



Single seed delineation of brain tumor using multi-thresholding



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ABSTRACT

A novel two-stage region of interest (ROI) segmentation is proposed for detecting glioblastoma multiforme (GBM) tumors from brain magnetic resonance images (MRIs). The method involves multi-level thresholding followed by post-processing. Initially discrete curve evolution (DCE) identifies multiple intervals around the significant (or visually critical) points, with a threshold being selected in each such interval using Otsu's method or Li and Lee's entropy. Next a post-processing on the segmented image, based on connected-component analysis and flood-fill operation, helps to extract each refined ROI around a single seed inserted by the user. The segmented ROI is more accurate, both quantitatively and qualitatively, as compared to related methods – in spite of using only a single seed. This is evaluated (i) visually, (ii) in terms of the Jaccard and Dice indices (on the ROI), and (iii) over time complexity of the algorithm. The experimental results on contrast enhanced T1-weighted MRI slices of 25 patients, each having the corresponding ground truth about the tumor regions, establish the effectiveness of our algorithm.

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1. Introduction

Identifying specific organs or anatomical features (like anomalies, tumors) in medical images requires considerable expertise concerning their shapes and locations. Image segmentation and detection, of such different regions or volumes of interest (ROI or VOI), is typically performed manually by expert radiologists as part of diagnosis, classification, treatment planning, prognosis and post-treatment evaluation. However the increasing amount of available data and the complexity of the features of interest, make it essential to develop automated delineations that assist and speedup image understanding while enhancing its reproducibility. Besides, the existence of inter- and intra-observer, inter-patient and inter-scanner variability, coupled with relatively low spatial resolution, make computer-guided delineations (based on objective criteria) desirable for outlining the tumor boundary. Computer-based quantitative image analysis is thus becoming an important field, with an increasing reliance on it by the biomedical community [1,10,12,29,34,37].

Image segmentation is an essential and crucial process for facilitating the delineation, characterization, and visualization of the region of interest (ROI) in any medical image, because its output affects all subsequent processes of image analysis. The goal of segmentation is to simplify and/or change the representation of an image into something that is more understandable. It is the process of assigning a label to every pixel in an image, such that those having the same label share certain visual characteristics. It plays an important role in computer-aided detection (CADe) and computer-aided diagnosis (CADx) of radio images, encompassing computed tomography (CT), positron emission tomography (PET) and magnetic resonance imaging (MRI). In the present context we focus our research on the segmentation of tumors from MR images of the brain.

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MRI uses a combination of a strong magnetic field, radio-frequency waves and a computer, to make the body tissues emit their own radio waves of differing intensities (depending on their chemical makeup), in order to reconstruct and display detailed 3D images of soft tissues like the brain. It can provide high spatial resolution of molecular signatures of normal and diseased tissue (as in solid tumors). Due to its dependence on the biologically variable parameters like proton density (PD), longitudinal relaxation time (T1), and transverse relaxation time (T2), the variable image contrast can be achieved by using different pulse sequences while changing the imaging parameters.

Glioblastoma multiforme (GBM) is the most common and lethal primary brain tumor in adults. The diagnosis and treatment of GBM is still largely guided by histopathology and immunohistochemistry,¹ with the overall survival remaining poor. Imaging has always played a critical role in assessing glioma response to treatment. While repeated tumor biopsies are challenging in brain tumor patients, imaging has the advantage of noninvasively capturing the heterogeneity of gliomas. MRI, a powerful and noninvasive diagnostic imaging tool, is routinely used in the diagnosis, characterization, and clinical management of the disease. It is able to capture multidimensional *in vivo* portraits of GBMs by simultaneously extracting structural, compositional, and physiological information [28]. It is also safe, as it does not involve any exposure to radiation.

The extracted ROI corresponding to the affected organ/tissue is manually evaluated by a radiologist during diagnosis. Manual segmentation of medical images is not only tedious and time consuming, but also not very accurate and reproducible – given the increasing number of imaging modalities used and the unmanageable quantity of images that needs to be regularly examined. It has been established [32] that semi-automatic segmentation is more robust than manual segmentation, with reference to inter-user variability, while providing comparable output accuracy. Therefore, it becomes necessary to study current methodologies in medical image segmentation [3,14,30,33,40], using automated algorithms which are generally more accurate and require negligible user intervention.

The simplest segmentation algorithms involve low-level techniques with negligible prior information [40], and includes intensity thresholding [35] and region growing [33]. Intensity-based methods identify local features, like edges and textures, in order to extract the ROI. A threshold is judiciously chosen to separate the target from the background. Region growing methods start from a seed point (usually determined manually) on the image and perform segmentation by clustering neighborhood pixels based on a similarity criterion.

Among the various segmentation strategies, thresholding remains the most efficient in terms of its simplicity, implementation, as well as processing time. When a target is clearly distinguishable from the background then the histogram of the image is bimodal, with the threshold corresponding to its *valley*. In such cases, typically the bi-level nonparametric thresholding algorithms exhaustively search for the optimum threshold. There exist many bi-level thresholding methods in literature [35,36], including those based on histogram shape, clustering, entropy, and minimum error. For selecting the optimum threshold (i) Otsu's method [31] maximizes the between-class intensity variance in the gray level image, (ii) Kapur's method [17] maximizes the total entropy of the foreground and background objects, (iii) the cross entropy between the image and its thresholded version gets minimized in Ref. [21], and (iv) the total misclassification error is minimized via an iterative search in Refs. [8,18].

A survey of 40 selected image thresholding methods [36] has demonstrated that Otsu's between-class variance [31] and Li and Lee's entropy (LLE) [21] are capable of attaining relatively stable performance measures – both in the context of medical and document images. Otsu's method is stated to be one of the popular thresholding techniques for image segmentation [11,35], with respect to uniformity and shape measures. Recently it has been claimed [41] that Otsu's algorithm performs better than many other 2D based thresholding methods.

However, for real-world images often a single threshold may not suffice to generate a satisfactory segmentation of the ROI. Also there may not exist any traceable valley. Such scenario led to the development of multi-level thresholding, which computes multiple thresholds to segment images into several classes. Nevertheless determining appropriate values for multiple thresholds, considering all possible combinations, causes the computational complexity to increase exponentially. Thereby an automatic determination of the appropriate number and values of multiple thresholds, that can preserve most relevant details in the original image, becomes a difficult task [16,23–25]. Applying new ideas and concepts to multi-level image thresholding is, therefore, an interesting and challenging research area.

Some well-known region growing approaches require post processing steps like split and merge [2], watershed [6], connected-component analysis and flood fill [33] to extract the ROI while removing small pieces (or holes) from the segmented object(s). In recent years interactive segmentation algorithms have also become very popular in case of medical images, particularly for delineating ROIs. Some such algorithms include Grow-Cut [9,39], Tumor-Cut [13] and graph-based seeded segmentation methods like Graph-Cut [7]. Interactive segmentation requires the user to select seed points on both the object and the background regions, with the accuracy of the final segmentation being completely dependent on the initial selection of seed pixels (encompassing their location as well as number). As this is an interactive process, therefore, the time required for the computation and manual correction is quite large. Hence a major challenge is to reduce user intervention without compromising on the output result.

The contribution of this research lies in developing a new semi-automatic, minimally interactive tumor delineation method from MR images. The algorithm produces fast segmentation of the ROI, as compared to that obtained by other interactive segmentation methods. The output is almost as good as those generated manually by radiologists. Multi-level thresholding is initially

¹ The process of detecting antigens (e.g., proteins) in cells of a tissue section by exploiting the principle of antibodies binding specifically to antigens in biological tissues.

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