Review article

A review on brain tumor segmentation of MRI images

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A B S T R A C T

The process of segmenting tumor from MRI image of a brain is one of the highly focused areas in the community of medical science as MRI is noninvasive imaging. This paper discusses a thorough literature review of recent methods of brain tumor segmentation from brain MRI images. It includes the performance and quantitative analysis of state-of-the-art methods. Different methods of image segmentation are briefly explained with the recent contribution of various researchers. Here, an effort is made to open new dimensions for readers to explore the concerned area of research. Through the entire review process, it has been observed that the combination of Conditional Random Field (CRF) with Fully Convolutional Neural Network (FCNN) and CRF with DeepMedic or Ensemble are more effective for the segmentation of tumor from the brain MRI images.

1. Introduction

Image segmentation plays a crucial role in image understanding, feature extraction, analysis and interpretation for many applications. It has widespread applications in medical science, for example, tissue classification, localization of tumors, tumor volume estimation, delineation of blood cells, surgical planning, atlas matching, and image registration [1]. Mathematical algorithms of feature extraction, modeling and measurement can be exploited in the images to detect pathology, an evolution of the disease, or to compare a normal subject to an abnormal one [2]. The accurate and reproducible quantification and morphology of tumors are of crucial importance for diagnosis, treatment planning as well as monitoring of response to oncologic therapy for brain tumors [3]. Brain tumor segmentation consists of separating the different tumor tissues (active tumor, edema and necrosis) from normal brain tissues: GM, WM, and CSF [4].

A brain tumor is a cancerous or non-cancerous growth of abnormal cells in the brain. A brain tumor can be benign or malignant. The benign brain tumor has a uniformity in structure and does not contain active (cancer) cells, whereas malignant brain tumors have a non-uniformity in structure and contain active cells. The gliomas and meningiomas are the examples of low-grade tumors, classified as benign tumors. They look like normal brain cells and grow slowly. Glioblastoma and astrocytomas are a class of high-grade tumors, classified as malignant tumors [5]. They tend to grow rapidly.

Clinicians plan the most responsive and viable treatment for patients by acquiring the data from various restorative diagnostic imaging modalities like MRI, CT, and PET [6]. The advancement of medical imaging devices especially MRI provides comprehensive analysis and extract pertinent information from images of most human body structures. A significant development in computational techniques helps the specialists to investigate the tremendous measure of information contained in medical images [2]. Imaging techniques like MRI are used to find the position and degree of extent of brain tumors. MRI provides noteworthy contrast for different brain tissues in comparison to other imaging modalities like CT [7, 8]. Moreover, MR images typify significant information regarding various tissue parameters (PD, spinlattice (T1) and spinspin (T2) relaxation times, flow velocity and chemical shift), which prompt more precise brain tissue portrayal. T2 weighted (T2) images are generally utilized for giving an underlying evaluation, recognizing tumor types, and segregating tumors from non-tumor tissues. The contrast material in T1 weighted images (T1c) helps to enhance tumor boundaries from the neighbouring normal tissues [9]. The T2 weighted scan in axial viewing with FLAIR is used to show non-enhanced tumors [10]. In the light of these special features, MRI gives an edge for decision in brain tumor studies [11].

Brain MRI segmentation is an essential basic step that has many applications in neurology such as quantitative analysis, operational planning, and functional imaging [1]. Although MRI can describe the structures of the brain accurately, however medical image segmentation is a tough task because of poor spatial resolution, low contrast, ill-defined boundaries, inhomogeneity, partial volume effect, noise, variability of object shapes and some other acquisition artifacts in the retrieved data as well as the lack of models of the anatomy that entirely

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capture the possible deformations in each structure [1, 12, 13]. These limitations can be dealt with by implementing few simple approaches as proposed in Refs. [13-16]. The heterogeneous appearance of tumors incorporating the expansive changeability in location, size, shape and recurrence makes it difficult to devise effective segmentation rules [12]. Notwithstanding these issues, a notable success is recorded in this field as a result of continuing advancement in instrumentation and computer technology.

Many researchers have classified schemes of image segmentation under different heads. One of such classifications as discussed in Refs. [4, 6] are threshold-based, region-based, pixel classification and model-based techniques. The other such classifications as presented in Refs. [17-19] are threshold-based, boundary-based and region-based methods. Threshold-based methods are based on the postulate that the pixels that lie within a certain range belong to one class [20, 21]. Boundary-based methods use the assumption that pixel properties change abruptly at the boundary of two regions [2, 22-33]. Region-based methods assume that a region is composed of adjacent pixels with similar properties [17, 34-36]. In pixel classification techniques [37, 38], segmentation depends upon feature space using pixel attributes that may consist of gray level, local texture and color components for each pixel in the image. In model-based techniques as in Refs. [22, 39-41], a model is formed incorporating a-priori knowledge such as shape, size, texture, orientation about the object or specific anatomical structure. There are some hybrid approaches that concatenate two or more of the aforementioned methods [42-45].

Depending upon the degree of human interaction required in segmentation of an image, segmentation techniques are classified as manual, semi-automatic [34, 46-48] and fully automatic [1, 3, 9, 42, 49, 50]. In manual segmentation, the clinicians locate tumors on their own using their experience and knowledge of anatomy, thus consuming a lot of time. The results through manual segmentation vary from person to person as it relies on the knowledge of operator and also requires a lot of expertise. It is regarded as ground truth for semi-automatic and automatic methods. Semi-automatic methods combine computers and human expertise whereas in fully automatic methods, computers determine the segmentation without any human intervention. The former requires human intervention in the form of initialization or manually correcting or modifying the outcomes which results in efficient segmentation; however, user intervention may tend segmentation results to suffer variations from person to person and even within the same user. The latter requires anatomical knowledge like the shape, size, appearance and location of tumor for construction of a model and performing the task. Moreover, it should be able to adapt to variations in the characteristics which makes it challenging [4]. Clinically, semi-automatic methods with least user intervention are more acceptable.

Depending on the use of manually labelled training data, segmentation methods are classified as supervised [5, 51, 52] and unsupervised methods [53-55]. Supervised methods utilize the labelled data in the construction of a model that maps the extracted features to labels or classes in the training phase which are then used to determine the classes of the unlabelled data in the testing phase. The training phase requires human intervention which ends up in variability of results. The reference is made to understand the details of the supervised learning based method proposed by Raschke et al. [56]. In unsupervised segmentation, no training data is available to group pixels with homogeneous attributes together. The number of classes are automatically decided by an algorithm, making the use of features like intensity and texture. These methods are useful to handle more complicated cases.

It is impossible to develop only one standard method that suits all imaging applications. It is in this context that an overview of the methodologies of image segmentation is presented. This paper focuses on the brain tumor segmentation of data obtained from MRI using different techniques for segmentation. Reference is made to Table 1 for abbreviations used throughout in this review work.

Table 1
List of abbreviations.

