Multi-Feature Guided Brain Tumor Segmentation Based on Magnetic Resonance Images

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SUMMARY In this paper, a novel method of high-grade brain tumor segmentation from multi-sequence magnetic resonance images is presented. Firstly, a Gaussian mixture model (GMM) is introduced to derive an initial posterior probability by fitting the fluid attenuation inversion recovery histogram. Secondly, some grayscale and region properties are extracted from different sequences. Thirdly, grayscale and region characteristics with different weights are proposed to adjust the posterior probability. Finally, a cost function based on the posterior probability and neighborhood information is formulated and optimized via graph cut. Experiment results on a public dataset with 20 high-grade brain tumor patient images show the proposed method could achieve a dice coefficient of 78%, which is higher than the standard graph cut algorithm without a probability-adjusting step or some other cost function-based methods.

key words: tumor segmentation, feature fusion, graph cut, MRI

1. Introduction

Magnetic resonance images (MRI) are extensively used in brain tumor localization in surgery planning for their non ionizing radiation to patients and the ability to provide complementary information for diagnosis, which generally consists of T1-weighted (T1), T2-weighted (T2), T1 with gadolinium contrast agent (T1C) and fluid attenuation inversion recovery (FLAIR) sequences. As manual segmentation is subjective and time-consuming, automatic segmentation has been an important but challenging task due to the complexity of tumor shape, size, location and appearance.

Methods of brain tumor segmentation can be grossly classified into three categories [1], [2]: region- or edge-based, classification or clustering, and atlas-based. The first usually makes use of edge information, and one representative method is to use active contour model [3]. For tumor segmentation based on classification or clustering voxels, the features usually include voxel grayscale, local textures, as well as symmetry [4]. The classification or clustering can be further divided into learning-based [4]–[6] and cost function-based [2], [7], [8] methods. In [2], Closed-Form Metric Learning is employed to learn a task-specific distance metric in the feature space. And a Real-AdaBoost technique with the learned distance metric is used to estimate the probability density of the tumor and the background through learning high-dimensional feature set. In [7], the segmentation task is modeled as an energy minimization problem in a conditional random field (CRF) formulation. They make use of random forests to obtain a probabilistic output instead of hard label separations. Then they use the probabilistic output for the weighting factor. Pairwise potentials are also computed. In [8], random walker algorithm is formulated on a weighted graph and optimized by solving a Dirichlet problem. The user has to select two groups of seeds which locate tumor and edema respectively to initialize the hierarchical RW. Then the hierarchical RW algorithm is performed to identify the tumor and edema. An atlas-based method is commonly used in tumor-growth modeling [9].

An energy cost function-based segmentation method is adopted in this paper, which can incorporate meaningful visual information into the cost function and guide the segmentation specifically. The grayscale is one of the most popular features used in tumor segmentation. Unfortunately, there is much overlap between the intensity values of the grayvalues of tumor, edema and health brain issues which would lead to inaccurate segmentation. In our research, complementary information among different modalts (T1, T2, T1C, FLAIR) could enhance the performance in a suitable fusion way.

In this paper, we propose a tumor segmentation through setting up a cost function by fusing multi-characteristics with different weights. Unlike [2], [7], [8], firstly, a Gaussian mixture model (GMM) is introduced to estimate the posterior probabilities of tumor for each grayscale of fluid attenuation inversion recovery (FLAIR) images, as the white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) can be well modeled by Gaussian functions [10]. Secondly, other features extracted from multi-sequence images are adopted to adjust the posterior probability of each voxel. Then, a cost function-based on probability and neighborhood information is formed and minimized through graph cut. Finally, a post-processing step is employed to refine the segmentation results.

The paper is organized as follows. Section 2 describes the proposed method. Section 3 reports the results based on multi-feature guided segmentation in comparison with other cost function-based methods and presents our discussions with other methods. Finally, Sect. 4 concludes the paper and future research line.
2. Materials and Methods

The flow chart of the proposed method is shown in Fig. 1: 1) pre-processing to normalize grayscales and approximate the main peak of the grayscale histograms; 2) feature extraction to approximate CSF in T1, the enhanced region in T1C, and the symmetric map; 3) estimation of initial probability from the GMM curve fitting of the grayscale histogram on FLAIR images; 4) adjusting initial probabilities by fusing features with a weighted power law transformation; 5) designing the cost function-based on probability and neighborhood and minimizing the cost by graph cut; and 6) post-processing to remove noise and differentiate edema from tumor for high-grade brain tumor. Some images of tumor and result are shown in Fig. 2. Details of these steps are given below.

