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Effect of bulk modulus on deformation of the brain under rotational accelerations

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Abstract

Traumatic brain injury such as that developed as a consequence of blast is a complex injury with a broad range of symptoms and disabilities. Computational models of brain biomechanics hold promise for illuminating the mechanics of traumatic brain injury (TBI) and for developing preventive devices. However, reliable material parameters are needed for models to be predictive. Unfortunately, the properties of human brain tissue are difficult to measure, and the bulk modulus of brain tissue in particular is not well-characterized. Thus, a wide range of bulk modulus values are used in computational models of brain biomechanics, spanning up to three orders of magnitude in the differences between values. However, the sensitivity of these variations on computational predictions is not known. In this work, we study the sensitivity of a 3D computational human head model to various bulk modulus values. A subject-specific human head model was constructed from T1-weighted MRI images at 2 mm³ voxel resolution. Diffusion tensor imaging provided data on spatial distribution and orientation of axonal fiber-bundles for modeling white-matter anisotropy. Non-injurious, full-field brain deformations in a human volunteer were used to assess the simulated predictions. The comparison suggests that a bulk modulus value on the order of GPa gives the best agreement with experimentally measured *in vivo* deformation in the human brain. Further, simulations of injurious loading suggest that bulk modulus values on the order of GPa provide the closest match with the clinical findings in terms of predicated injured regions and extent of injury.

Keywords

Brain bulk modulus; computational head model; *in vivo* brain deformation; comparison of strain fields; prediction of injury

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1. Introduction

Traumatic brain injury (TBI) has been a major public health concern worldwide. In the United States alone, an average of 1.7 million Americans sustain a TBI per year, leading to 52,000 deaths, 275,000 hospitalizations, and 1.36 million emergency department visits [1]; of these, an estimated 124,000 experience the onset of long-term disability. TBI is largely caused by falls, motor vehicle crashes, sports collisions, blast and firearm assaults [1], but the precise mechanisms associated with the injury remain a matter of intense study [2,3]. Computational models hold promise to determine severity and locations of injury, either a priori or post-injury, in patient-specific human heads. This simulation capability is even more important in reliably and consistently predicting TBI as injury-causing deformations cannot be generated in live humans. As a result, computational models of the head have become increasingly elaborate, in terms of anatomical details and constitutive response [4–6]. However, efforts in regards to reliable material parameters are still ongoing.

Much of the brain characterization literature has focused on shear properties [7], with little attention on bulk properties (Table 1a). Instead, the brain tissue is often assumed to be incompressible, or nearly so. As a consequence, a wide range of bulk modulus values, spanning up to three orders of magnitude difference, are used in computational head models of brain biomechanics (Table 1b). Most of these values were chosen in an ad-hoc manner to mimic near incompressibility, with the aim of achieving numerical stability and convergence. However, the influence of such computational adjustments on computational predictions, especially on shearing deformations within the brain, has not been investigated.

Wave propagation within the human head plays an important role in intracranial dynamics and deep brain injuries. Interestingly, shear wave speeds within the brain are orders of magnitude smaller than the bulk and longitudinal wave speeds due to the large difference between shear and bulk moduli. One consequence of this significant difference in wave speeds is that there is a timescale separation [6] that is developed in terms of potential injury-causing mechanisms in the brain. This timescale separation is particularly apparent in the case of blast loading. For example, consider a blast wave incident on the head, with a typical blast wave speed in air; the entire head observes the passage of the wave over and around the head within a time on the order of a few milliseconds. This fluid-structure boundary condition generates a pressure [27,28] and shear waves [29] within the brain. A pressure wave within the brain traverses the brain quickly (wave speed ~ 1000 m/sec) and establishes a pressure field inside the brain within less than a millisecond. However, the shear waves in the brain generated by the blast loading boundary condition move much more slowly (wave speed ~ 1 m/sec), and the shear fields that develop the rotational motions of the brain are established much later, after timeframes of over ten milliseconds. Numerous recent investigations elude to rotational-acceleration-induced brain injuries as a result of blast load [30,31]. Since these rotational motions can lead to mild TBI through deep brain injuries in the white matter, it is important to understand such deformations and motions while studying TBI under blast. Thus, in this manuscript, we focus on the effects of rotational loading and shear wave propagation within the head. Further, we focus on shear strains as opposed to intracranial pressure, since intracranial pressure does not provide a significant constraint on

the material properties [32,26]. Also, brain being much compliant in shear, larger deformations are sustained in shear and hence the brain is more prone to injury under shear.

