

Biomechanics of the brain for computer-integrated surgery

KAROL MILLER*, ADAM WITTEK, GRAND JOLDES

Intelligent Systems for Medicine Laboratory, School of Mechanical Engineering, The University of Western Australia.

This article presents a summary of the key-note lecture delivered at Biomechanics 10 Conference held in August 2010 in Warsaw. We present selected topics in the area of mathematical and numerical modelling of the brain biomechanics for neurosurgical simulation and brain image registration. These processes can reasonably be described in purely mechanical terms, such as displacements, strains and stresses and therefore can be analysed using established methods of continuum mechanics. We advocate the use of fully non-linear theory of continuum mechanics. We discuss in some detail modelling geometry, boundary conditions, loading and material properties. We consider numerical problems such as the use of hexahedral and mixed hexahedral–tetrahedral meshes as well as meshless spatial discretisation schemes. We advocate the use of Total Lagrangian Formulation of both finite element and meshless methods together with explicit time-stepping procedures. We support our recommendations and conclusions with an example of brain shift computation for intra-operative image registration.

Key words: brain, biomechanics, finite element method, meshless methods, surgical simulation, image registration

1. Introduction

Mathematical modelling and computer simulation are standard tools commonly used in engineering. Computational mechanics has had a profound impact on science and technology. It allows simulation of complex systems that would be very difficult or impossible to treat using analytical methods. A challenging task for the future is to extend the success of computational mechanics to fields outside traditional engineering, in particular to biology, biomedical sciences, and medicine [1].

In computational sciences, the selection of the physical and mathematical model of the phenomenon to be investigated has a major influence on the accuracy of the simulation results. Model selection is often a very subjective process; different modellers may choose different models to describe the same phenomenon. Nevertheless, valid computer simulations of a physical reality cannot be obtained without a proper model selection [1].

In this paper, we show how various aspects of computer-integrated neurosurgery can benefit from the application of the methods of computational mechanics. We discuss issues related to the model selection and the numerical algorithms used for obtaining the solution. We chose to focus on the following two application areas: neuroimage registration and neurosurgical simulation.

1.1. Computational radiology

NAKAJI and SPELTZER [2] list the “accurate localisation of the target” as the first principle in modern neurosurgical approaches. Neurosurgical interventions have extremely localised areas of therapeutic effect. As a result, they have to be applied precisely in relation to the patient’s current (i.e. intra-operative) anatomy, directly over the specific location of anatomic or functional abnormality [3].

If only pre-operative anatomy of the patient is precisely known from medical images (usually Magnetic

* Corresponding author: Karol Miller, Intelligent Systems for Medicine Laboratory, School of Mechanical Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA 6009, Australia. Phone: + (61) 8 6488 7323, e-mail: kmiller@mech.uwa.edu.au

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Resonance Images (MRI)), it is now recognised that the ability to predict soft organ deformation (and therefore intra-operative anatomy) during the operation is the main problem in performing reliable surgery on soft organs. We are particularly interested in problems arising in image-guided neurosurgery (figure 1). In this context, it is very important to be able to predict the effect of procedures on the position of pathologies and critical healthy areas in the brain. If displacements within the brain can be computed during the operation, they can be used to warp pre-operative high-quality MR images so that they represent the current, intra-operative configuration of the brain.

1.2. Simulation for neurosurgery planning, medical training and skill assessment

The goal of surgical simulation research is to model and simulate deformable materials for applications requiring real-time interaction. Medical applications for this include simulation-based training, skills assessment and operation planning.

Surgical simulation systems are required to provide visual and haptic feedback to a surgeon or trainee. Various haptic interfaces for medical simulation are especially useful for training surgeons for

