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Biofidelic white matter heterogeneity decreases computational model predictions of white matter strains during rapid head rotations

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Abstract

The finite element (FE) brain model is used increasingly as a design tool for developing technology to mitigate traumatic brain injury. We developed an ultra high-definition FE brain model (>4 million elements) from CT and MRI scans of a 2-month-old pre-adolescent piglet brain, and simulated rapid head rotations. Strain distributions in the thalamus, coronal radiata, corpus callosum, cerebral cortex gray matter, brainstem and cerebellum were evaluated to determine the influence of employing homogeneous brain moduli, or distinct experimentally derived gray and white matter property representations, where some white matter regions are stiffer and others less stiff than gray matter. We find that constitutive heterogeneity significantly lowers white matter deformations in all regions compared with homogeneous properties, and should be incorporated in FE model injury prediction.

Keywords

biomechanics; traumatic brain injury; computational model

INTRODUCTION

Finite element (FE) models of the human brain are important tools in the development and evaluation of safety systems such as seat belts and air bags in automobiles. (Zhou, Khalil et al. 1995, Willinger, Kang et al. 1999, Zhu, Prange et al. 2006, Kleiven 2007, Takhounts, Ridella et al. 2008, Coats, Eucker et al. 2012). Such a method must yield timely results, so as not to be a limiting factor in the safety system design process. At least one regulatory body has suggested that a FE brain model should yield injury prediction results within 2 hours of providing the model with the kinematic input, and should do so on a high-end

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personal computer (Takhounts, Eppinger et al. 2003). Loading conditions, such as the kinematics of the head of an anthropomorphic test device during a crash test are readily available, typically measured via an array of 9 or 12 linear accelerometers (Padgaonkar, Krieger et al. 1975), angular velocity sensors or optical motion tracking systems (Arbogast, Balasubramanian et al. 2009). FE models have been used to calculate deformation based measures for common traumatic brain injuries including diffuse axonal injury, subdural hematoma, and focal contusions.

Morphologically, the gyrencephalic structure of human brain creates sulci in the cortex, and deep fissures exist between the hemispheres and at the cerebro-cerebellar interface to accommodate the falx cerebri and tentorium, respectively. The state-of-the-art of finite element modeling permits simulation of each of these physical characteristics, but it often comes at the expense of increased simulation time and/or research resources to validate the model performance with each incremental “improvement” in the model. The question then arises, “What level of physical fidelity to the human is necessary for an FE brain model used for safety system design?”

Many researchers have conducted parametric studies to quantify the effect of FE brain geometric fidelity on mechanical quantities such as stress, strain and pressure. Ho and Klieven (2009) created two FE models - one with and one without the sulci – and found reductions in strain deep in the brain range from 4 to 48%. Bradshaw et al (Bradshaw, Ivarsson et al. 2001) developed a physical model of the brain using gel-filled cylinders exposed to coronal rotations, and found the addition of sulci doubled bridging vein strains, and a similar study using physical models found the addition of lateral ventricles reduced strains in tissue adjacent to the ventricles by 26 to 63 percent from the strains at the same locations in a model without ventricles (Ivarsson, Viano et al. 2002).

In addition to changes in structural fidelity, many researchers have performed parametric analyses by varying material properties while holding geometry constant. Brain tissue is heterogeneous, anisotropic, incompressible, nonlinear, and viscoelastic (Prange and Margulies 2002, Hrapko, van Dommelen et al. 2008, Chatelin, Vappou et al. 2012), and undergoes large deformations during traumatic insults (Margulies, Thibault et al. 1990, Miller, Margulies et al. 1998, Willinger, Kang et al. 1999, Zhu, Prange et al. 2006, Takhounts, Ridella et al. 2008).