The goal of this work is to study sensitivity of brain (shear) deformations to various values of bulk modulus. We perform three-dimensional (3D) head simulations under mild rotational accelerations and compare model response against non-injurious, full-field brain deformations in a human volunteer. We use this validated model to assess sensitivity of model response to bulk modulus values for both non-injurious and injurious loading. Simulations are performed until 100 ms in order to fully capture the effects of shear wave propagation [33,6], which are often neglected in computational simulations of the head in studying blast. The manuscript is organized as follows. In section 2, we briefly describe mild acceleration experiments on human volunteers, followed by detailed description of the 3D head model including descriptions of geometry and constitutive models, solution scheme, and loading and boundary conditions. In section 3, computational results from the 3D head model are presented and compared with experimentally obtained non-injurious brain deformations in human volunteers. Later in this section, results of injurious loading are presented. Specific observations regarding sensitivity of brain deformations to various brain bulk modulus values are also made for both non-injurious and injurious loading. Key conclusions of this work are summarized in section 4.

2. Methods

2.1 Head rotation experiments in human volunteers

Mild head rotation experiments were performed with healthy human subjects with the objective of obtaining full-field, *in vivo* deformations in the brain. Human volunteers were recruited by the Center for Neuroscience and Regenerative Medicine (CNRM) under the CNS Institutional Review Board at the National Institutes of Health. Dynamic motions during head rotation were captured using tagged Magnetic Resonance Imaging (tagged-MRI) [36,37]. Full-field brain deformations were obtained from these tagged-MRI images using the harmonic phase (HARP) method [36]. This data was used to validate a computational model of a human head. Note that, there is a one-to-one correspondence between the experiment and the model in terms of morphology and fiber orientation of the brain tissue, loading conditions, and measured deformations. Additional details of these experiments are available in [38] and avoided here for brevity.

2.2 Computational modeling of human head

2.2.1 Construction of Subject-specific 3D head model—A 3D human head model was created from MRI images of a human volunteer (age: 22 years). T1-weighted MRI images were segmented into different substructures (Fig. 1b), namely, white matter, grey matter, caudate, putamen, thalamus, ventricles, and cerebrospinal fluid (CSF). A topology-preserving, atlas-based technique described in Bazin et al. [39] was used for the segmentation. In addition to these segmented structures, an approximate, artificial “skull” was generated by dilation of a brain mask. Stiff membranes of the falx and tentorium were also added to the head model. The falx and tentorium in the MRI images of the human volunteer were unclear due to insufficient contrast, so these structures were segmented from

MRI images of a post-mortem human subject (PMHS) and incorporated into the head model.

2.2.2 Constitutive Modeling—The white matter of the brain consists of fiber bundles and shows anisotropic response in shear [40,41]. On the other hand, the grey matter contains the cell bodies and shows isotropic response [41,42]. White matter shear anisotropy was modeled using the Holzapfel-Gasser-Ogden (HGO) strain energy function (1) [43,44]. All other substructures of the head, with the exception of the CSF, were modeled using an isotropic limit of the HGO model [41,42]. In (1), the first two terms account for shear behavior while the third term accounts for volumetric behavior. A form of volumetric strain energy was chosen such that it satisfies all the physical requirements for a volumetric strain energy function, as described in Doll and Schweizerhof [45].

$$W = \underbrace{\frac{\mu}{2}(\bar{I}_1 - 3) + \frac{k_1}{2k_2} \left(e^{k_2(\bar{E}_1)^2} - 1 \right)}_{\text{shear}} + \underbrace{\frac{K}{2} \left(\frac{J^2 - 1}{2} - \ln J \right)}_{\text{volumetric}} \quad (1)$$

with

$$\bar{E}_1 = \kappa(\bar{I}_1 - 3) + (1 - 3\kappa)(\bar{I}_4 - 1) \quad (2)$$

where μ is the shear modulus of the isotropic matrix, k_1 is the stiffness of the fibers, k_2 is the dimensionless material parameter that controls the nonlinearity of the anisotropic response, K is the effective bulk modulus, J is the volume change ratio, and κ is the structural parameter that defines the degree of fiber dispersion. In the current work, it was assumed that only a single family of fibers existed in the material, and the original HGO model is reduced accordingly while arriving at a form presented in equation 1.

