



Review

Survey of Brain Tumor Segmentation Techniques on Magnetic Resonance Imaging

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Abstract

Brain tumor extraction is a challenging task because brain image and its structure are complicated that can be analyzed only by expert physicians or radiologists. Brain tumor detection and segmentation is one of the most challenging and time-consuming tasks in medical image processing. The image segmentation is a very difficult job in the image processing and a challenging task for clinical diagnostic tools. MRI (Magnetic Resonance Imaging) is a visualization medical technique, which provides plentiful information about the human soft tissue, which helps in the diagnosis of brain tumor. Accurate segmentation of the MRI images is extremely important and essential for the exact diagnosis by computer-aided clinical tools. There are different types of segmentation algorithms for MRI brain images. This paper is to check existing approaches of brain tumor segmentation techniques in MRI image for computer-aided diagnosis.

Keywords: Magnetic resonance imaging; Medical imaging; Brain tumor; Segmentation; Image processing; Computer-aided diagnosis

Introduction

The National Brain Tumor Foundation (NBTF) for research in the United States estimated the death of 13000 patients while 29000 underwent primary brain tumor diagnosis every year [1]. Depending on the origin and growth, brain tumor is classified into two types: The primary brain tumor develops at the original site of the tumor, and the secondary brain tumor is the cancer that spreads to the other parts of the body. Nowadays, biomedical imaging has been very important for many applications for radiologists to diagnose the patient treatment-related problems. At present, imaging technology is a must for patient

diagnosis. The various medical images like magnetic resonance imaging (MRI), ultrasound, computed tomography (CT), X-ray, etc. play an important role in the process of disease, diagnosing and treating. The recent revolution in medical imaging results from techniques such as CT and MRI, can provide detailed information about disease, and can identify many pathologic conditions to give an accurate diagnosis. For the diagnosis and treatment of patients suffering from brain tumor, specialists take the assistance of MRI scans of the brain. In any case, the analysis of MRI scan is done manually by the specialist, which is tedious, and the precision of the outcome depends on the experience of the specialist. The conclusions

may differ from one doctor to another. Thus, there is a need to overcome these issues and to automate or robotize the investigative procedure of brain tumor in MRI images. For this purpose, biomedical image processing techniques are applied to MRI scans. Thus, the segmentation and further characterization of brain tumor from MRI scans remain a broad range of research in the field of medical science. Computer aided diagnosis system has been developed for automatic detection of brain tumor through MRI. Improving the ability to identify early-stage tumors is an important goal for physicians, because early detection of class of disease is a key factor in producing successful treatments.

Segmentation is a prime task of MRI processing. It is a process of dividing an image into multiple parts: Different tumor tissues (solid tumor, edema and necrosis) and normal brain tissues; Gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). Moreover, the tumor cell characteristics, such as complex shape, heterogeneous intensity distribution, variability of the position of the tumor, and artifacts in the tumor also have a significant effect on diagnosis. Tumor heterogeneity describes the observation that different tumor cells show distinct morphological and phenotypic profiles, including cellular morphology, gene expression, metabolism, motility, proliferation, and metastatic potential. The heterogeneity of cancer cells introduces significant challenges in designing effective treatment strategies. Modalities, like T1-weighted, T2-weighted, or proton density (PD) images are utilized for various segmentation methods. Due to the good contrast of the T1-weighted images, they have been widely tested for different segmentation methods [2].

In recent years, many research publications describe the different segmentation approaches for medical image analysis which are reported by Al-Tamimi et al. [3]. Fig. 1 shows the number of research papers published between 2000 and 2018.

