ABSTRACT

The finite element (FE) modeling is a powerful tool for investigating the physical process producing head trauma, and a well validated model would, thus, be a valuable tool to aid in injury diagnosis and design of protective devices. Many FE head models with various degrees of simplification have been developed in the past several decades. There are, however, two common problems with the existing models. First, the mesh generation method is often time-consuming, and the generated mesh is unable to represent the important geometric characteristics of the complex human head. Second, existing models are validated using either intracranial pressure or deformation measured by cadaver experiments, but the extent to which the experimental results may be applied to live human brains is uncertain due to discrepancies between material properties of in vivo and cadaver brains.

In the first part of this work, we develop a 3D FE head model that accounts for important geometric characteristics of the head using an efficient magnetic resonance imaging (MRI) voxel-based mesh generation method. The model is validated against intracranial pressures measured in a previous cadaver frontal impact experiment. The model is run under either of two extreme assumptions—free or fixed—concerning the head-neck junction, and the experimental measurements are well bounded by computed pressures from the two boundary conditions. The presence of a spherically convergent shear wave pattern in the brain is uncovered through our FE simulation, and that provides the first computational mechanics support for the centripetal hypothesis of cerebral concussion. It is concluded that the frontal impact gives rise not only to a fast pressure wave but also a slow and spherically convergent shear stress wave that is potentially more damaging to the brain tissue.
In the second part of this work, we first study *in vivo* human brain deformation under mild impact induced by a 2-cm head drop using tagged MRI and the harmonic phase (HARP) imaging analysis technique originally developed for cardiac motion analysis. The FE simulation of mild impact is then carried out using the proposed 3D head model. The predicted deformation field from FE modeling correlates reasonably well with the results of MRI-based assessments. To our knowledge, this study is the first attempt in which the deformation field obtained by MRI-based assessment is correlated with the prediction of a corresponding FE model, and it is also the first validation of an FE brain injury model on *in vivo* human brain deformation data. It is found in this study that the maximum deformations occur within a few milliseconds following the impact, which is during the first oscillation of the brain within the skull, with maximum displacements of 2-3 mm and maximum strains of 5-10%.
To My Family
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# TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION ......................................................................................1

CHAPTER 2: MODEL DEVELOPMENT .....................................................................6

CHAPTER 3: MODEL VALIDATION I – INTRACRANIAL PRESSURE OF FRONTAL
IMPACT ..................................................................................................................11

CHAPTER 4: MODEL VALIDATION II – BRAIN DEFORMATION UNDER MILD
IMPACT ..................................................................................................................16

CHAPTER 5: DISCUSSION AND CONCLUSIONS ....................................................23

REFERENCES ..........................................................................................................27

APPENDIX ................................................................................................................30

FIGURES AND TABLES ...........................................................................................34
CHAPTER 1
INTRODUCTION

Traumatic brain injury (TBI) is a serious public health problem that has enormous social and economic impact. Each year over 1.5 million people sustain a TBI in the United States alone. Among them, 20% to 25% are moderate and severe TBIs that may result in death and life-long disabilities. Although the remaining 75% to 80% are mild TBIs that can recover fully in most cases, there are still a portion of people who experience long-term physical, cognitive, and psychological problems due to poor early diagnosis and treatment. TBI often occurs in traffic accidents, falls, assaults, and sports activities. In these traumatic events, a blow to the head or sudden acceleration/deceleration of the head without a direct impact may lead to brain lesions such as cerebral contusion, tears in arteries and veins, and tears of axons in brain white matter. In some cases of mild TBI, brain function impairments such as attention, emotional, and memory problems may exist without any visible brain lesions.

The TBI has received much attention from various disciplines. While clinicians focus on collecting pathological and physiological data, physicists and engineers employ the principles of mechanics to study the physical phenomena involved in injury process and provide explanations for the cause of brain damage. The different methods the researchers have used to study the mechanics of brain injury include animal and cadaver experiments, physical modeling, and mathematical modeling. In particular, finite element (FE) modeling has become a powerful tool for studying mechanics of brain injury. By numerically solving initial-boundary value problems modeling head trauma events, FE solutions provide spatial and temporal distribution of the field variables such as stress, strain, and displacement throughout the head model; however, these mechanical parameters of biological tissues are difficult to measure by experimental studies. The
resultant stress and strain from FE solutions may be taken as a quantitative measure of tissue
damage and correlated with pathological and physiological findings from clinical investigations.
Once good correlations are established and the FE model is well validated against experimental
data, the model may eventually become a valuable tool for better understanding of injury
mechanisms, better injury diagnosis and design of protective devices.

While the need for an FE model for head trauma research is obvious, the development of such
a model has been a challenging task due to the human head’s complex geometry, material
compositions, boundary/interface conditions, as well as insufficient experimental data for model
validation. The anatomy shown in Fig. 1 illustrates the multiscale complexity of the human head.
From exterior to interior, the human head consists mainly of scalp, skull, membranes (dura,
arachnoid, and pia mater), cerebrospinal fluid (CSF), and brain. Each component has its own
unique structure and complex geometry. For example, the skull is a three-layer structure
consisting of an inner and an outer table of cortical bones and an inner layer of cancellous bone.
Moreover, the skull bone varies significantly in its thickness from location to location. The brain
is known to be one of the most complex biological structures. Its tissues can be divided into two
types: one is gray matter made up mainly of the cell bodies of neurons, and the other is white
matter primarily comprising of the axons of neurons. Apart from the complex geometry,
biological tissues are often inhomogeneous, anisotropic, nonlinear, and their well-defined
mechanical properties are still lacking. In addition, interactions between different material
compositions such as solid skull, gel-like brain, and fluids pose additional challenges in FE
modeling. Finally, head injury experiments are difficult and expensive to carry out and very
limited data, especially, experimental data on in vivo human brain, are available for FE model
validation.
Despite the aforementioned challenges, many FE head models with various degrees of simplification have been developed in the past several decades. The early FE models used a simple fluid-filled spherical shell to represent the skull/brain complex. Complexity was gradually added to the models as more geometric and material information, as well as the required computing power became available. Among the advanced 3D FE head models developed in recent years are the models of Zhang et al. (2001), Willinger et al. (1999), Kleiven and von Holst (2001), and Horgan and Gilchrist (2004). All these models include the major anatomical components of the human head along with different material properties for individual components. Their geometric representations are based on anatomical drawings and medical images such as Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) images. A surface-based mesh generation method is generally used in which outer surfaces of individual components are first defined and internal meshes are then generated using certain techniques.

