model was designed for use paired with physical reconstructions of sporting events and was shown to produce a unique response compared to the scaled adult model in brain motion and strain measures. The new model showed reasonable agreement with adult experimental data with NISE scores showing the model response in the range of “fair” to “excellent” biofidelity and scoring higher than the scaled UCDBTM. With accurate complex contours of the white matter inside the brain, the new model better represents the relative volumes of grey and white matter of children and better reflects the developmental stage of a 6-year-old brain compared to any scaled adult model. The use of the new 6-year-old model is reasoned to be more appropriate than a scaled adult model when investigating brain injuries in children using physical reconstructions.

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Appendix

Table S1- 7. Peak excursion comparisons between the new 6-year-old model with increased shear moduli and the cadaveric experimental data from Hardy⁶²

		C1							C2						
C064-T1		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Cadaver peak excursions (mm)	X	0.90	0.12	1.16	0.33	0.99	0.51	1.35	1.20	11.23	-	0.54	2.31	11.31	0.96
		-0.25	-0.86	-0.29	-0.70	-1.58	-0.31	-2.31	-3.99	0.00	-	-2.79	-0.93	0.00	-1.79
	Z	0.00	2.19	1.34	0.59	2.52	0.59	1.93	2.72	5.51	-	2.66	2.15	5.70	2.92
		-2.84	-1.35	-1.49	-1.90	-2.26	-1.89	-2.02	-1.88	0.00	-	-1.32	-0.12	0.00	-1.87
Average 6YO model peak excursions (mm)	X	0.65	1.13	0.29	1.90	0.93	1.50	1.17	1.92	2.58	-	1.94	3.60	1.99	3.00
		-1.89	-1.47	-0.75	-2.70	-1.48	-2.17	-2.96	-4.03	-2.97	-	-2.29	-3.55	-2.08	-2.28
	Z	1.91	1.43	0.51	3.04	1.81	2.57	2.28	1.47	1.28	-	1.41	1.56	0.67	1.27
		-1.43	-1.26	-0.40	-2.55	-1.23	-1.87	-1.77	-1.28	-1.19	-	-1.49	-1.61	-1.00	-1.22
Stiff 6YO model peak excursions (mm)	X	0.70	1.15	0.37	1.53	0.75	1.20	1.20	2.33	2.51	-	2.06	3.15	1.94	2.72
		-1.69	-1.04	-0.85	-1.73	-1.40	-1.87	-2.40	-3.20	-2.48	-	-2.06	-2.81	-1.94	-2.17
	Z	1.65	1.20	1.03	2.25	1.42	1.88	1.91	2.26	1.10	-	1.59	0.89	0.66	0.69
		-1.34	-1.18	-0.59	-2.20	-1.06	-1.65	-1.65	-1.23	-0.73	-	-1.16	-1.38	-0.92	-0.78
C064-T4		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Cadaver peak excursions (mm)	X	-	0.37	0.00	0.31	0.00	0.12	0.00	2.92	-	-	2.42	1.81	-	-
		-	-1.73	-4.20	-3.37	-3.77	-4.03	-4.06	-3.71	-	-	-3.25	-2.40	-	-
	Z	-	0.49	0.55	0.64	0.69	1.17	0.42	0.31	-	-	0.45	0.70	-	-
		-	-3.00	-3.13	-1.36	0.00	-0.05	-0.77	-3.41	-	-	-2.86	-4.27	-	-
Average 6YO model peak excursions (mm)	X	-	0.45	0.42	1.21	0.27	0.75	0.68	1.81	-	-	1.71	2.29	-	-
		-	-1.08	-1.19	-2.79	-1.37	-2.37	-2.57	-2.90	-	-	-2.33	-3.18	-	-
	Z	-	1.25	0.89	1.79	1.08	1.61	1.36	0.22	-	-	0.18	0.85	-	-
		-	-1.31	-1.14	-1.06	-1.49	-1.06	-1.23	-0.65	-	-	-0.95	-1.34	-	-
Stiff 6YO model peak excursions (mm)	X	-	0.56	0.43	1.01	0.32	0.69	0.50	1.13	-	-	1.18	1.33	-	-
		-	-0.95	-1.07	-2.29	-1.25	-2.00	-2.18	-2.44	-	-	-2.03	-2.65	-	-
	Z	-	0.95	0.72	1.37	0.91	1.27	1.08	0.22	-	-	0.38	1.11	-	-
		-	-0.72	-0.57	-0.89	-0.42	-0.73	-0.42	-0.54	-	-	-0.68	-1.15	-	-

Table S1- 8. Viscoelastic material properties of the brain used in the UCDBTM

	Shear modulus (kPa)		Decay constant (s ⁻¹)	Bulk modulus (GPa)
	G_0	G_∞		
Grey matter	10	2	80	2.19
Cerebellum	10	2	80	2.19
White matter	12.5	2.5	80	2.19
Brain stem	22.5	4.5	80	2.19

NISE method

The NISE method is based on the cross correlation between two signals with measures shown below:

$$NISE_{phase} = \frac{\max\{2R_{xy}(\tau)\} - 2R_{xy}(0)}{R_{xx}(0) + R_{yy}(0)} \quad (2)$$

where

$$\begin{aligned} R_{xy}(\tau) &= \frac{1}{N-n} \sum_{i=1}^{N-n} X_i Y_{i+n} & R_{xx}(0) &= \frac{1}{N} \sum_{i=1}^N X_i X_i \\ R_{xy}(0) &= \frac{1}{N} \sum_{i=1}^N X_i Y_i & R_{yy}(0) &= \frac{1}{N} \sum_{i=1}^N Y_i Y_i \end{aligned} \quad (3)$$

$$\tau = n\Delta t$$

with X_i representing the i^{th} point of a data set (experimental), and Y_i representing the i^{th} point of the second data set (simulated). N is the total number of discrete points and τ is the time lag. Following the computation of the NISE score for amplitude and shape are calculated after the phase shift has been eliminated. The NISE scores for amplitude and shape are below:

$$NISE_{amplitude} = \frac{\max\{R_{xy}(\tau)\}}{\sqrt{R_{xx}(0)R_{yy}(0)}} - \frac{\max\{2R_{xy}(\tau)\}}{R_{xx}(0) + R_{yy}(0)} \quad (4)$$

$$NISE_{shape} = 1 - \frac{\max\{R_{xy}(\tau)\}}{\sqrt{R_{xx}(0)R_{yy}(0)}} \quad (5)$$

The NISE scores are then used to calculate a Correlation Score (CS) shown below

$$CS_{shape} = 100 \times (1 - |NISE_{shape}|)$$

$$CS_{amplitude} = 100 \times (1 - |NISE_{amplitude}|) \quad (6)$$

$$CS_{phase} = 100 \times (1 - |NISE_{phase}|)$$

Study 2 - Sensitivity of a 6-year old child finite element model to simulate fall events for three levels of surface compliance

David Koncan, Anna Oeur, Michael D Gilchrist, T. Blaine Hoshizaki

Abstract

A newly developed finite element model of a 6-year-old child simulated the brain response to physical impacts onto three levels of surface compliance representing unhelmeted falls, helmeted falls, and well-padded conditions. Results for this model were compared against a scaled version of a currently available adult finite element model used in previous research. The purpose of this study was to compare trends of response and assess how material property definitions, model geometry, and anatomical differences between models affect the peak strain response. The new model of a 6-year-old showed lower peak maximum principal strains for most impact conditions, with the exception of side impacts at the highest level of compliance, representative of a gymnastics mat. The increases in compliance caused the model responses to converge for maximum principal strain results in the grey matter, however in the white matter the new 6-year-old model showed sustained lower responses compared to the scaled adult model. The newly developed model of a 6-year-old child showed stable responses and created a different response compared to scaling of an adult model.

Introduction

By the age of 6 years old, many children are enrolled in sports programs to promote physical activity and learn new skills. As with all sporting and recreational activities, there are inherent risks of accidental injury from falls, collisions with other children, and falls after colliding with children or objects. Regardless of the cause, falls often result in a head impact. The impacting surface is influential in how forces are transmitted to the head and brain (Oeur et al., 2018). Different surfaces have varying levels of compliance, which change the impact characteristics as well as the resulting strain on the brain tissue (Oeur et al., 2018). Impacts to rigid, low-compliance surfaces typically result in high-magnitude short duration events, and softer surfaces yield lower magnitude longer duration events. Using finite element (FE) models, a representation of the strain response of the brain can be calculated to see how the magnitude and duration of the impact interact to cause brain tissue strain. Since concussions are reported to be a strain-based injury (Holbourn, 1943; Ommaya and Gennarelli, 1974; King et al., 2003; Kleiven, 2007; Post and Hoshizaki, 2015), FE modelling offers a method to understand and quantify the trauma experienced by the brain from head impacts causing concussion in children.

Finite element models are used extensively in adult concussion research, using reconstructions of impact events to determine stresses and strains in brain tissue (Willinger and Baumgartner, 2003; Zhang et al., 2004; Viano et al., 2005; Kleiven, 2007; Oeur et al., 2015). There are limited studies surrounding the biomechanics of concussion involving young children, including FE models. Two models of 6-year-olds have been developed in addition to the model developed in the previous study of this thesis (Cui et al., 2015; Giordano and Kleiven 2016). The PIPER scalable model was designed for ages 1.5-6 years old (Giordano and Kleiven, 2016), where the 6-year-old model by Cui et al. (2015) have both been used in car crash scenarios (Cui et al., 2015; Giordano and Kleiven, 2017). More recently, an FE model designed for concussion research paired with physical reconstruction techniques was developed in the previous study. The only validation data for child models is from Loyd (2010) who conducted skull compressions and drop tests, without intracranial measures. The validation data often do not cover a large range of impact velocities, compliances, or locations, likely due to limitations and complexities of conducting cadaver research. In addition to validation tests, testing FE models using parametric tests over a wider range of impact parameters can help to ensure the response is stable and sensitive to the changes to physical impact conditions and their durations. Impact duration is important to consider for FE modeling as the viscoelastic parameters of the brain tissue govern the time dependent shear modulus, which influences the resulting strains in the brain (Zhao et al., 2018). The rate at which the shear moduli change depends on the viscoelastic parameters that are used, drawn from brain tissue studies. For very short duration impacts, the initial shear modulus may be the most influential parameter on peak strain. When moderate to high levels of compliance are added resulting in longer impact durations (~40 ms), the viscoelastic parameters become more influential.

Sensitivity tests can serve to identify a limit of stability for the model, like that reported by Zhang et al. (2001), finding the Wayne State University Brain Injury Model was stable up to and including inputs accelerations of 200 g and 12 000 rad/s². In addition to stability, running the model using parametric tests including variety of impact magnitudes with varying impact durations will help to establish trends in the brain response. Identifying differences in trends is important for new FE models of children, as it can shed light on how documented differences in size (Lenroot and Giedd, 2006), material properties (Gefen et al., 2003; Sack et al., 2009; Thibault and Margulies, 1998; Prange and Margulies, 2002), and the arrangement of grey and

white matter in the brain (Lenroot and Giedd, 2006; Reiss et al., 1996) interact to create risk for concussive injury. Scaling adult models has been used to study concussive impacts in children (Dawson, 2016; Post et al., 2017a; 2017b), but only size is addressed using this method.

The purpose of this study was to test the sensitivity and stability of response of the newly developed FE model of a 6-year-old child for falls at three levels of surface compliance. The 6-year-old model was also compared against a scaled version of the University College Dublin Brain Trauma Model (UCDBTM) (Horgan and Gilchrist, 2003; 2004). Comparisons between models will be used to assess the influence of the differences in material properties, tissue arrangement, and geometry on the brain strain response.

Methods

The 6-year-old model being tested in this study was developed and validated in the previous study. The model was created using an MRI of a 6-year-old child and includes the skull, CSF, pia, tentorium and falx, grey matter, white matter, cerebellum, and brainstem. The model employs 1st order shell elements (skull), 1st order membrane elements (falx, tentorium, pia), and 2nd order tetrahedral elements (cerebrum, cerebellum, CSF). Triangular and tetrahedral elements were used to mesh the complex geometry of the folds of white matter inside the brain compared to the scaled UCDBTM, which does not have sufficient mesh density to represent the folds of the white matter using an 8-node brick mesh for the brain matter. The 6-year-old model contains 148,562 nodes and 169,849 elements in total, compared to the scaled UCDBTM which contains 32,279 nodes and 32,994 elements in total.

A subset of physical impact tests conducted on the Hybrid III 6-year-old head form were taken from a previous study and were simulated in this current study (Oeur et al., 2018). Impacts were conducted at three levels of surface compliance to elicit three groupings of impact durations typical of sports: short (~5 ms), moderate (~15 ms), and long (~25 ms) (Oeur and Hoshizaki, 2016; Oeur et al., 2018). Steel was used to represent a low compliance, characteristic of unprotected falls onto rigid surfaces. A 0.025 m thick vinyl nitrile (VN) foam was used to represent a moderate compliance, characteristic of a protected or helmeted fall (Hodgson and Thomas, 1972). A 0.067 m thick Rubatex R338 rubber foam was used to represent a high compliance for falls onto well-padded surfaces such as a gymnastics mat. Each impact surface

was assessed to determine the relative stiffness of each material using Shore A testing (ASTM Standard D2240), where 99.3, 17.8, and 3.0 correspond to the steel, VN foam, and Rubatex rubber foam respectively (Oeur and Hoshizaki, 2016; Oeur et al., 2018).