Description	Abbreviation
Active Contour Models	ACM
AdaBoost Algorithm with Random Forests	ADBRF
Adaptive Fuzzy Inference System	ANFIS
Artificial Bee Colony	ABC
Artificial Bee Colony-Standard Particle Swarm Optimization	ABC-SPSO
Artificial Neural Network	ANN
Berkeley Wavelet Transform	BWT
Boundary Vector Flow	BVF
Cerebrospinal Fluid	CSF
Computerized Tomography	CT
Conditional Random Field	CRF
Conditional Random Fields - Recurrent Neural Network	CRF-RNN
Content-Based Active Contour	CBAC
Convolutional Neural Network	CNN
Darwinian Particle Swarm Optimization	DPSO
Deep Neural Network	DNN
Dice Similarity Coefficient	DSC
Directional Spectral Distribution	DSD
Diffusion Tensor Image Segmentation	D-SEG
Diffusion Tensor Imaging	DTI
Discrete Wavelet Transform	DWT
Edge Stop Function	ESF
Enhanced Fuzzy C-Means Algorithm	EnFCM
Fast Generalized Fuzzy C-Means	FGFCM
Feed-forward Neural Network	FNN
Fluid-Attenuated Inversion Recovery	FLAIR
Fluid Vector Flow	FVF
Fractional Anisotropy	FA
Fractional Order Darwinian Particle Swarm Optimization	FODPSO
Fully Convolutional Neural Network	FCNN
Fuzzy C-Means	FCM
Fuzzy local information C-Means	FLICM
Gaussian Mixture Models	GMM
Genetic Algorithm	GA
Glioblastoma Multiforme	GBM
Gradient Vector Flow	GVF
Gray Matter	GM
Gray-Level Co-Occurrence Matrix	GLCM
Hierarchical Centroid Shape Descriptor	HCSD
High-Grade Gliomas	HGG
Hybridization of PSO and ABC	HPA
Integrated Algorithm Based on ABC and PSO	IABAP
Intensity Inhomogeneity	IIH
k-Nearest Neighbour	k-NN
Leaky Rectified Linear Unit	LReLU
Least Squares Support Vector Machines	LSVM
Level Set Function	LSF
Levenberg-Marquardt	LM
Low-Grade Gliomas	LGG
Magnetic Resonance Imaging	MRI
Modified Region Growing Method	MRGM
Multi-Fractal Analysis	MFA
Multi-modal Magnetic Resonance Imaging	mMRI
Multi-parametric Magnetic Resonance Imaging	mpMRI
Multi-Population Cuckoo Search Strategy	MCSS
Multi-Population Particle Swarm Optimization Strategy	MPSOS
Neighbourhood Intuitionistic FCM Clustering Algorithm with GA	NIFCMGA
Particle Swarm Optimization	PSO
Pizza-Slice Shaped Search Windows	PSSW
Positron-Emission tomography	PET
Principal Component Analysis	PCA
Probabilistic Neural Network	PNN
Proton Density	PD
Radial Basis Function	RBF
Random Forest	RF
Rectangular Shaped Search Windows	RSSW
Recurrent Neural Network	RNN
Region of Interest	ROI
Selective Binary Gaussian Filtering Regularizing Level Set	SBGFRLS
Signal-to-Noise Ratio	SNR
Stationary Wavelet Transform	SWT
Support Vector Machines	SVM
Volume of Interest	VOI
White Matter	WM

Table 2
Overview of recent methods on the basis of different features.

References	MRI modalities	Method	Time (s)	Dim	Supervision	Type of abnormality
[108]	T1c,T2,FLAIR	FCNN + CRF-RNN	–	2D	–	HGG, LGG
[51]	T1, T1c, T2, FLAIR	Incremental CNN	21 (Approx.)	2D	Automatic	High and low grade glioblastomas
[52]	T1c, T2, FLAIR, isotropic (p) and anisotropic (q) components derived from the diffusion tensor imaging (DTI)	Supervoxel based random forests	–	3D	–	All grade tumors
[12]	T1, T1c, T2, FLAIR	CNN + fully connected CRF (DeepMedic + CRF)	< 180	3D	Automatic	Traumatic brain injuries, brain tumors (HGG, LGG) and ischemic stroke
[105]	T1, T1c, T2, FLAIR	DNN	25 to 180	2D	Automatic	High and low grade glioblastomas
[83]	T2	FODPSO-DSDMSA	< 5	2D	Automatic	Gliomas
[5]	T1, T2, FLAIR, PD	BWT + SVM	–	2D	–	Glial Tumors
[50]	FLAIR	Superpixel based extremely randomized trees	–	2D	Automatic	HGG, LGG
[54]	T1, T1c	SBGFRLS	–	2D	Semi-automatic	Homogeneously-enhanced, non-enhanced, heterogeneously-enhanced and ring- enhanced tumor
[149]	T1, T1c, T2, FLAIR	LACM-BIC	448.57 s per patient and 15.82s per image slice	2D	Semi-automatic	All grade tumors
[150]	FLAIR, T1, T1c, T2	FCNN + Texton + RF	–	2D	Automatic	HGG, LGG
[104]	FLAIR, T1, T1c, T2	U-Net based DNN	2 to 3	2D	Automatic	HGG, LGG
[100]	T1, T1c, T2, FLAIR	CNN	–	2D	Automatic	HGG, LGG
[90]	T2	DWT + PPCA + ADBRF	0.0243	2D	Automatic	Gliomas
[9]	T1, T1c, T2, FLAIR	Three-dimensional active contour without edge	243 s per slice	3D	Automatic	various types
[85]	T1, T1c, T2, FLAIR	Symmetric Multimodal Templates + Concatenated Random Forests	–	2D	Automatic	HGG, LGG
[87]	T1, T2, FLAIR	GMM feature extraction + NB/SVM/PNN classifier	–	2D	Automatic	Glioblastoma
[86]	T1, T1c, T2, FLAIR	Extremely Randomized Forest with High-Level Features	–	2D	Automatic	Gliomas
[99]	T1, T1c, T2, FLAIR	Deep CNN	480	2D	Semi-automatic	HGG, LGG

Table 3

Comparative study of recent schemes on BRATS 2015 data sets.

Methods	Dice			Precision			Sensitivity		
	Comp.	Core	Enh.	Comp.	Core	Enh.	Comp.	Core	Enh.
110 cases [108]									
	0.84	**0.73**	0.62	**0.89**	0.76	0.63	0.82	**0.76**	0.67
DeepMedic + CRF in Ref. [12]	0.85	0.67	0.63	0.85	0.85	0.63	0.88	0.61	0.66
Ensemble + CRF in Ref. [12]	**0.85**	0.67	**0.63**	0.85	**0.86**	**0.63**	**0.88**	0.60	**0.67**
274 cases									
DeepMedic + CRF in Ref. [12]	**0.90**	**0.75**	0.72	**0.93**	0.84	**0.76**	**0.90**	0.72	0.73
Ensemble + CRF in Ref. [12]	0.90	0.75	**0.73**	0.92	**0.86**	0.76	0.89	0.72	**0.74**
[154]	0.88	0.77	0.68	0.90	0.84	0.68	0.89	0.76	0.75
[99]	0.87	0.73	0.68	0.89	0.74	0.72	0.86	0.77	0.70

*Comp. — Complete, Enh. — Enhancing, Bold faces for good performance.

Table 4

Comparative study of recent schemes on BRATS 2013.