2.1 Pre-Processing

The grayscales of MR images are normalized into \([0, 255]\) by linear transformation to facilitate subsequent processing. A histogram pan is also adopted to eliminate the influence of illumination variations between slices. Curve fitting is employed on the grayscale histogram of the normalized images. As WM is the main body of the brain, the main peak of histogram can be fitted by a Gaussian function. The red dotted line is the approximate distribution of WM (Fig. 3 (a)). Tumor and edema are always hyperintense in T2 and FLAIR, but hypointense in T1, as compared to WM (Fig. 2 (a,c)). By fitting the main peak of the histograms, we can obtain the important parameters of the Gaussian distributions: the mean values and variances, denoted as \(\mu_{T1}\), \(\sigma_{T1}\), \(\mu_{T1C}\), \(\sigma_{T1C}\), \(\mu_{T2}\), \(\sigma_{T2}\), \(\mu_{FLAIR}\), \(\sigma_{FLAIR}\).

2.2 Estimation of Initial Probability

This process is expected to obtain the initial probability of a voxel to be a part of the lesion, which consists of tumor and edema. FLAIR provides the most significant difference between object and healthy tissues. In addition, the brain is considered to consist of five types of tissue as CSF, WM, GM, tumor and edema. Gaussian Mixture Model (GMM) could be employed to estimate the initial probability, which can be calculated as

\[
p(I_v) = \sum_{i=1}^{M} \alpha_i N(I_v; \mu_i, \sigma_i),
\]

where \(M\) is the number of gaussian, and \(\alpha_i\) the contribution of the \(i\)th gaussian model with \(\sum_{i=1}^{M} \alpha_i = 1\).

The \(N(I_v; \mu_i, \sigma_i)\) means the probability density function of the grayscale \(I_v\), given by

\[
N(I_v; \mu_i, \sigma_i) = \frac{1}{\sqrt{2\pi\sigma_i}} \exp\left[-\frac{(I_v - \mu_i)^2}{2\sigma_i^2}\right].
\]

As shown in Fig. 3 (b), five Gaussian functions yield an accurate approximation of the histogram on FLAIR. In our case, tumor and edema correspond to the forth and fifth gaussian model as the lesion is brighter than CSF, WM, and GM.
where in our case, to CSF region is membrane (Fig. 2 (e)). The probability that a voxel belongs and CSF, a mathematical dilation can be used to include the membrane around the CSF is always hyperintense in T1 sequence. And Bayesian criterion is adopted to abstract the CSF region. In addition, the grayscale distribution of CSF, mixture of GM and lesion, the biggest grayscale value in the 3×3 neighborhood of v as IC. As glioma and edema are hyperintense on these two sequences, FLAIR symmetric map is calculated as

\begin{align}
I_c(symFLAIR) &= I_c(FLAIR) - I_c(FLAIR),
\end{align}

and the T2 symmetric map is produced in the similar way. However, to some degree the intensity of CSF is the highest in T2 but the lowest in FLAIR, and it will disturb the symmetric map (shown as Fig.4(c)(d)). The intersection can remove CSF interferences effectively. The final symmetric map is given as

\begin{equation}
I_c(symmap) = \begin{cases} 
1, & \text{if } \min(I_c(symT2), I_c(symFLAIR)) > T_{sym}, \\
0, & \text{otherwise.}
\end{cases}
\end{equation}

where \(T_{sym}\) is a constant. Figure 4(e) shows the intersection of the symmetric maps of T2 and FLAIR (red region).

The Specificity metrics \(S_{pec}\) is adopted to measure the reliability of the symmetric map, which is calculated as

\begin{equation}
S_{pec} = \frac{TN}{TN + FP}.
\end{equation}
where $TN$ and $FP$ are defined in Eq. (32). The higher Specificity the fewer false positive voxels there are. With the proposed method, the $Spec$ of the symmetric map can reach as high as 99.85\%. Due to the high Specificity value, the symmetric map can be employed to adjust the probability of voxels in step 2.7 as well as filter the object from segmentation in step 2.9.

### 2.7 Adjusting Probabilities

The initial probabilities are coarse because voxels with the same grayscale would have the same possibility with lesion. Due to the presence of noise and grayscale similarity between GM and edema, the segmentation error will be large. The features aforementioned can be employed for adjusting probabilities, with the magnitude of adjustment being dependent on the reliability of the feature.

Features can be divided into two categories: increase the probability (IP) of lesion; decrease the probability (DP) of lesion. Table 1 lists the effect of some features. For a voxel $v$, the grayscale on each sequence and region features constitute the feature vector $I_v$ with component denoted as $I_v(s), s \in \{T1, T1C, T2, FLAIR, CSF, enhance, symmap\}$.

A power law transformation is exploited for adjusting the probability. We assign a value $w_k$ to feature $F_k$. For a voxel $v$, the final probability $P_{fin}(obj|v)$ is calculated as

$$P_{fin}(obj|v) = P_{ini}(obj|v)^w,$$

with

$$w = \prod_{k=1}^{N} w_k,$$

where

$$w_k \begin{cases} < 1, & \text{if } F_k \text{ is IP} \\ > 1, & \text{if } F_k \text{ is DP} \end{cases}$$

and $N$ is the number of features.