In the current survey, we present briefly different stages in brain tumor detection, and we explicitly analyze the developed automated MS lesion segmentation approaches through a comprehensive up-to-date state-of-the-art review. To this end, the approaches are categorized, in terms of their main features and properties. Furthermore, a qualitative and quantitative comparison of the state-of-the-art approaches is provided, while their strengths

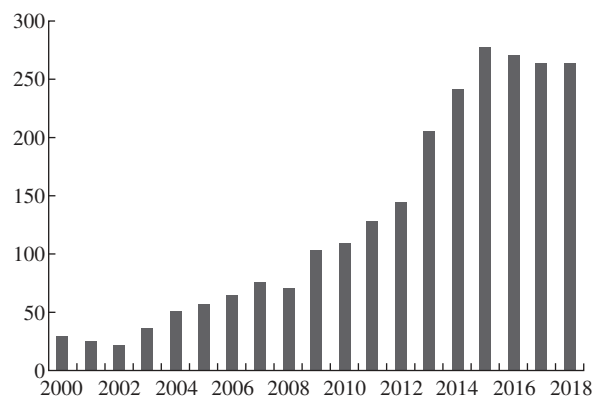


Fig. 1 Number of papers on brain tumor segmentation approaches published in 2000-2018 (edusol 2018 [4]).

and weaknesses are illustrated. The ultimate goal of this survey is to provide aid in identifying the most promising research directions in the field.

There are very extensive reviews on the methodologies published. Table 1 summarizes the number of methodologies reviewed by previous state-of-the-art as well as the current surveys. The current survey is focused mostly on automated MS lesion segmentation techniques published since 2010. Thus, a lot of categorizations of the related techniques are provided. The bibliography is very rich and a relatively large number of new methods have been published since 2013.

Table 1 Survey since 2012

Survey papers	Year	Number of methods reviewed in each survey papers
[5]	2012	44
[6]	2012	34
[7]	2013	55
[8]	2013	39
[3]	2014	31
[9]	2014	49
[10]	2015	32
[11]	2018	45
[12]	2018	31
[2]	2018	36
[13]	2018	61
Current survey	2019	72

Methodology

Detection of brain tumor from MRI images involves various phases such as preprocessing, feature extraction, segmentation and classification. Fig. 2 shows different stages in brain tumor detection.

One of the most important tasks for the tumor detection is preprocessing. Usually medical images appear inhomogeneous and of poor contrast, and require preprocessing for image enhancement. This

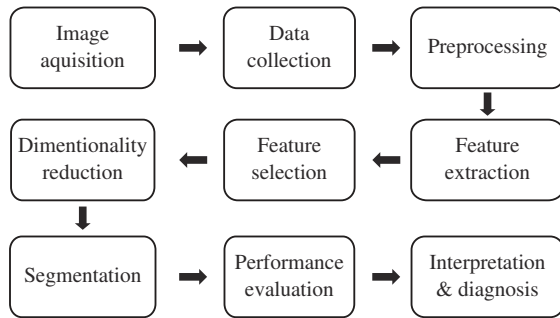


Fig. 2 Stages in brain tumor detection.

stage is used for reducing image noise, highlighting edges, or displaying digital images. The removal of unwanted parts from the brain MR image, finding edge position for removing labels and smoothing the image will be processed by using innovatively new pre-processing methods. A wide variety of pre-processing techniques like linear, non-linear, fixed, adaptive, pixel-based or multi-scale, are applicable in different circumstances [14].

Segmentation methods have the ability to detect or identify the abnormal portion from the image, which is useful for analyzing the size, volume, location, texture and shape of the extracted image. Segmentation guides the result of the whole analysis, because the proceeding steps depend on the segmented regions. The main principle of segmentation algorithms is the intensity or texture variations of images using region growing, deformable templates, thresholding, and pattern recognition techniques like fuzzy clustering and neural networks. Also, techniques like region-based and edge segmentation, adaptive and global thresholding, gradient operators, watershed segmentation, hybrid segmentation and volumetric segmentation, supervised and unsupervised segmentation exist. Several researchers are currently working on this medical image segmentation area [15].

