A Proposed Injury Threshold for Mild Traumatic Brain Injury

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Traumatic brain injuries constitute a significant portion of injury resulting from automotive collisions, motorcycle crashes, and sports collisions. Brain injuries not only represent a serious trauma for those involved but also place an enormous burden on society, often exacting a heavy economical, social, and emotional price. Development of intervention strategies to prevent or minimize these injuries requires a complete understanding of injury mechanisms, response and tolerance level. In this study, an attempt is made to delineate actual injury causation and establish a meaningful injury criterion through the use of the actual field accident data. Twenty-four head-to-head field collisions that occurred in professional football games were duplicated using a validated finite element human head model. The injury predictors and injury levels were analyzed based on resulting brain tissue responses and were correlated with the site and occurrence of mild traumatic brain injury (MTBI). Predictions indicated that the shear stress around the brainstem region could be an injury predictor for concussion. Statistical analyses were performed to establish the new brain injury tolerance level. [DOI: 10.1115/1.1691446]

Introduction

Traumatic brain injury (TBI) due to blunt impact is a major cause of morbidity and mortality. In the United States, approximately 2 million TBI cases occur each year [1]. The great majority of all traumas treated in emergency room, outpatient departments and physician's offices in the United States [2,3] are classified as mild traumatic brain injury (MTBI) or concussion. It has been recognized that there is an increase in MTBI resulting from recreational sports even while protective devices are in use. Sports-related TBI is an important public health problem because of the large number of people affected and the potential for serious sequelae. Brain injuries not only represent a serious disability for those involved but also place an enormous burden on society, often exacting a heavy economical, social, and emotional price. Since a cure is not attainable at this time, the only alternative is to develop intervention strategies to prevent or minimize these injuries.

Current standards for head injury protection are the Gadd Severity Index (GSI) [4] and the Head Injury Criterion (HIC) [5]. These criteria are based on the Wayne State University tolerance curve [6], which in turn was based on head acceleration results from animal concussion tests and cadaveric skull fractures due to rigid, flat surface impact on the forehead. They cannot fully account for the complex motion of the brain within a deformable skull. In addition, the criteria neglect the contribution of the angular acceleration of the head to injury production. Furthermore, the directional sensitivity of the head to a direct impact is not specified. Apparently, current football helmets have an effective padding system which can prevent severe head injuries but do not effectively prevent concussion.

A biomechanical study of human concussion that attempts to relate mechanical input to localized tissue deformation, such as pressure, stress/strain responses, is needed for a proper assessment of brain injury outcome. A specified insult known to interrupt brain function should be capable of being quantified, at least in principle. In other words, there must be a threshold below which no loss of function occurs and a ceiling beyond which irreversible changes in brain function would occur. Such information is crucial when human tolerance data are used to design protective systems.

There is no question that computer models capable of simulating impact events can be of major assistance to researchers in the study of brain injuries. Recently, several possible injury predictors based on head response variables have been suggested using finite-element (FE) head models. Ruan et al. [7,8] and Zhou et al. [9,10] indicated that shear stress/strain response could be the injury indicator for subarachnoid hematoma and diffuse axonal injury (DAI). Bandak and Eppinger [11] suggested that an accumulated volume of those elements exceeding a pre-determined maximum principal strain, referred to as the Cumulative Strain Damage Measure (CSDM), was related to strain-induced DAI. Al-Bsharat et al. [12] modified the model developed by Zhou et al. [10] to simulate large relative motion between the brain and the skull and implied that relative motion can play a role in brain injury. However, none of the above studies utilized data and injury from actual field incidents to predict injury.

In this study, an attempt was made to delineate injury causation and establish a meaningful injury criterion through the use of actual field accident data. Mild traumatic brain injuries from American football provide a unique living ''laboratory'' to study concussion mechanisms and tolerance levels in the human, with possible extrapolation to the general population. Performing an accident reconstruction using an anatomically detailed model facilitates the prediction of the extent and severity of brain response as a consequence of a particular impact. Therefore, the appropriate injury predictors based on this response can be used to establish a variety injury tolerance levels by a statistical approach. This approach is unlike previous studies which proposed tolerance limits for human head injury based on input kinematics either scaled from animal data or noninjurious volunteer test results. It is anticipated that the findings derived from this current study can improve helmet design and thus further reduce brain injury severity.

Methods

Traumatic Brain Injury Data From Football Field Accident Every team of the National Football League (NFL) plays sixteen regular games and four preseason games during each season. These games are videotaped and televised routinely. Each year, approximately 150 athletes are diagnosed as having sustained an apparent or suspected MTBI. During the past few years, a research program funded by NFL Charities has identified several concussion cases gathered from team physicians who treated the

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players when they were injured. The recorded events were then scrutinized in detail. Video recordings of the game during that event, involving varying degrees of concussion severity were examined in the course of this investigation. Confirmed injury cases were then used to determine the head impact kinematics by film analysis, including impact speed and locations of impact. This impact information was then used later to reconstruct the impact utilizing automotive crash dummies.

Laboratory-Based Accident Reconstruction. Laboratory-based accident reconstructions of football head impact were conducted using two Hybrid III Anthropomorphic Test Devices (ATDs), at Biokinetics and Associates, Ltd. (Ottawa, Canada). Although the MTBI can be the result of a head impact with a variety of contact surfaces, including the helmet, ground, knees, and elbows, the majority of MTBI injuries occurred due to an impact with another helmeted player, based on surveys of data from the past few seasons. Thus, in the current laboratory reconstruction, helmeted head-to-head collision associated with MTBI was the primary focus. Detailed descriptions of the methodology can be found in Newman et al. [13,14]. For the sake of completeness, a brief description of the laboratory based reconstruction procedure is provided below.

To reconstruct these head-on collisions, two Hybrid III dummy heads wearing exemplar football helmets worn by the injured and non-injured players during the incident were used. The two Hybrid III heads were instrumented with nine linear accelerometers and the heads were attached to Hybrid III necks instrumented with typical six axes load cells. To reenact the incidents, the video taken of the incident was analyzed to determine the kinematics of the players. The velocity of one player's head relative to the other was determined through frame-by-frame analysis. In the laboratory reconstruction, one head-neck assembly was mounted to a rigid base, and the other to a vertical twin-wire guided free-fall system. The injured (usually the struck) player was represented as a stationary helmeted headform, and the noninjured (usually the striking) player head was represented by a helmeted headform that moved at the full relative velocity as shown in Fig. 1. As such, the impact kinematics were unchanged from those of the two players who were both moving in most of the cases. The carriage was raised to an appropriate height so that upon release it fell freely and attained the desired impact. In the event that there was not enough ceiling height, a bungee cord was used to provide the additional acceleration needed to reach the desired speed. In this way, both helmeted headforms were impacted in a manner similar to the one recorded on video. In terms of relative velocity, the potential error in the entire reconstruction process was within 11.3% [15].

