Serial Registration of Intraoperative MR Images of the Brain

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The increased use of image-guided surgery systems during neurosurgery has brought to prominence the inaccuracies of conventional intraoperative navigation systems caused by shape changes such as those due to brain shift. We propose a method to track the deformation of the brain and update preoperative images using intraoperative MR images acquired at different crucial time points during surgery. We use a deformable surface matching algorithm to capture the deformation of boundaries of key structures (cortical surface, ventricles, and tumor) throughout the neurosurgical procedure, and a linear finite element elastic model to infer a volumetric deformation. The boundary data is extracted from intraoperative MR images using a real-time intraoperative segmentation algorithm. The algorithm has been applied to a sequence of intraoperative MR images of the brain exhibiting brain shift and tumor resection. Our results characterize the brain shift after opening of the dura and at the different stages of tumor resection, and brain swelling afterwards. Analysis of the average deformation capture was assessed by comparing landmarks identified manually and the results indicate an accuracy of $0.7 \pm 0.6$ mm (mean ± standard deviation) for boundary surface landmarks, of $0.9 \pm 0.6$ mm for landmarks inside the boundary surfaces, and $1.6 \pm 0.9$ mm for landmarks in the vicinity of the tumor.

1. Introduction

1.1. Role of registration during surgery

Image guided neurosurgery systems are increasingly being used in the operating room (OR), and have been shown to improve surgical visualization and navigation, and to reduce post-surgery remaining tumor (Jolesz, 1997; Knauth et al., 1999). To improve visualization of salient characteristics, image-guided neurosurgery relies on the registration of pre-operative images (magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), etc.) with the patient’s position in the OR (Peters et al., 1996). This can be done using a stereotactic frame (Kelly, 1986), or with frameless registration systems (Zamorano et al., 1992; Zinreich et al., 1993; Grimson et al., 1996). After registration, it is possible to visualize, and navigate into the anatomy of the patient in a coordinate system consistent with the position of the patient during surgery.

However, during surgery deformation of the brain occurs, leading to misalignment between the subject and the preoperative images. The major factors influencing this deformation include (Roberts et al., 1998; Paulsen et al., 1999; Nimsky et al., 2000; Naba vi et al., 2001):

- physical manipulation of the brain: dura opening, retraction and resection, draining and leakage of the cerebrospinal fluid (CSF) and,
- physiological reactions of the brain due to the properties of living tissue: anaesthetics and osmotic agents, as well conditions which are different from normal state.

The opening of the dura and cerebrospinal fluid...
(CSF) leakage cause a gravitational shift that is due to the disappearance of tension and pressure forces at the brain and ventricular boundaries (Bucholz et al., 1997; Hill et al., 1998; Maurer et al., 1998; Nabavi et al., 2001). Tissue retraction places brain tissue under constraint, while tissue resection consists of removing tissue, and both cause deformations of neighboring brain tissue (Roberts et al., 1998; Nabavi et al., 2001; Miga et al., 2001). Drugs the anaesthesiologist may administer to the patient can change the blood pressure and hydrate or dehydrate the brain, causing it to swell or to shrink (Roberts et al., 1998; Paulsen et al., 1999).

These factors lead to surface and body forces that deform the brain during surgery. As a result, cortical surface shifts ranging between 1.2 mm and 20 mm have been observed (Nabavi et al., 2001; Roberts et al., 1998), while subsurface shift can range up to 7 mm at the level of the lateral ventricles and the mid-hemispheric plane (Hill et al., 1998; Roberts et al., 1998; Hata et al., 2000; Nimsky et al., 2000; Nabavi et al., 2001).

Recently, using intraoperative MR images, studies (Nimsky et al. (2000); Nabavi et al. (2001)) demonstrated that these deformations develop and aggregate over the course of surgery, while they remain unrecognized by navigational systems. Beside the intraoperative shift due to CSF drainage and leaking, the other deformations induced by physical manipulation of the brain (e.g. tumor resection) compound and continuously change the brain shape. To be able to follow and understand these deformations, as well as to update preoperative images, it is necessary to perform imaging at crucial time points during surgery. Simply interpolating deformation from pre-operative and single post- or intraoperative images cannot be used to understand how the brain deforms across the entire course of a typical neurosurgery.

All these studies demonstrate that the accuracy of image-guided surgical navigation based upon preoperative images is seriously compromised over the course of surgery by intraoperative brain deformation at the cortical surface level as well as in subcortical regions of the brain. It is therefore of great importance for the image-guided neurosurgical systems to be able to correct for these deformations, and update preoperative images and planning according to the shape changes of the brain during surgery.

Prior to the surgical procedure, high quality images (MRI, CT, PET, functional MRI, digital subtraction angiography, etc.) are acquired for planning the surgery, but the data that can be acquired during the procedure is often less complete and less detailed. This data can be in the form of intraoperative MRI (IMRI), CT (ICT), ultrasound (IUS), or through fiducial markers.

Previous algorithms developed to capture brain deformation for neurosurgery can be categorized as those that deform preoperatively acquired images using image-based models and those using biomechanical simulation models. Image-based models are typically used when intraoperative image acquisition is available. The main challenge with those methods is that they require an image similarity criterion which is capable of tackling issues related to the limited contrast and spatial resolution of the intraoperatively acquired images, and problems due to intensity discontinuities with respect to preoperative images.

The following sections will first review methods that have been developed for the general purpose of non-rigid image registration, and outline the limitations of such techniques in the context of intraoperative registration (subsection 1.2). The next sections cover current image-based registration techniques that have been proposed for intraoperative registration (subsection 1.3) and biomechanical models that have been developed for correction and prediction of brain shift (subsection 1.4).

### 1.2. Review of Image Registration Methods

Much effort has been devoted to the non-rigid registration of images. There are two main components needed for doing this: an image similarity criterion and a regularization constraint that serves as an interpolation function between local image structure that is deformed using the image similarity criterion. Early work for recovering image deformation was based on the minimization of the sum of squared differences (SSD) between the images to be matched using a quadratic regularizer (Horn and Schunck, 1981). Successive evolutions of similar techniques have been proposed, and are often being referred to as optical flow methods (see Bauchemin and Barron (1995) for a complete review). Dengler and Schmidt (1988a) first proposed to minimize SSD in a multiresolution fashion with smoothing as a regularization constraint,
allowing to speed up the computations and to robustly capture larger deformations.

However, such methods tend to only establish correspondences between local image structures and arbitrarily interpolate between these, without accounting for prior knowledge one has about the behavior of the objects represented by the image, which can help produce a volumetric mapping which is closer to reality. Selecting a physics-based model for the deformation between local image structures imposes an additional constraint on the deformation. For instance, a rigid part of the body represented by the image will rather translate or rotate than smoothly bend to accommodate the deformation of the image data. To take advantage of prior knowledge one has about the objects represented by the image, Broit (1981) first proposed to model the image as an elastic object. Exploiting a suggestion of Dengler and Schmidt (1988a), Bajcsy and Kovacic (1989) and Gee et al. (1993) subsequently implemented multiresolution versions of Broit’s system where the deformation of the image proceeds step-by-step in a coarse to fine strategy, improving the robustness of the technique. The elastically deformable volumes have become a very active area of research and have been extended to viscous fluid deformable volumes (Christensen, 1994; Bro-Nielsen and Gramkow, 1996; Christensen et al., 1997) in an attempt to overcome the small deformation assumptions inherent in the linear elastic formulations.

