MATHEMATICAL MODELING OF CEREBRAL CONCUSSION: CORRELATIONS OF REGIONAL BRAIN STRAIN WITH CLINICAL SYMPTOMS

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ABSTRACT

To address the relationship of clinical symptoms and the location and magnitude of brain strains, the Wayne State University human head finite element model was used with loading conditions predicted to produce either mild (AIS 1) or classical (AIS 2) concussion. Sinusoidal accelerations using 3,000 rad/s^2 at 25 rad/s or 4,500 rad/s^2 at 50 rad/s, respectively were applied in sagittal and coronal planes to evaluate the effect of loading directions on strain magnitudes and distribution. High principal strains began at the surface and later migrated subcortically, eventually maximizing in parietal cortex, basal ganglia, thalamus and parahippocampal areas. Strain magnitude increased as angular velocity increased and peaked 8 ms after the peak of angular velocity. Large principal strains were in caudate, thalamus, midbrain and hippocampus for coronal and corpus callosum, hippocampus and fronto-temporal cortex for sagittal loading. In AIS 1 concussion, peak strain in all brain regions was <0.30 while in AIS 2 concussion, large areas had strains >0.35 (especially the brainstem-thalamic and hippocampal regions). These areas seem to correlate well with observed clinical symptoms of memory dysfunction and altered awareness associated with concussion.

Keywords: BRAINS, ACCELERATIONS, FINITE ELEMENT METHOD, TOLERANCES

TRAUMATIC BRAIN INJURY (TBI) is one of the leading causes of death and disability worldwide (Murray et al., 1996). In the US, there are approximately 300,000 new cases of TBI admitted to hospitals each year (Kraus and McArthur, 1996; Horn and Scherer, 2000). Currently about 6 million Americans are living with neurobehavioral sequelae or other losses of brain from TBI. Although TBI is a significant health problem, no effective treatments exist which target the underlying pathophysiology to prevent the progression of neural damage initiated by mechanical injury (Faden, 2002). This lack of therapeutic options highlights the importance of more efficacious strategies and equipment to prevent TBI from occurring in the first place.

Current regulations use the Head Injury Criterion (HIC) to assess head/brain injury severity. However, the HIC only takes translational acceleration into account, not rotational acceleration, and TBI is attributed to both types of motion. Diffuse brain injury (DBI) forms a broad spectrum of injuries from mild concussion, which is not associated with loss of consciousness, to classical cerebral concussion with transient disturbance of consciousness, to diffuse axonal injury (DAI) with prolonged loss of consciousness of varying duration. Several rotational acceleration limits for diffuse brain injury have been proposed based on the animal, cadaver, or physical model studies (Ommaya et al., 1967; Ommaya and Gennarelli, 1974; Lowenhielm, 1975, 1978; Margulies and Thibault, 1992; Newman et al., 2000; Zhang et al., 2004a). Recently Gennarelli et al. (2003) and Ommaya et al. (2002) reanalyzed previously published thresholds suggested for components of DBI and establish tolerances for the entire spectrum of DBI.

Many animal models, *in vitro* neural tissue models, and finite element (FE) models have been used to estimate neural tissue damage thresholds and their relation to neuropothological outcomes (Margulies and Thibault, 1992; Bandak and Eppinger, 1994; Mendis et al., 1995; Maxwell et al., 1997; Miller et al., 1999; Bain and Meaney, 1999; Willinger et al., 1999; Franklin et al., 2005; Singh et al., 2006; Mao et al., 2006; Elkin and Morrison III, 2007). Recently, validated Wayne State

University (WSU) human head FE model was utilized to investigate the mechanisms of concussions sustained by American football players using on-field accident data obtained from the National Football League (NFL) (Zhang et al., 2003; King et al., 2003; Zhang et al., 2004a; Viano et al., 2005). Subsequently, the model was used to estimate the brain response of an Indy race car driver during a severe frontal, side and rear crash (Zhang et al., 2004b). The model was further applied to predict various types of brain injury using the data from reconstructions of real-world automotive crashes and to relate the localized tissue strain to the actual injury sustained by the occupant (Franklyn et al., 2005). The correlation of the regional strain with clinical symptoms and injury severity demonstrated the applicability of the current model to predict the risk of DBI caused by given mechanical conditions.

The present investigation was performed to relate proposed rotational parameters to localized strain measures for mild to classical concussion injuries using a validated finite element model of the human head. Our hypothesis is that the differences found in the anatomical areas and magnitudes of brain strains for mild and classical concussion levels would correspond to regional symptoms common in humans with those conditions.