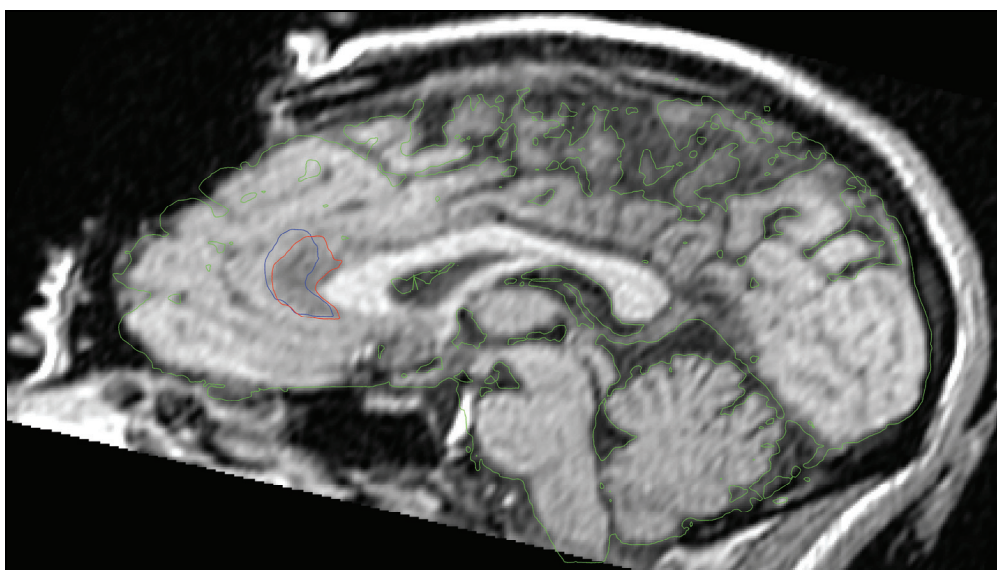


Fig. 1. Comparison of the brain surface determined from images acquired pre-operatively with the intra-operative images acquired after craniotomy. The pre-operative position of the tumor is shown against the intra-operative tumor segmentation. MRI images were provided by the Department of Surgery, Brigham and Women's Hospital (Harvard Medical School, Boston, Massachusetts, USA)

The neuroimage registration problem involves large deformations, non-linear material properties and non-linear boundary conditions as well as the difficult issue of generating patient-specific computational models. However, it is easier than the surgical simulation problem in two important ways: we are interested in accurate computations of the displacement field only, accuracy of stress computations is not required; and the computations must be conducted intra-operatively, which practically means that the results should be available to an operating surgeon in less than 40 seconds [4]–[7]. This still forms a stringent requirement for computational efficiency of the methods used, but is much easier to satisfy than a 500 Hz haptic feedback frequency requirement for neurosurgical simulation [8].

minimally invasive procedures (laparoscopy/interventional radiology) and remote surgery using teleoperators. These systems must compute the deformation field within a soft organ and the interaction force between a surgical tool and the tissue to present visual and haptic feedback to the surgeon. Haptic feedback must be provided at the frequencies of at least 500 Hz [8]. From a solid-mechanical perspective, the problem involves large deformations, non-linear material properties and non-linear boundary conditions. Moreover it requires extremely efficient solution algorithms to satisfy stringent requirements imposed on the frequency of haptic feedback. Therefore, surgical simulation is a very challenging problem of solid mechanics.

When a simulator is intended to be used for surgeon training, a generic model developed from aver-

age organ geometry and material properties can be used in computations. However, when the intended application is for operation planning, the computational model must be patient-specific. This requirement adds to the difficulty of the problem – the question of how to rapidly generate patient-specific computational models still awaits a satisfactory answer.

Following the Introduction (Section 1), in Section 2 we discuss the issues related to modelling geometry, boundary conditions, loading and material properties of the brain, and numerical algorithms devised to efficiently solve brain deformation behaviour models. In Section 3, we consider an example application in the area of computational radiology – brain shift computation for neuroimage registration. We conclude with some reflections about the state of the field.

2. What is and what is not important in modelling the brain biomechanics?

2.1. Geometry discretisation

Detailed geometric information is needed to define the domain in which the deformation field needs to be computed. In applications that do not require patient-

specific data (such as neurosurgical simulators for education and training), the geometric information provided by brain atlases [9]–[12] is sufficient. However, other applications such as neurosurgical simulators for operation planning and image registration systems require patient-specific data. Such data are available from radiological images (for example, see figure 2); however, they are significantly inferior in quality to the data available from anatomical atlases. The brain model should contain the brain parenchyma, ventricles and tumour (if present) that need to be identified in radiological images (in practice, magnetic resonance images).

The accuracy of neurosurgery is not better than 1 mm [3]. Voxel size in high quality pre-operative MR images is usually of similar magnitude. Therefore, we can conclude that patient-specific models of the brain geometry can be constructed with approximately 1-mm accuracy, and that higher accuracy is probably not required.

A necessary step in the development of the numerical model of the brain is the creation of a computational grid which in most practical cases is a finite element mesh or a cloud of points required by a meshless method. Because of the stringent computation time requirements, the mesh must be constructed using low order elements that are not computationally intensive. The linear under-integrated hexahedron is the preferred choice.

Many algorithms are now available for fast and accurate automatic mesh generation using tetrahedral elements, but not for automatic hexahedral mesh gen-

