AUTOMATIC SEGMENTATION OF OPTIC PATHWAY GLIOMAS IN MRI

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ABSTRACT
This paper presents an automatic method for the segmentation of Optic Pathway Gliomas (OPGs) from multi-spectral MRI datasets. The method starts with the automatic localization of the OPG and its core with an anatomical tumor atlas followed by a binary voxel classification with a probabilistic tissue model whose parameters are estimated from MR images. The method effectively incorporates prior location, shape, and intensity information to accurately identify the sharp OPG boundaries and to delineate in a consistent and repeatable manner the OPG contours that cannot be clearly distinguished on conventional MR images. Our experimental study on 15 datasets yield a mean surface distance error of 0.67mm and mean volume overlap difference of 28.6% as compared to manual segmentation by an expert radiologist. To the best of our knowledge, this is the first method that addresses automatic OPG segmentation.

Index Terms— multi-spectral MRI, brain tumor, segmentation, Optic Pathway Glioma

1. INTRODUCTION
Optic Pathway Gliomas (OPGs) are the most common tumors of the central nervous system in patients with Neurofibromatosis (NF). OPGs are low-grade pilocytic astrocytomas arising in the optic nerve and chiasm and may involve the hypothalamus and post-chiasmal regions. OPGs may be asymptomatic, but may become very aggressive [1]. OPG growth may cause severe complications depending on its localization [2]. In NF patients, the most common site of involvement of the optic pathway is the optic nerve, while in combined NF and non-NF groups, the most common site is the chiasm. Patients with known OPGs are typically screened serially for progressive visual loss and for changes on MR images.

To determine the proper treatment for NF patients with OPGs, it is crucial to accurately quantify the tumor volume and its components [3]. Precise follow-up of OPG evolution may serve as a marker for disease progression and may be used to determine the efficacy of a treatment. Currently, OPG volume is coarsely estimated manually by the physician with a few measurements on axial, coronal, and sagittal slices. This is inaccurate, time consuming, error prone, user dependent, and may compromise the follow-up of the disease progression and its treatment.

Brain tumor detection, characterization, and follow-up using CT and MR images is the current standard of care in radiology. The ample spectrum of tumor types and locations has given rise to a plethora of methods for tissue classification and quantification [4]. Most studies focus on the automatic detection of Glioblastoma Multiforme (GBM) tumors, e.g. [3, 5, 6], since they account for about 40% of all brain tumors [7]. Additional studies address the automatic detection of other brain lesions, including astrocytoma [8], low-grade glioma [9] and meningioma [10]. While effective, most of these methods do not take into account the anatomic location of the tumor, which is essential for the detection and segmentation of the OPG. A common problem of OPGs and other tumors is the delineation of their boundaries due to the tumor inhomogeneity, the surrounding tissues with overlapping signal intensity values, the uneven tumor ingrowth into nearby structures, and the imaging partial volume effect.

In this paper we describe an automatic method for the segmentation of OPG from multi-spectral MRI datasets. The method starts with the automatic localization of the OPG and its shape with an anatomical atlas followed by a binary voxel classification with a probabilistic tumor model whose parameters are estimated from MR images. The method effectively incorporates prior location, shape, and intensity information to accurately identify the sharp OPG boundaries and to delineate in a consistent and repeatable manner the OPG contours that cannot be clearly identified on the MR images. Experimental results on 15 datasets yield a mean surface distance error of 0.67mm and a mean volume overlap difference of 28.6% as compared to manual segmentation by an expert radiologist. To the best of our knowledge, this is the first method that addresses automatic OPG segmentation.