Such methods assume constant intensity between the images to be matched. To circumvent that problem, methods have been proposed so as to be able to cope with images imaged with different parameters or modalities (e.g. Guimond et al. (2001)).

Similarity metrics allowing images from different modalities to be non-rigidly matched have also been proposed, such as mutual information (e.g. (Maintz et al., 1998; Gaens et al., 1998; Rueckert et al., 1999; Thiran and Butz, 2000)), and normalized cross-correlation (e.g. (Bajcsy and Kovacic, 1989; Collins et al., 1994; Rexilius and Warfield, 2001)). An issue for the design of a similarity metric suitable for intraoperative matching is the need to incorporate a method for dealing with significant discontinuities in intensities of the images from which the deformation field needs to be estimated. Only a few reports have approached this issue (Dengler and Schmidt, 1988b; Kaus, 2000).

Other authors have proposed to use deformable surface models in conjunction with a physics-based model to infer a volumetric deformation field from surface-based deformations (e.g. (Davatzikos, 1997; Thompson and Toga, 1996)) that provide a way to match boundaries of common image structures in the images.

Another class of registration methods using physical-based models to constrain image registration is those using statistical shape information of the objects to be matched (e.g. (Wang and Staal, 2000; Papademetris et al., 1999a)). These methods use statistical boundary shape information to match images and appear to be less sensitive to noise, while significantly improving non-rigid registration.

The cardiac image analysis community has also used physics-based constraints - primarily FEM formulations - that they deform with image-derived forces. These models then provide quantitative, and physically interpretable 3D deformation estimates from image data. Papademetris et al. (1999b) derive the forces they apply to the FE model from Ultrasound (US) images using deformable contours they match from one image to the next one using a shape-tracking algorithm. Metaxas (1997) derives forces from MRI-SPAMM data for doing motion analysis of the left or right ventricle (Park et al., 1996; Haber et al., 1998). These approaches fit a generic parameterized FEM onto the image sequence before doing the analysis, and are used as deformation analysis tools rather than for doing non-rigid registration.

1.3. Intraoperative registration methods

Relatively little work has addressed the challenge of intraoperative volumetric brain image alignment. There are two main issues when matching intraoperative images to pre-operative images:

- **Intensity variations** between the pre-operative and intraoperative images or between the intra-operative images themselves. These contrast variations can be due to the image acquisition: different imaging parameters, the presence of objects distorting the magnetic field, etc. The variations can also be caused by the injection of contrast agents during the procedure, which can change the intensity distribution of similar tissues.
Disappearance of image parts also causes important intensity differences between preoperative images and intraoperative images as well as between intraoperative images. The opening of the skull and the dura cause several parts of the brain to be removed on the image, creating black holes, and thus sudden discontinuities at some locations in the image sequence. The same problem occurs when retraction and resection start, creating black gaps within the brain tissue. Such discontinuities may lead to estimation of implausible deformations when matching an earlier image onto that acquired after skull or dura opening, or after tissue retraction or resection.

Our laboratory has had extensive experience with image-based matching models for a variety of brain matching applications (Warfield et al., 1995; Warfield, 1996; Nakajima et al., 1997; Hata et al., 1998; Warfield et al., 1999; Ferrant et al., 1999b; Hata et al., 2000; Kaus, 2000; Ruiz-Alzola et al., 2001; Rexilius and Warfield, 2001). However, in the context of intraoperative brain matching, such methods have not yet been able to provide a robust and clinically applicable solution. Using a volumetric optical flow approach, Hata et al. (2000) showed that because of the varying contrast intensity of the intraoperative images, the method was performing best when the skin was segmented out before applying the matching method. The method was only applied on intra-operative images acquired under similar conditions, and no experiments to match pre-operative data onto intraoperative data were carried out. Also, only images acquired intraoperatively before and after opening of the dura mater were considered, and therefore discontinuities caused by surgically induced deformations (such as tissue resection) are not being dealt with.

Previous experience using multi-modal image similarity criteria (i.e. mutual information (MI), see Hata et al. (1998); Hata (1998)) has also shown that this cannot fully solve the contrast variation problems either. Hastreiter et al. (2000) propose to use a MI based matching algorithm, but the images need to be acquired under very similar conditions for the algorithm to work. For improved visualization of the brain shift, they use a deformable surface model. Hill et al. (1999) use a B-spline deformation model and MI as a similarity criterion. In order to correct for different intensity gains in the intraoperative images, they iteratively determine an intensity scale value that minimises the mean square difference in voxel intensities. However, motion around control points is independent, and therefore, the model does not yield physics-based constraints on the deformation field. Also, there is no consideration about tissue resection, and the obtained deformation fields therefore do not reflect actual physical deformations.

It is only recently that biomechanical models (i.e. linear elasticity models discretized using the Finite Element (FE) Method) have been explicitly proposed to constrain image registration (Kyriacou et al., 1999; Hagemann et al., 1999). In these studies, the deformation from one image to the next is enforced by manually, or semi-automatically defining correspondences between contours in the images to register. The biomechanical model is then used to infer a deformation field in the rest of the image. Their advantage is that they propose a physics-based interpolation between features that are brought into correspondence in two images. Differences in material properties included in the biomechanical model (such as hard/soft materials, anisotropy, etc.) can therefore be used to constrain the interpolation between image-based correspondences in a physically plausible way. Also, by establishing correspondences between image structures in a different way than with a similarity measure computed all over the image volume, one can provide the deformation model with physically better constrained deformations. The current disadvantages of these methods is that they have only been tested in 2D, with computations done on a pixel basis by Hagemann et al. (1999), which causes the FE computations to be particularly computationally expensive.

What these examples show is that image based models could be a solution for intraoperative brain matching if image acquisition and contrast variation problems can be solved for. Also, in the case of partial tissue loss or if only part of the volume has been imaged, solutions need to be found so that the image matching models can overcome these issues and still provide physically plausible deformation estimates.
1.4. Intraoperative Registration methods using biomechanical simulation

There has also been a significant amount of work directed towards simulation (see Delinguette (1998) for a review) using models driven by physics-based forces such as gravity. The motivating concept for these models has been to avoid the acquisition of intraoperative images. Miller (1999) proposed a viscoelastic dynamic FE model capable of accurately reproducing the actual deformation of brain tissue under compression levels reaching 30% and for loading velocities varying over five orders of magnitude. Such a model is very promising, but to our knowledge, no simulations have been performed to simulate the behavior of brain tissue during surgery.

Skrinjar and Duncan (1999) have proposed a model consisting of mass nodes interconnected by Kelvin models\(^2\) to simulate the behavior of brain tissue under gravity, with boundary conditions to model the interaction of the brain with the skull. Recently, they proposed steps towards automatic intraoperative update of pre-operative images using stereo camera images of the intraoperative shift (Skrinjar et al., 2001). The shift measured with the stereo cameras is then imposed as a boundary condition to the brain model in order to produce a volumetric mapping that can serve to update pre-operative images.