Accident Reconstruction by Modeling. Case-by-case computer simulations were carried out using the head kinematics obtained from laboratory testing as input to the FE model. Brain tissue response was calculated throughout the entire brain. If the induced local mechanical response variable correlated with the site of injury, it can be used as an injury predictor to assess the potential injury severity. A validated FE model along with tissue tolerance data can offer a means of identifying and quantifying the hazardous mechanical agents that can cause concussion. Because concussion is the primary injury which occurs most frequently in isolation, and because it appears to be a threshold injury in most cases, results from this simulation can be used to derive a minimal brain tolerance criterion. Using such a biomechanical analysis to study tissue-injury as a consequence of head impact is illustrated in the following paradigm (Fig. 2). Football accident reconstruction using FE modeling techniques described in this study is a step toward accomplishing the stated goals.

Model Description. The Wayne State Brain Injury Model (WSUBIM) simulates all essential anatomical features of a 50th percentile male head, including the scalp, skull with an outer table, diploë, and inner table, dura, falx cerebri, tentorium and falx cerebelli, pia, venous sinuses, CSF, lateral and third ventricles, cerebrum (white and gray matter), cerebellum, brain stem, and parasagittal bridging veins. The WSUBIM used in this study was modified from the one used in direct head impact simulation studies reported by Zhang et al. [16]. Major changes made to the model were essentially to improve mesh quality and material definitions adapted to the current application. The model was prevalidated against cadaveric intracranial and ventricular pressures data from cadaveric head impact tests published by Nahum et al. [17] and Trosseille et al. [18].

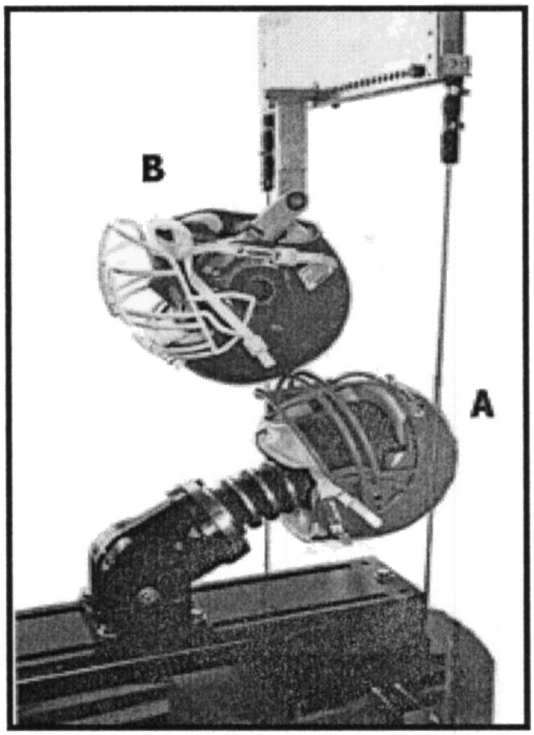

Fig. 1 Laboratory accident reconstruction set up. Helmeted headform A represents a struck player's head and helmeted headform B represents a striking player's head

Material Properties. Brain tissue is naturally inhomogeneous and anisotropic and such material definitions should be incorporated into a brain model to obtain a more realistic injury response. The inhomogeneity of the brain is based on the fact that gray matter consists of cell bodies while white matter is more fibrous in nature. Thus, this neuroarchitecture can be considered as macroscopically inhomogeneous. To incorporate this feature in the modeling of a viscoelastic brain tissue, the shear moduli for the white matter were assumed to be 20% higher than those for the gray matter. The reported mechanical properties of the brain tissue in shear varied considerably from one study to another due to various test methodologies, conditions and samples selected [19,20,21,48,49]. Arbogast et al. [19] reported that the instantaneous shear moduli were 1040 Pa for white matter and 680 Pa for gray matter in an experimental study on pig brains. In their study, brain tissues sliced from adult pigs were placed between two parallel plates and subjected to oscillatory shear forces. Shear moduli were calculated for these tissues as a function of excitation frequency. Although the design of this study was quite elegant, its results did not fully reflect the tethering effect of the blood vessels. The material properties chosen for the current study, as shown in Table 1, were higher than reported data obtained from using dissected brain tissue [19,20] but are in the same range of

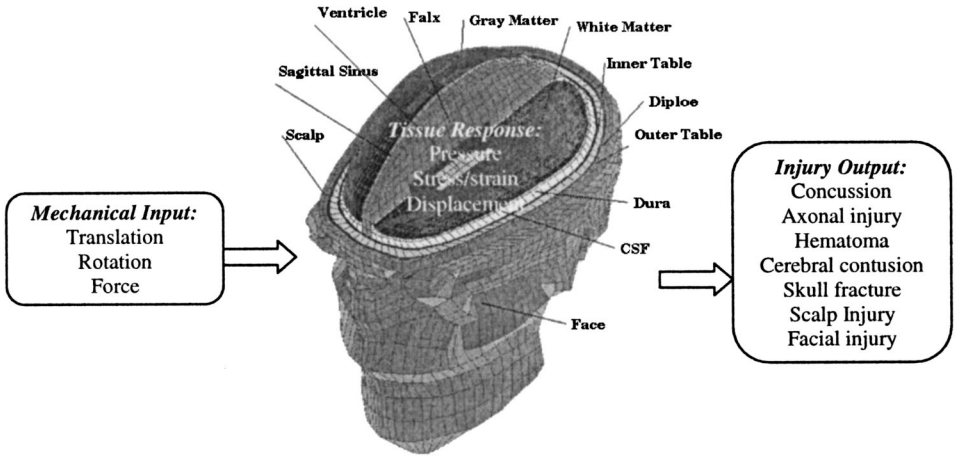

Fig. 2 Block diagram illustrating the tissue-injury response to traumatic input loading as a biomechanical analysis process using a computer surrogate

results reported by Fallenstein et al. [48], Galford and McElhaney [49], and Shock and Advani [21] and consistent with those used in previous modeling studies [7,10,12,16,22,23].

Another shortcoming of previous brain material definitions was the failure take into account regional differences in brain properties. This regional difference can affect the stress or strain fields during impact. Based on magnetic resonance diffusion tensor images of the brain neuroarchitecture, Pieropaoli and Basser [24] indicated that some regions of white matter could be modeled as transversely isotropic and gray matter as isotropic structures. Furthermore, it has been shown that the axonal fibers of white matter at the brainstem and the corpus callosum have primarily longitudinal arrangements. Oscillatory shear tests of the pig brain tissue revealed that the complex shear modulus for the brainstem region was 80% greater than that for cerebrum tissue [19]. In the current investigation of concussive brain injury, the brainstem and diencephalon are the two critical regions where large deformation of these tissues may alter the state of consciousness. To better mimic the regional tissue response under dynamic loading, the short-term shear modulus of the brainstem region was assumed to be 40% higher than that for the cerebrum white matter. Other viscoelastic material properties assumed for the brain are listed in Table 1. Material properties of remaining components of the WSUBIM used in this study were consistent with those of previous simulations [12,16,22].

