

Review article

State of the art survey on MRI brain tumor segmentation

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ABSTRACT

Brain tumor segmentation consists of separating the different tumor tissues (solid or active tumor, edema, and necrosis) from normal brain tissues: gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). In brain tumor studies, the existence of abnormal tissues may be easily detectable most of the time. However, accurate and reproducible segmentation and characterization of abnormalities are not straightforward. In the past, many researchers in the field of medical imaging and soft computing have made significant survey in the field of brain tumor segmentation. Both semiautomatic and fully automatic methods have been proposed. Clinical acceptance of segmentation techniques has depended on the simplicity of the segmentation, and the degree of user supervision. Interactive or semiautomatic methods are likely to remain dominant in practice for some time, especially in these applications where erroneous interpretations are unacceptable. This article presents an overview of the most relevant brain tumor segmentation methods, conducted after the acquisition of the image. Given the advantages of magnetic resonance imaging over other diagnostic imaging, this survey is focused on MRI brain tumor segmentation. Semiautomatic and fully automatic techniques are emphasized.

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1. Introduction

The ultimate goal of brain tumor imaging analysis is to extract the patient-specific important clinical information, and their diagnostic features. This information embedded within the multidimensional image data, can guide and monitor interventions after the disease has been detected and localized, ultimately leading to knowledge for clinical diagnosis, staging, and treatment of disease [1]. These processes can be represented diagrammatically as a pyramid. At each level of the pyramid, specific techniques are required to process the data, extract, label, and represent the information. Additionally it is necessary to represent the information in a high level of abstraction in order to obtain relevant clinical knowledge or datasets from which medical diagnosis and decision can be made. Effective management, processing, visualization, and analysis of the obtained datasets cannot be accomplished without high-performance computing infrastructure that should be composed of high-speed processors, storage, network, image display unit, as well as software programs. Development and implementation of the related techniques require detailed understanding of the underlying problems, and knowledge about the acquired data, as: nature of data, goal of the study, and scientific or medical interest, etc.

The effective extraction of useful information and attributes contained in different types of multidimensional images plays a crucial role in image segmentation. As Bhandar states [2]: The main objective of image segmentation is to partition an image into mutually exclusive regions such that each region is spatially contiguous and the pixels within the region are homogeneous with respect to a predefined criterion. This definition is in itself a major limitation of most of the segmentation methods, especially when defining and delineating “abnormal tissue types”, because the tumors to be segmented are anatomical structures which are often non-rigid and complex in shape, vary greatly in size and position, and exhibit considerable variability from patient to patient.

In the specific case of brain tumors, segmentation consists of separating the different tumor tissues such as solid or active tumor, edema, and necrosis (Fig. 1), from normal brain tissues, such as gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF). In brain tumor studies, the existence of abnormal tissues may be easily detectable most of the time. Nevertheless, accurate and reproducible segmentation and characterization of abnormalities are not straightforward.

In the last years many researchers in the field of medical imaging and soft computing have made significant advances in the field of brain tumor segmentation. Both semiautomatic and fully automatic methods have been proposed. Clinical acceptance of segmentation techniques has depended on the simplicity of computation and the degree of user supervision [4]. Until better solutions are proposed,

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semi automatic or interactive methods will likely be dominant in practice for a long time to come, because erroneous interpretations are not acceptable under any circumstances. This paper presents an overview of the most relevant existing brain tumor segmentation methods applied after the acquisition of the image. Given the advantages of magnetic resonance imaging (MRI) over other diagnostic imaging techniques, this survey is focused on MRI brain tumor segmentation. Semiautomatic and fully automatic techniques are emphasized. This work is divided into four sections. First, [section 2](#) gives an introduction of manual and automated segmentation methods. Then, in [section 3](#), the concepts of unsupervised and supervised segmentation are presented. Subsequently, the most relevant existing methods for the segmentation of brain tumors are introduced in [section 4](#) and discussed in [section 5](#). Finally, the paper conclusions are summarized in [section 6](#).

2. Manual and automated brain tumor segmentation

Brain tumor segmentation methods can be classified into three categories according to the degree of required human interaction as described by Foo et al. [5], Olabarriga et al. [6], and Yao [4]: manual segmentation, semiautomatic segmentation, and fully automatic segmentation. The next sections give a description of each category, some of their principal advantages and inconveniences are delineated.

2.1. Manual segmentation

Manual segmentation of brain tumors involves manually drawing the boundaries of the tumor and structures of interest, or painting the region of anatomic structures with different labels [4]. In manual segmentation, human experts (radiologists/anatomists/trained technologists) not only make use of the information presented in the image but also make use of additional knowledge such as anatomy. Manual delineation requires software tools with sophisticated graphical user interfaces to facilitate drawing regions of interest and image display. In practice, the selection of the tumor region, which is the region of interest (ROI), is a tedious and time-consuming task. MRI scanners generate multiple two-dimensional cross-sections (slices), and the human expert has to go through the dataset slice by slice for choosing the most representative ones from

which the relevant regions are carefully delineated [1]. Manual segmentation of brain tumors is also typically done based on a single image with intensity enhancement provided by an injected contrast agent [7]. However if the person drawing the ROI is not a radiologist/anatomist/trained technologist who is well versed with that brain anatomy, it will most likely yield poor segmentation results.

The task of marking the tumor regions slice by slice sometimes limits the human rater's view and generates jaggy images. As a result, the segmented images are less than optimal showing a "stripping" effect [7]. Needless to say, manual ROI delineation is also operator dependent and the selected regions are subject to large intra and inter rater variability [8]. For example, the study in [9] quantified an average of $28\% \pm 12\%$ variation in quantified volume between individuals performing the same brain tumor segmentation task (the variation ranged from 11% to 69%), and quantified a $20\% \pm 15\%$ variation within individuals repeating the task three times at 1 month intervals. [Fig. 2](#) gives an example presented in [10] of inter rater variability, where four different experts performed a manual segmentation of a glioma on the same slice and patient. The resulting segmentation of each expert presents notable differences.

In spite of the possible intra and inter rater variability, manual segmentation is habitually used as validation ground truth for semi and fully automatic segmentation methods; in which segmentation results are qualitatively and quantitatively evaluated by comparison with manual segmentations. Methodologies providing semi automated or, ideally, fully automated segmentation will present clear advantages over the manual delineation. However, manual segmentation is still widely used in clinical trials, especially where a lot of human knowledge and expertise are required to distinguish tissues.

2.2. Semiautomatic segmentation

In semiautomatic brain tumor segmentation, the intervention of a human operator is often needed to initialize the method, to check the accuracy of the result, or even to manually correct the segmentation result. Most of the current research is targeted at semiautomatic segmentation of brain tumors with the intention of having the least human interaction possible. According to Olabarriga et al. [6], the main components of an interactive brain tumor segmentation

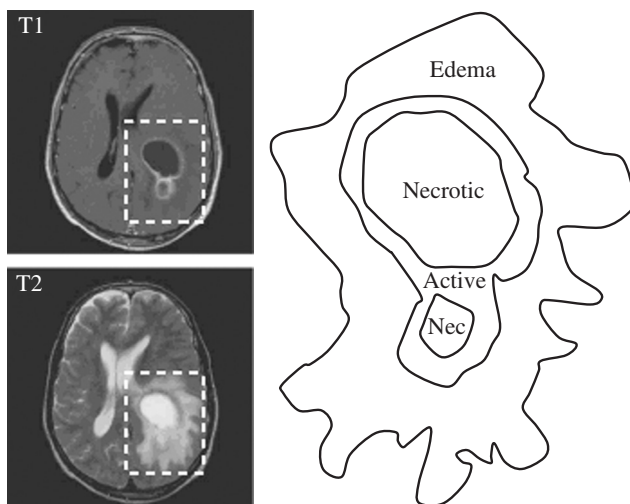


Fig. 1. Labeled example of a brain tumor in the T1 with contrast and T2 modalities (adapted from [3]).