The modified invariants, $\bar{I}_1$ and $\bar{I}_4$, are defined as,

$$\bar{I}_1 = \text{tr}(\bar{\mathbf{C}}) \quad (3)$$

$$\bar{I}_4 = \mathbf{a}^0 \cdot \bar{\mathbf{C}} \cdot \mathbf{a}^0 \quad (4)$$

where $\bar{\mathbf{C}}$ is the deviatoric component of the right Cauchy–Green deformation tensor and $\mathbf{a}^0$ is a unit vector representing the fiber direction in the undeformed configuration. The fiber direction after deformation is given by the unit vector $\mathbf{a}$. The fiber stretch, λ , is then defined as,

$$\lambda \mathbf{a} = \mathbf{F} \cdot \mathbf{a}^0 \quad (5)$$

Because $\mathbf{a}$ is a unit vector,

$$\lambda^2 \mathbf{a} \cdot \mathbf{a} = \lambda^2 = \mathbf{a}^0 \cdot \mathbf{F}^T \mathbf{F} \cdot \mathbf{a}^0 = \mathbf{a}^0 \cdot \bar{\mathbf{C}} \cdot \mathbf{a}^0 = \bar{I}_4 \quad (6)$$

The fiber orientation map and Fractional Anisotropy (FA) map from the DTI provide the information on fiber alignment and fiber dispersion, respectively, for each voxel (Fig. 1b). The fiber dispersion parameter κ can be related to FA from DTI using a following relation [44],

$$\kappa = \frac{1}{2} \frac{-6 + 4\text{FA}^2 + 2\sqrt{3\text{FA}^2 - 2\text{FA}^4}}{-9 + 6\text{FA}^2} \quad (7)$$

The lower limit of $\kappa = 0$ represents perfectly aligned fibers, whereas the upper limit of $\kappa = 1/3$ represents randomly oriented fibers. In this work, both fiber direction and fractional anisotropy are incorporated based on DTI data for this particular human volunteer. In addition to anisotropy, the constitutive model also incorporates the viscoelasticity in shear using a quasilinear viscoelastic function [46]. The shear relaxation is defined using a Prony series,

$$\mu(t) = \mu_0 \left[1 - \sum_{i=1}^n g_i (1 - \exp(-t/\tau_i)) \right] \quad (8)$$

$$\text{as } t \rightarrow \infty; \quad g_1 + g_2 + \dots + g_n + \frac{\mu_\infty}{\mu_0} = 1 \quad (9)$$

where μ_0 is the instantaneous shear modulus, g_i are constant parameters, and τ_i are relaxation time constants.

The CSF was modeled using the Tait equation of state [48], given by,

$$P = \frac{K_0}{n} \left[\left(\frac{\rho}{\rho_0} \right)^n - 1 \right] \quad (10)$$

where, P is the pressure, K is the bulk modulus, and ρ is the density. The subscript 0 indicates values at zero pressure or initial density. For fluids similar in composition and viscosity to that of water, the value of the constant n is 7.15 [48]. The Tait equation of state is commonly used to model fluids under large pressure variations.

Constitutive model parameters: In these simulations, we use a baseline bulk modulus value based on our own measurements on human tissue samples (Ramesh, unpublished work). We obtain a dynamic bulk modulus value of 1.46 GPa for the human cerebrum and a bulk modulus value of 1.19 GPa for the human cerebellum, at a strain rate of $\sim 10^3 \text{ s}^{-1}$. These values are consistent with values reported in the literature (Table 1). The anisotropic properties and viscoelastic properties are based on Velardi et al. [40] and Lee et al. [49], respectively. All of the material properties used in the simulations are tabulated in Table 2 [48–51,40].

