SEGMENTATION OF BRAIN TUMOR IMAGES BASED ON ATLAS-REGISTRATION COMBINED WITH A MARKOV-RANDOM-FIELD LESION GROWTH MODEL

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ABSTRACT

We present an automatic method to segment brain tissues from volumetric MRI brain tumor images. The method is based on non-rigid registration of an average atlas in combination with a biomechanically justified tumor growth model to simulate soft-tissue deformations caused by the tumor mass-effect. The tumor growth model, which is formulated as a mesh-free Markov Random Field energy minimization problem, ensures correspondence between the atlas and the patient image, prior to the registration step. The method is non-parametric, simple and fast compared to other approaches while maintaining similar accuracy. It has been evaluated qualitatively and quantitatively with promising results on eight datasets comprising simulated images and real patient data.

Index Terms— Brain Tumor, Brain Tissue Segmentation, Atlas Registration, Markov Random Field

1. INTRODUCTION

Automatic and accurate segmentation of brain tissues and important brain structures is of major interest for many tasks in physiological and biomechanical modeling in cancer research, surgical planning or clinical studies. Many different approaches to achieve this task exist, e.g. classification, atlas-based segmentation or segmentation based on deformable models. Atlas-based segmentation has several advantages compared to other methods: not only can it provide the different tissue types, but it inherently also contains the segmentation of smaller subcortical structures which are of interest for surgical planning. Additionally, after matching an atlas to the patient image, the same deformation can also be applied to superimpose other modalities of the same atlas on the patient. For example the atlas diffusion image can be mapped to the patient, which is important in tumor modeling. Atlas-based segmentation of different tissue types, such as grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) is an established way to classify different tissues in magnetic resonance images (MRI) of healthy subjects. The atlas labels are propagated to the patient image through warping with a deformation-field obtained by non-rigid registration techniques. However, in case of tumor-bearing brain images this approach fails due to the missing tumor prior in the atlas.

In general, it is not possible to simply mask out the tumor area and perform non-rigid registration on the rest of the healthy brain, because non-rigid methods need a sufficiently good initialization to converge to a good solution. Additionally, the error in structures in the immediate tumor vicinity will be largest. However, this is the most important region because accurate delineation of the structures around the tumor is of major interest in cancer research and surgical planning. A general idea to overcome the problem, is to introduce a tumor seed into the atlas and grow the tumor to its approximate shape. Solutions have been suggested by several groups [1, 2, 3]. Cuadra et al. [1] use a model of lesion growth that does not consider any mechanical tissue properties, while Mohamed et al. [2] use a finite element method (FEM) model to calculate tissue displacements induced by the tumor mass effect according to the mechanical properties of surrounding tissues. After the introduction of a tumor prior into the atlas, this modified atlas image is warped to the patient image using non-rigid registration algorithms, thus implicitly performing segmentation.

It is desirable to incorporate mechanical tissue properties into models of tumor-induced deformations. Although FEM-based methods offer this capability, they suffer from the need of transforming the data into a mesh. Automatic mesh generation is challenging and error-prone, while semi-automatic mesh generation is time-consuming and tedious. It is difficult to handle large deformations of the mesh and frequent remeshing has to be undertaken. A completely voxel-based method, which does not require any meshing would greatly simplify the task. An appealing approach is presented in [3]. However, it runs on a subsampled version of the input image for reasons of computation speed and it suffers from difficult parameterization. Additionally, it requires a pre-segmented tissue image to guide the deformation process.

The aim of this work is to provide a tool to segment the healthy tissues in tumor-bearing brain images, which can be easily used by clinicians while avoiding difficult parameter settings. The proposed method only needs a delineation of the solid tumor area as an input, which can be easily done manually or using a previous automatic segmentation step.

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2. METHODS

We show the application of a clinically-oriented, new mesh-free method for modeling soft-tissue deformations to tumor induced deformation and segmentation of tumor-bearing brain images. It is based on finite differences in a local neighborhood of each voxel using Markov Random Fields (MRF).

2.1. The displacement model

In [4] Seiler et al. outlined the idea of formulating soft-tissue deformations as an energy minimization problem in the MRF sense with the energy to be minimized being

$$U_{\text{total}} = U_{\text{prior}} + U_{\text{observation}} \tag{1}$$

In this case, U_{prior} models the biomechanical properties of the underlying tissues and $U_{observation}$ introduces boundary conditions. The total energy U_{total} is minimized in cliques surrounding a center voxel. Tissue characteristics are based on Young's modulus. A clique and the interactions between the individual voxels is shown for 2 dimensions in figure 1.