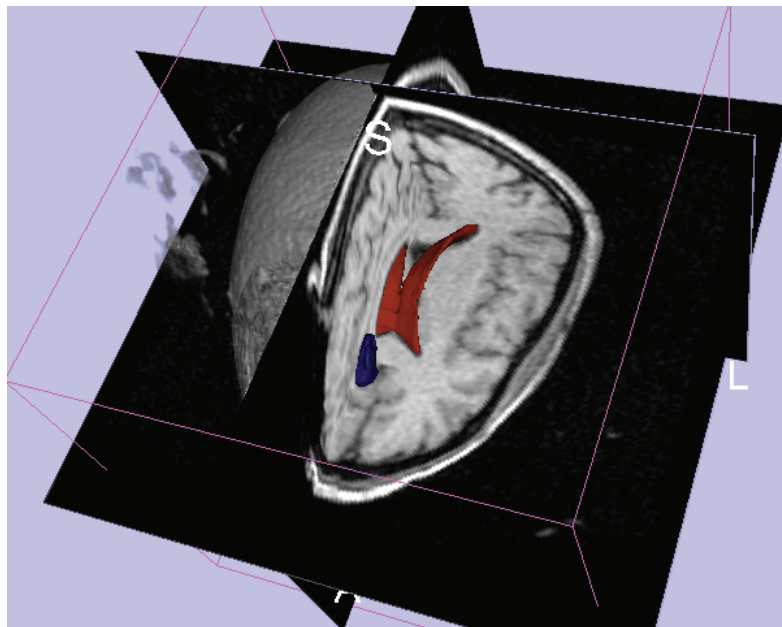


Fig. 2. 3D magnetic resonance image presented as a tri-planar cross-section. Parts of the tumor and ventricles are clearly visible. Public domain software Slicer (www.slicer.org) developed by our collaborators from Surgical Planning Laboratory, Harvard Medical School, was used to generate the image

eration [13]–[15]. Template-based meshing algorithms can be used for meshing different organs using hexahedrons [16]–[18], but these types of algorithms work only for healthy organs. In the case of severe pathologies (such as a brain tumour), such algorithms cannot be used, as the shape, size and position of the pathology are unpredictable. This is one reason why many authors propose the use of tetrahedral meshes for their models [4], [5], [19], [20]. In order to automate the simulation process, mixed meshes having both hexahedral and linear tetrahedral elements are the most convenient (see figure 3).

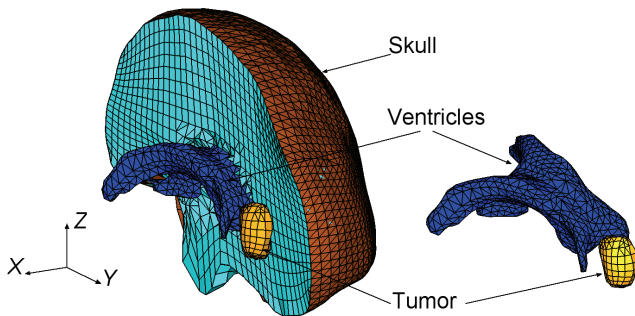


Fig. 3. Patient-specific hexahedron-dominant brain mesh, including ventricles and tumor

The under-integrated hexahedral elements require the use of an hourglass control algorithm in order to eliminate the instabilities, known as zero energy modes, which arise from the single-point integration. One of the most popular and powerful hourglass control algorithms, that is currently available in many commercial software finite element packages, is that proposed in [21]. This method is applicable to hexahedral and quadrilateral elements with arbitrary geometry undergoing large deformations. We adapted

this method to the Total Lagrangian Formulation so that many quantities involved can be pre-computed [22], making the hourglass control mechanism very efficient from the computational point of view.

In the modelling of incompressible continua, artificial stiffening (often referred to as volumetric locking) affects many standard elements, including the linear tetrahedral element, see, e.g., [23]. This phenomenon occurs also for nearly incompressible materials and therefore introducing slight compressibility does not solve the problem. A number of improved linear tetrahedral elements with anti-locking features have been proposed by different authors [24]–[27]. The average nodal pressure (ANP) tetrahedral element proposed in [24] is computationally inexpensive and provides much better results for nearly incompressible materials compared to the standard tetrahedral element. Nevertheless, one shortcoming of the ANP element and its implementation in a finite element code is the handling of interfaces between different materials. We extended the formulation of the ANP element so that all elements in a mesh are treated in the same way, requiring no special handling of the interface elements [28].

An alternative to using the finite element method is to use our recently developed Meshless Total Lagrangian Explicit Dynamics algorithm (MTLED) [29]. The problem of computational grid generation disappears as one needs only to drop a cloud of points into the volume defined by a 3D medical image [30]–[35], see figure 4.

