Automated Model-Based Segmentation of Brain Tumors in MR Images

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Abstract. We present a novel fully-automated generative brain tumor segmentation method that makes use of a widely available probabilistic brain atlas of white matter, grey matter and cerebrospinal fluid. An Expectation Maximization-approach is used for estimating intensity models for both normal and tumorous tissue. A level-set is iteratively updated to classify voxels as either normal or tumorous, based on which intensity model explains the voxels' intensity the best. No manual initialization of the level-set is needed. The overall performance of the method for segmenting the gross tumor volume is summarized by an average Dice score of 0.68 over all the patient volumes of the BRATS 2015 trainings set.

1 Introduction

Routine use of automated MR brain tumor segmentation methods in clinical practice is hampered by the large variability in shape, size, location and intensity of these tumors. Reviews of MR brain tumor segmentation methods are provided by Bauer et al. [1] and Menze et al. [2].

Brain tumor segmentation methods in Menze et al. [2] are grouped into generative and discriminative methods. Discriminative segmentation methods require a set of manually annotated training images from which the appearance of tumors is implicitly learned by the algorithm. Generative models on the other hand don't require a set of annotated training images. Explicit prior knowledge of anatomy or intensity appearance is directly incorporated into the algorithm [3]. In the past BRATS challenges [2], discriminative methods have largely outperformed generative methods, which sparked increased development in discriminative methods. Although it is clear that existing methods need to be improved in terms of accuracy, the methods also need to be developed and broadened in order to be deployable in clinical settings where access to a training set is limited or non-existent.

We present a novel fully-automated generative tumor segmentation method that only makes use of a widely available probabilistic brain atlas of white matter (WM), grey matter (GM) and cerebrospinal fluid (CSF) and for which no manual initialization is needed. The probabilistic prior is fully exploited by searching globally for voxel intensities that cannot be explained by the normal tissue model. The method is outlined in Sec. 2 and results are presented in Sec. 3.

2 Method

Classification is based on an EM-estimation of normal and tumorous intensity models. An evolving level-set determines which of both intensity models applies to what regions in the image (Fig. 1).

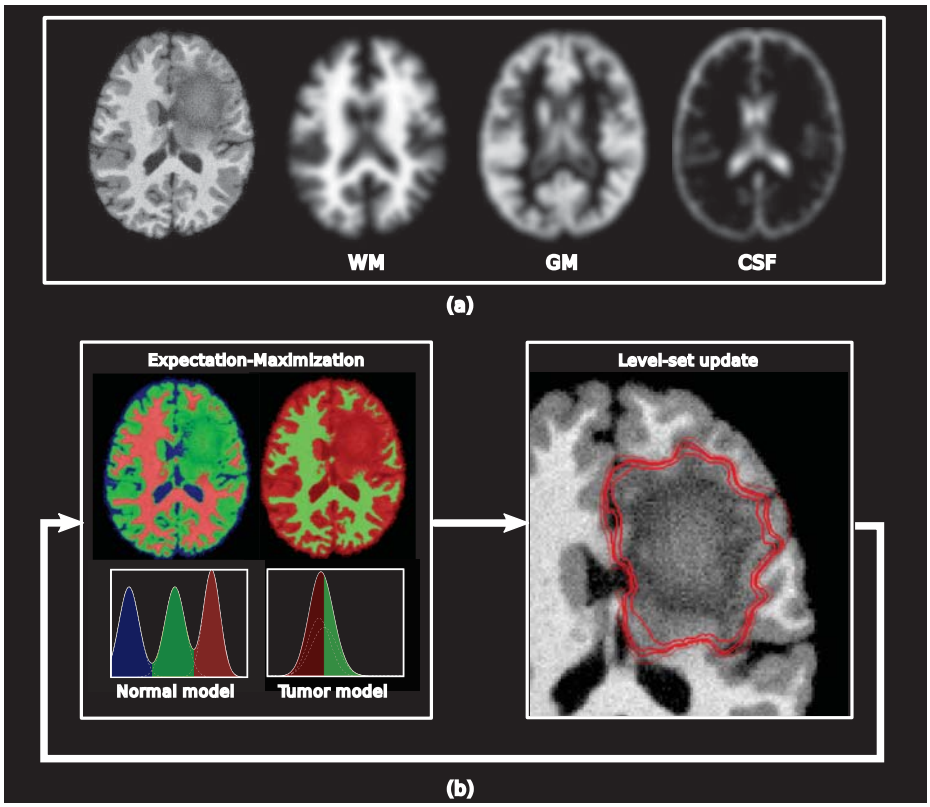

Fig. 1. (a) Spatial priors are non-rigidly registered to the patient image. (b) A full Expectation-Maximization estimation of the normal and tumorous intensity models is done, after which a level-set is updated. This process is repeated until convergence.

