E-ISSN: 2321–9637
Volume 1, Issue 5, December 2013
International Journal of Research in Advent Technology
Available Online at: http://www.ijrat.org

ESTIMATION OF BRAIN SHIFT CAUSED BY MENINGIOMA

Melanie Patsy Fernandes[1], Pavithra M. N.[2], Prof. Anand Jatti[3]
[1 2 3] Department of Biomedical Signal Processing and Instrumentation
[1 2 3] R.V. College of Engineering, Bengaluru-India
[1 2] Mtech student, [3] Professor
[1] 25melaniefernandes@gmail.com
[2] pavithramn@gmail.com
[3] anandjatti@rvce.edu.in

***Abstract*— Meningioma is one of the most frequent tumors and grows on the surface of the brain. This pushes the brain leading to stress changes in the brain causing it to shift from its region. On a broader scale, two methods of estimation of brain shift are used. One is the non-linear model and the other is linear model. Linear model is further optimized to produce better results. Better accuracy and its close estimation of the shift makes non-linear model a better approach.**

Keywords— tumor, meningioma, deformation, segmentation, tetrahedral, elasticity, linear, non-linear

1. INTRODUCTION

Tumor growth can cause brain deformation and change stress distribution in the brain which leads to brain shift. Therefore important achievements in engineering have been achieved by mathematical modeling and computer simulation of brain shift. Soft tissue deformation modeling has received increasing attention in the biomedical imaging community [1].

The surgical simulation research goals are to model and simulate deformable tissues for applications requiring real-time interaction. Medical applications for modeling and simulation include simulation-based training, skills assessment and operation planning [1] Image guided intervention systems can help surgeons improve the clinical outcomes of surgery. Modeling and simulation are particularly important in certain areas, such as tumor growth, oedema, hematomas and craniotomy motion tracking and segmentation. However, soft tissue simulations are often plagued by imprecise geometric information, unknown constitutive laws, boundary conditions and distributed forces [1].

Several approaches have been developed to address brain deformation. Recently, biomechanical models have been developed that estimate displacements. These models are based on physical brain deformation and thus require measurements after deformation. Tissue deformation simulation usually starts with segmentation of the target geometry from a medical image, which is then used to reconstruct a representation of the target geometry's boundary surface. Some models can model brain responses to strain and stress. Some such models are linear and assume that the stress and strain relationship is linear, while others assume a non-linear relationship. Linear models assume that the brain's response to stress and strain is similar to that of elastic or solid materials [2].

Computer Aided Therapy (CAT) requires a better understanding of the characteristics of brain cancer progression based on phenotypic cancer profiles derived from imaging, histopathology and other sources, which can ultimately help determine predictive factors of cancer invasiveness. Significant tools for understanding such

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cancer profiles are statistical atlases. In brain tumor patients, such atlases have the potential to assist surgical and treatment planning [3].

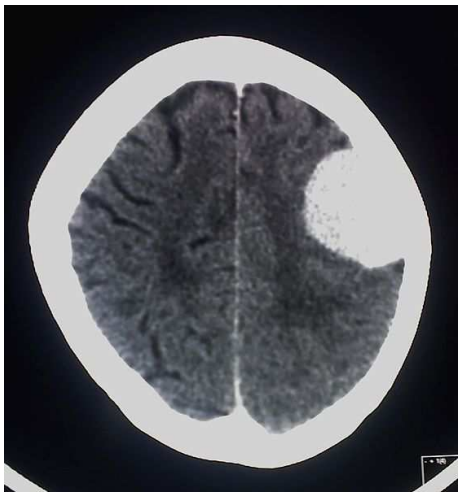

Figure 1: A contrast enhanced CT scan of the brain, demonstrating the appearance of a meningioma (Courtesy Wikipedia)

The decision of whether and how to best treat a brain tumor is based on multiple factors, including size and location of the tumor, tumor type, symptoms, growth rate and age of the patient (among others). In general, there are two basic options: surgical removal and radiation. In both cases (surgical and radiation) segmentation has an impressive impact on Image Guided Surgery (IGS) and CAT systems. Brain MRIs that reveal tumors are difficult to segment because of brain tissue deformation caused by tumor mass effect or volume expansion [4].

To model and estimate deformation of brain structure, we focused on one type of brain tumor, meningiomas, because they are a good representative of brain tumors in general and possess several attractive characteristics [5] [7].