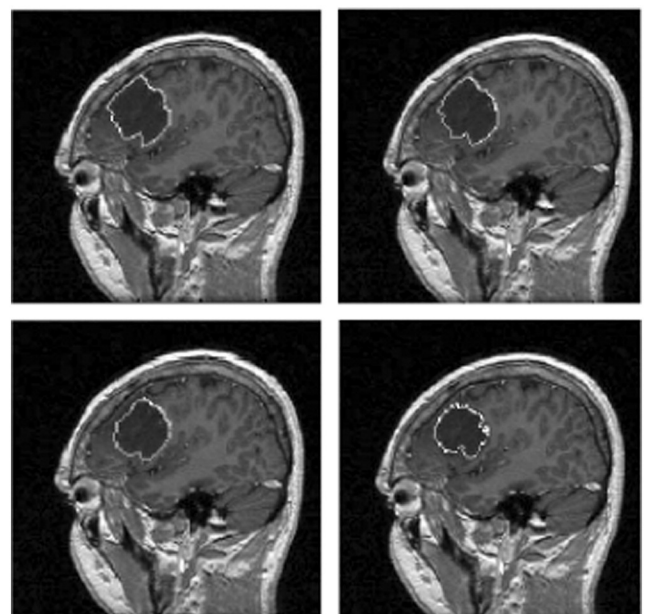


Fig. 2. Manual segmentation by four different experts of a glioma on the MRI [10].

method are the computational part, the interactive part, and the user interface. The computational part corresponds to one or more pieces of program capable of generating a delineation of the tumor given some parameters. The interactive part is responsible for mediating information between the user and the computational part. It translates the outcome produced by the computational part into visual feedback to the user and the data input by the user into parameters for the program. The actual communication between the computer and the user is done via the output and input devices controlled by the user interface. The user analyzes the visual information displayed on the screen and reacts accordingly, providing feedback for the computation.

The user interaction in brain tumor segmentation was grouped by Foo [5] into three main categories: initialization, intervention or feedback response, and evaluation. Most methods will consist of one or more types of interaction and can be summarized as:

- **Initialization:** Input of arguments or parameters (either from keyboard, mouse or other forms of input devices); some pre-processing of image data to enhance quality (sharpening or noise removal); evaluation of the complexity of the image data to improve decision making during input of arguments/parameters; user selecting the object from the first slice of the data set to be processed or from a three-dimensional representation.
- **Intervention/Feedback response:** Steering of the process continuously or intermittently towards a desired result; giving a response to feedback data from process; stopping the process midway when undesired results are obtained to make corrections, and then resume the process.
- **Evaluation:** Evaluating the final result of the process to determine if it is correct or satisfactory. If not satisfactory, necessary changes are made to the arguments or parameters and the process is repeated, modifications are made to the results, or in some cases results are simply rejected.

Since the semiautomatic methods use different strategies to combine computers and humans' expertise, the outcome of these methods depends on the strategy as much as on computation. These strategies could include involving the user in the initialization of segmentation process, keeping the user in the control during the whole process, or adding intelligent behavior to elevate the abstraction of interaction. Although it is true that by using these strategies efficient brain tumor semiautomatic segmentation methods can be obtained, semi automatic segmentation like manual segmentation is subjected to variations both between expert users and within the same user.

2.3. Fully automatic segmentation

In fully automatic methods, the computer determines the segmentation of tumor without any human interaction. Fully automatic methods generally incorporate human intelligence and prior knowledge in the algorithms, and are usually developed making use of soft computing and model-based techniques such as deformable models. Soft computing techniques such as fuzzy systems, and deformable models will be reviewed in [section 4](#).

The study of automatic brain tumor segmentation represents an interesting research issue in Machine Learning and Pattern Recognition, since it represents a problem that humans can learn to do effectively. However, developing highly accurate automatic methods remains a challenging problem. This is easily explained by the fact that humans must use high-level visual processing, and must incorporate specialized domain knowledge to perform this task [7], which makes developing fully automatic methods extremely difficult. Although this is true for many pattern recognition and

vision problems, brain tumor segmentation has several properties that reduce the advantage that humans have over machines. For example, from the brain anatomical properties can be emphasized that the head's appearance in MR images is relatively predictable, the brain is well quantified structurally, and the behavior of different tissue types in different MR modalities is well characterized. Additionally, there is no temporal component and the brain remains stationary, therefore being able to visually track objects over time has no advantage. Another property which reduces the advantage of humans over machines is that the viewpoint is known and that humans view the data as a series of two-dimensional slices. Therefore the ability of humans to use three-dimensional information in segmentation is also reduced in this task since there is no three-dimensional modeling of structures based on a large range of views of the object. Concerning the illumination, although local magnetic inhomogeneities of the coils system and susceptibility effects can cause severe problems for post-processing of the data sets and medical diagnostics [11], in the last decade several robust algorithms for correcting intensity inhomogeneities in MRI images have been proposed [12–15], making the ability to compensate for differences in illumination less of an advantage.

The use of implicit or explicit anatomical knowledge such as size, shape, location, expected appearance of the tumor, and bilateral symmetry to guide the segmentation is especially important for robust automatic methods. This knowledge may be incorporated into the segmentation model in the form of initial conditions, constraints on the model shape parameters, data constraints, or into the model fitting procedure. For automatic segmentation, it is essential to have a model that not only describes the size, shape, location and appearance of the tumor but that also permits expected variations in these characteristics. However, no completely automatic segmentation algorithm has yet been adopted in the clinic environment. [Table 1](#) gives a list of the prior art in fully automatic tumor segmentation. These approaches will be reviewed in [section 4](#) according to their segmentation method.

Currently, fully automatic segmentation methods are desirable in processing large batch of images and are mainly restricted to the research environment. However, it must be pointed out that these methods have not gained wide acceptance among the practitioners (radiologists, neurologists, and to a very lesser extent pathologists) for every day clinical practice. It has been mainly due to the lack of interpretability and transparency in the segmentation process, two characteristics that make a segmentation method a convenient tool for every day clinical practice [26].

3. Unsupervised and supervised segmentation

As previously mentioned, the main objective of image segmentation is to partition an image into mutually exclusive and exhausted regions which are homogeneous with respect to a predefined criterion. In the case of brain tumors, the segmentation consists of separating the different tumor tissues such as solid or active tumor, edema, and necrosis, from the normal brain tissues such as gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF). The brain tumor segmentation requires an objective measure that can be used to define the homogeneity of each tissue. There exist two ways of obtaining the objective measure, namely the unsupervised and supervised segmentation methods [27]. The difference between them is that unsupervised methods do not make use of training data that have been manually labeled, as is the case of supervised methods. In unsupervised segmentation the number of classes is automatically specified by an algorithm that groups numerically similar pixels. The next sections give a description of unsupervised and supervised segmentation methods.

