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SHORT COMMUNICATION

On the unimportance of constitutive models in computing brain deformation for image-guided surgery

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Abstract Imaging modalities that can be used intra-operatively do not provide sufficient details to confidently locate the abnormalities and critical healthy areas that have been identified from high-resolution pre-operative scans. However, as we have shown in our previous work, high quality pre-operative images can be warped to the intra-operative position of the brain. This can be achieved by computing deformations within the brain using a biomechanical model. In this paper, using a previously developed patient-specific model of brain undergoing craniotomy-induced shift, we conduct a parametric analysis to investigate in detail the influences of constitutive models of the brain tissue. We conclude that the choice of the brain tissue constitutive model, when used with an appropriate finite deformation solution, does not affect the accuracy of computed displacements, and therefore a simple linear elastic model for the brain tissue is sufficient.

Keywords Brain · Constitutive models · Finite element method · Craniotomy-induced brain shift · Displacement boundary conditions

1 Introduction

Therapeutic technologies that are entering neurosurgical practice now (e.g. nanotechnology devices, focused radiation, lesion generation and robotic surgery) have extremely localized area of therapeutic effect (Bucholz et al. 2004) and therefore have to be applied directly over specific location of anatomic/functional abnormality, precisely in relation to the current (i.e. intra-operative) patient's anatomy. As surgical intervention tends to distort the pre-operative anatomy and often leads to misalignment between the actual position of pathology and its position determined from pre-operative images, an image-guided surgery requires intra-operative images and/or update of the pre-operative images to the current position of the brain internal structures. Such update is known as registration.

To achieve an accurate image update, the organ (e.g. the brain) deformations must be taken into account. Since the late 1990s significant research effort has been directed towards the prediction of such deformations using biomechanical models (Miga et al. 1997; Hagemann et al. 1999; Paulsen et al. 1999; Warfield et al. 2000; Ferrant et al. 2001, 2002; Castellano-Smith et al. 2001; Xu and Nowinski 2001; Miga et al. 1999, 2000; Warfield et al. 2005; Wittek et al. 2005, 2007; Dumpuri et al. 2007). Typically, in such models, the Finite Element (FE) method (e.g. Bathe 1996) is employed to discretize and solve the related differential equations of continuum mechanics.

In our previous studies (Wittek et al. 2005, 2007), we applied non-linear finite element procedures in computing brain deformation for image-guided neurosurgery and showed that accurate computation of brain deformation during craniotomy-induced brain shift can be done by defining load through the prescribed displacements on the brain surface in the craniotomy area.

When the load is defined through the prescribed deformation of the brain surface, the problem of computing the brain deformations for image-guided surgery can be formulated in the following way:

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- Known: initial position of the entire domain [as imaged by magnetic resonance images (MRIs)] and current position of some parts of the boundary, e.g. the displacement of the exposed surface of the brain. No surface tractions are applied;
- Unknown: deformation field within the domain (the brain), in particular, current position of the tumor.

Problems of this type have been previously referred to as "displacement–zero traction problems" (Miller 2005a,b; Miller and Wittek 2006), since they are very special cases of "displacement–traction problems" (Ciarlet 1988).

Elementary reasoning based on dimensional analysis proves that for linear elastic, isotropic materials, whose properties are described by a stress parameter (e.g. Young's Modulus) and Poisson's ratio, the solution of the static (or quasi-static) displacement–zero traction problem is independent of the stress parameter. In displacement–zero traction problems, the load is applied through the motion of boundary that has dimension of length (meters), and the computed results are nodal displacements, that also have dimension of length (meters).

In case of non-linear materials the above argument does not hold because such materials may have more than one stress parameter (e.g. Ogden-type models) and stress – history of strain functional dependencies may vary significantly depending on the choice of the constitutive model. However, our previous experience (Miller 2001, 2005a,b) gained from modeling of uni-axial tension and compression of homogenous cylindrical samples whose constitutive behavior was represented using different types of hyperelastic constitutive models allows us to hypothesize that the solution of displacement–zero traction problem very weakly depends on the constitutive model even for non-linear materials. This suggests that the brain tissue incompressibility (Holbourn 1943; Pamidi and Advani 1978; Walsh and Schettini 1984; Sahay et al. 1992; Mendis et al. 1995; Miller and Chinzei 1997; Farshad et al. 1999; Miller 1999; Darvish 2000; Miller 2000; Miller and Chinzei 2002; Takhounts et al. 2003) rather than the stress parameters is the key material property affecting such solution.