2. MENINGIOMA

Meningioma is the most frequent tumor of neuroectodermal origin in humans. It is usually benign [6]. Meningiomas arise from a layer of tissue (the meninges) that covers the brain and spine. Meningiomas grow on the surface of the brain (or spinal cord) and therefore push the brain away rather than growing from within. Meningiomas represent about 25 percent of all tumors originating in the head. Meningiomas are often slow growing, increasing in size only 1-2 mm per year, therefore we can assume that the tumor growth rate is 1-2 mm per year, and their growth behavior can most closely be described as linear, so we can assume that their growth rate is linear [5] [7].

It is generally a sporadic tumor. They show an unexpectedly high recurrence rate. Also, completely removed low-grade tumors can recur. Recurrence and multiplicity are correlated with the formation of a peritumoral edema. On the cytogenetic level, it is the best-studied tumor in humans. Corresponding to their origin, they grow extracerebrally and outside the medulla, mostly displacing, rather than infiltrating, the neural parenchyma and are very common tumors, with an approximate annual incidence of 1 in 16,000 [6]. Pressure induced on the tissue by the tumor and edema is proportional to the added volume [8].

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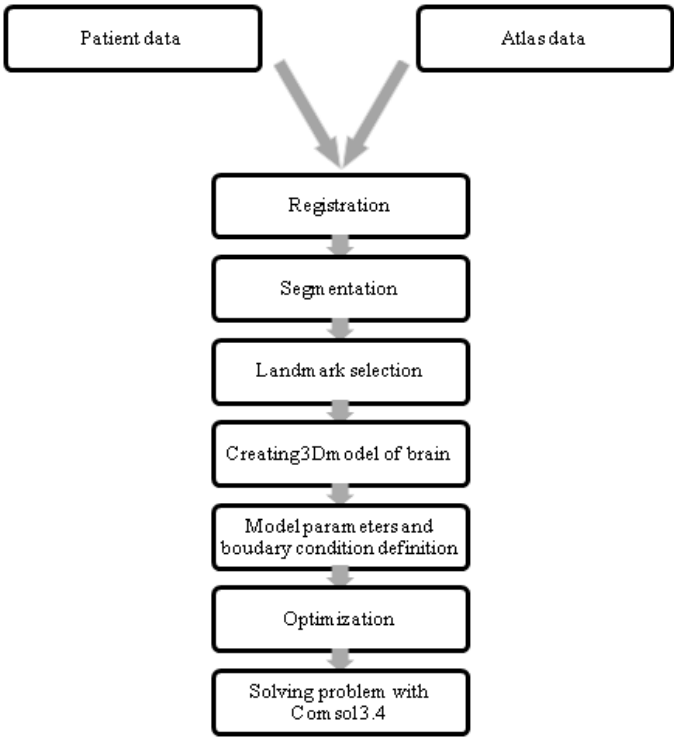

Figure 2: Block diagram method for estimation of brain deformation [7]

3. MATERIALS AND METHODS

1. Preprocessing

Because MRI images only elucidate tumoral brain anatomy, the ability to predict soft tissue deformation, and therefore tumoral brain anatomy during tumor growth, is a primary requirement for reliable treatment. If displacements within the brain can be computed, they can be used to simulate tumors in healthy atlases [7].

The atlas data were registered non-rigidly with patient data to reduce misalignment errors. The non-rigid B-spline method was used to register atlas data to the patient dataset, as detailed in "Eq. (1)". Fig. 3 shows the results of the registration process for cases 2, 3 and 4, which had tumors in the right parietal, right parietal and right frontal lobes, respectively.

$$D(x)=\sum_{i=0}^{3}\sum_{j=}^{3}\sum_{k=0}^{3}B_l(u)B_m(v)B_n(w)P_{i+l,j+m,k+n}$$

$$l=\left[x/n_x\right]-1 \quad m=\left[y/n_y\right]-1 \quad n=\left[z/n_z\right]-1$$

$$B_0(t)=\left(-t^3+3t^2-3t+1\right)/6$$

$$B_1(t)=\left(3t^3-6t^2+4\right)/6$$

$$B_2(t)=\left(-3t^3+3t^2+3t+1\right)/6$$

$$B_3(t)=t^3/6 \qquad (1)$$

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Where i =[x/n_x] – 1, j =[y/ n_y]-1, and k = [z/ n_z]-1, denote the index of the CP cell containing (x, y, z) and u, v and w, which are relative positions of (x, y, z) in three dimensions. B_0 through B_3 are cubic B-splines "Eq. (1)" [9] [7].

In order to specify brain tissue displacement, anatomical landmarks are defined in both patient data and registered as shown in Figure 3. Landmarks, such as ventricle borders and the brain midline, are chosen close to tumor regions so that deformation can be effectively tracked as the tumor shifts these landmarks [7].