Methods	Dice			Precision			Sensitivity		
	Comp.	Core	Enh.	Comp.	Core	Enh.	Comp.	Core	Enh.
Challenge									
Zhao et al. [108]	**0.88**	**0.84**	**0.77**	0.90	0.87	**0.76**	0.86	0.82	0.80
Pereira et al. [100]	0.88	0.83	0.77	0.88	0.87	0.74	**0.89**	0.83	0.81
Havaei et al. [105]	0.86	0.77	0.73	0.88	0.85	0.76	0.78	0.68	0.58
Tustison et al. [85]	0.87	0.78	0.74	0.85	0.74	0.69	**0.89**	**0.88**	**0.83**
Kwon et al. [155]	0.88	0.83	0.72	**0.92**	**0.90**	0.74	0.84	0.78	0.72
Davy et al. [156]	0.85	0.74	0.68	0.85	0.74	0.62	0.85	0.78	0.77
Leaderboard									
Zhao et al. [108]	**0.86**	0.73	**0.62**	**0.89**	0.77	0.60	0.85	0.77	**0.69**
Pereira et al. [100]	0.84	0.72	**0.62**	0.85	0.82	0.60	**0.86**	0.76	0.68
Havaei et al. [105]	0.83	0.69	0.59	0.86	0.78	0.55	0.84	0.71	0.67
Tustison et al. [85]	0.79	0.65	0.53	0.83	0.7	0.51	0.81	0.73	0.66
Kwon et al. [155]	**0.86**	**0.79**	0.59	0.88	**0.84**	**0.60**	**0.86**	**0.81**	0.63
Davy et al. [156]	0.72	0.63	0.56	0.69	0.64	0.5	0.82	0.68	0.68

*Comp. — Complete, Enh. — Enhancing, Bold faces for good performance.

1.1. Key contributions

The present work is devoted to providing an abstract idea, particularly, the analysis of the existing methods that are used to segment the tumor present in MRI images. A number of methods are available to segment the tumor from brain MRI images. Although, the survey paper [4] provides information on different methods of segmentation with their advantages and disadvantages, there is still scope not only for comparative analysis but also for the contribution of recent methods. The highlights of this study are as follows:

1. It presents an exhaustive study of recent methods for brain tumor segmentation from brain MRI images.
2. It helps the clinicians to take the decision of correct diagnosis and further treatment accordingly.
3. Quantitative analysis through different metrics shows the effectiveness and appropriateness of recent schemes.
4. It also gives readers new directions of research for brain tumor segmentation.

The remaining paper is organized as: Section 2 presents various segmentation methods used in literature, Section 3 focuses on comparison and discussions. Finally, Section 4 depicts the conclusions.

2. Methods of segmentation

2.1. Conventional methods

2.1.1. Thresholding

Thresholding is one of the simplest techniques of image segmentation. It is fast, easy to implement and understand. It works upon the idea of converting a scalar image into a binary image, in which a threshold value is decided based upon the intensity values of the image. The intensity values of the pixels are compared with the threshold value. The pixels with intensity value same-as or higher than threshold value are assigned the value 1, whereas the pixels with lower intensity values are assigned 0, thus separating the foreground (white pixels) and the background region (black pixels), respectively.

Consider the original gray scale image, say $f(i,j)$. Depending upon the intensity values, an initial threshold value T is chosen. Partition the image into two sets H_1 and H_2 where H_1 and H_2 contains the set of pixels that are brighter and darker than the threshold value respectively. Further, the mean intensities h_1 and h_2 of H_1 and H_2 respectively are evaluated depending upon which a new threshold value is calculated as $T_1 = \frac{h_1 + h_2}{2}$. If $\|T - T_1\| \geq \Delta T$, (a pre-decided parameter), then the above procedure is repeated else the binary image $h(i,j)$ is obtained as

$$h(i, j) = \begin{cases} 1 & if \quad f(i, j) \geq T_F \\ 0 & if \quad f(i, j) < T_F \end{cases}$$

(1)

where T_F is the final threshold value. This is an iterative way of selecting a threshold as used in Refs. [57, 58].

When a single threshold value is chosen for the entire image, it is

called a global threshold. This is the most intuitive approach for thresholding of an image. It is computationally easy and fast. It does not incorporate any local relationship between pixels. It does not require any prior shape knowledge so it is appropriate for segmentation of images that do not have any fixed shape. Otsu's method [20] quests for finding the optimum value of the global threshold to segregate object from the background in the image. The histogram is assumed to be bimodal in Otsu's method. This method fails if two classes are of different sizes or with variable illumination across the image [59]. Sujan et al. [21] have used Otsu's thresholding along with morphological operations like dilation and erosion to detect brain tumor from MRI image. A new threshold method is presented in Ref. [60] to produce more accurate results. The authors in Ref. [61] have attempted to find a global threshold using level sets for segmentation of tumor and non-tumor regions. It requires only zero level set to be fed into it to perform the task. But, its efficiency becomes questionable if the difference of the intensity levels of tumorous and non-tumorous regions is lower. The performance of global thresholding approach deteriorates if the intensity of image pixels is of low contrast and not homogenous or in high noise levels.

It is not always possible to divide an image into two regions by using a single threshold value. An image may have more than two types of regions, wherein the objects in the image do not share same intensity values. In such a scenario, multiple threshold values are used to segment an image into various regions of interest. To meet the requirement in these situations, several thresholding methods are proposed in literature as local and dynamic threshold [62]. These methods are suited for segmentation when it is not possible to predict a single threshold value from the histogram of the image.

Thresholding is mostly used as a pre-processing step to segmentation of complex images like those of brain MRI because of their incapability to exploit all the relevant information from the image.

2.1.2. Region growing

Region growing is a fundamental and a popular method of image segmentation used to segment homogeneous regions that have the same intensity values. It does not require any prior shape knowledge so it can be implemented on any object that varies in shape. The main principles of working include that every pixel must be in some region, pixels in a region must be connected and should satisfy some specific similarity conditions, regions should be disjoint, and two different regions must not have the same properties [17]. It initializes with a seed point in each region of interest that can be selected manually or automatically. Then the neighbouring pixels or regions are connected to the seed point according to some predefined similarity criteria. The method is kept progressing till all the pixels are classified in one of the regions maintaining the connectivity of all the pixels grown from the seed point. It incorporates local relationships between pixels. Its computational simplicity enhances the use of this method; however, it is sensitive to seed initialization and noise. It does not perform well for images with neighbouring regions sharing similar intensities and non-smoothly varying regions like textured images. It can be applied to the images affected by lighting variation but only after suitable pre-processing. Partial volume effect is also an important factor that limits the accuracy of segmentation as it blurs the intensity distinction at the border of the two tissue types, thereby making a voxel to represent more than one tissue type [35]. This is overcome by the introduction of MRGM [63] by using gradient information for identification of boundaries. A comparative analysis of traditional region growing and MRGM is presented in Ref. [34] which proves MRGM to give better results of tumor segmentation in 3D T1 MRI images.

An effective choice of threshold for selecting similarity condition between two regions plays an important role in efficient segmentation. This gap is filled by Deng et al. [64] by minimizing the variance between homogeneous regions and *ximising* the gradient along the boundary. A fixed threshold value is used by Weglinski and

Fabijanska [65] in seeded region growing method for tumor segmentation along with some pre-processing, yielding satisfactory results. However, the adaptive threshold may prove to be more reliable. In spite of considering only intensity constraint, inclusion of orientation constraint in Ref. [66] has lead to improved results. An enhanced version of traditional region growing has been developed in Ref. [36]. A brain MRI is processed from generation of threshold T2 and PD image of a brain MRI using seeded region growing algorithm, which is further processed by Markov Logic Algorithm leading to classification based on tumor's existence.