However, the realities of the actual neurosurgery modeling —such as complex geometry, boundary conditions (contact between the brain and skull) and deformation state, as well as the necessity to take into account material non-homogeneity (e.g. one has to distinguish between the brain parenchyma, tumor and ventricles)—are very different from simple tension or compression of a homogenous cylinder used in the studies by Miller (2001, 2005a,b).

Therefore, in this contribution, we apply a patient-specific model of brain undergoing craniotomy-induced shift previously developed by Wittek et al. (2005, 2007) to investigate how strongly the computed deformation field within the brain depends on the constitutive models of brain tumor and parenchyma. We consider the following models in the decreasing order of complexity:

1. Hyperviscoelastic material model;
2. Hyperelastic material model;
3. Linear elastic material model.

The rationale for starting the analysis from a state of the art hyperviscoelastic model instead of the simplest linear elastic one was that the brain and other soft tissues exhibit non-linear stress–strain relationship and strain rate dependency (Bilston et al. 2001; Fung 1993; Miller 2000; Miller and Chinzei 2002; Takhounts et al. 2003).

As neurosurgery can result in brain surface deformations of over 10 mm (Miga et al. 2003), geometrically non-linear finite element procedures (i.e. finite deformation formulation of continuum mechanics) were used for all three constitutive models analyzed.

2 Methods

2.1 Boundary conditions and loading

Following Wittek et al. (2007), we modeled the brain–skull interface during craniotomy-induced brain shift by introducing a gap with thickness equaled to thickness of the subarachnoidal space (as determined from the magnetic resonance images MRI—approximately 3 mm) between the brain and skull.

The load was defined by prescribing the displacements on the brain surface in the craniotomy area as previously explained in Wittek et al. (2007).

2.2 Patient-specific mesh

Patient-specific brain mesh developed in the previous studies by Wittek et al. (2004, 2005, 2007) was used (Fig. 1). This mesh was created from a set of 60 pre-operative MRIs of a patient undergoing brain tumor surgery at the Department of Surgery, Brigham and Women's Hospital (Harvard Medical School, Boston, MA, USA). The skull was treated as a rigid body.

2.3 Constitutive models

The behavior of the healthy brain parenchyma (hereafter referred to as parenchyma) and tumor was described using three distinct constitutive models: (1) hyperviscoelastic, (2) hyperelastic, and (3) linear elastic. For all three models, the parenchyma and tumor Poisson's ratios were designated a value of 0.49.

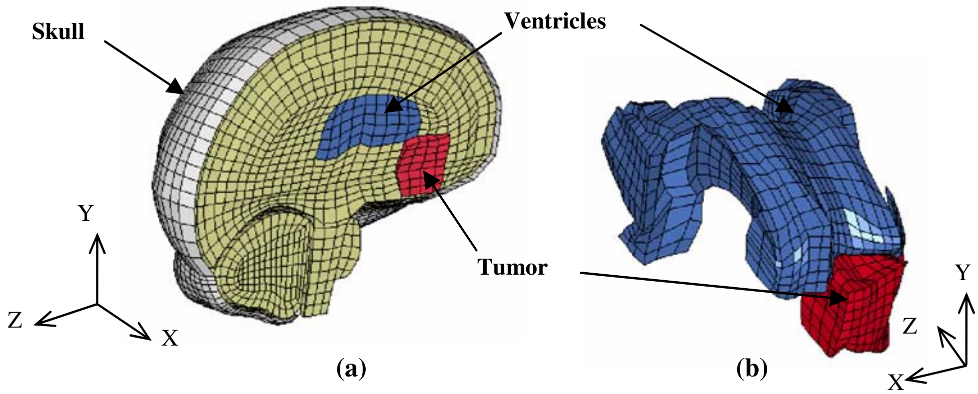

Fig. 1 Patient specific meshes of **a** left hemisphere of brain, and **b** ventricles and tumor. The entire mesh comprises of 16,925 nodes, 15,031 hexahedral (8-noded bricks) and 19 pentahedral elements defining the brain parenchyma, ventricles and tumor. The elements' characteristic length varied between 0.6 and 6 mm. For 85% of the elements, the characteristic length was between 2 and 4.5 mm. During the craniotomy, gravity acceleration acted in the XZ plane and formed a 24.5° angle with the Z axis