METHODS

The finite element model of the human head developed by Zhang et al. (2001) was exercised to investigate the tissue strain responses at various anatomical regions resulting from a set of applied rotational threshold loadings. This anatomically inspired, high resolution FE model features fine anatomical details including the scalp, skull with an outer table, diploë, and inner table, dura, falx cerebri, tentorium, pia, sagittal sinus, transverse sinus, cerebral spinal fluid (CSF), hemispheres of the cerebrum with distinct white and gray matter, cerebellum, brainstem, lateral ventricles, third ventricles, and bridging veins. The facial model consists of facial bones, nasal cartilage, temporal mandibular joint, ligaments, soft tissue and skin. The entire head model is made up of over 315,000 elements and uses 15 different material properties for various tissues of the head. The model has been subjected to rigorous validation against available cadaveric intracranial and ventricular pressure data, relative displacement data between the brain and the skull, and facial impact data (Zhang et al., 2001; Viano et al., 2005).

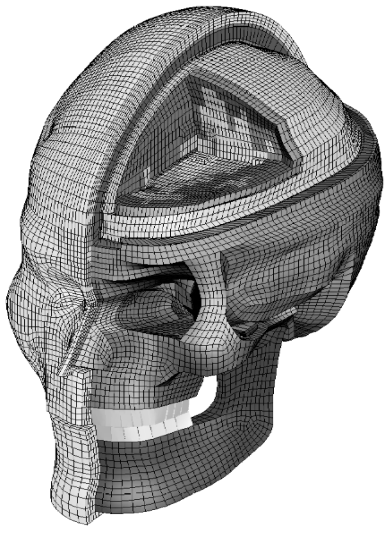

Fig. 1 - Anatomically Detailed Finite Element Model of Human Head

The accelerations used as input to the WSU head model were based on the rotational acceleration thresholds proposed for a spectrum of diffuse brain injury (Gennarelli et al., 2003). As depicted in

Figure 2 and Table 1, the entire DBI is divided into six injury categories, namely mild cerebral concussion (mCC), classical cerebral concussion (cCC), severe cerebral concussion (sCC), mild diffuse axonal injury (mDAI), moderate diffuse axonal injury (MDAI) and severe diffuse axonal injury (sDAI). Six sets of peak angular acceleration and angular thresholds were established to describe each injury severity. In the current study, two rotational acceleration (velocity) levels, 4,500 rad/s2 at 50 rad/s and 3,000 rad/s2 at 25 rad/s thresholds for classical concussion (AIS 2) and mild concussion (AIS 1) were simulated and compared.

The acceleration-time profile used was based on a standard sinusoidal function α(t) as following:

$$\alpha(t) = \frac{2\pi A}{T}\sin\left(\frac{2\pi t}{T}\right)$$

where A is the peak acceleration amplitude and T is the pulse duration. The duration of the pulse was determined based on the magnitude of the acceleration and velocity. Figure 3 shows the rotational acceleration, rotational velocity and angular rotation-time histories.

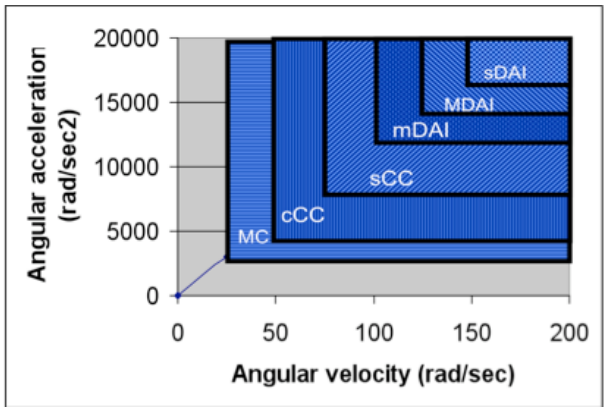

Table 1. DBI Categories and AIS Scale

AIS	Angular Acceleration	Angular Velocity	Injury
0	0	0	0
1	3,000	25	mCC
2	4,500	50	cCC
3	8,000	75	sCC
4	12,000	100	mDAI
5	14,500	125	MDAI
6	16,500	150	sDAI

Fig. 2 – Angular Tolerances for the Entire Spectrum of Diffuse Brain Injury as listed in Table 1.