There are, however, two common problems with these models in terms of the quality of the geometric representation and the efficiency of the mesh generation. Concerning the first issue, some important geometric characteristics are not well represented. The unique folding structure of the cerebral cortex is not taken into account and the brain is modeled as having a ‘smooth’ surface. Consequently, the CSF in the subarachnoid space between the skull and the brain is modeled as a uniform layer, while, in reality, it has a non-uniform distribution due to the ‘hills and valleys’ (i.e. gyri and sulci) on brain’s surface. Studies have suggested that the folding structure of the brain surface and the non-uniform distribution of the CSF greatly influence both the distribution and the magnitude of the maximum stress and strain in the brain subjected to impact (Gilchrist et al., 2000; Cloots et al., 2008; Lauret et al., 2009). A second and separate problem with the previous FE models is that the surface-based mesh generation employed is
generally quite time-consuming which makes generation of patient-specific head models infeasible. However, patient-specific models for biological structures are important due to large individual variations, and this is particularly the case when the human head is concerned (Kleiven and von Holst, 2001),

In terms of model validation, all the previous head injury models are validated on either intracranial pressure or brain displacement from cadaver experiments. However, the extent to which the experimental results may be applied to human brain in vivo is uncertain due to discrepancies between material properties of in vivo and cadaver brains. To obtain a better understanding of brain injury mechanisms and better validation of FE brain injury model, knowledge of deformation patterns of in vivo human brain is essential and such measurements have become possible since the invention and advancement of MRI technique. MRI is known to be the most powerful tool for non-invasive assessment of biological soft tissues in vivo, which makes it suitable for brain research. In fact, in the field of cardiac research, a special MRI pulse sequence called tagging (Zerhouni et al., 1988; Axel and Dougherty, 1989) has been developed and has become a well established technique to image cardiac motion. MRI tagging is used to spatially modulate the longitudinal magnetization of the subject to create temporary features called tags in the myocardium. The tag pattern is deformed by the underlying heart motion and can be shown from an image sequence reconstructed from sufficient data acquired over many heartbeats in a single breath hold (Osman et al., 2000). Various image processing techniques have also been developed to analyze the tagged cardiac MRI images to estimate the motion quantities such as displacements and strains of the myocardium. In particular, a novel image processing technique called harmonic phase (HARP) image analysis developed by Osman et al. (1998; 2000) provides a fast and automated means to estimate dense motion quantities from
tagged cardiac MRI images. The tagged MRI and the HARP image processing techniques
developed for cardiac motion tracking has been applied to obtain deformation fields of \textit{in vivo}
human brain during mild acceleration by Bayly \textit{et al.} (2005), Sabet \textit{et al.} (2008), and Feng \textit{et al.}
(2010).

Our study is aimed at problems with the existing models described above. In the first part of
this work, we propose a 3D FE human head model that accounts for important geometric
characteristics of the head using an efficient MRI voxel-based mesh generation method. The
proposed model is then validated on intracranial pressure measurements from a previous cadaver
experiment of frontal impact. The wave propagation in the brain following the impact is also
studied. In the second part of this work, we obtain deformation fields of \textit{in vivo} human brain
under mild impact induced in a 2-\textit{cm} vertical head drop using tagged MRI and the HARP
technique; these results are compared with the predicted deformation fields from our proposed
FE model. The significance of the comparison is two-fold. On one hand, to our knowledge, this
is the first attempt where the deformation field obtained by MRI-based assessment (i.e., tagged
MRI images and HARP analysis) is correlated with predictions of a corresponding FE model.
Note that a good correlation would provide a validation of the sensitivity of the tagged MRI and
HARP analysis to the deformations caused by the mild impact loading. On the other hand, our
work is also the first attempt to use deformations of \textit{in vivo} human brain for FE head injury
model validation. A good correlation would serve as another validation of our proposed FE head
model.
CHAPTER 2
MODEL DEVELOPMENT

2.1 MRI voxel-based FE mesh

The geometry of the FE mesh is based on T1- and T2-weighted structural MRI scan data of a healthy adult. Image segmentation is performed to differentiate five tissue types: scalp, skull, cerebrospinal fluid (CSF), gray matter, and white matter. As a result, each image voxel is associated with a particular tissue type. The FE mesh shown in Fig. 2 is created by directly converting image voxels into eight-node hexahedral elements through a custom C++ code. The FE mesh consists entirely of hexahedral elements with element size of $1.33mm \times 1.33mm \times 1.30mm$ which is identical to the MRI resolution. Each FE is assigned a particular material property according to the tissue type of its corresponding image voxel. The scalp and facial structures are excluded, and structures such as membranes and blood vessels are not explicitly modeled. Globally, the model has a total of 1,061,799 elements and 1,101,599 nodes. To the best of our knowledge, our MRI voxel-based FE head model is the first FE head model that has the MRI resolution. The voxel-based mesh generation method provides an efficient and accurate means of generating a patient-specific head mesh that can describe the important features of the highly complex head geometry, such as the folding structure of the cerebral cortex and realistic separation of CSF, gray, and white matter. The very fine mesh of our model also makes it possible to capture stress wave propagation during a head impact process.

2.2 Mesh smoothing

The direct conversion of image voxels to hexahedral FEs provides a fast, automated means of

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* Based on Chen and Ostoja-Starzewski, 2010.
generating 3D FE mesh of complex biological structures. However, the hexahedral FE mesh introduces jagged edges on mesh surface and material interfaces, which would lead to numerical artifacts in the solution (Guldberg et al., 1998; Jacobs et al., 1993). Thus, in order to improve numerical accuracy, a mesh smoothing technique is applied to smooth out the jagged edges on the outer surface and material interfaces. A C++ program is developed based on the smoothing algorithms proposed in Boyd et al. (2006) and Taubin (1995; 2000). Figure 3 shows the original and smoothed meshes of the brain.

The mesh smoothing algorithm includes the following three major steps:

1) Classify and label surface, interface and interior nodes of the FE mesh. Nodes are labeled in a hierarchical order. For example, surface nodes, interface nodes, and interior nodes can be labeled as 3, 2, and 1, respectively.