3.1. Unsupervised segmentation

When image data are unlabeled, the image can be segmented using clustering algorithms. In this case, no human finds and labels subsets of training data. Instead, the entire set of pixel vectors is submitted to a cluster analysis scheme, and the clusters are found algorithmically. Moreover, once found, algorithmic clusters (regions that have the same labels) must somehow be assigned physical (tissue) labels [28]. Unsupervised segmentation can be performed using an anatomic objective measure or an image-based objective measure to assess segmentation quality. In the former the goal is to segment the image into regions that have homogeneous and known anatomic properties, whereas in image-based objective the segmentation quality is based on the evaluation of regions having similar intensities or textures.

Brain tumor unsupervised segmentation approaches that use an anatomic objective measure aim to segment the image into at least two anatomically meaningful regions, one of which is tumor or edema. These approaches have been of limited applicability; because most of the proposed methods have been focused solely on the segmentation of enhancing tumor areas. This limitation is primarily due to the difficulty in translating the visual processing and anatomic knowledge used by human experts into operations that yield the desired results.

The unsupervised segmentation methods that use image-based features, rather than dividing the image along anatomically meaningful distinctions, divide the images into homogeneous regions using image-based features such as intensities and/or textures. These methods can handle more complicated cases, for example producing an accurate segmentation of the different regions present in a heterogeneous tumor [29]. In the case of brain tumor segmentation, the lack of shape or intensity priors on the tumors makes unsupervised segmentation more challenging [30], for this reason there has been narrow research effort directed towards techniques for unsupervised brain tumor segmentation in MR images that do not use an anatomic objective measure.

Three major disadvantages have been pointed out [27] when using unsupervised segmentation methods using image-based features: the number of regions often needs to be pre-specified, tumors can be divided into multiple regions, and tumors may not have clearly defined intensity or textural boundaries. These disadvantages can be reduced by making use of pre-processing techniques such as intensity inhomogeneity correction and intracranial segmentation commonly referred to as “skull stripping”. Various techniques of intensity inhomogeneity correction have been proposed in the last three decades. Reviews of these methods can be found in [31–33]. Skull stripping aims to segment the brain tissue from the skull and non-brain intracranial tissues in magnetic resonance images of the brain.

Skull stripping is an important pre-processing step in neuroimaging analysis [34–38] because brain images must typically be skull stripped before other processing algorithms can be applied.

3.2. Supervised segmentation

Image segmentation supervised methods differ from unsupervised methods through the use of labeled training data. Supervised classification involves both a training phase that uses labeled data to learn a model that maps from features to labels, and a testing phase that is used to assign labels to unlabeled data based on the measured features. In supervised segmentation the choice of accurate training data is crucial because different training sets can lead to great disparities in training time, as well as potential differences in segmentation results [28]. In the supervised manner, the operator decides, based on the MR data being inspected, how many tissue classes exist in the image.

When formulating the brain tumor segmentation task as a supervised classification problem, one straightforward method is to use the labels normal and tumor as classes, and to use the intensities in the different MR images as features. Under this formulation the training phase consists of learning a model that uses the MR image intensities to discriminate between normal and tumor pixels. The testing phase would consist of using this model for classifying unlabeled pixels into one of the two classes based on their intensities.

The source of the training and test data has a major influence on the performance of a supervised method. Two major sources of training and test are patient-specific training, and inter-patient training. In patient-specific training, the training data are obtained from the images to be segmented. Several of the subclasses of patient-specific training that will be examined include: training and testing data are the same, training uses a subset of the pixels within the test slice, and training is performed based on slices that are adjacent to the test slice. Inter-patient training is to perform training on several patients, and testing in one [39]. Subclasses for inter-patient training include: training and testing data are the same, training on the same slice and tumor type from different patients, and training on the same tumor type from different patients.

A major advantage of using a supervised formulation is that supervised methods can perform different tasks simply by changing the training set. Supervised methods have the potential of reducing the manual engineering task by providing labeled data, appropriate features, and appropriate parameters for the learning algorithm. Although highly effective and versatile, supervised methods for brain tumor segmentation in MR images often suffer from the disadvantage of requiring patient-specific training. The human variability associated with manual training data, could also be a disadvantage.

4. Segmentation methods

Detection, localization, diagnosis, staging, and monitoring treatment responses are crucial procedures in clinical medicine and oncology. Early detection and localization of the diseases, and accurate disease staging could lead to changes in patient management that will impact on health outcomes. Accurate quantification of regional physiology depends on accurate delineation or segmentation of the tumor structure or region of interest in the images. According to Wong [1], the fundamental roles of segmentation are: (1) permit quantification, (2) reduce the dataset by focusing the quantitative analysis on the extracted regions that are of interest, and (3) establish structural correspondences for the physiological data sampled within the regions.

A wide variety of brain tumor segmentation techniques has been proposed. However, there is no standard segmentation technique

Table 1
Summary of related methods in automatic brain tumor segmentation.

Authors	Description
Ho 2002 [16]	3D Level Sets
Prastawa 2004 [17]	Knowledge-based/outlier detection
Lee 2005 [18]	Discriminative Random Fields and Support Vector Machines
Dou 2007 [19]	Fuzzy Region Growing Framework
Khotanlou 2009 [20]	Model-based Fuzzy classification
Iftekharuddin 2009 [21]	Self Organizing Maps
Gordillo 2010 [22]	Knowledge-based Fuzzy classification
Vijaya 2011 [23]	Knowledge-based/Neural Networks
Wang 2011 [24]	Region-based active contour models
Kumar 2012 [25]	Genetic Algorithm Clustering/Region Growing

that can produce satisfactory results for all imaging applications. Quite often, methods are optimized to deal with specific imaging modalities such as magnetic resonance imaging. In general, segmentation techniques have been divided for diverse authors [1,4,40,41] into four major classes:

- Threshold-based techniques
- Region-based techniques
- Pixel classification techniques
- Model-based techniques

Threshold-based, region-based and pixel classification techniques are commonly employed in two-dimensional image segmentation [21,23,37,42]. Model based techniques such as parametric and geometric deformable models (level sets), are mostly employed in volumetric (3D) image segmentation [16,43,44].

There has been a large amount of research effort directed towards the segmentation methods. Many of the approaches that will be discussed here represent prototypical examples of state of the art methods in the general area of brain tumor segmentation. A review of threshold-based, region-based and pixel classification techniques will be given in this section. Model-based techniques such as parametric and geometric deformable models (level sets), as well as their applications, will be introduced and discussed latter in this section. Semiautomatic and fully automatic image segmentation techniques are emphasized.

4.1. Threshold-based methods

Thresholding is a simple and effective region segmentation method, in which the objects of the image are classified by comparing their intensities with one or more intensity thresholds. These thresholds can be either global or local. If the histogram of an image expresses a bimodal pattern, the object can be separated from the background in the image by a single threshold called global thresholding. However, if the image contains more than two types of regions, corresponding to different objects, the segmentation must be carried out using local thresholding. The image may be segmented by applying several individual thresholds or by using a multi-thresholding technique.