After segmentation, 3D models of surfaces of the brain parenchyma and tumors were created [7].

A necessary step in obtaining the numerical model of the brain is the creation of a computational grid, which in most practical grids is a finite element mesh. Because of the long computation time requirements, meshes with low-order elements must be constructed that are not computationally costly. Many algorithms are available for fast and accurate automatic mesh generation using tetrahedral elements [1] [7].

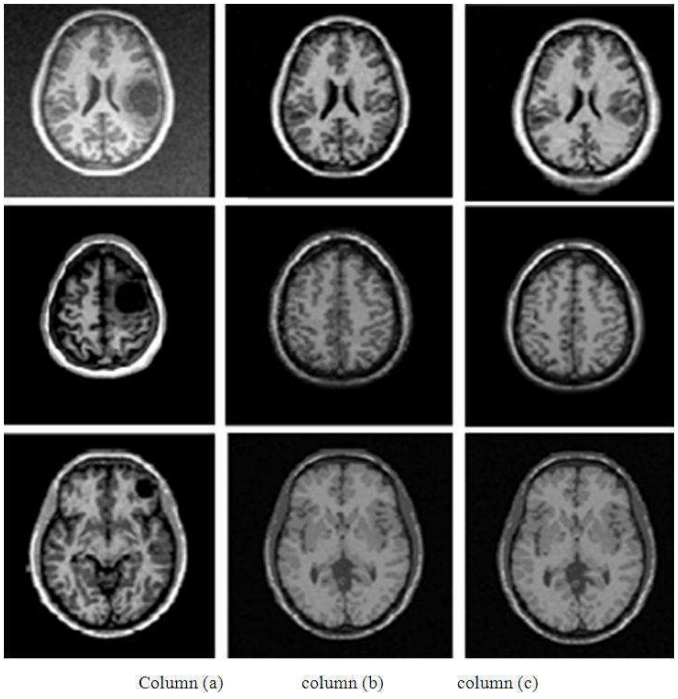

Figure 3: Registration of atlas data with patient data (case 2, 3, and 4) left column patient data middle atlas data right column registered data [7].

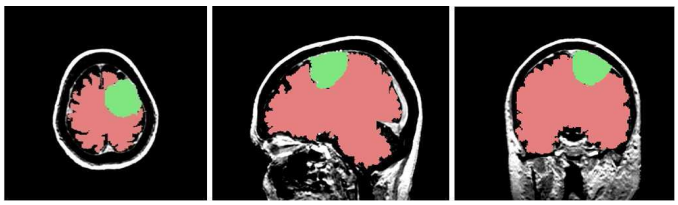

Figure 4: Segmented MRIs of the patient head used for building patient specific brain mesh. The tumor segmentation is indicated by whit green color [7].

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2. *Non-Linear model*

Brain shift behaves in a non-linear manner and is modeled as a viscoelastic material. Nonlinear models closely approximate real shift, and in comparison with linear models they achieve more accurate results, but have higher computational costs. Brain shifts can be detected by the following non-linear methods.

2.1 DR method

Dynamic Relaxation (DR) is an explicit iterative method for obtaining the steady state solution. It can be used for finding the deformed state for a discretised continuum mechanics problem. The method relies on the introduction of an artificial mass dependent damping term in the equation of motion, which attenuates the oscillations in the transient response, increasing the convergence towards the steady state solution.
The DR method is especially attractive for highly nonlinear problems (including both geometric and material nonlinearities) solved using the finite element method. Because of its explicit nature there is no need for solving large systems of equations. All quantities can be treated as vectors, reducing the implementation complexity and the memory requirements. Although the number of iterations to obtain convergence may be quite large, the computation cost for each iteration is very low, making it a very efficient solution method for nonlinear problems [14].

The DR method is combined with the Total Lagrangian formulation of the Finite Element method, for computing intra-operative organ deformations. It includes a number of iteration parameters which must be estimated. These parameters are especially hard to estimate for a nonlinear problem, as their optimal values (which ensure the fastest convergence rate) change during the iteration process [13, 14].

The estimation is done using an estimated value of the load, which might not lead to the optimum value of the iteration parameter. A simple and efficient method of estimating the value of the minimum Eigen value during the iteration process was proposed. As the iterations progress, the estimated minimum Eigen value converges fast to its optimal value. This leads to a very efficient DR procedure, while eliminating the need for separate simulations for parameter estimation. The proposed estimation method involves only vectors, preserving the computational advantages of an explicit method. These features make the proposed DR a perfect candidate for parallel implementation on a Graphics Processing Unit (GPU), which offers very high computation power at a low cost [14].