2) Define neighborhoods for each of the surface and interface nodes with hierarchical constraints. Generally, each node is surrounded by six neighboring nodes. In this smoothing process, only the neighboring nodes with higher or same hierarchical orders are defined as the neighborhoods of the central node. For instance, surface nodes only consider other surface nodes as their neighbors. Interface nodes may consider surface nodes or other interface nodes as their neighbors. The set of neighborhoods of node $i$ is denoted as $i^*.$

3) Apply a Laplacian smoothing in two consecutive steps with two different scaling factors, $\lambda$ and $\mu.$ The algorithm is described as follows:

$$\Delta x_i = \sum_{j \in i^*} w_{ij} (x_j - x_i);$$

if $k$ is even

$$\text{(1)}$$
\[ x_i = x_i + \lambda \Delta x_i; \]

else

\[ x_i = x_i + \mu \Delta x_i; \]

end;

where \( \lambda = 0.6307 \), \( \mu = -0.6732 \) (Taubin, 2000), \( N \) is the number of iterations, and \( w_0 \) is taken as the inverse of the total number of neighborhoods of node \( i \).

Too many iterations of mesh smoothing can result in severely distorted elements, and so the limit of smoothing iterations is found to be eight in this study. The conventional Laplacian smoothing method usually causes mesh volume shrinkage while the smoothing algorithm implemented here has the advantage of conserving the mesh volume.

### 2.3 Material properties

Most biological tissues are recognized as inhomogeneous, anisotropic and nonlinear; however, the complete material characterization of biological tissues is still a challenging task. Hence, assumptions of material behavior have to be made for the sake of FE model development. The material data of different tissues used in this study are taken from literature and listed in Table 1. All material phases in the model are assumed to be homogeneous and isotropic.

The human skull consists of an inner and an outer table of relatively stiff and high-density cortical bones and a middle layer of relatively compliant and low-density cancellous bone, or diploë. In this study, the three-layer cranial bone is modeled as a single-layer structure with the effective properties taken from Khalil & Hubbard (1977).

The CSF is a Newtonian fluid composed of 99% water with a specific gravity of 1.0032-1.0048 and a relative viscosity of 1.020-1.027 at 37°C (Turitto et al., 1998). It flows within the
subarachnoid space and the ventricles of the brain. The subarachnoid space, existing between arachnoid and pia mater, is not only occupied by most of the CSF, but also traversed by the delicate fibrous arachnoid trabeculae and large blood vessels (Fig. 1(b)). Given the evident spatial complexity, the CSF layer representing the entire subarachnoid space is modeled by a homogenized solid material with bulk modulus of 21.9 MPa and shear modulus of 50 KPa while the use of solid FEs to model the CSF layer can account for the shear resistance provided by the arachnoid trabeculae and large blood vessels in the subarachnoid space.

Brain tissues have long been recognized as viscoelastic materials with strong strain rate dependence. Studies have also shown their nonlinear behavior at large deformation. The structure difference between gray and white matter gives rise to the hypothesis that they have different mechanical properties. In this study, we use a material model which assumes linear viscoelastic behavior for both gray and white matter. The shear relaxation modulus is described by

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

where $G_0$ is the short-term shear modulus, $G_\infty$ is the long-term shear modulus, and $\beta$ is a decay constant. The material parameters used are the same as those in Zhang et al. (2004).

**2.4 Interface/Boundary conditions**

Traction and displacement continuity at material interfaces are assumed for the FE model, hence neither tangential sliding nor normal separation is allowed at any two-tissue interfaces. The interface condition can be described mathematically as follows:

$$u^{(p)} = u^{(q)},$$
$$t^{(p)} = t^{(q)},$$

for all $p$ and $q$ phases in contact,
where $\mathbf{u}$ is the displacement vector and $\mathbf{t}$ is the traction vector.

Traction and displacement boundary conditions depend on specific head injury cases that are being simulated. Different traction and displacement boundary conditions are prescribed for different simulations and will be described in Chapter 3 and 4. It should be noted here that the effect of the neck on the response of the head to external loading needs to be considered by prescribing appropriate boundary condition at head-neck junction since the neck is not included in the model.
CHAPTER 3
MODEL VALIDATION I - INTRACRANIAL PRESSURE OF FRONTAL IMPACT

3.1 Cadaver experiment of frontal impact

A frontal cadaveric impact experiment conducted by Nahum et al. (1977) is used to validate our proposed model. In that experiment, seated stationary cadaver subjects were impacted at the frontal bone of the skull in the mid-sagittal plane in an anterior-posterior direction by a rigid mass traveling at a constant velocity. The skull was rotated forward and the Frankfort anatomical plane was inclined 45° to the horizontal. The recorded impact force as shown in Fig. 4 lasts approximately 9 ms with the peak of 6.8 KN around 5 ms. Intracranial pressures were recorded by pressure transducers placed at the following five locations in the subarachnoid space: in the frontal bone adjacent to the impact area, immediately posterior and superior to the coronal and squamosal sutures respectively in the parietal area, inferior to the lambdoidal suture in the occipital area (one in each side), and at the posterior fossa in the occipital region. The frontal region, which is right under the impact region, is named coup site and the posterior fossa region, which is opposite to the impact site along the impact axis, is named contrecoup site.

3.2 FE simulation of frontal impact

To simulate Nahum’s experiment, the recorded impact force from the cadaver test is directly applied to the mid-frontal area of the model in the anterior-posterior direction. The impact force is applied in the form of a distributed load over an area of 1556 mm$^2$ and the peak pressure load is 4.37 MPa.

As for the boundary condition at the head-neck junction, two extreme assumptions – i.e., free and fixed boundary conditions – are considered respectively. Most 3D FE head models in the

* Based on Chen and Ostoja-Starzewski, 2010
literature consider the free boundary condition only with the supporting argument being that the neck constraint has negligible influence on the dynamic response of the head model in a short time interval. However, the head model subjected to frontal impact without any constraint at the neck will undergo predominantly rectilinear motion and the rotational acceleration occurring in actual head motion can not be properly represented. Therefore, we also consider the fixed boundary condition, the other extreme case in which the nodes around an area of the foramen magnum are fully constrained. Since rotation about the occipital condyles is involved in actual head motion, motivated by variational principles of mechanics, we argue that the responses predicted by these two extreme cases provide bounds on the actual response.

The FE analysis is carried out using ABAQUS with a dynamic, explicit procedure. The simulation is run for 15 ms. A typical simulation of 15 ms required about 1.5 hrs using an SGI Altix supercomputer with 16 parallel CPUs.

3.3 Results

Comparisons of pressure-time histories between model predictions and experimental measurements at coup and contrecoup sites are shown in Figs. 5 and 6. We can see that the experimental data are well bounded by the numerical results of two extreme boundary conditions as expected since the actual response at the head/neck junction has an intermediate behavior. At the coup site, the model with free boundary condition predicts tensile pressure in nearly the whole duration with a peak pressure of 180 KPa at 5 ms; the model with fixed boundary condition shows variations of compression and tension and the peak pressure reached is 80 KPa. We see that the model with free boundary condition gives better correlation of coup pressure with experimental results. At the contrecoup site, the model with free boundary condition predicts
mostly tensile pressure for the 15ms simulation and the response for the first 6ms is in good agreement with the test data. However, the transition from tension to compression found in the cadaver experiment for the contrecoup site is replicated better by the model with fixed boundary condition. The maximum and minimum contrecoup pressures obtained by the simulations are 65KPa and -60KPa, respectively.