2. METHOD
Our automatic OPG segmentation method consists of four steps. The input is a multi-spectral MRI dataset consisting of k MRI pulse sequences, such as T1-weighted, T2-weighted, Fluid Attenuated Inversion Recovery (FLAIR), among others. The output is the set of OPG voxels. Since OPG bound-
aries are not always clear, the algorithm uses a probabilis-
tic tissue model generated from training datasets. The ini-
tial location of OPG is found using an anatomical OPG atlas.
The OPG atlas consists of a set of points in the chiasm core, $O = \{o_1, ..., o_{n_O}\}$, and a set of points the OPG Region Of Interest (ROI), $M = \{m_1, ..., m_{n_M}\}$. These two sets were defined by an experienced radiologist on the Johns Hopkins Univ. Int. Consortium of Brain Mapping T2 atlas [11].

In the first step, the MR images from the different pulse sequences are co-registered and normalized. In the second step, the core of the chiasm and the OPG Region Of Interest (ROI) are defined by registering the MR images to the anatomical OPG atlas. In the third step, the OPG sharp boundaries are found. In the fourth step, the missing OPG boundary segments are found using a probabilistic tumor intensity model. Fig. 1 shows two representative examples of OPG segmentation. Fig. 2 illustrates the algorithm steps.

2.1. MRI sequences co-registration and normalization

Since the patient may move during image acquisition, we first co-register the MR images with an affine registration method using the SPM package [12]. To standardize the patient MRI intensity values and the probabilistic OPG intensity model, we apply Dynamic Histogram Warping (DHW) [13]. This results in intensity-normalized and aligned MR images.

2.2. MRI sequences registration to OPG atlas

The chiasm core and OPG ROI are generated by first regis-
tering the MR images to the OPG atlas using the SPM nor-
malization tool [12], and then mapping back the OPG atlas points $O$ and $M$ to the MR images space. The resulting sets $\hat{O} = \{\hat{o}_1, ..., \hat{o}_{n_O}\}$ and $\hat{M} = \{\hat{m}_1, ..., \hat{m}_{n_M}\}$ represent the chiasm core and the OPG ROI in the patient image space.

2.3. OPG sharp boundaries detection

The OPG is mostly surrounded by the Cerebral Spine Fluid (CSF), whose intensity value in the FLAIR pulse sequence is very low. Consequently, the OPG boundary is clearly distin-
guishable where the CSF surrounds the OPG. The CSF voxels are identified in FLAIR by fixed-value thresholding. Once the sharp OPG boundary voxels have been identi-
fied, $\hat{M}$ is reduced to include only the OPG voxels that do not lie beyond a sharp border. The voxels are selected as follows. For every voxel $\hat{m}_i \in \hat{M}$, we find the shortest Euclidean distance path to $\hat{O}$ and label it as $P = \{p_1, ..., p_i\}$. If at least one of the voxels in $P$ is a CSF voxel, then $\hat{m}_i$ is deleted from $\hat{M}$. The resulting $\hat{M}$ has all the voxels in the OPG ROI that do not lie beyond the CSF borders around the OPG.

2.4. OPG boundary completion

To find the OPG boundary in areas where a clear border with CSF does not exist, we use the Generalized Likelihood Ratio Test (GLRT) [14]. In GLRT, two hypotheses are defined; the most likely is chosen based on a probabilistic measure calculated from an estimate of their unknown model parameters. 

Probabilistic tissue model

We represent an MRI dataset consisting of MR images ac-
quired with $k$ pulse sequences, each with $n$ voxels, as set $V = \{v_1(r), ..., v_n(r)\}$ where $v_j(r)$ is a $k$-dimensional vector, $v_j(r) = (v_{j1}, v_{j2}, ..., v_{jk})$, where $v_{ji}$ represents the intensity value of the voxel $v_i$ in the $j$-th pulse sequence. The parameter $r$ denotes the spatial location of the voxel $v_i(r)$. We postulate two hypotheses for voxel $v_j(r)$:

$$H_0 : \text{voxel } v_j(r) \text{ corresponds to healthy tissue.}$$

$$H_1 : \text{voxel } v_j(r) \text{ corresponds to OPG.}$$

Thus, the probability of $v_j(r)$ to be OPG depends on its spa-
tial location and the voxel intensity values in the MR images. Assuming that the spatial location of a voxel is independent of its intensity level, the Probability Density Function (PDF) of $v_j(r)$ for a given hypothesis is:

$$f(v_j(r), r|H_i) = f_I(v_j(r)|H_i) \cdot f_S(r|H_i), \quad i = 0, 1$$

where $f_I(v_j(r)|H_i)$ and $f_S(r|H_i)$ are the contributions of
the intensity and the spatial location of \(f(v_j(r), r|H_i)\).