2.2. Supervised methods

Supervised methods utilize the accurately labelled data obtained in the training phase to decide classes for unlabelled data of testing phase [4]. It involves two phases: training and testing. In the training phase, a model is constructed that maps the extracted features of data points to labels or classes. The model is then used to determine the classes of the unlabelled data in the testing phase. The training phase demands human intervention which ends up demonstrating the variability of results. Supervised classification performs better than unsupervised classification in terms of classification accuracy. Few classifiers are discussed as:

2.2.1. k-Nearest Neighbour

k-NN algorithm is a memory-based supervised learning algorithm that directly compares the new unlabelled problem instances with a collection of labelled samples in the training set. k-NN classification is performed in two stages. In the first stage, nearest neighbours for an unlabelled instance are identified and then in the second stage, the class or label of the instance is determined using those neighbours. The training phase of the algorithm consists of storing the feature vectors and class labels of the training samples. The training data is being stored and then the similarity or distance between the new unlabelled test point and the training instances is computed to predict the label of the test point. k Nearest neighbours to the unlabelled data from the training set are identified and their labels are used to assign the label or class to the unknown record by majority voting. The parameter k depends upon the number of extracted features and the number of cases [67]. The distance metric to be used depends upon the problem domain [68]. k-NN is used in Ref. [67] to segment light and dark abnormalities within both medium and low background gray level values in the FLAIR-MRI brain images. Significant improvement in the segmentation of white matter lesions has been noticed in Ref. [69] due to inclusion of tissue type priors in feature set and use of variance scaling for intensity normalization.

2.2.2. Support vector machines

SVM splits the image into two classes by finding a hyperplane that best classifies the data [70]. For instance, the hyperplane which has the maximum distance from the nearest data point on each side is chosen [71]. SVM requires solving the following optimization problem:

$$\min_{w,b,\xi}, \frac{1}{2}w^T w + C \sum_{i=1}^{l} \xi_i, \tag{2}$$

subject to $y_i(w^T \phi(x_i) + b) \geq 1 - \xi_i$, with $\xi_i \geq 0$, where (x_i, y_i) are labelled pairs in data set, w is the normal vector of separating hyperplane, ξ is error term, C is penalty parameter for error term and b is the offset of the hyperplane [72]. SVM uses a kernel function $K(x_i, x_j) = \phi(x_i)^T \phi(x_j)$ to transform the data into a higher dimensional feature space so that the data can be linearly separated with a maximum margin [73].

Kharrat et al. [74] used spatial gray level dependence method to extract the texture features which are then chosen by GA to be fed into SVM for classification of brain tissues into a normal, benign or malignant tumor. SVM is combined with hierarchical regularization using

CRFs in Ref. [73] to give much promising results in separating healthy and tumor tissue and then sub-classifying both regions into the CSF, WM, GM and necrotic, active, edema region respectively in a novel hierarchical way. Zhang et al. [75] contributed in the literature by introducing a novel feature selection algorithm fusing multi-input data. However, this system is modeled based on 2D information to segment each pixel in 3D MRI volumes which limits its validation on large data sets.

In SVM, points are classified based upon the proximity with separating hyperplane which takes longer computational time to solve linear or quadratic problems so formed. In lieu of reducing the number of calculations, Wu et al. [76] emphasized on segmenting the image into superpixels rather than processing on voxels. SVM is trained using features extracted by multi-level Gabor wavelet filter and the relationship between the neighbouring superpixels is learned. The output from SVM and affinity model is combined with CRFs and structural noise is removed, resulting in final segmentation of GBM. Recently, an effort reducing the classification error using SVM is presented by Soltaninejad et al. [77]. Classification of tumor grades(such as II, III and IV) is performed using the first and second order statistical features extraction. Whereas, the ROI segmentation is incorporated using either manually or through a superpixel based approach. Enhanced version of MRI brain tumor grading is presented in Ref. [78].

An efficient method for brain tumor classification based on D-SEG is proposed by Jones et al. [79]. This technique uses a combined application of k-means clustering and SVM. To delineate VOI of abnormal tissues, the k-means clustering approach with similar isotropic and anisotropic diffusion properties is applied. Whereas, SVM is used for classifying various types of tumors such as LGG, glioblastomas, metastases, and meningiomas. D-SEG is also used in Ref. [80] to identify tumor core ROIs to further discriminate GBMs from solitary metastasis using the selected 2-D shape features extracted from DTI data assuming that the 2-D shape features are normally distributed. However, this is the limitation of presented work which is later suppressed by Yang et al. [72] with the use of 3D shape descriptors to improve the accuracy in the discrimination between the two.

Like the standard SVM where data points are classified by finding a single hyperplane, points can also be classified by assigning them to the closest of the two parallel lines which are pushed apart as far as possible [81]. Vaishnavee and Amshakala [13] have used this proximal SVM classifier to solve a linear system of equations for generating a linear or non-linear classification. The classifier performs its task with much more accuracy and in lesser time. Bahadure et al. [5] also used SVM for tumor detection. The quality of the image is firstly enhanced using the modified sigmoid function. Then BWT is applied for effective segmentation of brain MR image after using suitable threshold operation for skull stripping. Textural features are extracted using GLCM and fed into SVM that gave an accuracy of 96.51% in contrast with an accuracy of 90.54% without feature extraction. The results are compared with the ANFIS [82], Back Propagation, and k-NN which gave an accuracy of 90.04%, 85.57% and 87.06% respectively.

Lahmiri [83] has used PSO, DPSO and FODPSO to segment the glioma affected area from the normal region in the image. DSD signatures from the segmented image are computed and its features are extracted by means of MFA and further, the classification is performed by SVM. The results show the achievement of highest accuracy in the case of FODPSO for segmentation.

2.2.3. Random forests

Random forest, an ensemble learning scheme is a simple, supervised classification technique which runs efficiently on large data sets, handles thousands of input variables without variable deletion and estimates important features for classification. It is relatively robust to outliers and noise. Breiman [84] defined a random forest as "a classifier consisting of a collection of tree structured classifiers $\{h(x,\Theta_k), k = 1,$ …} where the Θ_k are independent identically distributed random

vectors and each tree casts a unit vote for the most popular class at input x". In literature, several techniques (such as Refs. [50, 85-89]) are developed using the application of RF based classification. Tustison et al. [85] applied several features including intensity, geometry, and asymmetry from multiple modalities to a random forests classifier. The use of symmetric multivariate templates has enhanced its performance. The work presented by Chaddad [87] uses GMMs to identify GBM features using different individual modalities (T1 and T2 weighted images, FLAIR MR images) separately. Multithresholding segmentation with morphological operations of MR images has been used to detect infected regions. GMM features demonstrated better performance resulting in early treatment of GBM. Koley et al. [89] implemented RF for pattern classification after the identification and extraction of tumor area. The tumor region is quantified with 86 features to develop the training data set, which are then given as input to the classifier. The ADBRF has been used in Ref. [90] which promises to give quite accurate results with only 13 discriminant features. Goetz et al. [88] proposed a new random forest-based method which uses domain adaptation to reduce sample selection errors introduced by the sparse sampling. Extremely randomized trees [91] (extra trees classifier) are used in Refs. [50, 86]. They are computationally efficient and reduce the variance due to more randomization. Pinto et al. [86] includes high level local features including intensities in all sequences and context-based features calculated over non-linear transformation of the images while Soltaninejad et al. [50] considered different types of features like intensity statistics, textons, and curvature features. Instead of using voxels, supervoxels are formed in Ref. [52] using multimodal MRI to reduce computations. Information from multimodal images is combined to produce supervoxel boundaries across multiple image protocols. Statistical and texton features provide improved performance for classification of brain tumor supervoxels using RFs.