2.2.3 Solution Scheme—The material point method (MPM) [52–54] was used for transient, dynamic analysis of a human head subjected to rotational acceleration. The MPM approach incorporates salient features of both Lagrangian and Eulerian formulations. In this technique, the material points are used to represent a material continuum, and a background grid is used to solve governing equations of elastodynamics. The grid (mesh) is held fixed and is used to determine spatial gradients. The updated field variable advects material points in and out of a grid cell. Boundary conditions are applied on the grid nodes that are populated by material points. Constitutive equations are used to update stress using a finite deformation framework to handle large deformations. The background mesh in MPM does not encounter any mesh-degeneration, and thus provides stable and efficient numerical solution despite material points undergoing very large deformations. MPM assumes no-slip contact between various interfaces. In this work, we have used the public domain Uintah MPM package to perform high-performance simulations on a parallel computing cluster. The segmented MRI images in the form of voxels were imported in MPM. Simulations were performed with a background mesh size of 2 mm^3 . A mesh convergence study was conducted to arrive at this mesh size. Less than 5% change in field variables (i.e., stresses and strains) was used as a convergence criterion.

The capability of MPM for handling large deformation problems in soft materials has already been demonstrated [55,56]. In this work, we use MPM over conventional FEM for several reasons listed here: (a) In MPM, conforming meshes are not required, thus one can directly import voxelated information from MRI images and explicit meshing is not required. Hence, the cost associated with developing subject-specific head models in MPM is minimal. Developing subject-specific head models using conventional FEM can be time consuming and costly. (b) In MPM, as the background grid is fixed, it does not suffer from the excessive distortion limits and associated errors. (c) MPM can handle a very large ratio between the bulk modulus and the shear modulus of the brain tissue with minimal volumetric locking artifacts. Note that, modeling the entire blast event including fluid-structure interaction is not fully developed and validated in the current Uintah MPM framework. Thus, in this work we do not explicitly simulate the blast event. Efforts will be made in the future to fully develop this capability in the Uintah MPM framework.

2.2.4 Pressure Stabilization—A numerical artifact known as volumetric locking is typical in simulations of nearly incompressible materials undergoing deformation. Locking refers to the build-up of fictitious stiffness due to the element's inability to reproduce correct deformation mode shapes. Locking can result in poor kinematics and erroneous pressures

and subsequent strains. Due to the many orders of magnitude difference between the shear modulus ($\sim 1\text{--}3$ kPa) and bulk modulus ($\sim 1\text{--}2$ GPa) of the brain tissue, volumetric locking can generally occur in the computations of the brain dynamics. Some finite element procedures rely on the use of reduced integration techniques in order to circumvent locking. However, use of reduced integration can result in spurious singular or hourglass modes. In MPM, volumetric locking is addressed by Mast et al. [57]. They provide a generalized solution to regularize volumetric and deviatoric parts of stress. In this work, we use the simplest scheme of volumetric averaging of a kinematic variable over a certain length to alleviate effects of volumetric locking. In our computations, we average the Jacobian measure for material points belonging to a background cell (Fig. 2). The Jacobian, $J = \frac{dV}{dV_0} = \det(F)$ is defined for an individual material point, because material points “carry”

with them all the field variables in MPM. The deformation gradient for each material point is scaled based on the average value of the Jacobian for the cell (equation 11).

$$\mathbf{F}_{\text{mp}}^{\text{new}} = \sqrt[3]{\frac{J_{\text{cell}}}{J_{\text{mp}}}} \times \mathbf{F}_{\text{mp}}^{\text{old}} \quad (11)$$

where,

$\mathbf{F}_{\text{mp}}^{\text{old}}$: old deformation gradient at a given time

$\mathbf{F}_{\text{mp}}^{\text{new}}$: new deformation gradient after stabilization

J_{mp} : Jacobian for a material point

J_{cell} : average Jacobian for the cell $= \frac{1}{n} \sum_{i=1}^n (J_{\text{mp}})_i$

As shown by Mast et al. [57], use of this pressure stabilization technique reduces the numerical artifacts associated with the orders of magnitude difference between the normal and shear components of stress values.

2.2.5 Loading and Boundary Condition—Simulations are exact replicates of head rotation experiments in human volunteers described in section 2.1. The MPM head model was subjected to an angular deceleration history obtained from head-rotation experiments [38]. The head initially rotates with finite velocity (Fig. 1d) ω_0 and then decelerates according to the deceleration history shown as in Fig. 3, resembling a half sinusoidal wave. Note that magnitude and duration of the loading pulse are different for injurious loading (Fig. 7a); however, the shape and loading direction remain the same. The head/neck is free at the bottom as dictated by the experiment.