Impacts were conducted at three different velocities: 1.5 m/s, 3.0 m/s, and 4.5 m/s, covering a low to high range of fall velocities which are consistent for children from fall simulations (Koncan et al., 2016; Koncan et al., 2017). Impacts to steel were not conducted at 4.5 m/s to prevent equipment damage. The front and side of the head were chosen as impact locations to reflect common impact sites in children's falls (Figure S2- 1). Finite element model responses of the 6-year-old model were compared to a scaled version of the UCDBTM.

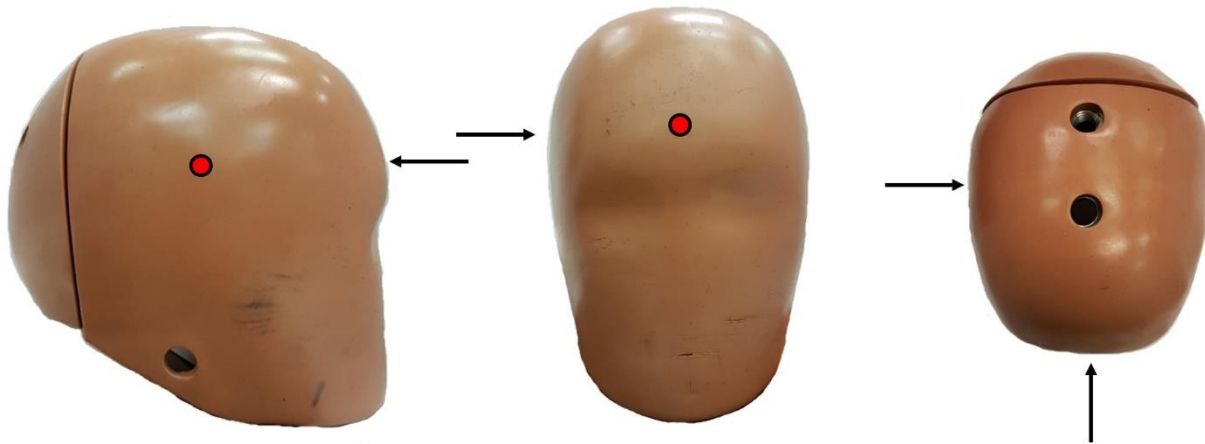


Figure S2- 1. Side, front, and top views of a Hybrid III 6-year-old head form showing the front and side impact locations used for this study.

Monorail

Impacts were conducted using a monorail drop rig. The head and neck form were attached to a drop carriage, which were then lifted to the prescribed height and dropped onto the anvils. The drop carriage was attached to the monorail by ball bushings, allowing low friction movement upon release. Impact velocity was determined using a photoelectric time gate positioned within 0.02 m of the impact anvil.

Head form

An instrumented Hybrid III 6-year-old head form was used in this study, attached to an unbiased neck form. The head form was instrumented with nine Endevco 7264C-2KTZ-2-300 single-axis accelerometers arranged in a 3-2-2-2 array, capable of capturing three-dimensional

impact kinematics (Padgaonkar et al., 1975). Accelerometer signals were sampled at 20 kHz using a DTS TDAS system and were filtered using a CFC class 1000 filter. The head form was attached to an appropriately sized non-directional neck form (University of Ottawa, Ottawa, Canada) composed of alternating aluminum and butyl rubber discs held together using a standard Hybrid III neck cable (Walsh et al., 2012). To prevent any directional influence on the impact kinematics due to the neck, the non-directional neck was used since the standard Hybrid III neck form has a directional design to properly reflect flexion and extension movements from car crash environments (Mertz et al., 1971; Mertz et al., 1989; Kang et al., 2005). The neck form is further described by Oeur et al. (2018).

Finite element models

Two finite element models were used in this study, a new 6-year-old FE model developed in the previous study, and a scaled version of the UCDBTM (Horgan and Gilchrist, 2003; 2004). The 6-year-old model was developed using medical images of a 6-year-old child, and the response was partially validated against adult cadaveric data of intracranial pressure and brain motion (Hardy 2007; Hardy et al., 2007) with results presented in the previous study. The stiff version of the model presented in the previous study was used for this study. Material properties of the 6-year-old model are shown below in Table S2-6 and Table S2-. For further details regarding model development and validation, see the previous study of this thesis.

Table S2-6. Elastic material properties for tissues in the 6-year-old model.

Material	Young's modulus (MPa)	Poisson's ratio	Density (kg/m ³)
Skull	Rigid		2000
Dura	31.5	0.45	1130
Pia	11.5	0.45	1130
Falx and Tentorium	31.5	0.45	1130
Brain	Hyper Elastic	~0.5	1060
CSF	0.015	~0.5	1000

Table S2-2. Material properties of the brain for the 6-year-old model.

	Initial shear modulus (kPa)	Ogden material constant α	Viscoelastic parameters				
			g_1	τ_1 (s)	g_2	τ_2 (s)	g_∞
Grey matter	11.5						
White matter	14.4	0.59	0.451	0.021	0.301	0.199	0.249
Brain stem	25.9						
Cerebellum	11.5						

The 6-year-old model was compared against the scaled version of the UCDBTM (Horgan and Gilchrist, 2003; 2004). The scaled version of the UCDBTM was created by modifying the model to 90% of its original size. While the scaled model does not match the size of the new 6-year-old model, it was scaled based on a brain size study (Uchiyama et al., 2013), and is being used to serve as a benchmark of response since it has been used in previous studies of concussion in young children (Dawson, 2016; Post et al., 2017a; Post et al., 2017b). Material properties for the scaled model were not altered from the original UCDBTM and are shown in the appendix in Tables S2-8 and S2-9.

The model responses were compared based on commonly used metrics in concussive research, maximum principal strain (MPS), and cumulative strain damage measure (percentage of cerebrum elements surpassing 0.15 maximum principal strain). Comparisons of MPS were made for responses in the grey and white matter for each model, assessing how strain patterns differ between models, with cumulative strain damage measure comparisons being conducted for the cerebrum. A response stability assessment was conducted using the ratio of the artificial

strain energy (which includes hourglassing) to the internal energy, with under 10% used as a benchmark limit, similar to Zhang et al. (2001) for hourglassing energy.

Statistics

Three factorial ANOVAs were run to identify main effects of velocity, location, and compliance on the model strain responses in the grey matter, white matter, and CSDM measures. One-way ANOVAs were then run, splitting the data set where main effects were observed to identify each specific impact case that created different responses in the two FE models. Since the aim of the study was to examine how the new 6-year-old model response differed from the scaled adult model, interactions were not investigated though it is acknowledged that there are interactions between the impact parameters of compliance, location, and velocity that affect the strain response as was investigated by Oeur et al. (2018). Statistical tests were run using IBM SPSS Statistics V 19.0 (Armonk, New York, USA) using an alpha level of 0.05 to determine accepted significance ($p < 0.05$).

Results

Peak resultant linear acceleration, and peak resultant rotational acceleration results are shown for frontal impacts in Table 3, and for side impacts in Table 4 for all compliance conditions. Strain increased with increasing impact velocity for all cases except in the white matter for frontal impacts to the VN foam at 3.0 and 4.5 m/s. A summary of the strain responses in the grey and white matter are shown in for front and side impacts in Figure S2- 2 and Figure S2- 3 respectively. Main effects were observed for CSDM, maximum principal strain in the grey matter, and maximum principal strain in the white matter for impact location, velocity, and compliance ($p < 0.05$).

Table S2-7. Peak resultant linear and rotational acceleration for frontal impacts at three levels of compliance impacts using the Hybrid III 6-year-old head form

	Steel		VN foam		Rubatex rubber foam	
	Linear acceleration	Rotational acceleration	Linear acceleration	Rotational acceleration	Linear acceleration	Rotational acceleration
1.5 m/s	115.7	4451	17.7	977	9.2	560
3.0 m/s	354.5	17075	41.1	3712	22.4	1445
4.5 m/s	-	-	97.5	7411	46.2	2845

Table S2-8. Peak resultant linear and rotational acceleration for side impacts at three levels of compliance impacts using the Hybrid III 6-year-old head form

	Steel Linear acceleration	Rotational acceleration	VN foam Linear acceleration	Rotational acceleration	Rubatex rubber foam Linear acceleration	Rotational acceleration
1.5 m/s	172.5	24359	21.7	2408	10.1	830
3.0 m/s	519.8	85969	48.2	5403	20.4	1993
4.5 m/s	-	-	89.2	9169	41.4	3816

Differences in MPS values between the 6-year-old model and scaled UCDBTM were largest for steel impacts, decreasing as compliance was increased. For most impact conditions, values from the 6-year-old model were lower than the scaled UCDBTM, with the exceptions of the VN foam impact to the side at 1.5 m/s, and all Rubatex rubber foam impacts to the side.

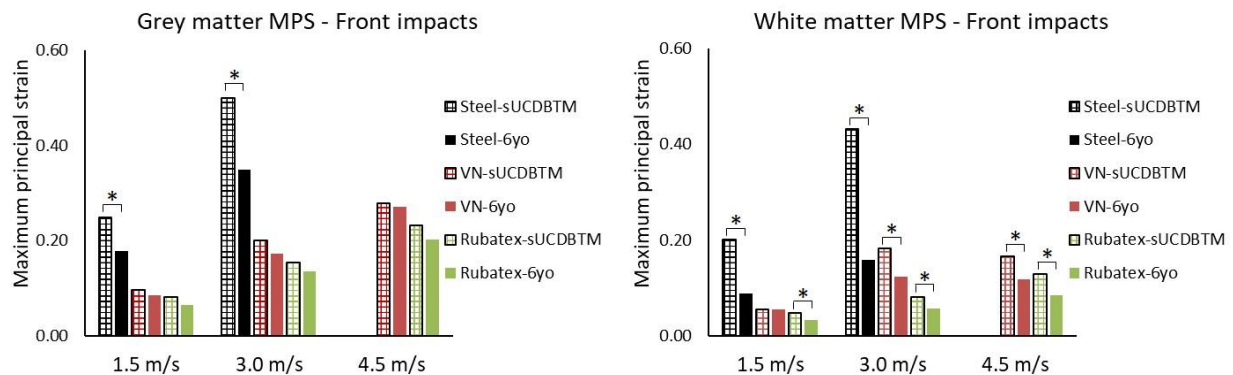


Figure S2- 2. Maximum principal strain values for front impacts to low (steel), moderate (VN foam), and high (Rubatex rubber foam) compliance for the 6-year-old model (6yo) and scaled University College Dublin Brain Trauma Model (sUCDBTM). Statistical significance marked by *

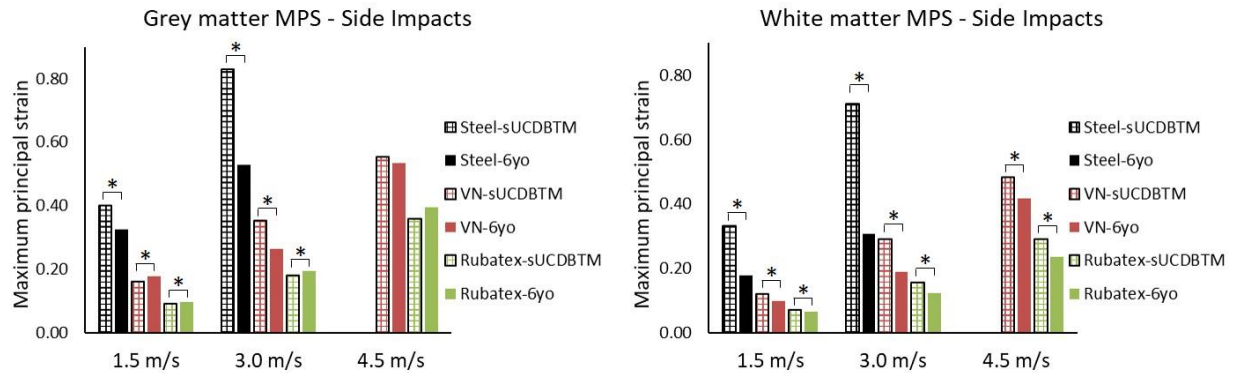


Figure S2- 3. Maximum principal strain values for side impacts to low (steel), moderate (VN foam), and high (Rubatex rubber foam) compliance for the 6-year-old model (6yo) and scaled University College Dublin Brain Trauma Model (sUCDBTM). Statistical significance marked by *

Peak MPS responses from the 6-year-old model were on average, 29% lower for steel, 8% lower for the VN foam, and 14% lower for the Rubatex rubber foam for frontal impacts. For side impacts, the 6-year-old model showed 31% lower responses for steel, 9% lower responses for the VN foam, and 9% higher responses for the Rubatex rubber foam.

Results of CSDM are presented in Table S2-5 and showed minimal differences in volumes of strain within the cerebrum. Statistical significance ($p < 0.05$) was reached for two impacts, the front impact on steel at 3.0 m/s, and the side impact on VN foam at 4.5 m/s.