The proposed adaptive method was applied to compute brain shift estimations using non-linear biomechanical models. The simulations prove the high computational efficiency of the adaptive method [13, 14].

The proposed method offers fast convergence, computational efficiency and the possibility to control the accuracy of the results. These characteristics make it an ideal method for solving image registration problems using bio-mechanical models. A GPU implementation of the algorithm can perform complex brain shift simulations in less than 2s [14].

2.2 Ogden-based Hyper-viscoelastic constitutive model

To model deformations induced by tumors more precisely, the Ogden-based Hyper-viscoelastic constitutive model was used in the following Equations 2 and 3[1, 10-12, 7]:

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

$$\mu = \mu_0[1 - \sum_{k=1}^{n} g_k(1 - e^{\frac{-t}{\tau_k}})] \quad (3)$$

Table 1: Nonlinear brain tissue model parameters

Instantaneous response	k= 1	k= 2
$\mu 0$ =842[Pa] α= -4.7	characteristic time t1=.5[s] g1= 0.450	characteristic time t2=50[s] g2= 0.365

Where W is the strain energy. λ_1, λ_2, λ_3 (directions 1, 2, 3 corresponding to x, y, z) are principal extensions and their values are 1 for no deformation, greater than 1 for extension and smaller than 1 for compression. α is a material coefficient without physical meaning. The value of α was found to be -4.7, see Table 1[1, 11, 7], t and τ denote time. "Eq. (3)" describes viscous response of the tissue. μ_0 is the instantaneous shear modulus in the un-deformed state. τ_k are characteristic relaxation times. Stress-strain relationships are obtained by differentiating the energy function W with respect to strains [1, 11, and 7].

The stress-strain rate relationships are non-linear, and the stiffness of the brain in compression is much higher than in extension. To compute the external force, the tumor growth rate was used. An interesting consequence of the basic model assumptions is that the profile of the concentration of tumor cells depends on the ratio of the growth rate "Eq. (4)" [17, 15, and 7]:

$$\frac{\partial c}{\partial t} = \frac{\rho(c_s - c)}{c_s} \quad (4)$$

In which c(x, t) designates the tumor cell density at location x and time t and ρ denotes the net proliferation rate. This computation makes our method more accurate due to proper force calculation for each patient. Therefore, brain displacement due to tumor growth can be measured by this method. Displacement by tumor is defined as a homogenous force applied to the brain that must satisfy the following condition [16, 7]:

$$f(ext) + div(\sigma - \lambda Ic(t)) = 0 \quad (5)$$

Where f (ext) is external force, σ is internal stress, c (t) is tumor growth model and λ is coupling factor. A coupling factor was chosen that minimizes the quantitative difference between the model and the real deformations: 1.4 N mm/Cells [17, 7]. This equation is the differential version of the law proposed by Wasserman [16, 7] and can be locally interpreted as a tissue internal pressure proportional to the tumor concentration.

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2.3 Deformable Surface Approach

Deformable surfaces are used to generate models of the brain surface in the pre- and the intra-operative stage. Color encoding after efficient distance calculation further enhances the visual impression. The overall work flow of the deformable surface approach consists of four steps: surface generation, surface registration, distance computing and visualization. Surface generation consists of an iterative process which requires a coarse approximation of the brain surface. Therefore, a few vertices are specified in a slicing view, which are then connected using a Delaunay tetrahedrization method. Non-convex parts of the target object are modeled by interactively deleting some of the tetrahedra. Finally, the boundary surface of the tetrahedral complex is the approximation required by the deformable surface module. The distortions caused by the actual brain shift should to be taken into account. Otherwise the registration is severely falsed. In order to avoid the compensation of the deformation phenomenon those vertices are excluded from the registration which is directly related to the location of the brain shift. They are defined by interactively specifying a maximum distance between vertices to be considered. However, this requires a deformation of the brain which is larger than the registration error that has to be compensated. As this is not the case in most situations, an additional manual rigid pre-registration is provided. To visualize the brain shift, annotate every vertex of one brain surface with the distance it has moved away from the other surface, the distance, we have to determine by following equation:

$$d(x, Y) = \min_{y \in Y} \|x - y\|_2 \quad (6)$$

In order to calculate this distance we would have to compute the smallest distance of the regarded vertex to each of the triangles, which is quite expensive. The resulting values are used to color-code the registered surfaces. Either the whole distance value spectrum is mapped to different colors ranging from blue to red, or a threshold is visualized using two colors. It appeared to be useful to draw one brain surface colorized and the second one in a transparent way. This technique provides a good visual impression of the brain shift [18].