Paulsen et al. (1999) and Miga et al. (1999) proposed a FE model based on consolidation theory where the brain is modeled as an elastic body with an interstitial fluid. They also use gravity induced forces, as well as experimentally determined boundary conditions. In a later study (Miga et al., 2000b), an attempt towards modeling the postoperative behavior of tissue resection was done by adding a depression stress at the boundaries of the resected cavity. A further extension by this group has investigated modeling retraction and resection (Miga et al., 2001). Retraction is modeled by applying boundary conditions, and retraction is modeled by the deletion of mesh elements. This work is a promising post-operative simulation of the behavior of these neurosurgical events. However, this work does not yet incorporate intraoperative force measurements so as to effectively validate their model. Also, in order to generate their segmentations and FE mesh from pre-operative images they report up to five hours operator input and over 25 minutes of running time for the simulations they carry out (Miga et al., 2001).

Even though these models are very promising, it remains difficult to accurately estimate all the forces and boundary conditions that interact with the model, especially during the course of surgery. For instance, it is very difficult to model the shrinking of the lateral ventricles during brain shift. This phenomenon is probably due to a pressure change of the cerebrospinal fluid (CSF) inside the ventricles, but it is extremely complicated to effectively measure this pressure continuously during neurosurgery. Also, only the state of the brain before and after opening of the dura has been considered so far in most studies, therefore not considering the dynamic evolution of the shape of the brain during surgery.

Finally, even if all biomechanical parameters could be measured, the brain deformation is also partly caused by physiologic changes induced by surgery, and hence the patient physiology would most likely need to be modelled accurately in order to demonstrate accurate prediction of brain deformation. Such models will be challenging to develop. As an alternative to such models, we have explored the use of intraoperative imaging to provide the information necessary to enable reliable and accurate updates of pre-operative images.

1.5. Proposed solution

To correct for intraoperative brain deformation and characterize the shape changes the brain undergoes during surgery, we use a biomechanical finite element (FE) model driven by surface correspondences, which we automatically extract from the intraoperatively acquired MR images. The surface correspondences are computed using a deformable surface matching algorithm that we apply on segmentations of the intraoperative images. The advantage of the method is that it circumvents the contrast variation problem mentioned in section 1.3 by matching image structure using segmentations of the intraoperative images. Body forces could be used here as well to drive the deformation of the model, but we currently have no means to directly measure them. In Ferrant et al. (2001, 2000b), we present an algorithm for registering two intraoperative scans showing only brain shift in the direction of...
gravity after opening of the dura, without any surgically induced deformations. The segmentation of the intraoperative images was done semi-automatically. In this paper, we are tracking the deformation of the brain during an entire surgical procedure by deforming the initial FE brain model successively onto intraoperatively acquired MR images taken at crucial moments during the course of surgery so as to dynamically update preoperative images according to the shape changes the brain has undergone. Matching problems induced by tumor resection are solved by updating our biomechanical brain model accordingly with topological changes. The topological changes are modeled by removing the elements of the FE brain model covering resected areas. Furthermore, we use a new segmentation algorithm capable of doing accurate segmentation of intraoperative scans automatically in a limited amount of time. Finally, so that the algorithm can run within the time constraints of neurosurgery, our algorithms have been optimized and parallelized. Thus our algorithm can cope with all the challenges related to image based matching algorithms, and presents the following features:

- it overcomes the intensity variation problem by using a robust real-time intraoperative segmentation algorithm,
- it automatically computes correspondences between image-based features with a deformable surface matching algorithm,
- it uses a biomechanical model to infer a volumetric deformation field between matched image-based features,
- it overcomes problems related to tissue removal, and can be used with limited intraoperative image data as well.

Our ultimate goal is to update pre-operative images given intraoperative brain deformations at arbitrary stages with less information than described in this study (such as a limited number of slices, or orthogonal slices of CT or MR at critical locations, intraoperative ultrasound (US) images, or surgical localizers). In order to achieve this we need to verify and validate our deformation model. We believe Intraoperative MR imaging (IMRI) is an ideal testbed for this because it provides reasonable contrast and spatial resolution, therefore enabling a thorough validation of the deformation algorithms.

2. Algorithms

In order to successfully capture brain deformation from intraoperative images, we have developed a set of image processing tools that allow us to track the boundary deformation of the images, as well as biomechanical deformation tools that allow us to estimate the volumetric deformation the brain undergoes given boundary deformations. Body forces could readily be included in our model when a reliable mechanism to measure or estimate such forces becomes available. Figure 1 describes our algorithm using a flow diagram. The main idea is that we track the boundary surfaces of key objects as they deform during surgery, and that we use these boundary displacements to infer a volumetric deformation field using a biomechanical model. The volumetric deformation we then obtain can be used to update pre-operative images (e.g. MRI, functional MRI, PET, etc.) so it matches the shape changes that have been induced by surgery.

![Figure 1. Block scheme for our intraoperative deformable tracking and registration algorithm.](image-url)
the vertical line can be executed pre-operatively, and hence more time is available to perform them. The tasks to be executed preoperatively include the extraction from pre-operative images of the objects the neurosurgeon wishes to track and characterize over the course of surgery (typically the brain, the tumor, and the ventricles), and the generation of a FE tetrahedral model of these objects. This model will be deformed during surgery to match the shape changes of the objects it represents. Different biomechanical properties could be assigned to the different objects and the boundary surfaces of these key objects can be extracted from the model.

On the right side of the vertical line of Figure 1, every column depicts the different operations to be carried out during neurosurgery each time a new intraoperative MR scan is acquired. The different boxes are executed from top to bottom: first an intraoperative segmentation of the scan is done to extract the key objects, then the boundary surfaces of the model are deformed to match the shape changes the segmentation reflects, these deformations are eventually used to infer a volumetric deformation field with the biomechanical model, which can be used to update the preoperative scan(s). This sequence of operations depicted by the vertical sequence of boxes is repeated each time a new intra-operative scan is acquired.

Tissue retraction and resection introduce topology or major shape changes for the brain, since tissue is being displaced, cut and removed. Tissue resection is approximated by removing elements of the finite element (FE) model covering retracted and resected areas so as to reflect the changes. The areas of resection appear as black holes within the brain tissue image and are thus easy to segment from the intraoperative images. Those elements of the FE model remaining on the resected areas between the tumor boundary surface and the brain surface are removed to account for the topology change introduced by cutting the brain tissue. Special care has been taken to ensure that the model remains consistent with respect to its earlier configuration, so that deformation can still be characterized from the model at previous time points.

Our algorithm consists of seven main components:

- **Preoperative segmentation**: key objects whose shape will change over the course of surgery are precisely segmented from preoperatively acquired images using the algorithm described by Warfield et al. (2000a),

- **Tetrahedral mesh generation**: an initial FE model of the brain is generated using the preoperative segmentation (Ferrant et al., 1999b, 2000a).

- **Intraoperative segmentation**: the key objects are segmented out intraoperatively each time new images are acquired using the algorithm described by Warfield et al. (2000b).

- **Deformable surface matching**: the boundary surfaces of the key objects in the model are deformed towards the corresponding boundaries in the next image of the sequence (Ferrant et al., 1999a, 2000a) using an improved algorithm that better captures the changes of complicated shapes such as the ventricles.