4.1.1. Global thresholding

The simplest property that pixels in a region can share is intensity. So, a natural way to segment such regions is through thresholding, the separation of light and dark regions. Thresholding creates binary images from gray-level ones by turning all pixels below some threshold to zero and all pixels about that threshold to one. If $g(x, y)$ is a thresholded version of $f(x, y)$ at some global threshold T ,

$$g(x, y) = \begin{cases} 1 & \text{if } f(x, y) \geq T \\ 0 & \text{otherwise} \end{cases} \quad (1)$$

in which pixels with value of 1 correspond to the ROI, while pixels with value 0 correspond to the background.

The major problem with thresholding is that only the intensity is considered, not any relationships between the pixels. There is no guarantee that the pixels identified by the thresholding process are contiguous. Extraneous pixels that are not part of the desired region can easily be included, and sometimes isolated pixels within the region (especially near the boundaries of the region) are ignored. These effects get worse as the noise gets worse, simply because it is more likely that a pixel intensity does not represent the normal intensity in the region. When thresholding is used, it is necessary to play with it, sometimes losing too much of the region and sometimes getting too many extraneous background pixels. Shadows of objects

in the image are also a problem, not just where they fall across another object but where they mistakenly get included as part of a dark object on a light background. Another problem with global thresholding is that changes due to intensity inhomogeneity across the scene may cause some parts to be brighter (in the light) and some parts darker (in shadow) in ways that have nothing to do with the objects in the image.

Global thresholding performs well if the image contains objects with homogeneous intensity or the contrast between the objects and the background is high. However, it may not lead itself to fully automatic segmentation, and may fail when two or more tissue structures have overlapping intensity levels. The accuracy of the ROI is also questionable because it is separated from the background based on a single threshold value which may be subject to very large statistical fluctuations. With the increasing number of regions or noise levels, or when the contrast of the image is low, threshold selection will become more difficult.

Gibbs et al. [45] presented an unsupervised approach for the segmentation of enhancing tumor pixels from T1-weighted post-contrast images. The system first applied an intensity threshold to a manually selected region of interest, and represents a clearly justified approach for segmenting image objects that are different in intensity from their surroundings. Although the requirement of manual slice or region of interest selection is a disadvantage, a more severe drawback is that the method does not effectively take into account the presence of hyper-intense pixels representing normal structures in T1 post-contrast images.

4.1.2. Local thresholding

Apart from global thresholding, there are several thresholding methods which can be classified as local thresholding. A local threshold is determined adaptively in a local region around a pixel. These techniques maybe useful when a thresholding value cannot be determined from a histogram for the entire image or a single threshold cannot give good segmentation results. Local threshold can be determined by estimating a threshold value for the different regions from the intensity histogram. According to Yao [4] the values of thresholds are generally estimated by the prior knowledge. Local threshold values can also be estimated using the local statistical properties such as the mean intensity value in T1-weighted MRI as in [37] or by calculating partial volumes of each region to determine the threshold for the segmentation of each component on brain PD and T2 MR images [46]. Stadlbauer et al. [47] used the Gaussian distribution of data values as threshold in normal brain T2-weighted MRI. The limit threshold value for normal brain tissue was the mean plus three times the standard deviation. Based on this threshold, an area was calculated which was delineated as pathologic tissue.

Generally threshold-based segmentation methods, local or global, are considered unable to exploit all the information provided by MRI, and are used as a first step in the segmentation process.

4.2. Region-based methods

Region-based segmentation approaches examine pixels in an image and form disjoint regions by merging neighborhood pixels with homogeneity properties based on a predefined similarity criterion [1]. These methods can be sketched in a general way as follows: Let X be an image that is segmented into N regions, each of which is denoted as R_i where $i = 1, 2, \dots, N$. The original image can be exactly assembled by putting all regions together and there should be no overlapping between any two regions R_i and R_j for $i \neq j$. The logical predicate $L(\cdot)$ contains a set of rules (usually a set of homogeneity criteria) that must be satisfied by all pixels within a

given region, and it fails in the union of two regions since merging two distinct regions will result in an inhomogeneous region. The regions must satisfy the following properties:

$$\begin{aligned} X &= \bigcup_{i=1}^N R_i \\ R_i \cap R_j &= \emptyset \quad \forall i, j = 1, 2, \dots, N \\ L(R_i) &= \text{TRUE} \quad \text{for } i = 1, 2, \dots, N \\ L(R_i \cup R_j) &= \text{FALSE} \quad \text{for } \forall i, j = 1, 2, \dots, N; i \neq j \end{aligned} \quad (2)$$

where $L(\cdot)$ is a logical predicate.

The region growing and the watershed segmentation methods are part of the region-based methods [4], and are the most commonly used for brain tumor segmentation. The next sections give a description of these methods, and some applications in the literature for brain tumor segmentation.

4.2.1. Region Growing

The simplest region-based segmentation technique is the region growing, which is used to extract a connected region of similar pixels from an image [48]. Region growing starts with at least one seed that belongs to the structure of interest. Neighbors of the seed are checked and those satisfying the similarity criteria are added to the region. The similarity criteria are determined by a range of pixel intensity values or other features in the image. Seeds can be chosen manually or provided by an automatic seed-finding procedure. The procedure iterates until no more pixels can be added to the region. The advantage of region growing is that it is capable of correctly segmenting regions that have similar properties and generating connected region.

Kaus et al. [49] implemented a region growing technique for segmenting MR Images of brain tumors. The technique involved the iteration of statistical classification to divide an image into different tissue classes on the basis of the signal intensity value. Objects of interest were identified on the classified images with local segmentation operations (mathematic morphology and region growing). Other studies [50–52] have proved that the region growing is an effective approach and less computation intensive than other non region-based methods for brain tumor segmentation, especially for the homogeneous tissues and regions. The primary disadvantage of region growing method is the partial volume effect [53,54] which limits the accuracy of MR brain image segmentation. Partial volume effect blurs the intensity distinction between tissue classes at the border of the two tissues types, because the voxel may represent more than one kind of tissue types.

S. Lakare et al. [54] introduced the modified region growing method (MRGM), which is used to remove the partial volume effects and to incorporate gradient information for more accurate boundary detection and filling holes occurred after segmentation. In [55] Salman presented a comparative analysis of the traditional region growing segmentation and the MRGM, addressed to brain tumor segmentation in 3D T1 MR images. In his study Salman proved that the MRGM increases the accuracy of the volumetric measurements of brain tumors, producing lower relative errors than traditional region growing method when compared with manual segmentation.

Other approaches incorporate the region growing process as a refinement step. A good example is the work presented by Dou et al. [19], wherein they proposed a fuzzy information fusion framework for the automatic segmentation of tumor tissues of human brain from multiple MR image sequences (T1, T2 and PD). This framework consists of the registration of multispectral images, the creation of fuzzy models (based on a priori knowledge), fuzzy feature fusion and an adjustment by fuzzy region growing. Rexilius et al. [56] propose a fast multispectral (T1, T2 and FLAIR) segmentation of brain tumors by means of a probabilistic intensity model, followed by an iterative

refinement of the initial segmentation. The refinement step is performed by a progressive region growing that combines probability and distance information. An adaptive region growing method based on the gradients and variances along and inside of the boundary curve is proposed in [57]. They use the anisotropic diffusion filter to preserve the edge information. Then the new model is given, which chooses the mean variance inside of the boundary curve and the reciprocal of the mean gradient along the curve as the research subjects. The objective function of the model is to add two elements about gradient and variance mentioned above. The minimum of the sum is the optimum result which corresponds to the desirable threshold. In region growing processing step, the threshold is increased gradually and the set of the coarse contour is obtained. Finally, through optimizing the model, the optimal segmentation result can be acquired from the set of contours. In [25] a genetic algorithm based dynamic clustering is first used for the segmentation of tumor region, then the clusters with highest average intensity value are retained and the seed is located by examining the Asymmetry Map. Finally the tumor pixels are extracted by region growing method.