Loading Boundary Conditions. Twelve cases involving 24 players were replicated by a modified version of the WSUBIM to predict the response of the player's brain during impact. The kinematics of the helmeted Hybrid III headform were expressed in terms of its three translational and three rotational acceleration components in an anatomical (body-fixed) reference frame. These data were measured directly from the laboratory reenactment of the head collisions and were used as input to the WSUBIM. By defining the outer surface of the skull as a rigid body and applying the head kinematics at the center of gravity (CG) of the head, the loading boundary conditions of the head were prescribed. A total of 12 pairs of head kinematics obtained from the 12 laboratory reconstructions were used in the model reconstruction. Figure 3 shows a sample set of input translational and rotational acceleration time histories. All simulations were computed using Pam-Crash™ (ESI, Paris, France), an explicit finite element analysis code. Problems of convergence commonly associated with implicit FE analysis are not an issue in explicit analysis as long as the time step selected is sufficiently small. Nevertheless, the convergence of the solution was tested using an ideal model loaded in a typical loading condition. It was found that model responses were comparable when characteristic length of the element was 5 mm or less. The current model has an average size of 5 mm and the model results are considered acceptable.

Results

In the literature, mechanically relevant parameters in terms of intracranial pressure, stress, and strain have been postulated as head injury mechanisms resulting from blunt impact. There is evidence that sudden changes of intracranial pressure, shear stress concentration, and relative motion between the brain and skull do indeed cause surface contusions, concussion, DAI, as well as acute subdural hematoma. In this study, the mechanical responses, including intracranial pressure and brain shear stress were directly calculated as intracranial responses to varying degrees of loading severity. The magnitude of the response parameters were used to determine injury severity and to quantify a particular dose of insult with respect to the corresponding injury observed.

Head Kinematics. The average values of head acceleration in translation and rotation used in the simulation were analyzed for the injury and noninjury groups. The mean values and standard deviations ($\pm$SD) along with the peak head acceleration were calculated. The peak resultant translational acceleration ranged from 61 to 144 G for injury cases, and from 32 to 102 G for noninjury cases. The mean resultant translational acceleration was 103 $\pm$30 G for injury cases and 55$\pm$21 G for noninjury cases. As for the rotational component, the peak resultant rotational acceleration of the head varied from 4168 to 12,832 rad/s^2 with a mean of

Table 1 Viscoelastic material properties of brain tissues used in the head model

	Density ρ (kg/mm^3)	Bulk modulus K (GPa)	Short-term shear modulus G_0(Pa)	Long-term shear modulus G_∞(Pa)	Decay constant β (s^{-1})
White Matter	1.04E−06	2.19	4.1E+4	7.8E+3	400
Gray Matter	1.04E−06	2.19	3.4E+4	6.4E+3	400
Brainstem	1.04E−06	2.19	5.8E+4	7.8E+3	400

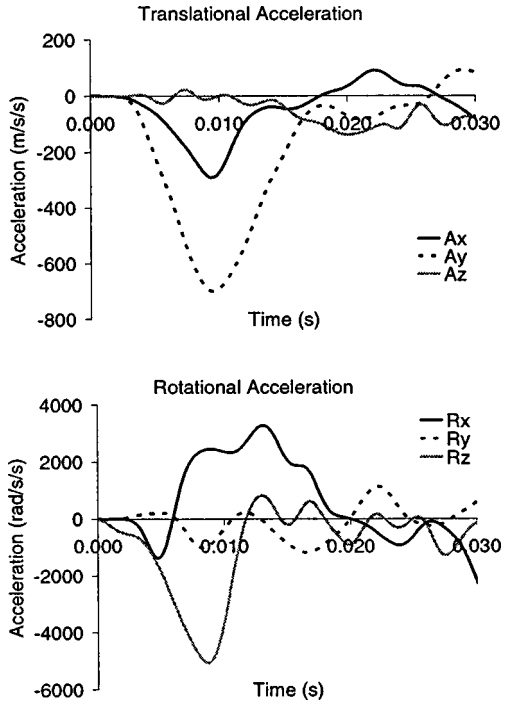

Fig. 3 A sample set of the input head translational and rotational acceleration time histories

7354 ± 2897 rad/s^2 for injury cases and from 2087 to 6265 rad/s^2 with a mean of 4204 ± 1411 rad/s^2 for noninjury cases. The mean values of head accelerations for injury cases were higher than those of noninjury cases.

HIC values were calculated for each case. Hodgson and Thomas [25], Prasad and Mertz [26] and Mertz and Irwin [27] suggested that the HIC time interval should be limited to 15 ms. This proposal was based on analyses of cadaveric and volunteer data in which it was found that an impact duration of 15 ms or less was critical to skull fracture and concussion. Thus, a time interval of 15 ms was used to calculate HIC_{15}. The HIC_{15} and GSI averaged 441 (± 224) and 351(± 169) in the injury cases and 137 (± 124) and 110(± 103) in the noninjury cases, respectively.

Intracranial Pressure Response. Typical intracranial pressure time traces at the coup and contrecoup sites predicted by the model are shown in Fig. 4*a*. The peak pressure values were based on the average of three selected elements in the area where the maximum pressure occurred. As depicted in this simulation, predicted intracranial pressure reached its peak at about 9 ms with a positive maximum value of 66 kPa and a negative maximum value of -52 kPa. The total duration of apparent pressure wave lasted about 16 ms for a typical impact.

Predicted intracranial pressure distribution as viewed from the top of the whole brain, at the time of peak pressure response is shown in Fig. 4*b*. As clearly depicted in this figure, the pressure gradient stretched uniformly across the brain with the peak positive pressure occurring in the fronto-temporal lobe while the peak negative pressure was located in the right-occipital lobe near the posterior cerebellum. The pressure distribution indicated a coup and contrecoup pattern.

For all cases simulated, the peak positive pressures at the coup site ranged from 53 to 130 kPa for cases with injury outcome and from 40 to 101 kPa for noninjury cases. The mean values of coup pressure were 90 ± 24 kPa and 61 ± 17 kPa for injury and noninjury cases, respectively. In the contrecoup region, the peak negative pressures varied from 48 to 128 kPa for injury impact and varied from 20 to 78 kPa for noninjury cases. The mean values of contrecoup pressure were 76 ± 26 kPa and 41 ± 18 kPa corresponding to injury and noninjury cases, respectively. The observed apparent duration of intracranial pressure pulses ranged from 10 to 20 ms depending on the duration of the applied head acceleration. The pressure duration was primarily related to the translational acceleration pulse. Table 2 summarizes the predicted maximum and minimum intracranial pressure along with calculated means and standard deviations for all simulations.