The comparison of intracranial pressures shows the significant influence of different boundary conditions on the mechanical response of the human head complex subjected to transient loads. One or more of the following factors may also contribute to the discrepancy between the model responses and the experimental measurements: exclusion of anatomical structures such as membranes, simplified models of material behavior, and the imprecise information of the exact pressure transducer locations.

3.4 Discussion: spherically convergent shear waves

As is well known, the Helmholtz resolution of a displacement vector into the gradient of a scalar and the curl of a zero-divergence vector leads to the decoupling of dilatation (pressure) and distortion (shear) in the equation of motion of a homogeneous isotropic material. This then leads to equations for scalar and vector potentials. The scalar potential is associated with the propagation of dilatational (pressure) waves, while the vector potential is associated with the propagation of distortional (shear) waves. For linearly viscoelastic materials, the maximum speeds of propagation of these two types of waves are given by Christensen (1982),

\[
c_1 = \left( \frac{K(0) + \frac{4}{3} \mu(0)}{\rho} \right)^{\frac{1}{2}} \quad \text{(Dilatational)}
\] (4a)
\[ c_2 = \left( \frac{\mu(0)}{\rho} \right)^{\frac{1}{2}} \]  
(Distortional)  
(4b)

where \( \rho \) represents material density, \( K(0) \) and \( \mu(0) \) are instantaneous bulk and shear modulus, respectively.

Based on the material properties used for brain tissues in this study, the speed of pressure wave propagation is around 1450\( m/s \), so that the pressure wave transits in less than 0.1\( ms \), taking 14\( cm \) as the anterior-posterior dimension of the brain. On the other hand, the maximum speed of shear wave propagation in the brain is around 6.3\( m/s \), which is three orders of magnitude less than the speed of pressure waves. Therefore, the frontal impact gives rise not only to a fast pressure wave but also a slow wave of distortion. As shown in Fig. 7, a marked difference in the shear stress between two boundary conditions was found. The model with fixed boundary at the head/neck junction predicts larger shear stress in the brain throughout the duration. This difference in shear stress magnitude is attributed to the fact that fixed boundary causes the rotational motion of the head model while the free boundary leads to nearly translational motion. What is also observed is that both free and fixed boundary conditions give rise to complex patterns of shear stress waves which converge spherically away from the skull towards the brain center following the impact. Evidently, the highly heterogeneous brain structure introduces extra complexities, i.e. local fluctuations in stress levels. In the case of free boundary condition, the amplitude is lower and it is higher for a fixed boundary condition. However, the shear waves do not increase in intensity as they converge inward. This can be explained from the standpoint of a competition of wave amplification due to spherically convergent implosion with wave damping due to brain tissue viscoelasticity.
The maximum pressure in the brain obtained from the FE simulation is on the order of 10-100 KPa and the maximum shear stress is on the order of 1 KPa. Although the shear stress is 1-2 orders lower than the pressure, it is potentially more damaging because brain tissues have very small resistance to shear compared with its resistance to pressure (Holbourn, 1943).

In order to better understand the spherically converging shear wave pattern found in the above simulation, but free of the local heterogeneities due to complex brain structure, we construct a simple idealized FE model. The model consists of an inner sphere with a radius of 7 cm representing the brain and two outer spherical shell layers with thicknesses of 5 mm and 8 mm that represent the CSF layer and skull, respectively. The same material properties as listed in Table 1 are adopted for this simplified model except the shear modulus of the brain is the average values of gray and white matter. The same impact pulse as used in previous analysis is employed here and it acts along one of the center axes of the sphere. The whole model is freely supported. Figure 8 shows the resulting spatial distribution of von Mises shear stress in the inner sphere at different time points during the 15 ms duration, in which the spherically convergent shear wave is clearly seen. We conclude that the solid shell enclosing a CSF layer and the solid brain core, leads to a partial conversion of the energy of the axial impact to the head into a shear wave imploding towards the center.
CHAPTER 4

MODEL VALIDATION II – BRAIN DEFORMATION UNDER MILD IMPACT

In this part of our study, we carried out the head drop experiments using human volunteers, acquired tagged MRI images during the head drop, applied the HARP analysis to the tagged MRI images, and obtained the brain motion estimates. In addition, we built a mathematical model of mild impact of the human head using our proposed MRI voxel-based FE head mesh, and compared the predicted deformation fields with that from MRI-based HARP estimates.

4.1 MRI-based assessment of brain deformation

A healthy adult with no history of head trauma was recruited to participate in the 2-cm vertical head drop experiment. The experiment was carried out at the Biomedical Imaging Center (BIC) at the University of Illinois at Urbana-Champaign in accordance with the institutional review board. All MRI data collection was performed on a Siemens Allegra 3 T scanner. During the 2-cm vertical head drop, a custom-made MRI-compatible head drop device (HDD) was secured to the MRI head coil to guide the motion of head (Fig. 9). At the start position, the HDD was raised to the elevated position and locked. As the head began to drop after activation of a release mechanism, a fiber optic system of the HDD triggered the dynamic imaging sequence of the MRI unit. The dynamic scans utilized a multi-shot spiral FLASH sequence with spatial modulation of magnetization (SPAMM) grid-tagging (Axel and Dougherty, 1998) and the grid-tagging lines are applied in synchrony with the head drop. The imaging sequence parameters were: TR=10 ms, TE=1.5 ms, flip angle=8°, 240 mm field of view, 128×128 acquisition matrix, 1.8 mm spatial resolution, 10 ms temporal resolution, 4 mm tag period, and 8 mm slice thickness. A 12-shot spiral acquisition was used where a single shot at each time point was acquired per
head drop and the drop was repeated 12 times per image time series. Four series of dynamic images were acquired. They include one axial slice and one sagittal slice, and two tagging orientation per image slice. Slice prescription is determined by examining the lowest point of the skull in a scout image taken with the HDD in the down position. 200 tagged images are acquired in a time series, covering the first two seconds after the head drop with 10 ms temporal resolution. Figure 10 shows the SPAMM-tagged images corresponding to the 7th time point (70 ms) after the drop.