Our laboratory has characterized the mechanical tissue properties of newborn, toddler and adult pig brain tissue undergoing large deformation in 6 regions: thalamus, coronal radiata, corpus callosum, cerebral cortex gray matter, brainstem and cerebellum (Prange and Margulies 2002, Coats and Margulies 2006), and found properties did not change between toddler and adults (Gefen and Margulies 2004). These published material properties (Table 1) reveal substantial differences between gray and white matter, and even between white matter regions, with a greater than two fold difference between the lowest (corpus callosum) and highest (corona radiata) white matter regional shear moduli, and clear evidence of anisotropy in the white matter. In the next sections, we summarize several parametric studies which examined the influence of regional heterogeneity and anisotropy on predicted local brain tissue strains.

Kleiven (2007) investigated the sensitivity of strain and pressure to changes in homogeneous brain material properties in a 3-dimensional FE model (7,128 brain elements), and found that a halving of the Ogden Hyperelastic material constants μ_1 and μ_2 led to a 40% increase in resulting maximum principal strain in the model but no change in maximum or minimum pressure; similarly, doubling of these same Ogden material constants led to a 40% decrease in maximum principal strain but no change in maximum or minimum pressure. Chafi and colleagues (Chafi, Dirisala et al. 2009) studied three different isotropic constitutive models of CSF (a linear elastic fluid, linear viscoelastic, or nearly incompressible linear elastic constitutive model), and found that a two-order of magnitude reduction in bulk modulus in any of the three constitutive models led to a 6 to 70% increase in peak intracranial coup pressure, a 40 to 200% increase in peak intracranial shear strain, and 400 to 600% increase in relative brain motion.

Researchers at Wayne State University compared homogeneous with heterogeneous brain tissue properties by creating a two-dimensional FE model of the pig brain exposed to coronal rotations (Zhou, Khalil et al. 1995). Although no data is presented, the authors stated that simulation results qualitatively matched the location of diffuse axonal injury (DAI) in the experiments when white matter was 1.6 times stiffer than gray matter, as compared to a model with equal gray and white matter moduli. They compared the mechanical response of a homogeneous brain model, where all tissue regions were assigned the same bulk (2.19×10^5 kPa) and shear (168 kPa) moduli, to a heterogeneous model with the white matter bulk modulus and shear modulus increased 1.6 times that of gray matter (Zhou, Khalil et al. 1995); the material moduli of all other tissue regions in the heterogeneous model remained the same as the homogeneous model. The authors exposed both models to two different impact conditions – a blunt strike to the forehead and a rapid rotation in the sagittal plane. The analysis of regional response was limited to the maximum pressure and maximum shear stress in a single element at each of four locations – the frontal pole, occipital pole, the corpus callosum, and the brain stem. In both the blunt strike and rapid rotation simulations, the difference in peak pressure between the heterogeneous and homogeneous models at the four locations was less than 5%. In contrast, there was a substantial increase in the shear stress in the heterogeneous brain model with stiffer white matter, to 1.14–1.59 times that of the homogeneous brain model at all four locations, with the smallest effect at the poles. These data highlight the sensitivity of FE model stress to material property variance. However, as described above and in Table 1, data from adult swine brain tissue stress relaxation tests at large (50%) strains suggest that gray and white matter may be more similar than Zhou and colleagues assumed, with the isotropic shear modulus of the corona radiata only about 1.15 times that of the cortical gray matter, and the corpus callosum white matter is actually *less* stiff (0.84 times) than gray matter (Coats and Margulies 2006). Consequently, while Zhou's observed differences in tissue stress between the homogeneous and heterogeneous two-dimensional FE models in 4 elements reinforce the importance of considering heterogeneous material properties when developing an FE brain model, the lack of biofidelity with their 1.6 times stiffer white matter may not yield realistic insight.

Colgan and colleagues (Colgan, Gilchrist et al. 2010) developed a modest-density (7318 element) transversely isotropic hyperelastic finite element model of the brain to investigate the influence of anisotropic white matter bundles on the deformation response of the brain.