- **Biomechanical simulation of volumetric deformation**: the obtained displacements of the surfaces are used as boundary conditions to drive our biomechanical model (Ferrant et al., 2000b, 2001).

- **Interpolate deformation field and deform image**: the deformation field of the FE model is interpolated back onto the image grid to deform pre-operative image data so as to update the preoperative planning on the current shape of the brain (Ferrant et al., 2000b, 2001).

- **Tumor resection modeling**: at the stage at which tissue resection starts, based on the intraoperative segmentation of retracted and resected areas, the topology of the FE model is updated so as to reflect the topology changes this induces.

Steps 1 and 2 are executed pre-operatively and can be more time-consuming, while steps 3, 4, 5, 6 are to be executed during the course of surgery, and repeated each time a new scan is acquired. Step 7 is executed each time resection significantly modifies the shape or topology of one of the key objects in the model.

The following sections describe these elements of our algorithm.
2.1. Preoperative segmentation

The primary object the neurosurgeon sees during the surgery is the surface of the brain. It is shape changes of the brain that the neurosurgeon wants to be able to track. As CSF drainage and/or leakage occurs during surgery, shape changes at the brain/ventricle boundary also needs to be modelled. As reported earlier (Ferrant et al., 2000b; Hata et al., 2000; Nabavi et al., 2001), significant shifts and CSF volume losses have been reported at the level of the ventricles, hence it is important to segment the ventricles from the intraoperative image sequence as well. Since tumor tissue will be resected, the surgeon is particularly interested in brain tissue surrounding the tumor. Therefore, the tumor is also segmented from the image sequence. We thus will consider 3 key objects for segmentation: brain tissue, tumor, and ventricular CSF.

Since preoperative data is acquired before surgery, the time available for segmentation is longer. This means we can use segmentation approaches that are robust and accurate but are time consuming and hence impractical to use in the operating room. In our laboratory, preoperative data is segmented with a variety of manual (Gering et al., 1999), semi-automated (Kikinis et al., 1992) or automated (Warfield et al., 1995, 2000a; Kaus et al., 2000) approaches. We select the most robust and accurate approach available for a given clinical application.

2.2. Tetrahedral mesh generation

Within a FE modeling framework, the bodies on which one is working need to be discretized using finite elements, e.g. tetrahedra. As available meshing software did not produce satisfactory results on biomedical structures, we developed our own tetrahedral mesh generation algorithm. Unlike Hagemann et al. (1999), we use elements covering several image voxels so as to limit computational complexity without sacrificing accuracy.

We generate tetrahedral meshes with a multi-resolution volumetric version of the marching tetrahedra algorithm (Ferrant et al., 2001). It starts by first subdividing the image into cubes of a given size (specifying the size of the largest tetrahedra in the mesh), which are further divided into five tetrahedra using an alternating pattern so as to avoid diagonal crossings on the shared quadrilateral faces. Next, this initial mesh is iteratively refined in the regions of the image where refinement allows improved accuracy at lower computational cost, e.g. in the neighborhood of object boundaries. Finally, a volumetric marching tetrahedra-like approach is applied to this multiresolution mesh. For each tetrahedron of the multiresolution mesh, the image label value of each vertex is checked, if the vertex labels are different, the tetrahedron is divided along the edges for which the node labels are different.

Special care is taken so that the quality of the elements guarantees minimal errors in further FE computations. This is done by Laplacian smoothing of the vertices of mesh, starting with the tetrahedra located on the boundary surfaces, and iteratively proceeding next with those located next to those that have been processed.

For more details, the reader is referred to Ferrant et al. (2000a, 2001).

2.3. Intraoperative segmentation

In order to be able to successfully track and characterize the deformation of the key objects the neurosurgeon is interested in, we need to segment them out of the intraoperative images. This task is extremely difficult because the intraoperatively acquired data has limited resolution and contrast, and it is therefore often difficult to distinguish between tissue types. It is also difficult because of contrast variation between pre-operative and intraoperative images as well as between intraoperative images.

We use an algorithm that exploits preoperative MR acquisition and preoperative segmentation to generate a patient-specific model for the segmentation of intraoperative data. The algorithm uses the segmentation of preoperative data as a template for the segmentation of intraoperative data (Warfield et al., 2000a,b). Each preoperative segmented tissue class is converted into an explicit 3D volumetric spatially varying model of the location of that tissue class, by computing a saturated distance transform (Ragnelnam, 1993) of the tissue class. This model is used to provide robust automatic local context for the classification of intraoperative data (Warfield et al., 2000a).

During surgery, intraoperative data is acquired and the preoperative data (including any MRI/fMRI/PET/MRA that is appropriate, the tissue class segmentation and the spatial localization model derived from it) is aligned with the intraop-
erative data using a mutual information (MI) based rigid registration method (Wells III et al., 1996; Ger- ing et al., 1999). The intraoperative image data then together with the spatial localization model forms a multichannel 3D data set. Each voxel is represented by a vector with components from the intraoperative MR scan, the spatially varying tissue location model and if relevant to the particular application, any of the other preoperative image data sets.

When an intraoperative scan is to be segmented, a statistical model for the probability distribution of tissue classes in the intensity and anatomical localization feature space is built. The statistical model is encoded implicitly by selecting groups of prototypical voxels which represent the tissue classes to be segmented intraoperatively (this typically requires less than five minutes of user interaction preoperatively). This multichannel data set is then segmented by tissue classification (Duda and Hart, 1973; Warfield et al., 1998a,b, 2000a).

2.4. Deformable surface matching

Our deformable surface matching algorithm deforms the boundary surfaces of the model at a given time point towards the corresponding boundaries in the image at the next time point. The algorithm models the surfaces as elastic membranes to which image-derived forces are applied iteratively until the surface matches the shape of the target object as well as possible. The elastic membrane model is discretized using FE, and the temporal variation of the surface is discretized using forward Euler integration, which yields the following semi-implicit iterative equation (Cohen and Cohen, 1993):

\[(I + \tau A)\mathbf{v}^t = \mathbf{v}^{t-1} - \tau \mathbf{F}^{v^{t-1}}\]  

where \(\mathbf{v}^t\) is the vector representing the node positions of the mesh at time \(t\), \(A\) the elasticity matrix of the membrane, \(I\) the identity matrix, and \(\mathbf{F}^{v^{t-1}}\) the vector representing the image-derived forces applied to the surface computed at timestep \(t - 1\). This equation converges to the right minimum provided time step \(\tau\) is small enough and the initial surface not too far from its target shape.

Classically, the image force \(\mathbf{F}\) is computed as a decreasing function of the gradient of the target image so as to be minimized at the edges in the target image (Kass et al., 1988; Cohen and Cohen, 1993). To increase the robustness and the convergence rate of the surface deformation, we compute our forces as a steepest gradient descent on a Euclidean distance transform of the edges of the object to be tracked in the target image. The distance transform is computed with optimal efficiency (linear computational cost with respect to the amount of voxels in the image) using a fast Euclidean distance transformation algorithm (Cuisenaire and Macq, 1999; Cuisenaire, 1999). To prevent the surface from sticking on a wrong edge, or to prevent two sides of a thin surface from sticking together on the same edge, we have included the expected gradient sign of the edges of the structure to be segmented in the force expression (Ferrant et al., 1999a, 2000a). Hence the criterion to be minimized is the distance of the deformable surface to the target object.