2.2.4. Artificial neural networks

Animals respond to the environment because of very small connected units called neurons in the nervous system. Like animals, artificial neural network imitates the behaviour of neurons and respond to the surroundings to achieve an optimal state. The artificial neurons, like the originals, process the input signals and then transmit them from one to another, thus traversing multiple intermediate hidden layers of connections to get the relevant output at the final layer. The known characteristics are fed into input nodes and mathematical operations are performed on them to get a final classification. The output of each artificial neuron is a non-linear function of the sum of its inputs. Similar to a person who learns from his experiences, the technique is trained to evaluate the parameters involved in mathematical operations so that the errors at the final stage can be minimized. As the learning proceeds, the weights with which these artificial neurons are connected to each other in different layers also vary. These weights are found out by using optimization methods. As the size of the network becomes very large, the complexity of the technique increases and is time-consuming. Moreover, efficient training of the network requires a large number of images. However, its ability to model any arbitrary, non-trivial distribution is of practical advantage. Different types of neural networks are being used currently [92, 93].

FNN classifier has been used in Refs. [66, 94-96]. The FNN is one of the simplest ANNs. In this network, the flow of information is unidirectional, from the input nodes, through the hidden nodes, and to the output nodes. It can classify separable non-linear patterns and can approximate any arbitrary continuous function. Various algorithms like Back Propagation algorithm, GA, PSO and ABC are used to train FNN but they easily end up in giving local optimum values of the parameters. Moreover, they suffer a drawback of high computational costs. FNN and RBF neural network have been used with the modified region growing involving both intensity and orientation constraint in Ref. [66] and gave satisfactory results.

El-Dahshan et al. proposed a fast and robust hybrid intelligent

machine learning technique in Ref. [42] for automatic detection of brain tumor. It is based on feedback pulse-coupled neural network for segmentation, DWT for feature extraction, the PCA for reducing the dimensionality of the wavelet coefficients and the feed forward back-propagation neural network to classify inputs into healthy or pathologically cases. The experiments showed the classification accuracy to be 99%. Damodharan and Raghavan claim in Ref. [94] that FNN performs better than k-NN classifier and Bayesian classifier, measured on the basis of sensitivity, specificity and accuracy graphs. Skull stripping and morphological operations are applied to remove the noise from the input image after which thresholding is used to segment the constituents of the brain; CSF, WM, GM. Statistic features like mean, variance, entropy and energy functions are calculated and fed into the classifier to get the segmentation of the abnormal part from the normal one.

Wang et al. have used SWT to extract features from brain MRI images in Ref. [95]. SWT helps in better extraction of features resulting in improved classification [97]. The authors have then used PCA for feature reduction to reduce the dimensionality and hence, the computational cost. FNN is trained by three different algorithms: an IABAP, ABC-SPSO and HPA. The classification results are shown to be excellent in terms of sensitivity, specificity, precision, and accuracy when FNN is trained with HPA.

Shree and Kumar [98] have focused on removing noise and smoothening the image that has improved SNR. In this scheme, the DWT for extracting wavelet coefficients and GLCM for statistical feature extraction are used after region growing segmentation to improve the performance and to reduce the complexity. This was followed by morphological operations which remove the noise that can be formed after segmentation. The PNN classifier also implemented in Ref. [7] was then used to train and test the performance accuracy in the detection of tumor location in brain MRI images. The proposed technique is proved to be effective since the experimental results recorded nearly 100% and 95% accuracy in training and testing data sets respectively while identifying normal and abnormal tissues from brain MR images.

S. Pereira et al. [99, 100] introduced an automatic method for segmentation into five classes: necrosis, edema, non-enhancing, enhancing tumor and normal tissue. For the evaluation, three tumor regions; Enhancing tumor, Core (necrosis + non-enhancing tumor + enhancing tumor) and the Complete tumor (all tumor classes) are considered. The process is automatic except for the initial stage in which the user needs to identify the grade of glioma manually. The authors have used the standardizing method proposed by Nyul et al. [101] as a pre-processing step so that similar intensities depict the same tissue type in an image. Two CNN architectures, one for LGG and another (deeper than LGG) for HGG are trained wherein LReLU activation function is applied to all the layers except the last where softmax is used. The use of small kernels along with more convolutional layers has been proposed which requires a smaller number of weights to be trained. Moreover, regularization and data augmentation are used to reduce overfitting. DSC metric for two data sets BRATS 2013 and BRATS 2015 for the complete, core, enhancing regions are 0.88, 0.83, 0.77 and 0.78, 0.65, 0.75, respectively.

Intensity distribution in an image for various tissue types does not allow adaptation to variations in scanners or individuals or time. To overcome this problem, Zhang et al. [102] have used multi-modality information from T1, T2, and FA images as input to deep CNN for segmenting isointense stage brain tissues. A 3D deep CNN has been used in Ref. [103] that can handle an arbitrary number of modalities. A 3D CNN with 11 layers and two parallel pathways has been presented in Ref. [12] which incorporates local and contextual information thus, resulting in improved segmentation results. 3D fully connected CRFs are used as a post-processing step that helps to get better prediction results. It helps to overcome computational burden while processing 3D medical scans. Although, a 3D information of the MRI data is an advantage to 3D-CNNs but an increase in the network size and

computational cost is its major disadvantage. Therefore, 2D-CNNs have been widely adopted in the brain tumor segmentation methods. In continuation of these methods, Dong at al. [104] contributed by proposing a fully automatic brain tumor segmentation method using U-net based deep convolution network. Here, it is shown that their results are good for core region and comparable for the complete region of the tumor.

A new DNN is presented in Ref. [105]. Since, the distribution of tumor labels is unbalanced, a two-phase training procedure has been used to train CNNs efficiently. The authors have explored two types of architecture: two-pathway and cascaded architecture. Two-pathway architecture models both local features and global contextual features simultaneously. Cascaded architecture took into consideration the dependence of labels of pixels. Two CNNs are stacked wherein the segmentation outputs from one CNN are taken as input to the following CNN which has helped to achieve higher performance.

CNNs are powerful, features are not required to be fed into the system, rather it extracts the required information for classification from the provided data [106]. However, few loopholes, including the amount of hyper-parameters, requirement of a large amount of training data that demands memory and a lot of computations that too increase further with deeper networks, discourage the employment of CNNs on medical imaging data [107].

Zhao et al. [108] have used image patches and image slices to train FCNNs and CRF-RNN, respectively. The three segmentation models are trained using patches and slices in axial, coronal and sagittal views. Image patches have been used in training to handle millions or billions of parameters involved in deep models. Three results are obtained corresponding to each view which are then combined using voting based fusion strategy. Fusion results have shown improvement. An improved variant of nonparametric nonuniform intensity normalization (N3) algorithm, denominated N4ITK, for bias field correction and intensity normalization method as proposed in Ref. [91] has been used as a pre-processing step. Thresholding is used as a post-processing step to correct the false labels. The authors have evaluated the positive effects of the pre and post processing steps in the process, but at the same time, they add to the implementation time of segmentation. The authors also witnessed that the results obtained by using 3 modalities T1c, T2, FLAIR are highly competent with those obtained by using all the 4 modalities. So, T1 is proved to be almost redundant which can result in reduction of storage and data acquisition cost.