The use of meshless methods is motivated by simple, automatic computational grid generation for patient-specific simulations. We use a modified Element-Free Galerkin method [29] that is meshless in the sense that deformation is calculated at nodes that

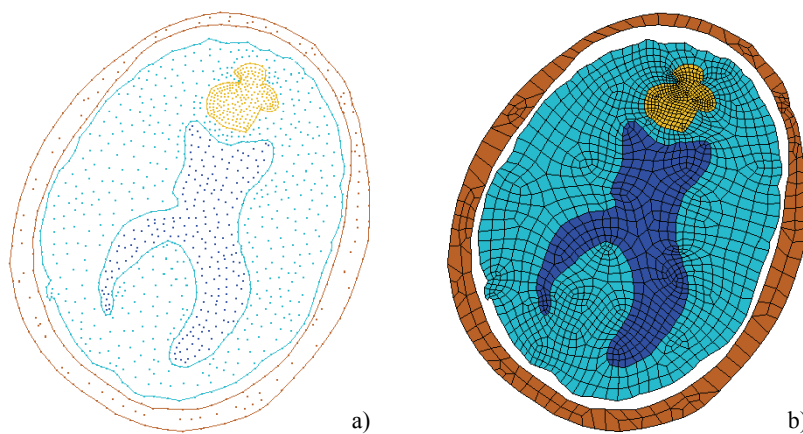


Fig. 4. A 2D slice of the brain discretised by nodes of MTLED [29] method (a); and quadrilateral finite elements (b). Development of a good-quality finite element mesh is time-consuming. Generation of the meshless grid is almost instantaneous

are not any part of an element mesh. Node placement is almost arbitrary. Volumetric integration is performed over a regular background grid that does not conform to the simulation geometry.

2.2. Boundary conditions

The formulation of appropriate boundary conditions for computation of brain deformation constitutes a significant problem because of complexity of the brain–skull interface, see figure 5.

almost independent of the mesh density of the skull surface.

2.3. Loading

We advocate loading the models through imposed displacements on the model surface [7], [41], [44], see figure 6. In the case of neurosurgical simulation, this loading will be imposed by a known motion of a surgical tool. In the case of intra-operative image registration, the current (intra-operative) position of the

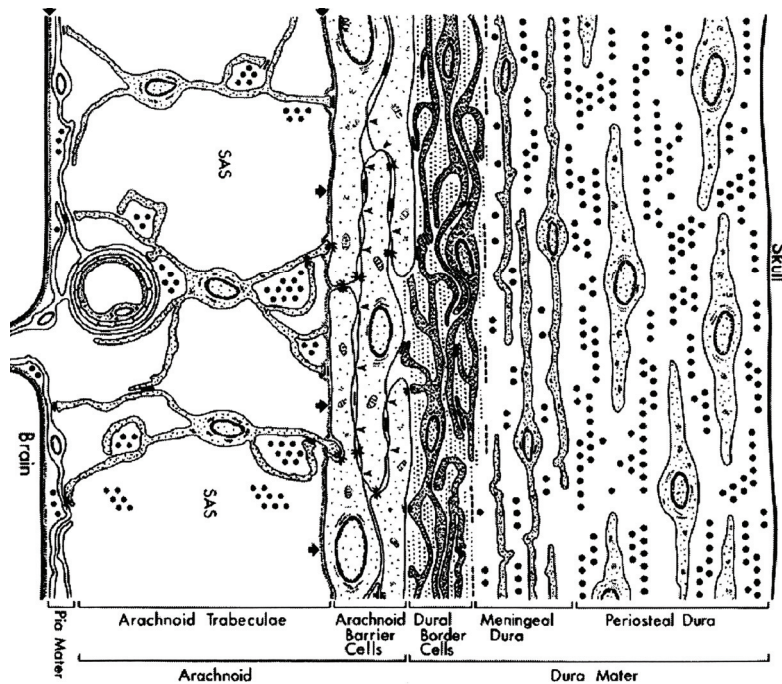


Fig. 5. Structure of the brain–skull interface, adapted from [36]

A number of researchers fix the brain surface to the skull [37], [38]. We do not recommend this approach. Our experience [7], [39]–[42] suggests that a small gap between the brain and the skull allows the motion of the brain within the cranial cavity. Therefore a simple and effective model of the brain–skull interface is a frictionless contact that allows separation.

As the skull is orders of magnitude stiffer than the brain tissue, its rigidity can be assumed. In order to handle the brain–skull interaction we developed a very efficient algorithm that treats this interaction as a finite sliding, frictionless contact between a deformable object (the brain) and a rigid surface (the skull) [43]. Unlike contacts in commercial finite element solvers (e.g. ABAQUS, LS-DYNA), our contact algorithm has no configuration parameters (as it only imposes kinematic restrictions on the movement of the brain surface nodes) and is very fast, with the speed

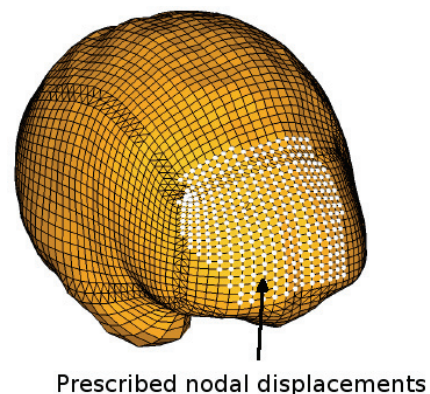


Fig. 6. Model loading through prescribed nodal displacements at the exposed brain surface

exposed part of the brain surface can be measured using a variety of techniques [45]. This information can then be used to define model loading.