Table S2-9. Cumulative strain damage (CSDM 15) measures for the two FE models, the 6-year-old model (A) and the scaled UCDBTM (B)

	Steel				VN foam				Rubatex rubber foam			
	Front		Side		Front		Side		Front		Side	
	A	B	A	B	A	B	A	B	A	B	A	B
1.5 m/s	0.0	0.01	0.03	0.05	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3.0 m/s	0.02	0.23	0.72	0.70	0.0	0.0	0.03	0.04	0.0	0.0	0.0	0.0
4.5 m/s					0.0	0.0	0.063	0.043	0.0	0.0	0.04	0.03

For all impacts to the VN foam and the Rubatex rubber foam, the artificial strain energy averaged under 9% of the internal energy and showed stable responses. For steel impacts at 3.0 m/s, the artificial strain energy averaged 16% and 14% of the internal energy for the front and side impacts respectively. For steel impacts at 1.5 m/s, the artificial strain energy averaged under 10% and 11% of the internal energy for the front and side impacts respectively.

Discussion

The 6-year-old model showed similar trends in MPS results in the grey matter, though lower in magnitude compared to the scaled UCDBTM. On average, MPS results from the 6-year-old model were 30% lower for the steel impacts, 9% lower for the VN foam impacts, and 1% lower for the Rubatex rubber foam impacts, averaged across both locations. Though the differences in MPS in the grey matter decreased with increasing compliance, the same did not occur in the white matter. On average, strains in the 6-year-old model were 56% lower than the scaled UCDBTM for the steel impacts, and 23% lower for both the VN foam and Rubatex rubber foam impacts. The unique response of the 6-year-old model highlights that although MPS trends are similar between the two FE models, differences in the strain patterns are present from the different model construction. For longer impact durations, though the strains in the grey matter are similar, differences remain in the white matter. The accurate representation of the folds of white matter of the 6-year-old model were influential in the response, adding some structural rigidity to the cerebrum since all white matter is connected, whereas in the scaled UCDBTM the white matter is not necessarily connected.

In addition to the connected white matter in the 6-year-old model, other factors that likely influenced these results include the differences in the brain material properties, and the pia-CSF interface. The 6-year-old model has shear moduli 15% larger than those of the scaled UCDBTM. For the shorter impact durations, the effective shear moduli would not change considerably from the initial shear moduli, resulting in lower strains than the scaled UCDBTM. As the impact durations were elongated with increasing compliance, the viscoelastic properties become more influential and the resulting strains are closer in value. The tied interface used in the 6-year-old model could reduce the penetration of strain into the white matter due to the forces being better distributed along the surface of the brain. Comparatively, the scaled UCDBTM could have more localized strain resulting from contact that could then be transmitted into the white matter in thinner cortical regions. Though a contact surface may be an effective boundary condition when assessing model response to cadaveric data, highly localized strain concentrations are an unlikely result from brain motion through the CSF. Contact between the brain and skull would cause strain concentrations, however modelling of the CSF using solid elements with low shear moduli

prevents this type of effect and is not possible in either the 6-year-old model or the scaled UCDBTM.

Low values of CSDM can be attributed to the lower impact velocities tested in this study, as well as the maximum strains being concentrated in smaller regions of the brain. The CSDM threshold of 0.15 sits between conservative and optimal thresholds for functional disruption of axons without damage by Bain and Meaney (2000), and at the suggested level for functional disruption by Maxwell et al. (1997). Children at play often experience head impacts but do not display discomfort or symptoms, which would be expected if considerable functional disruption of axons were occurring. The low impact velocities (~ 1.5 m/s) to padded surfaces conducted in this study reflect this point, with zero CSDM measures. If the threshold for the CSDM measure was lowered to 0.10 MPS, it is possible that more differences would be observed, however the measure could saturate for higher energy impacts such as those to steel at 3.0 m/s. In the current study, the cumulative strain damage measure, using a strain threshold 0.15 was not as sensitive to the changes in impact magnitude and duration as maximum principal strain.

Geometric differences between models were not directly assessed in this study, however geometry is unlikely to affect responses to the extent of other factors, such as material model differences, and interface conditions. Geometric influence was investigated in a study by Danelson et al. (2008), finding that size differences were more important than shape, however shape could influence the distribution of the strain. Geometry is an important factor (Franklyn, 2007), however between a scaled adult model and the 6-year-old model, boundary conditions, material models, discretization of the white matter, and size were more influential parameters.

For the stability tests, material models that employ both hyperelastic and viscoelastic properties contain viscous dissipation within the artificial strain energy term in Abaqus, so it inflates the calculated value. The percentage that viscous damping contributes to the artificial strain energy is unknown. Despite this unknown, for the more compliant impacts to VN and Rubatex foams, the artificial strain energy remained below 10% of the internal energy. The steel impacts at 3.0 m/s created a minimum of 350 g and $17\,000\text{ rad/s}^2$, so it was reasoned that response stability is not critical at this level due to the known severity of impacts of this magnitude, including skull fracture (Kleiven, 2013), and brain bleeds (Post, 2013). At this level,

the FE model will output high strain values, simply underscoring the impact severity by another measure. Impacts to the two foam levels of compliance showed results in line with the stability tests conducted by Zhang et al. (2001) with results under 10%.

Limitations

This study uses two finite element models, a 6-year-old model that was benchmarked against a scaled version of the UCDBTM. Comparisons between models are always difficult since different model constructions yield different results for identical loads (Ji et al., 2014). Of more value are the trends of response, identifying what aspects of the models influence the results. These trends can then be extended and used to interpret real-world data, or other model-predicted brain responses. While no model-to-model comparison will ever be completely valid, these comparisons allow for an informed interpretation of the data.

Only two impact locations were tested in this study, choosing frequent impact locations for children's head impacts rather than a comprehensive set of locations. While impact location does affect impact kinematics and subsequently, strain responses, similar trends in response were found for the 6-year-old model and UCDBTM for the two locations that were tested. The authors decided not to test additional locations, because they should show similar trends of comparison between the two models, with some variations of the magnitude of strain output.

Conclusions

The 6-year-old model was shown to respond to changes in impact magnitude and duration, creating a unique strain response compared to a scaled adult model. The highly accurate representation of the white matter of the 6-year-old model showed lower levels of strain through all levels of impact velocity and surface compliance, due to the white matter adding extra stiffness to the system. The 6-year-old model on average, yielded lower strains compared to the scaled UCDBTM, and showed different patterns of strain within the cerebrum. Increased compliance reduced strain, and peak results converged towards those from the scaled UCDBTM at the highest level of compliance. If comparisons are being made between different FE models, caution should be exercised. Particular attention must be given to the impact duration, as the viscoelastic parameters are influential in the strain outputs. Expected differences between models may decrease with longer impact durations and depending on the viscoelastic parameters. The 6-

year-old model presents a more anatomically precise tool to investigate concussion further in young children.

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Appendix

Table S2-10. Elastic properties of the brain used in the UCDBTM

Material	Young's modulus (MPa)	Poisson's ratio	Density (kg/m ³)
Brain	Viscoelastic	0.49998	1060
CSF	0.015	0.5	1000
Cortical bone	15000	0.22	2000
Trabecular bone	1000	0.24	1300
Facial bone	500	0.23	2100
Dura	31.5	0.45	1130
Pia	11.5	0.45	1130
Falx and tentorium	31.5	0.45	1130
Scalp	16.7	0.42	1000

Table S2-11. Viscoelastic material properties of the brain used in the UCDBTM

	Shear modulus (kPa)		Decay constant (s ⁻¹)	Bulk modulus (GPa)
	G_0	G_∞		
White matter	12.5	2.5	80	2.19
Grey matter	10	2	80	2.19
Cerebellum	10	2	80	2.19
Brain stem	22.5	4.5	80	2.19

Study 3 - Differences in brain strain between young children and adults for head impacts from falls resulting in concussion

David Koncan, Dr. Michael Gilchrist, Dr. T.Blaine Hoshizaki

Abstract

Researchers are divided on whether children are more, less, or equally susceptible to concussive injury. Falls are a common event to cause concussive injury in people of all ages, who experience debilitating symptoms following the impact events. Compared to adults, it has been documented that children are at elevated risk for concussion, experience longer recovery times, and are at higher risk for repeated concussions compared to adults. What is unknown, is whether the developing brain may be injured at differing strain levels compared to adults. This study examined peak and cumulative brain strain from 20 cases of concussion in both young children and adults. Physical reconstructions of 40 real-world concussive events were conducted, first using MADYMO simulations to establish the head impact velocity for each case. Several fall simulations were conducted for each case to establish a conservative estimate of the impact velocity that caused the concussive injury. Falls were then reconstructed using a monorail drop tower to measure the 3D impact kinematics, which were used to load FE models of the brain. Two different models were used; a newly developed 6-year-old model for the child cases of concussion, with adult cases of concussion run using a published adult brain model. The concussion cases in children showed lower responses for all impact kinematics as well as strain metrics examined. All the cases were falls from standing, yielding a velocity driven relationship that showed children can experience concussive injury at lower strain levels compared to adults. The results suggest that play structures that put children in elevated positions without adequate padding on the ground create significant risk of concussive injury. Equipment manufacturers should also investigate age-specific head protection as scaling adult products may not adequately reduce risk of concussive injury.

Introduction

There are an estimated 750,000 annual pediatric concussion visits to emergency departments in the United States (National Center for Injury Prevention, 2003; Gilchrist et al., 2011). Following these brain injuries, there are often debilitating effects such as cognitive deficits (Stancin et al., 2002; Savage et al., 2005; McClincy et al., 2006; Shrey et al., 2011; Treble et al., 2013) or behaviour problems (Savage et al., 2005) that can last long after the initial injury (National Institutes of Health, 1999). Though adults may experience deficits following a concussion, they are typically less severe than those in children (Choe et al., 2012). Children are

at an elevated risk for concussion, prolonged recovery, and repeat concussive injury compared to adults (Gilchrist et al., 2011), however researchers are divided on whether children are more susceptible (Meyers et al., 2007; Maxwell 2012), less susceptible (Ommaya et al., 1967; Ommaya et al., 2002; Sparrey et al., 2009), or equally susceptible to these types of injuries compared to adults, and how that relates to impact biomechanics.

Falls are a common event that can result in concussion for people of any age. In many countries, falls account for over 20-50% of all head injuries, including concussions (O’Riordain et al., 2003), which cost up to 60 billion dollars annually in the United States (Langlois et al., 2006). With children, many concussive injuries are a result of recreational play, or sports (Browne and Lam, 2005; Adelson and Kochanek, 1998). Sporting impacts are important to investigate since children are six times more likely to suffer a severe concussion from falls or collisions during organized sports compared to other physical leisure activities (Browne and Lam, 2005). For sports manufacturers, children are often treated as small adults, designing products at one size and simply scaling it down to accommodate the differences in size of the age groups. While this approach may be effective for some products, with head injuries the same assumption is misplaced. Further understanding of what contributes to injury to the developing brain and how it differs from adults is required. There are differences in the developing brain of a child compared to an adult that may reflect a unique brain response to head impact.

The mechanical properties of brain tissue change with age (Gefen et al., 2003; Thibault and Margulies, 1998; Prange and Margulies, 2002; Sack et al., 2009) and continually remodels as we learn and develop new skills. Myelination and significant remodelling of grey and white matter in the brain have been shown to continue into the 3rd decade of life (Lenroot and Giedd, 2006). With concussion reported to be a strain-based injury (Holbourn 1943; Ommaya and Gennarelli 1974; King et al. 2003; Kleiven 2007; Post and Hoshizaki 2015), the variations in mechanical characteristics and patterns of grey and white matter in the brain will elicit a unique mechanical response for different age groups. Grey and white matter are mechanically different as a result of their underlying microstructure; grey matter is highly isotropic while white matter is anisotropic (Prange et al., 2002; Hrapko et al., 2008). As connections are reinforced and white matter tracts develop, the mechanical response of the brain tissue under load from events such as falls will be affected.

In adults there are many published FE models of the brain (Horgan and Gilchrist, 2003; Mao et al., 2013; Kleiven and Hardy, 2002; Sahoo et al., 2014; Giordano and Kleiven, 2017b), but relatively few child models. Two FE models exist of 6-year-old children that have been used to study car crash events (Cui et al., 2015; Giordano and Kleiven, 2016), as well as a newly developed model of a 6-year-old child, validated in the first study of this thesis designed for use with physical models. Adult models have been used to calculate risk of concussion using maximum principal strain (MPS), and cumulative strain damage measure (CSDM) (Takhounts et al., 2003; Zhang et al., 2004; Kleiven 2007; Kimpara and Iwamoto, 2012; Patton et al., 2015), however there is little data for children and risk assessments based on adult data may not be appropriate. Scaled adult models have been used to study concussion in children between the ages of 5-18 (Dawson 2016; Post et al., 2017a; Post et al., 2017b), but scaling does not adequately represent the developmental stage of young children. The newly developed 6-year-old model allows for in-depth investigations of concussion in youth. In the simulation of car crash events by Giordano et al. (2017a), two of three events yielded loading curves lasting over 100 ms. Car crashes differ greatly from falls, as falls can result in forces over an order of magnitude larger than impulsive loads transferred through the torso and neck such as those experienced by car crash (Ommaya et al., 2002). Falls resulting in concussion from impacts to non-compliant surfaces yield high forces lasting less than 5 ms (Hoshizaki et al., 2016). Falls and sporting impacts have not been adequately studied in young children, and the impacts differ from those experienced in car crash events.