They used diffusion tensor images and tractography to establish white matter bundle orientation and anisotropic uniformity (via fractional anisotropy values) in two white matter regions in a previously published mesh (Horgan and Gilchrist 2004). Compared to isotropic properties, anisotropy in the brainstem and corona radiata increased shear strains significantly in those regions. More recently, Giordano and colleagues (Giordano and Kleiven 2014) also used a modest density (7128 brain elements) FE model examined the white matter in two brain regions (brainstem and corpus callosum), and found that, compared to isotropic properties, adding stiff fibers to invoke anisotropy in these regions increased principal strains in those regions, but decreased the axon-oriented strains only slightly when white matter in these regions was represented as a hyper-viscoelastic fiber-reinforced anisotropic material. Together, these previous studies underscore the potential importance of regional anisotropic properties on deformation responses in those regions.

To complement these previous studies, we performed parametric simulations to compare the maximal principal strain response in *every element* of a finely meshed, 3-dimensional FE brain model with homogeneous (uniform) and heterogeneous regional cerebral material properties, where properties of the corona radiata, corpus callosum, thalamus, and cortex were replaced by published values for those regions. Second, we extend the field by introducing an ultra high-definition FE brain model (>4 million elements) directly from CT and MRI scans of a 2 month old pig brain (Figure 1), increasing geometric fidelity. A third unique feature of this communication is that, because results may be sensitive to the relative alignment of white matter regions varies with head rotation kinematics, we simulated two previously published rapid rotation experiments (Sullivan, Eucker et al. 2015) one each in the axial and sagittal rotation planes (Figure 2). Finally, we also examined 6 anatomic regions (cortical gray matter, coronal radiata, corpus callosum, thalamus, cerebellum, and brainstem, see Figure 1) to capture both local and remote influence of constitutive property representation on brain tissue deformation. Results for each region and head rotation direction were compared across three high-resolution models: either homogeneous properties or one of two heterogeneous material property compositions based upon the upper and lower bounds of published regional material data, with the goal of capturing the effect of minimal and maximal heterogeneity on the distribution of local and more remote regional principal strain values.

METHODS

Mesh development

Animal protocols were approved by the University of Pennsylvania Institutional Animal Care and Use Committee. Images of a decapitated 2 month old piglet head were captured at the University of Pennsylvania Veterinary Hospital CT scanner (0.63mm between slices, 0.34mm² in-plane resolution, 173mm × 173mm × 151.25 mm field of view). After en bloc removal of the brain, MRI images were obtained at the Small Animal Imaging Facility at the University of Pennsylvania (9.4 T 31 cm horizontal bore MR system, 110 × 55 × 48 mm³ FOV, resolution: 0.15mm³). The dimensions of the test subject brain were 73mm in anterior-posterior length, 57.2mm in lateral width, and 47.6 mm in superior-inferior extent, which was within the mean ± one standard deviation of a group previously reported for a low

resolution model (Sullivan, Eucker et al. 2015). MR and CT images were imported into ScanIP (ScanIP with +FE Module 5.0.931, Simpleware LTD, United Kingdom). Voxels were segmented into one of the following neuroanatomical regions: skull, CSF, falx, cortical gray matter, coronal radiata, corpus callosum, thalamus, cerebellum, or brainstem (illustrated in Figure 1), including most of the olfactory bulbs, the entire cerebrum and cerebellum, and most of the brainstem. In addition to the brain, the falx cerebri and skull were represented by rigid hexahedral solid or shell elements in the pre-processor (MSC Patran 2008r1, MSC Software Corporation, Santa Ana, CA). CSF was modelled as a linear viscous fluid sandwiched between the brain and skull. A finite element mesh was generated from the segmented images, consisting of 4.1 million elements and 1.2 million nodes. By volume, 74% of the elements were hexahedral and 26% were tetrahedral. The mesh geometry was optimized by ScanIP to control for distortion, and the resulting inscribed-to-circumscribed sphere aspect ratio for all elements was greater or equal to 0.1 (average = 0.79), and only 71 elements out of 4.1 million elements had an edge length aspect ratio (longest edge length / shortest edge length of a single element) greater than 10 (average = 1.6).

