UNSUPERVISED SEGMENTATION OF BRAIN TISSUE IN MULTIVARIATE MRI

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ABSTRACT

In this paper, we present an unsupervised, automated technique for brain tissue segmentation based on multivariate magnetic resonance (MR) and spectroscopy images, for patients with gliomas. The algorithm uses spectroscopy data for coarse detection of the tumor region. Once the tumor area is identified, further processing is done on the FLAIR image in the neighborhood of the tumor to determine the hyper-intense abnormality in this region. Areas of contrast enhancement and necrosis are then identified by analyzing the abnormal FLAIR region in a gadolinium-enhanced T1-weighted image (GAD). Once the tumor regions are removed, the remaining tissue is segmented into white matter, gray matter, and cerebrospinal fluid (CSF) using a hierarchical graphical model whose parameters are estimated using the EM algorithm.

Index Terms—segmentation, glioma, brain, spectroscopy

1. INTRODUCTION

Magnetic resonance imaging has wide uses in the diagnosis, characterization, and planning of treatment for brain tumors. It offers the ability to visualize the internal structure and function of the brain by providing contrast between different soft tissues. One of the best features of MR is the ability to exploit several different contrast mechanisms, thereby acquiring multiple views of the same tissue within a single examination. The contrast mechanism used to generate these images relies upon different physical and physiological properties. Images such as Fluid Attenuated Inversion Recovery (FLAIR) and T1- and T2-weighted MR images are used in order to approximate the boundary and features of tumor, edema, and healthy tissue. Magnetic Resonance Spectroscopy (MRS) provides insight into the chemical composition of brain tissue, which allows for the evaluation of metabolic alterations that are correlated with the nature and malignancy of tumors [1]. Combining the information from these different images can improve the diagnosis and tumor boundary delineation beyond what is achievable from any single image.

When dealing with multivariate magnetic resonance exams, the conventional practice is for the images to be manually segmented by radiologists who apply a combination of experience with previous images and prior knowledge of the contrast mechanisms of each image in order to formulate an opinion about the regions of interest and their borders. The process is subjective and often very time-consuming. It can take as much as three to five hours to identify the regions of interest (ROIs) for one patient.

A large amount of research has been devoted to automated brain tissue segmentation. Supervised segmentation methods use classification algorithms such as k-nearest-neighbor [3], Bayes classifier [3], Neural Networks [3], and Support Vector Machines (SVMs) [4], to learn models of the characteristics of different brain tissue types from labeled examples and use the models to segment new images. Supervised algorithms are usually very slow to train and require a lot of manually segmented data. These algorithms are often inadequate for the segmentation of gliomas, because the heterogeneity within and between different MR images of the same type makes it difficult to distinguish between different tissue types based on pixel intensity values alone. Unsupervised segmentation methods divide an image into homogenous regions based on an objective measure of homogeneity. The simplest unsupervised segmentation method is thresholding, during which individual pixels are labeled as belonging to an object if their value is greater than or smaller than some threshold value [5]. Zhang [6] provides a survey of various methods for setting the threshold automatically. Statistical approaches that label pixels according to probability values determined based on the intensity distribution of the images are very popular approaches to the segmentation problem [7]. Unsupervised segmentation techniques do not require any training data, but can lead to groupings that do not correspond to the desired conceptual brain tissue categories. A great deal of work has been done in the development of unsupervised brain tissue segmentation algorithms that combine information from different images, but there has been somewhat less work in combining imaging data with spectroscopy.

In this study, we use spectroscopy data for the coarse detection of the tumor region. Once the tumor area is identified, the FLAIR abnormality region is finely determined using thresholding with morphology and surface smoothing. Areas of contrast enhancement and necrosis are then identified by analyzing the abnormal FLAIR region in a gadolinium-enhanced T1-weighted image (GAD). Once the tumor regions are removed, the remaining tissue is segmented into white matter, gray matter, and cerebrospinal fluid (CSF) using a hierarchical graphical model whose parameters are estimated using the EM algorithm.
matter, gray matter, and cerebrospinal fluid (CSF) using a hierarchical graphical model based on the intensity values in the pre-gadolinium T1-weighted image (T1v), the T2-weighted image (FSE), and the GAD image. The novel aspects of this algorithm include the use of spectroscopy for coarse tumor detection, which makes it possible to use fast thresholding methods with high accuracy, as well as the identification of regions of interest within the tumor. Together, the pieces of this segmentation algorithm provide a framework for accurately segmenting MR images into healthy and abnormal regions of interest. The method can be used with few corrections to replace the manual segmentation of such images used in the medical field.