This yields the following relation for the external force:

\[\mathbf{F}(\mathbf{x}) = S_{\text{min}} G_{\text{exp}} \nabla \mathcal{D}(\mathbf{x})\]  

where \(\mathcal{D}(\mathbf{x})\) represents the distance transform of the boundaries of the segmentation of the target image \(I\) at point \(\mathbf{x}\). \(S_{\text{min}}\) is chosen so that the gradient points towards a point with a smaller distance value:

\[S_{\text{min}} = \begin{cases} +1 & \text{if } \mathcal{D}(\mathbf{x}) > \mathcal{D}(\mathbf{x} + \nabla \mathcal{D}(\mathbf{x})) \\ -1 & \text{if } \mathcal{D}(\mathbf{x}) < \mathcal{D}(\mathbf{x} + \nabla \mathcal{D}(\mathbf{x})) \end{cases}\]

\(G_{\text{exp}}\) is the contribution of the expected gradient sign on the labeled image:

\[G_{\text{exp}} = \begin{cases} +1 & \text{if } k\mathbf{n} \nabla I(\mathbf{x}) > 0 \\ -1 & \text{if } k\mathbf{n} \nabla I(\mathbf{x}) < 0 \end{cases}\]

where \(\mathbf{n}\) is the normal to the surface at point \(\mathbf{x}\), \(k = +1\) if the region to be matched has a higher label value than the surrounding tissues; \(k = -1\) if the region to be matched has a lower label value than the surrounding tissues. This means that if a surface whose normal points in the opposite direction to that of the expected image gradient, it will not be attracted towards that edge.

We solve the system of equations with the Portable, Extensible Toolkit for Scientific Computation (PETSc) package (Balay et al., 2001) using the Generalized Minimal Residual (GMRES) solver with block Jacobi preconditioning.
2.5. Biomechanical modeling of volumetric brain deformation

Assuming a linear elastic continuum with no initial stresses or strains, the deformation energy of an elastic body submitted to externally applied forces can be expressed as (Zienkiewicz and Taylor, 1987):

\[
E = \frac{1}{2} \int_\Omega \sigma^T \epsilon \, d\Omega + \int_\Omega F \epsilon \, d\Omega
\]

(3)

where \( F = F(x, y, z) \) is the vector representing the forces applied to the elastic body (forces per unit volume, surface forces or forces concentrated at the nodes of the mesh), \( \epsilon = \epsilon(x, y, z) \) the displacement vector field we wish to compute, and \( \Omega \) the body on which one is working. \( \epsilon \) is the strain vector, which can be expressed as \( \epsilon = L \sigma \), and \( L \) the stress vector, linked to the strain vector by the material’s constitutive equations.

In the case of linear elasticity, with no initial stresses or strains, this relation is described as

\[
\sigma = \sum_{m} A_{m}^{\text{el}} \epsilon_{m} = \sum_{m} B_{m}^{\text{el}} \epsilon_{m} \epsilon_{m}
\]

(4)

which can be rewritten in a global linear equation system the solution of which provides us with the displacements resulting from the forces applied to the body:

\[
K \epsilon = -F
\]

(5)

The displacements at the boundary surface nodes are fixed to match those generated by the deformable surface model. Let \( \bar{\epsilon} \) be the vector representing the displacement to be imposed at the boundary nodes. The elements of the rows of the rigidity matrix \( K \) corresponding to the nodes for which a displacement is to be imposed need to be set to zero, and the diagonal elements of these rows to one. The force vector \( \bar{F} \) is then set to be equal to the displacements vector for the boundary nodes: \( \bar{F} = \bar{\epsilon} \) (Zienkiewicz and Taylor, 1987). This way, solving Eq. 8 for the unknown displacements will produce a deformation field over the entire FE mesh model that matches the prescribed displacements at the boundary surfaces.

We solve the system of equations with the Portable, Extensible Toolkit for Scientific Computation (PETSc) package (Balay et al., 2001) using the Generalized Minimal Residual (GMRES) solver with block Jacobi preconditioning.

2.6. Modeling tissue resection

During neurosurgery, the surgeon often needs to retract and resect tissue, for instance for removing tumor. Practically, the surgeon first retracts the brain, bringing neighboring tissue under constraint. Tumor tissue is then resected until no more remains. This means that the shape and topology of the brain change after tumor resection starts. This change needs to be
included into our model so as to be able to track further deformations faithfully.

The way we cope with this topology change is by updating our model so it reflects the changes at the time point where they appear. We do this by clipping the existing mesh model (deformed onto the shape of the brain at the time point where resection appears) at the boundary of the resected areas. The clipping is done the same way as at the meshing stage: tetrahedra lying inside resection areas are removed from the mesh, and those lying across the boundary between brain are cut so as to have a precise boundary representation of the brain with the resected areas. This however is an approximation as tissue retraction is not modeled. This operation thus only partially reflects what the surgeon does. After that stage, in our model, the tumor boundary and the brain boundary merge and form one new single boundary surface.

To ensure that we are able to link between the model at the previous time point, our topology modification algorithm keeps track of the correspondence between elements and nodes of the new resected FE model with the FE model before removal of the elements. This is essential for further tracking and characterization of the deformation.

2.7. Updating preoperative images
Once the volumetric FE model has been deformed from one time point to the next, the obtained deformation field is only computed at the discretization nodes of the FE model. This deformation field can then be interpolated back onto the image grid using the shape functions of every element of the FE mesh (using Eq. 4) linking the displacement at the nodal points to continuous space. This is needed in order to update the preoperative images so that they match the shape changes of the brain the model reflects.

2.8. Timeline analysis of the deformable registration algorithm
All the components of our non-rigid deformation and tracking algorithm were implemented to run on parallel hardware so as to be able to provide results to the surgeon within the time constraints of neurosurgery. Figure 2 presents a typical timeline of the image processing, analysis and simulation tasks executed during neurosurgery. It must be noted that the image analysis and simulation tasks are altogether taking up a time which is of the same order of magnitude as that of the intraoperative image acquisition. This timeline analysis demonstrates that with the parallel implementation of our algorithms, the intraoperative image analysis methods are sufficiently fast to provide feedback to the surgeon at a rate which is practical to use during neurosurgery.

3. Experiments

3.1. Input data
The left column of Figure 3 shows the same spatial location of intraoperative MR images (256x256x60 matrix - 60 slices scanned from inferior to superior, voxel size 0.9375x0.9375x2.5 mm³) taken at five critical time points during surgery (see Nabavi et al. (2001) for method) after rigid alignment using mutual information (Wells III et al., 1996). The first scan (top, time point 1) was taken at start of surgery, the second one (time point 2) after the dura had been opened and some CSF drained, showing significant brainshift in the direction of gravity (downwards), the third (time point 3, 70 minutes after time point 2) and fourth (time point 4, 60 minutes after time point 3) scans show two stages of tissue retraction and tumor resection also causing the brain to slightly shift in the direction of gravity, and the fifth scan (time point 5, 45 minutes after time point 4) shows the brain swelling up again after dural closure. Note that a contrast agent had been injected after the first scan was taken.