Feature extraction can be defined as the process of transforming or converting an image into its group of features. The different methods employed for feature extraction include texture features, co-occurrence matrix, Gabor features, wavelet transform based features, decision boundary feature extraction, minimum noise fraction transform, nonparametric weighted feature extraction and spectral mixture analysis. For feature reduction principal component analysis, linear discriminant analysis and independent component analysis are used. Integration of the feature extraction with the feature reduction algorithms leads to accurate systems that uses less number of features

that can be extracted with less computational cost [8].

Feature selection algorithms popularly used are genetic algorithm, sequential backward selection (SBS), sequential forward selection (SFS), and particle swarm optimization (PSO), while principal component analysis (PCA), kernel PCA and ICA help in dimensionality reduction. Many methods used for feature selection are appropriate for biomedical image classification [16]. Three different techniques are often used, namely multiple kernel learning, a GA based approach having an SVM as decision function, and recursive feature elimination using many classifiers.

The biomedical image classification is a very important stage for automated CAD system. In some approaches, segmentation problem is transformed into a classification problem and a brain tumor is segmented by training and classifying. Generally, a machine learning classification method for brain tumor segmentation requires large amounts of brain MRI scans with known ground truth from different cases to train on. Mainly, artificial intelligence and prior knowledge are combined to solve the segmentation problem. Currently, high segmentation performances are obtained by deep learning methods [13]. The brain MRI classification is achieved using supervised techniques like ANN, SVM, k-NN and unsupervised classification techniques such as self-organizing map (SOM) and FCM.

Several algorithms and techniques have been developed for segment brain tumor regions from MR images. The most commonly used techniques were the C-means and fuzzy sets combined with other techniques to achieve better performance with the MR images uncertainties and regions. In fact, hybrid techniques and soft computing techniques as fuzzy logic, neural network and genetic algorithms have found wide applications in image segmentation. Also, PCNN and its modification forms are widely applied to image segmentation.

Current Trends in MRI-CAD Scheme Methods

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

Although it is hard to explicitly categorize the state-of-the-art MRI based MS lesion segmentation techniques because of large overlaps between them, the classification of methods is based on the following characteristics that all methods have: Input data handling, main strategy, and existence of supervision. Four categorizations are presented below.

The first categorization is detailed by Danelakis and co-workers [11]. The categorization is based more on supervised and unsupervised methods, 2D and 3D volume based, than on the strategy used. Table 2 illustrates the proposed categorization of the state-of-the-art MS lesion segmentation techniques.

Table 2 Categorization proposed in [11]

Supervised		Unsupervised	
3D volume	2D image	3D volume	2D image
Feature-based	Feature-based	Lesion-based	Lesion-based
Data-driven	Data-driven	Tissue-based	Tissue-based
Atlas-based	Atlas-based	Data-driven	Data-driven
Statistical	Statistical	Atlas-based	Atlas-based

The second categorization is presented by Mohan et al. [13]. The methodologies are subdivided into categories as fully automatic (fuzzy logic, adaptive neuro-fuzzy inference system, support vector machines, artificial neural networks, self-organizing maps, particle swarm optimization, random forest, miscellaneous methods, etc.) and semi-automatic (FCM, SVM, ANN) for 2D & 3D user interaction methods. This survey reveals that brain MRI segmentation method scan are classified into 6 major categories: Threshold based segmentation, region based segmentation, edge detection, clustering (hard and soft clustering, algorithms used FCM and K-means), statistical models (EM algorithm, MRF model) and ANN [17].

The third categorization is described by El-Dahshan et al. [9]. This study illustrates the classification of human brain in MRI is possible via supervised techniques such as artificial neural networks and support vector machine, and unsupervised classification techniques such as SOM and fuzzy C-means. Other supervised classification techniques, such as k-NN can be used to classify the normal/pathological T2-weighted MRI images. Also, hybrid intelligent systems using soft computing techniques are used for classifier

design. Soft computing consists of several intelligent computing paradigms, including fuzzy logic, neural networks, and bio-inspired optimization algorithms (genetic algorithm and genetic programming), which can be used to produce powerful hybrid intelligent classification systems. Table 3 summarizes the segmentation techniques [9].