2.3. Quantitative comparison between the simulations and the experiment

We use the following measures to compare brain deformations from the simulations with the experiment: (a) peak values, (b) area-fraction distribution, and (c) correlation score. Out of these measures, the first measure takes into account peak values at discrete spatial points; whereas the latter two measures take into account full-field spatial information. For area

fraction measure, we consider 2D sections along the axial plane for comparison of the model with the experiments. The area-fraction, ϕ , for a given 2D section that has a shear strain, E , within the specified range m to n , is defined as:

$$\phi_{m < E \leq n} = \frac{\iint E \, dx dy, \text{ for } m < E \leq n}{\iint dx dy} \quad (12)$$

Area fraction measure presented above tend to integrate out the heterogeneity of the strain field distribution. A more robust way to compare full-field 3D data between the model and the experiment is to use statistical measures that take into account point-wise spatial variations between the model and the experiment. Here, we use two such measures, namely, root mean square error (RMSE) and correlation score (CS) for model evaluation. RMSE and CS are defined as,

$$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^N (O_i - P_i)^2}{N}} \quad (13)$$

$$\text{CS} = (1 - |\text{NISE}|) \times 100 \quad (14)$$

Where, NISE is the normalized integral square error, which is defined as,

$$\text{NISE} = 1 - \frac{2 \sum_{i=1}^N O_i P_i}{\sum_{i=1}^N O_i^2 + \sum_{i=1}^N P_i^2} \quad (15)$$

Variables P and O represent spatially varying simulated (predicted) dataset and experimentally measured (observed) dataset, respectively. CS has a range from 0 to 100. For CS, the validity rating in terms of a qualitative index (such as excellent, unacceptable) is available in the literature [58]. The qualitative index is categorized into five classifications as: Excellent: 86 CS 100; Good: 65 CS <86; Fair: 44 CS <65; Marginal: 26 CS <44; Unacceptable: 0 CS <26.

3. Results and Discussion

3.1 Validation of model against human volunteer data

We validate the computational head model against full-field brain deformations [59,60,37] obtained in a human volunteer [38]. The experiments were performed with spatial and temporal resolutions of 8 mm and 18 ms, respectively, to obtain spatial displacements [38]. This information was used to calculate shear strains throughout the head. Shear strains from the simulation were then compared with the experimentally obtained shear strains. Even

though simulations were run with a much finer resolution of 2 mm^3 , simulation results were coarsened to match the experimentally tagged-MRI resolution of 8 mm^3 . In this way, comparisons are made at the same length scale. The qualitative comparison of radial-circumferential shear strain (E_{rt}) is shown in Fig. 4. From Fig. 4, it is evident that the computational model is able to capture the overall dynamics and the magnitudes of the experimentally observed shear strain fields in the human brain. The agreement between the experiment and simulation is less definitive at $t = 63 \text{ ms}$, likely due to the fact that viscoelastic time constants that are used in this work are not comprehensive. In both experiments and simulations, a shear wave starts to propagate from the outer boundary towards the inside. Peak shear occurs at 45 ms and, as time proceeds, shearing in other directions (sign change) starts due to the reflection of waves from the center. Note that, entire wave propagation dynamics plays out in 100 ms , thus the shear wave propagation within the brain has a timescale of $\sim 100 \text{ ms}$.

More robust quantitative comparisons in terms of peak radial-circumferential shear strain (E_{rt}) and correlation score are shown in Table 3 and 4, respectively, and quantitative comparison in terms of area fraction distribution of shear strain is shown in Fig. 5. The comparison between experiment and simulation is reasonable using each of these quantitative measures.

3.2. Sensitivity of simulations to bulk modulus

We use quantitative measures described in section 2.3 to study the sensitivity of brain deformations to various values of bulk modulus. Bulk modulus values are changed by orders of magnitude to cover all the values typically used in computational simulations of brain biomechanics. Table 5 tabulates peak radial-circumferential shear strain (E_{rt}) from the simulations as the bulk modulus value is changed with order of differences in the magnitude from 10^{10} Pa to 10^6 Pa . Peak radial-circumferential shear strain (E_{rt}) from the experiment is also tabulated. As indicated in the table, bulk modulus on the order of 10^{10} Pa under-predict the measured magnitude of peak shear strain, whereas bulk modulus on the order of 10^8 Pa or lower over-predict the measured magnitude of peak shear strain. To quantify the differences in distributions of strains, the area fraction distribution is plotted in Fig. 6, and again it is apparent that the best overall comparison with experiment is obtained with simulations using the GPa bulk modulus. Table 6 tabulates root mean square error (RMSE) and correlation score (CS) along with the qualitative rating for various bulk modulus values. Best model performance is obtained for a bulk modulus value of 10^9 Pa . These results suggest that a realistic bulk modulus value on the order of GPa is necessary to reproduce the experimentally observed shear deformations in the brain. This is especially important because shear and rotation-related injury modes and the axonal-injury criteria based on strain measures [44,10,12] are now widely accepted.