The HARP method is based on the fact that the SPAMM–tagged MRI images have a collection of distinct spectral peaks in the Fourier domain, and each of these spectral peaks carries information about a particular component of tissue motion. The inverse Fourier transform of one of these peaks is a complex image called the harmonic image. It can be shown that the phase of the harmonic image is linearly related to a directional component of the tissue motion and this phase-motion relation is the key to the ability of the HARP method to track motion with sub-voxel resolutions. The summary of the methodology of the HARP image processing technique developed by Osman et al. (1998; 2000) and implementation details of our brain motion estimates are given in Appendix. The implementation of the HARP method for displacement estimates using tagged MRI images include the following five major steps: Fourier transform SPAMM-tagged images to get isolated spectral peaks; apply a band-pass filter to isolate one of the off-center harmonic peaks; take inverse Fourier transform of the isolated peak to get a harmonic image; obtain the HARP angle image which is the principal value of the phase of the harmonic image; use the HARP angle images to estimate the 2D displacement fields. As an example, Fig. 11(a) shows the spectral peaks for the tagged image in Fig. 10(a). Figure 11(b) shows the harmonic magnitude image extracted from tagged image shown in Fig. 10(a) using the
filter in Fig. 11(a). The HARP angle image corresponding to the spectral peak circled in Fig. 11(a) is shown in Fig. 11(c), and a mask created using a crude segmentation of the harmonic magnitude image in Fig. 11(b) is applied to remove noise outside the region of interest.

A custom Matlab code was developed for implementing the HARP method for motion estimate. Given four series of SPAMM-tagged images described earlier in MRI data collection, a sequence of 2D displacement fields for both axial slice and sagittal slice were obtained. We see that the brain experiences downward displacements in the direction of the impact at each time point during the first 60 ms, which is the free fall period of a 2-cm vertical drop. At 70 ms, the brain starts to have upward displacement, which indicates it has begun to bounce from the impact. This observation seems reasonable since a particle dynamics analysis shows it takes about 63 ms for a rigid body to impact with a rigid surface after a 2-cm drop. We also see that the brain continues to move upward at 80 – 100 ms, but the rate of change of displacements slows and stops. After 100 ms, the brain falls back down until it hits the lowest position at around 140 ms. After 140 ms, the upward displacements of the brain resume, indicating the start of the second oscillation, which ends around 200 ms when the brain hits the lowest position again. Then a few more small oscillations follow before the brain motion diminishes. Since the brain motion after impact is of our primary interest, we safely assume 60 ms is the instant right before impact, based on the above analysis, and recalculate the displacements using the time frame at 60 ms as our reference time frame.

4.2 FE simulation of mild impact

The FE mesh, material properties, and interface condition are the same as described in Chapter 2. Besides the head model, a rigid surface that the head will impact is also defined. Since the
brain deformation after impact is of more interest than its behavior during the free fall before impact, we model the head at an initial position very close to the rigid surface and specify an initial velocity of $0.626 \text{ m/s}$ to simulate the $2\text{-cm}$ drop. To model the interaction between the human head and the rigid surface, a friction coefficient of 0.3 is specified for tangential behavior. Since the neck is not included in our model, an appropriate boundary condition must be prescribed to simulate the constraint of the neck on the head movement during the head drop. In this simulation, fixed boundary condition is prescribed around the region of foramen magnum to represent the restraining effect of the neck. The simulation is run using ABAQUS with a dynamic, explicit procedure for $150 \text{ ms}$.

### 4.3 Results

The 2D displacement fields obtained by MRI-based HARP analysis for both axial and sagittal slices from $70 \text{ ms}$ to $200 \text{ ms}$ using $60 \text{ ms}$ as the reference time frame are shown in Fig. 12 (a), (c) and Fig. 13 (a), (c). For axial slice, the maximum displacements in the anterior-posterior direction reach over $1 \text{ mm}$ after impact, whereas the displacement in the left-right direction is not significant throughout the duration. For sagittal slice, the displacements in the anterior-posterior direction reach over $2 \text{ mm}$ in the top portion of the brain whereas the displacement in the head-feet direction is within $2 \text{ mm}$ range. Comparing the displacement fields between the first oscillation of the brain ($70 \text{ ms} – 140 \text{ ms}$) and the second oscillation ($150 \text{ ms} – 200 \text{ ms}$) for all cases, we see that a larger portion of the brain experiences large displacements during the first oscillation. Notice that the anterior-posterior displacements in the sagittal slice (Fig. 13(a)) is vertically varied, and the top portion of brain tissues has larger displacements than the lower portion. This pattern is understandable since the lower portion of the brain, the brain stem,
extends to the neck which provides some degree of constraint to the movement around that region. Another reason can be that the base of the skull is very rough while the top of the skull is relatively smooth, so lower portion of the brain cannot move much compared to its upper portion.

Axial plane and sagittal plane in the FE model that are close to the slice prescription in the MRI data collection are determined. In-plane displacement fields obtained by FE simulation for the first 60 ms with 10-ms interval are shown in Fig. 12(b), (d) and in Fig. 13(b), (d) for comparison with the results from MRI image-based HARP analysis. We find that, at 5 ms, the displacements (not shown in Figs. 12 and 13) in the direction of the impact in both the axial and sagittal slice are negative. This initial downward displacement is due to the fact that the head model is placed initially at a position above the rigid surface. However, at 10 ms we start to see upward displacements. Therefore, we consider the time frame at 10 ms in the FE simulation to correspond approximately to the time frame at 70 ms in the HARP analysis, but note that the reference position in the FE simulation is not exactly the same as the reference position in the HARP displacement estimates. This discrepancy can be one of the factors for possible differences in the results obtained through these two different methods.

The magnitude of the maximum displacement predicted by the FE simulation is on the same order as that obtained by HARP analysis, i.e., in the range of 1-2 mm for the axial slice and 2-3 mm for the sagittal slice. For the sagittal slice, the patterns of displacement distribution from the HARP analysis are also predicted by the FE simulation, which involve vertically varying displacements in the anterior-posterior direction and horizontally varying displacements in the head-to-feet direction. One may also notice the displacements in the anterior-posterior direction for the axial slice as shown in Fig. 13(d) are not perfectly symmetric about the midline. The
asymmetric displacements may be caused by an imperfectly symmetric brain dropping at a slightly tilted angle.