Material Properties

For our parametric analysis comparing a homogeneous and heterogeneous brain, we developed three finite element models and used each model to simulate the axial and sagittal experiment. In all models, the material properties were based upon previously published moduli values for brain tissue (Table 1), with a Poisson's ratio of 0.49999 and density of $1.04\text{E-}6 \text{ kg/mm}^3$. Falx and tentorium were represented with a linear viscoelastic solid with a density of $1.130\text{E-}6 \text{ kg/mm}^3$, Poisson's ratio of 0.45 and modulus of 15MPa. The skull was considered rigid. CSF was modelled as a Newtonian fluid with $\rho = 1.0 \text{ g/cm}^3$, $K = 22.0 \text{ GPa}$, $\eta = 0.727 \text{ mPa s}$. First, a homogeneous model (Ho) was developed based upon the material properties for mixed gray-white matter reported by Prange (Prange and Margulies 2002) and Coats (Coats and Margulies 2006) (Table 1). Second, a heterogeneous-low model (Ht-Lo) was generated by defining all regional material properties in accordance with Table 1, choosing the least of the D1 and D2 values for anisotropic regions (Coronal Radiata and Corpus Callosum). Third, a heterogeneous-high model (Ht-Hi) was generated like the Ht-Lo model, choosing the *greater* of the D1 and D2 values for anisotropic regions. Some of the experimentally derived published regional modulus values in the Ht-Low and Ht-High models were lower than the same region in the Ho model, and some were stiffer. Because we previously have shown that material properties of 5 times those values measured in the material property experiments were required to achieve a good match between model and hemi-section experiments (Coats, Eucker et al. 2012), the models were constructed with material properties that were $5\times$ those shown in Table 1. CSF was modelled with $10\times$ the published CSF bulk modulus value (Bloomfield, Johnston et al. 1998). The brain material properties used for the Ho, Ht-Lo, and Ht-Hi models are presented in Table 2.

Simulations

The finite element solver used for all three models was for each of the two experiments (6 simulations total) Abaqus Explicit v6.9-EF1 (Dassault Systèmes, Vélizy-Villacoublay, France) running on the Children's Hospital of Philadelphia's Research Cluster ($32 \times$ Dell SC-1435 nodes each with two Opteron 2.5 GHz 2380 quad core processors with 32 GB of

RAM and the CentOS 5.3 operating system). The rapid rotation of the head lasts 12 to 17 milliseconds (Figure 2), but we simulated 30 milliseconds of the experiment to allow sufficient time for strains to dissipate. Each simulation ran on 8 processors in parallel and took approximately 22 days to complete the finite element solution. Maximum principal strain was written to the Abaqus output database file every 0.33 milliseconds (ms) of simulation time. Custom Python scripts and Matlab software were written to extract the strain time-history of every element from the Abaqus output database for visualization of the results.

RESULTS

Maximum principal strain distributions were examined in 6 regions: cortical gray matter, coronal radiata, corpus callosum, thalamus, cerebellum, and brainstem. Results for both axial and sagittal head rotations are presented in Figures 3–6. In all combinations of region and plane of rotation, the Ho strain distribution was always statistically significantly different from either Ht-Low or the Ht-High strain distribution ($p < 0.0001$ – Kolmogorov-Smirnov test of two distributions). To examine the response with finer granularity, we performed element-by-element comparisons (Figure 5 and Figure 6) between homogeneous and each of the two heterogeneous models, where two strains – one from the homogeneous and one from either of the two heterogeneous models – from the same element are plotted with the line of identity shown (dashed line) to qualitatively assess the correlation between the model strains for every element in a region. Data points that fall below and to the right of the line of equality indicate that strains in the heterogeneous model in that element are less than the strains in the homogeneous model. To quantify these overall regional differences between the homogeneous and heterogeneous models, we also performed linear regressions of the element-by-element comparisons shown in Figure 5 and Figure 6 (provided in Table 3 and Table 4, respectively). Regression fit (R^2) was greater than 0.96 in all cases.