Currently, it is unknown whether children are more susceptible or possibly more resilient to concussive injuries. Some have cited the developing brain is more susceptible to damage (Adelson and Kochanek, 1998; Meyers et al., 2007), while others have supported the developing brain to be more resilient to strains (Sparrey et al., 2009). Falls resulting in concussion have not been adequately studied in young children. Without knowledge of the tolerance to impacts of children in comparison to adults, it is difficult to assess protective capacity of equipment as well as assess risk of injuries with certain types of events. The purpose of this study was to assess whether finite element responses from falls resulting in concussion are different between children and adults, quantified using maximum principal strain, and cumulative strain damage measure (CSDM).

Methods

Forty concussive cases resulting from falls were used for this study, 20 of adults, and 20 of young children (ages 5-7). Concussive cases of adults were drawn from The Ottawa Hospital, recruiting patients that had suffered a concussion and were referred to a clinic for treatment persistent concussion symptoms. Concussive cases of children were drawn from nine pediatric emergency departments inside the Pediatric Emergency Research Canada (PERC) network. Approval for this study was granted by the Research Ethics Board. Patients included in the study must have been diagnosed with a concussion and had accurate and complete eyewitness or personal accounts of the injury to fill out a summary on a Neurotrauma Injury Report Form, or modified version filled out using a tablet device (Zemek et al., 2017). The individual, parent/guardian, or child filled out the forms with the attending physician, providing details of the impact event. These forms were electronic documents that were used as a standardized data collection method to inform laboratory reconstructions. The descriptions on the forms were required to contain sufficient detail to ensure an accurate estimation of the following parameters: head impact velocity, location, and impact surface. If details were insufficient, the case was excluded from the dataset. In all cases, patients were confirmed to have a concussion, diagnosed by a physician.

Using the data from the Neurotrauma Injury Report forms, simulations were run to determine the fall impact velocity. Using Mathematical Dynamic Models (MADYMO)(TASS International), a set of kinematic simulations were run to estimate the head velocity on impact for each case. Impact reconstructions were then conducted using an appropriately sized head form, either the Hybrid III 6-year-old, Hybrid III 5th percentile female, or Hybrid III 50th percentile male, depending on the age and gender of the patient. Finite element model responses were obtained by loading the newly developed 6-year-old model, and the University College Dublin Brain Trauma Model using the recorded impact kinematics for child and adult cases respectively. Overall, 8 of 20 child cases were females, with 15 females in the adult cases. The fall directions of the child cases included 15 front falls, 3 to the side and 2 to the rear, and for adults there were 3 impacts to the front, 1 to the side, and 16 to the rear. Case description summaries for the adult and child cases are located in the appendix, in Tables 4 and 5 respectively.

Monorail drop rig

A monorail drop rig was used to conduct the reconstructions of concussions resulting from falls. The monorail drop rig consisted of a carriage attached to a single rail with two ball bushings, allowing for low friction motion upon release by a pneumatic switch. The appropriately sized head and neck form for each case were attached to the carriage. Impact velocity was determined using a photoelectric time gate, positioned within 0.02 m of the impacting surface. For each case, the specified impact surface was replicated, or simulated, and attached to the anvil. A 1/2" MEP anvil was used to simulate impacts to the ground, as well as one case where the patient fell on a boat deck. For impacts to wooden surfaces, a small section of hardwood floor was constructed using standard thickness 3/4" plywood covered by hardwood flooring, supported by wooden joists with a 12" separation.

Head forms

Fall reconstructions were conducted using the Hybrid III 6-year-old, Hybrid III 5th percentile female, or Hybrid III 50th percentile male, with an attached unbiased neck form. For all child cases, male or female, the Hybrid III 6-year-old head form was used. For adults, female cases used the Hybrid III 5th percentile female, where male cases used the Hybrid III 50th percentile male. The head forms were instrumented with nine single-axis accelerometers (Endevco 7264C-2KTZ-2-300, (Endevco, San Juan Capistrano, CA, USA)) arranged in a 3-2-2 array, to capture three-dimensional impact kinematics (Padgaonkar et al., 1977). A DTS TDAS data collection system was used that sampled accelerometer signals at 20 kHz, and filtered using a CFC 180 filter. The head forms were attached to an appropriately sized non-directional neck form (University of Ottawa, Ottawa, Canada) composed of alternating aluminum and butyl rubber discs held together using a standard Hybrid III neck cable (Walsh et al., 2012). The non-directional neck was used to prevent directional bias since the standard Hybrid III neck forms have a directional design to properly reflect flexion and extension movements from car crash environments (Mertz et al., 1971; Mertz et al., 1989; Kang et al., 2005). The neck forms are described by Oeur and Hoshizaki (2018).

Mathematical Dynamic Models

In order to establish the range of possible impact velocities for falls, MADYMO (Tass International, Livonia, USA) simulations were conducted. The simulations were conducted using

different orientations of the limbs and body in order to find a conservative estimate of the impact velocity that caused the concussive injury. For frontal and side impact locations, horizontal velocities were assigned between 0.5 m/s to 3.5 m/s, as 3.57 was an average 20 m sprint speed for children aged 6 (Roman et al., 2014). For impact locations to the rear of the head, horizontal velocities were assigned between 0.2 to 2.0 m/s, similar to a published 1.91 m/s being a “fast walking speed” of children aged 9-12. Frictional properties between the shoes and contact surface for the simulations were altered from the default coefficient of 0.5 for cases involving slips on ice. In these cases, a value of 0.15 was used, the coefficient of friction between rubber and ice.

Fall direction was determined using the recorded data from the Neurotrauma Injury Report Form, or based on the impact location if a summary was missing or insufficient. In addition to the location grid (shown in Figure 1), check boxes were included on the Neurotrauma Injury Report Form to specify impact vector with options of front, front 45, side, back 45, back, unknown. Based on the reported impact vector, paired with the location grid, fall directions were determined.

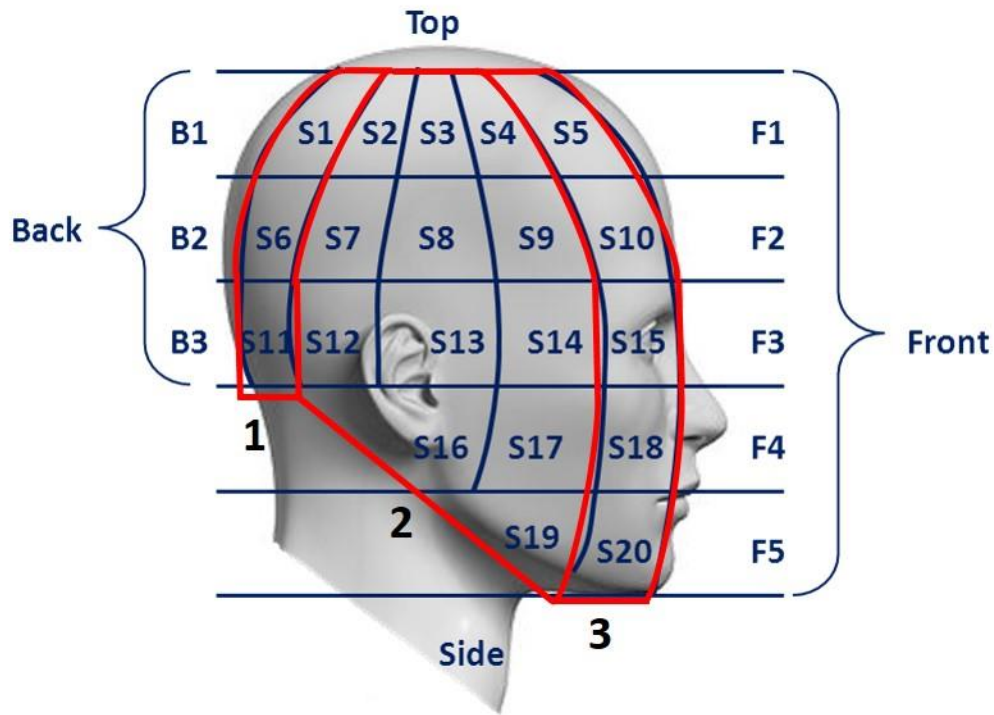


Figure S3- 1. Impact location grid on the Neurotrauma Injury Report Form, sectioned into three regions used for determining fall direction.

For impact locations specified only as F1-F5, or B1-B3, front and rear falls were simulated respectively. For locations in region 1 in Figure 1, rear falls were conducted if combined with a B1-3 code or if there was a back or back45 direction specified. Unknown or other directions were treated as side falls. For region 2, only side falls were conducted. If there was overlap between region 2 and either 1 or 3, side falls were simulated. In all cases, rotation of the head and body was applied as necessary to ensure a proper impact location. All kinematic simulations were conducted with limbs placed in a way so they impact before the head but offer little bracing effect during the fall to create a variety of scenarios for falling. For locations in region 3, front falls were conducted if combined with a F1-F5 code or if there was a front or front45 direction specified. Unknown directions were treated as side falls. A flow chart detailing the analysis from event description to the FE simulations is shown in

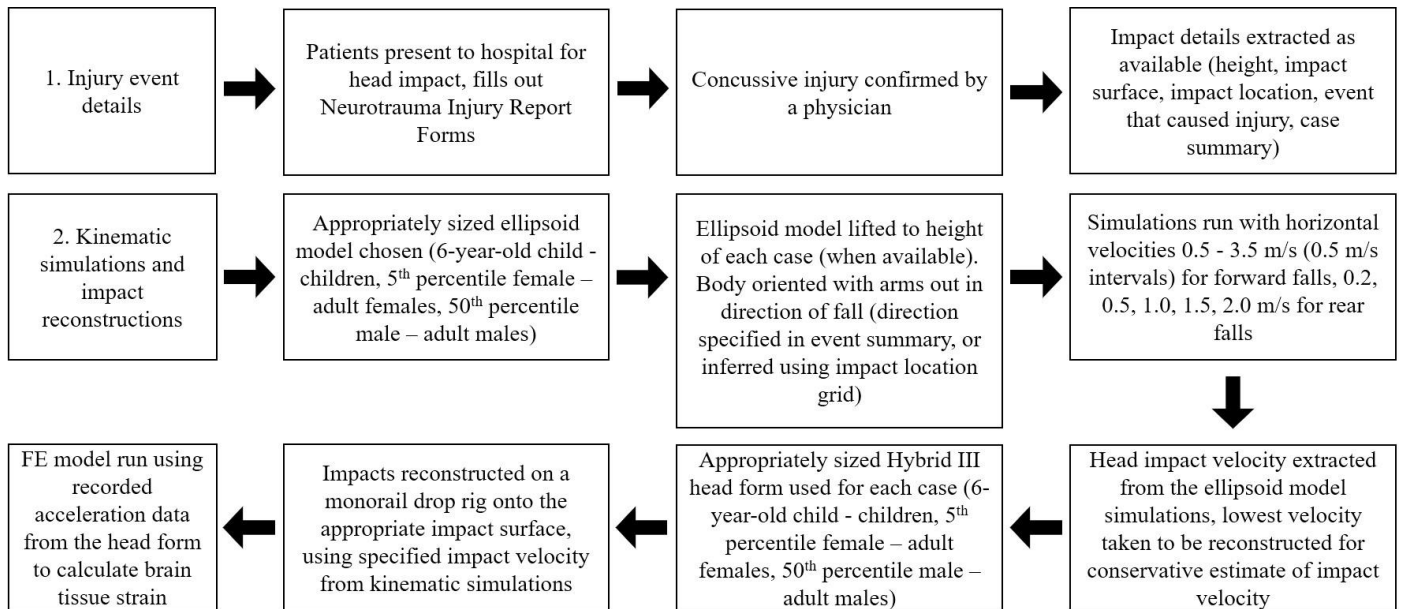


Figure S3- 2. Flow chart showing the analysis method from case event details on Neurotrauma Injury report forms, to fall kinematic simulations, to reconstructions of the events, to FE simulations to calculate brain tissue strain.

Finite element models

Two finite element models were used in this study, the stiff version of the 6-year-old model developed and validated in the first study of this thesis, and the University College Dublin Brain Trauma Model (UCDBTM) (Horgan and Gilchrist, 2003; 2004). The 6-year-old model was partially validated against cadaveric data of intracranial pressure and brain motion (Hardy et al., 2007), yielding an average score of 78.340 out of 100 using a modified version of the Normalized Integral Square Error method (Donnelly et al., 1983; Giordano and Kleiven, 2017). The validation procedures yielded an overall rating in the “good biofidelity” category (Giordano and Kleiven, 2017). The stiff version of the 6-year-old model was used to reflect the argument that youth brain tissue is stiffer than adult tissue at large strains, a result found by Prange and Margulies (2002). The stiff 6-year-old model has an initial shear modulus 15% larger than the UCDBTM as well as different viscoelastic parameters. Material properties of the 6-year-old model are shown below in Table 1 and Table 2. For further details regarding model development and validation, see the first study in this thesis.