As suggested in papers [44], [46]–[48] for problems where loading is prescribed as forced motion of boundaries, the unknown deformation field within the domain depends very weakly on the mechanical properties of the continuum. This feature is of a great importance in biomechanical modelling where there are always uncertainties in patient-specific properties of tissues.

2.4. Mechanical properties of brain tissue

Experimental results show that the mechanical response of brain tissue to external loading is very complex. The stress–strain relationship is non-linear with the stiffness of the brain in compression much higher than in extension. There is also a non-linear relationship between stress and strain rate. To account for such complicated mechanical behaviour we proposed the Ogden-based hyper-viscoelastic constitutive model of the following form [49], [50]:

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

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

where W is the strain energy, $\lambda_1, \lambda_2, \lambda_3$ are the principal extensions, α is a material coefficient without physical meaning. We identified the value of α to be -4.7 (see table 1). t and τ denote time. Equation (2) describes viscous response of the tissue. μ_0 is the instantaneous shear modulus in the undeformed state. τ_k are characteristic relaxation times.

The material constants (identified from experiment) are given in table 1.

One advantage of the model proposed is that the implementation of the constitutive equation presented here is already available in commercial finite element software [51]–[53] and can be used immediately for larger scale computations.

It is important to examine the simplifying assumptions behind the model described by equations (1) and (2), and table 1: *incompressibility* and *isotropy*.

1. *Incompressibility*. Very soft tissues are most often assumed to be incompressible, see, e.g., [54]–[60]. In experiments on brain tissue at moderate strain rates, we have not detected a departure from this assumption [61].

2. *Isotropy* (i.e. mechanical properties are assumed to be the same in all directions). Very soft tissues do not normally bear mechanical loads and do not exhibit directional structure (provided that the sample considered is large enough: for the brain we used the samples of 30-mm diameter and 13 mm in height). Therefore, they may be assumed to be initially isotropic, see, e.g., [49], [54], [60], [62]–[67].

Average properties, such as those described above, are not sufficient for patient-specific computations of stresses and reaction forces because of the very large variability inherent to biological materials. This is clearly demonstrated in the biomechanics literature, see e.g., [49], [50], [68], [69]. Unfortunately, despite recent progress in elastography using ultrasound [70] and magnetic resonance [71], [72], reliable methods of measuring patient-specific properties of the brain are not yet available.

2.5. Solution algorithms

The algorithms implemented in the great majority of commercial finite element programs use the Updated Lagrangian formulation, where all variables are referred to the current (i.e. from the end of the previous time step) configuration of the system (Ansys [73], ABAQUS [51], ADINA [74], LS-DYNA [52], etc.). The advantage of this approach lies in the simplicity of incremental strain description and low internal memory requirements. The disadvantage is that all derivatives with respect to spatial coordinates must be recomputed in each time step, because the reference configuration is changing.

We use the Total Lagrangian Formulation, where all variables are referred to the original configuration of the system. The decisive advantage of this formulation is that all derivatives with respect to spatial coordinates are calculated with respect to the original configuration and therefore can be pre-computed – this is particularly important for time-critical applica-

Table 1. List of material constants for the constitutive model of brain tissue, equations (1) and (2), $n = 2$ [49]

Instantaneous response	$k = 1$	$k = 2$
$\mu_0 = 842$ (Pa) $a = -4.7$	characteristic time $t_1 = 0.5$ (s) $g_1 = 0.450$	characteristic time $t_2 = 50$ (s) $g_2 = 0.365$

tions such as surgical simulation and intra-operative image registration.

Because biological tissue behaviour can be described in general using hyper-elastic or hyper-viscoelastic models, such as that given in equations (1) and (2), the use of the Total Lagrangian Formulation also leads to a simplification of material law implementation as these material models can easily be described using the deformation gradient.

The integration of equilibrium equations in the time domain can be done using either implicit or explicit methods [75]–[77]. The most commonly used implicit integration methods, such as Newmark’s constant acceleration method, are unconditionally stable. This implies that their time step is limited only by the accuracy considerations. However, the implicit methods require the solution of a set of non-linear algebraic equations at each time step. Furthermore, iterations need to be performed for each time step of implicit integration to control the error and prevent divergence. Therefore, the number of numerical operations per each time step can be of three orders of magnitude larger than that for explicit integration [75].

On the other hand, in explicit methods, such as the central difference method, treatment of non-linearities is very straightforward and no iterations are required. By using a lumped (diagonal) mass matrix [75], the equations of motion can be decoupled and no system of equations must be solved. Computations are done at the element or support domain level eliminating the need for assembling the stiffness matrix of the entire model. Thus, the computational cost of each time step and internal memory requirements for explicit integration are substantially smaller than those for implicit integration. There is no need for iterations anywhere in the algorithm. These features make explicit integration suitable for real time applications.