4.2.2. Watershed

Basic watershed segmentation method can be explained by a metaphor based on the behavior of water in a landscape. When it rains, drops of water falling in different regions will follow the landscape downhill. The water will end up at the bottom of valleys. For each valley there will be a region from which all water drains into it. In other words: each valley is associated with a catchments basin, and each point in the landscape belongs to exactly one unique basin. At points where water coming from different basins meets, dams will be built. When the water level has reached the highest peak in the landscape, the process is stopped. As a result, the landscape is partitioned into regions separated by dams, called watershed lines or watersheds. It produces a complete contour of the images and avoids the need for any kind of contour joining.

Watershed applications have been widely used in brain tumor segmentation, for example, Letteboer et al. [58] and Dam et al. [59] performed segmentation of brain tumors using multi-scale watershed transformation. Dam presented an interactive method for T1 MRI brain tumor segmentation, the method builds blocks at different scales that the user can select (and deselect) in order to sculpt the desired anatomical object. Supervised learning is used to predict which building blocks are to be included in the segmentation. Cates et al. [60] performed an analysis of user-assisted hierarchical watershed segmentation of brain tumors from MRI data. The quantitative and qualitative results showed improvements on the segmentation time and precision over manual segmentation. The analysis also identified some failures in the watershed technique, where edges were poorly defined in the data, and noted a trend in the manual segmentation results toward systematically larger segmentations. The analysis raised questions about the wisdom of using expert segmentations to define ground truth. Bhattacharya and Das [42] implemented a marker-based improved watershed algorithm utilizing the prior knowledge of the test images for the segmentation of brain tumors; seeded region-growing method was used as the marker of ROIs. Later Ratan et al. [61] proposed a watershed segmentation based algorithm that was used for detection of tumor in 2D and in 3D brain MRI. A simple supervised block-based and image-based (shape, texture, and content) technique was used to analyze MRI brain images with relatively lower computational requirements.

The watershed transform usually suffers from over-segmentation. As any local maximum in the image will generate a shape boundary (or part of) it is obvious that watershed segmentation has

a strong potential for over segmentation, if not for other reasons then because of noise. To avoid over-segmentation some pre or post processing methods have been proposed in order to produce a more reasonable segmentation that reflects the layout of objects [62,63]. Kong et al. [64] applied on brain tumor MRI a merging process for the over segmented regions using Fuzzy C-Means clustering algorithm.

4.3. Pixel Classification Methods

Another type of segmentation method is based on pixel classification. Pixels in an image can be represented in feature space using pixel attributes that may consist of gray level, local texture, and color components for each pixel in the image. In the case of single-channel (or single-frame) image, pixel classification is typically based on gray level and image segmentation can be performed in a one-dimensional feature space. For multichannel (multiple-frame) images or multispectral (multimodality) images the segmentation can be performed in multidimensional feature space.

In brain tumor segmentation the methods based on pixel classification are constrained to the use of supervised or unsupervised classifiers to cluster pixels in the feature space. Clustering is the process of grouping similar objects into a single cluster, while objects with dissimilar features are grouped into different clusters based on some similarity criteria. The similarity is quantified in terms of an appropriate distance measure. An obvious similarity measure is given by the distance between two vectors in the feature space which can be expressed as:

$$d(x_i, x_j) = \left(\sum_{k=1}^n \|x_i - x_j\|^p \right)^{\frac{1}{p}} \quad (3)$$

where $x_i = (x_i^1, \dots, x_i^n) \in R^n$ and $x_j = (x_j^1, \dots, x_j^n) \in R^n$ are the two vectors in the feature space. It can be seen that the above measure corresponds to Euclidean distance when $p = 2$ and Mahalanobis distance when $p = 1$.

Another measure that is commonly used as similarity criterion is the normalized inner product, which is given by:

$$nd(x_i, x_j) = \frac{x_i^T x_j}{\|x_i\| \|x_j\|} \quad (4)$$

where T denotes the vector transpose operation. This measure provides information regarding the cosine between the vectors x_i and x_j in the feature space.

Each cluster is represented by its centroid (or mean) and variance, which indicates the compactness of the objects within the cluster, and the formation of clusters, is optimized according to a cost function that typically takes into account the similarity within individual cluster and dissimilarity between clusters.

There are many clustering techniques proposed in the literature. Basic techniques include unsupervised methods such as: Fuzzy C-Means (FCM), k-means, and statistical methods as Markov Random Fields (MRF) among others. The supervised methods include Bayes and Artificial Neural Networks (ANN). In this section the FCM, MRF and ANN clustering techniques are presented and analyzed.

4.3.1. Fuzzy C-Means

In many situations, it is not easy to determine if a pixel should belong to a region or not. This is because the features to determine homogeneity may not have sharp transitions at region boundaries [65]. To alleviate this situation fuzzy set concepts can be introduced into the segmentation process, as is the case of Fuzzy C-Mean technique. FCM clustering is a very popular technique in the area of

unsupervised image segmentation by pixel classification, particularly in the case of brain tumor segmentation [64,66].

When the FCM method is applied for brain tumor segmentation, the first step consists of determining a set of tissue classes. Each pixel is then assigned membership values to the tissue classes according to its attributes (intensity, texture, etc.). The fuzzy membership functions, constrained to be between 0 and 1, reflect the similarity degrees between the data value at a specific location and the prototypical data value, or centroid, of its class. Thus, a membership value near one means that the data value at that location is close to the centroid of the class. If the initialization can be carried out by accurate estimation of cluster centers, the algorithm converges faster and the clustering results are improved. Supoot et al. [66] applied the splitting technique of discrete curve evolution (DCE) in order to find the most accurate estimation of cluster centers for T1, T2 and PD MR brain image segmentation. The proposed technique reduced the convergence time resulting in lower computational time.

Phillips et al. [67] gave an early proof-of-concept fuzzy clustering for brain tumor by operating on the raw multisequence data. They visually demonstrated that even with multisequence data the intensity distributions for tumor and normal tissues overlap. This led other researchers to incorporate additional knowledge into the feature vectors being clustered using FCM. Clark et al. [68] integrated knowledge-based techniques and multispectral histogram analysis to segment glioblastoma multiforme (GBM) tumors in a multichannel feature space (T1, T2 and PD). The level of correspondence between ground truth measurements and isolated tumor pixels was incremented by their segmentation method. Fletcher-Heath et al. [69] also implemented a knowledge-based fuzzy clustering approach for the segmentation of T1, T2 and PD MRI of non-enhancing tumors followed by 3D connected components to build the tumor shape. Veloz et al. [70] applied Fuzzy C-Means and Mathematical Morphology to extract patterns of intensities of the GBM and to select seed points automatically to perform the Fuzzy Spatial Growing in T1, T1c and T2 MR images. Additionally, a Fuzzy similarity criterion was considered to measure the memberships degrees of the voxels to the tumor.