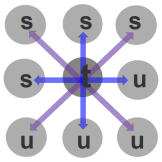

Fig. 1. Different cliques C_i belonging to the center voxel t in 2D.

For each clique C_i at voxel t, the prior energy is calculated depending on its neighbors s and u as

$$\begin{aligned} V_{pC_i} &= \left| \frac{m_t}{m_u}(\mathbf{d_t} - \mathbf{d_s}) - (\mathbf{d_u} - \mathbf{d_t}) \right|^2 \\ &+ \left| \frac{m_t}{m_s}(\mathbf{d_t} - \mathbf{d_u}) - (\mathbf{d_s} - \mathbf{d_t}) \right|^2 . \end{aligned} \tag{2}$$

Equation (2) describes a linear relation with $m_{\{s,u,t\}}$ representing the material property and $\mathbf{d}_{\{s,u,t\}}$ a displacement vector representing the local voxel displacement. By summing over all cliques C_i in the complete image region Ω we obtain the overall prior energy

$$U_{prior} = \sum_{t \epsilon \Omega} \sum_i V_{pC_i} . \tag{3}$$

The observation energy of each clique is calculated as

$$V_{oC_i} = p_{\mathbf{x}_s} \mid \mathbf{b}_{\mathbf{x_s}} - \mathbf{d}_{\mathbf{x_s}} \mid . \tag{4}$$

p_{x_s} acts as a mask and determines at which voxels boundary conditions are applied, $\mathbf{b}_{\mathbf{x_s}}$ is the boundary conditions vector and $\mathbf{d}_{\mathbf{x_s}}$ the displacement vector at position x_s. The overall observation energy in the complete image region is calculated as

$$U_{observation} = \sum_{t \epsilon \Omega} \sum_i V_{oC_i} . \tag{5}$$

We process the image in a hierarchical way in order to be able to use fast and stable local optimizers for the MRF energy. This results in a hierarchical Markov Random Field (HMRF) approach. The iterated conditional modes (ICM) [5] optimization algorithm is used for finding the minimum energy at each level of hierarchy. This solution is employed for the initialization of the next hierarchical level. Thanks to its inherently parallel nature, the ICM algorithm is well suited for implementation on the GPU. Therefore we also implemented a parallelized version of the optimization algorithm on a NVidia® Tesla GPU using Cuda.

2.2. Application of the displacement model to tumor growth modeling in 3D

The mass effect of brain tumors is simulated using the above mentioned model. In this study, we concentrate on the mass effect of gliomas because it has the largest impact on the deformation. Conversely, diffusion effects are neglected. The tumor is grown from a small circular seed, where an outward-pushing force is applied inside the tumor. This displacement deforms the surrounding tissues depending on the mechanical properties they have been assigned.

We adopt a radial expansion force, which is accepted as a good approximation for glioma growth [1]. Growth is performed in an iterative way until the approximate shape and volume of the tumor in the patient image is attained. This means, the hierarchical displacement model, discussed in section 2.1, is applied iteratively with a small displacement at each step.

We would like to emphasize that the presented method is not intended to be a viable model for biomechanical tumor growth. It is used as an efficient and biomechanically justified method to introduce tumor-induced deformations into an atlas image, in order to be able to perform atlas-based segmentation of tumor-bearing brain images.

Material properties of brain tissues are taken from Clatz et al. [6] who report a value of 694 Pa for both GM and WM. The fluid properties are set to a Young's modulus of 0.001 Pa. The skull is assumed to be rigid.

2.3. The complete segmentation pipeline

Before applying the dedicated segmentation algorithm, the images undergo a preprocessing pipeline. In a first step, the brain region is extracted from the images using a customized skull stripping algorithm based on atlas-registration and level-set refinement.[1] Subsequently, bias-field correction is per-

[1] available at www.istb.unibe.ch/content/surgical_technologies/medical_image_analysis/software

formed in order to achieve a homogeneous intensity distribution across the whole image volume using [7]. To cope with noise, anisotropic diffusion filtering is applied as described in [8]. After rescaling the image intensities, the histogram of the atlas image is matched to the histogram of the patient image.

The atlas is initially aligned with the patient image using an affine registration algorithm with a mutual information based similarity metric. After this rough alignment, the atlas is automatically seeded with a tumor prior. This tumor seed is chosen to lie in the center of mass of the patient tumor. If the tumor seed happens to be chosen outside a grey or white matter region, this is corrected automatically so that the seed lies in the vicinity of the initially estimated seed position. Subsequently the tumor is grown to its approximate shape in the patient, which is provided as an input to the algorithm. Tumor growth is governed by the displacement model presented in section 2.2. The patient tumor is eroded by 3 pixels, which allows for better results because the final exact displacement can be handled by the non-rigid registration algorithm. The growth process is stopped when the volume of the artificially grown tumor matches the one of the eroded patient tumor.