In the axial plane rapid rotations, for all regions, strains from each heterogeneous model were less than strains in the homogeneous model (Figure 3 and 5), typically with lowest levels in the Ht-High model (0.61 to 0.73 times Ho strains), followed by the Ht-Low (0.80 to 0.93 times the Ho strains across all regions). The exceptions were in the corpus callosum, where strains approach the line of equality, indicating little difference between homogeneous and one or both heterogeneous model strains.

The sagittal direction exhibited similar trends, with heterogeneous models generally showing smaller strain values than the homogeneous model across models, but the regional differences were less pronounced (Figure 6). Across all regions, the Ht-High strains were 0.56 to 0.74 times the Ho strains, and Ht-Low strains were 0.63 to 0.89 times the Ho strains. For most regions, Ht-High model strains were often smaller than Ht-Low, as in the sagittal rotations. The exception was the cerebellum where Ht-High and Ht-Low strains were nearly identical, and in the brainstem, where for strains < 0.1 mm/mm heterogeneous models predicted larger strains than the homogeneous (Ho) model (Figure 6, top left pane).

For each region, we examined the population distribution (POP) of maximum principal strain, determined by rank ordering the maximum strain values from all elements in that

region. Near the lower end of the strain distribution for the region, we defined the POP90 value as that strain value that 90% of the tracers in a region achieved or exceeded; sometimes referred to as the 10th percentile strain in the region. The POP50 value was defined as the median maximum principal strain. Near the high end of the strain response for the population of elements in the region, we defined the POP10 value as the strain that only 10% of the tracers achieved or exceeded. When POP 10 and POP90 are close, the population distribution in that region is narrow, consistent with a more uniform response in the region.

To assess the relative impact of model heterogeneity on deformation distribution within a region, we calculated the POP criteria for all regions and models and the percent change in POP strain values between models (Table 5 and Table 6). Positive percent changes indicate the POP strain values were higher (more deformation predicted) in the heterogeneous models than in the homogeneous models. Negative percent changes indicate the POP strain values were lower (less deformation predicted) in the heterogeneous models than in the homogeneous models. We examined the difference between POP10 and POP90, and smaller differences indicated more uniform responses.

In the axial direction, the POP strain values were reduced 2% to 43% in the two heterogeneous models compared to the Ho model, again with larger reductions in the Ho-High than Ho-Low comparisons. The heterogeneous models had more uniform regional responses than the Ho model for all regions except the corpus callosum, where the POP10-POP90 value varied little by model. The regions with the least uniform response (largest POP10-POP90) were the cerebrum and cerebellum.

In the sagittal direction, model heterogeneity again reduced strains, but the differences between the two heterogeneous models were not consistently remarkable. Generally, as in the axial direction, the uniformity of the maximum principal strain responses increased within a region for the heterogeneous models compared to the Ho model. In the sagittal direction, the brainstem, cerebrum and cerebellum had the least uniform intra-regional strain response (largest POP10-90).

Within model type, we compared the influence of head rotation on the strain uniformity in each region, and found that the regional strain response was more uniform in axial rotations than sagittal rotations (smaller POP10-POP90), with the most dramatic directional dependence in the thalamus. The exceptions were in the cerebrum, where axial rotations produced larger intra-regional variability than sagittal rotations, and in the brainstem, where variability within region was not affected by head rotation direction.

DISCUSSION

We have developed a high-resolution finite element model of the 2-month-old pig brain derived directly from CT and MRI scans. Developing the model using CT and MRI images allowed us to define brain geometry with high fidelity to the pig, including segmentation into gray and white matter, brainstem, thalamus, and cerebellum, and study the influence of material mechanical property heterogeneity on the maximum principal strain response of the model. In general, heterogeneity reduced strains in every region compared with the