Many authors have considered that standard FCM for MR image segmentation is not efficient by itself, as it fails in dealing with the significant strong correlation of neighboring pixels that is given in MR images. Ignoring this specificity leads to strong noise sensitivity and several other imaging artifacts. Several solutions have been proposed to overcome this problem [71,72]. Most of the proposed improvements involve the consideration of local spatial information based on the fact that besides the gray level value of the considered pixel, the information provided by its neighbors also contribute to its assignment to a given cluster [73]. In [74] the authors make use of genetic algorithms and particle swarm optimization to determine the optimum value of degree of attraction. The quantitative and qualitative comparisons performed on simulated and real brain MR images with different noise levels demonstrate unprecedented improvements in segmentation results compared to other FCM-based methods.

Since Fuzzy C-Means is an iterative algorithm, it is considered a very time consuming clustering technique. Aiming at reducing the execution time, several particular implementations have been developed. Szilágyi et al. [75], and Chen and Zhang [76] proposed to evaluate the neighborhoods of each pixel as a pre-filtering step, and perform FCM afterwards. This latter quick approach, combined with an averaging pre-filter, is referred to as enhanced Fuzzy C Means (EnFCM) [77].

4.3.2. Markov Random Fields

Most clustering methods do not consider spatial information or the dependency between the pixels in the image surface. The

unsupervised clustering method of Markov Random Fields (MRF) provides a way to integrate spatial information into the clustering process. In many cases, this reduces both the possible problem of clusters overlapping and the effect of noise on the clustering result [78]. In the particular case of brain tumor segmentation, if a pixel is strongly labeled as tumor (non-tumor), it suggests that its neighbors will have a tumor (non-tumor) label. This has motivated some researchers to apply Markov Random Fields and Conditional Random Fields (CRFs) to various segmentation tasks. MRF and CRF techniques are able to represent complex dependencies among data instances, giving a high accuracy on brain tumor's segmentation task [18].

Cappelle et al. [79] presented an unsupervised approach by means of an MRF model that statistically used influences that neighboring pixels should have on each other's labels removing the need of morphological operations. In their work the authors assumed that the tissue classes in T1 and T2 MRI: gray matter, white matter, CSF, tumor, and edema could be modeled by a Mixture Model (of Gaussians), and trained the Markov Random Field with the Iterated Condition Modes (ICM) algorithm. Gering et al. [80] proposed a method that detects abnormalities in the brain using a multi-layer MRF framework. The information layers included pixel intensities, structural coherence, spatial locations, and user input. In their work, it was considered that a given voxel would change its high-level classification in the evolving presence of tumor if the attributes of lower-level layers shared strong similarities. In [81] a spatial accuracy weighted Hidden MRF and Expectation Maximization algorithm (SHE) was proposed. In this algorithm, a spatial accuracy, representing the spatial-resample accuracy of each voxel of re-sampled low-resolution images, was introduced and used in the model updating and classification. Segmentation was achieved by first aligning low resolution images such as T2-weighted and FLAIR images onto T1-weighted images and then applying the SHE algorithm to segment the tumor. More weights were given to the voxels with high-interpolation accuracy and vice versa. In this way, the tumor segmentation results were more accurate than treating the voxels equally. Bauer et al. [82] presented an automatic method to segment brain tissues from volumetric T1-weighted datasets of brain tumor MR images. The tumor growth model was formulated as a mesh-free MRF Energy Minimization problem, ensuring correspondence between the atlas and the patient image, prior to the registration step. Compared to other approaches, the method is non-parametric, simple and fast while maintaining similar accuracy.

One difficulty associated with MRF models is that they usually require algorithms computationally intensive. There are approximation techniques that can deal with these computational challenges. Conditional Random Field variants such as Discriminative Random Fields (DRFs) and Support Vector Machines (SVMs) [83] are coupled with a set of knowledge-based features to perform the segmentation and classification. Despite these disadvantages, the Markov Random Fields are widely used not only for modeling classes of segmentation, but also to model texture properties and inhomogeneities of the intensities.

4.3.3. Artificial Neural Networks

Another relevant supervised clustering method is the Artificial Neural Network (ANN) technique. This classifier feeds the features through a series of nodes, where mathematical operations are applied to the input nodes and a classification is made at the final output nodes. The training step for this technique consists of determining the values of the parameters considered (or involved) in the mathematical operations such that the error in the predictions made by the output nodes is minimized. Since no parametric distribution (such as a Gaussian distribution) is assumed for the data, ANN approaches are non-parametric techniques. Moreover, the use

of “hidden” layers of nodes allows the modeling of non-linear dependencies in the features. Although ANN training is complex, the ability to model non-trivial distributions offers clear practical advantages. This is noteworthy in the case of tumor segmentation since assuming the data follow a simple Gaussian distribution may not be appropriate for segmenting heterogeneous tumors [27].

Clarke [84] was one of the first researchers to introduce a supervised classification using an ANN approach for brain tumor segmentation in MR images. Ozkan et al. [85] also made use of ANN classification methods. Their system first used patient-specific training of a neural network classifier on a single slice. When segmenting an adjacent slice, this neural network was first used to classify all pixels in the adjacent slice, after that the locations of pixels that received the same label in both slices were then determined. These pixels in the adjacent slice were used as a new training set for the neural network classifier used to classify the adjacent slice. Dickson and Thomas [86] presented one of the uncommon supervised methods that do not require patient-specific training. The authors used a set of 50 hand-labeled MR slices from the same area of the head from different patients with acoustic neuromas, and learned to automatically label this type of tumor without patient specific training. The features used in this system included not only the pixel intensities, but also the intensities of neighboring pixels and the pixel location within the image.

Implementing Artificial Neural Networks for brain tumor segmentation involves problems of complexity and it is a time consuming task: the size of network becomes very large, training time is unacceptable, and large number of images is required for training the network. Some methods to solve these problems have been introduced, as is the case of the neuro difference fuzzy model proposed by Tayel [87], which purpose is reducing complexity, time, and storage space in determining the critical points of ROI contour using an ANN.

A particular case of ANN is the self-organizing map (SOM). In contrast with other neural network models, it has a strong physiological inspiration, as it is based on the topological map that exists in the brain cortex. The cortex is organized so that topologically closer neurons tend to produce answers to the same kind of stimulus; this is one of the reasons why SOM technique is largely employed in visual pattern recognition [88]. The self-organizing map training method is based on competitive learning, which is a type of neural network unsupervised learning. Reddick et al. [89] developed a pixel-based two stage approach where a SOM was trained to segment multispectral MR images which were subsequently classified into white matter, gray matter, etc., by a feed-forward ANN. In their work Vijayakumar et al. [88] proposed a method based on SOM to segment tumor, necrosis, cysts, edema, and normal tissue in T2 and FLAIR MRI. Their approach also graded the tumors simultaneously. The overall sensitivity and specificity of the Vijayakumar's method were observed as 0.86 and 0.93, respectively. More recently, Iftikharuddin et al. [21] presented a work where the effectiveness of two novel fractal and fractal-wavelet features is exploited to segment and classify tumor and non-tumor regions along with intensity values in multimodal (T1, T2 and FLAIR) MR images. The features are fused and the segmented tumor clusters are obtained exploiting a SOM neural network.