Brain Shear Stress Response. During the impact, the shear stress in the brain had a different response pattern as compared to the intracranial pressure gradient generated across the brain. Initially, the shear stress on the cortical surface of the brain was high; gradually high shear stresses were concentrated at the central core region of the brain. Comparing the magnitude of shear stress throughout the whole impact duration, the midbrain and the thala-

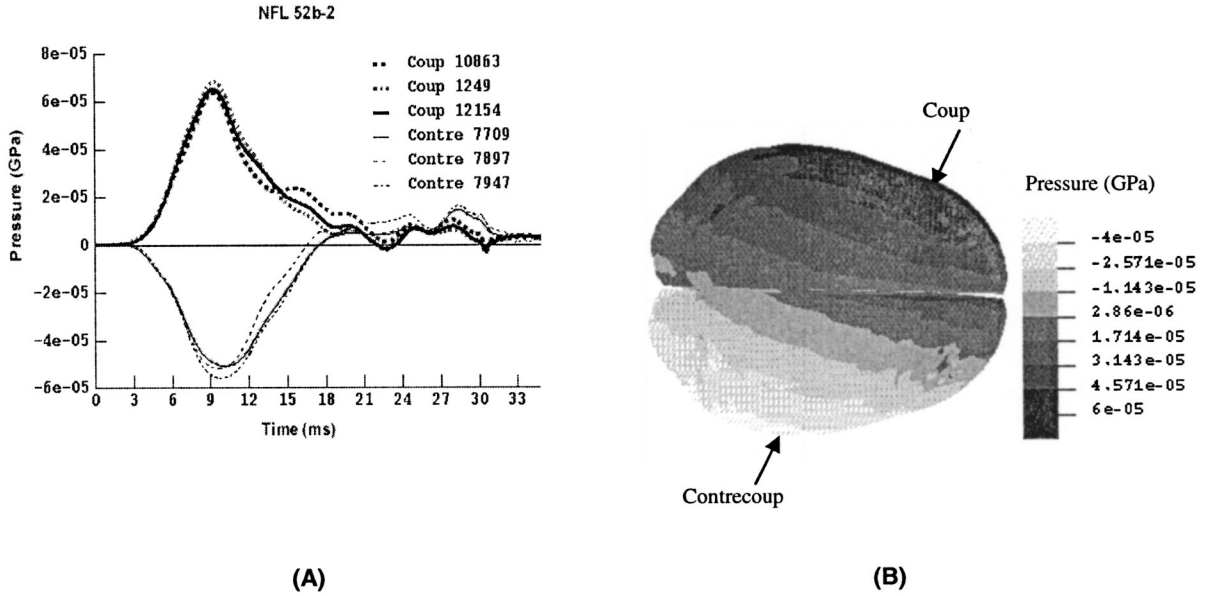

Fig. 4 (*A*) Predicted peak positive and peak negative intracranial pressure-time histories; (*B*) Predicted intracranial pressure distribution 9 ms after the impact

Table 2 Predicted intracranial pressure for injury and noninjury cases

		Peak Intracranial Pressure (kPa)	
		Coup	Contrecoup
Injury	Range	53–130	48–128
$N=9$	Mean	90 (±24)	76 (±25)
Noninjury	Range	40–101	20–78
$N=15$	Mean	61 (±17)	41 (±18)

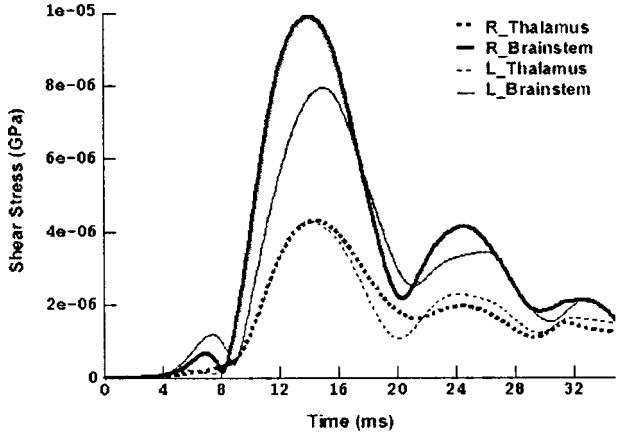

Fig. 5 The predicted shear stress histories in the brainstem and the thalamus regions from a typical case

Table 3 Predicted peak shear stress for injury and noninjury cases

		Shear Stress (kPa) Midbrain Brainstem)	Thalamus
Injury	Range	6.2–12.0	3.1–6.4
$N=9$	Mean (±SD)	8.4 (±2.2)	4.5 (±1.2)
Noninjury	Range	2.6–9.5	1.5–4.6
$N=15$	Mean (±SD)	5.3 (±1.9)	2.8 (±0.9)

mus were the two regions that experienced the highest shear stresses. Figure 5 shows typical shear stress histories predicted in the thalamus and the midbrain regions from one simulation. Peak values were calculated based on the average value of two elements in the thalamus and the midbrain areas, respectively. As depicted in this figure, the peak maximum shear stress was about 9.0 kPa in the midbrain of the brainstem. The thalamus region also sustained a high shear stress of about 4.0 kPa during the impact. The predicted peak shear stress responses in the thalamus and the midbrain of the brainstem region for all 24 simulations are listed in Table 3. The locations of the elements in the brain model used for analysis are indicated in Figs. 6*a* and 6*b*. Among all the injury cases simulated, the predicted shear stress at critical regions ranged from 3.1 to 6.4 kPa in the thalamus with a mean value of 4.5 ± 1.2 kPa. It varied from 6.2 to 12.0 kPa around the midbrain area with a mean value of 8.4 ± 2.2 kPa. For noninjury cases, the predicted shear stresses varied from 1.5 to 4.6 kPa in the thalamus, and from 2.6 to 9.5 kPa in the upper brainstem area. The mean values were 2.8 ± 0.9 kPa and 5.3 ± 1.9 kPa for the thalamus and the midbrain regions in the noninjury cases, respectively.

Shear stress contours in a parasagittal and a sectional view are shown in Fig. 6. As demonstrated in the figure, high shear stresses were concentrated in the core region of the brain, particularly in the upper brainstem and over most of the diencephalon. The corpus callosum region, where the diffuse axonal injury is commonly reported, did not experience significantly high shear stresses in the current simulations.

Relationship Between Brain Response and Head Kinematics.. The relationship between model predicted brain responses and head kinematics was investigated using linear regression approach. If well correlated, the intracranial distortion could be predicted from the translational acceleration and/or the rotational acceleration of the head.

