Recent Advancements in the Automatic Detection and Segmentation of GBMs from Multimodal Brain MRI Images

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Abstract *- Segmentation of tumors from multimodal MRI images is a challenging and time consuming task done manually by radiologists. Automation of this task is challenging because of the high variance in appearance of glial cells, among different patients and, similarity between tumor and normal tissue. In this paper we present the results of our survey on recent progress in the segmentation of brain tumors from multimodal MRI images Multimodal Brain Tumor Segmentation.*

Keywords — *BRATs, Generative model, Discriminative model, SVMs.*

I. INTRODUCTION

Glioblastoma multiformes are the frequent brain tumors in humans, originating from glial cells and invading the surrounding tissues [1]. In spite of advances in glioma research, diagnosis of the patient remains very poor. The patients with GBMs, require immediate treatment, because they have a median survival rate of two years or less [2], [3]. For low grade gliomas treatment is often delayed as long as possible. To evaluate the progress of the disease and the success of the treatment modal, neuroimaging methods are used for both categories. In clinical routines and clinical studies, the resulting images are evaluated either based on qualitative criteria only or by relying on quantitative measures as the largest diameter visible from axial images of the lesion [4], [5].

Tumor segmentation in Brain MRI is one of the crucial procedures in surgical and treatment planning. However, at present, tumor segmentation in brain images is performed manually in clinical practice. Apart from being time consuming, manual tumor delineation process is complex and depends on the expert. Currently, multimodal MRI images are used by clinical experts in segmenting brain tumor images because they provide various data on brain tumors. In GBMs, the tumor portion is divided into necrosis, contrast-enhancing tumor, nonenhancing tumor, and edema [6]. Different image modalities reveal different parts in the tumor area. For example, T1-C (T1-weighted modal images with contrast enhancement) highlights contrast-enhancing regions, whereas T2 highlights edema regions. Though multimodal MRI images can provide complementary information in the tumor region, brain tumor segmentation is still a challenging and difficult task.

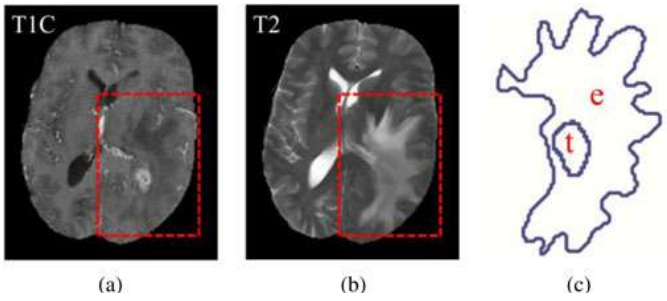

Fig. 1. Different modalities reveal different parts in the tumor area. The edge of the tumor area is visually vague. In addition, the brain structure is deformed because of the occurrence of edema. (a) T1C-weighted brain tumor MRI image. (b) T2-weighted brain tumor MRI image. (c) Contour of the actual brain tumor. "t" represents the combination of contrast-enhancing and necrotic parts, and "e" represents the edema part.

Tumors in brain can have various shapes and sizes and may appear at different locations. In addition to tumor heterogeneity, tumor edges can be vague and visually complex (Fig. 1). Moreover, some tumors may infiltrate surrounding tissues in the brain because of the mass effect or edema (Fig. 1). Additionally, artifacts and noise in brain MRI images increase the difficulty of segmentation process. Thus, designing of a semiautomatic or automatic brain tumor segmentation approach is necessary to provide an acceptable performance.

By replacing the current assessment methods with highly accurate and reproducible measurements of the tumor structures, image processing algorithms that can automatically

analyze brain tumor image slices would be of great potential value for treatment planning, improved diagnosis, and follow-up of individual brain tumor patients. However, design and development of automated brain tumor segmentation techniques is challenging, because tissue areas are defined through intensity variations that are relative to surrounding normal lesions, and even manual segmentations by experts show significant changes when intensity variations between adjacent lesion structures are smooth or suppressed by partial voluming and field artifacts. Further, tumor lesions vary considerably across tumor patients in terms of shape, size, extension, and localization, hindering the use of strong priors on shape and location that are important components in the segmentation of many other anatomical lesion structures. Moreover, the mass effect induced by the growing tissue may infiltrate normal brain tissues, thereby limiting the reliability of spatial prior knowledge for the healthy part of the brain. Finally, a variety of MRI imaging modalities can be used for mapping tumor affected tissue changes, including T2 and FLAIR MRI (highlighting changes in tissue water relaxational properties), post-Gadolinium T1 MRI (showing pathological intratumoral take-up of contrast agents), perfusion and diffusion MRI (local water diffusion and blood flow), and MRSI (relative concentrations of selected metabolites). These imaging modalities provide different types of biological information, and therefore poses somewhat different important information processing tasks.