Table S3-12. Elastic material properties for tissues in the UOBTM-6

Material	Young's modulus (MPa)	Poisson's ratio	Density (kg/m ³)
Skull	Rigid		2000
Dura	31.5	0.45	1130
Pia	11.5	0.45	1130
Falx and Tentorium	31.5	0.45	1130
Brain	Hyper Elastic	~0.5	1060
CSF	0.015	0.49998	1000

Table S3-13. Material properties of the brain for the UOBTM-6

	Initial shear modulus (kPa)	Ogden material constant α	Viscoelastic parameters				
			g_1	τ_1 (s)	g_2	τ_2 (s)	g_∞
Grey matter	11.5						
White matter	14.4	0.59	0.451	0.021	0.301	0.199	0.249
Brain stem	25.9						
Cerebellum	11.5						

Two different sizes of the UCDBTM were used for the adult cases, a full size for the male cases and a model scaled to 93% of the original size for the female cases. The 5th percentile female head form has a circumference that is 93% of the 50th percentile male head form (54 cm vs 58 cm). The scaled model reflects the difference in size of the head forms that were used for physical reconstructions. Material properties were not altered for the scaled model, with the properties of the UCDBTM shown in the appendix in Tables 6 and 7.

Concussive cases were compared based on commonly used metrics in concussive research using maximum principal strain, and cumulative strain damage measure. Cumulative strain damage measure used a threshold of 0.15, from Takhounts et al., (2003) that showed correlation between strain exceeding this level and mild DAI injury in animals, and is also reported to be a good predictor of concussion in American football reconstructions (Sanchez et al., 2018). Maximum principal strain comparisons were conducted for both the grey and white matter for each model, assessing how strain waves penetrate into the brain tissue in the two models, with CSDM being measured for the cerebrum.

Statistics

A one-way MANOVA was run to identify differences in impact parameters of impact velocity, peak linear acceleration, peak rotational acceleration, and strain metrics of CSDM, and maximum principal strain (grey and white matter) with acceptance set at $p < 0.05$. One-way ANOVAS were then run to identify differences in impact parameters and strain metrics, using a Bonferroni correction to adjust the acceptable alpha level to $p < 0.05/6$, $p < 0.008$.

Results

There was a statistically significant difference between children and adults concussive cases ($F = 31.68$, $p < 0.05$, Wilk's $\Lambda = 0.275$, partial $\eta^2 = 0.725$). The one-way ANOVAS showed significant differences for all six metrics collected between child and adult concussive cases ($p < 0.008$). There was an average difference in impact velocity of 0.90 m/s between adult and child cases, and child cases showed lower impact kinematics as well as strain values compared to the adults. An averaged summary of the results is shown in Table 3.

Table S3-14. Averaged summary of biomechanical metrics for reconstructions of 20 concussive cases of children and adults. Average values shown, with standard deviations in brackets.

	Impact velocity (m/s)	Peak Linear Acceleration (g)	Peak Rotational Acceleration (krad/s ²)	Cumulative strain damage measure	Maximum Principal Strain (Grey matter)	Maximum Principal Strain (White matter)
Children	3.04 (0.53)	193.3 (84.2)	10.18 (6.31)	0.19 (0.29)	0.374 (0.145)	0.211 (0.089)
Adults	3.94 (0.57)	323.2 (49.8)	20.47 (6.1)	0.65 (0.18)	0.688 (0.128)	0.511 (0.108)

Maximum principal strain and cumulative strain damage measure responses for individual cases are shown for children in Figure 2, and for adults in Figure 3. In addition to the differences in the peak strain in the grey and white matter, the cumulative strain damage measures were also lower in the children compared to the adults.

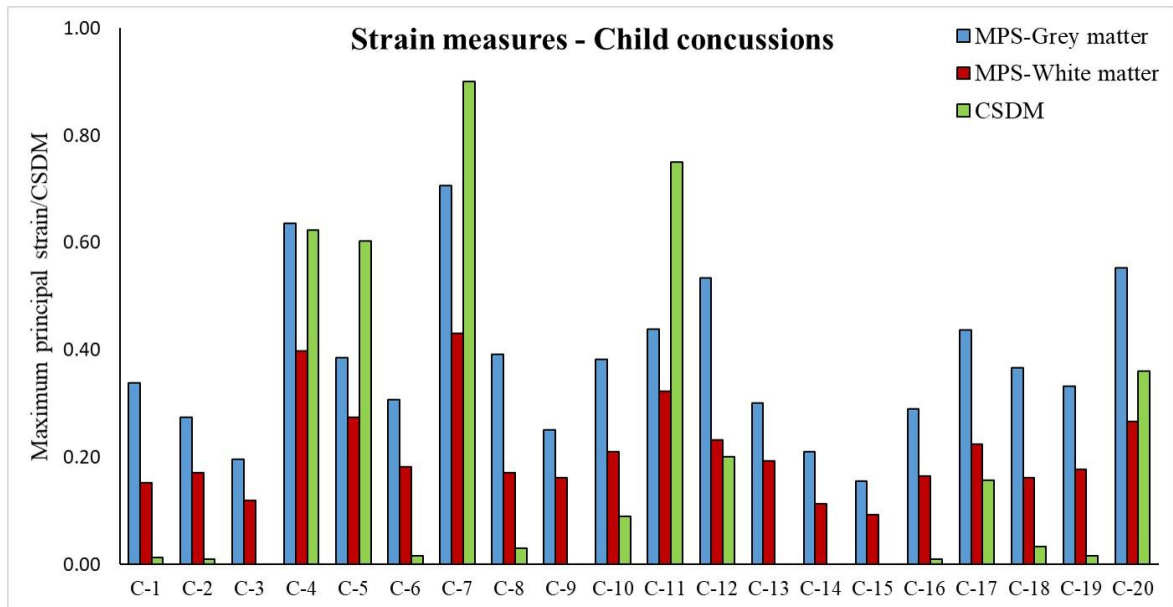


Figure S3- 3. Maximum principal strain and CSDM results for 20 cases of concussions in children, using the 6-year-old FE model

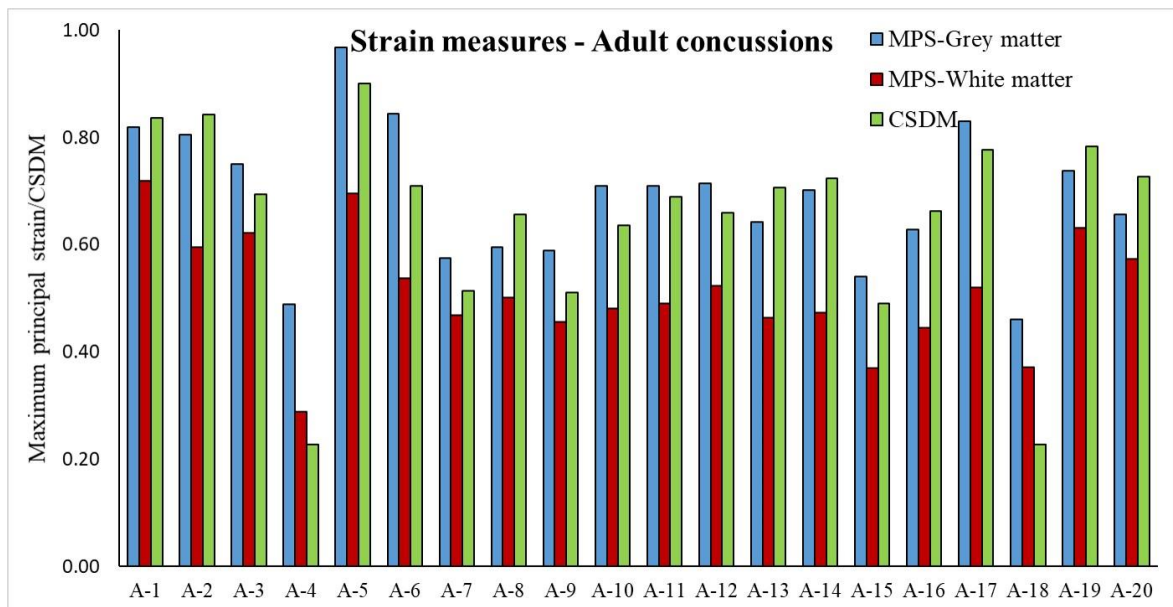


Figure S3- 4. Maximum principal strain and CSDM results for 20 cases of concussions in adults, using the UCDBTM

Discussion

As expected, all metrics from the reconstructions of concussive events examined in this study showed child responses to be lower than those of the adult cases. With an average difference in impact velocity of 0.90 m/s between children and adult cases, the relationship is

partially driven by impact velocity and lower impact energies. Another factor distinguishing the child and adult cases is impact locations, with 15 impacts to the front, 2 to the side, and 3 to the rear for the child cases, and 3 impacts to the front, 1 to the side, and 16 to the rear for the adults. The proportion of child concussions occurring from frontal falls (75%) was similar to a study of minor head injuries in children under the age of 4, finding over 70% occurred from frontal impacts (Hughes et al., 2016). Similarly, Hughes et al. (2016) documented close to 40% of the falls being impacts to concrete, compared to 30% in the current data set. The many impacts to the front of the head could be attributed to balance issues, since children's heads are larger compared to the rest of their body relative to adults. Also, children may exhibit riskier behaviour and test their physical limits more often than adults resulting in falls and frontal head impacts.

Examining the strain patterns, differences in magnitude as well as cumulative strain measures were observed. On average, the child cases had 44% and 58% lower MPS values than those in adults for the grey and white matter respectively. Differences in model responses from different constructions were examined in the previous study of this thesis, finding that the 6-year-old model shows 30% and 56% lower strains in the grey and white matter respectively than a scaled version of the UCDBTM for non-compliant impacts. With a 30% and 56% increase in strain added to the 6-year-old model responses, MPS values would be 0.486 and 0.329 in the grey and white matter respectively; values that are still lower than the adult MPS values of 0.688 and 0.511. The differences found in this study are noteworthy, and unlikely solely the result of differences in model construction.

For CSDM, the child cases averaged 72% lower values than those of the adult cases. Notably, 14 child cases had MPS results over 0.30, and 6 of these had CSDM measures under 0.05 showing that higher strain magnitudes did not necessarily translate to a cumulative strain effect in the whole brain. Overall strain was lower in children, but also more localized as it did not penetrate as deep into the white matter or spread as widely throughout the cerebrum. Of the child cases, only four cases had CSDM results of 0.20 and above, three of which were impacts to the side of the head, known to cause more severe strains (Zhang et al., 2001; Takhounts et al., 2008). All adult cases had CSDM results above 0.20.

To illustrate differences in strain pattern response, two subsets of cases can be more easily compared, impacts between 3.0 and 3.5 m/s, and between 3.5 and 4.0 m/s to non-

compliant surfaces (concrete, steel, ice). In the first subset, there are four child cases (C-2, C-3, C-6, C-8), and three adult cases (A-4, A-9, A-15) that fit these criteria. For the second subset, there were five child cases (C-7, C-10, C-12, C-17, C-20), and nine adult cases (A-3, A-6, A-10, A-11, A-13, A-14, A-16, A-17, A-18) that fit the criteria. The results for the subset of data is shown below in Table S3-15.

Table S3-15. Strain variables for two subsets of concussion cases of adults and children with similar impact velocities

	Impact velocity (m/s)		MPS (grey matter)		MPS (white matter)		CSDM (cerebrum)	
	Adults	Children	Adults	Children	Adults	Children	Adults	Children
Subset 1	3.08	3.05	0.54	0.35	0.37	0.18	0.42	0.02
Subset 2	3.73	3.75	0.70	0.52	0.49	0.27	0.64	0.34

Despite the similarity in impact velocity and impact surface, the child cases of concussion yielded lower peak strains, and cumulatively less strain in the brain when compared to adults.

Though all the data used in this study came from emergency department records, one reason the child concussion metrics could be lower than adults is that adults are less likely to go to a hospital without experiencing severe symptoms, where parents of young children would be more likely to get their child assessed after seeing them experience a head impact. This could lead to a bias towards more severe impacts in adults, and potentially lower severity impacts in children. Despite this potential bias, there is a separation in the metrics examined in this study and the trends are unlikely to be affected if more severe impacts in children and lower severity impacts in adults were added.

Comparing the strains to published adult values associated with risk of concussion, all adult cases are above 50% risk of concussion and the results for the child cases are mixed. Values associated with 50% risk of concussion that can be compared to data in this study are MPS of 0.26 in the grey matter (Kleiven, 2007), 0.32 (Kimpura and Iwamoto, 2012), 0.26 in the white matter (Patton et al. 2015), and 0.31 for mild risk of DAI (Deck and Willinger, 2008). With 16 cases exceeding MPS of 0.26 in the grey matter, 5 exceeding 0.26 in the white matter, and 12 exceeding both 0.31 and 0.32 in the cerebrum, no metric predicts all cases but the most appropriate comparison appears to be strain above 0.26 in the grey matter.