3.2. Preoperative and intraoperative segmentation
The segmentation of the intraoperative scans (Warfield et al., 2000b) is done to extract the key objects we are interested in, i.e. brain tissue, ventricles and tumor. The right column of Figure 3 shows the corresponding segmentation for the 2D slices corresponding to those of the left column in the same figure. Since no contrast agent had been injected before the first scan was taken, the tumor is not clearly visible in the first intraoperative scan, and so the tumor segmentation of a corresponding preoperative scan was used.

3.3. FE tetrahedral model generation
Next, a multi-resolution FE tetrahedral mesh model is generated from the first intra-operative segmented image. In this study, the initial coarse mesh has been
refined at the location of the ventricles and of the tumor so as to ensure sufficient precision for matching these structures throughout the sequence. Figure 4 shows orthogonal images along the coordinate axes through the generated tetrahedral mesh overlayed on the corresponding images of the gray-level MR scan. The mesh shown on this figure was not yet post-processed so as to illustrate the initial partition of the domain into cubes, with refinement in the selected regions. The size of the longest edges in this mesh is approximately 10 mm, while that of the smallest is 0.1 mm. The average length of the edges is 3.8 mm.

We model brain tissue as an isotropic linear elastic material, characterized by two parameters: Young’s elasticity modulus \( E \) and Poisson’s ratio \( \nu \) (Zienkiewicz and Taylor, 1987). They determine its behavior and are of course critical to the reliability of the deformation model. As in our previous work (Ferrant et al., 2000b, 2001), we rely on the study of Paulsen et al. (1999) and Miga et al. (1999) for choosing our coefficients \( (E = 3\, k\, Pa, \nu = 0.45) \).

### 3.4. Deformable surface tracking

The boundaries of the key structures can now be tracked all over the sequence. The initial surfaces are extracted from the initial FE model and successively deformed towards the corresponding boundaries of the objects in the intraoperative segmented image sequence using our deformable surface algorithm. Figure 5 shows cuts through the 3D deformable boundary surfaces at the different time points during surgery overlayed on the corresponding images from the volumetric intraoperative MRI.

In Figure 6, one can clearly observe the cortical surface shift aggregating in the direction of gravity until the 4th scan (time point 4), and slightly reacting in the opposite direction from the 4th to the 5th scan (time point 5). The same applies for the lateral ventricles, whose volume diminishes until time point 4, and slightly increases from time point 4 to time point 5.

Figure 7 shows the deformation of the brain and ventricular boundary surfaces from one time point to the next over the entire course of surgery in 3D. The surface renderings are colorcoded according to the intensity of the actual deformation, with the sign indicating whether the surface is shrinking (positive deformation) or swelling (negative deformation).

In Figure 8, the same color-coding is used to illustrate the full deformation from time point 1 to time point 4 of the brain surface, as well as from the lateral ventricles. The 3D arrows represent the deformation field the surface has undergone. These visualizations clearly show that the deformations happen
Figure 3. First column (subfigures a to e): an axial image at the level of the tumor and right lateral ventricle in each of five intraoperative volumetric MR scans (time point 1 to time point 5) taken sequentially during neurosurgery. Second column (subfigures f to j): corresponding intraoperative segmentations of the images.
mainly in the direction of gravity, but as Figure 7 indicates, there might also be a small circumferential sinking and swelling movement associated.

From time point 1 to time point 2, after dural opening, a significant shift of the upper part of the brain (ranging between 4 and 7.5 mm) can be observed in the direction of gravity. This shift propagates down to the lateral ventricle located in the upper hemisphere of the brain (shift ranging between 1.5 and 3 mm) (see Figures 7a, and 5a,b,c). This downward shift aggregates and amplifies both in amplitude and in extension as tumor resection starts and progresses. Between time point 2 and time point 3, tumor resection starts along with an extension of the previous shift both in amplitude (2 mm in average for the brain, 2 mm for the ventricles) and extension (see Figures 7b, 5c,d,e). As tumor resection progresses towards time point 4, the phenomenon slightly expands further (see Figures 7c and 5e,f,g). From time point 1 to time point 4, the total shift of the cortical surface in the direction of gravity is of about 12 mm, while that of the lateral ventricles sums up to about 6 mm (see Figures 8 and 6).

From time point 4 to time point 5, the brain reacts and swells up in the opposite direction to that of the previous shifts. Figure 7d shows the brain surface at time point 5 with the blue color indicating that the deformation from time point 4 to time point 5 corresponds to a swelling of the cortical surface (see also Figures 5g,h,i and Figure 6). The area swelling up from time point 4 to time point 5 roughly corresponds to the area that had been sinking from time point 1 to time point 4.

A small region of enhancement still appears at the end of surgery. This is an issue of major importance for image-guided neurosurgery. In some cases there is a discrepancy in the contrast distribution at the beginning of surgery and after resection. The evidence is currently inconclusive as to whether this neoenhancement is due to contrast leakage, or late enhancement of tumor cells. This is currently under investigation.

The boundary surface of the tumor is not deformed independently until tumor resection starts. Before that, the tumor is included into the brain model and treated identically to normal brain tissue.

3.5. **Modeling topological changes for tissue resection**

From the scan at time point 2 to scan at time point 3 a topology change occurs due to tissue retraction and resection. This can be seen on the scans as black areas within the brain (as visible in Figure 9). To model the tissue resection, the FE mesh deformed onto the scan showing resection (third scan) is clipped and elements covering the resection areas are removed so as to reflect the surgically induced topological change. Practically, this means that the brain boundary now expands into the tumor area through a small pathway. Figure 9 illustrates this on 2D images, while Figure 10 shows 3D surface renderings of the topo-
Figure 5. Illustration of axial MRI and corresponding deformable boundary surfaces, showing the initial boundary surfaces, their distance from the target surfaces and the closeness of the match achieved. From left to right, top to bottom: (a) 1st scan (time point (TP) 1) with initial boundary surfaces (at TP 1), (b) 2nd scan (TP 2) with same surfaces (at TP 1), (c) 2nd scan (TP 2) boundary surfaces deformed onto scan at TP 2, (d) 3rd scan (TP 3) with same surfaces (at TP 2), (e) 3rd scan (TP 3) with deformed surfaces (at TP 3), (f) 4th scan (TP 4) with same surfaces (at TP 3), (g) 4th scan (TP 4) with deformed surfaces (at TP 4), (h) 5th scan (TP 5) with same surfaces (at TP 4), (i) 5th scan (TP 5) with deformed surfaces (at TP 5).
Figure 6. Top image: enlargement of axial image from intraoperative MRI at time point (TP) 4 and corresponding deformable boundary surfaces at TP 1 (red), TP 2 (green), TP 3 (yellow), TP 4 (blue) illustrating the progressive shift of the brain and ventricles. Bottom image: same slice at TP 5 with boundary surfaces at TP 4 (blue) and TP 5 (pink) illustrating the upwards shift of the cortical and ventricular surfaces.
Figure 7. 3D surface renderings of the cortical surfaces with color coding of the deformation from one scan to the next. Positive values indicate a deflation of the surface, negative values indicate an inflation of the surface. a) shows the brain at time point (TP) 2 with deformation field from matching the 1st scan (TP 1) to the 2nd (TP 2), b) brain at TP 3 with deformation field from matching scan at TP 2 to scan at TP 3, c) brain at TP 4 with deformation field from matching scan at TP 3 to scan at TP 4, d) brain at TP 5 with deformation field from matching scan at TP 4 to scan at TP 5.
logically changed boundary surface of the brain. The hole created by the tissue resection can very well be observed.