3.3 Dynamic brain deformations during injury-causing loading

In the earlier sections, we have focused on studying the sensitivity of brain deformations to values of bulk modulus for mild rotational loading. However, it is also important to understand how bulk modulus values affect the prediction of injury and injured regions. Thus, the head model presented above is further used to simulate injurious loading that

resulted in definitive concussion during collegiate football impacts [67]. Figure 7a shows loading pulse for injurious loading [67,63]. Figure 7b shows the shear strain in the brain for injurious loading for a specific 2D slice ($z = 0$) and for the baseline bulk modulus value on the order of 10^9 . Peak radial-circumferential shear strains on the order of $\pm 30\%$ are seen for this loading. Further, overall wave propagation dynamics is similar to the non-injurious case.

Injured regions within the brain are quantified using axonal strain injury criterion, as recent investigations suggest that axonal strain is the best predictor of mild traumatic brain injuries [44,10,12]. We use white matter axonal strain injury threshold values of 18% and 13% based on the works of Wright and Ramesh [44] and Giordano and Kleiven [10], respectively. Using these thresholds, the white matter regions that would be injured, are shown in Fig. 7c. Notable damage regions include the corpus callosum, corticospinal tract, cingulum, corona radiata, and internal capsule. The injured regions found in this work are consistent with DTI findings in blast TBI patients. Ivanov et al. [68] collected DTI data in Iraq and Afghanistan veterans scanned on an average of 3.7 years after trauma exposure. They found DTI abnormalities in several white matter (WM) regions including the corpus callosum, the corticospinal tract, the internal capsule, and the cingulum. Mac Donald et al. [69–71] collected DTI data in service members deployed to the combat operations in Iraq and Afghanistan. Data was collected in acute/sub-acute stages and during one-year and five-year follow ups. They found DTI abnormalities in several white matter regions including internal and external capsules, longitudinal fasciculus, corpus callosum, and right middle frontal gyrus white matter.

Sensitivity of injury to the value of bulk modulus—Table 7 tabulates total cumulative injury (damage) in the white matter of the brain for various bulk modulus values. Cumulative injury is based on the entire volume of the brain and for the entire simulation time of 100 ms. The total volume of the injured regions increases as the bulk modulus is decreased. As a consequence, many white matter regions indicate damage for bulk modulus values of 10^8 or smaller. However, clinical evidence [72,73,68,71,74] does not support WM damage over such a large volume and a large number of regions.

4. Conclusions

Computational models of brain biomechanics hold promise for overall management of TBI, including their use in diagnostics and prevention of injury. However, models have predictive value only if they are able to capture the biomechanics of the brain as both a material and a structure. Even though significant progress has been made in terms of accurately incorporating the morphology and constitutive relationships of the brain, the understanding regarding accurate material parameters is uncertain. One such parameter is a bulk modulus of the brain tissue; bulk modulus values spanning up to three orders of magnitude differences have been used in the computational models. However, their sensitivity to model predictions is not known. In this work, we have studied the sensitivity of brain deformations to bulk modulus values using a subject-specific computational head model. The model incorporated detailed morphology of the brain tissue, including anisotropy of the white matter. The model was validated against sub-injurious brain deformations in a living human volunteer. Simulation results show that a bulk modulus on the order of GPa gave the best

agreement with experimental data from tagged MRI. A bulk modulus value of 10^{10} Pa underestimated magnitudes of peak strains and distribution of area fractions. On the other hand, bulk moduli of 10^8 Pa and lower overestimated the magnitudes of the peak strains and the distribution of area fractions. Further, based on statistical measures such as RMSE and CS, the simulations with a bulk modulus value of 10^9 Pa gave the best overall agreement with respect to the experimentally measured deformations. The model was further used to simulate injurious loading that results in a definitive concussion. For the injury simulations, a bulk modulus value on the order of 10^9 Pa provided the results that are consistent with clinical findings of injury. These results underscore the importance of using accurate bulk modulus values in computational head models.