Because of its high clinical relevance and its challenging nature, the process of computational brain tumor segmentation has attracted attention during the past 20 years, resulting in a wealth of different techniques for automated, semi-automated segmentation of tumor tissues. All of these methods were validated on small private datasets with varying metrics for performance quantification, making comparisons between these methods a highly challenging task. Exacerbating this problem is the fact that various combinations of imaging modalities are used in validation studies, and that there is no consistency in the tumor sub-regions that are considered. Because of this, it remains difficult to judge which image segmentation techniques may be worthwhile for use in clinical practice and research; what exactly the performance is of the best image processing algorithms available today; and how well current automated segmentation algorithms perform in comparison with groups of expert clinical raters.

In order to review the current state-of-the-art in automated brain tumor segmentation and compare between different strategies, in 2012 and 2013 a Multimodal Brain Tumor Image Segmentation Benchmark (BRATS) challenge in conjunction with the international conference on Medical Image Computing and Computer Assisted Interventions (MICCAI) was organized. For this, a unique dataset of MR scans of low- and high-grade glioma patients with repeat manual tumor delineations by several human experts was prepared, as well as realistically generated synthetic brain tumor datasets for which the ground truth segmentation is known. On this data set, each of twenty different brain tumor segmentation methods was optimized by their respective developers. In this paper we report the results of this BRATS benchmark.

The paper is organized as follows. We briefly review the current state-of-the-art in automated brain tumor segmentation in Section II. Evaluation process is described in Section III. Section VI concludes the paper.

II. Related Work

Brain tumor segmentation techniques can be divided into two categories — automatic and semiautomatic. Automatic segmentation algorithms for segmenting and classifying brain tumors include fuzzy c-mean clustering [7–9], region-growing methods [5–9], atlas-based methods [10,11], neural network-based techniques [12,13] and watershed methods [14,15]. These methods generally require postcontrast T1-weighted images (where the tumor is either fully enhanced or shows peripheral enhancement) and work on lesion homogeneity. They still remain a challenge for heterogeneous brain tumors and for other MR modalities.

Research on semiautomatic methods has been done for medical image segmentation (for segmentation of brain tumors on MRI images). Most of these works have used parametric active

contour models [16–20] and level-set active contour models [21–23]. These semiautomatic methods provide more accurate results than the automatic methods because the initial region of interest is labeled by humans. This reduces the search space and helps in locating and segmenting brain tumors with more accuracy.

Caselles[17] have conducted experiments using geodesic active contours. His approach used a snake based on energy minimization and the level-set technique for segmenting an object. The interior and exterior edges of the object are detected without contour-tracking process. The similar experiments were conducted on tumor images, but the tumor was not extracted properly as the evolved curve did not stop at the exact location due to the large changes of the gradient along the brain tumor boundary.

Xu and Prince [18] have conducted experiments using gradient vector flow (GVF). In their work contour was initialized across the object boundary. by the bidirectional nature of the vector field. In this bidirectionality prevented the contour from leaking through small boundary holes or weak edges. However, the same bidirectionality caused GVF contour to collapse on approach to the same object boundary. The contour failed to evolve at saddle points. GVF active contour performance was tested on MR of the left ventricle of a human heart; however, due to the presence of irregular boundary, many details of the endocardia border were left out. Xie and Mirmehdi's [23] have proposed magneto static active contour (MAC). Their model is based on magnetostatics and hypothesized magnetic interactions between the active contour and object boundaries. This MAC model is able to capture complex geometries, weak edges and broken boundaries. However, this MAC model is slower than parametric methods and detects multiple false objects in the presence of noise, leading to the arising of multiple zero-level sets (as in the case of heterogeneous brain tumors).