The studies on feature extraction and classification of brain MRI were suggested by El-Dahshan et al. [9] for a comparative study, where it can be seen that:

- The commonest methods for feature extraction are discrete wavelet transform and texture analysis.
- The commonest methods for classification are hybrid systems that give the best accuracy combined with a pre-feature extraction and different machine learning techniques.
- Hybrid intelligent systems (especially soft computing systems) have an impact on the efficiency and accuracy of classification systems. It gives very high accuracy (in the range 97-100%).

In the fourth categorization, the segmentation techniques have been divided by Gordillo et al. [18] into four major classes:

- Threshold-based techniques (global thresholding; local thresholding);
- Region-based techniques (region growing; watershed);
- Pixel classification techniques (fuzzy C-Means; Markov random fields; artificial neural networks);
- Model-based techniques (parametric deformable models; geometric deformable models or level sets).

The first categorization can be adapted, based on input data handling, main strategy and existence of supervision, while the others use only main strategy.

The advantages and disadvantages of the most used classifiers for human brain MR images are summarized in Table 4 [9, 18]. Hybrid techniques that combine two or more techniques and soft computing techniques like NN, fuzzy logic and GA have found wide applications in image segmentation. Kumar and co-workers [17] presented a review on the various hybrid segmentation methods, revealing that K-means had better performance and less computational complexity. Hence by applying K-means in conjunction with other methods, it is possible to increase the segmentation performance.

Table 3 Overview of the most commonly used segmentation techniques in CAD [9, 10]

Groups of the methods	General principles	Methods with example papers
Contour and shape based techniques	Boundary and edge based image segmentation.	Deformable model [20] ; Active contour [21, 22] Level set [23, 24] ; Atlas-based [25]
Region based techniques	Its classified as a pixel-based method (initially select the seed points)	Thresholding [26]; Edge based [27] Watershed [28]; Seed region [29]
Statistical based techniques	Label pixel determine based on intensity distribution of the image.	EM (Expectation-maximization) [30, 31] MRF (Markov random field) [32] GMM (Gaussian mixture model) [33]
Multiresolution based techniques	Multiple scales based segmentation.	DWT (Discrete wavelet transform)[34, 35]
Machine learning based	The algorithms that can learn and make predictive data.	Supervised classifiers based ANN (artificial neural network) [36, 37] SVM (support vector machine) [38] DT (decision tree) [39] KNN (k-nearest neighbors) [40] LVQ (learning vector quantization) [41] Deep learning (CNN, U-Net) [37, 42-44]
		Unsupervised clustering based FCM (fuzzy C-mean) [45, 46] SOM (self organizing map) [47] K-mean [48] PCNN (pulse-coupled neural network) [44] FPCNN (feedback PCNN) [49]
Hybrid based techniques	Two or more approaches used to segment the image.	EM+PCNN [50] FFT(fast fourier transform) + EM - GMM [51] FCM + LVQ [52] DWT + FCM [53] AC (active contour) + SVM [54] DWT + SOM [55] GA + SVM [56, 57] Level set + ANN [58] GA + ANN [59] GR (generalized rough) + FCM [60] DWT + GA + SVM [61] SOM + LVQ [55] PCM (probabilistic CM) + FCM [62] FCM + Level set [63] DWT + PNN [64, 65] Level set + RG (region growing) [66] fully convolutional neural network (FCNNs) + Conditional random fields (CRFs) [67]

Validation and comparison

Validation and comparison of the state of the art is crucial for any newly developed method. We would like to briefly cover the possibilities and challenges for evaluating and validating methods in the brain tumor image analysis.

It would be optimal to compare any method against the real case. However, this is a big challenge in this field, if not impossible. In the lack of a well-accepted ground truth, the current gold standard for the evaluation is to compare with manual segmentations by an expert. However, this is an extremely time-consuming and tedious task; additionally, it is not objective. Another possibility for a first sanity check is to assess results on a synthetic dataset including ground truth. Generally, synthetic data lack important

characteristics of real images. In the lack of a brain tumor database with ground-truth segmentations, that is available to a broad community of clinicians and researchers, so far most authors validated their algorithms on a limited number of cases from their own data. This makes it difficult to compare the performance of different methods against each other in an unbiased way.