The power law transformation would transform the probability in the range of [0, 1], shown as Fig. 5.

### 2.8 Graph Cut-Based Energy Optimization

In computer vision, tumor segmentation is to find a labeling $f$ that assigns each voxel $v \in V$ a label $f_v \in \mathcal{L}$, where $f$ is both smooth and consistent with the observed data [12]. In consequence, the cost function should be in the form of

$$E(f) = E_{data}(f) + E_{smooth}(f).$$

According to the work of Boykov et al. [12]–[14], graph cut has been verified to be an effective approximation algorithm to find the global minimization of this kind of energy functions in the form of Eq. (22). In the proposed method, a binary label non-grid graph cut is therefore adopted for optimization, in which 1 represents lesion region and 0 represents background. 6-neighborhood is chosen to obtain a piecewise smoothness in three-dimensional (3D) images. The form of $E_{data}(f)$ in Eq. (22) is given by

$$E_{data}(f) = \sum_{v \in V} D_v,$$

while the form of $E_{smooth}(f)$ is

$$E_{smooth}(f) = \sum_{(u,v) \in \mathcal{N}} V_{u,v}(f_u, f_v),$$

where $\mathcal{N}$ is the set of pairs of neighbor voxels, and $u, v$ corresponds to a pair of neighbor voxels [12]. Data cost of each
voxel is calculated as
\[
D_a(\omega) = -\ln P(\omega|\omega)v, \quad (25)
\]
and
\[
D_a(\omega g) = -\ln P(\omega g|\omega)v, \quad (26)
\]
where the \( P(\omega|\omega)v \) and \( P(\omega g|\omega)v \) are the posterior probabilities computed in step 2.7.

Smoothing term is used to make the segmentation result smooth and is defined as
\[
V_{ux} (f_u, f_v) = \exp\left(-\frac{(I_u - I_v)^2}{\sigma^2}\right) * \delta(f_u, f_v), \quad (27)
\]
where \( I_u \) and \( I_v \) represent the grayscales of voxel \( u, v \in V \) in T2, and \( \sigma \) is a constant, and
\[
\delta(f_u, f_v) = \begin{cases} 0, & \text{if } f_u = f_v, \\ 1, & \text{if } f_u \neq f_v. \end{cases} \quad (28)
\]

By setting non-zero voxels as a node set \( V \) and assembling them by edges \( E \) according to physical positions, a graph \( G = (V, E) \) can be built. Min-Cut/Max-Flow algorithm [14] is used to optimize the cost function. A lesion map \( I(\text{lesion}) \) is derived during this processing, in which 1 represents lesion region and 0 represents background. For a voxel \( v \), the label \( I_v(\text{lesion}) \) is expressed as
\[
I_v(\text{lesion}) = \begin{cases} 1, & v \in \text{foreground}; \\ 0, & \text{otherwise}. \end{cases} \quad (29)
\]

2.9 Post-Processing

The lesion region obtained from graph cut contains glioma, edema and some noise. This step intends to eliminate noise and differentiate edema from glioma.

2.9.1 Removing Noise

The foreground obtained in step 2.8 can be divided into several disconnected regions. The symmetric value \( S_k \) of the region \( K \) can be calculate as
\[
S_k = \sum_{v \in K} I_v(\text{symrmap}). \quad (30)
\]

The region would be judged as noise if \( S_k < T_s \) and set to background, where \( T_s \) is a constant.

2.9.2 Differentiating Tumor from Edema

The enhanced region and the necrosis surrounded by enhancing region should be marked as tumor, while the remaining are edema for high grade glioma. The final labeling \( f \) of the voxel \( v \) can be calculated as
\[
f(v) = \begin{cases} 2, & \text{if } I_v(\text{lesion}) = 1 & \text{& } I_v(\text{enhance}) = 1; \\ 1, & \text{if } I_v(\text{lesion}) = 1 & \text{& } I_v(\text{enhance}) = 0; \\ 0, & \text{otherwise}. \end{cases} \quad (31)
\]

where label 2 represents for the tumor region, while 1 for edema and 0 for background, respectively.

3. Results and Discussion

Brain tumor image data used in this work were obtained from the MICCAI 2012 Challenge on Multimodal Brain Tumor Segmentation (BraTS, http://www.imm.dtu.dk/projects/BRATS2012) organized by B. Menze, A. Jakab, S. Bauer, M. Reyes, M. Prastawa, and K. Van Leemput. The challenge database contains fully anonymized images from the following institutions: ETH Zurich, University of Bern, University of Debrecen, and University of Utah.