Wang et al. [20] proposed a model for brain tumor segmentation based on fluid vector flow (FVF). Their model simulates fluid flowing along object boundary and generates external force field to drive the contour evolution. Their FVF model works well on postcontrast T1-weighted images, particularly in extracting brain hemorrhage and tumor (high-intensity regions). However, their method was not tested on other MRI modalities(T1-weighted and T2-weighted brain tumor MR images) and with different tumor types (isointense and heterogeneous tumors).

A. Context-sensitive Classification Forests for Segmentation of Brain Tumor Tissues

Zikic et al [24] proposed the segmentation as a classification task, and the discriminative power of context information was used. They realize this idea by modeling the classification forest with spatially non-local features to represent the data, and by providing the CF with initial probability estimates for the single tissue classes as additional input (along-side the MRI channels). The initial probabilities are patient-specific, and computed at test time based on a learned model of intensity. Through the combination of the initial probabilities and the non-local features, their approach was able to capture the context information for each data point. Their method was fully automatic, with segmentation run times in the range of 1-2 minutes per tumor patient.

B. Segmentation of Brain Tumor mages Based on Integrated Hierarchical Classification and Regularization

S.Bauer et al [25] presented a fully automatic method for brain tumor segmentation, which is based on classification with integrated hierarchical regularization. Their method not only offer to separate healthy from pathologic tissues, but it also subcategorizes the healthy tissues into CSF, WM, GM and the pathologic tissues into necrotic, active and edema compartment.

C. Spatial Decision Forests for Glioma Segmentation in Multi-Channel MR Images

A fully automatic algorithm was proposed by Geremia [26] for the automatic segmentation of gliomas in 3D MR images. Their algorithm was built on the discriminative random decision forest framework to provide a voxel-wise probabilistic classification of the volume. Their method uses multi-channel MR intensities (T1, T1C, T2, Flair), spatial prior and long-range comparisons with 3D

regions to discriminate lesions. A symmetry feature was introduced accounting for the fact that gliomas tend to develop in an asymmetric way.

D. *Multimodal Brain Tumor Segmentation Using The "Tumor-cut" Method on The BraTS Dataset*

Hemamci et al. used "Tumor-cut"[28] method to multi-modal data which includes edema segmentation. Their method was semi-automatic, requiring the user to draw the maximum diameter of the tumor. Their algorithm takes about a minute user-interaction time per case. The typical run-time for each patient case is around 10-20 minutes depending on the size of the brain tumor. The Dice overlap with the expert segmentation is 0.36 ± 0.25 for the edema and 0.69 ± 0.20 for the tumor region.

E. *Brain tumor segmentation based on GMM and active contour method with a model-aware edge map*

A model for tumor segmentation was proposed by Zhao [28] based on GMM. Their method integrates the model of gray distribution of pixels (Gaussian Mixture Models, GMM) with the edge information between two difference classes of tissue in the brain. They reported that High detection precision could be achieved.

F. *Probabilistic Gabor and Markov Random Fields Segmentation of Brain Tumours in MRI Volumes*

N. K. Subbanna et al [29] presented a techniques for segmenting tumors from brain MRI using probabilistic and MRFs. Their method was a two stage process for segmenting tumors from multispectral brain magnetic resonance images (MRIs). From the training volumes, they modeled the tumor, edema and the other healthy brain tissues using space characteristics. They reported that their segmentation technique worked on a combination of Bayesian classification of the Gabor decomposition of the MRI volumes to produce an initial classification of tumors, along with the other classes. They followed their initial classification with a MRF classification of the Bayesian output to resolve local inhomogeneities, and impose a smoothing constraint. Their results show a Dice similarity coefficient of 0.668 for the brain MRI tumors and 0.56 for the edema.

G. *Hierarchical Random Walker for Multimodal Brain Tumor Segmentation*

A Random Walker (RW) based method was proposed for brain tumor MR images segmentation with interaction by Xiao [01]. Their method was not only designed to achieve the final segmentation result, but also it was a convenient tool for users to modify their final results on iterative basis. They have extended their model to feature space for soft clustering to overcome the shortcoming of typical RW algorithm, and they carried out pixel-wise segmentation in image space. Their proposed technique was performed on multimodal brain MR images, including T2- weighted, contrast enhanced T1-weighted, and FLAIR sequences.