In order to reduce the inference time, a sequential CNN architecture has been implemented in spite of parallel CNN architecture in Ref. [51]. The proposed Incremental XCNet develops and trains CNN models simultaneously rather than working on conventional trial and error technique. It incorporates ensemble learning. It incorporates no post-processing and least pre-processing steps.

2.3. Unsupervised methods

Unsupervised segmentation requires no training data to group pixels with homogeneous attributes together. The number of classes is automatically decided by an algorithm, making the use of image-based features like intensity, gradient or texture. These methods can tackle more complex problems. The unsupervised methods of segmentation are discussed as:

2.3.1. Clustering

Clustering is an unsupervised pixel-based method for image segmentation that partitions an unlabelled image data into clusters in which the pixels share some common characteristics. It is of two types: hard clustering and soft clustering. In hard clustering, a data point either belongs to a cluster or not. Clusters do not overlap as in k-means clustering whereas in soft clustering, in spite of putting a data point into a cluster completely, the probability of belonging to a cluster is assigned to it. Clusters can overlap. A single data can belong to two or

more clusters at the same time as in Fuzzy C-Means clustering.

2.3.1.1. k-Means clustering.

k-Means clustering is a key technique in pixel-based methods [38]. Segmentation is done using k-means algorithm in following few steps. Initially, k means $m_1^{(1)}, m_2^{(1)}, \ldots, m_k^{(1)}$ are considered corresponding to the k clusters of the image. Then, the distance between each observation x_i, $i = 1, 2, \ldots, n$ where each x_i is a d-dimensional real feature vector and the means $m_j^{(t)}$, $j = 1, 2, \ldots, k$ for each cluster at t^{th} iteration, is calculated. An observation says x_1 belongs to that cluster whose mean has the least distance with x_1. So, a cluster of observations is formed at each iteration and new means are calculated. The above steps are repeated until the new means do not change further. Hence, the image is finally partitioned into k clusters.

k-Means algorithm, though simple and computationally efficient, may not give an optimum value even after a large number of iterations. The use of a different distance function other than Euclidean distance may lead to convergence of the result in some cases. The time complexity of the algorithm is given by $O(knt)$, where k is number of clusters, n is number of data points and t is number of iterations usually requiring $k \ll n$ and $t \ll n$ [109, 110]. The value of t depends on the initial starting cluster centres [110]. k-Means algorithm has few limitations, say, the number of clusters k has to be initialized, the initial means also have to be chosen and it is affected by noise also.

Determining the actual number of clusters requires a-priori knowledge about the image. If the number of clusters chosen is the same as the real number of clusters, then k-means algorithm gives correct segmentation; else, it ends up in giving faulty results. While clustering the real data, the number of clusters is unknown beforehand, so the algorithm is run several times by performing clustering using different number of clusters which adds to computational cost and time. Moreover, a lot of computations are required at every iteration to calculate the distance of each data point from its nearest cluster.

k-Means and hierarchical clustering are used to separate the position of tumorous tissues from the healthy ones in Ref. [111] by first rendering the original MRI image and then applying pseudo-color transformation to convert it into RGB image to enhance its features. Juang and Wu [112] also works on the same idea and gave encouraging results to determine exact lesion size and region. Ahmed and Mohamad [113] combined Perona and Malik [114] anisotropic diffusion model for image enhancement and k-means clustering for classifying different tissues and tumors and reliable results are witnessed.

Accurate determination of size and stage of tumor helps in taking necessary and immediate steps to save the lives of tumor patients. Selvakumar et al. [115] have worked in this direction by using k-means and Fuzzy C-Means algorithm. J. Vijay and J. Subhashini [38] proposed a method which gave efficient results in a comparatively lesser number of iterations. Madhukumar and Santhiyakumari [116] suggested k-means, with histogram guided initialization has been proved to differentiate all the six tissue classes (GM, WM, CSF, necrosis, enhancing edema and background) on tumor edema complex MR images. In order to tackle the drawback of initialization of cluster centres, Dhanachandra et al. [117] have implemented the use of subtractive clustering for initialization of k-means algorithm. It is accompanied by preprocessing step of partial stretching enhancement and post-processing step of median filtering to remove undesired regions, which finally results in improved segmentation quality.

2.3.1.2. Fuzzy C-Means clustering.

FCM clustering algorithm was proposed by Bezdek in 1993 [118]. It works on the principle of assigning membership values u_{ij} to each feature data point $x_i, i = 1, 2, \ldots, n$, $x_i \in \mathbb{R}^d$ corresponding to the centres of the clusters c_j, $j = 1, 2, \ldots, k$ where $k < n$ depending upon the Euclidean distance of the data point from the centre of the corresponding cluster expressed by $\|\cdot\|$. The membership values satisfy the following properties:

1. $0 \leq u_{ij} \leq 1, for all\ i, j,$
2. $\sum_{j=1}^{k} u_{ij} = 1, for\quad all\quad i,$
3. $\sum_{i=1}^{n} u_{ij} < n, for\quad all\quad j.$

The larger membership value signifies higher propinquity to belong to the particular cluster. One piece of data may belong to two or more clusters. The initial membership values are assigned to each data point x_i to belong to a cluster j. Then, the centres of the clusters and the membership values are updated. Now, the fuzzy partitioning is done through an iterative minimization of the objective function. The process terminates when the membership values in consecutive iterations are close enough.

The major disadvantages of the standard FCM algorithm are that it uses the non-robust Euclidean distance and it is sensitive to noise. The former problem is dealt in Refs. [119, 120] by adopting some robust distance measures such as L_p norms ($0 < p \leq 1$) that helped to reduce the effect of outliers on results. In addition to it, Mahalanobis distance has been used in Ref. [121] to reduce the influence of the geometrical shape of the different classes. The second limitation is dealt by designing algorithms incorporating spatial information into account by many researchers as in Refs. [37, 47, 121-124].

Ahmed et al. redesigned the standard FCM algorithm incorporating spatial contextual information, later called FCM_S [37] by using the modified objective function to recoup intensity inhomogeneity and acknowledging the labels of pixels to be influenced by those of their immediate neighbouring pixels. However, it computes the neighbourhood term at each iteration which takes a lot of time. In order to overcome this problem, FCM_S is modified to FCM_S1 and FCM_S2 by introducing mean and median filtering (as proposed in Ref. [123]) that has also increased the robustness to outliers and noise. Computational time was further reduced by Benaichouche et al. [121] using EnFCM by working on gray level histogram rather than the image pixels.

Blending the ideas of FCM_S1, FCM_S2 and EnFCM, W. Cai et al. [47] have proposed FGFCM clustering algorithm in which segmenting time is significantly reduced by considering its dependency only on gray values rather than the image size. Moreover, a parameter α is used to balance between sensitivity to noise and preserving image information, that demands expertise to be chosen, has been replaced by a new factor S_{ij}, introduced as a local similarity measure that has reduced uncertainty of correct segmentation. The method was suitable when prior knowledge of noise does not exist, which generally happens. Furthermore, in spite of using the usual distance metric, a new dissimilarity index influenced by local and non-local information is proposed by Wang et al. [125] which is proved to be better than above algorithms but it is computationally expensive. Various variants of FCM have been developed to make the standard FCM algorithm more robust to noise. Forouzanfar et al. [126] presented a neighbourhood attraction dependent on the relative location and features of neighbouring pixels. FLICM algorithm that incorporates the local spatial information and gray level information in a fuzzy way was developed in Ref. [127]. Its performance is independent of the type of noise. The adaptive control factors introduced in objective function are achieved automatically without any parameter selection like α which makes the segmentation process crisp. Song [128] improved segmentation accuracy by incorporating modified spatial constraints between the centre pixel and neighbourhood pixels in similarity measurement.