2. IMAGE ACQUISITION AND PREPROCESSING

Sixty-nine patients with a diagnosis of high grade glioma received MRI examinations preceding surgery. Thirty-two were scanned on a 1.5 T MR scanner, and thirty-seven were scanned on a 3T MR scanner. The MR examination included a three-dimensional T1-weighted sequence, acquired both with and without gadolinium contrast agent, a 3D T2-weighted sequence, and a 3D fluid attenuated inversion recovery (FLAIR) sequence. These images had a nominal resolution of $1\text{mm} \times 1\text{mm} \times 3\text{mm}$. Chemical shift imaging was performed using point-resolved spectroscopy volume-section techniques ($10\text{mm} \times 10\text{mm} \times 10\text{mm}$ nominal spatial resolution). For the spectroscopy, water suppression was achieved either through the use of spectral-spatial spin-echo pulses or CHESS and outer volume suppression was performed using very selective suppression pulses [8]. The spectral amplitudes and line-widths of choline (Cho), creatine (Cr), and N-Acetyl-Aspartame (NAA), lactate (Lac), and lipid (Lip) were estimated. A spectroscopy-based abnormality index is derived for the relative levels of Cho to NAA (CNI) using a robust linear regression algorithm [8]. All images were rigidly registered to the post-contrast T1-weighted image. The registration was performed through the maximization of normalized mutual information using a gradient ascent algorithm [9]. The images were stripped of the skull using the Brain Extraction Tool (BET) [10].

3. TUMOR SEGMENTATION

The patients considered in this paper have glioblastoma multiforme (GBM), which is the most common and most aggressive type of brain tumor [11]. Scans of GBM usually show a heterogeneous mass with a hypo-intense or necrotic center (dead cells) and a variable ring of enhancement surrounded by edema (an excess accumulation of water) [11]. In this study, the regions of interest within a GBM are the contrast-enhancing lesion (CEL) and the necrotic tissue (NEC).

The tumor segmentation algorithm uses the relative levels of Choline to NAA to detect the tumor. A thresholding algorithm with morphology is then used to find the boundaries of the tumor. Surface smoothing is then applied as a last step correction. The algorithm is described in more detail next and the pseudocode is provided below. The algorithm uses spectroscopy data for coarse detection of the tumor region. Spectroscopy data has a much coarser resolution than structural images, and therefore cannot be used for an accurate delimitation of the boundary of tissue abnormality. Furthermore, spectroscopy data is only available for a part of the structural image. In order to obtain high quality spectroscopy data, lipid has to be avoided during the acquisition process, which means that part of the tumor might not have spectroscopic information. Even though spectroscopy data cannot be used to finely determine the boundaries of tumors, this data reflects metabolite information that is a lot more reliable in detecting abnormal tissue than the information available in the structural images. Therefore, using spectroscopy for tumor detection and structural images for boundary delineation can lead to more accurate results than using each modality on its own. An abnormality index is derived for the relative levels of Cho to NAA (CNI) as described in Section 2. Once the areas of abnormal CNI are identified, further processing is done on the FLAIR image in the neighborhood of the tumor to determine the FLAIR abnormality region. In FLAIR images of patients diagnosed with GBMs, the abnormal region is typically brighter than the rest of the image. A thresholding algorithm is used to identify the bright FLAIR areas in the vicinity of abnormal CNI. A Gaussian distribution is fitted through to the FLAIR intensity values, and a threshold is selected based on this distribution. The rough area of the abnormal FLAIR region is estimated using the area of the abnormal CNI region. This area is used to select an initial thresholding value. The threshold is then optimized by maximizing the inter-region contrast between the area of high FLAIR intensity and the adjacent regions. The contrast is measured in terms of the average gray-level intensity of the region of interest, $I_{ROI}$, and the average gray-level intensity of the local background, $I_{BG}$, and can be computed as $C = \frac{I_{ROI} - I_{BG}}{I_{ROI} + I_{BG}}$. In order to obtain the intensity of the local background, the bounding box

Algorithm 1 Tumor Segmentation Algorithm

1: compute mask $C_{\text{abnormal}}$
2: fit Gaussian distribution through FLAIR intensity values
3: select threshold $t_0$ fitted based on Gaussian distribution
4: threshold FLAIR image: $I_{t_0} = I_{\text{FLAIR}} > t_0$
5: fill holes, erode, then dilate $I_{t_0}$
6: find disjoint regions in the binary image $I_{t_0}$
7: select regions of $I_{t_0}$ which contain abnormal CNI: $L_0$
8: define small windows around connected regions in $L_0$
9: optimize threshold $t$ on local window
10: select final abnormal region $L$ and smooth boundary
11: threshold CEL in region $L$ of GAD image
12: threshold NEC in region $L$ of GAD image
around the region of interest is computed and its edges are increased by 5% in each direction. This provides a local analysis window that is large enough to accurately recompute the tumor boundaries, yet small enough to keep the noise levels reduced. The pixels inside the extended box that do not belong to the region of interest are considered local background pixels. After thresholding, 3D morphological operations are used for spatial correction: the region of interest is dilated and eroded and gaps are filled. The surface of the region of interest if modeled by a surface tessellation using connected triangles. This model is used to smooth the boundaries of the FLAIR abnormality. Areas of contrast enhancement and necrosis are then identified by analyzing the FLAIR abnormality region in a gadolinium-enhanced T1-weighted image. A thresholding algorithm is used to identify the contrast enhancing lesion as the brighter region in the abnormal tissue. Necrosis is identified through thresholding as the darker region within the abnormal tissue. The same goodness of segmentation metrics are used to determine appropriate thresholding values.