Differences in the displacement fields obtained from these two methods are also observed. First, the duration of the first oscillation of the brain in FE simulation is about 60 ms, which is less than that (~80 ms) in the HARP analysis. Figure 14 shows the displacement time history of a node of the brain close to the impact region. The period of the first oscillation of the FE model can be attenuated by changing the prescribed fixed boundary condition around foramen magnum. A more compliant boundary condition would result in a longer period of the first oscillation. Second, the displacement pattern in left-right direction in the axial slice (Fig. 12(a) and (b)) obtained from these two methods seems to be reversed. In the HARP analysis, displacement is positive in the anterior portion and negative in the posterior portion for most of the duration. The FE simulation gives just the opposite results. While this discrepancy in lateral displacements is small in magnitude, and therefore of secondary importance, the reason for it to occur is not clear. Third, the negative displacements seen at 10 ms and 60 ms in the axial slice (Fig. 12(d)) do not appear in the displacement estimates by HARP analysis. This difference can be attributed to different reference positions for displacement calculations. Fourth, in the sagittal slice, the FE simulation predicts the switch of signs of displacements at the beginning of the second oscillation (from 50 ms to 60 ms as shown in Fig. 13(b) and (d)), but the displacement sign switching is not seen in the results obtained by the HARP analysis.

Given the complexity of the problem, we have obtained a reasonably good correlation of in-plane brain displacements between the prediction of the FE model and the estimates of the MRI-based HARP analysis, especially during the first oscillation of the brain within the skull.
4.4 Discussion

Besides displacements, strain fields are also obtained by FE simulation, which provides a better measure of brain deformation. Brain tissue is most vulnerable to shear strains due to its high bulk modulus and low shear modulus. In addition, tensile strains are believed to be more dangerous than compressive strains. Here we show the in-plane shear strain and the maximum principal strain distribution in the prescribed axial and sagittal slice for the first 60 ms after impact with 5-ms interval in Figs. 15 and 16, respectively. For the axial slice, the maximum shear strains are within 3% and the maximum principal strains are within 5%. Larger shear strains and maximum principal strains are seen in the sagittal slice, which are more than 5% but within 10%. In both the axial and sagittal slices, we see the maximum strains to occur in the first few milliseconds after impact, which is during the first oscillation of the brain within the skull. Under moderate or severe impact, we would expect the brain to experience strains larger than 10% during the initial time following the impact, which can be the cause of immediate functional or structural damage to brain tissues.

A few limitations of the current study should be noted. First, only in-plane displacement fields of the prescribed axial and sagittal slices are obtained through MRI-based HARP analysis due to the limitation of current MRI tagging technique. Once 3D tagged image data becomes available, a full comparison of 3D spatio-temporal displacement fields can be made with the results from FE modeling. Second, the mild impact considered in this study is well under brain injury threshold and high strength impact can only be studied using physical models such as human cadavers and animal models. However, our study of mild impact can provide some insight into the deformation patterns of the brain under more severe impact.
CHAPTER 5
DISCUSSION AND CONCLUSIONS

A side impact simulation is also carried out to check the existence of the spherically convergent shear wave pattern in the brain. In the side impact simulation, the proposed FE model is subject to the same impact pulse as in the frontal impact simulation but the pulse is applied on the temporal region of the skull. It is found that the side impact simulation also gives rise to a similar spherically convergent shear wave pattern previously observed in the frontal impact simulation. It is believed that the presence of shear wave pattern uncovered in this study provides the first computational mechanics support for the centripetal hypothesis of cerebral concussion (Ommaya and Gennarelli, 1974; Ommaya, 1995). Concussion is a head injury with a temporary loss of brain function and it is the most common type of brain injury. Although concussion has been a well recognized clinical problem for centuries, its underlying mechanism is still under debate. As one of the main hypotheses of concussion, the centripetal theory was formulated based on a huge amount of experimental data on subhuman primates. The theory is stated as follows, “Concussive brain injuries include the phenomena of cerebral concussion and constitute a graded set of clinical syndromes following head injury wherein increasing severity of disturbance in level and content of consciousness is caused by mechanically induced strains affecting the brain in a centripetal sequence of disruptive effects of function and structure. These effects begin at the surface of the brain and extend inward to the diencephalic-mesencephalic core at the most severe coma-producing levels of trauma” (Ommaya and Gennarelli, 1974). Before the centripetal theory was proposed, the classical view was that the main mechanism producing traumatic unconsciousness was an isolated brainstem injury (Sahuquillo and Poca, 2002). Therefore, the most important concept introduced in this theory is that damage to the
brainstem (coinciding with the core of the brain) never occurs in isolation, but is associated with diffuse brain damage to the hemispheres. This concept is supported by the finding of the spherically convergent shear stress wave pattern in this study. From the FE simulation, we see that following an impact, the shear stress/strain with large magnitude occurs at the surface of the brain first, and then converges towards the brain center. The centripetal theory of concussion has been validated by a series of experimental and clinicopathologic observations, as well as the MRI brain imaging data in head injury patients (Ommaya and Gennarelli, 1974; Ommaya, 1995), but has not been validated before from a mechanics standpoint. Therefore, our finding of spherically convergent shear waves by FE simulation provides the first computational mechanics support for the centripetal hypothesis of cerebral concussion.

In summary, we have developed a 3D FE model of the human head using an MRI voxel-based mesh generation method. The proposed mesh generation method provides an efficient and accurate means of generating a patient-specific head mesh that can describe the important features of the highly complex head geometry, such as the folding structure of the cerebral cortex and realistic separation of CSF, gray, and white matter. To the best of our knowledge, our proposed model is the first FE head model that has the MRI resolution. The very fine mesh of our model also makes it possible to capture the stress wave propagation during a head impact process. In order to remove numerical artifacts, a mesh smoothing technique which conserves mesh volume was applied to create a smooth mesh surface and material interfaces. The proposed model was first validated on intracranial pressure data from a previous cadaver frontal impact experiment. It was found that the experimental data are well bounded by the responses computed from the models with free and fixed boundary conditions. Most interestingly, this simulation reveals a spherically convergent shear wave pattern in the brain that provides the first
computation mechanics support for the centripetal hypothesis of cerebral concussion. We conclude that the frontal impact gives rise not only to a fast pressure wave but also to a slow, and potentially more damaging, spherically convergent wave of distortion.

The second part of this work investigates deformation patterns of human brain under mild impact through two different methods: MRI-based assessment of *in vivo* human brain and FE modeling. The 2 cm vertical head drop experiments were carried out in the MRI tunnel to induce mild impact to the human head. Tagged MRI images were acquired and the HARP image processing technique was implemented to obtain displacement estimates of the brain under mild impact. The simulation of the mild impact event using our proposed FE model was performed to predict the spatio-temporal distribution of deformation fields including displacements and strains of the brain. A reasonably good correlation was found between the displacement fields obtained through MRI-based HARP analysis and through the FE simulation. To the best of our knowledge, our study is the first validation of an FE brain injury model on *in vivo* brain deformation data, and it is also the first attempt in which the deformation field obtained by MRI-based assessment is correlated with the prediction of a corresponding FE model. It was found in this study that the maximum deformations occur within a few milliseconds following the impact, which is during the first oscillation of the brain within the skull, with the maximum displacements of 2-3 mm and the maximum strains of 5-10%.