Intracranial Pressure Response vs. Head Kinematics. The relationships between the peak intracranial pressure and the maximum translational and rotational acceleration in x, y, and z directions and the resultant for all 24 cases were calculated. In general, linear regression curves show that increasing head translational and rotational accelerations resulted in an increase of the intracranial pressure. The highest R^2 was found when the resultant translational acceleration was used to predict the intracranial pressure ($R^2=0.77$) (Fig. 7*a*). The translational acceleration in the lateral (y) direction also had a stronger correlation ($R^2=0.53$) than the other two translational accelerations in the postero-

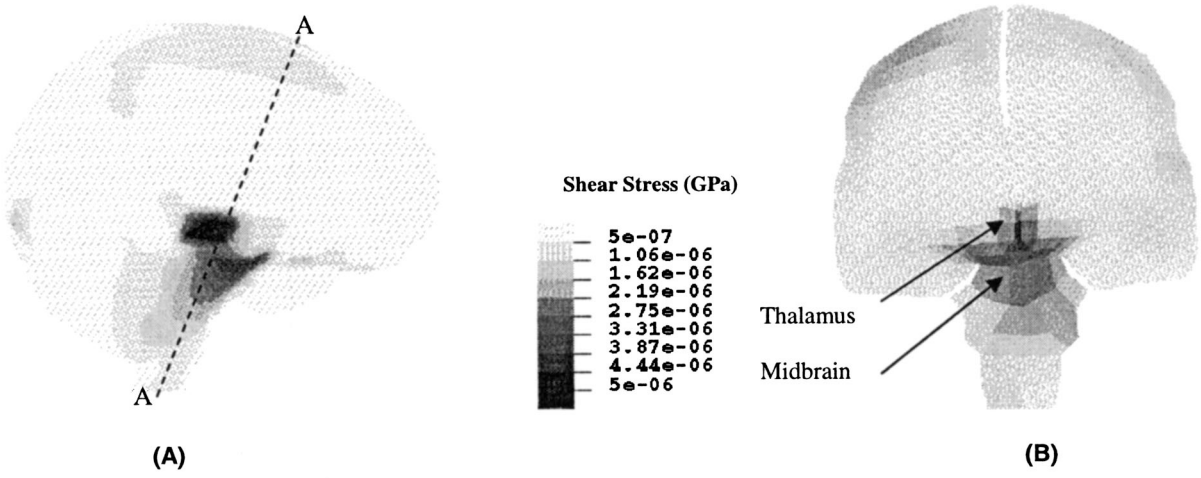

Fig. 6 Shear stress contours predicted by the model at 16 ms for: (*A*) a parasagittal section; (*B*) Sectional view through A-A which represents a section through the mamilothalamic tract

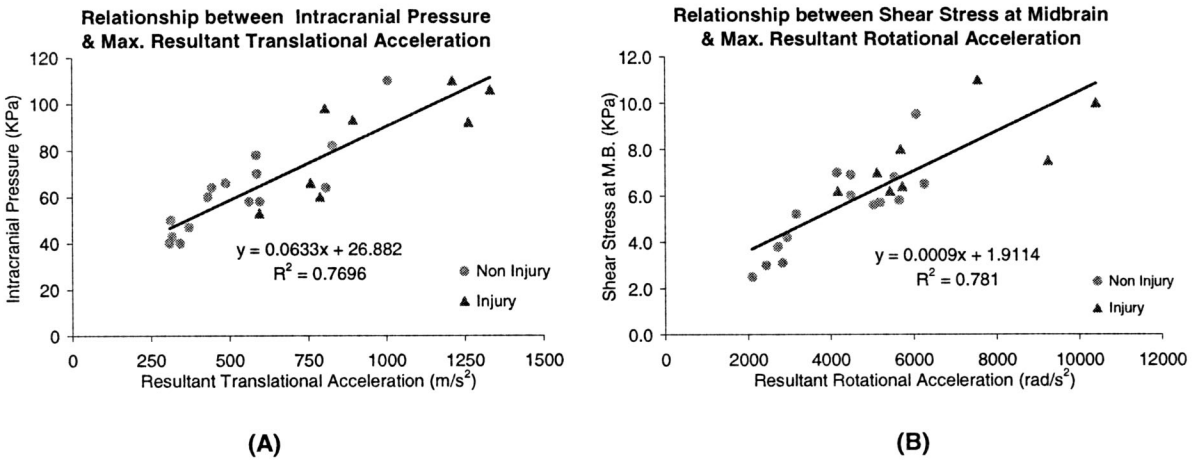

Fig. 7 Relationship between intracranial pressure and the maximum translational acceleration (*A*) and between shear stress at the midbrain and the maximum rotational acceleration of the head (*B*)

anterior (x) ($R^2=0.31$), and the inferior-superior (z) ($R^2=0.31$) directions. The high coefficients of correlation suggested that intracranial pressure could be predicted by resultant translational acceleration of the head. The relationship between intracranial pressure and rotational motion did not show a good correlation, with low R^2 values of 0.297, 0.109, 0.382, and 0.303 for the three rotational components about the x-, y- and z-axis, and the resultant, respectively.

Shear Stress Response vs. Head Kinematics. The linear regression lines and scatter of data points between maximum shear stress at the brainstem and head input kinematics are illustrated in Fig. 7*b*. The regression lines show that the maximum shear stress tended to increase with the maximum head input kinematics. By comparing the R^2 values, a strong correlation ($R^2=0.78$) was found between shear stress at the brainstem and resultant rotational acceleration. There was no significant relationship between the maximum shear stress and peak translational acceleration. The regression model suggests that the maximum shear stress is highly sensitive to rotational acceleration and appears to have a very low correlation with translational acceleration.

Logistic Regression Analysis. Logistic regression is a form of regression which is used when the dependent variable is a dichotomy and the independent variables are continuous, categorical, or both. Logistic regression estimates the probability of occurrence for a given event. The estimation is based on the maximum likelihood principle rather than on the least-squares principle. The maximum likelihood estimation (MLE) is a maximization process to calculate the logistic regression coefficients and to determine the relationships between outcome and the independent variables. It seeks to maximize the likelihood, which reflects how likely it is that the observed values of the dependent variables may be predicted from the observed values of the independent variables. The logistic model for the probability of injury (p) takes the form:

$$p=\frac{1}{1+e^{-\hat{y}(x)}}$$

where $\hat{y}(x)=\beta_0+\Sigma_{i=1}^{n}\beta_i x_i$ is the logistic function, x_i are the dependent variables, and β_i are the logistic regression coefficients.

In this study, a logistic regression analysis was conducted to determine strong injury predictors and to establish injury tolerance or criterion for MTBI. To form the regression model, the dichotomous dependent variable or outcome was the occurrence of concussion or MTBI. The independent or predictor variables tested were: shear stress in the midbrain of the brainstem (SSS), shear stress in the thalamus (SST), intracranial pressure (ICP), the Head Injury Criterion (HIC), the Gadd Severity Index (GSI), the maximum resultant translational acceleration (Ar), and the maximum resultant rotational acceleration (Rr). Various univariate and multivariate models were assessed to find a single predictor variable, or a set of variables (a combination of the variables), which best explained the data. The sample size used in logistic analyses was all available data sets. Variations in impact location and direction were not studied separately in order to have a large enough sample size. The regression models were evaluated to determine significance and fit of predicted head response parameters against observed injury outcome. Sigmastat, a commercial statistical software package (SPSS Inc. Chicago, Illinois), was used to perform the logistic regression analysis.

