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Iteration Method for Registration of Brain Tumor Images with Parallel Optimization

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Abstract

The motivation of this work is to register MR(magnet-resonance) brain tumor images with a brain atlas. Such a registration method can make possible the pooling of data from different brain tumor patients into a common stereotaxic space. The shape, size and location of the initial seed are critical for achieving topological equivalence between the atlas and patients images. We focus on the automatic estimation of these parameters, pertaining to tumor simulation and propose an objective function reflecting feature-based similarity and elastic stretching energy and optimize it with APPSPACK (Asynchronous Parallel Pattern Search), for achieving significant reduction of the computational cost.

Keywords: Brain Tumor, DFO, Deformable Registration, APPSPACK, Optimization.

2010 MSC: 34A36 34K10.

Introduction

Studying the tumor origin and location relative to brain structures for different types of tumors could help gain insight into the brain tumor disease. Moreover, the spatial normalization of tumor diseased images into a common template space, before and after treatment and especially when tumor has recurred, could help studying the tumor progression in relation to the applied treatment (Gray et al., 2006; Jenkinson et al.,2002).

Thus, atlases with segmented structures of interest or with integrated information about anatomical and functional variability can be mapped into the patients image space in order to minimize the risk for significant functional impairment. In this study, (i) we apply a biomechanical model, developed in an Eulerian formulation and solved using regular grids in a fictitious domain method and (ii) focus on the automatic estimation of the tumor model parameters pertaining to tumor simulation. We propose an objective function for assessing the optimality of tumor simulation / registration and optimize it with the parallel optimization method, APPSPACK (Ellingwood et al.,2016; Jenkinson et al.,2002).

Main results

Tumor growth simulation and deformable registration of brain tumor images:

Fig (1) illustrates the whole framework for registration of a normal atlas with a tumor-bearing brain image (patients image). which involves three components: (i) simulation of tumor growth in the atlas image, (ii) deformable registration between the atlas with simulated tumor and the patients image, and (iii) assessment of the output (i.e. deformation field and registered atlas) for estimation of the tumor model parameters. Tumor growth is simulated by seeding the atlas. The approach we use to simulate the tumor induced deformation (mass effect) is based on a biomechanical model employing incremental linear elasticity.

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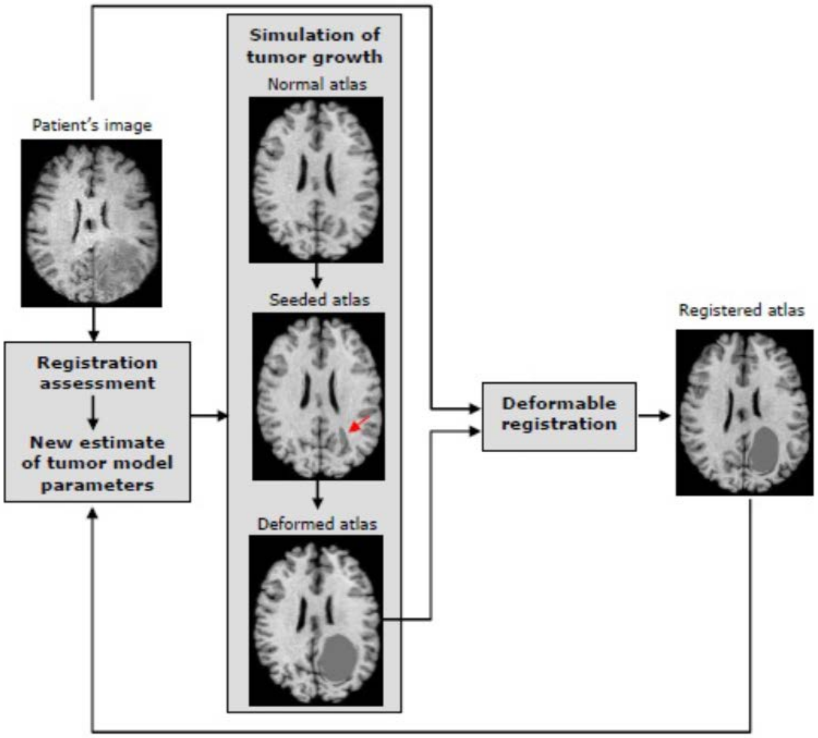

Fig. 1: Illustration of our framework for registration between a normal brain atlas and a patient's image. The red arrow shows the seed that is placed in the atlas for simulating tumor growth. The atlas with simulated tumor (deformed atlas) is then registered to the patient's image.