homogeneous model, in some cases as low as 0.56× the homogeneous strains, and strains within a region were more uniform. These findings contrast with those of Zhou (Zhou, Khalil et al. 1995), who found ~50% increase in shear strains in a heterogeneous FE brain model as compared to a homogeneous FE brain model. However, there are a few important differences between Zhou's work and the study presented herein. First, Zhou increased the stiffness of only the white matter (60% increase) in accordance with the available knowledge at the time of their publication (1995), whereas we changed the stiffness of the cerebral gray matter, corona radiata, corpus callosum, and thalamus in accordance with material property experiments on pig brain, whereby some regions were stiffer and some regions less stiff than homogeneous models. Second, Zhou examined changes at only 4 individual elements in the brain (one each at the frontal pole, occipital poles, corpus callosum, and brainstem), whereas we examined all elements in each region. Finally, Zhou compared maximum shear stress whereas we compared maximum principal strain, so direct comparisons should be approached cautiously, because others have shown in parametric studies that the direction of the effect of local material properties may depend on the output variable examined (Giordano and Kleiven 2014).

Intuition might suggest that change in strain in a particular region is dependent upon change in the material modulus for that region. However, we found that the brainstem and thalamus, both of which have the same shear modulus (1083 Pa) in the homo- and heterogeneous models, exhibited substantial changes in strain (0.57 to 0.87 times) from the homo- to heterogeneous models. Further, the corpus callosum had a large reduction (and the largest absolute change of all regions) in shear modulus from Ho to Ht-Low models (1083 to 657 Pa), but the corpus callosum strains were relatively immune to regional property changes. These results suggest that local regional response may depend on properties of adjacent and remote regions. In addition, the brainstem response may also be influenced the displacement boundary condition permitted at the foramen magnum. Future parametric studies could vary regional constitutive properties and boundary conditions individually, to tease out the relative influences of geometry, material property representation and boundary influences on local, neighboring and distant brain regions.

We also found that some of the regional strain responses were influenced by the plane of rotation, despite the fact that the pig FE model has no falx or tentorium. Similarly, Ho and Kleiven (Ho and Kleiven 2009) created two FE models - one with and one without the sulci - and found reductions in strain deep in the brain were dependent upon the plane of rotation. Coronal (human anatomical plane) rotations in that study yielded only 4% change in maximum principal strain, while sagittal rotations yielded up to a 48% change in strain. In the case of the human, the falx likely has an important role; head motion in sagittal rotations is parallel to the falx, and brain motion is likely also parallel to the falx. The direction of coronal head rotation is perpendicular to the falx and it is likely that the falx tends to restrain the motion of the brain in the coronal direction in such a way that the presence or absence of the sulci has little effect on the strains deep in the brain. Future studies in the pig FE could focus on additional directions of motion, and use more than one kinematic time-history for each direction to characterize the influence of direction in more detail.

In this communication, we report changes in strain due to the introduction of heterogeneity and identify the regional response influence by local and remote tissue properties. In brain injury biomechanics FE brain models are used to mimic life-like tissue deformations to develop injury thresholds and for evaluating injury mitigation strategies, such as protective equipment, such as helmets and playing surfaces. Therefore, it is important that there is consistency between the constitutive model descriptions used to develop the thresholds, and the actual properties of the tissues injured. Without experimentally derived material property descriptions, FE models might over or under-predict brain tissue deformations, and lead to erroneous injury thresholds. Based on our study, we conclude that gray and white matter heterogeneity is an important feature of a FE brain model, and should be included in future injury threshold development efforts.

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Figure 1.

Cutaway images of the finite element brain model. Six distinct regions are shown - cortical gray matter (purple), coronal radiate (blue), corpus callosum (brown), thalamus (magenta), cerebellum (green), and brainstem (tan). Skull, falx and CSF elements not shown.

Figure 2.

Velocity time histories rapid rotation experiments simulated in the current study – experiment 080402 (left) and experiment 071106 (right). “Start time” and “end time” bound the portion of the velocity signal that was used as input to the model; at all other times the velocity input was zero.

Figure 3. Percent volume of the brain that has achieved a certain strain in axial rapid rotation simulations, stratified by brain region.

Figure 4. Percent volume of the brain that has achieved a certain strain in sagittal rapid rotation simulations, stratified by brain region.

Figure 5.