The modified surface is then deformed onto the next scans as shown in Figure 5. Figure 11 shows the results of the matching at the next time points on the corresponding axial and coronal images from the volumetric MRI.

### 3.6. Inferring a biomechanical volumetric deformation field from surface deformations

Once the boundary surface deformations have been computed, we use them as a boundary condition to our biomechanical FE model. Figure 12 shows the color-coded 3D deformation field from one image of the sequence to the next. The color coding maps the norm of the actual deformation intensity throughout the brain model with the sign indicating whether the dot product of the deformation vectors with the gravity vector is positive (i.e. downwards deformation, positive scalars) or negative (i.e. upwards deformation, negative scalars).

It can be clearly observed that the deformations at the boundary surfaces computed in the previous section propagate into the brain volume. From time point 1 to time point 2, the sinking propagates from the brain surface down to the mid-sagittal plane, also affecting the left lateral ventricle. The same applies until time point 4. This is illustrated with the positive green-yellow-red color-coding of the upper hemisphere of the brain in Figure 12a,b,c. The swelling of the brain after dural closure is very clearly illustrated with the negative blue color coding of the upper hemisphere of the brain (Figure 12d). Visualization of the volumetric deformation field using 2D orthogonal planes provides ready comparison of the underlying MRI and the estimated deformation. This will be described in the next section.

Figure 13 illustrates the effect of turning off the ventricular surface deformation when simulating a volumetric deformation for the deformation from time point 1 to time point 2. When compared to the results with the ventricular boundary surface displacements applied (as visualized in Figure 12a), one can very clearly see that the CSF draining and leakage causing the shrinking of the ventricles needs to be accounted for in order to obtain better accuracy in the vicinity of the ventricles.
Figure 9. 2D axial (a,b) and coronal (c) images through topologically adapted boundary surface of the brain overlayed on corresponding images from 3rd MR scan (time point 3).

Figure 10. a) 3D rendering of the brain surface after topological change modeling tissue resection, and b) wireframe rendering of the same surface which more clearly illustrates the merger of the tumor and brain surfaces.
3.7. Updating preoperative images

The volumetric deformation field of the FE model can then be used to deform pre-operative images, so the surgeon can have an updated view of pre-operative planning he had done before hand.

Figure 16c,f,i,l shows updated axial images at the different timepoints during surgery, on the areas covered by the brain model (with the rest of the image outside the brain model simply copied from the previous image). The two other columns of Figure 16 illustrate the accuracy of the deformation algorithm with difference images between the successive intra-operative scans (subfigures a,d,g,j) and between the intraoperative scans and the images updated with the computed deformation field (subfigures b,e,h,k).

Figure 14 shows the 2D deformation field from one image to the next overlayed on the image the deformation originates from. This provides the doctor with a comprehensive way to visualize the deformation the brain is undergoing from one time point to the next. Enlargements of regions where the deformation field is less visible are also shown. As discussed previously, the deformation field propagates below the brain surface down to the left lateral ventricle. Until time point 4, the brain shifts in the direction of gravity (e.g. downwards in Figure 14), increasing progressively. From time point 3 to time point 4, a lateral shift can also be observed. This lateral shift may be caused by tumor resection. From time point 4 to time point 5, after dural closure the brain slightly swells in the opposite direction to gravity. Even though this deformation has a very small amplitude, it is clearly not only located around the cortical surface, it also affects sub-surface tissue.

In Figure 15, enlarged images of deformation fields in regions neighboring the tumor and resected areas are shown. One can observe that the brain swells towards the interior of the resection cavity. In the bottom row of Figure 15 showing the deformation field from scan 4 to scan 5 (time point 4 to time point 5), the swelling of the cortical surface can be seen along with the shrinking of the boundary of the brain with the tumor and resected areas.
Figure 12. Orthogonal images along the coordinate axes of the color-coded deformation field estimated at each of the different time points (TP 2 to TP 5) for which images were acquired during surgery, transparently overlayed on corresponding images from the volumetric intraoperative MRI. Positive deformation values indicate a deformation in the direction of gravity, negative values indicate deformation in the opposite direction. The deformation fields shown illustrate the deformation from a) TP 1 to TP 2, b) TP 2 to TP 3, c) TP 3 to TP 4, d) TP 4 to TP 5.
Figure 13. Orthogonal images as in Figure 12 through volumetric MRI acquired at time point (TP) 2. a) Color-coded deformation field computed from TP 1 to TP 2 without accounting for ventricular deformation. b) Difference of deformation fields computed using ventricular deformation (as in Figure 12a) and that computed without using ventricular deformation (shown in subfigure a of this Figure). This illustrates that the deformation field estimation using the brain surface only, differs slightly from that estimated using the brain surface and the ventricle surface almost everywhere except close to the ventricles. Around the region of the ventricles, including the ventricle surface match leads to improved estimation of the true deformation field.
Figure 14. Left column: 2D deformation field overlayed on axial slice at different time points (TP 1 to TP 4, top to bottom) during surgery. Right column: enlarged images of the same deformation field on the same slice. Deformation vectors are from a,e) TP 1 to TP 2, b,f) TP 2 to TP 3, c,g) TP 3 to TP 4, d,h) TP 4 to TP 5.
3.8. Performance analysis

In order to assess the accuracy of our algorithm and the validity of our deformation model, we have manually placed sets of landmarks on the different intraoperative scans and tracked them using our algorithm. A total of about 400 landmarks were carefully picked in 3D by an expert in an orthogonal image viewer on zoomed (3 times) versions of the images, which allowed for accurate fully 3D positioning of the landmarks. The landmarks were placed in both hemispheres of the brain and have been divided into 3 separate categories: those that were lying on the boundary surfaces (37% of all landmarks consisting of 16% on the ventricles, and 21% on the cortical surface), reflecting the accuracy of the deformable surface matching algorithm, those that were located inside the boundary surfaces (41% of all landmarks were in mid volume), reflecting the estimation accuracy of the volumetric FE model, and those that were located in the vicinity of the tumor and resection areas (22% of all landmarks). Due to the limited amount of visible structure in these regions of the intraoperative images, the landmark localization was not as accurate as for the other landmarks.

The distance between the landmarks before and after registration has been measured and the results are reported in Table 1 for the successive time points of the intraoperative image sequence.

The average distance of all the deformed landmarks to the target landmarks was \(0.9 \pm 0.7\) mm (mean ± standard deviation), which can be considered as quite accurate given the imprecision of the manual landmark picking. One can notice that the best accuracy was obtained for the landmarks located on the boundary surfaces, and the worst results were obtained in the vicinity of the tumor and resection areas. We believe this inaccuracy is due to the limited accuracy of the landmark picking in that area, but also because our model currently does not take retraction into account.