3. Linear model

Linear models assume that the stress and strain relationship is linear and brain's response to stress and strain is similar to that of elastic or solid materials solid mechanical model is more reliable than the elastic model.
The energy of the brain's deformation caused by externally applied forces is given by

$$W = \int_{\Omega} \sigma^T \varepsilon d\Omega + \int_{\Omega} F^T u d\Omega \quad (7)$$

where F = F(x, y, z) is the total force applied to the brain, external force obtained from Ω is the brain, u is the displacement vector, and ε is the strain vector that can be defined as ;

$$\varepsilon = \left(\frac{\partial u}{\partial x}, \frac{\partial u}{\partial y}, \frac{\partial u}{\partial z}, \frac{\partial u}{\partial x} + \frac{\partial u}{\partial y}, \frac{\partial u}{\partial y} + \frac{\partial u}{\partial z}, \frac{\partial u}{\partial x} + \frac{\partial u}{\partial z}\right) \quad (8)$$

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In case of linear elasticity with no initial stresses or strains the stress vector (σ) relates to the strain vector by the linear equation σ = Dε, where D is the elasticity matrix describing the material properties and is described by below equation:

$$D=\frac{E(1-\nu)}{(1+\nu)(1-2\nu)}\begin{bmatrix} 1 & \frac{\nu}{1-\nu} & \frac{\nu}{1-\nu} & 0 & 0 & 0 \\ \frac{\nu}{1-\nu} & 1 & \frac{\nu}{1-\nu} & 0 & 0 & 0 \\ \frac{\nu}{1-\nu} & \frac{\nu}{1-\nu} & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1-2\nu}{2(1-\nu)} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1-2\nu}{2(1-\nu)} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1-2\nu}{2(1-\nu)} \end{bmatrix} \quad (9)$$

The value of D can be obtained by two material parameters: Young's modulus(E) that relates tension and stretch in the main orthogonal directions, and the Poisson ratios (ν), which represent the ratio of the lateral contraction due to longitudinal stress in a given plane [7].

4. Optimized Linear Model

Tumor sizes and brain anatomy can change the brain model parameters, called Poisson ratio and Young's modulus from different patient to patient and for different tumor. Therefore, to obtain the best model parameters optimization process is utilized in combination with the conventional linear model to obtain the best parameters for each patient. Meningioma tumors from different patients are analyzed. The cost function was defined as the mean square difference of distance between the landmark position manually selected in the real image data and their corresponding estimated positions in the model. Landmarks were selected in a non-uniform manner around the tumor contour focusing on the areas with large deformations. One half of the landmarks are used in the optimization process and the other half were used for error calculation. The Matlab optimization to optimize the following cost function:

$$MSE=\frac{1}{M}\sum_{i=1}^{M}(x_{iE}-x_{iD})^2 \quad (10)$$

Where M is the number of landmarks, XiE is the estimated landmark position and XiD is the corresponding landmark position the in real data [7].

4. DISSCUSSION

The linear models have low computational complexity, and are easy to implement but have relatively more estimation error than non-linear models, which are more complex, and time consuming. They provide numerical formulations that sufficiently describe brain tissue behavior and are simpler to implement and run relatively fast. Tumor sizes and brain anatomy can change the brain model parameters. Therefore, to obtain the best model

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parameters optimization process is utilized in combination with the conventional linear model to obtain the best parameters for each patient. From the biomechanical point of view linear model is confronted to clinical data. The need to take into account large deformations has to be studied.

Accuracy rates were 92% in the optimized linear model and 95% in the non-linear model but the computation time of the linear model is three times less than nonlinear model. Brain shift behaves in a non-linear manner and is modeled as a viscoelastic material. Nonlinear models closely approximate real shift. The advantages of non-linear method make it the best method to estimate brain shift. The need to reduce computational costs should be taken into account.

5. CONCLUSION

In estimation of brain deformation, model selection and optimization of model parameters are important steps toward obtaining accurate and reliable results. Here, we computed the deformation of brain tissue resulting from meningiomas. We used tumor growth model to compute the external forces and we choose the tumor seeds manually in the regions that tumor exists in real data. Linear models have lower computational costs but has less accuracy compared to that of non-linear. Non-linear models estimate the shift at a much closer level and have 95% accuracy which makes it a better model to be used for the estimation of brain shift and the size of the tumor for removal.

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