Future improvements of the model will address increasingly complex challenges: (i) a more realistic boundary condition at the head-neck junction and interface condition between the skull and the brain; (ii) modeling of membranes and other substructures based on better imaging and processing techniques (Helms *et al.*, 2006); (iii) better constitutive models of human brain tissues. Furthermore, the current model is really based on the assumption of a separation of scales, which
does not hold everywhere in the brain structure, and itself, like many other biological systems, is known to be fractal; e.g. human brain’s surface has a fractal dimension of about 2.7-2.8. Thus, in the future work a scale-dependent homogenization of disordered, fractal materials (Ostoja-Starzewski, 2008; Li and Ostoja-Starzewski, 2009) will have to be implemented in setting up rheological properties of the FE model according to the location and size of each and every voxel.

From an engineering point of view, the final objective of brain injury research is to provide a predictive tool such as an FE model that can aid in injury diagnosis and design of protective devices. A well validated FE model can be such a powerful tool, especially when brain injury experiments are difficult and expensive to carry out. Our proposed 3D patient-specific MRI-based FE head model has been validated using both the intracranial pressure data of human cadavers subject to frontal impact and the in vivo brain deformation data under mild impact, which thus provides us a certain degree of confidence of using our proposed FE model as an effective predictive tool for future brain injury research.


APPENDIX: SUMMARY OF HARP IMAGE PROCESSING TECHNIQUE FOR DISPLACEMENT ESTIMATES

An image point can be defined by a 2D vector \( \mathbf{y} = [y_1, y_2]^T \), where \( y_1 \) is the coordinate in the readout direction and \( y_2 \) the coordinate in the phase-encoding direction. In order to relate 2D tagged images to actual 3D tissue motion, a fixed rectangular Cartesian coordinate system, \( \mathbf{x} \in \mathbb{R}^3 \), representing the scanner frame is also defined. The actual 3D position \( \mathbf{x} \) of an image point \( \mathbf{y} \) is therefore given by the function

\[
\mathbf{x}(\mathbf{y}) = y_1 \mathbf{h}_1 + y_2 \mathbf{h}_2 + \mathbf{x}_0 = \mathbf{H} \mathbf{y} + \mathbf{x}_0,
\]

where \( \mathbf{h}_1 \in \mathbb{R}^3 \) and \( \mathbf{h}_2 \in \mathbb{R}^3 \) are the readout and phase-encoding directions of the image plane, respectively, \( \mathbf{H} = [\mathbf{h}_1 \mathbf{h}_2] \), and \( \mathbf{x}_0 \in \mathbb{R}^3 \) is the origin of the image plane. At time \( t = 0 \), let every material point be marked by its position \( \mathbf{p} \in \mathbb{R}^3 \). As the brain tissue deforms, a material point moves from its reference position \( \mathbf{p} \) to current position \( \mathbf{x} \) at time \( t \). If the one-to-one mapping function \( \mathbf{p}(\mathbf{x}(\mathbf{y}), t) \), which gives the reference position \( \mathbf{p} \) at time \( t = 0 \) of a spatial point \( \mathbf{x} \) at time \( t \), is known, brain deformation can then be completely characterized. The key to the HARP method is to utilize the relationship existing between the local phase information and the mapping function to estimate the tissue deformation.

Now let \( I(\mathbf{p}) \) represent the intensity of a SPAMM-tagged MRI image passing through point \( \mathbf{p} \) immediately after tagging. The tagged image can be written as a finite cosine series having a certain fundamental frequency in the following manner,

\[
I(\mathbf{p}) = \sum_{k=1}^{K} D_k(\mathbf{p}) e^{i\omega_k \mathbf{p}},
\]

(A2)
where $K$, $D_k$, and $\omega_k$ are related to the parameters of the tagging pulse sequence. Replacing $\mathbf{p}$ with $\mathbf{p}(x(y),t)$, we can find that Eqn. A2 can be written in terms of spatial coordinates $x$ or $y$ instead of material coordinates $\mathbf{p}$ in the following,

$$I(\mathbf{p}(x,t)) = \sum_{k=1}^{K} D_k(\mathbf{p}(x,t))e^{i\omega_k \mathbf{p}(x,y)}$$

or

$$I(y,t) = \sum_{k=1}^{K} D_k(y,t)e^{i\omega_k \mathbf{p}(x(y),t)}. \quad (A3)$$

From the above equation one can see that the SPAMM-tagged image is the sum of $K$ complex images, which is called the harmonic images, each corresponding to a distinct spectral peak identified by the frequency vector $\omega_k$. The pattern of cosines in the SPAMM-tagged image is the cause of the isolated spectral peaks in its Fourier domain, and the number and distribution of the spectral peaks vary according to the specific tagging pulse sequence.

One can see from Eqn. A3 that the $k$ th harmonic image corresponding to the frequency vector $\omega_k$ can be written as

$$I_k(y,t) = D_k(y,t)e^{i\omega_k \mathbf{p}(x(y),t)}, \quad (A4)$$

where $D_k$ is called the harmonic magnitude image, and $\omega_k^T \mathbf{p}(x(y),t)$ is called the HARP image and denoted by $\phi_k$. The HARP image is rewritten for clarity in the following,

$$\phi_k(y,t) = \omega_k^T \mathbf{p}(x(y),t). \quad (A5)$$

The $k$ th harmonic images can be approximately determined by taking inverse Fourier transform of the spectral peak in the direction of $\omega_k$, which is isolated using a band-pass filter. The magnitude image contains geometry information of the tissue without the presence of tag pattern; therefore, it is used to provide a crude segmentation that distinguishes tissue from the
background for the HARP image. One can see from Eqn. A5 that HARP image $\phi_k$ is linearly related to the mapping function $p(x(y),t)$, so it can be used to characterize tissue motion. In actual implementation, the principal values of $\phi_k$, denoted by $a_k$, are used since they are easily calculated from the harmonic images. Here, $a_k$ is called the HARP angle image, and it is restricted to the range $[-\pi, \pi)$. HARP angle image $a_k$ is related to HARP image $\phi$ by

$$a_k(y,t) = \nu(\phi(y,t)),$$  \hspace{1cm} (A6)

where the nonlinear wrapping function is given by

$$\nu(\phi) = \text{mod}(\phi + \pi, 2\pi) - \pi.$$  \hspace{1cm} (A7)