The ultimate shape of the tumor and a segmentation of all other brain tissues is obtained using a non-rigid registration step, accounting for the final precise deformation of tumor and surrounding tissues. In our implementation, we use ITK's version of the Diffeomorphic Demons non-rigid registration method by Vercauteren et al [9]. The method yields a dense-deformation field, which is used to register the modified atlas to the pathologic patient image. The Demons method has the advantage of being fast and producing physically justifiable and realistic deformations by ensuring the invertibility of the deformation field. Additionally, it only needs the image intensities to guide the registration process.

3. RESULTS

We analyzed eight volumetric T_1-weighted datasets of brain tumor MR images. Four datasets consisted of simulated images, kindly provided by [10]. For these images a ground-truth tissue classification is available. We also analyzed four real patient cases from the ContraCancrum project database [11]. The atlas for registration was chosen from [12].

Dice similarity coefficients are measured in table 1 to quantify the overlap of the results produced by the proposed method with the ground truth provided by the simulated datasets. Dice coefficients were in the range between 0.7 and 0.82 for the relevant tissues (WM, GM, CSF).

Figure 2 shows one slice of a real-patient case from the ContraCancrum database. Each step of our method is depicted separately (affine alignment and seeding of the atlas - tumor growth in the atlas - non-rigid registration of the atlas). Since no ground-truth segmentation is available for the patient cases, we compared the registration error of manually selected landmark points with and without applying the MRF tumor-growth method. Five landmarks were selected close to the tumor border, whereas five landmarks were annotated in regions further away from the tumor. Results are shown in table 2. When using the MRF growth model, the landmark error in the tumor border region decreased on average by 12% while in regions further away from the tumor it decreased significantly less. The absolute landmark error decreased up to 7mm. As expected, the absolute decrease was larger in the tumor vicinity than in other regions. Additionally, it should be mentioned that without the growth model, landmarks were present inside the tumor area in some cases, which is obviously wrong.

Computation times on a single 2.3 GHz CPU ranged be-

Table 1. Dice similarity coefficient achieved by the proposed method for the four simulated datasets under study.

	CSF	GM	WM	Tumor
Case-1S	0.71	0.77	0.8	0.93
Case-2S	0.7	0.78	0.78	0.94
Case-3S	0.71	0.77	0.8	0.95
Case-4S	0.72	0.79	0.82	0.87

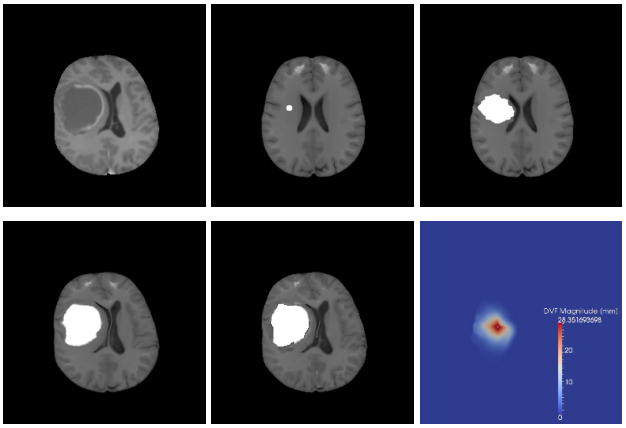

Fig. 2. Results for one slice of ContraCancrum patient Case-1. Top row, left to right: Patient image, seeded atlas after affine registration, deformed atlas after tumor growth. Bottom row, left to right: Deformably registered modified atlas, tissue checkerboard of final result, magnitude of the displacement field after tumor growth.

Table 2. Relative decrease in landmark error after registration using the tumor growth model compared to not using the growth-model for the four ContraCancrum datasets.

	Case-1P	Case-2P	Case-3P	Case-4P
Tumor vicinity	-22%	-15%	-14%	-7%
Other regions	-4%	-11%	0%	0%

tween 20 minutes and five hours, depending on the size of the tumor. The vast majority of the time is spent for the tumor growth process. Previous analyses on 2D slices have shown that the method is approximately twice as fast compared to a FEM method while maintaining similar accuracy [13]. Preliminary results of the GPU implementation in 3D have shown a speed-up-factor of more than 10 (compared to the CPU version) for the total computation time when running on a NVidia® Tesla GPU.