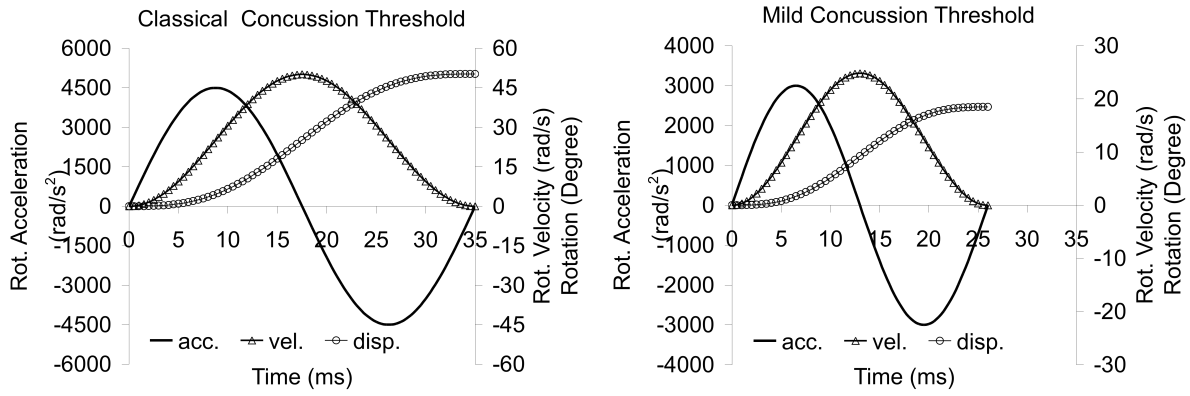

Fig. 3 - Applied Rotational Acceleration, Rotational Velocity and Angular Displacement Time Histories at the Center of the Gravity of the Head Model

The two rotational acceleration pulses were applied to the c.g. of the head model in the sagittal (about y-axis), and coronal (about x-axis) planes. The effect of the loading direction on the magnitude and distribution of strains were compared. The severity of affected brain regions were evaluated based on tissue strain damage criterion in order to assess concussion risk. First principal strain of 0.35 previously proposed as the tolerance threshold for mild traumatic brain injury (MTBI) or concussion was used as strain damage threshold to assess the injury severity (Zhang et al., 2003; King et al., 2003; Viano et al., 2005). The locations of neural tissue experiencing strain above this level were then correlated to the anatomic structures associated with common symptoms of concussion (loss of consciousness, amnesia/memory and cognitive dysfunction). In addition, the extent of injury was quantified in the affected regions using the cumulative strain damage measure proposed by Bandak and Eppinger (1994). The cumulative strain damage is the measure of the accumulation of strain response over the period of loading. The measure calculates the volume fraction of the brain that experiences maximum principal strain level greater than a strain damage tolerance level as a consequence of the total event. The strain damage tolerance level used was 0.35 first principal strain.

RESULTS

The distribution of first principal strain responses in the brain exhibited regionally specific patterns after the two loading conditions were applied. At the same loading severity, the induced strain magnitude did not vary substantially between coronal and sagittal motions. However, the loading direction did produce different strain distributions. Figure 4 shows the composite maps of the cumulative strain predicted by model in the transverse (A and B) and coronal (C) sections throughout the entire acceleration duration. For coronal rotation, the highest strains occurred in the thalamus, midbrain, caudate, hippocampus and temporal lobe regions. In the sagittal loading condition, the hippocampus, corpus callosum and cortex at inter-hemispheric fissure experienced the highest strains.

At the higher AIS 2 rotational condition, using a critical strain threshold of 0.35, it was found that the thalamus and the midbrain were affected regions due to a coronal rotation and the hippocampus and cortex region were highly strained due to a sagittal rotation. The overall affected brain volume fraction (ratio of damaged tissue to whole brain tissue) reached to 17% and 15% respectively, for coronal and sagittal loadings. The affected brain volume was only 1.0% and 0.8% for coronal and sagittal direction, respectively, in the mild AIS 1 loading condition.

In terms of temporal profiles of the brain response, it was observed that the localized tissue strain was initiated at the surface of the brain earlier in the loading. Later, strains migrated to the white matter and deep gray matter structures with increased magnitude and, eventually accumulated in specific loci of the brain, notable in the midbrain, thalamic pathway and parahippocampal areas. The strain magnitude increased as angular velocity increased. The strain reached peak at about 7-8 ms after the angular velocity reached maximum. Figure 5 shows the timing of the strain predicted by the model in the regions sustained critical strain due to rotation in the coronal and sagittal planes. The strain magnitude at each region was determined by averaging the strain magnitude for a tissue size of 6x6x6 mm at every time increment.