Of all the cases examined in this study, 31 of 40 were to non-compliant surfaces of ice, steel, or concrete, with the remaining nine impacts to minimally compliant surfaces, either the ground, or wood. These represent one end of a spectrum of impact durations typical of sport, encompassing the 5-15 ms range, where sport impacts lie in the 5-30 ms range (Hoshizaki et al., 2016). The data used to calculate risk of concussion in adults drew mostly from American football collisions. Kendall (2016) showed that collisions produce the lowest strains out of collisions, helmeted falls, punches, and unhelmeted falls. For this reason, it is expected that the unhelmeted falls reconstructed in this study show higher strains than studies that included collision data. For this reason, though the strain value of 0.26 in the grey matter predicts risk reasonably well for the data in this study, it is assumed that if more compliant impacts were included in the data set the comparison will not hold. Risk of concussive injury in children requires a separate analysis from adults as the developing brain cannot withstand the same level of strain.

This study supports the hypothesis by Zhou et al. (2016) that young children are at risk of injury at comparatively lower strains compared to adults. The strain data from this study follows the results of Dawson (2016), who found child cases of concussion to have lower strains than adults when using a scaled version of the UCDBTM. These data suggest that because the children sustained concussions at lower strains, it is important to note that when children are in elevated positions, such as on play structures, or on a bicycle for example, the risk of head injuries from falling will increase based on the increased impact velocity from the additional fall height. For activities that place children at height, this study reinforces that protective equipment would be beneficial since even higher responses would be expected, leading to risk of more severe head injuries. It may also be prudent for equipment manufacturers to create youth specific protective equipment, not simply sizing a single product.

Limitations

One limitation of this study is that the data was collected using two different finite element models with different constructions, requiring some interpretation of the results. Direct comparisons of results from different FE models are not possible, or recommended (Ji et al., 2014). With the limited amount of published concussion data in children, there are no comparable data sets to use, and so the comparisons were done with full knowledge of the

limitation of comparing different model responses as well as child data to adult data. This study also only included low compliance falls resulting in concussion and represents the lower end of impact durations typical in sport. Further work is required to collect quality concussive event data across differing levels of compliance to help establish how strain and risk changes with differing levels of compliance. In addition, to further define concussive injury in children and adults, it would be beneficial for further work to strive for reconstructing head impacts of non-concussive fall events.

The use of MADYMO simulations to obtain a head impact velocity is not necessarily a true response, but rather a conservative estimate of the head impact velocity. In reality, without video there is no way to accurately model the fall and obtain a more accurate head impact velocity. In practice, these simulations produce a reasonable response that has been used in many studies to establish head impact velocity (Doorly and Gilchrist, 2006; Dawson 2016; Koncan et al., 2016; Koncan et al., 2017; Post et al., 2017a; Post et al., 2017b). Additionally, the physical head forms that were used to measure the impact kinematics do not capture the geometric variance of the humans being studied. Repeated use of the head form allows for a reliable response to impacts but does not address how geometric variation of the head contributes to differences in impact response.

Finally, the conclusions of this study are predicated on the mechanical properties used in the child model, with more similar responses expected if a softer material model was used. It is postulated that the differences in impact velocity and impact kinematics will still yield lower strain results in children, however the strain values could be closer to those of adults.

Conclusions

This study shows that children between the ages of 5-7 sustain concussive injuries at comparatively lower strains than adults, and less volume of brain tissue experiencing strain overall. Children sustained concussive injuries from falls at lower impact velocities than adults due to their lower stature. All cases included in this study were to non-compliant (steel, concrete, ice) or low compliance surfaces (ground, wood), and resulted in higher strains than many published studies involving concussion of professional athletes. Values associated with 50% risk of concussion in adults were not appropriate for predicting risk of concussive injury in children,

and it is not recommended to continue to use adult values associated with concussive risk to predict injury for children. The authors stress the importance of wearing protective equipment when engaging in activities that put children in an elevated position where they can easily fall, since concussive injuries occur when falling from standing height.

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Appendix

Table S3-16. Adult concussion case summary with gender, impact surface, velocity, and locations. Location codes refer to those shown in Figure 1.

Case label	Gender	Impact surface	Impact velocity	Impact location
A-1	Male	Concrete	4.71	B2
A-2	Male	Concrete	4.75	B2/S11
A-3	Male	Concrete	3.76	B2
A-4	Male	Concrete	3.07	F3/S15
A-5	Male	Ice	4.91	S8
A-6	Female	Concrete	3.64	B2/S6
A-7	Female	Concrete	4.02	F2/S10
A-8	Female	Boat deck - MEP	3.89	B2
A-9	Female	Concrete	3.16	B2
A-10	Female	Concrete	3.69	B2
A-11	Female	Concrete	3.79	B2
A-12	Female	Concrete	4.37	B2
A-13	Female	Ice	3.67	B2
A-14	Female	Ice	3.87	B2
A-15	Female	Ice	3.01	B2
A-16	Female	Ice	3.61	B2
A-17	Female	Ice	3.78	B2/S6
A-18	Female	Ice	3.75	F2/S10
A-19	Female	Ground - MEP	4.75	B2
A-20	Female	Soccer field - MEP	4.59	B2

Table S3-17. Child concussion case summary with gender, age, height, impact surface, velocity, and location. Location codes refer to those shown in Figure 1.

Case label	Gender	Age (yrs)	Height (cm)	Impact surface	Impact velocity	Impact location
C-1	Male	5.09	107	Concrete	2.63	B2/B3
C-2	Female	5.1	109	Wood	3.30	S10
C-3	Female	5.25	97	Wood	3.04	F2
C-4	Female	5.53	117	Concrete	2.80	S4
C-5	Female	5.57	104	Ice	2.31	S9
C-6	Male	5.59	97	Concrete	3.01	F1
C-7	Male	5.8	122	Ice	3.83	F2-F5
C-8	Male	5.94	99	Steel	3.09	F1
C-9	Male	6.18	91	Wood	2.93	F2
C-10	Female	6.26	117	Concrete	3.60	F1/S10
C-11	Male	6.6	114	Ice	2.39	S9
C-12	Male	6.67	112	Ice	3.58	S5
C-13	Female	6.91	117	Wood	3.64	F1
C-14	Male	6.94	107	Wood	2.86	F1-F5
C-15	Male	6.95	119	Wood	2.24	S10
C-16	Male	7.18	91	Concrete	2.54	F1
C-17	Female	7.19	137	Steel	3.77	S10
C-18	Male	7.39	122	Ice	2.59	B2/B3
C-19	Male	7.91	119	Concrete	2.77	B2
C-20	Female	7.91	130	Ice	3.95	F3

Table S3-18. Elastic properties of the brain used in the UCDBTM

Material	Young's modulus (MPa)	Poisson's ratio	Density (kg/m ³)
Brain	Viscoelastic	0.49998	1060
CSF	0.015	0.5	1000
Cortical bone	15000	0.22	2000
Trabecular bone	1000	0.24	1300
Facial bone	500	0.23	2100
Dura	31.5	0.45	1130
Pia	11.5	0.45	1130
Falx and tentorium	31.5	0.45	1130
Scalp	16.7	0.42	1000

Table S3-19. Viscoelastic material properties of the brain used in the UCDBTM

	Shear modulus (kPa)		Decay constant (s ⁻¹)	Bulk modulus (GPa)
	G_0	G_∞		
White matter	12.5	2.5	80	2.19
Grey matter	10	2	80	2.19
Cerebellum	10	2	80	2.19
Brain stem	22.5	4.5	80	2.19

PART IV

Global discussion and conclusions – Study summaries

The purpose of this thesis was to assess how the mechanical response of the brain in young children around 6 years old differs from an adult brain in cases resulting in concussive injury. A new model was created, validated, tested, and finally compared to adult responses, with these tasks separated into three studies. The purpose of the first study was to create and validate a novel FE model developed specifically for children around 6 years of age to be used alongside physical models to investigate concussive injuries, and compare the new model with a scaled adult model used in previous studies for sport concussion in children. The purpose of the second study was to test the sensitivity and stability of response of the newly developed FE model of a 6-year-old child for falls at three levels of surface compliance consistent with head impact events typical of sport that cause concussion in children. The purpose of the third study was to assess whether finite element responses from falls resulting in concussion are different between children and adults, quantified using maximum principal strain, and cumulative strain damage measure (CSDM).

The first study developed and partially validated a new 6-year-old model, using comparisons to cadaveric data of intracranial pressure and relative brain-skull motion from Hardy et al. (2001; 2007). Two different versions of the model were evaluated using different material properties, one “stiff” version and one “average” version. Comparisons were made to a scaled adult brain model used in previous research of children to use as a reference to identify how the new model differed in response, and how strains in specific locations in the brain differed between the models. Using a modified version of the normalized integral square error method to assess biofidelity (Donnelly et al., 1983; Giordano and Kleiven, 2016b), both the stiff and average models were classified to have “good” biofidelity, scoring 78.340 and 75.762 respectively, where the scaled adult model scored the lowest at 70.497. The biofidelity measures identified the stiff model as performing better than the three other models, despite being stiffer than many published studies reporting material properties of the brain. With biofidelity measures corresponding to “good” biofidelity, the model performs sufficiently well to be used in further studies of brain injury. The stiff and average model created acceptable responses in biofidelity

measures, and deemed suitable for consideration for future investigations involving youth. The cadaver data that was used to validate the new model was obtained using adult specimens, a limitation of this study. Until intracranial measures for youth are published, assumptions must be made and adjusted as studies are published in the future.

The second study tested the model at three levels of compliance to two impact locations, at three impact velocities, using a subset of previously published data that investigated interactions between impact parameters. Characterizing the model response across these parameters was important, since different impact events have unique impact parameters and may require event specific strain values to associate to risk of concussive injury (Kendall, 2016). Again, the responses were compared to a scaled adult model to further document how the new model differs from a model that had been previously published with youth data. The new 6-year-old model showed on average, 30% lower strains for low compliance impacts (steel), 9% lower strains for moderate compliance impacts (VN foam), and 1% lower strains for high compliance impacts (Rubatex rubber foam). Trends were different between frontal and side locations, with the high compliance impacts to the side showing 9% higher responses than the scaled adult model. Strain in the white matter of the brain as well as cumulative strain damage measures for the 6-year-old model were consistently lower than the scaled model. The 6-year-old model showed similar peak strains for high compliance impacts, but the strain did not penetrate as deep into the brain. It was hypothesized the accurate representation of the folds of the white matter were influential in reducing the overall strain, as well as penetration of strain into the brain. The study offered a method to interpret differences in model results, based on levels of impact velocity and compliance, allowing for better comparisons between the new model and the UCDBTM.

The third study compared the brain response from concussive cases in children and adults resulting from falls. Physical reconstructions of 40 real-world concussive events were conducted; 20 involved children aged 5-7, and 20 involved adults. Simulations of the brain tissue response were conducted using the newly developed 6-year-old model for the child cases, and two sizes of the UCDBTM for the adult cases, with a 93% scaled version used for females to account for size differences. The child cases showed lower responses across all measured metrics, for impact kinematics and strain variables. The lower strains were a result of a velocity driven relationship,

with the child concussions occurring from lower velocity impacts compared to the adults, since all events were falls from standing. Even for subsets of cases matched for velocity and surface compliance, child strains were lower than the adults. This study ultimately provides an argument that based on impact kinematics and strain variables, children are at higher risk of concussive injury than adults. In adult studies of concussion, values of maximum principal strain in the range of 0.20-0.30 have been correlated to ~50% risk of concussive injury. In tissue studies, functional impairment has been documented at strains near 0.15, with damage occurring near a strain of 0.20. With the child responses being lower than adults, 50% risk of concussion may lie closer to strains of 0.15-0.25 in children, overlapping with adults, but beginning at lower values, however this value is purely observational. Putting children at elevated height with risks of falls such as jungle gyms, would be putting children at higher risk of concussion if steps are not taken to manage the impact forces from falls with padding or other solutions. Helmet designers can also benefit from this study, aiming at creating a youth-specific helmet in order to reduce risk of concussion.

Conclusion

The purpose of this research was to investigate whether or not children are more susceptible to concussive injuries when compared to adults. With the development of a novel 6-year-old model with age-appropriate material properties, accurate geometry, and highly discretized folds of the white matter within the cerebrum, a unique strain response was elicited when compared to a scaled adult model. The response of the new model was found to show different responses across three levels of compliance, with smallest differences for the highest compliance condition. In low compliance conditions, the new model showed lower peak strains, and lower strains penetrating into the white matter.

When used in reconstructions of real-world concussive events, the 6-year-old model showed consistently lower responses than the adult cases of concussion. The children sustained concussive injury at lower impact velocities, translating into lower impact energy, and lower strains in the brain tissue. The results demonstrated that children sustain a concussion at lower strains when compared to adults. Risk of elevated positions pose significant risk of concussive injury as falls from height produce higher impact velocities. On play structures, where children are at an elevated height, fall protection systems should be put in place, or padded floors may be

beneficial to help reduce the possibility of injury from falls that occur during sports and play and improve overall safety.

PART V

Statement of Contributions

List of Collaborators:

David Koncan (PhD student) was involved in all aspects of this thesis, from conception to data collection, analysis, and writing.

Dr. Thomas Blaine Hoshizaki was involved as the thesis supervisor and was involved in a supervisory role in all aspects of the thesis.

Dr. Michael D. Gilchrist provided support for finite element modelling related queries, and was a committee member for the thesis.

Dr. Anna Oeur was involved in the impact data collection that was used in the second study, as this data was collected as a part of her PhD thesis.

Dr. Michael Vassilyadi was involved in the acquisition of the MRI that was used to develop the finite element model in the thesis.