The researchers in the field of MRI brain tumor segmentation have used SOM or FCM separately as segmentation process tools. In [90] Murugavalli and Rajamani implemented a hybrid technique combining the advantages of a Hierarchical Self Organizing Map (HSOM) and FCM to detect various tissues like white matter, gray matter, CSF and tumor in T1 MR images. HSOM is the combination of self organization and topographic mapping techniques. This technique combines the idea of regarding the image segmentation

process as one of data abstraction where the segmented image is the final domain independent abstraction of the input image. The value of the tumor pixels detected with both implementations, HSOM and SOM combined with FCM is higher than the number of tumor pixels detected for the SOM k-means and HSOM k-means. This increment is due to the abstraction level and fuzzy clustering process.

4.4. Model-Based Segmentation Techniques

In previous sections the most successful solutions for the extraction of brain tumor boundary were analyzed, mainly for 2D MRI data. The segmentation of volumetric (3D) image data is a challenging problem that has been mainly approached by model-based segmentation techniques as parametric deformable models and geometric deformable models or level sets. In model-based segmentation, a connected and continuous model is built for a specific anatomic structure by incorporating a priori knowledge of the object such as shape, location, and orientation. Some models incorporate prior statistical information drawn from a population of training datasets [4]. The statistical parameterization provides global constraints and allows the model to deform only in ways implied by the training sets.

Segmenting structures from medical images and reconstructing a compact geometric representation of these structures are difficult due to the sheer size of the datasets and the complexity and variability of the anatomic shapes of interest [91]. The challenge is to extract boundary elements belonging to the same structure and integrate these elements into a coherent and consistent model of the structure. Deformable models involve the formulation of a propagating interface (a closed curve in 2D and a closed surface in 3D) that moves under a speed function determined by local, global and independent properties. Given the initial position of a propagating interface, and the corresponding speed function, deformable models track the evolution of the interface during the segmentation process. Existing deformable models can be broadly divided into two categories: parametric and geometric. The following sections explain the parametric and geometric deformable models including some approaches appearing in the literature for brain tumor segmentation.

4.4.1. Parametric Deformable Models

The strength of parametric deformable models (also known as active contour models or snakes) stems from their ability to segment, match, and track images of anatomic structures by exploiting constraints derived from the image data together with a priori knowledge about the location, size, and shape of these structures. Parametric deformable models are capable of accommodating the often significant variability of biological structures over time and across different individuals. Furthermore, these models support highly intuitive interaction mechanisms that allow medical scientists and practitioners to bring their expertise to bear on the model-based image interpretation task when necessary [91]. Deformable models are parametrically defined curves or surfaces that move under the influence of weighted forces that have two components named internal and external forces. The internal forces are used to assure the smoothness of the model during deformation process, while external forces are defined to push/pull the model toward the boundaries of the structure. Parametric representations of the models allow accurate and compact description of the object shape, while the continuity, connectivity, and smoothness of the models compensate the irregularities and noise in the object boundaries. The active contour model, or snake, is defined as an ordered collection of n points in the image plane $V = \{v_1, \dots, v_n\}$, $v_i = (x_i, y_i)$, $i = \{1, \dots, n\}$.

The points in the contour iteratively approach the boundary of an object through the solution of an energy minimization problem. For each point in the neighborhood of v_i , an energy term is computed:

$$E_{snake}(V) = E_{int}(V) + \beta E_{ext}(V) \quad (5)$$

where $E_{int}(V)$ is an energy function dependent on the shape of the contour and $E_{ext}(V)$ is an energy function dependent on the image properties, such as the gradient, near point v_i . α and β are constants providing the relative weighting of the energy terms.

E_{snake} , E_{int} , and E_{ext} are matrices. The value at the center of each matrix corresponds to the contour energy at point v_i . Other values in the matrices correspond (spatially) to the energy at each point in the neighborhood of v_i . Each point, v_i , is moved to the point, v_i' , corresponding to the location of the minimum value in $E_{snake}(V)$. If the energy functions are chosen correctly, the contour, V , should approach, and stop at, the object boundary.

Contour deformable models have been widely used for its sensitivity in searching the boundary of brain tumors. In fact, the sensitivity of the boundary found by the snake is better than the conventional edge detection methods, such as the Sobel and Laplacian. The external energy of snake function is only positive in homogeneous regions, and zero at the edges [92]. A number of methods have been proposed to improve the snake's performance. Luo et al. [10] implemented two of these improved methods for tumor segmentation on 2D T1 brain MRI: the balloon model, and the Gradient Vector Flow snake (GVF). The improvement provided by these methods is that the balloon model permits to enlarge the snake's capture range, and the GVF uses a spatial diffusion of the gradient of an edge map of the image, instead of using image gradients as an external force. Later in [93], Luo et al. extended their approach to 3D. Law et al. [94] presented a modified deformable region model for the extraction of brain tumor boundary in 2D MR images. The model used a point sampling technique in order to reduce the number of boundary points processed. The time required for the extraction of brain tumor boundary in MR image was greatly reduced compared with traditional active contour models.

In some applications, the initial position of the model needs to be manually placed close enough to the desired boundary to avoid converging to wrong boundaries. Khotanlou et al. [20] proposed a parametric deformable model constrained by spatial relations as refinement step to provide an accurate estimation of the boundaries of any type of brain tumors on T1 MRI.

4.4.2. Geometric Deformable Models or Level Sets

One disadvantage when using parametric deformable models for the segmentation of volumetric (3D) image, is the difficulty of naturally handling topological changes for the splitting and merging of contours. This problem was solved by introducing the use of geometric deformable models, or level sets. The main component of the level set method is the implicit representation of the interface. If the interface is given by Γ , Γ is represented as the zero level set $\{\phi = 0\}$ of a level set function ϕ . The function is a surface defined over the image area with the following property:

$$\phi(x, y, t = 0) = \pm d(x, y) \quad (6)$$

where d is the distance function from (x, y) to $\Gamma(t = 0)$, and the plus (minus) sign is chosen if the point (x, y) is outside (inside) the initial interface. Thus, the surface ϕ evolves along its normal direction with speed F as:

$$\frac{\partial \phi}{\partial t} + F|\nabla \phi| = 0 \text{ given } \phi(x, y, t = 0) \quad (7)$$

and at any time the propagating front is given by the zero level set:

$$\Gamma(t) = \{(x, y) | \phi(x, y, t) = 0\} \quad (8)$$

Caselles et al. [95] and Malladi et al. [96] proposed a geometric deformable contour with an image gradient stopping force based upon the Osher–Sethian [97] level set framework. Although the Caselles method notably improved the initialization of parametric active contours, provided that the initial contour was placed symmetrically with respect to the boundaries of interest, in practice this is not easy to achieve since many medical image segmentation problems are not dealing with regularly shaped objects. Diverse approaches were proposed to overcome this problem. So, Kichenassamy et al. [98] and Yezzi et al. [99] added a term to efficiently attract the evolving contour to the desired feature. Siddiqi et al. [100] subsequently modified the speed function by adding a term based upon the gradient flow derived from a weighted area functional so that the contour could more flexibly evolve toward the desired edges. Chang and Valentino [101] used the simulation of a charged fluid framework, governed by Poisson's equation, as a deformable model to perform general image segmentation. Later Chang et al. [43] proposed the Charged Fluid Model (CFM), a new deformable model that extends and modifies the charged fluid framework for T2 MRI brain tumor segmentation.