Nevertheless, our algorithm reduced the distance between landmarks from up to 7.2 mm before deformation down to 2.6 mm or less for surface-based landmarks, and significant improvements were also observed for subsurface landmarks. This compares well with the acquisition voxel size which was 0.9375x0.9375x2.5 mm^3.
Figure 16. Left column: difference between successive images from original MR image sequence (difference between images at time points (TP) 1 and TP 2, TP 2 and TP 3, TP 3 and TP 4, TP 4 and TP 5). Middle column: difference between intraoperative MR images and deformed images at time TP 2, TP 3, TP 4, TP 5. This illustrates how well our algorithm is capable of capturing deformation, both at the level of the ventricles, and at the level of the cortical surface. Right column: updated intraoperative MR image after deformation at TP 2, TP 3, TP 4, TP 5.
Table 1
Measurements of distances between deformed landmarks and manually placed landmarks. $i \rightarrow j$ refers to distance measurements of landmarks placed in image $i$ and image $j$, while $i^{def} \rightarrow j$ refers to those placed in image $i$ deformed onto image $j$ and image $j$. The table presents the average and associated standard deviation of the deformation measurements on the different landmark sets, as well as the maximum deformation within each set.

Total deformation measurements are reported both for each time point transition and for each landmark category. The first two result columns refer to landmarks on the boundary surfaces (Surface and max columns), next two refer to landmarks between both surfaces (Volume and max columns), next two refer to landmarks in the vicinity of the tumor (Tumor and max columns). The last two columns report results on the entire set of landmarks.

<table>
<thead>
<tr>
<th>Time pt.</th>
<th>Surface</th>
<th>max</th>
<th>Volume</th>
<th>max</th>
<th>Tumor</th>
<th>max</th>
<th>Total</th>
<th>max</th>
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<td>$1 \rightarrow 2$</td>
<td>1.9±1.5</td>
<td>7.2</td>
<td>2.2±1.1</td>
<td>4.7</td>
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<td>1.0±0.6</td>
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<tr>
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<td>3.8</td>
<td>2.0±1.4</td>
<td>4.5</td>
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<td>2.8</td>
</tr>
<tr>
<td>$3 \rightarrow 4$</td>
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<td>6.4</td>
<td>1.4±0.9</td>
<td>3.0</td>
<td>1.7±1.3</td>
<td>3.8</td>
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</tr>
<tr>
<td>$4 \rightarrow 5$</td>
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<td>2.7</td>
<td>0.9±0.7</td>
<td>2.7</td>
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<td>1.4±1.5</td>
<td>8.7</td>
</tr>
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<td>2.6</td>
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</table>

4. Discussion

Our algorithm is capable of characterizing and tracking intraoperative brain deformation, and update preoperative images with clinically acceptable accuracy. However, certain aspects of the algorithm need to be discussed.

The overall accuracy we obtain depends on the accuracy of the different components of our algorithm:

- **The intraoperative segmentation**: given the resolution of the data, a segmentation error of 1 voxel in the slice acquisition direction can result in an incorrect deformation of 2.5 mm, which explains, for instance, some of the implausible deformation obtained at the bottom of the brain. However, because the voxel-size in the direction of gravity is 0.9375 mm, we are able to track deformations of the order of 1 – 2 mm, such as those showing the brain swelling from scan 4 to scan 5. It must be noted that in the case analysed, the intraoperative segmentation of the left (upper on the axial slices) cortical hemisphere was particularly accurate. The presence of large sulci in the other hemisphere caused some inaccuracies and inconsistencies from one scan to the next in the segmentation, therefore also affecting the surface matches causing errors to propagate throughout the hemisphere. Nevertheless, these errors do not affect the accuracy of the matching in the left hemisphere where the surgical procedure was carried out, and hence are of less importance for surgical guidance.

- **The deformable surface matching**: the deformable surface matching algorithm performs quite well on simplified objects such as those we used in the experiments presented in this paper, but it would be much less robust on more complicated structures with deep and sharp folds for instance. Also, there is no guarantee that the deformable surface provides us with the actual deformation of the boundaries of the objects in the image. Therefore, we are currently investigating multi-resolution surface representations for improved surface matching (Jaume et al., 2001).

- **The biomechanical model**: the model we cur-
rently use is limited to linear elasticity. For larger displacements, we are intending to investigate non-linear elasticity models such as the models described by Picinbono and Ayache (2000) and Miller and Chize (1997); Miller et al. (2000). Also, we currently consider the brain as an homogeneous body, while tumor and other structures can have a very different biomechanical behavior that our model currently does not incorporate. For intraoperative use, modeling extra structures would require a real-time intraoperative segmentation able to robustly identify them. Finally, anisotropy should be included into the model. To this effect, tensor diffusion images are currently being acquired before and during surgery (Mamata et al., 2001), and can help measure anisotropy directions within white and gray matter.

- **Tissue resection and retraction:** tissue resection represents tissue removal, and therefore our algorithm approximates this correctly by removing elements from the model. However, it must be noted that the pathway leading to the tumor for instance is not resected but just retracted. For maximum accuracy, this would require tracking the surgical instruments intraoperatively, but this data is currently not collected at our institution. This should be modeled as well to faithfully capture the deformation of the brain and hence improve updates of preoperative images.

5. Conclusion

In this study, we have tracked brain deformation using a fully 3D finite element biomechanical model during the course of neurosurgery so that preoperative images could be updated faithfully, so as to provide improved image-guided navigation to the neurosurgeon. Deformations in the presented case were analysed extensively.

Our deformable registration algorithm is capable of tracking intraoperative deformations with an average accuracy of less than 1 mm, which is clinically acceptable. It is able to overcome the limitations of most non-rigid registration methods, that are related to intensity variations and tissue removal visible in the intraoperative images. Moreover, due to our efficient parallel implementation, we are able to perform all the computations within the time constraints of neurosurgery.

One of the advantages of our method is that due to the fully volumetric deformation field the algorithm produces, other imaging modalities acquired preoperatively (such as PET, CT, fMRI, etc.) can be updated and viewed during surgery as well.

To our knowledge, this is the first time brain deformation has been analysed by deriving high resolution deformation fields from serial volumetric intraoperative acquisitions acquired over the entire course of a neurosurgery. This has enabled us to analyze the behavior of deformations of brain tissue, and to carry out preoperative and intraoperative image fusion on a timescale compatible with use during neurosurgery.

The results of our algorithm show that the brain surface progressively sinks during surgery, and swells back after tumor resection is complete. Moreover, cortical shift propagates to subcortical areas, down to the ventricles. Much more complicated deformations were observed on brain tissue around the tumor and resected areas. The brain has been observed to swell at the boundaries with the tumor and resection areas, shrinking them.

Our study also demonstrates that one cannot interpolate deformation from preoperative and single intraoperative (or postoperative) images to understand what happens during surgery. It is necessary to perform imaging at critical timepoints (Nabavi et al., 2001) during surgery to track brain deformation and understand how it deforms.

The areas we are planning to further investigate are to include tissue heterogeneity, which should be straightforward within the finite element formulation. With more complete intraoperatively computed segmentations, it will be easy to assign different material properties and anisotropy to the elements of the mesh covering the different parts of the brain. Other possible areas of investigation are the modeling of the falk, which has been observed to play a role similar to that of a barrier against which brain tissue slides or gets compressed. However, as discussed by Miga et al. (2000a), there is only limited data in the literature reporting on differences in mechanical properties of brain tissue. We believe serial IMRI acquisition and biomechanical modelling may offer a mechanism
to estimate these parameters in the future.

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