Following Wittek et al. (2007), the tumor was simulated using the same constitutive model as the parenchyma and its shear modulus was designated a value three times larger than that of the healthy tissue. This value is consistent with the experimental data by Sinkus et al. (2005) who reported that the ratio of shear modulus of tumor to that of the healthy tissue varies from 1.4 to 3.3 depending on the tumor type.

Following Miller et al. (2000) and Miller and Chinzei (1997, 2002), no distinction was made between the properties of grey and white matter. Both the brain parenchyma and tumor were treated as isotropic single-phase continua.

The ventricles were modeled as very soft linear elastic continuum with a shear modulus of 100 Pa (Wittek et al. 2005, 2007).

The following constitutive models for the brain parenchyma and tumor were considered in the order of decreasing complexity:

1. *Hyperviscoelastic material*—the model proposed by Miller and Chinzei (2002). For strains of up to 30%, this model represents the main features of brain tissue mechanical behavior such as non-linear stress–strain relationship, bi-modal response (i.e. larger stiffness in compression than in tension), and non-linear stress–strain rate relationship:

$$W = \frac{2}{\alpha^2}\int_0^t \left[\mu(t-\tau)\frac{\mathrm{d}}{\mathrm{d}\tau}\left(\lambda_1^\alpha+\lambda_2^\alpha+\lambda_3^\alpha-3\right)\right]\mathrm{d}\tau, \quad (1)$$

$$\mu = \mu_0\left[1-\sum_{k=1}^{n} g_k\left(1-\mathrm{e}^{-\frac{t}{\tau_k}}\right)\right], \quad (2)$$

Table 1 Constitutive constants for hyperviscoelastic model of brain tissue (Miller and Chinzei 2002)

Instantaneous response	$k = 1$	$k = 2$
$\mu_0 = 842$ Pa	$\tau_1 = 0.5$ s	$\tau_2 = 50$ s
$\alpha = -4.7$	$g_1 = 0.450$	$g_2 = 0.365$

Compare Eqs. (1) and (2)

where W is a potential function, λ_i's are principal stretches, μ_0 is the instantaneous shear modulus in undeformed state, τ_k's are characteristic times, g_k's are relaxation coefficients, and α is a material coefficient which can assume any real value without restrictions.

The constants for Eqs. (1) and (2) were taken from the experiments using samples of swine brain tissue by Miller and Chinzei (2002) (Table 1).

2. *Hyperelastic material*—during surgical procedures, the strain rates are relatively small and do not vary strongly. One may argue that in such a case, strain rate dependency is unlikely to play a major role. If the strain rate dependency is not of interest, the viscoelastic terms can be deleted from Eq. (1), which yields the hyperelastic model described by the following formula:

$$W = \frac{2\mu}{\alpha^2}\left(\lambda_1^\alpha+\lambda_2^\alpha+\lambda_3^\alpha-3\right). \quad (3)$$

The constants $\mu = \mu_0 = 842$ Pa and $\alpha = -4.7$ were the same as for the hyperviscoelastic material model (Table 1).

3. *Elastic material*—the linear elastic almost incompressible (Poisson's ratio of 0.49) constitutive model that obeys the Hooke's law. Shear modulus $\mu = \mu_0 = 842$ Pa was used.

2.4 Integration of equations of continuum mechanics

Following Wittek et al. (2005, 2007), non-linear dynamics finite element solver available in the LS-DYNA 970 (revision 5434) software package (Livermore Software Technology Corporation, Livermore, CA, USA) (LSTC 2004) was applied in this study. We used the explicit (central difference) time integration (Crisfield 1998) as it requires no iterations and its effectiveness in brain deformation computation was demonstrated by Wittek et al. (2007).

3 Results

To obtain a quantitative assessment of the accuracy of three biomechanical brain models used in the present study, the displacements of gravity centers of the ventricles and tumor predicted using these models were compared with the ones determined from the MRIs (Table 2).