The displacement is defined by the difference between the current position $x$ and the original position $p$, and expressed by

$$u(x,t) = x - p(x,t).$$  \hspace{1cm} (A8)

HARP angle image can be used to obtain displacement fields of the tissue motion. Given a sequence of HARP angle image $a_k(y,t)$, the following quantity can be calculated:

$$\Delta a_k(y,t) = \nu[\omega_k^T x(y) - \phi_k(y,t)].$$  \hspace{1cm} (A9)

Substituting Eqns. A5 and A8, we find that Eqn. A9 becomes

$$\Delta a_k(y,t) = \nu[\omega_k^T u(x(y),t)].$$  \hspace{1cm} (A10)

Only when $\omega_k^T u(x(y),t) \in [-\pi, \pi)$, no wrapping will occur and $\Delta a_k(y,t) = \omega_k^T u(x(y),t)$. This is the only case discussed in Osman et al. (2000). Here we consider the more general case when $\omega_k^T u(x(y),t)$ is not restricted in the range $[-\pi, \pi)$. For this case phase unwrapping of $\Delta a_k(y,t)$ is necessary to extract displacement from equation A10, leading to,

$$\nu[\Delta a_k(y,t) + \pi] = \omega_k^T u(x(y),t).$$  \hspace{1cm} (A11)
Next, let \( \mathbf{u}_2(y, t) = [u_1, u_2] \) represent the 2D displacement within the image plane, then \( \mathbf{u}_2(y, t) = \mathbf{H} u_2(y, t) \), and Eqn. A11 can be rewritten as

\[
\mathbf{H} \mathbf{u}_2(y, t) = \mathbf{W}^{\mathbf{H}} \mathbf{u}_2(y, t).
\]

If another sequence of angle image having a linearly independent frequency vector \( \omega_i \) is also available, the 2D displacement field is then calculated by

\[
\mathbf{u}_2(y, t) = (\mathbf{W}^{\mathbf{H}} \mathbf{H})^{-1} \begin{bmatrix} \mathbf{H} \mathbf{u}_k(y, t) + \pi \\ \mathbf{H} \mathbf{u}_k(y, t) + \pi \end{bmatrix},
\]

where \( \mathbf{W} = [\omega_k, \omega_l] \). Equation A13 is the key equation that calculates 2D displacements from the HARP angle image.

The specific slice prescription and tagging orientation in our MRI acquisition lead to the following \( \mathbf{W} \) and \( \mathbf{H} \) matrices for axial slice and sagittal slice, respectively.

**Axial slice:**

\[
\mathbf{H} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 0 & 0 \end{pmatrix}, \quad \mathbf{W} = \frac{2\pi}{S_p} \begin{pmatrix} 0 & 1 \\ 1 & 0 \\ 0 & 0 \end{pmatrix};
\]

**Sagittal slice:**

\[
\mathbf{H} = \begin{pmatrix} 0 & 0 \\ 1 & 0 \\ 0 & 1 \end{pmatrix}, \quad \mathbf{W} = \frac{2\pi}{S_p} \begin{pmatrix} 0 & 0 \\ 1 & 0 \\ 0 & 1 \end{pmatrix},
\]

where \( S_p = 4 \text{ mm} \) is the tagging period.
### FIGURES AND TABLES

#### TABLE 1. Mechanical properties of different tissues used in the FE model

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Density $\rho$ (kg/m$^3$)</th>
<th>Bulk modulus $K$ (Pa)</th>
<th>Short term shear modulus $G_0$ (Pa)</th>
<th>Long term shear modulus $G_\infty$ (Pa)</th>
<th>Decay factor $\beta$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull</td>
<td>2070</td>
<td>3.61E+9</td>
<td>2.7E+9</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>CSF</td>
<td>1004</td>
<td>2.19E+7</td>
<td>5.0E+4</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Gray matter</td>
<td>1040</td>
<td>2.19E+9</td>
<td>3.4E+4</td>
<td>6.4E+3</td>
<td>400</td>
</tr>
<tr>
<td>White matter</td>
<td>1040</td>
<td>2.19E+9</td>
<td>4.1E+4</td>
<td>7.8E+3</td>
<td>400</td>
</tr>
</tbody>
</table>
Figure 1. (a) Sagittal cross-sectional view of the human head (from Hanaway et al. (1998)); (b) coronal cross-sectional view of a top portion of the human head (from Hargreaves (2006)).
Figure 2. (a) FE model of the human head; (b) FE model of the human head – axial view.
Figure 3. (a) FE mesh of the brain before smoothing; (b) FE mesh of the brain after eight smoothing iterations.
Figure 4. Input force time history (from Nahum et al. (1977)).
Figure 5. Coup pressure time histories from Nahum et al. (1977) (broken line) and from the model (two continuous lines).
Figure 6. Contrecoup pressure time histories from Nahum et al. (1977) (broken line) and from the model (two continuous lines).
Figure 7. The von Mises stress distribution in the brain (mid-sagittal view) during a 15ms frontal impact simulation. Left column – free boundary; right column – fixed boundary.
(d) 11ms

(e) 13ms

(f) 15ms

Figure 7. (cont.)
Figure 8. The von Mises stress distribution in the inner sphere of the idealized spherical model of the head (mid-sagittal view) during a 15 ms axial impact simulation.
Figure 9. HDD complete unit CAD model
Figure 10. MR SPAMM-tagged images corresponding to 70 ms after tagging. (a) Anterior-posterior SPAMM tags and (b) left-right SPAMM tags in the axial slice. (c) Anterior-posterior SPAMM tags and (d) head-feet SPAMM tags in the sagittal slice.
Figure 11. (a) Magnitude of Fourier transform of Fig. 10(a). (b) Harmonic magnitude image of a harmonic image corresponding to the spectral peak inside the circle in (a). (c) Harmonic phase angle image of the harmonic image corresponding to the same spectral peak as in (b).
Figure 12. In-plane displacement fields for the axial plane obtained from HARP analysis and FE simulation.
Figure 13. In-plane displacement fields for the sagittal plane obtained from HARP analysis and FE simulation.
Figure 14. Displacement time history of a node on the brain close to the impact site obtained from FE simulation.
Figure 15. In-plane shear strains and maximum principal strains for the axial slice predicted by FE simulation.
Figure 16. In-plane shear strains and maximum principal strains for the sagittal slice predicted by FE simulation.