Prior Registration Spatial priors of WM, GM and CSF are non-rigidly registered to the patient image. The prior information is relaxed by smoothing the spatial priors with a Gaussian kernel.

Intensity models and the Expectation-Maximization algorithm Normal and tumorous tissue intensities are modeled separately. Let $G_{\mathbf{\Sigma_j}}$ be a zero-mean multivariate Gaussian with covariance matrix $\mathbf{\Sigma_j}$, then normal and tumorous tissue are both modeled by a Gaussian mixture model

$$p(\mathbf{y_i}|\theta) = \sum_{j}^{K} G_{\mathbf{\Sigma_j}}(\mathbf{y_i} - \mu_\mathbf{j}) p(\Gamma_i = j), \tag{1}$$

with $\mathbf{y_i} = (y_{i_1}, \ldots, y_{i_N})$ the intensity of voxel i and $\Gamma_i = \{j|j = 1 \ldots K\}$ the tissue class. The intensity model parameters $\theta = \{(\mu_\mathbf{j}, \mathbf{\Sigma_j})|j \in 1 \ldots K\}$ are iteratively updated using an EM-approach [3]. For normal tissue, $K = 3$ and $p(\Gamma = j) = \pi_j$ are the spatial priors for WM, GM and CSF. For tumorous tissue, the number of Gaussians is a free parameter and the weights of the Gaussians are updated according to the volume fraction of each of the tumor classes.

Convex level-set formulation The image I is subdivided into two regions Ω_{in} and Ω_{out} for which the intensities are modeled by the probability distributions described in the previous paragraph [4]. The regions are separated by a boundary $\partial\Omega$ that is implicitly represented by a level-set function. The boundary and intensity model parameters are found by minimizing the energy functional

$$\underset{\theta_{in},\theta_{out},\partial\Omega}{\operatorname{argmin}} \quad \lambda \int_{\Omega_{in}} -\log p_{in}(I|\Omega_{in}, \theta_{in})\, d\mathbf{x} + \lambda \int_{\Omega_{out}} -\log p_{out}(I|\Omega_{out}, \theta_{out})\, d\mathbf{x} + \kappa \mathrm{L}(\partial\Omega), \tag{2}$$

where $L(.)$ is the length of the boundary. The first two terms penalize the negative loglikelihood of the image I evaluated in respectively the tumorous and normal intensity model. The third term penalizes the length of the boundary. Parameters λ and κ determine the relative importance of the energy terms. For each iteration to update the level-set, a full Expectation-Maximization estimation of the parameters θ_{in} and θ_{out} is done.

The energy functional is non-convex and the gradient flow finds a solution that depends on a manual initialization of the level-set. It is unclear how close the initialization needs to be to the ultimate tumor segmentation. In this work, this problem is overcome by using a convex level-set formulation that performs a global search over the image and makes a manual initialization superfluous. A global minimum is guaranteed by replacing the gradient flow by another gradient flow with the same steady-state solution and by restricting the level-set to lie in a finite interval [5]. The problem is thus reformulated as an L_1-minimization problem that is solved by the Split Bregman-numerical scheme [5]. It is important to note that, by using spatial priors of WM, GM and CSF, the global optimum coincides with the clinically meaningful notion of normal and tumorous regions.

3 Experiments and Results

The method is validated on the BRATS 2015-trainings data set [2] that holds 54 low-grade and 220 high-grade glioma patient volumes that are already skull-stripped and registered intra-patient. No further pre-processing is done. Since the method is designed to segment gross tumor volume, the modalities that are used are the T2-weighted MR image and the T2-weighted FLAIR MR image. The spatial priors are relaxed by a Gaussian kernel with standard deviation of $\sigma = 3$ voxels. The number of Gaussians for modeling the tumor intensities is set to 1. The energy functional hyperparameters are $\lambda = 1e1$ and $\kappa = 1e1$. For each update of the level-set, a full EM-estimation for both the tumorous and normal

intensity model is performed. The computation time for a single patient volume is about 15 minutes on a 2×2.66Ghz Quad-Core CPU, out of which 10 minutes are spent for the non-rigid registration of the priors to the patient volume.

The overall average Dice score for the gross tumor volume on the training data set is 0.68. This score is comparable to fully-automated generative methods from the past BRATS challenges that were validated on a data set that is very similar [2]. However, we should note that currently available discriminative algorithms can reach Dice scores of over 0.80.

4 Discussion and Conclusion

In plenty of clinical settings only a handful of patient images needs to be processed without the availability of an annotated training set. Generative methods have therefore an enormous practical value. In this work, we have presented a generative method for segmenting the gross tumor volume in glioma patients. A global search is performed and spatial prior information of healthy human adults is exploited in order to do the segmentation in a fully-automated way.

References

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