4. HEALTHY TISSUE SEGMENTING

After the abnormal brain region is identified using the FLAIR image, the healthy tissue is further segmented into white matter, gray matter, and cerebrospinal fluid based on three images: the T1-weighted image before and after the contrast enhancing agent is administered, and the T2-weighted image. A hierarchical graphical model is used to model the intensity values of the three healthy tissue types in the three types of MR images, and the parameters of the model are estimated using the EM algorithm.

The image classification problem involves assigning to each voxel a class label taking a value from the set \( \mathcal{L} \). Each pixel in an image is characterized by an intensity value \( Y \). The true and unknown labeling of the image is denoted as \( Y^* \), and \( \tilde{X} \) is an estimate of \( X^* \), both of which are interpreted as particular realizations of a random field \( X \), which is a Markov Random Field (MRF) with a specified distribution \( P(X) \). The observable image is denoted by \( Y \), which is a realization of a Gaussian Hidden Markov Random Field (GHMRF). The problem of classification is recovering \( X^* \) given the observed image \( Y \).

The algorithm used for single channel segmentation was introduced in [7] and is briefly described next. This algorithm is then extended to multichannel segmentation. The EM algorithm can be used to iteratively fit the parameters of the model. The strategy underlying the EM algorithm is the following: estimate \( X \) given the current \( \theta \) estimate, then estimate the new parameters \( \theta \) by maximizing the expectation of the complete-data log likelihood, \( E[\log P(X,Y|\theta)] \). The E-step of the EM algorithm calculates the conditional expectation \( Q(\theta|\theta^t) \), while the M-step maximizes it to obtain the next estimate.

### Algorithm 2 EM algorithm

**E-step:** \( Q(\theta|\theta^t) = E[\log P(X,Y|\theta)|Y,\theta^t] \)

**M-step:** \( \theta^{t+1} = \arg \max_{\theta} Q(\theta|\theta^t) \)

<table>
<thead>
<tr>
<th>ROI</th>
<th>with CNI</th>
<th>without CNI</th>
</tr>
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<tbody>
<tr>
<td>T2all</td>
<td>0.95</td>
<td>0.95</td>
</tr>
<tr>
<td>CEL</td>
<td>0.85</td>
<td>0.88</td>
</tr>
<tr>
<td>NEC</td>
<td>0.87</td>
<td>0.85</td>
</tr>
<tr>
<td>WM</td>
<td>0.98</td>
<td>0.90</td>
</tr>
</tbody>
</table>

**Table 1. Segmentation Results**

Given several types of images of the same structure, a hierarchical model can be formed that combines complementary brain tissue type information from several imaging modalities. The data from \( m \) imaging modalities is denoted as \( Y = Y_1,\ldots,Y_m \). Each of the imaging modalities has its own parameters, \( \Theta = \theta_1,\ldots,\theta_m \). The remaining parameters of the model are the labels corresponding to the underlying tissue types, \( \theta_L \). Then, according to Bayes’ rule \( p(\Theta,\theta_L|Y,M) \propto \prod_{i=1}^{m} p(Y_i|\theta_i,\theta_L)p(\theta_L|M) \). The marginal posterior for the common parameters is obtained by marginalizing over the parameters specific to each distribution: \( p(\theta_L|Y,M) \propto \int_{\theta_1} \cdots \int_{\theta_m} p(\Theta,\theta_L|Y,M)d\theta_1 \cdots d\theta_m \).

5. RESULTS

The segmentation algorithm was run on the data described in Section 2. The segmentation results for the abnormal region (T2all), the contrast enhancing lesion (CEL), necrosis (NEC), and white matter (WM) were then compared to expert manual segmentation. These four types of tissue are the regions of interest that get manually segmented for all the acquired scans. White matter is of interest because it can be used for normalization. The precision (P), recall (R), and F-measure results of this comparison are summarized in Table 1 and some examples are illustrated in Figure 1. Table 1 also illustrates the benefits of using CNI for tumor detection, by contrasting the results with those of using FLAIR alone for the abnormality detection.

6. DISCUSSION

The algorithm proposed in this paper is able to obtain the FLAIR abnormality with high accuracy, as compared to manual segmentation. This algorithm is fast, and does not require any training. The use of spectroscopy data for tumor detection eliminates the need for a slow, complicated algorithm for tumor detection or for correcting spatial segmentation errors. The possible drawback in the use of spectroscopic images is the extra acquisition time. However, spectroscopic images are routinely acquired for glioma patients in or-
Fig. 1. Segmentation Results. Each row corresponds to one patient. The columns, from left to right, illustrate the abnormal brain region on a FLAIR image, the CEL and NEC on a GAD image, and an overlay of the abnormal, white matter, gray matter, and CSF automated segmentation on top of a T1-weighted image. The ROIs segmented by our algorithm have red outer boundaries and green inner boundaries. The manually segmented ROIs have yellow outer boundaries and blue inner boundaries. The tumor is red, the CSF is blue, the white matter is green, and the gray matter is yellow.

7. REFERENCES