Initially, univariate analyses were performed using the single independent variables listed above. The estimated logistic function for univariate models took the general form as $\hat{y}(x)=\beta_0+\beta_1 x_1$. Then, multivariate analyses were conducted. Translational and rotational accelerations as well as the intracranial pressure and the shear stress were selected and formed as two multivariate models. For the multivariate model, the logistic function took the form $\hat{y}(x)=\beta_0+\beta_1 x_1+\beta_2 x_2$.

To determine whether or not relationships between outcome and the predictor variables were statistically significant, significance tests of -2 Log Likelihood ratio and Wald Chi-Squared were performed. The model goodness of fit was used to compare the model's relative predictive ability as suggested by Hosmer and Lemeshow [28]. The null hypothesis is that a logistic regression coefficient β_1 is zero for univariate model, or the addition of a further terms β_{i+1} is zero for multivariate logistic model. Using the null hypothesis, -2 log likelihood ratio has a chi-squared distribution from which the probability (P-value) of incorrectly rejecting these null hypotheses was determined. The test statistics and P-values acquired from the significance test for each model along with the predictor variables are summarized in Table 4.

Based on these analyses, the occurrence of concussion can be best predicted by the shear stress in the midbrain (SSS). The Wald Chi-squired test also revealed that SSS was the best predictor. All the other predictors, which had the lower statistic values, were of less significance when compared to SSS variable. The multivariate models were also analyzed. It was found that although the multivariate model of resultant translational plus rotational acceleration was better than the two univariate models based on the -2 log

Table 4 Significance tests for univariate and multivariate logistic regression models

No.	Predictor Variables	d.f.	−2 log Likelihood Ratio		Wald Statistic	
			p	Statistic	p	Statistic
1	SSS	1	<0.001	17.799	0.010	8.112
2	SST	1	0.001	12.136	0.015	6.949
3	ICP	1	0.016	7.703	0.032	6.282
4	HIC	1	0.001	12.758	0.021	7.344
5	GSI	1	0.001	12.633	0.028	7.093
6	Ar	1	0.001	14.571	0.018	7.040
7	Rr	1	0.001	12.388	0.026	5.924
8	ICP+SSM	2	0.020	11.926	0.018	6.569
9	Ar+Rr	2	0.001	15.794	0.016	5.780

likelihood ratio test, the Wald Chi-squared test statistic was not. Figure 8 shows the predicted injury probabilities based model response and head input kinematics.

Discussion

Twenty-four real world football helmet-to-helmet field collisions were reconstructed using a partially validated FE model of the human head. The FE analysis allowed predictions of the intracranial pressure distribution, local stress, and strain of intracranial contents for a given impact associated with either a concussive or a noninjurious outcome. By relating the localized stress and strain to the injury site in the brain tissue, a FE model can offer a promising means of identifying hazardous mechanical agents responsible for this transient but usually reversible of neural impairment sustained by football players. If this correlation can be done successfully, the derived injury tolerance or criterion indeed will reflect real accident conditions and thus provide biomechanical data to set up a basis for head injury prevention. The remainder of the discussion section is related to issues of brain response and tolerance to impact.

Intracranial Pressure Response. In all 24 cases simulated, the patterns of the predicted pressure response within the cranial cavity showed distinct pressure gradients across the entire brain. The coup and contrecoup pressure phenomenon was also predicted by the model. This pressure phenomenon has been suggested in the literature as a mechanism for cerebral contusion. In the published studies, a large amount of information is available regarding the existence of pressure gradients in the cranial cavity of the head. Its role in relation to the mechanism of brain injury has been studied using animal models, physical models, cadaver skulls, and cadaver subjects. Denny-Brown and Russell [29] demonstrated the existence of positive pressures at the impact site and the negative pressures at the opposite site of the brain during experiments that induced animal concussion. Holbourn [30] showed the observed pressure and stress gradients in a gelatin-filled model of the human skull due to the angular acceleration. Gross [31] enunciated a cavitation theory by photographing through water-filled glass containers of several shapes. Lindgren [32] observed pressure distribution in water-filled spherical and hemispherical models constructed with aluminum and thermoplastics materials. Based on the observation that pressures gradients existed as a result of external insult, those researchers concluded that a sudden change in the intracranial pressure, during and after an impact to the head, plays an important role in the causation of a cerebral contusion or concussive brain injury.

In the current study, model simulations showed a progression of pressure gradients within the cranial cavity. The peak value and duration of the pressure response were closely related to the level of applied head translational acceleration. Additionally, the coup and contrecoup location showed correlation with the direction of translational acceleration at its CG. In a published study by Ward et al. [33], an intracranial pressure injury index was suggested to assess brain injury severity and the occurrence of the cerebral contusion. This index was based on combined analytical and live animal experimental investigation of brain injury. According to this intracranial pressure tolerance criterion, serious brain injury occurred when the peak intracranial pressure exceeded 235 kPa, while minor or no brain injuries would occur when the resulting intracranial pressure was below 173 kPa. In the present study, the predicted peak pressures at the coup and contrecoup sites ranged from 43 kPa to 130 kPa in compression, and from 32 kPa to 128 kPa in tension, respectively. Predicted intracranial pressure responses for all cases simulated were no higher than 173 kPa. It was deduced from model responses that the players were not at a great risk of suffering a minor contusion or cerebral cortex hem-

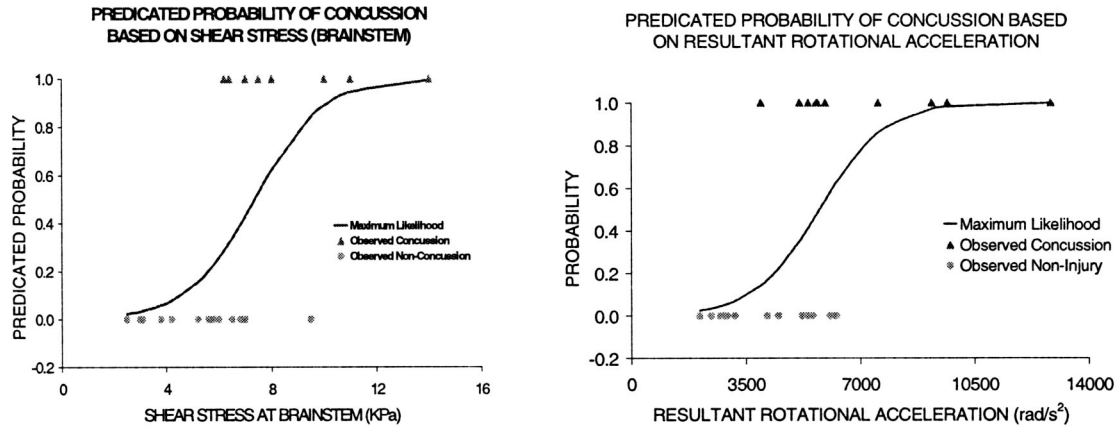

Fig. 8 Logist plots of the predicted injury probability based on shear stress at brainstem predicted by model and the input head rotational acceleration

orrhage based on the criterion proposed by Ward et al. [33]. However, it should be noted that the intracranial pressure duration (between 1 and 10 ms) in their experiments and simulations were shorter than those in this study. In a typical football head impact, the duration is usually longer than 10 ms, in part because of the use of protective helmets. In addition, their data were derived from frontal and occipital impacts only. Therefore, the proposed threshold for contusion may not be applicable to concussive brain injury resulting from a variety of impact locations, directions, and longer duration impacts.