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PART VI

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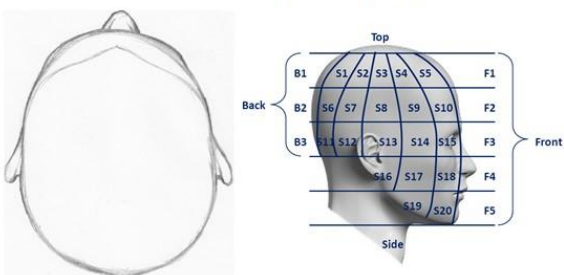
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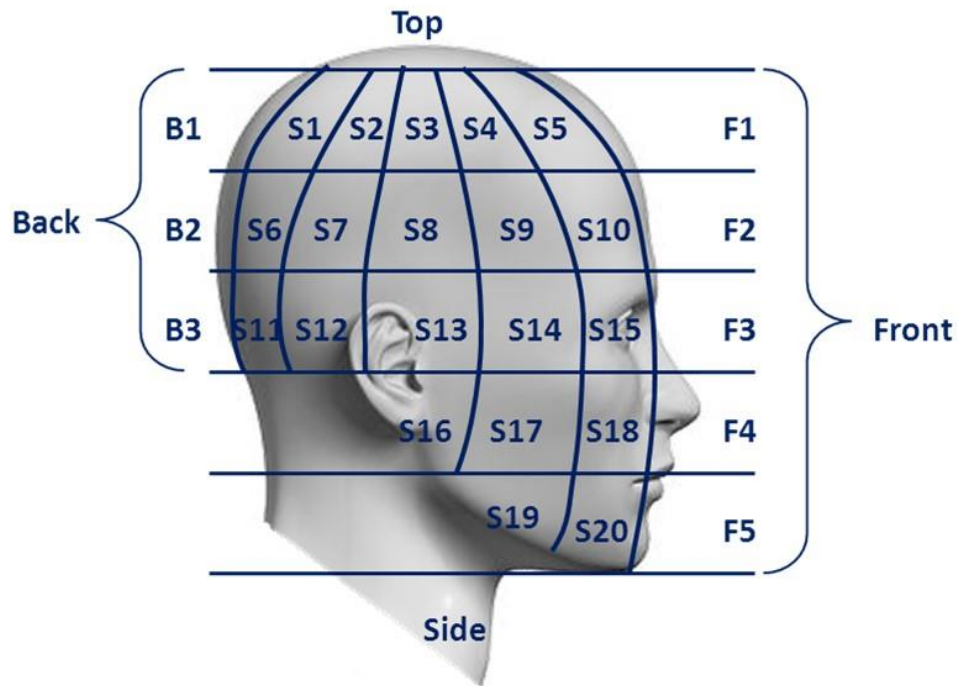
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Appendix A

Neurotrauma injury report forms and case data

Neurotrauma Injury Report

Patient Information Age: _____ Gender: ☐ Male ☐ Female Weight: _____ Height: _____ Previous Head Injury: ☐ No ☐ Yes – Number _____ Pre-existing Medical Conditions _____ _____ _____ Diagnosis and Description Injury Diagnosis: _____ Incident Description: Sports/Recreational Play. Recreational Play (gym, recess) _____ _____ _____ Primary Impact Location- Please indicate the location of primary impact.  Question 1a: Select the location where you were hit using the image shown on the right and the direction using the left image Question 1b: If you were hit on the side, which side was it? ☐ Left ☐ Right Question 2: Circle the orientation of the hit Downward Straight Upward	Glasgow Coma Scale Eyes: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ Closed Verbal: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Tube Motor: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 Loss of Consciousness ☐ No ☐ Yes – Duration _____ minutes Amnesia ☐ No ☐ Yes – Duration _____ minutes Symptoms of Confusion ☐ No ☐ Yes – Duration _____ minutes Fall ☐ N/A Drop: _____ Initial Contact: ☐ Head ☐ Other Impact Surface: ☐ Sand ☐ Grass ☐ Gravel ☐ Concrete ☐ Ice ☐ Steel ☐ Other: _____ Collision ☐ N/A Object: _____ Weight: _____ kg Speed: ☐ Slow ☐ Moderate ☐ Fast Material: _____ Mode: ☐ Walk ☐ Run ☐ Bike ☐ Skate Helmet ☐ N/A Make: _____ Model: _____ Size: _____ Available for Analysis: ☐ No ☐ Yes Supporting Documents (if available) Injury Picture: ☐ No ☐ Yes Incident Video: ☐ No ☐ Yes
Documentation Physician: _____ Hospital: _____ Date: (Y Y Y Y / M M / D D)	



Question 1a: Select the location where you were hit using the image shown above.

Question 1b: If you were hit on the side, which side was it?

- ☐ Unknown
- ☐ Midline
- ☐ Left
- ☐ Right

Question 2: In which direction were you hit?

- ☐ Front
- ☐ Front 45°
- ☐ Side
- ☐ Back 45°
- ☐ Back

Question 2: What was the orientation of the hit?

- ☐ Downward
- ☐ Straight
- ☐ Upward

Case: C-1

Age: 5.09
Gender: Male
Height: 107 cm

Impact speed: 2.63 m/s
Impact location: B2/B3
Impact surface: Concrete

Impact direction: Back
Weight: 17.3 kg



Event description:

Slipped/fell/tripped on floor/ground

Case: C-2

Age: 5.10
Gender: Female
Height: 109 cm

Impact speed: 3.30 m/s
Impact location: S10
Impact surface: Hardwood floor

Impact direction: Front
Weight: 19 kg



Event description:

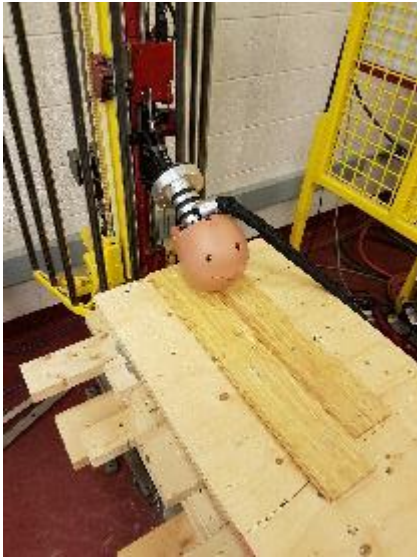
Slipped/fell/tripped on floor/ground

Case: C-3

Age: 5.25
Gender: Female
Height: 97 cm

Impact speed: 3.04 m/s
Impact location: F2
Impact surface: Hardwood

Impact direction: Front
Weight: 18.3 kg



Event description:
Struck head against wall/door

Case: C-4

Age: 5.53
Gender: Female
Height: 117 cm

Impact speed: 2.80
Impact location: S4
Impact surface: Concrete

Impact direction: Side
Weight: 27 kg



Event description:
Struck head against wall/door

Case: C-5

Age: 5.57
Gender: Female
Height: 104 cm

Impact speed: 2.31
Impact location: S9
Impact surface: Ice

Impact direction: Side
Weight: 19.2 kg



Event description:

Slipped/fell/tripped on floor/ground

Case: C-6

Age: 5.59
Gender: Male
Height: 97 cm

Impact speed: 3.01
Impact location: F1
Impact surface: Concrete

Impact direction: Front
Weight: 21.5 kg



Event description:

Fall down stairs

Case: C-7

Age: 5.80
Gender: Male
Height: 122 cm

Impact speed: 3.83
Impact location: F2-F5
Impact surface: Ice

Impact direction: Front
Weight: 17.3 kg



Event description:
Struck head against household object (e.g. furniture)

Case: C-8

Age: 5.94
Gender: Male
Height: 99 cm

Impact speed: 3.09
Impact location: F1
Impact surface: Steel

Impact direction: Front
Weight: 23.8 kg



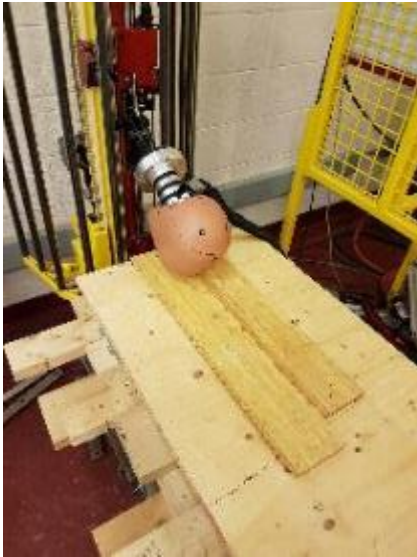
Event description:
Slipped/fell/tripped on floor/ground

Case: C-9

Age: 6.18
Gender: Male
Height: 91 cm

Impact speed: 2.93
Impact location: F2
Impact surface: Wood

Impact direction: Front
Weight: 18.5 kg



Event description:
Struck head against household object (e.g. furniture)

Case: C-10

Age: 6.26
Gender: Female
Height: 117 cm

Impact speed: 3.60
Impact location: F1/S10
Impact surface: Concrete

Impact direction: Front
Weight: 29.6 kg



Event description:
Struck head against household object (e.g. furniture)

Case: C-11

Age: 6.6
Gender: Male
Height: 114 cm

Impact speed: 2.39
Impact location: S9
Impact surface: Ice

Impact direction: Side
Weight: 23.3 kg



Event description:
Slipped/fell/tripped on floor/ground

Case: C-12

Age: 6.67
Gender: Male
Height: 112 cm

Impact speed: 3.58
Impact location: S5
Impact surface: Ice

Impact direction: Front
Weight: 23 kg



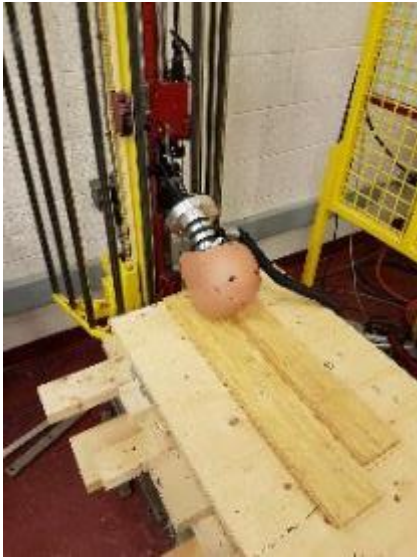
Event description:
Slipped/fell/tripped on floor/ground

Case: C-13

Age: 6.91
Gender: Female
Height: 117cm

Impact speed: 3.64
Impact location: F1
Impact surface: Wood

Impact direction: Front
Weight: 19.7 kg



Event Description:

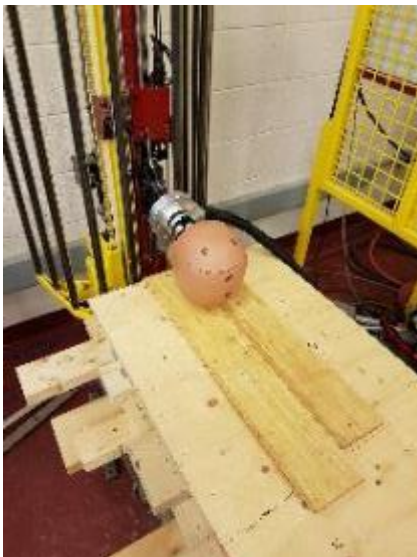
Fall from height (e.g. fall from bed or tree)

Case: C-14

Age: 6.94
Gender: Male
Height: 107 cm

Impact speed: 2.86
Impact location: F1-F5
Impact surface: Wood

Impact direction: Front
Weight: 20 kg



Event Description:

Fall from height (e.g. fall from bed or tree)

Case: C-15

Age: 6.95
Gender: Male
Height: 119 cm

Impact speed: 2.24
Impact location: S10
Impact surface: Wood

Impact direction: Front
Weight: 20 kg



Event description:

Struck head against household object (e.g. furniture)

Case: C-16

Age: 7.18
Gender: Male
Height: 91 cm

Impact speed: 2.54
Impact location: F1
Impact surface: Concrete

Impact direction: Front
Weight: 21 kg



Event description:

Slipped/fell/tripped on floor/ground

Case: C-17

Age: 7.19
Gender: Female
Height: 137 cm

Impact speed: 3.77
Impact location: S10
Impact surface: Steel

Impact direction: Front
Weight: 57.7 kg



Event description:
Struck head against household object (e.g. furniture)

Case: C-18

Age: 7.39
Gender: Male
Height: 122 cm

Impact speed: 2.59
Impact location: B2/B3
Impact surface: Ice

Impact direction: Back
Weight: 22.5 kg



Event description:
Slipped/fell/tripped on floor/ground

Case: C-19

Age: 7.91
Gender: Male
Height: 119 cm

Impact speed: 2.77
Impact location: B2
Impact surface: Concrete

Impact direction: Back
Weight: 25.6 kg



Event description:

Slipped/fell/tripped on floor/ground

Case: C-20

Age: 7.91
Gender: Female
Height: 130 cm

Impact speed: 3.95
Impact location: F3
Impact surface: Ice

Impact direction: Front
Weight: 24.2 kg



Event description:

Slipped/fell/tripped on floor/ground

Case: A-1

Age: 58
Gender: Male
Height:

Impact speed: 4.71 m/s
Impact location: B2
Impact surface: Concrete

Impact direction: Back



Case: A-2

Age: 22
Gender: Male
Height:

Impact speed: 4.75 m/s
Impact location: B2/S11
Impact surface: Concrete

Impact direction: Back



Event Description:

Fell backwards and hit head on curb, hit curb
level not ground

Case: A-3

Age: 49
Gender: Male
Height:

Impact speed: 3.76 m/s
Impact location: B2
Impact surface: Concrete

Impact direction: Back



Case: A-4

Age: 52
Gender: Male
Height:

Impact speed: 3.07
Impact location: F3/S15
Impact surface: Concrete

Impact direction: Front



Case: A-5

Age: 37
Gender: Male
Height:

Impact speed: 4.91
Impact location: S8
Impact surface: Ice

Impact direction: Side



Case: A-6

Age: 65
Gender: Female
Height:

Impact speed: 3.64
Impact location: B2/S6
Impact surface: Concrete

Impact direction: Back



Case: A-7

Age: 54
Gender: Female
Height:

Impact speed: 4.02
Impact location: F2/S10
Impact surface: Concrete

Impact direction: Front



Case: A-8

Age: 50
Gender: Female
Height:

Impact speed: 3.89
Impact location: B2
Impact surface: Boat deck (Impacted MEP)

Impact direction: Back



Event description:
Slipped on boat deck

Case: A-9

Age: 51
Gender: Female
Height:

Impact speed: 3.16
Impact location: B2
Impact surface: Concrete

Impact direction: Back



Case: A-10

Age: 59
Gender: Female
Height:

Impact speed: 3.69
Impact location: B2
Impact surface: Concrete

Impact direction: Back



Case: A-11

Age: 57
Gender: Female
Height:

Impact speed: 3.79
Impact location: B2
Impact surface: Concrete

Impact direction: Back



Case: A-12

Age: 21
Gender: Female
Height:

Impact speed: 4.37
Impact location: B2
Impact surface: Concrete

Impact direction: Back



Event description:

Slipped on ice, hit first concrete step – hit step
level not ground

Case: A-13

Age: 26
Gender: Female
Height:

Impact speed: 3.67
Impact location: B2
Impact surface: Ice

Impact direction: Back



Event description:
Slipped on ice

Case: A-14

Age: 51
Gender: Female
Height:

Impact speed: 3.87
Impact location: B2
Impact surface: Ice

Impact direction: Back



Event description:
Fell backwards on ice, hit buttocks, then head

Case: A-15

Age: 43
Gender: Female
Height:

Impact speed: 3.01
Impact location: B2
Impact surface: Ice

Impact direction: Back



Event description:

Fell backwards while running on ice

Case: A-16

Age: 62
Gender: Female
Height:

Impact speed: 3.61
Impact location: B2
Impact surface: Ice

Impact direction: Back



Case: A-17

Age: 52
Gender: Female
Height:

Impact speed: 3.78
Impact location: B2/S6
Impact surface: Ice

Impact direction: Back



Case: A-18

Age: 65
Gender: Female
Height:

Impact speed: 3.75
Impact location: F2/S10
Impact surface: Ice

Impact direction: Front



Event description:

Slipped on ice, fell forward onto right forehead
and right knee

Case: A-19

Age: 27
Gender: Female
Height:

Impact speed: 4.75
Impact location: B2
Impact direction: Back
Impact surface: Ground and rocks (Impacted MEP)



Event description:
Slipped on a rock, fell backwards and hit head

Case: A-20

Age: 18
Gender: Female
Height:

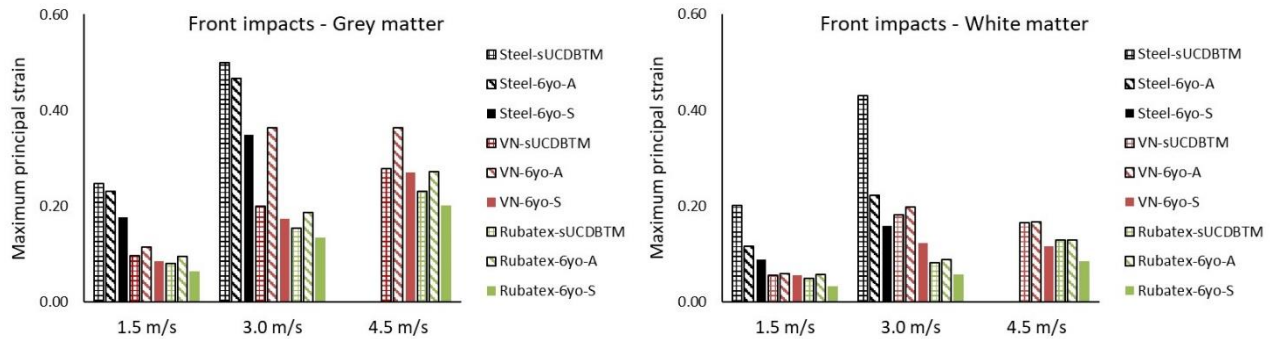
Impact speed: 4.59
Impact location: B2
Impact direction: Back
Impact surface: Soccer field (Impacted MEP)



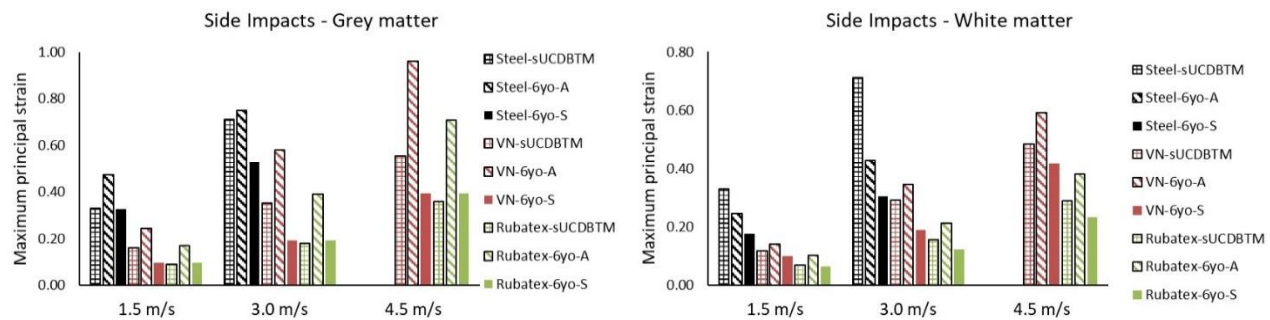
Event description:
Fell and hit the back of her head while playing soccer

Appendix B

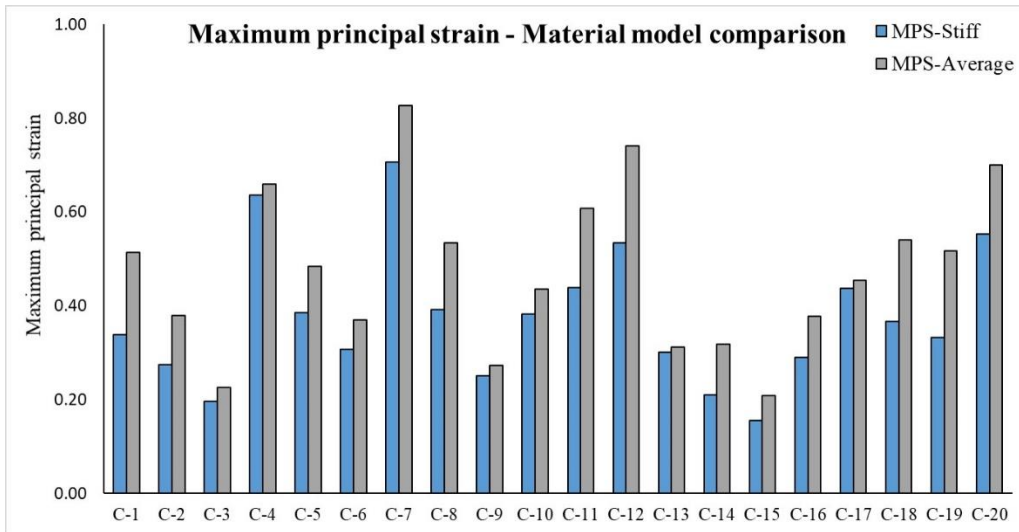
Results for study 2 and study 3 using a more compliant material model



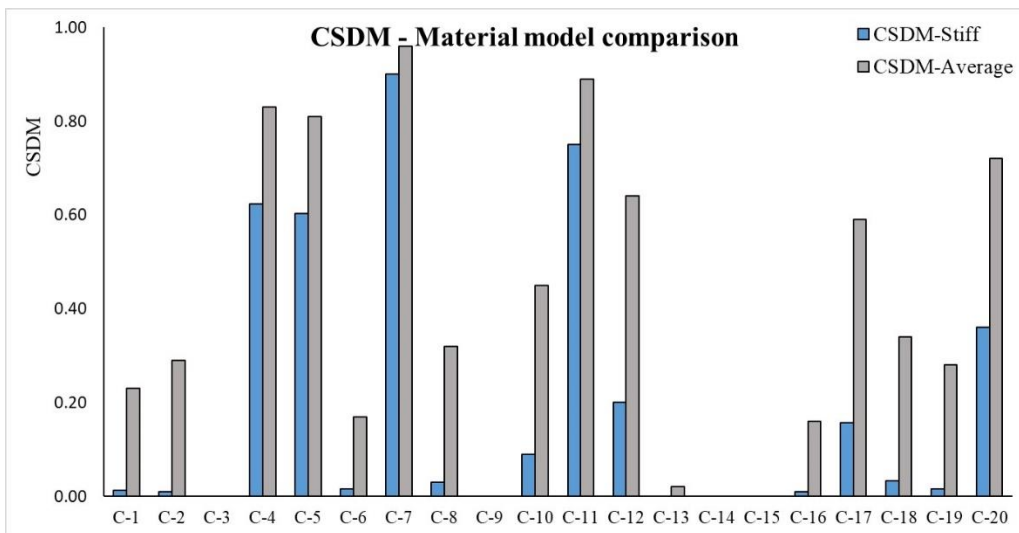
Maximum principal strain results for front impacts to low (steel), moderate (VN foam), and high (Rubatex rubber foam) compliance for the average 6-year-old model (6yo-A), stiff 6-year old model (6yo-S), and scaled University College Dublin Brain Trauma Model (sUCDBTM)



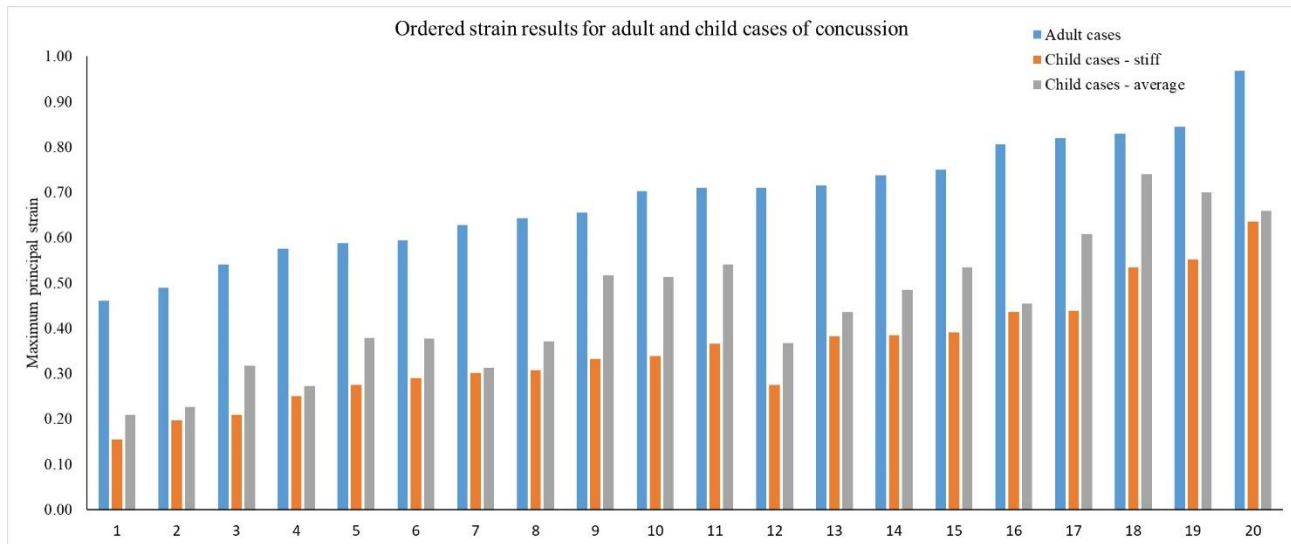
Maximum principal strain results for front impacts to low (steel), moderate (VN foam), and high (Rubatex rubber foam) compliance for the average 6-year-old model (6yo-A), stiff 6-year old model (6yo-S), and scaled University College Dublin Brain Trauma Model (sUCDBTM)



Maximum principal strain results for the 20 concussive cases of children using the stiff and average shear moduli presented in study 1.



Cumulative strain damage measure results for the 20 concussive cases of children using the stiff and average shear moduli presented in study 1.



Maximum principal strain results, ordered from lowest to highest for both child and adult cases, presenting both the stiff material model responses (orange) and the average material model responses (grey) compared to the adult responses (blue).