Therefore, and due to the different metrics used, the accuracy and speed of the individual methods, which have been collected from the respective publications, cannot be directly compared with each other. Table 5 summarizes a variety of databases and modalities used in the validation [13]. According to Mahesh et al. [2], analysis based on datasets and modalities utilized for experimentation of tumor recognition

Table 4 The advantages and disadvantages of the most used classifiers for human brain MR images are summarized

Groups of the methods	Techniques	Advantages	Disadvantages
Threshold-based	Global and local thresholding	Simple and computationally fast.	Limited applicability to enhancing tumor areas.
	Region-growing	Simple and capable of correctly segmenting regions that have similar properties and generating connected region.	Partial volume effect. Noise or variation of intensity may result in holes or over-segmentation.
Region-based	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.	Over-segmentation.
	Fuzzy C means	Unsupervised. Always converges the boundaries of tumor. It determines a membership degree of data to each class.	Long computational time, sensitivity to noise . The requirement for initialization of several initial parameters.
	Artificial neural networks	Ability to model non-trivial distributions and non-linear dependences. Self-adaptive methods.	Gathering training samples is not straightforward and learning phase is slow.
Pixel-based	Markov random fields	Are able to represent complex dependencies among data instances.	Difficulty when selecting the parameters that control the strength of spatial interactions. Usually require algorithms computationally intensive.
	k-nn	It is a simple and powerful.	The choice of k affects the performance of the k-NN algorithm. severely degraded by the presence of noisy.
	SVM	It minimizes the number of misclassifications. It offers a possibility to train generalizable, nonlinear classifiers in high dimensional spaces using a small training set.	Depends on the kernel that has been used.
	SOM	The advantages of SOM are simple and easy to understand and good for visualization	The trained network may converge to some local optimum.
	EM	The main advantages of this algorithm are its simplicity and speed which allows it to run on large datasets.	Sensitive to noise and intensity in-homogeneities.
Model-based	Parametric Deformable Models	Capable of accommodating to the variability of biological structures over time and across different individuals.	The model may converge to wrong boundaries in case of inhomogeneities.
	Level Sets	Topological changes are naturally possible.	Computationally expensive.
Hybrid techniques		Hybrid methods aim at combining the advantages of different paradigms within a single system. Hybrid methods which combined the relative strengths from the different classifiers and applied them in a sequence in such a way that the overall accuracy was maximized.	High computational costs.

system is deliberated. Fig. 3 presents analysis based on the modality of MRI image used for validation of

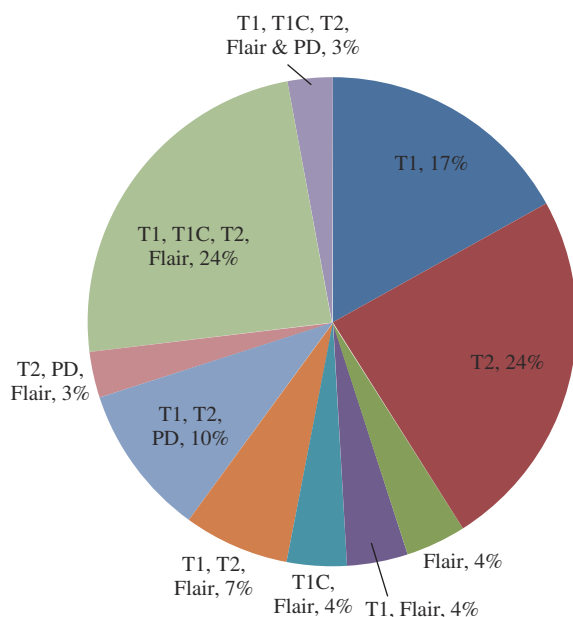


Fig. 3 Analysis based on the modality used.

segmentation and classification techniques adopted for brain tumor recognition. Fig. 4 depicts pie chart for analysis based on datasets utilized.