However, the explicit methods are only conditionally stable. Normally, a severe restriction on the time step size has to be included in order to receive satisfactory simulation results. Stiffness of soft tissues is very low [49], [50], [64], [78], e.g. stiffness of the brain is of about eight orders of magnitude lower than that of common engineering materials such as steel. Since the maximum stable time step is (roughly speaking) inversely proportional to the square root of Young’s modulus divided by the mass density [52], it is possible to conduct simulations of brain deformation with much longer time steps than in typical dynamic simulations in engineering. This was confirmed by our previous simulations of brain shift using the commercial finite element solver LS-DYNA [7], [40]. Therefore, when developing the suite of finite element

algorithms for computation of brain tissue deformation, we combined Total Lagrange Formulation with explicit time integration.

A detailed description of the Total Lagrange Explicit Dynamics (TLED) algorithm is presented in [79]. The main benefits of the TLED algorithm are:

- the possibility of pre-computing many variables involved (e.g. derivatives with respect to spatial coordinates and hourglass control parameters),
- no accumulation of errors – increased stability for quasi-static solutions,
- easy implementation of the material law for hyper-elastic materials using the deformation gradient,
- straightforward treatment of non-linearities,
- no iterations required for a time step,
- no system of equations needs to be solved,
- low computational cost for each time step.

3. Application example

3.1. Modelling the brain for image registration – computer simulation of the brain shift

A particularly exciting application of non-rigid image registration is in intra-operative image-guided procedures, where high resolution pre-operative scans are warped onto sparse intra-operative ones [6], [80]. We are in particular interested in registering high-resolution pre-operative MRI with lower quality intra-operative imaging modalities, such as multi-planar MRI and intra-operative ultrasound. In achieving the accurate matching of these modalities, accurate and fast algorithms to compute tissue deformations are fundamental.

Here we present the examples of computational results of brain shift. To account for various types of situations that occur in neurosurgery, we analyzed five cases of craniotomy-induced brain shift with tumor (and craniotomy) located anteriorly (cases 1 and 2), laterally (case 3) and posteriorly (cases 4 and 5) (figure 7). For the cases studied the maximum craniotomy-induced displacement of the cortical surface, as observed on intra-operative MR images, was about 7.7 mm. Three-dimensional patient-specific brain meshes were constructed from the segmented pre-operative magnetic resonance images (MRIs). The segmentation was done using seed growing algorithm followed, in some cases, by manual corrections (fig-

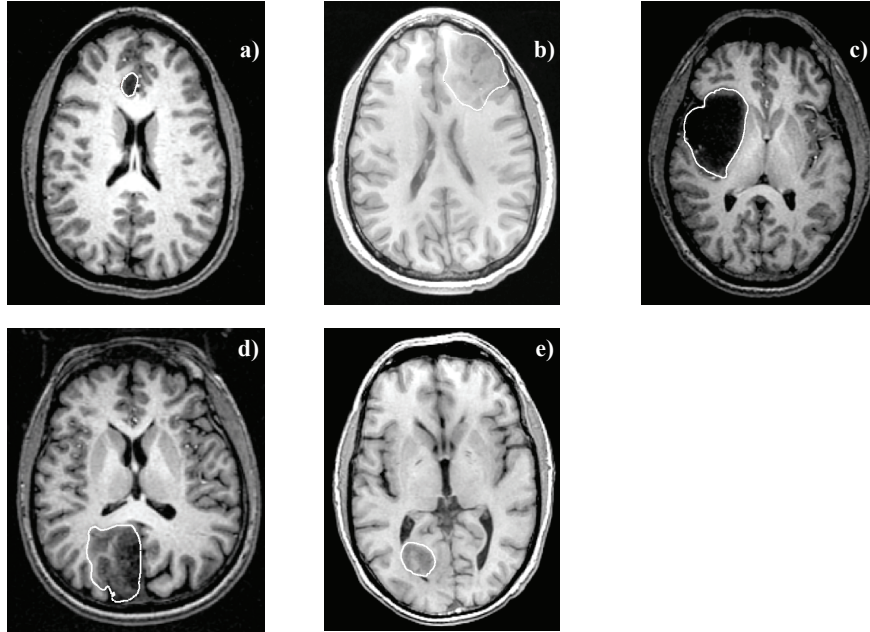


Fig. 7. Preoperative T1 MRIs (inferior view) showing tumor location in the cases analysed in this study. White lines indicate the tumor segmentations. a) Case 1, b) Case 2, c) Case 3, d) Case 4, and e) Case 5

Table 2. Summary of the patient-specific brain meshes built in this study

	Case 1	Case 2	Case 3	Case 4	Case 5
Number of hexahedral elements	14447	10258	10127	9032	8944
Number of tetrahedral elements	13563	20316	23275	23688	21160
Number of nodes	18806	15433	15804	14732	14069
Number of degrees of freedom	55452	45315	46896	43794	42018

ure 7). A detailed presentation of the meshes' properties is given in table 2.