Due to the current unavailability of clinical and somatic symptoms of players who sustained an MTBI as well as an absence of a detailed quantitative assessment of their neurological status, grading the concussion level for each injury case could not be done. Thus a direct link between the predicted intracranial pressures and the threshold of concussion could not be established until such data become available.

Brain Shear Stress Response. The underlying pathology of diffuse brain injury is widespread damage to axons in the brain. The level of immediate neurologic impairment is correlated with the extent and severity of axonal damage [34]. The concept of the shearing of axons at the time of blunt injury was postulated more than 30 years ago [35–37]. Morphological study of axonal injuries using non-human primates subjected to head acceleration have shown that axonal fragmentation or perturbation occurs within minutes of injury which supports the concept that shear can produce various degrees of diffuse axonal injury and petechiae [38].

Mechanically induced brain deformation at a particular region or site as a consequence of applied loading may determine a particular type of brain injury. Gurdjian et al. [39] observed that a high shear stress concentration was generated at the brainstem when a sagittal section of the human skull, filled with milling yellow (a fluid that has photoelastic properties), was subjected to an impact. Edburg et al. [40] also reported that the brainstem was the region to experience high concentration of shear stress in a skull model. From the medical literature, clinical observations and neuropathological studies have demonstrated that the corpus callosum, the midbrain-pons tegmentum, the inferior colliculus, and the dorsolateral quadrant of the rostral brainstem at the superior cerebellar peduncle are regions most often associated with diffuse neuronal and vascular damage [41–45].

For the incidents simulated, high shear stresses were initially in the cortical region of the brain. They then moved to the central core areas after the impact reached its peak. The midbrain sustained the highest localized shear stresses in comparison to other regions of interest. This model prediction agrees with clinical and pathophysiological observations and biomechanical investigations using experimental animals, physical and analytical models. The development of a highly localized shear stress can be due to the structural and anatomic features of the midbrain. It is surrounded by a relatively stiff tentorium opening and the brainstem itself is shaped as a narrow bridge or structure. Also it is noted that the midbrain is bounded by white matter, gray matter, and the ventricles. It is likely that a high stress/strain concentration can develop in this area of the brain.

The experimental work of Denny-Brown and Russell [29] pointed to the brainstem as the probable anatomical substratum of concussion, as demonstrated by the work of Magoun [46] on the reticular system. Rosenblum et al. [47] stressed that the midbrain regions are neural relay stations and centers for vital functions. Thus, shear in these areas can be responsible for brain dysfunction if the level is sufficiently high. The severity and extent of such brain dysfunction could be as severe as DAI when shear stress/strain exceeds the tissue injury threshold, or as minor as a mild concussion in which brain tissues (cells) are not irreversibly destroyed but remain alive with cerebral functions altered to varying degrees. The model predicted that the level of shear stress experienced by football players associated with injury could be used as a meaningful measure to predict the possibility of incurring a concussion during an impact, if more cases are studied and a statistically significant correlation can be determined.

Injury Predictor and Tolerance Level Assessment. The biomechanical injury predictors and their respective tolerance levels proposed in this study are based on results of a reconstruction of actual field incidents which covered both injury and noninjury cases. Existing tolerance values using input parameters do not consider the brain as a deformable body, and are, thus, at best only indirectly and incompletely related to brain injury. In contrast, the proposed tolerances based on the current study use tissue response parameters and are thus not only more reliable but also capable of relating a particular level of tissue response to a specific type and probability of injury.

However, the limitations of the current study should be recognized. First, it should be noted that head kinematics used as model input were measured from a laboratory accident reconstruction, by drop tests. The exact location and direction of the impact just before and at the moment of contact cannot be accurately ascertained. Second, tissue responses were predicted by an FE head model which has not been subjected to extensive validation. In addition, complete knowledge of in vivo material properties of brain tissue is still lacking. Third, the sample size was limited. Fourth, accurate information regarding recidivism is unavailable. It is possible that some of the injured players suffered a recurrent injury (repeated concussion, e.g., a second concussion in a season, or a larger number of concussions in a career), and can thus have a lower injury threshold. Additionally, the influence of the model/brain size on the resulting tolerance levels was not considered in this study [48,49].

Injury Predictors for MTBI. The injury predictors for MTBI evaluated in this study were biomechanical parameters, including brain tissue response, head input kinematics, and existing head injury criteria. Based on statistical analyses, the maximum shear stress response at the brainstem region provided the strongest correlation with the occurrence of MTBI. In the multivariate analysis, it was found that no other multivariate model was significantly better than the univariate models, except that the combination of resultant translational acceleration and rotational acceleration model did show a better outcome than the two respective univariate models. This may imply that both translational and rotational acceleration are essential elements for an injury to occur. Further examination of this effect should be directed towards the study of the relative contribution of each acceleration component on injury outcome. However, a larger sample size of real-life injury and noninjury cases will be needed.

Injury Tolerance Level. Using logistic regression analysis, the probability of injury can be ascertained. Therefore, the thresholds for a number of probability values of MTBI can be established. The thresholds of injury predictors that would result in a 25%, 50%, and 80% probability of MTBI were determined for shear stress in the midbrain and for translational acceleration, rotational acceleration, and HIC_{15}.

The estimated tolerable SSS levels were 6.0, 7.8, and 10.0 kPa for 25%, 50%, and 80% probability of MTBI. In addition, at each probability level, the number of true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN) were calculated based on whether the actual incidents reconstructed were injury cases or noninjury cases and shear stress responses predicted for these cases were either above or below the threshold value [50]. At a threshold having a probability level of 25%, the specificity was 0.743 while sensitivity reached 1. At the 50% probability level, specificity and sensitivity levels were 0.56 and 0.93, respectively, while at 80% probability, the specificity was 1.000 and the sensitivity was 0.711. The threshold level which balanced (the best overall threshold) the accurate prediction of injury/noninjury cases was found to be at a probability of 31% or a SSS of 6.6 kPa.