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Figure 1. 3D computational human head model. The model was constructed from the T1 and diffusion MRI images of a human volunteer. T1-weighted images were used to segment brain tissue into different substructures (a). Diffusion images provided information on fiber orientation and fractional anisotropy of the brain tissue (b). Individual images were stacked together to generate a 3D model (c). Resulting model was subjected to mild angular acceleration and solved using Material Point Method (MPM) (d).

Figure 2.

Cell-averaging-based approach for stabilization. (a) Material point and background cell configuration in MPM (b) the Jacobian for the cell is determined by averaging the Jacobian for each material point within a cell. Old deformation gradient is scaled based on the Jacobian for the cell to obtain new deformation gradient for each material point.

Figure 3.
Deceleration-time history for head deceleration

Figure 4.

Qualitative comparison of radial-circumferential shear strain (E_{rt}) between the experiment and the simulation. Simulation results are based on baseline bulk modulus value on the order of 10^9 Pa.

Figure 5.

Quantitative comparison in terms of area fraction distribution of radial-circumferential shear strain (E_{rt}) between the experiment and the simulation. A representative result for a midaxial slice ($z = 0$) at a representative time ($t = 45$ ms) is shown. This trend extends throughout the head.

Figure 6.

Sensitivity of model response based on area fraction distribution of radial-circumferential shear strain (E_{rt}) to various bulk modulus values. A representative result for a midaxial slice ($z = 0$) at a representative time ($t = 45$ ms) is shown. This trend extends throughout the head.

Figure 7.

Simulations of injurious loading that resulted in definitive concussion. (a) Input acceleration for injurious loading. (b) Radial-circumferential shear strain shear strain (E_{rt}) pattern in the brain for injurious loading. (c) Regions of white matter fiber tracts exceeding axonal strain injury criterion. Injured regions are marked in red.

Table 1

Summary of bulk modulus values of brain in the literature

(a) Experimentally measured bulk modulus values			
Source	Bulk modulus value	Frequency/strain rate *	Method of obtaining bulk modulus value
McElhaney et al. (1973) [75]	2.06 GPa	0–100 Hz (10^2 s^{-1})	hydrodynamic compression tests on human and monkey brains within 10 hours of post mortem
Stalnaker (1969) [64]	2.10 GPa (human) 2.08 GPa (monkey)	0–100 Hz (10^2 s^{-1})	hydrodynamic compression tests on human and monkey brains within 10 hours of post mortem
Etoh et al. (1994) [65]	2.7 GPa	1.7 MHz (10^6 s^{-1})	ultrasonic testing of bovine gray matter

(b) Values of bulk modulus used in computational head models		
Source	Bulk modulus value	Remarks regarding choice of bulk modulus value
Ruan et al. (1994) [25]	21.9 to 219 MPa	by fitting the results of computational model to intracranial pressure measurements in post mortem human subjects
Claessens et al. (1997) [8]	0.83 to 83.3 MPa	rationale for choice not stated
El Sayed et al. (2008) [9]	2.19 MPa	rationale for choice not stated
Zoghi-Moghadam and Sadegh (2009) [11]	50 MPa	rationale for choice not stated
Giordano and Kleiven (2014) [10,5]	50 MPa	bulk modulus is lowered with respect to the acknowledged value of 2 GPa to account for numerical stability
Ji et al. (2015) [12]	219 MPa	rationale for choice not stated
Takhounts et al. (2003, 2008) [13,14]	560 MPa	bulk modulus was chosen to simulate near incompressibility
Sahoo et al. (2014) [15]	1.125 GPa	rationale for choice not stated
Kleiven and Hardy (2002) [16]	2.1 GPa	based on the experimental works of Stalnaker [64] and McElhaney et al. [75]
Horgan and Gilchrist (2004) [17], Zhang et al. (2004) [18], Mao et al. (2013) [4], Sarvghad-Moghaddam et al. (2015) [11]	2.19 GPa	rationale for choice not stated
Taylor and Ford (2009) [23]	2.37 GPa	by citing Zhang et al. [76]

* Since frequencies are reported in aforementioned papers, approximate strain rate is stated in the brackets