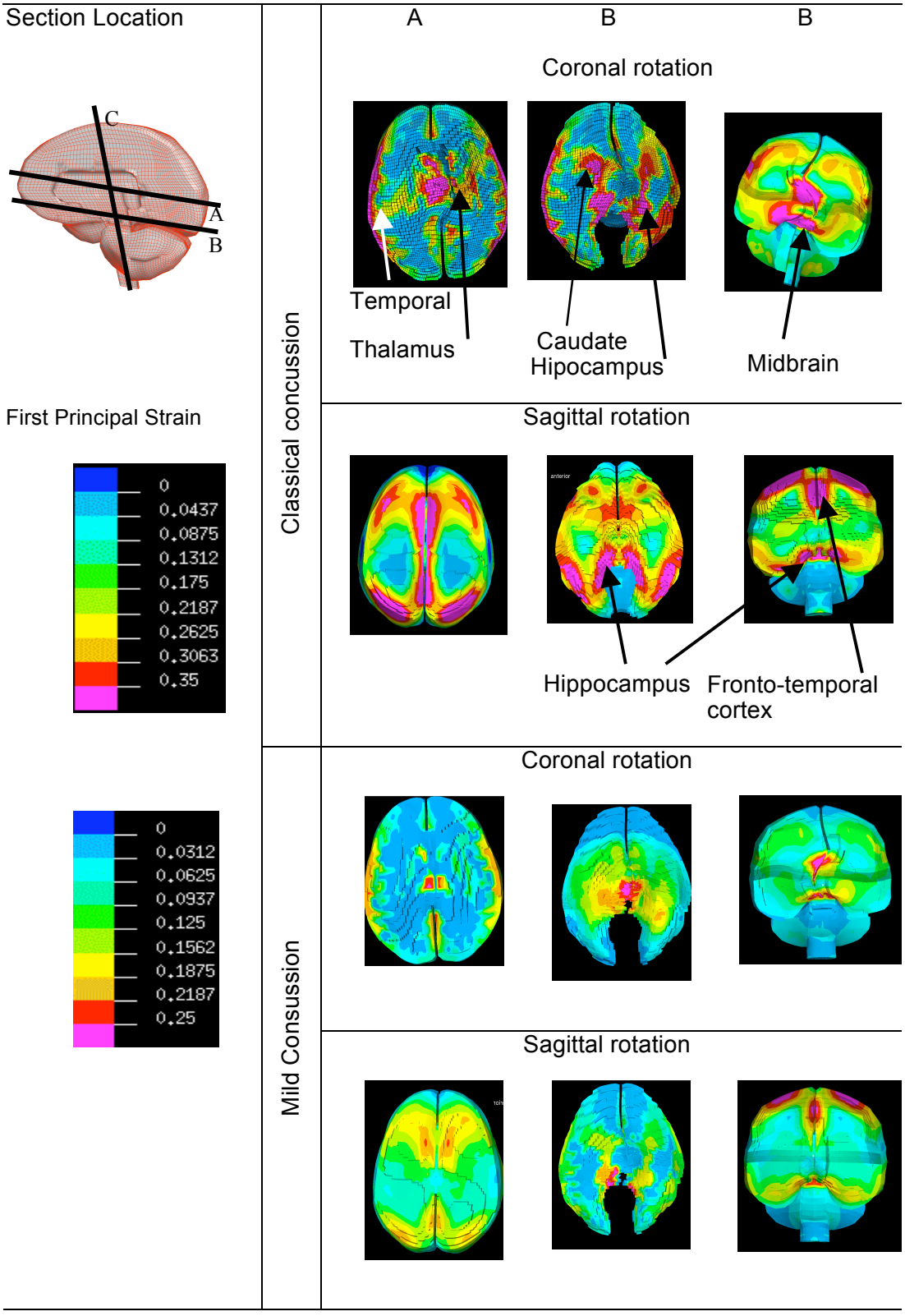

Fig. 4 - Accumulative Strain Map throughout the Entire Pulse Duration

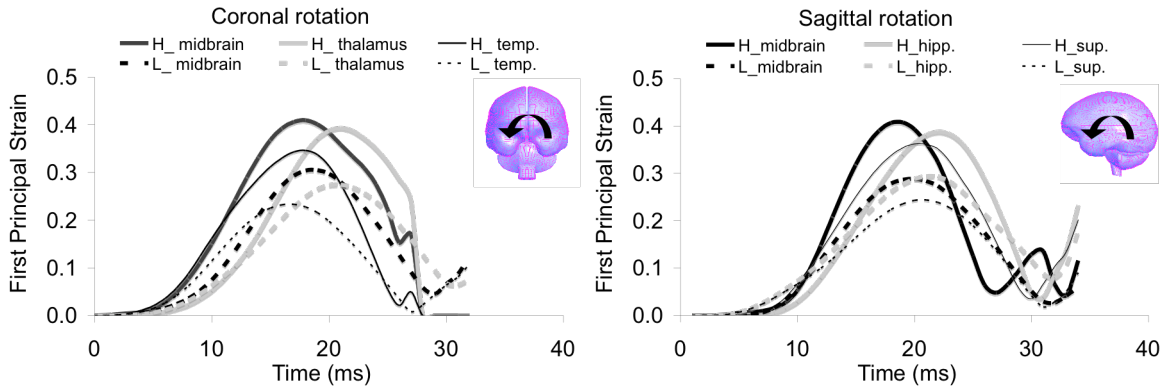

Fig. 5 - First Principal Strain Time Histories Experienced by Certain Regions of the Brain During Applied Coronal and Sagittal Rotational Motion at Two Threshold Levels (H For Classical Concussion and L For Mild Concussion)

DISCUSSION

The objective of this study was to use the WSU head FE model to relate defined head rotational parameters to localized brain strain patterns for specific grades of diffuse brain injury, specifically, mild concussion and classical concussion (Gennarelli and Wodzin, 2005).

Many FE head models have been developed and applied to study brain contusion, subdural hematomas, brain edema, and brain deformation (Chu et al., 1994; Mendis et al., 1994; Huang et al., 1999; Willinger et al., 1999; Kleiven et al., 2001; Taktounts et al., 2003). However, there has been limited FE analysis of concussion and diffuse brain injury using human injury data. This is, due in part to lack of a high resolution model that is capable of localizing the injury. The head model applied in this study is constructed with over 300,000 elements and thus has the capability of predicting tissue level response of various brain regions with a level of sophistication not available in other FE models. Recent studies on the mechanisms of the concussion provide first of its kind to correlate the mechanical condition occurring in concussion with the clinical symptoms (Zhang et al., 2003; King et al., 2003; Zhang et al., 2004a; Viano et al., 2005).