In Table 2, the computation results are presented to one decimal place as this is approximately the accuracy of the finite element computations presented in this study. This accuracy was determined by conducting a modeling example based on the one used by Miller et al. (2007). In this example, an ellipsoid of approximately brain size (long axis of 200 mm and short axis of 100 mm) with constitutive behavior described as in Eqs. (1) and (2) and Table 1 was indented using a prescribed nodal displacement. It was found that when the ellipsoid was discretized using hexahedral elements of approximately the same size as in the brain model shown in Fig. 1, the calculated deformations differ by around 0.1 mm from the solution obtained using a very dense mesh consisting of 140,000 elements (element size approximately four times smaller than in the presented study). We estimated the accuracy of our computations by comparing them to the solution obtained using the mesh with 140,000 elements that can be regarded as accurate and converged.

When interpreting the results summarized in Table 2 one should take into account that the accuracy of determining positions of centers of gravity of tumor and ventricles is limited by the voxel size in the MRI images used in this study—0.85 mm × 0.85 mm × 2.5 mm. Therefore, for practical purposes, values differing by less than 0.80 mm can be considered the same.

The results summarized in Table 2 confirm our expectations that the predicted intra-operative positions of the tumor and ventricles centers of gravity were essentially the same regardless of the constitutive model used. The predictions of these positions were accurate for all three constitutive models used.

The above interpretation of the results summarized in Table 2 is confirmed by detailed comparison of the transverse and coronal cross-sections of the actual tumor and ventricle surfaces acquired intra-operatively with the ones predicted in the presented simulations. Varying the material model exerted very little effect on the computed deformation field and the differences between the computed and MRI-derived intra-operative cross-sections were very small (Figs. 2, 3).

To assess the effects of material model (i.e. hyperviscoelastic, hyperelastic, linear elastic) on computation times, the times needed to compute deformation field within the brain were obtained (Table 3). The computation times reported here do not include the time for writing output files on the computer hard drive, i.e. they are the times needed to solve the system of finite element equations. The right-hand side column of Table 3 summarizes the percentage variation of computation time with respect to the simulation in which the non-linear hyperviscoelastic material model was used.

All three constitutive models produce essentially the same results (Table 2, Figs. 2, 3). Therefore, we recommend using linear elastic constitutive model (and geometrically non-linear analysis) for the brain tissue as it leads to approximately 29% saving in computational time and causes no loss of accuracy as compared to the hyperviscoelastic model of Miller and Chinzei (2002).

4 Discussion and conclusions

During image-guided neurosurgery it is often possible to obtain partial, sparse information about the current, intra-

Table 2 Observed and computed centers of gravity displacements for ventricles and tumor

Center of gravity displacements (mm)						
Material model	Ventricles			Tumor		
	ΔX	ΔY	ΔZ	ΔX	ΔY	ΔZ
MRI determined	3.4	0.2	1.7	5.5	−0.2	1.7
Hyperviscoelastic material	2.6	−0.1	2.1	5.2	−0.4	2.7
Hyperelastic material	2.6	−0.1	2.1	5.2	−0.4	2.7
Linear elastic material	2.6	−0.1	2.1	5.0	−0.5	2.7

X, Y, and Z directions are as in Fig. 1. The computations were done using geometrically non-linear finite element procedures. During the craniotomy, gravity acceleration acted in the XZ plane and formed a 24.5° angle with the Z axis