Since brain tumor images often exhibit large tumors, the biomechanical simulator needs to be robust to large deformations and also computationally efficient. This problem is solved using a regular grid discretization with a fast matrix-free multigrid solver for the resulting algebraic system of equations (Mohamed et al., 2006). we assume that the parameters pertaining to the biomechanical model, such as material properties of brain and ventricles, are similar across patients and we do not include them in the optimization process. The remaining parameters, that need to be estimated, relate to the patient-specific tumor characteristics.

Specifically, the tumor seed is created by eroding the tumor in the patients image and placing it in the atlas. The size of the eroded tumor and the location in the atlas are the 4 parameters pertaining to the tumor seed. The tumor mass effect is calculated by the act of outward forces normal to the tumor boundary. In order to avoid overlapping forces, the convex hull of the tumor seed is used in the simulations. In order to simplistically distinguish between tumor mass effect (causing brain tissue displacement) and tumor infiltration (not causing displacement) we introduce a 5th parameter, the tumor growth factor. The tumor growth factor is a parameter that allows the simulation of tumor mass effect to terminate before the tumor in the atlas has reached the size of the tumor in the subject[5,6]. The similarity criterion is designed based on the similarity of attribute vectors, which are defined for each voxel in the image in order to capture the anatomical context (including healthy and malignant tissue) around it. The attribute vector, $\mathrm{a(x)} = [\mathrm{a_1(x)}\ \mathrm{a_2(x)}\ \mathrm{a_3(x)}\ \mathrm{a_4(x)}\ \mathrm{a_5(x)}]$, reflects edge type ($\mathrm{a_1}$); tissue type ($\mathrm{a_2}$), and geometric moment invariants ($\mathrm{a_3} = \{\mathrm{a_3}^{(j)},\ \mathrm{j} = 1, \dots, \mathrm{K}\}$) from all tissue types, respectively. $\mathrm{a_1}$ and $\mathrm{a_2}$ are scalars taking discrete labels, whereas $\mathrm{a_3}$ is a $1 \times \mathrm{K}$ vector comprising the geometric moment invariants of each tissue and is used to capture shape information. Also a4 is used to reflect the signed distance from the tumor boundary, and a5 to reflect the angular location with respect to the tumor center. The elastic deformation field that spatially warps the template to the patients image is calculated by maximizing a similarity criterion reflecting the distance of attributes. Specifically, The similarity of two voxels x and y is defined as the weighted summation of a similarity criterion matching the brain structures, $\mathrm{Sim_B}$, and a similarity criterion matching the tumor geometry, $\mathrm{Sim_T}$, as given below in (Croft et al.,2015):

$$Sim(x,y) = (1-\omega(x,y)).Sim_B(x,y) + \omega(x,y).Sim_T(x,y) \quad (1)$$

Where

$$Sim_B(x,y)=\begin{cases}0 & a_1(x)=a_1(y)\\ (1-|a_2(x)-a_2(y)|).\prod_{j=1}^{K}\left(1-\left|{a_3}^{(j)}(x)-{a_3}^{(j)}(y)\right|\right) & otherwise\end{cases}$$

$$Sim_T(x,y)=\exp\left(-c_1.|a_4(x)-a_4(y)|\right).exp(-c_2.|a_5(x)-a_5(y)|)$$

$$\omega(x,y)=\begin{cases}1 & x\ or\ y\ inside\ in\ tomur\\ \dfrac{c_3}{a_4(x).a_4(y)} & otherwise\end{cases}$$

$w(x,y)$ is a weighting factor which decreases with the distance of x and y from each tumor respectively, and c_i are positive constants. If at least one of the two images is normal (without tumor), the distance from tumor boundary (a_4) becomes infinite, w becomes zero (for the region outside the tumor) and the similarity criterion matches only the brain structures. The use of spatially adapted weights ensures that the identification of corresponding points is driven mainly by one of the two matching criteria, whereas the spatially smooth decrease of w makes the total similarity, Sim, smooth. Regarding the intrinsic difference between the similarity criteria, we should note that the function values of both Sim_T and Sim_B are normalized in the range [0,1]. Moreover, the con-stants c_1 and c_2 determine the sensitivity (gradient) of Sim_T .