Model predictions indicated that different regions of the brain were susceptible to higher strain responses after applied rotational acceleration loading. Such regional strain response patterns were further influenced by the direction in which the head rotated. Coronal rotation induced mutifocal high strain in the midbrain, thalamus and caudate regions perhaps indicating an effect of the falx on the strain propagation. In the case of head rotation in the sagittal plane, the critical strain was mainly located in the hippocampus and upper brainstem region. This strain localization was likely dictated by the presence of the tentorium opening and its transverse orientation affecting the tissue deformation in the sagittal plane.

The FE model predicted high strain in specific regions of the brain, notably, the midbrain, thalamus and hippocampus. These anatomical structures are important functional units closely associated with memory (hippocampus), and the state of consciousness (midbrain, thalamus), the two most common symptoms in concussion. Our model predicted higher strains in these regions than in other parts of the brain, suggesting that an alteration in cerebral function in these regions is highly associated with tissue distortion in these areas. The severity of such responses exceeds tolerance levels and therefore direct strain damage is certainly possible. Thus, alternative explanations for the observed physiological changes such as a "selective vulnerability," diminished injury tolerance, venous hypertension, hyperemia or ischemia need not be considered. The brain function may be directly impaired by injury to that region or may disrupt the neural pathways that communicate between multiple brain structures. Thus, injury to the midbrain could have widespread effects because it is interconnected to diencephalon, the temporal lobe, the limbic system and multiple other areas of cerebrum. In this way, behavioral, cognitive or memory impairments could arise secondarily

to the affected midbrain. This mechanism may imply the diffuse nature of clinical signs and symptoms for concussion of various severities.