Numerous researchers have made an exclusive use of optimization techniques to achieve better classification results. The researchers in Ref. [121] proposed to initialize the FCM algorithm with the help of PSO so that the system is not trapped in local minima. It helped to choose the nearest initial solution to the global optimum. Menon and Ramakrishnan [129] proposed the segmentation of MRI image using Artificial Bee Colony (ABC) with fitness function given in Ref. [130] along with FCM clustering. It not only segments the tumor but also provides with its intensity. A NIFCMGA is proposed in Ref. [131] which

not only helps to evaluate the optimal parameters for IFCM, but also reduces the effect of noise and outliers through neighbourhood membership. Superiority in segmentation results of MRI image in presence of noise and IIH has been achieved in Ref. [124] by incorporating a conditional variable with each pixel which describes its significance in generating the local membership values and the clusters. But, high IIH levels cannot be dealt in with this approach. Incorporation of local contextual information and Gaussian function into the objective function in Ref. [55] has proved to be beneficial in IIH estimation and bias field correction.

2.3.2. Active contour models /deformable models

ACM is a model-based segmentation technique, which is often called Deformable Models in its 3D version. It is mostly used in 3D image segmentation [132]. A connected and continuous model is built for a specific anatomic structure in model-based segmentation by incorporating a-priori knowledge of the object such as shape, location, and orientation. Given an initial propagating surface, deformable models involve the evolution of the surface with the given speed function such that it matches with the structure of the original object. Deformable models are capable of accommodating the significant variability of biological structures over time and across different individuals. They are classified as parametric ACMs and geometric ACMs. Parametric ACMs are implemented using techniques like finite element method or splines whereas geometric models use the Eulerian framework like level sets [133].

2.3.2.1. Parametric active contour models.

Active contour models have been widely used for segmentation since its inception. The parametric active contour model, also called snakes, was originally given by Kass, Witkin and Terzopoulois [22] based on the gradient descent method. Active contours are simply connected closed curves which track the boundary by matching the deformable model to the image curve, influenced by weighting forces (external and internal forces), in order to minimize the defined energy functional. The energy function involves the parameters which control the elasticity and rigidity of the curve respectively [24, 134]. External forces push the initial contour towards object contours and internal forces resist deformation.

Though the model is simple and consistent, it has few limitations too. For instance, the snake has to be initialized close to the desired contour, else, it may find local minima away from the contour [133]. The problem is solved by Cohen in Refs. [23, 25]. Dual active contour models use two snakes to approach the desired contour from both inner and outer sides so as to improve the detection of global minima, however low computational efficiency and complexity in its implementation restrict its use [2].

Snakes did not perform well in presence of concavities and sharp corners in the gray-level image which was overcome by the introduction of GVF as suggested by Xu and Prince [28, 30, 31]. However, GVF requires prior object knowledge and appropriate parameter selection for good and reliable results. Moreover, it requires high computations. Many researchers have introduced novel external force fields to overcome the drawbacks of snakes. Sum et. al. proposed BVF [135] to deal with problems of concavities and capture range. It used the interpolation scheme to compute the potential values which helped reduce computational burden. Wang et.al. proposed FVF in Ref. [136] to extract concave shaped tumors. It also addressed the issue of limited capture range. It outperformed GVF and BVF based on the quantitative measures; mean, median and standard deviation. In Ref. [134], a robust method combining region based fuzzy clustering for getting an initial contour and deformable model for segmenting tumor region using GVF as external force field has been proposed that has solved the problems associated with initialization and poor convergence to boundary concavities. Sachdeva et. al. [137] introduced CBAC that uses intensity as well as texture information in order to handle the problems like

preconvergence in case of ill-defined edges, oversegmentation in case of weak and diffused edges and noise, failure to segment heterogeneous tumors and homogeneous tumors against the similar background. The comparisons with GVF, FVF and BVF proved the remarkable performance of CBAC.

Many nature-inspired optimization techniques have been used to overcome the limitations and solve the energy minimization problem. The control points in the traditional ACMs search in a small window for its new position to locate the edges which hinders accuracy in locating concavities. A large search window is accompanied with more computational time. In view to reduce this computational time, a MPSOS has been proposed in Ref. [138]. Evolutionary algorithms followed by Greedy Algorithm have been used in Ref. [139] to automate the process of selecting an optimal value for parameters to allow good detection of edges. A MCSS has been introduced in Ref. [53] which is implemented with two geometries for search windows, RSSW and PSSW, out of which PSSW is preferred. MCSS was compared with traditional snakes and MPSOS. The assessments of the ACM strategies were performed through similarity metrics; Jaccard coefficient, Dice coefficient, and Hausdorff distance.

2.3.2.2. Geometric deformable models.

Geometric models are based on curve evolution theory and level set methods [40]. Instead of parameterizing a curve, it is depicted as a zero level set of a higher dimensional function whose evolution defines the initial value problem. Contour evolution is associated with speed function of level sets. Here, the contour is independent of the curves parameterization [39]. So, they can handle topological changes. However, in case of tumor segmentation of MRI images wherein images are generally noisy with ill-defined edges, geometric deformable models may result in an inconsistent topology with respect to the actual object [140]. Caselles et. al. [24] proposed a model for active contours based on a geometric partial differential equation called mean curvature motion equation. This scheme works well for objects having good contrast. When the object boundary is indistinct or has gaps, this contour tends to leak through the boundary. When boundaries of an object are not defined by gradient or with very smooth boundaries, classical active contour models [22, 24, 27] are not applicable. In the concerned direction, a method proposed by Tony F. Chan [33] can be applied. In order to work well in case the boundaries are ill-defined, a framework that uses edge-based information obtained from gradients along with probability scores obtained from classifiers has been proposed in Ref. [141]. The method can acquire probability scores from any classifier and can construct ESFs for any edge-based active contour model using any level set method. Instead of using just one ESF, it uses a group of ESFs which makes the process robust.

Traditional level set methods generally develop irregularities in the LSF during its evolution which hampers its stability. In order to fix this issue, re-initialization of LSF as and when required (when the LSF degrades and requires reshaping for its evolution) has been proposed as a correcting measure. However, determining when LSF degrades and how it should be corrected is itself of serious concern. In lieu of this, a distance regularization term has been introduced in potential function in Ref. [142] that maintains the shape of LSF. Moreover, the problem of poor convergence to boundaries has also been encountered which is dealt in Ref. [134] by combining fuzzy clustering with deformable models.

An automated 3D active contour method without edge has also been proposed in Ref. [9] that can identify tumor slices and segment them in volumetric MRI brain scans. Modify Level Set method combining geometric method with the statistical method of active contours has been proposed in Ref. [1] to make initialization task automatic.