Heterogeneous vs. homogeneous strains for axial plane rapid rotation simulation, stratified by brain region. Each data point is the strain from the same single element in both models. Dashed line is line of equal strain between models.

Figure 6.

Heterogeneous vs. homogeneous strains for sagittal plane rapid rotation simulation, stratified by brain region. Each data point is the strain from the same single element in both models. Dashed line is line of equality between ordinate and abscissa strains.

Figure 7.
Exemplar maximum principal strain cumulative population distribution.

Table 1

Regional material properties of porcine brain*

Region		α	μ_0 (Pa)
Corona Radiata (Prange and Margulies 2002)	D1	0.0741	293
	D2	0.0360	211
	Avg	0.0614	254
Corpus Callosum (Prange and Margulies 2002)	D1	0.0497	131
	D2	0.0759	232
	Avg	0.0628	182
Cortex (Coats and Margulies 2006)		0.0382	211
Thalamus (Prange and Margulies 2002)		0.0382	264
Mixed Gray / White Matter (Prange and Margulies 2002)		0.0326	217

Force and displacement data were obtained from parallel plate shear tests and fit to a first order Ogden hyperelastic model:

$$T_{12} = \frac{2\mu(t)}{\alpha^2} \left(\frac{(\lambda^\alpha - \lambda^{-\alpha})}{\lambda + \lambda^{-1}} \right)$$

where the known quantities are the shear stress (T_{12}) is determined from the measured force and dimensions of the specimen, the maximum principal stretch ratio (λ) is determined from the prescribed motion of the parallel plates. The unknown quantities are α , which describes the nonlinear strain-magnitude sensitive behavior, and $\mu(t)$ which is the viscoelastic shear modulus of the material.

Table 2

Shear modulus (μ_0) for the Homogeneous (Ho), Heterogeneous Low Range (Ht-Lo), and Heterogeneous High Range (Ht-Hi) models. All units are Pascals (Pa).

	Model		
Region	Ho	Ht-Lo	Ht-Hi
Corona Radiata	1,083	1,055	1,463
Corpus Callosum	1,083	657	1,161
Cortex	1,083	1,055	1,055
Thalamus	1,083	1,318	1,318
Brainstem	1,083	1,083	1,083
Cerebellum	1,083	1,083	1,083

Table 3

Linear regression results for axial plots in Figure 5.

Region	Correlation	Slope	Offset	R ²
Brainstem	Ht-High vs. Ho	0.73	−0.0027	0.9986
	Ht-Low vs. Ho	0.87	−0.0031	0.9994
Cerebellum	Ht-High vs. Ho	0.72	0.0052	0.999
	Ht-Low vs. Ho	0.88	0.0029	0.9996
Cerebrum	Ht-High vs. Ho	0.64	0.0029	0.9995
	Ht-Low vs. Ho	0.85	−0.00082	0.9997
Corpus Callosum	Ht-High vs. Ho	0.7	−0.011	0.997
	Ht-Low vs. Ho	0.93	0.0051	0.9991
Thalamus	Ht-High vs. Ho	0.61	0.014	0.9995
	Ht-Low vs. Ho	0.80	−0.0065	0.9996
White Matter	Ht-High vs. Ho	0.63	−0.006	0.999
	Ht-Low vs. Ho	0.88	−0.01	0.9996

Table 4

Linear regression results for sagittal plots in Figure 6.

Region	Correlation	Slope	Offset	R ²
Brainstem	Ht-High vs. Ho	0.57	0.039	0.9636
	Ht-Low vs. Ho	0.65	0.035	0.9791
Cerebellum	Ht-High vs. Ho	0.74	0.014	0.9931
	Ht-Low vs. Ho	0.81	0.011	0.9961
Cerebrum	Ht-High vs. Ho	0.71	0.011	0.9976
	Ht-Low vs. Ho	0.85	0.0052	0.9979
Corpus Callosum	Ht-High vs. Ho	0.67	0.0035	0.998
	Ht-Low vs. Ho	0.85	0.00087	0.9959
Thalamus	Ht-High vs. Ho	0.56	-0.0046	0.9933
	Ht-Low vs. Ho	0.63	0.018	0.9973
White Matter	Ht-High vs. Ho	0.74	-0.012	0.9956
	Ht-Low vs. Ho	0.89	-0.012	0.9943

Table 5
Brainstem, cerebellum, and cerebrum POP Injury Criterion, stratified by region and rapid rotation plane.