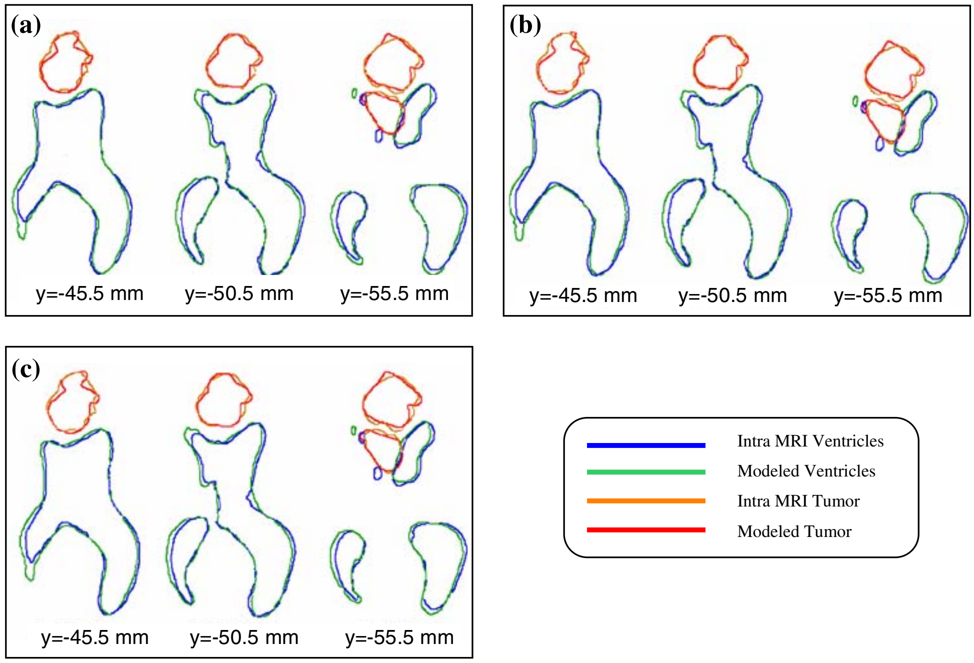

Fig. 2 Transverse contour sections: **a** hyperviscoelastic constitutive model, **b** hyperelastic constitutive model, and **c** linear elastic constitutive model. The computations were done using geometrically non-linear finite element procedures. Distance y is measured from most superior point of parietal cortex. y axis points superiorly

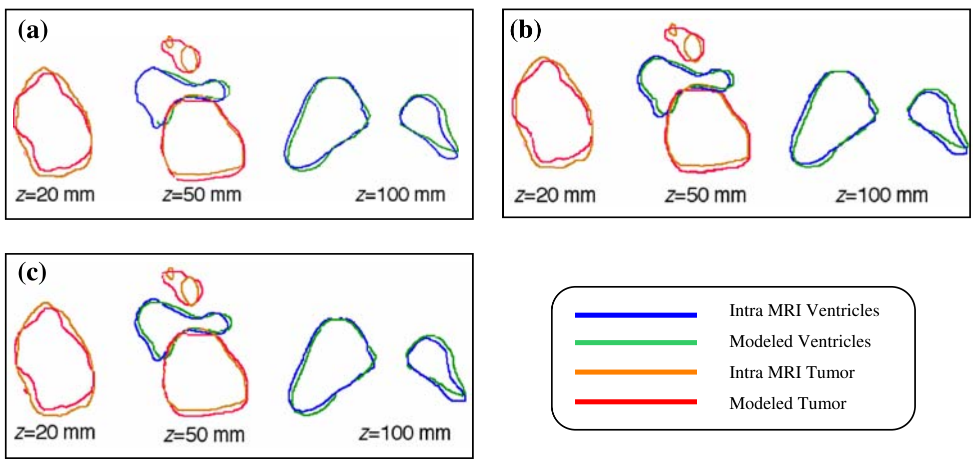

Fig. 3 Coronal contour sections: **a** hyperviscoelastic material model, **b** hyperelastic material model, and **c** linear elastic material model. The computations were done using geometrically non-linear finite element procedures. Distance z is measured from most anterior point of frontal cortex. z axis points posteriorly

Table 3 Comparison of the computation times of different analyses with the computation time in the simulation in which hyperviscoelastic material model was used

Material model	Computation time (s)	Variation (%)
Hyperviscoelastic material	2,411	–
Hyperelastic material	2,358	2.20
Linear elastic material	1,713	28.95

Geometrically non-linear finite element procedures were applied in all the analyses. The computations were performed on personal computer with 3.0 GHz Pentium 4 processor and 1,024 MB of internal memory. No attempt was made to optimize computational speed, therefore the results in this Table should be viewed as relative only

operative position of the brain. This information can be used to warp high quality pre-operative images, so that they correspond to the current (i.e. intra-operative) situation, through computation of the deformation field within the brain using a biomechanical model.