4. DISCUSSION AND CONCLUSION

We applied a clinically-oriented method to deform brain tissues in an atlas, in order to be able to perform atlas-based segmentation of tumor-bearing brain images. This is an extension of our previous work, which operated on 2D slices only, required some manual interactions, had less sophisticated preprocessing and was not parallelized [13]. The technique is generally applicable to simulate the tumor mass-effect. Its advantage is that it is non-parametric and easy to be used, especially in a clinical scenario.

Results were analyzed visually and quantitatively. The performance of the method was promising when comparing checkerboard images. Dice similarity coefficients were competitive or even better than for other methods published [3], however different data was used. Landmark errors in the tumor region decreased significantly when using the proposed growth method, which clearly shows its justification. As expected, landmark errors decreased more in the tumor vicinity than in regions further away from the tumor border. Case-1P exhibited the largest tumor area, while Case-3P and Case-4P were rather small tumors. This is reflected in the landmark error which decreased more for Case-1P than for the other cases. Preliminary tests showed that computation times could be drastically reduced to the order of minutes using a GPU implementation of the MRF tumor growth method. This renders the technique very useful for daily clinical practice.

4.1. Outlook

In the future, we plan to include a diffusion term into the growth-model in order to allow for more realistic simulations. We will also improve and further speed-up the GPU implementation of the MRF-growth method, and present more detailed comparison between CPU and GPU implementation.

5. REFERENCES

[1] M.B. Cuadra, C. Pollo, A. Bardera, O. Cuisenaire, J.G. Villemure, and J.P. Thiran, "Atlas-based segmentation of pathological MR brain images using a model of lesion growth," *IEEE Transactions on Medical Imaging*, 2004.

[2] A. Mohamed, E.I. Zacharaki, D. Shen, and C. Davatzikos, "Deformable registration of brain tumor images via a statistical model of tumor-induced deformation," *Medical Image Analysis*, 2006.

[3] E.I. Zacharaki, C.S. Hogea, D. Shen, G. Biros, and C. Davatzikos, "Non-diffeomorphic registration of brain tumor images by simulating tissue loss and tumor growth," *NeuroImage*, 2009.

[4] C. Seiler, P. Buechler, L.-P. Nolte, M. Reyes, and R. Paulsen, "Hierarchical markov random fields applied to model soft tissue deformations on graphics hardware," *Recent Advances in the 3D Physiological Human*, 2009.

[5] J. Besag, "Statistical analysis of dirty pictures," *Journal of Applied Statistics*, 1993.

[6] O. Clatz, M. Sermesant, P.Y. Bondiau, H. Delingette, S.K. Warfield, G. Malandain, and N. Ayache, "Realistic simulation of the 3d growth of brain tumors in mr images coupling diffusion with biomechanical deformation," *IEEE transactions on medical imaging*, 2005.

[7] J.G. Sled, A.P. Zijdenbos, and A.C. Evans, "A nonparametric method for automatic correction of intensity nonuniformity in MRI data," *Medical Imaging, IEEE Transactions on*, 2002.

[8] P. Perona and J. Malik, "Scale-space and edge detection using anisotropic diffusion," *IEEE Transactions on pattern analysis and machine intelligence*, 1990.

[9] T. Vercauteren, X. Pennec, A. Perchant, and N. Ayache, "Diffeomorphic demons: Efficient non-parametric image registration," *NeuroImage*, 2009.

[10] M. Prastawa, E. Bullitt, and G. Gerig, "Simulation of brain tumors in MR images for evaluation of segmentation efficacy," *Medical Image Analysis*, 2009.

[11] K. Marias et al., "Clinically oriented translational cancer multilevel modeling: The contracancrum project," in *World Congress on Medical Physics and Biomedical Engineering, 2009, Munich, Germany*, Dössel and Schlegel, Eds. 2009, IFMBE Proceedings, Springer.

[12] T. Rohlfing, N.M. Zahr, E.V. Sullivan, and A. Pfefferbaum, "The SRI24 multi-channel brain atlas: construction and applications," in *Proceedings-Society of Photo-Optical Instrumentation Engineers*, 2008.

[13] S. Bauer, C. Seiler, T. Bardyn, P. Buechler, and M. Reyes, "Atlas-based segmentation of brain tumor images using a markov random field-based tumor growth model and non-rigid registration," in *Proceedings of the 32nd Annual International Conference of the IEEE EMBS Buenos Aires, Argentina*, 2010.