The proposed data were compared with results obtained from animal models, and computer models in the literature. In a FE model simulation of motorcyclist accidents, Kang et al. [51] observed that the predicted areas of shear stress concentration correlated with the brain injury locations. The authors suggested that brain shear stress in the range of 11 kPa and 16.5 kPa was the brain injury limit. In an experimental and computational study of axonal injury using sheep, Anderson et al. [52] reported that the location of the shear stress predicted from a FE model showed some degree of correlation with the site of injury observed in the animal model. The predicted shear stress in the range of 8 to 16 kPa was suggested to be responsible for widespread axonal injury with a severity of 1+(mild DAI). It is worth noting that the reported injury thresholds in these two studies were for slightly more severe forms of brain injuries. The proposed injury tolerance for shear stress derived from current study fell well within the lower bound of these published results. Recently, Bain and Meaney [53] produced in vivo axonal injuries using the optic nerve of guinea pig. The strain based in vivo tissue-level thresholds for functional and morphological injuries of white matter were estimated by logistic regression analysis. The proposed conservative, optimal and liberal thresholds for functional impairment were 0.13, 0.18, and 0.28, respectively. In the current study, an approximate strain levels estimated from the proposed SSS at 25%, 50%, and 80% probability of MTBI were about 0.14, 0.19 and 0.24, respectively. It appears that the estimated strain at 25% and 50% was consistent with the in vivo tissue threshold levels for functional brain injury suggested by Bain and Meaney [53]. Notice that the shear stress and strain threshold derived from the current study was based on material properties assumed in this model. If different material properties were selected, the shear stress injury threshold could be altered.

The maximum resultant translational acceleration at the CG of the head was estimated to be 66, 82, and 106 G for a 25%, 50%, and 80% probability of MTBI, respectively. One et al. [54] produced the human concussion tolerance curve called JHTC based on data from a series of concussion experiments using primates. Dimensional analysis was utilized to extrapolate the animal data to the human level. Resultant average head accelerations of 220 G for 2 ms duration and 90 G for 9 ms were considered to be concussion thresholds for head impact. According to the Wayne State Tolerance curve (WSTC), an effective acceleration of 80 G was considered noninjurious while 90 G could produce concussion [55] for impacts with a padded surface, however, no upper limit of the time duration was specified. The injury tolerance estimated from the current study was primarily derived from a typical impact duration of 10 to 16 ms. The tolerable levels for MTBI proposed here compared fairly well with those from the JHTC and the WSTC.

The maximum resultant rotational accelerations for a 25%, 50%, and 80% probability of sustaining a MTBI were estimated to be 4.6×10^3, 5.9×10^3, and 7.9×10^3 rad/s^2, respectively. These values are for impact durations between 10 to 30 ms, when a helmet or padding was used. Reported head rotational acceleration limits available in the literature were obtained from different surrogates including animals, cadavers, mathematical models, and volunteers. Ommaya [56] proposed an angular acceleration tolerance of 1800 rad/s^2 for a 50% probability of concussion when he scaled data from several animal species to the human. The scaling procedure was unreliable and there was no associated translational acceleration applied to the head. A tolerance level of 4.5×10^3 rad/s^2 was suggested as a safe limit in the mid-sagittal plane rotation by Lowenhielm [57]. Ewing [58] showed that no adverse effects were observed in instrumented volunteers with head angular acceleration of 2.7×10^3 rad/s^2. Princemaille et al. [59] conducted an experimental study with volunteer boxers who were instrumented with multiple accelerometers. The maximum angular acceleration of 16,000 rad/s^2 with an angular velocity of 25 rad/s was tolerated by these boxers. Note that results from their studies were derived from the use of a small data set with no injured subjects. Margulies and Thibault [60] proposed a human injury tolerance for DAI using a scaling method based on experimental animals, physical models and analytical simulations of DAI. An angular acceleration of 1.6×10^4 rad/s^2 was suggested as tolerance to moderate to severe DAI for the human head subjected to a lateral motion. The proposed tolerable rotational acceleration or MTBI from current study fell well within the range of reported brain injury tolerance level.

The estimated HIC_{15} threshold levels for 25%, 50%, and 80% of probability of MTBI were 151, 240, and 369. Apparently, the threshold derived from this study was less than the regulatory limit for serious brain injury of 1,000, specified in FMVSS 208. By analyzing a number of published skull fracture and brain injury test data, Prasad and Mertz [26] suggested that a HIC_{15} value of 1000 represented a 16% risk of life-threatening brain injuries according to a derived Head Injury Risk Curve (HIRC). It can be seen that mild brain injury in football could occur even at seemingly low HIC values. This implies that the head linear acceleration, and thereby HIC is not the only injurious factor attributable to the causation of minor brain injury. This fact again raises concerns that the rotational components of head acceleration should be determined and be included in any injury criterion.

Overall, the tolerance level in terms of head kinematics proposed here are generally lower than those currently accepted or proposed. One possible reason may be related to the direction and location of head impacts simulated. These injury data mainly involve the lateral and frontal-lateral impacts. Injury severity can be different for other impact directions. This was shown by Zhang et al. [16] who demonstrated that the human head had a lower tolerance from a lateral impact in comparison to a frontal impact with the same energy. Observations from this study further provide evidence to support the concern that the direction of impact is an important factor in brain injury tolerance [61–63]. However, further investigation of other injury predictors is warranted when more MTBIs data become available.

Conclusions

In this study, actual field incidents from American football were reconstructed using a sophisticated finite element head model. Head kinematics measured from helmeted Hybrid III dummy heads were used as input to drive the FE model. The resulting mechanical response parameters, including the intracranial pressure and brain shear stress predicted by the model, were chosen as potential injury indicators of MTBI. Statistical analyses were performed to assess the relationships between injury outcome and brain tissue responses or head kinematics. Some injury predictors and injury tolerances for MTBI were proposed and were compared to the other studies in the literature. The following conclusions can be drawn from current investigation:

1. Intracranial pressure results from the model showed a typical coup and contrecoup pattern throughout the brain. The location and level of peak pressure in the brain were not well correlated with the sites of concussive brain injury. However, the magnitude of the resulting pressure reflected the severity and extent of resulting tissue response to a given impact. Therefore, intracranial pressure can serve as a global response indicator for head injury.
2. High shear stress concentrations were found to be localized in the upper brainstem and thalamus regions. The induced shear stress may alter brain function leading to a mild brain injury. The shear stress generated at the central core region of the brain is primarily related to the geometrical feature and material composition of the brainstem structure.
3. Based on linear regression analyses, translational head acceleration had a greater influence on intracranial pressure re-

sponses in comparison with rotational acceleration. Shear stress in the central part of the brain was more sensitive to rotational acceleration than to translational acceleration.

4. Based on linear logistic regression analyses, the predicted shear stress response in the upper brainstem was the best injury predictor over other brain response parameters, such as the existing injury criteria HIC, GSI, and the head acceleration. A shear stress of 7.8 kPa was proposed as the tolerance level for a 50% probability of sustaining a MTBI.

5. Injury tolerance for MTBI based on head kinematics and HIC_{15} can be estimated. If the head was exposed to a combined translational and rotational acceleration, with an impact duration of between 10 to 30 ms, the suggested tolerable reversible brain injury level was less than 85 G, for translational acceleration. For the rotational acceleration, it was less than 6.0×10^3 rad/s^2. The suggested HIC_{15} value was 240. These values may change as more human data become available.

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