A neo-Hookean material model was used for the brain tissue and tumor. Based on the published experimental data [49] a value of 3000 Pa was used for the Young's modulus of parenchyma. The Young's modulus of the tumor was chosen two times larger than that of the parenchyma, which is consistent with the experimental data of SINKUS et al. [71]. Following [7], we used Poisson's ratio of 0.49 for the brain parenchyma and tumor. It is worth noting that, as the model was loaded with the enforced motion of the exposed part of the surface of the brain, the resulting displacement field is almost insensitive to the mechanical properties of brain tissue. This is an important result that allows using biomechanical models for intraoperative image registration without knowing precisely patient-specific properties of the tissue [41].

Universally accepted "gold standards" for validation of nonrigid registration techniques have not been developed yet [81]. Objective metrics of the images' alignment can be provided by automated methods using image similarity metrics (such as, e.g., Mutual Information and Normalized Cross-Correlation). One

of the key deficiencies of such metrics is that they quantify the alignment error in terms that do not have any straightforward geometrical (in Euclidean sense) interpretation.

To provide an error measure that enables such interpretation, we compared X , Y and Z bounds of the ventricles determined from the intraoperative segmentations and obtained by registration (i.e. warping using the predicted deformation field) of the preoperative data. The bounds provide six numbers that can be geometrically interpreted as the X , Y and Z coordinates of vertices P_1 and P_2 defining a cuboidal box bounding the ventricles (see figure 8). The difference between the coordinates of these vertices determined from the intraoperative MRIs and predicted by our biomechanical models was used as a measure of the alignment error. The coordinates of the vertices P_1 and P_2 can be determined automatically, which makes such difference less prone to subjective errors than the measures based on anatomical landmarks selected by experts. We provide no error measure for the tumor registration as we were not able to quantify reliably the intra-operative bounds of tumors due to limited quality of the intra-operative images.

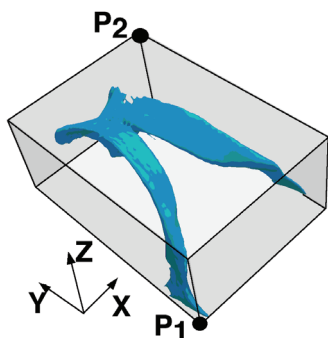


Fig. 8. Definition of ventricles' bounds. Vertices P_1 and P_2 define a cuboidal box that bounds the ventricles. The box faces are formed by planes perpendicular to X , Y and Z axes

The computation times on a PC (Intel E6850 dual core 3.00 GHz processor, 4 GB of internal memory, and Windows XP operating system) varied from 30 s (Case 1) to 38 s (Case 5). Following our earlier work

[82] on the application of Graphics Processing Units (GPUs) to scientific computations, we also implemented our algorithms using the NVIDIA Compute Unified Device Architecture (CUDA). Non-trivial details of this implementation are given in [83]. For the NVIDIA CUDA implementation of our algorithms, the computation times were shorter than 4 s for all the craniotomy cases analyzed in this study. The maximum errors when predicting the intraoperative bounds of the ventricles were 1.6 mm in X (lateral) direction, 1.6 mm in Y (i.e. anterior–posterior) direction and 2.2 mm in Z (inferior–superior) direction (table 3). These errors compare well with the voxel size ($0.86 \times 0.86 \times 2.5 \text{ mm}^3$) of the intraoperative images. A qualitative comparison of the contours of ventricles and tumor (predicted by the finite element brain models developed in this study) with the intraoperative images shows a remarkably good agreement (figure 9).