Estimation of the tumor model parameters:

We estimate the tumor model parameters by solving a bound-constrained nonlinear optimization problem

$$\begin{gathered}\min f(\theta)\\ s.t.\ L\leq\theta\leq U\end{gathered}\qquad(2)$$

where $f: \mathcal{R}^n\rightarrow\mathcal{R}^n$ is an empirical nonlinear function designed to rate the success of the coupled tumor simulation and inter-subject registration problem, $\theta\in\mathcal{R}^n$represents the parameters of the tumor simulation model applied, and L and U are lower and upper bounds on , respectively. We focus only on the model parameters that are patient-specific, such as the origin of the tumor, the amount of brain tissue that died due to the tumor appearance, and the tumor growth factor. The bounds L and U are putting some constraints on the validity of the simulations. Non-linear constraints describing the complex brain domain are not explicitly handled; instead, a penalty function is imposed to inhibit invalid tumor simulations (e.g., outside the brain). An upper bound on the tumor growth factor (amount of expansion) is the size of the tumor in the subjects image.

- *Objective function:*

The objective function used for optimizing the tumor model parameters is based on the hypothesis that the optimal tumor parameters minimize the discrepancies between the co-registered images and also produce realistic deformation maps when trying to match the atlas with simulated tumor with the patients image. The objective function,f, reflects the success of registration and the validity of the calculated deformation fields and is expressed as feature-based similarity and elastic stretching energy, respectively. is defined as the combination of three normalized measures:(i) the overlap of the co-registered segmented images (E_1),(ii) the feature-based similarity as in equation (1) (E_2),

Table 1. VN-dist (in mm)for 8 patient's images .In Table 1, has an error of 2:758 mm and 3:662mm respectively. It can be seen that this is a very difficult case, from image registration perspective, since the anatomy is highly obscured by tumor infiltration and edema.

Error total boundary	0.752	0.998	1.021	0.986	0.872	**2.758**	0.785	0.997
Error in tumor vicinity	0.657	1.098	2.350	1.349	1.099	**3.662**	0.578	1.430

And (iii) the Laplacian of the inter-subject deformation field which is used to rate the regularity of the solution based on smoothness properties (E_3) , as mathematically given below in:

$$f=\sum_{k=1}^{3}\sum_{x\in\Omega}c_k h_k(x)E_k(x;\theta)\qquad(3)$$

The constantsc_k are used to assign different weights on different measures, whereas $h_k(x)$ is used to assign different weights according to the voxels location x. $h_k(x)$is selected to decrease with the distance from the tumor boundary for all three measures, and to increase on voxels lying on edges particularly for the image-related measures, i.e., E_1 and E_2. The assignment of higher weights on voxels lying on edges is due to the distinctiveness of the features of those voxels (Zacharaki et al.,2008). The constants c_k are learned by evaluating the performance of each measure separately in the registration of patient images, i.e., how informative each measure is in estimating θ. Ω is the domain over which f is calculated, and it is defined in the subject brain within a specific distance from tumor boundary, where the effects of mis-registration are expected to be more prominent.

- *Optimization method and strategy applied:*

The tumor is manually delineated by an expert in the patients original image. Subsequently, the patients image is registered globally with the tumor-free template by applying an affine transformation. An affine transformation is a transformation which preserves straight lines and ratios of distances between points lying on a straight line. It does not necessarily preserve angles or lengths, but does have the property that sets of parallel lines will remain parallel to each other after an affine transformation. The transformed image is denoted as affine transformed subject in Fig 2. Then the tumor parameters are optimized by solving equation (2). We chose a derivative-free optimization (DFO) that designed for solving general nonlinear optimization problems that have the following characteristics:1) They are relatively small. 2) Their objective function is relatively expensive to compute and derivatives of such functions are not available and can’t be estimated efficiently. because the objective function contains discontinuities and the approximations of the derivatives with finite differencing may be unreliable and APPSPACK targets simulation-based optimization problems characterized by a small number of parameters.

The "asynchronous" property is important for our application, since the function evaluation cost varies significantly according to the parameters applied. We can use parallel computing to decrease time to solution by defining a custom parallel computing implementation of an optimization problem. For each resolution level, an initial estimate of the deformation field is obtained by elastically registering the affine transformed subject to the normal atlas in the whole image domain (Ellingwood et al.,2016;Zacharaki et al.,2008). Since the deformation field displays almost negligible changes in the regions far away from the tumor during the iterative process of optimizingθ, the optimization is performed only in a subdomain of the subject space in order to considerably speed up the implementation. The subdomain is larger than the tumor neighborhood, Ω, used to evaluate the optimality criterion.