Ho et al. presented in [16] a method for automatically segmenting blobby-shaped tumor structures in MR images. The segmentation was performed using a probability map of tumor versus background to guide a level set snake propagation. Prastawa et al. [17] presented a knowledge-based detection/segmentation algorithm, which is based on learning pixel-intensity distributions and uses level set snakes, for normal brain matter and detecting outlier pixels that are considered tumor, the distributions were learned with kernel-based density estimation methods, and the initial outlier detection was followed by a region competition algorithm. The input for the snake was obtained by sampling specific regions based on the probabilistic brain atlas, which is represented as the zero level set of the implicit function (Eq. 6).

Li et al. [12] proposed a region-based active contour model in a variational level set formulation for the segmentation of brain MRI. They defined a data fitting energy in terms of a contour and two fitting functions that locally approximated the image intensities on the two sides of the contour. The level set formulation included a regularization term, from which a curve evolution equation was derived for energy minimization. The regularity of the level set

function was intrinsically preserved by the level set regularization term to ensure accurate computation avoiding expensive reinitialization of the evolving level set function. Later in [13] from brain MRI and other images with intensity inhomogeneities, Li et al. derived a local intensity clustering property, and defined a local clustering criterion function for the intensities in a neighborhood of each point. The local clustering criterion was integrated over the neighborhood center to define an energy functional, which was converted to a level set formulation. Minimization of this energy was achieved by an interleaved process of level set evolution and estimation of the bias field.

Xie et al. [44] exploited a hybrid level set segmentation method driven by region and boundary information simultaneously. Region information served as a propagation force, and boundary information served as stopping functional. In this approach, the user selects an ROI and then a level set method is applied to segment the tumor. Lefohn et al. [102] proposed a semi-automatic method for tumor segmentation using level sets in which the user selects the tumor region to initialize the segmentation. Based on a visual inspection of the results, they tune the level set parameters and the segmentation process is repeated. Cobzas [39] and Popuri [30] presented a variational method for brain tumor segmentation. Their approaches used prior knowledge of the appearance of anatomical structures in the normal brain, in the form of templates and atlases. These templates and atlases were fully integrated into a level set variational segmentation.

5. Summary of Brain Tumor Segmentation Methods

Threshold-based techniques offer the possibility of conducting a simple and fast segmentation when good threshold values are defined. Although with restrictions, these techniques are generally used as a first step in the segmentation process (Table 2).

Region-based techniques for brain tumor segmentation are mainly used as refinement step for defining a connected boundary of the tumor [19,56]. Some region-based approaches such as watershed transform, have reported very accurate results in segmenting tumors, but generally these approaches are constrained to be semi-automatic [60].

Pixel classification techniques for brain tumor segmentation are limited to clustering nevertheless they are the most frequently used for brain tumor segmentation. The unsupervised technique of FCM, which is the most popular for medical image segmentation [64,66],

Table 2
Summary Table of Segmentation Methods.

Segmentation Method	Advantages	Disadvantages
Threshold-based Global and Local Thresholding	Simple and computationally fast.	Limited applicability to enhancing tumor areas [45].
Region-based Region-growing	Simple and capable of correctly segmenting regions that have similar properties and generating connected region [50].	Partial volume effect [53,54]. Noise or variation of intensity may result in holes or over-segmentation.
Watershed	Segments multiple regions at the same time. It produces a complete contour of the images and avoids the need for any kind of contour joining [59].	Over-segmentation [63].
Pixel-based Fuzzy C Means Artificial Neural Networks	Unsupervised. Always converges the boundaries of tumor. Ability to model non-trivial distributions and non-linear dependencies [27].	Long computational time, sensitivity to noise [72]. Gathering training samples is not straightforward and learning phase is slow [21].
Markov Random Fields	Are able to represent complex dependencies among data instances [83].	Difficulty when selecting the parameters that control the strength of spatial interactions. Usually require algorithms computationally intensive [34].
Model-based Parametric Deformable Models	Capable of accommodating to the variability of biological structures over time and across different individuals [91].	The model may converge to wrong boundaries in case of inhomogeneities [10].
Level Sets	Topological changes are naturally possible [97].	Computationally expensive [39].

permits the use of vague concepts in the definition of clusters, and gives highly accurate results in cases of non homogeneous tumors. The unsupervised method of MRF provides a way to integrate spatial information into the clustering process, reducing the overlapping of clusters and the effect of noise on the result [78]. A major difficulty in MRF is the selection of the parameters that control the strength of spatial interactions, which can result in very soft segmentation and a loss of structural details. The supervised clustering method of ANN has the ability to model non-trivial distributions offering clear practical advantages [21,88]. Implementing ANNs for brain tumor segmentation involves problems of complexity and it is a time consuming task.

Model-based techniques have been widely used for its sensitivity in searching the boundary of brain tumors. However, as in the case of region-based methods, these models are mainly used as refinement step in brain tumor segmentation [20]. Segmenting tumors by making use of geometric deformable models or level sets, permits the development of fully automatic and highly accurate segmentation approaches as in [16]. Unfortunately, these methods are still computationally expensive [39].

Based on the existing literature, several general conclusions can be drawn with regard to elements of a system that can be used to improve performance in brain tumor segmentation. First of all, it is important to address the segmentation towards a fully automated method. This can be done incorporating within the algorithms human intelligence and prior knowledge about intensity and other tissue information, shape, size, symmetry, and normal anatomic variability to improve segmentation results. Furthermore, it would be desirable to have an unsupervised fully automatic segmentation method to avoid the use of patient-specific training. The use of some pre- or post-processing methods has demonstrated to provide more reasonable segmentation results, which reflect the layout of regions of interest, as is the case of intracranial segmentation commonly referred to as skull stripping.

6. Conclusions

Detecting the existence of brain tumors from MRI in a fast, accurate, and reproducible way is a challenging problem. Medical image processing is a very active and fast-growing field that has evolved into an established discipline. Brain tumor segmentation techniques have already shown great potential in detecting and analyzing tumors in clinical images and this trend will undoubtedly continue into the future.

Medical image analysis needs to address real-world issues that have been outside the realm of computer vision [103]. These issues come largely from the fact that the end systems are mostly used by the physician. The human factor is essential, since any successful solution will have to be accepted by a physician and integrated into the medical procedural work flow. This puts strong constraints on the type of applicable methods. Due to it, there has been a discrepancy between the advanced frameworks presented in computer vision and the low-level methods used by researchers working on real medical application solutions.

One major goal in tumor imaging research is to accurately locate the cancer. Segmentation techniques have been applied according to the characteristics that allow distinguishing tumors from normal tissues. When tumors can be distinguished from normal tissues by their image intensity, threshold-based [37] or region growing [19] techniques have been employed. Other tumors can be identified by their shapes so that a model-based technique [30,43] was applied for the segmentation.

Although the reported accuracy on brain tumor segmentation of the proposed automated methods is quite promising, these ap-

proaches still have not gained wide acceptance among the pathologists for every day clinical practice. One of the principal reasons might be the lack of standardized procedures. Another two reasons could be the substantial differences with the traditional specialists' way of work, and the deficiency of the existing methods in assisting medical decision with a transparent and interpretable way. The latter two are very important for computer aided medical diagnosis where the demand for reasoning and explanation is of main priority.

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