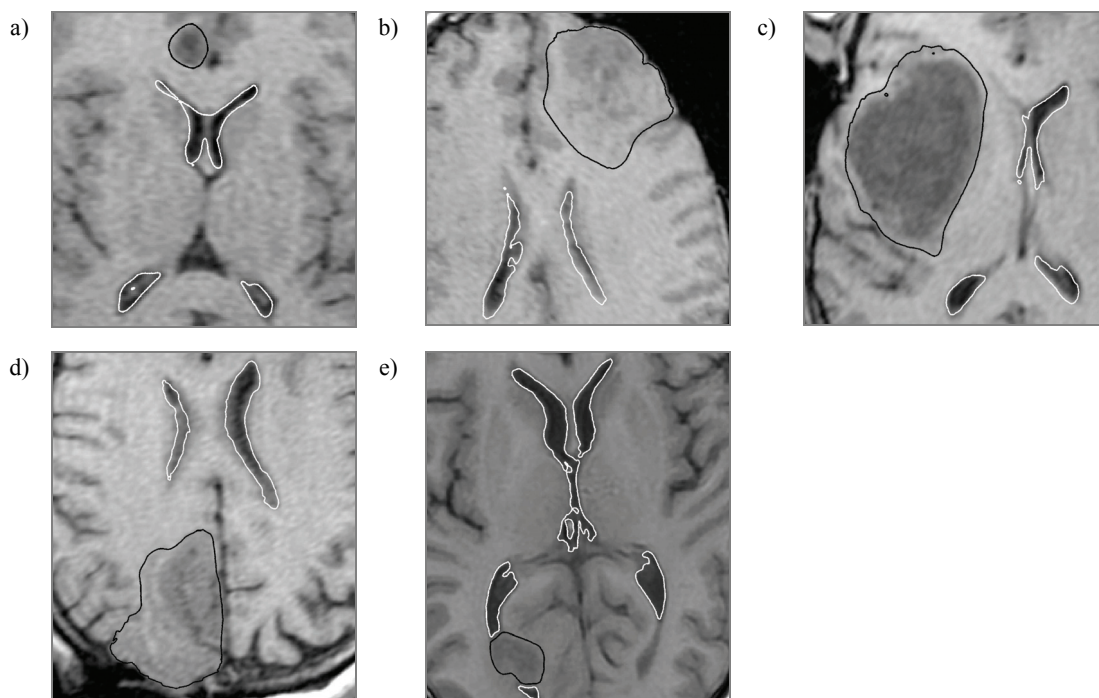


Fig. 9. The registered (i.e. deformed using the calculated deformation field) preoperative contours of ventricles and tumor are imposed on the intraoperative images. The images were cropped and enlarged. a) Case 1, b) Case 2, c) Case 3, d) Case 4, and e) Case 5

Table 3. Error in predicting the X , Y , and Z coordinates (in millimeters) of vertices P_1 and P_2 defining the bounds of the ventricles in the intraoperative MRIs (see figure 8). The directions of the X , Y , and Z axes are as in figure 8. The numbers in bold font indicate the maximum errors

	X coordinate error (mm)		Y coordinate error (mm)		Z coordinate error (mm)	
	P_1	P_2	P_1	P_2	P_1	P_2
Case 1	0.3	0.2	0.7	1.3	0.7	0.2
Case 2	0.0	0.5	1.2	0.5	0.6	0.5
Case 3	1.6	0.4	0.6	1.6	2.2	0.1
Case 4	0.5	0.0	0.5	0.4	0.1	0.7
Case 5	0.1	0.4	0.5	1.5	1.1	0.4

In table 3, the computation results are presented to one decimal place as it has been reported in the literature [7] that this is approximately the accuracy of finite element computations using the type of finite element algorithms applied in this study.

State-of-the-art image analysis methods, such as those based on optical flow [84], [85], mutual information-based similarity [86], [87], entropy-based alignment [88], and block matching [89], [90], work perfectly well when the differences between images to be co-registered are not too large. It can be expected that the non-linear biomechanics-based model supplemented by appropriately chosen image analysis methods would provide a reliable method for brain image registration in the clinical setting.

4. Conclusions

Computational mechanics has led to a better understanding and greater advances in modern science and technology [1]. It is now in a position to make a similar impact in medicine. We have discussed modelling approaches to two applications of clinical relevance: surgical simulation and neuroimage registration. Mechanical terms such as displacements and forces can be used to characterise these problems, and therefore the standard methods of continuum mechanics can be applied. Moreover, similar methods may be used for modelling the development of structural diseases of the brain [42], [91]–[93].

Because of the large displacements involved (from ca 10 to 20 mm in the case of a brain shift) and the strongly non-linear mechanical response of tissue to external loading, we use non-linear finite element procedures for the numerical solution of the models proposed.

The complicated mechanical behaviour of the brain tissue, i.e. non-linear stress–strain and stress–strain rate relationships and much lower stiffness in extension than in compression, requires sophisticated constitutive models for some applications. The selection of the constitutive model for surgical simulation problems is made based on the characteristic strain rate of the process to be modelled and, to a certain extent, on computational efficiency considerations. Fortunately, for intra-operative image registration, the precise knowledge of patient-specific mechanical properties of brain tissue is not required [41].

A number of challenges still prevent the wide acceptance of Computer-Integrated Surgery systems based on computational biomechanical models. As we

deal with individual patients, methods to produce patient-specific computational grids quickly and reliably must be improved. Substantial progress in automatic meshing methods is required, while meshless methods may provide an alternative solution. Computational efficiency is an important issue, as intra-operative applications, requiring reliable results within approximately 40 seconds, are most appealing. The use of the Total Lagrangian Formulation of the finite element method [76], [79], where all field variables are related to the original (known) configuration of the system and therefore most spatial derivatives can be calculated before the simulation commences, during the pre-processing stage, offers such a possibility. Implementation of these algorithms in graphics processing units leads to computation times well within the limits required for intra-operative applications.

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