Table 2

Material properties of head constituents

Substructure	Properties
White Matter	$G_0 = 1520$ Pa; $G_{\infty} = 286$ Pa; $g_1 = 0.81$; $\tau_1 = 2$ sec $k_1 = 121$ Pa; $k_2 = 0.0001$; fractional anisotropy (κ) and fiber direction ($\mathbf{a}$, unit vector) for each material point from DTI
Grey Matter	$G_0 = 2750$ Pa; $G_{\infty} = 385$ Pa; $g_1 = 0.625$; $g_2 = 0.055$; $g_3 = 0.182$; $\tau_1 = 2$ sec; $\tau_2 = 11$ sec; $\tau_3 = 47.5$ sec
Caudate, Putamen	$G_0 = 700$ Pa; $G_{\infty} = 110$ Pa; $g_1 = 0.61$; $g_2 = 0.135$; $g_3 = 0.103$; $\tau_1 = 1.45$ sec; $\tau_2 = 10$ sec; $\tau_3 = 110$ sec
Thalamus	$G_0 = 6700$ Pa; $G_{\infty} = 943$ Pa; $g_1 = 0.81$; $\tau_1 = 2$ sec
Common properties for brain substructures	$\rho = 1040$ kg/m ³ ; $K_{\text{cerebrum}} = 1.46$ GPa; $K_{\text{cerebellum}} = 1.19$ GPa
Falx, Tentorium	$\rho = 1133$ kg/m ³ ; $E = 60.67$ MPa; $\nu = 0.45$
Skull	$\rho = 2070$ kg/m ³ ; $E = 8$ GPa; $\nu = 0.22$
Ventricles, Cerebrospinal fluid (CSF)	$\rho = 1004$ kg/m ³ ; $K = 1.46$ GPa; $n = 7.15$; $\mu = 1.002\text{e-}3$ Pa-sec

Table 3

Comparison of peak radial-circumferential shear strain (E_{rt}) between the experiment and the simulation.

Simulation results are based on baseline bulk modulus value on the order of 10^9 Pa

	Peak positive shear strain (E_{rt})	% difference with respect to experimental value	Peak negative shear strain (E_{rt})	% difference with respect to experimental value
Experiment	0.060	–	0.018	–
Simulation	0.064	6.67	0.020	11.11

Table 4

Comparison of model performance between the experiment and the simulation using root mean square error (RMSE) and correlation score (CS) measures. Simulation results are based on a baseline bulk modulus value on the order of 10^9 Pa.

Time	Radial-circumferential shear strain (E_{rt})		Performance rating in terms of qualitative Index [58]
	Root mean square error (RMSE) %, E_{rt}	Correlation score (CS), E_{rt}	
$t = 27$	0.88	86.70	Excellent
$t = 45$	0.83	91.20	Excellent
$t = 63$	1.25	62.36	Fair
$t = 81$	0.96	78.90	Good
$t = 99$	1.03	72.55	Good

Table 5Sensitivity of model response, based on peak shear strain (E_{tt}) to brain bulk modulus values

Bulk Modulus	Peak positive strain	% difference with respect to experimental value	Peak negative strain	% difference with respect to experimental value
Experiment	0.060	–	0.018	–
10^{10}	0.049	–18.33	0.014	–22.22
10^9	0.064	6.67	0.020	11.11
10^8	0.084	40.00	0.038	111.11
10^7	0.097	61.67	0.046	155.56
10^6	0.107	78.33	0.052	188.89

Table 6

Sensitivity of model response, based on root mean square error (RMSE) and correlation score (CS) measures, to brain bulk modulus values. Representative result at $t = 45$ ms is shown.

	Radial-circumferential shear strain (E_{rt})		
Bulk Modulus	Root mean square error (RMSE) %	Correlation score (CS)	Performance rating in terms of qualitative Index [58]
10^{10}	1.40	60.82	Fair
10^9	0.83	91.20	Excellent
10^8	2.1	52.73	Fair
10^7	3.32	42.30	Marginal
10^6	3.97	33.54	Marginal

Table 7

Cumulative injury in white matter of a brain for various bulk modulus values

Bulk Modulus	Cumulative injury	
	Axonal strain injury using threshold defined by Wright and Ramesh [44]	Axonal strain injury using threshold defined by Giordano and Kleiven [10]
10^{10}	15 %	18 %
10^9	28 %	34 %
10^8	43 %	50 %
10^7	52 %	61 %
10^6	66 %	75 %