The parametric study conducted in this paper shows that in such computation the choice of the constitutive model is unimportant, and therefore we suggest using the simplest linear elastic model for the brain tissue. The differences between the displacements of the gravity centers of tumor and ventricles predicted using the linear elastic and hyperviscoelastic/hyperelastic constitutive models of brain tissue were negligible. They did not exceed 0.2 mm (Table 2), which is much below the resolution (0.5–1 mm) of state of the art imaging technologies applied in image-guided surgery.

The conclusion that the choice of the constitutive model of brain tissue has almost no influence on the computed deformation field is, in our view, an important and far-reaching one. It has been widely believed that every patient-specific finite element model of the brain must suffer from

Table 4 Observed and computed centers of gravity displacements for ventricles and tumor

Center of gravity displacements (mm)						
Material model/ analysis type	Ventricles			Tumor		
	ΔX	ΔY	ΔZ	ΔX	ΔY	ΔZ
MRI determined	3.4	0.2	1.7	5.5	−0.2	1.7
Linear elastic material/geometrically non-linear analysis	2.6	−0.1	2.1	5.0	−0.5	2.7
Linear elastic material/linear analysis	0.7	0.2	1.90	3.7	−0.3	2.6

X, Y, and Z directions are as in Fig. 1. Notice appreciable error in the results obtained using geometrically linear analysis (last row). During the craniotomy, gravity acceleration acted in the XZ plane and formed a 24.5° angle with the Z axis

uncertainties regarding non-linear, patient-specific mechanical properties of the brain tissue. The results of our parametric study show that for situations that can be adequately modeled as displacement–zero traction problems, as is often the case in image-guided surgery, this difficulty disappears. One can use the simplest linear elastic model with any reasonable value of the Young's modulus and Poisson's ratio close to 0.5.

As the brain shift results in brain surface deformations of over 10 mm (Miga et al. 2003), geometrically non-linear (i.e. using finite deformations) finite element analysis was used as a solution method in this study. However, it should be noted that a number of research laboratories have reported computing deformations of the brain undergoing the shift using geometrically linear solution methods (Miga et al. 1997; Hagemann et al. 1999; Paulsen et al. 1999; Warfield et al. 2000; Castellano-Smith et al. 2001; Ferrant et al. 2001, 2002; Miga et al. 1999; Clatz et al. 2005; Warfield et al. 2005; Dumpuri et al. 2007). Such methods assume that the brain deformations are infinitesimally small. This assumption is in obvious contradiction with large deformations and rigid body motion of the brain occurring during the brain shift we analyzed (Wittek et al. 2007), which is also confirmed in this study. Our attempt to apply the linear analysis yielded incorrect results in terms of the displacements of gravity centers of tumor and ventricles and overall brain deformations (Table 4, Fig. 4). The largest error occurred in predicting the ventricles and tumor centers of gravity displacements in x direction (Table 4)—the direction that experienced the largest rigid body motion. Highly localized, unrealistic brain deformation in the craniotomy area was predicted by geometrically linear analysis (Fig. 4).

Caution is required when extrapolating the conclusions of this study beyond craniotomy-induced brain shift. Clearly, the accurate constitutive model of brain tissue is essential in applications of biomechanical modeling that require stress prediction such as, e.g. computing forces acting on surgical tools. The presented modeling approach cannot be applied to surgical procedures involving topology changes, such as cutting and tissue removal. Therefore, the methods we applied cannot be used to simulate, e.g. tumor excision. However, the presented conclusions are applicable to the wide spectrum of problems, which includes not only the craniotomy-induced brain shift but also other neurosurgical situations for which sufficient information is available to deduce loading through the enforced motion of boundaries.

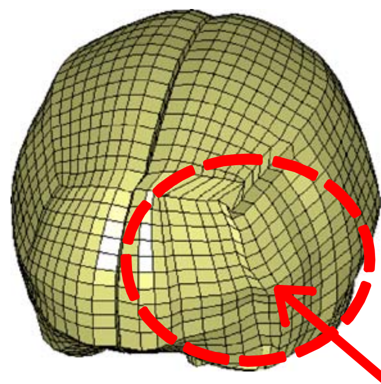

Fig. 4 Unrealistic localized brain deformation obtained using geometrically linear analysis

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