The results of the strain locations and associated magnitudes correlate well with the clinical symptoms specified in AIS 1 and AIS 2 concussions. In AIS 1 mild concussion, there is no loss of consciousness and indeed, the model results show low levels of strain in the midbrain-thalamic regions which subserve consciousness. The strains are higher in these areas in the AIS 2 condition, suggestive of loss of consciousness may occur. Similarly, the more severe memory disturbances (including retrograde and anterograde amnesia) that occur in AIS2 concussions are associated with higher strains in the medial temporal lobes (parahippocampal) regions than is the case in AIS 1 concussion where little or no amnesia occurs (Kelly, 1991; 1997).

Concussion is a clinical syndrome that may present with a broad spectrum of clinical signs and symptoms including at AIS levels >1, brief loss of consciousness. Reported concussion symptoms observed from NFL players in recent studies were consistent with the common forms of brain dysfunction noted after MTBI that occurred in non-athlete populations (Pellman et al., 2004). It is now generally appreciated that loss of consciousness, previously thought to be the most significant prognosticating factor of brain injury outcome, may have minimal post-injury consequences, and yet a seemingly more minor injury with photophobia and amnesia can lead to a prolonged syndrome. While fewer than 10% of concussed players experienced loss of consciousness, significant abnormalities of memory and cognitive function were observed for over 45% of the NFL players after concussion. The memory/cognitive problems were strongly correlated with delayed return to play (Pellman et al., 2005). FE model predicted strain and strain rate in the fornix, midbrain and corpus callosum showed significant correlations with the memory and cognitive impairments, loss of consciousness and increased intervals for full recovery (Viano et al., 2005). These correlations imply that local strain criteria could be the effective parameters capable of addressing specific symptoms and severity of concussion injury. The locations of the significant strain predicted from the current study were consistent with some of the common signs and symptoms occurred in football-related MTBIs and the general population after mild head injury.

Gennarelli et al. (2003) proposed the peak rotational acceleration and velocity based tolerances for various levels of diffuse brain injury in humans and related rotational limits with the abbreviated injury scale (AIS). AIS 2 and AIS 1 are related to the classical concussion and mild concussion with rotational thresholds at 4,500 rad/s^2 with 50 rad/s and 3,000 rad/s^2 with 25 rad/s, respectively. Although these values are estimates based on the literature, they are comparable to thresholds suggested by others. In the literature, several angular acceleration and velocity limits have been proposed for human concussion using the data derived from animal, cadaver, physical models or volunteer tests. Ommaya et al (1967) proposed 4,500 rad/s^2 for the human concussion threshold, on the basis of scaled primate data. Lowenhielm (1975, 1978) suggested 4,500 rad/ s^2 and 30 rad/s as a safe limit in sagittal rotation. Margulies and Thibault (1992) proposed angular acceleration of 16,000 rad/s^2 for moderate to severe DAI in lateral motion. Recent studies on concussive impact to the football players showed that concussed players were exposed to an average rotational acceleration of 6,400 rad/s^2 and angular velocity of 35 rad/s (Pullman et al., 2003; Viano et al., 2005). The typical duration of pulse was around 25 ms. Although this field of science may never achieve consensus about the thresholds for concussions, the magnitude and duration of angular thresholds applied in this study are comparable to the levels in other published concussion thresholds.

At applied AIS 2 loading, the model predicted strain levels of 0.35-0.45 consistent with the strain response predicted for the NFL players after concussion. These strain levels along with strain rate response were strongly associated with clinical memory, cognitive and cranial problems. For AIS 1 case, the model prediction implied that the applied rotational loading threshold was insufficient to induce strain above critical level (0.35 threshold) associated clinically severe signs and symptoms. First principal strain of 0.35 used in this study was based on the threshold determined from FE analysis of the NFL MTBI cases (Zhang et al., 2003; King et al., 2003; Viano et al., 2005). Published data on the strain thresholds measured from *in vitro* or *in vivo* models of TBI generally fell between

0.10 and 0.21. Recently, Tamura et al (2007) examined the relationship of strains measured between the axon and brain tissue. The results revealed that the strain level experienced by each axonal element was only one third of the total strain experienced by the brain tissue. This finding implies that directly incorporating a cellular level axonal threshold into an FE brain model could result in substantial over-prediction of injury occurrence. In terms of the cumulative strain measure, the current study only compared the difference in injury extent between AIS 1 and AIS 2 level injuries. Further studies using FE modeling of animal TBI would be required to establish volumetric strain-based threshold for quantifying injury extent and ultimate neurological outcomes.