The region-based ACM methods, unlike edge-based ACMs, do not depend on edges and gradient information of the image, hence more robust to noise. By incorporating the global image information, they become robust to initialization. However, they assume the image

intensity to be homogeneous which does not often occur in the real world. ACMs suffer from the limitation of handling IIH. Local image information is extracted through the introduction of a local binary fitting energy functional [143] and local image fitting energy functional [144] which helped in segmenting images with IIH. Wang et. al. took advantage of both global and local image information to frame a two-stage ACM [145]. In the first stage, a coarse segmentation contour is obtained by employing global energy fitting functional, which is then used as initial contour in second stage and local energy fitting functional is employed to finally extract the object boundaries. Bias correction is also an important method for addressing the IIH of MRI images. A modified model has been developed in Ref. [146] in which clustering criterion energy function is defined by considering the difference between the measured image and estimated image in local region to obtain accurate segmentation results and an accurate estimation of the bias field. The problem of IIH is also dealt with introduction of locally statistical ACM [147]. Furthermore, incorporation of the multiple image information into the singed pressure force term of SBGFRLS model has made a significant contribution in solving blurred edge problems in brain tumor segmentation [54]. The method effectively segmented homogeneously enhanced, non-enhanced, heterogeneously-enhanced and ring-enhanced tumor. A new LSM proposed by Kumar et al. [148], based on probabilistic C-mean objective function and incorporating lattice Boltzmann method is highly parallelizable, effective in tackling intensity inhomogeneity in image and robust to noise. It is computationally less complex. Region-based ACMs that use statistical intensity information are sensitive to high mean intensity difference between two consecutive regions. The difference in the mean intensities of the foreground and the background is quite significant which decreases the relevance of this method in MRI images. Therefore, Localized ACM with background intensity compensation integrating an additional automatic step to balance this difference is proposed in Ref. [149]. The introduction of HCSD enables the application of the approach on all sets of brain tumor images. It is compared to some state-of-the-art methods for segmentation tasks and claimed to outperform them on grounds of computational time, dice coefficient, sensitivity, specificity, and the Hausdorff distance.

2.4. Hybrid techniques

Hybrid techniques combine two or more techniques to provide segmentation results. It concatenates two or more methods by using their advantages and overcoming their disadvantages to get fruitful and reliable outcomes. Parveen [151] suggested that FCM and SVM are combined to acquire accurate classification of the diseased part of the brain. FCM is used for segmentation of doubtful, diseased region of the brain. Gray level run length matrix is used to extract features which are used by SVM for classification.

k-Means detects the tumor faster than FCM whereas FCM predicts tumor cells more accurately in comparison to k-means [43]. So, the proposed automatic algorithm in Ref. [43] uses the advantages of both the methods to carry out efficient segmentation in lesser execution time due to a reduced number of iterations. Tumor cluster is extracted and then contoured using thresholding and active contours respectively as post-processing step.

A hybrid technique constituting LSVM classifier with Multi-Layer perceptron based kernel functions and RBF kernel functions for classification, and Fast Bounding Box for segmentation has been proposed in Ref. [44]. Noise removal is done as a pre-processing step by median filtering followed by statistical based feature extraction using GLCM. The classification accuracy is claimed to be 96.63% which is quite promising.

Machine learning and region-based ACMs have been integrated for effective segmentation using their respective advantages. Machine learning helps to deal with intensity inhomogeneities whereas region-based ACMs deals efficiently with poorly defined boundaries and

misclassified pixels. Region-based ACM for segmentation and ANN based LM algorithm for classification process are integrated together to classify the MRI image efficiently as normal and tumorous as suggested by Shenbagarajan et al. [92]. k-NN and SVM are integrated with Chan-Vese method [45] in order to get accurate segmentation results in lesser amount of time. Soltaninejad et al. [150] proposed an automated segmentation of brain tumor in mMRI images. In this study, a combination of FCNN with RF is presented. FCNN is used to form machine-learned features while RF for classification of normal and tumor tissues. The method was tested on MICCAI-BRATS 2017 challenge data sets. However, the similar methodology for the desired objectives with improved results is presented in Ref. [152]. More recently, an article presented in Ref. [153] demonstrates the state-of-the-art techniques participated in BRATS challenge for the segmentation of brain tumors in mpMRI scans. The paper concludes the competition by comparing various methodology and their findings. In this paper, the statement is made that the approaches based on machine learning are a good contender than conventional methods at different levels of the competition. Finally, it is observed that on focusing the prediction of overall survival the Deep learning based techniques are superior to rest others.

The hybrid approach presented Sharma et al. [93] to retrieve information about the affected part and the size of a tumor from brain MRI images is based upon k-means and ANN. Fuzzy Inference System, that uses GLCM for feature extraction is created, followed by thresholding, morphological operator and watershed segmentation for brain tumor detection.

The combined approach of RFs and ACMs has been proposed in Ref. [107]. RFs are employed as feature learning kernels to learn multiscale feature representations iteratively from multimodal MR volumes. Tumor structure is inferred from concatenated forests which is taken as an initial contour to multiscale patch driven active contour model for the final segmentation. This method is robust to tissues with low contrast. They require lesser computations and memory in contrast to other machine learning methods like CNNs.

3. Comparison and discussion

Table 2 shows an overview of recent methods based on different parameters used for segmentation of brain tumor from brain MRI images. Here, a comparative analysis in terms of the methodology used, types of abnormality and the type of supervision is presented. One may observe here that most of the studies are focused towards high- and low-grade gliomas. It is also analyzed through this comparison that increasing the size of the network will require more computational time and complexity.

Tables 3 and 4 present a quantitative analysis of various state-of-the-art methods through different evaluation parameters such as Dice, Precision, and Sensitivity for brain tumor segmentation of MRI images. Table 3 presents the results for two different cases of 110 and 274 for BRATS 2015 data sets and Table 4 shows the comparative results for both Challenge and Leaderboard data sets of BRATS 2013.

However, very limited literature is available for comparing the results of BRATS 2015 data sets. Still, an effort is made to present the effectiveness of different methods for these data sets. Table 3 shows that the performance of the method proposed by Kamnitsas et al. [12] is better for almost all the evaluation parameters than the other existing schemes. Here, it may be observed that the performance of Ref. [12] for 110 cases is better when Ensemble with CRF is used while for 274 cases it is good for DeepMedic with CRF.

Table 4 depicts that the performance of Zhao et al. [108] integrating FCNN and CRF in a unified framework for Dice is better than others for Challenge data sets. However, the results of Tustison et al. [85] using the supervised learning capabilities of the RF model with regularized probabilistic segmentation and Kwon et al. [155] are good for sensitivity and Precision, respectively. For Leaderboard data sets, the performance of Kwon et al. [155] using the combination of segmentation

and registration seems much better than the others. However, Zhao et al. [108] also provides the good results at some places for Leaderboard data sets. As per authors' knowledge, no method is reported in the literature that provides the best result for all the evaluation parameters.

4. Conclusions

This paper presents an exhaustive study of various existing methods of brain tumor segmentation. The quantitative analysis through different evaluation parameters among state-of-the-art methods helps the readers and clinicians not only to set the new directions to develop the scope of research but also assists for accurate diagnosis of the tumor. Finally, reviewing different methods, it has been observed that the combination of CRF with FCNN and CRF with DeepMedic or Ensemble are more effective towards fulfilling the requirements of segmentation of brain tumor.

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