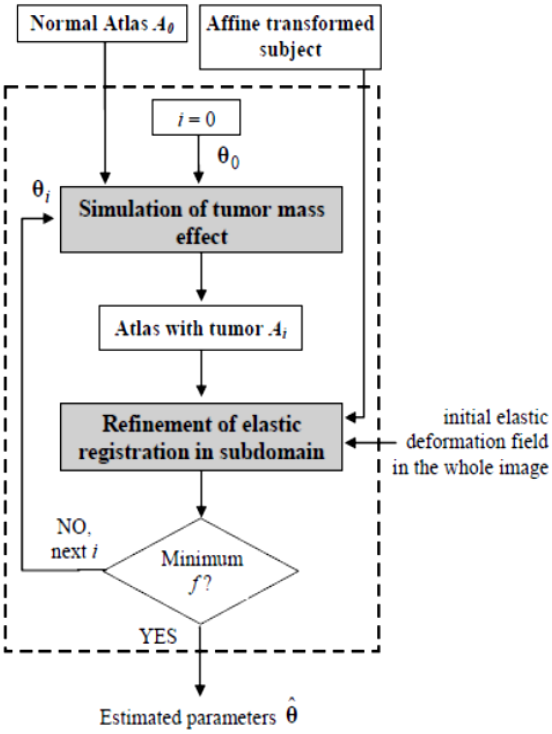

Fig. 2: Estimation of the tumor model parameters by evaluating and maximizing ***f*** in a subdomain of the subject space (region around the tumor).

Conclusion

1. Tumor simulation: The current framework uses a piecewise linear elasticity model and regular grids (PLE simulator)
2. Optimization of the tumor model parameters
3. Definition of the tumor model parameters
4. Registration method More importantly, the computational time is considerably decreased in comparison to our previous work , due to the use of parallel optimization for the parameters of the tumor growth model. The computational cost increases with the number of resolution levels applied in the optimization of the tumor model parameters and decreases with the number of parallel processors. The whole framework (starting from the segmented atlas and patients images), which includes the steps implemented serially in a single processor, required about 2 hours additionally to the optimization. These steps are the calculation of the global alignment, the calculation of the deformation field in the whole image domain before the estimation of θ(for initialization) and the calculation of the deformation field in the whole image domain after the estimation of θ (for refinement in the full resolution).

Methods that have been originally developed with the purpose of atlas-based segmentation often apply simplistic models of tumor growth. A current limitation of our approach is that it is based on the prior tissue segmentation, which poses considerable difficulties in practice, especially in the region around the tumor that often displays edema and infiltration. In this study we present Such a method that (i) makes possible the pooling of data from different patients into a common space (ii) allows the mapping of atlases with segmented structures of interest into the patient's image space for optimization of the surgical or radiotherapy treatment planning, (iii) estimates the brain tissue loss and replacement by tumor, as well as the mass effect of the tumor thereby helps identifying differences in the tumor growth process among populations of subjects The method is based on the idea of decoupling the total deformation into the tumor-induced deformation and the deformation due to inter-subject differences. We can use parallel computing to decrease time to solution by enabling built-inparallel computing support or by defining a custom parallel computing implementation of an optimization problem. For minimizing an expensive optimization problem using parallel computing, we solve the optimization problem by evaluating functions in serial fashion and solve the same problem by using the parallel for Loop feature with evaluating function in parallel. We have applied the proposed framework for registration of 16 brain MRI datasets including tumors. We calculated a quantitative rater-independent measure, such as the surface distance of the ventricles (VN-dist) between the co-registered images. We calculated VN-dist as the mean Euclidean distance of the ventricular boundaries in both directions, from the patients image to the warped atlas image and reversely. Table 1 shows VN-dist for 8 patients images. calculated over the whole ventricular boundary (top rows), as well as only on the part that lies closer to the tumor, in order to emphasize possible limitations of the method due to the presence of tumor (bottom rows). These results show that the distance of ventricles is larger in the tumor vicinity than over the total ventricular boundary. Specifically, the error is at voxel accuracy for the ventricular part that is far from the tumor and at the order of the diagonal voxel distance for the region close to the tumor, for all cases except for one. This worst case, which is highlighted in Table 1, has an error of 2.758 mm and 3.662 mm respectively. It can be seen that this is a very difficult case, from image registration perspective, since the anatomy is highly obscured by tumor infiltration and edema, and the ventricles cannot be clearly segmented.

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