H. *Automatic Brain Tumor Segmentation based on a Coupled Global-Local Intensity Bayesian Model*

Tomas-Fernandez [31] presented a technique for localizing and quantifying the tumor volume of brain from magnetic resonance images, which is a key task for the analysis of brain cancer. Based in the well established global gaussian mixture model of brain tissue segmentation. They proposed a tissue model which combines the patient global intensity model with a population local intensity model that was derived from an aligned reference of healthy subjects. They used the Expectation-Maximization algorithm to estimate the parameters which maximize the tissue maximum a posterior probabilities. Further, they modeled the brain tumors as outliers with respect to coupled global/local intensity model. Tumor segmentation from MRI was validated using the 30 glioma patients scans from the training dataset from MICCAI BRATS 2012 challenge.

I. *Segmenting Glioma in Multi-Modal Images using a Generative Model for Brain Lesion Segmentation*

B.H.Menze et al [32], proposed and evaluated a fully automated method for channel-specific tumor segmentation in multi-dimensional images. Their method represents a tumor appearance model for multi-dimensional sequences

that provides channel-specific segmentation of the tumor. Their generative model shares data about the spatial location of the tissue among channels while making use of the specific multi-modal signal of the healthy lesion classes to segment the normal tissues in the brain. For voxel encoding, their model includes a latent variable, the probability of observing tumor at that voxel, based on the ideas from [2, 3].

III. Evaluation Process

In MICCAI 2012 BRaTs workshop the following performance metrics were used for segmenting edema and tumor.

- Jaccard: This coefficient is used to compare diversity as well as similarity between sample objects.
- Sensitivity

This metric measures the proportion of positives that are identified as correct as such (e.g., the percentage of sick people who are correctly identified as having the sick condition). It is measured as the ratio of number of true positives to sum of true positives and false negatives.

- Specificity

This measures the proportion of negatives that are correctly identified as such (e.g., the percentage of healthy people who are correctly identified as not having that sick condition). It is measured as the ratio of number of true negatives to sum of true negatives and false positives.

- Dice similarity coefficient

Dice coefficient is used to compare the similarity between two objects.

- Hausdorff distance

Two sample sets are close in the Hausdorff distance if every point of either sample set is close to some point of the other sample set. Then the Hausdorff distance is the longest distance you can be forced to travel by an adversary who chooses a point in one of the two sample sets, from where you then must travel to the other sample set. It is the greatest of all the distances from a point in one sample set to the closest point in the other sample set.

Table 1 Performance evaluation of segmentation algorithms in MICCAI 2012.

Core				
	Clinical		Synthetic	
	High-grade	Low Grade	High Grade	Low Grade
Automatic				
Shin et al.	0.14391536	0.23246645	0.28434818	0.07247578
Bauer et al.	0.51166622	0.33183625	0.7787252	0.8577578
Zikic et al.	0.47582122	0.33885775	0.8688745	0.84243
Subbanna et al.	0.13343608	0.00095839	0.3978257	0.4199778
Xiao et al.	0.33688352	0.22405493	0.41422405	0.4689204
Zhao et al.	0.05811677	0	0	0
Semi automatic				
Hamamci et al.	0.69408752	0.32417005	0	0
Edema				
	Clinical		Synthetic	
Automatic				
	High-grade	Low Grade	High Grade	Low Grade
Shin et al.	0.03835941	0.06120145	0.31215886	0.21312157
Bauer et al.	0.53603	0.1790644	0.7852322	0.7460034
Zikic et al.	0.597521	0.32403075	0.8502734	0.7490424
Subbanna et al.	0.06922264	0	0.6953803	0.6451742
Xiao et el.	0.53900664	0.27857825	0.3433091	0.10039676
Zhao et al.	0.00348448	0	0	0
Semi-automatic				
Hamamci et al.	0.53916273	0.0330265	0	0

IV. Conclusion

In this paper we presented the report on the performance evaluation of segmentation techniques in BRATS brain tumor segmentation challenge. These techniques are evaluated on the largest dataset which was made available for

the public. Our results in the report indicate that, while tumor segmentation in brain MRI is difficult for human raters, currently available state of art techniques can reach Dice scores of over 80% for whole brain tumor segmentation. Segmenting the brain tumor core region, and especially the high active core region in GBMs, proved more challenging, with Dice scores reaching 70% and 60%, respectively. Of the segmentation algorithms tested, no single technique performed best for all tumor regions considered. However, the errors of the best algorithms for each individual region fell within human inter-rater variability.

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