Region	Model	Axial Simulation			Sagittal Simulation			POP10-POP90	POP10-POP90 (axial-sag)
		POP10	POP50	POP90	POP10	POP50	POP90		
Brainstem	Ho	0.376	0.224	0.052	0.324	0.265	0.06	0.298	0.026
	Ht-Low	0.32	0.197	0.041	0.279	0.211	0.083	0.233	0.046
	Ht-High	0.262	0.167	0.035	0.227	0.2	0.086	0.232	-0.005
	Ht-Low vs. Ho	-15%	-12%	-21%		-20%	38%		
	Ht-High vs. Ho	-30%	-26%	-33%		-25%	42%		
Cerebellum	Ho	0.506	0.325	0.079	0.427	0.393	0.076	0.536	-0.109
	Ht-Low	0.425	0.292	0.073	0.352	0.323	0.088	0.472	-0.12
	Ht-High	0.345	0.243	0.065	0.28	0.293	0.089	0.435	-0.155
	Ht-Low vs. Ho	-16%	-10%	-7%		-18%	16%		
	Ht-High vs. Ho	-32%	-25%	-17%		-25%	17%		
Cerebrum	Ho	1.1	0.457	0.22	0.88	0.959	0.195	0.764	0.116
	Ht-Low	0.82	0.392	0.183	0.637	0.387	0.169	0.596	0.041
	Ht-High	0.646	0.298	0.142	0.504	0.326	0.147	0.49	0.014
	Ht-Low vs. Ho	-25%	-14%	-17%		-20%	-13%		
	Ht-High vs. Ho	-41%	-35%	-36%		-34%	-25%		

Table 6
Corpus callosum, corona radiata, and thalamus POP Injury Criterion, stratified by region and rapid rotation plane

		Axial Simulation				Sagittal Simulation				
Region	Model	POP10	POP50	POP90	POP10-POP90	POP10	POP50	POP90	POP10-POP90	POP10-POP90 (axial-sag)
Corpus Callosum	H0	0.589	0.509	0.391	0.198	0.595	0.439	0.272	0.323	-0.125
	Ht-Low	0.58	0.477	0.364	0.216	0.537	0.373	0.233	0.304	-0.088
	Ht-High	0.426	0.345	0.25	0.176	0.437	0.295	0.191	0.246	-0.07
	Ht-Low vs. H0	-2%	-6%	-7%		-10%	-15%	-14%		
	Ht-High vs. H0	-28%	-32%	-36%		-27%	-33%	-30%		
Corona Radiata	H0	0.641	0.475	0.349	0.292	0.651	0.4	0.266	0.385	-0.093
	Ht-Low	0.555	0.411	0.3	0.255	0.576	0.357	0.216	0.36	-0.105
	Ht-High	0.367	0.299	0.215	0.152	0.441	0.291	0.181	0.26	-0.108
	Ht-Low vs. H0	-13%	-13%	-14%		-12%	-11%	-19%		
	Ht-High vs. H0	-43%	-37%	-38%		-32%	-27%	-32%		
Thalamus	H0	0.585	0.45	0.306	0.279	1.252	0.795	0.441	0.811	-0.532
	Ht-Low	0.456	0.356	0.242	0.214	0.874	0.549	0.305	0.569	-0.355
	Ht-High	0.373	0.289	0.201	0.172	0.779	0.472	0.258	0.521	-0.349
	Ht-Low vs. H0	-22%	-21%	-21%		-30%	-31%	-31%		
	Ht-High vs. H0	-36%	-36%	-34%		-38%	-41%	-41%		