It should be emphasized that this investigation studied only coronal and sagittal plane rotational accelerations with idealized time histories. The complex multi-planar motions often seen in real-world concussions can induce different distributions of strain in the non-uniform human head. While the contribution of the translational acceleration to the strain response appeared to be minimal, a thorough investigation of tissue strain response from a combination of translational and rotational acceleration in three-dimensional fashion is needed before a generalized mechanical thresholds can be determined with high confidence. In the future, these stain patterns will be compared to actual clinical cases where the concussion biomechanics and the symptoms are known.

Traumatic diffuse brain injuries range from damage which involves principally physiological disruption of brain function as in the case of concussion, to severe structural compromise as in axonal injury (Gennarelli, 1993). It can be postulated that the injury parameters affecting physiological function could also cause structural compromise in a continuum manner. The more severe forms of diffuse brain injury, including moderate and severe axonal injury need to be investigated to fully understand the entire spectrum of diffuse brain injury.

REFERENCES

Bain AC, Meaney DF. Thresholds for mechanical injury to the in vivo white matter. 43rd Stapp Car Crash Conf, SAE Paper 99SC19, 1999.

Bandak FA, Eppinger RH. A three-dimensional finite element analysis of the human brain under combined rotational and translational accelerations. 37th Stapp Car Crash Conference, SAE 942215, 1994.

Chu CS, Lin MS, Huang HM, Lee MC. Finite element analysis of cerebralcontusion. J Biomech 27, 1994, pp. 187-194.

Elkin BS, Morrison B. Region-specific tolerance criteria for the living brain. Stapp Car Crash Journal, 51, 2007, pp. 127-138.

Faden AI. Neuroprotection and traumatic brain injury: theoretical option and realistic proposition. Current Opinion in Neurology 15, 2002, pp.707-712.

Franklyn M, Fildes B, Zhang L, Yang KH, Sparke L. Analysis of finite element models for head injury investigation: Reconstruction of four real-world impacts. Stapp Car Crash Journal 49, 2005, pp. 1-32.

Gennarelli TA, Wodzin E. (eds). Abbreviated Injury Scale 2005, Association for the Advancement of Automotive Medicine, Barrington, IL, p. 51, 2005.

Gennarelli TA. Cerebral concussion and diffuse brain injury. In: *Head Injury* (Cooper PR, ed), 1993, pp 137-158. Batimore: Wiiliams and Wilkins.

Gennarelli, TA, Pintar FA, Yognandan N. Biomechanical tolerances for diffuse brain injury and a hypothesis for genotypic variability in response to trauma. Annual Proc Assoc Adv Automotive Med. (Lisbon, Portugal) 47, 2003, pp. 624-8.

Horn J, Scherer M. Rehabilitation of traumatic brain injury. In: Physical medicine and rehabilitation: the complete approach (Grabois, Hart, Lehmkuhl, eds), 2000, pp. 1281-99. Malden (MA): Blackwell Science.

Huang HM, Lee MC, Chiu WT, Chen CT, Lee SY. Three-dimensional finite element analysis of subdural hematoma. J Trauma 47, 1999, pp. 538–44.

Kelly JP et al. Report of the Sports Medicine Committee. *Guidelines for the Management of Concussion in Sports.* Denver, CO: Colorado Medical Society, May 1991.

Kelly JP. Practice parameter: the management of concussion in sports (summary statement). Report of the Quality Standards Subcommittee. Neurology 48, 1997, pp. 581-585.

King AI, Yang KY, Zhang L, Hardy WN, Viano DC. Is head injury caused by linear or angular acceleration? Bertil Aldman Lecture, International IRCOBI Conference on the Biomechanics of Impact, 2003.

Kleiven S, Hardy WN. Correlation of an FE model of the human head with local brain motion – consequences for injury prediction. Stapp Car Crash J 46, 2002, pp. 123-144.

Kraus JF, McArthur DL. Epidemiologic aspects of brain injury. Neurol Clin 14, 1996, pp. 435-450.

Lowenhielm P. Mathematical simulation of gliding contusions. J Biomechanics 81, 1975, pp. 351-356.

Löwenhielm P. Tolerance level for bridging vein disruption calculated with a mathematical model. J Bioeng 2, 1978, pp. 501-507.

Mao H, Zhang L, Yang KH, King AI. Application of a finite element model of the brain to study traumatic brain injury mechanisms in the rat. Stapp Car Crash J 50, 2006, pp. 583-600.

Margulies SS, Thibault LE. A proposed tolerance criterion for diffuse axonal injury in man. J Biomech 25, 1992, pp. 917-923.