Since the OPG spreads from the center of the core to the margins of the chiasm, we model \(f_S(r|H_1)\) as a Gaussian:

\[
(r|H_1) \sim N(r_S, C_S).
\]

Since \(H_0\) is the complementary hypothesis of \(H_1\), and we have no additional knowledge about the distribution of \(r\) for \(H_0\), we model the distribution of \(f_S(r|H_0)\) as:

\[
f_S(r|H_0) = 1 - f_S(r|H_1)
\]

Under hypothesis \(H_1\), an OPG voxel can be enhancing OPG, non-enhancing OPG, or cyst. Under hypothesis \(H_0\), a healthy voxel can be air, CSF, or non-enhancing healthy tissue.

We model the intensity levels of the voxels under hypotheses \(H_0\) and \(H_1\) as a mixture of three Gaussians. The distribution of the intensity values for the \(i\)-th hypothesis is:

\[
f_i(v_j(r)|H_i) = \sum_{q=1}^{3} a_{iq} \cdot g_1(C_{iq}) \cdot g_2(\mu_{iq}, C_{iq})
\]

\[
g_1(C_{iq}) = \frac{1}{(2\pi)^{k/2}|C_{iq}|^{1/2}}
\]

\[
g_2(\mu_{iq}, C_{iq}) = \exp\{-\frac{1}{2}(v_j(r) - \mu_{iq})^{T}C_{iq}^{-1}(v_j(r) - \mu_{iq})\}
\]

where the superscript \(T\) denotes the transpose. The parameters \(\mu_{0q}\) and \(C_{0q}\) denote the mean vector and covariance matrix of the relevant healthy tissue component, respectively, and \(\mu_{1q}\) and \(C_{1q}\) denote the mean vector and covariance matrix of the relevant OPG component. Since we do not have the prior probabilities of any of the three components for either of the healthy or the OPG hypothesis, we use an equal prior probability for these components, i.e.: \(\forall i, q \ a_{iq} = \frac{1}{3}\).

Unknown parameters estimation

The PDF of a voxel for a given hypothesis \(H_0\) or \(H_1\) requires the estimation of the mean vector and matrix covariances. To compute the value of these 14 parameters, we use Maximum Likelihood Estimator (MLE). We group the parameters estimators into three vectors:

\[
\hat{\theta}_0 = (\{\hat{\mu}_{0q}\}_{k=1}^{3}, \{\hat{C}_{0q}\}_{q=1}^{3})
\]

\[
\hat{\theta}_1 = (\{\hat{\mu}_{1q}\}_{q=1}^{3}, \{\hat{C}_{1q}\}_{q=1}^{3})
\]

\[
\hat{\theta}_2 = (\hat{r}_S, \hat{C}_S)
\]

representing the healthy tissue model, the OPG model, and the OPG location. Since we assumed Gaussian distribution of the healthy and OPG components, the MLEs of \(\hat{\theta}_1\) and \(\hat{\theta}_2\) in this case are as follows [14]. The parameters \(\{\hat{\mu}_{0q}\}_{q=1}^{3}\) and \(\{\hat{C}_{0q}\}_{q=1}^{3}\) are the sample mean and covariance matrix of the CSF, air, and healthy components of healthy tissues, respectively. Similarly, \(\{\hat{\mu}_{1q}\}_{q=1}^{3}\) and \(\{\hat{C}_{1q}\}_{q=1}^{3}\) are the sample mean and covariance of enhancing, non-enhancing, and cystic components of OPG, respectively. Based on Eq. 1, \(\hat{r}_S\) is the center of mass of \(\hat{O}\) (the origin of chiasm), i.e.:

\[
\hat{r}_S = \frac{1}{n_{\hat{O}}} \sum_{i=1}^{n_{\hat{O}}} \hat{r}_i
\]

and \(\hat{C}_s\) is the spatial sample covariance of \(\hat{O}\), the core of the chiasm. The GLRT is thus:

\[
\Lambda(v_j(r)) = \frac{f(v_j(r), r|\hat{\theta}_1, \hat{\theta}_2; H_1)}{f(v_j(r), r|\hat{\theta}_0, \hat{\theta}_2; H_0)} \cong \gamma
\]

where \(\gamma\) is a predetermined threshold that reflects the trade-off between false and missed detections. The notation \(\cong \gamma\) means that if \(\Lambda(s_i(r))\) is greater than \(\gamma\), \(H_1\) is chosen for voxel \(s_i(r)\), otherwise, \(H_0\).

The final segmentation result is the intersection between the GLRT result and \(M\). The set of voxels \(S = \{s_i(r)\}\) that are detected as OPG is:

\[
S = \{s_i(r) : \Lambda(s_i(r)) > \gamma \ \text{and} \ s_i(r) \in \hat{M}\}
\]

3. EXPERIMENTAL RESULTS

We conducted a quantitative evaluation of our method with 15 clinical multi-spectral MRI datasets acquired by a General Electric Signa 3T HDXT scanner. Subjects were pediatric patients 3-7 years old with OPGs. Each scan consists of the three pulse sequences that are mostly frequently used to detect, diagnose, and segment OPGs in the clinical setting: T1-weighted, T2-weighted, and FLAIR. Each dataset has 512 × 512 × 30 voxels with voxel size 0.5mm × 0.5mm × 5.0mm. An expert radiologist manually produced ground-truth segmentations for each scan. To separate the training and testing datasets and to provide robust performance of our methods, three additional data sets were used to estimate the unknown parameters for Eqs. 3-4. These datasets were also used to determine the CSF value in the FLAIR sequence to distinguish the OPG from CSF in their tangency region. Figs. 1 and 2 show representative results.

To quantify the results, we computed the Receiver Operating Characteristic (ROC) curve. It graphically shows the sensitivity versus false positives (FP) rate for a binary classifier system as its discrimination threshold varies [15]. Fig. 3 shows the free response ROC curve for the 15 datasets, where l-sensitivity is given in voxels/mm³ units. We determined from it that the optimal threshold is \(\gamma = 1.2\). For this value, the mean volumetric overlap error is 28.6%, and the mean surface distance is 0.67mm. These values are comparable to those of other fully automatic detection methods of brain tumors reported in the literature [4, 6].

4. CONCLUSIONS

We have presented a method for the automatic segmentation of Optic Path Gliomas from several MRI pulse sequences.
Our method effectively incorporates prior location, shape, and intensity information. It relies on an anatomical tumor atlas and on a probabilistic tissue model. Unlike other methods, ours relies on the tumor localization to define a tumor region of interest and combines the voxel information from several MRI modalities to delineate the ambiguous OPG boundaries. Our experimental results indicate that our method accurately identifies the sharp OPG boundaries and delineates in a consistent and repeatable manner the OPG contours that cannot be clearly identified on the MR images. Our method is the first of its kind for automatic OPG segmentation.

The potential clinical significance of the OPG segmentations is to save time and effort for clinicians and to provide an automatic tool to reliably determine the OPG shape boundary and measure its volume. In addition, since OPG contours often cannot be defined in the MR images even by an expert radiologist, the method can provide a consistent, repeatable, and unbiased tool for follow-up measurements. Future work includes the classification of the segmented OPG volumes into its three constituent components (cyst, enhancing, and non-enhancing tumors) and the comparative evaluation and comparison for accurate and quantitative OPG follow-up.

5. REFERENCES