The proposed algorithm has been validated on the high-grade glioma set of the BraTS dataset, which includes 20 patient images. Each patient data contains T1, T1C, T2, and FLAIR images. All volumes are linearly registered to T1, skull stripped, and interpolated to 1 mm isotropic resolution.

To quantify the performance of the segmentation, namely true positive (TP), true negative (TN), false positive (FP), and false negative (FN), which are computed as
\[
TP = R \cap G; \quad TN = \overline{R} \cap \overline{G}; \quad FP = R \cap \overline{G}; \quad FN = \overline{R} \cap G, \quad (32)
\]
where \( R \) is the segment result and \( G \) is the ground truth set. From these, Dice coefficient (Dice) is employed to measure the quality of the purposed method, which is defined as
\[
\text{Dice} = \frac{2 \cdot TP}{FP + FN + 2 \cdot TP}. \quad (33)
\]

The performance of different methods are shown in Table 2. The proposed method is compared with the general graph cut method without probability adjusting and some other cost function-based methods [7], [8], [15] as well as learning-based methods [5], [6].

Table 2 also shows that without probability adjusting the tumor segmentation performance is not as good as with probability adjusting. This may be interpreted as follows. The initial posterior probability is greatly dependent on the grayscale of FLAIR, in which the gray intensities of the tumor part vary a lot, resulting in incorrect segmentation of the tumor. The adjusting step degrades the importance of FLAIR and enhances that of other information such as T2, symmetric map, etc., which leads to improve the tumor segmentation performance. This effect of the probability adjusting can be seen in Fig. 6. The example shows a particular brain tumor image, in which active tumor part

<table>
<thead>
<tr>
<th>high grade glioma set</th>
<th>Dice (%)</th>
</tr>
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<tbody>
<tr>
<td>Classification forest [5]</td>
<td>( _ _ _ _ )</td>
</tr>
<tr>
<td>Spatial decision forest [6]</td>
<td>68</td>
</tr>
<tr>
<td>Hierarchical classification [7]</td>
<td>( _ _ _ _ )</td>
</tr>
<tr>
<td>Random walker [8]</td>
<td>( _ _ _ _ )</td>
</tr>
<tr>
<td>Bayesian method [15]</td>
<td>45</td>
</tr>
<tr>
<td>Our method (without probability adjusting)</td>
<td>75</td>
</tr>
<tr>
<td>Our method (with probability adjusting)</td>
<td>78</td>
</tr>
</tbody>
</table>

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was known, machine learning-based methods \cite{5}, \cite{6} might be better approached through complexity information. As that the features of high glioma are complicated and might other cost function-based algorithms, which reflects the fact posed method yielded a more accurate segmentation than other cost function-based methods \cite{7}, \cite{8}, \cite{15}. The proposed method shows that the proposed method has a better accuracy than formulated and optimized by graph cut. Comparative study given by GMM and other features, a cost function is for-

is hypointense in FLAIR. The posterior probability obtained by GMM can not reflect the lesion correctly and thus leads to error segmentation. Fusing the complementary features among other modals with probability adjusting can perform well in this kind of complicated situation.

Automatic glioma segmentation is challenging due to substantial variation of grayscales, variable and complex shape, texture and weak edges. GMM has been employed to fit the grayscale histogram and determine the initial probabilities. Complementary features from multi-sequence MR images are explored and fused in a new way to modify the initial probabilities. Based on the posterior probability given by GMM and other features, a cost function is formulated and optimized by graph cut. Comparative study shows that the proposed method has a better accuracy than other cost function-based methods \cite{7}, \cite{8}, \cite{15}. The proposed method yielded a more accurate segmentation than other cost function-based algorithms, which reflects the fact that the features of high glioma are complicated and might be better approached through complexity information. As was known, machine learning-based methods \cite{5}, \cite{6} might have over-fitting problem while the proposed fusion on complementary features might avoid. In addition, these complementary features, of which reliability has been testified, may also be used for classification-based segmentation. The moderate Dice coefficient of the proposed method might imply the following: 1) features can be fused with different weight in a good way; and 2) the method still has space to be improved since some effective but complicated features such as based on textures have not been fused yet.

The limitations of our method is as follows: Because public data is rare, the parameters in our experiment may rely on the dataset. The background of this problem is complicated. We designed a lot of intermediate process to obtain a good segmentation. If one process was interfered, following process may be interfered too.

4. Conclusions

A method to segment glioma from multi-sequence MR images have been proposed. The novelties lie in introducing GMM to estimate the initial probabilities, enhancing complementary features through adjusting probabilities by power-law functions, and fusing posterior probability and neighborhood information in a framework of graph cut. Experiment results on a public dataset with 20 patient images show the proposed method could achieve a dice coefficient of 78% to segment the sum of tumor and edema respectively for high grade glioma images. The method could also be explored as the initial segmentation for supervision-based segmentation for higher accuracy.

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