Maxwell WL, Povlish JT, Graham DL. A mechanistic analysis of nondestructive axonal injury: A review. J Neurotrauma 14(7), 1997, pp. 419-440.

Mendis K, Stalnaker RL, Advani AH: A constitutive relationship for large deformation finite element modeling of brain tissue. J Biomech Eng 117, 1995, pp. 279-285

Miller RT, Smith DH, Chen X, Xu BN, Leoni M, Nonaka M, Meaney DF. Comparing experimental data to traumatic brain injury finite element models. 43rd Stapp Car Crash Conf, SAE Paper 99SC20, 1999.

Murray CJ, Lopez AD. Evidence-based health policy-lesions from the Global Burden of Disease Study. Science 274(5288), 1996, pp. 740-743.

Newman J, Shewchenko N, Welbourne E. A proposed new biomechanical head injury assessment function-the maximum power index. Stapp Car Crash Journal 44, 2000, pp. 215-247.

Ommaya AK, Gennarelli TA. Cerebral concussion and traumatic unconsciousness: correlation of experimental and clinical observations of blunt head injuries. Brain 97, 1974, pp. 633-654.

Ommaya AK, Goldsmith W, Thibault L. Biomechanics and neuropathology of adult and paediatric head injury. British J Neurosurgery 16(3), 2002, pp. 220–242.

Ommaya AK, Yarnell P, Hirsch AE, Harris EH. Scaling of experimental data on cerebral concussion in sub-human primates to concussion threshold for man. 11th Stapp Car Crash Conference, SAE 670906, 1967.

Pellman EJ, Viano DC, Tucker AM, Casson IR, Waeckerle JF. Concussion in professional football: Reconstruction of game impacts and injuries. Neurosurgery 53(4), 2003, pp. 799-812.

Pellman EJ, Viano DC, Tucker AM, Casson IR. Concussion in professional football: Location and direction of helmet impact – Part 2. Neurosurgery 53(6), 2003, pp. 1328-1341.

Pellman EJ, Powell JW, Viano DC, Casson IR, Tucker AM, Feuer H, Lovell M, Waeckerle JF, Robertson DW. Concussion in professional football: Epidemiological features of game injuries and review of literature – Part 3. Neurosurgery 54(1), 2004, pp. 81-94.

Pellman EJ, Viano DC, Casson IR, Arfken C, Feuer H. Concussion in professional football:Players returning to the same game – Part 7. Neurosurgery 56(1), 2005, pp. 79-90.

Singh A, Lu Y, Chen C, Kallakuri S, Cavanaugh JM. A new model of traumatic axonal injury to determine the effects of strain and displacement rates. Stapp Car Crash Journal 50, 2006-22-0023, pp. 601-623. Dearborn, Michigan, USA.

Takhounts EG, Eppinger RH, Campbell JQ, Tannous RE, Power ED, Shock LS. On the development of the SIMon finite element head model. Stapp Car Crash J 47, 2004, pp. 107-133.

Tamura A, Nagayama K, Matsumoto T, Hayashi S. Variation in nerve fiber strain in brain tissue subjected to uniaxial stretch. Stapp Car Crash J 51, 2007, pp. 139-154.

Viano DC, Casson IR Pellman EJ, Zhang L, Yang KH, King AI. Concussion in professional football: Brain responses by finite element analysis – Part 9. Neurosurgery 57, 2005, pp. 891-916.

Willinger R, Kang HS, Diaw B. Three-dimensional human head finite element model validation against two experimental impacts. Ann Biomed Eng. 27, 1999, pp. 403-10.

Zhang L, Yang KH, Dwarampudi R, Omori K, Li T, Chang K, Hardy WN, Khalil TB, King AI Recent advances in brain injury research: A new human head model development and validation. Stapp Car Crash Journal 45, 2001, pp. 369-393.

Zhang L, Yang KH, King AI. A proposed injury threshold for mild traumatic brain injury. J Biomechanical Engineering 126(2), 2004a, pp. 226-236.

Zhang L, Begeman P, Melvin J. Brain injury prediction for Indy race car drivers using finite element model of the human head. SAE Transactions: J Passenger Cars, 2004b, Society of Automotive Engineers.

Zhang L, Yang KH, King AI, Viano DC. A new biomechanical predicator for mild traumatic brain injury – A preliminary finding. ASME Bioengineering Conference Proceedings, 2003, Key Biscayne, FL, USA.