The evaluation of performance can be done by comparison between automated segmentations and

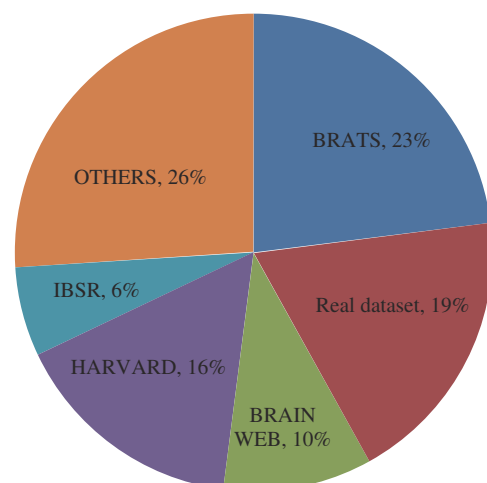


Fig. 4 Analysis based on the dataset source used.

Table 5 The database used in CAD

Data base source	Data set used	Modalities	Paper	Year
Harvard*	30 normal, 20 abnormal	axial T2w	[68]	2010
	320 slices	T2w, T2c	[69]	2014
	6 normal brains, 46 abnormal brains	axial T2w	[70]	2006
	70, 60 abnormal, 10 normal	axial T2w	[71]	2010
	75 transaxial image slices (39 normal brains, 36 pathological brain)	axial T2w	[56]	2015
	22 normal and 44 abnormal	axial T2w	[72]	2017
BRATS** (MICCAI)	30 patient (20 HG, 10 LG)	T1, T2, T1c, FLAIR	[9]	2014
	5 different slices of 22 high grade and 15 low-grade tumors and 20 synthetic data	T1w, T2w, T1c, FLAIR	[73]	2016
	10	T1w, T2w, T1c	[74]	2012
	255	T1, T2, PDw, FLAIR, T1c	[57]	2011
	660,000 data points from 11 cases	T1w, T2w, T1c, Flair	[35]	2006
	250 brain tumor MRI images	NA	[65]	2015
	BRATS 2013- 65 MR scans + BRATS 2015-327 MR scans	T1, T1c, T2, FLAIR	[37]	2015
	30 glioma patients, 10 LG, 20 HG	FLAIR, T1w, T1c, T2w	[32]	2012
	30 patient (20 HG, 10 LG), 30 simulated subjects	T1c, T2, FLAIR	[75]	2015
	30 patient (20 HG, 10 LG)	T1, T1c, T2 and Flair	[43]	2017
	220 (HG) and 54 (LG)	T1, T2 and FLAIR	[42]	2017
IBSR***	172	T1c	[76]	2014
	65 images of 40 Brain web data, 25 IBSR V2.0	T1w	[77]	2010
	IBSR 1.0- 20 images, IBSR 2.0- 18 images	T1w volumetric images	[21]	2012
	20 normal people	T1-w	[78]	2015
San Raffaele Hospital, Milan	15 patients (9 LG, 6 HG) and 6 healthy patients	T2w FSE (Fast Spin Echo), T1w FFE(fast field echo)	[59]	2012
PSG IMSR & Hospitals, Coimbatore, Tamilnadu, India	35 patients; 12 meningiomas and 23 gliomas	T1w, T1c, 1H-MRSI	[79]	2014
General Hellenic Airforce Hospital, MRI Unit, Katehaki, Athens, Greece	67 MR images	T1w	[80]	2014
Hua-Shan Hospital in Shanghai of China.	DS1-280 glioma (169 LG, 111 HG), DS2-154 cases (85 LG, 69 HG)	T1, T2	[81]	2016
Dr.Shajis MRI & Medical Research 709 Centre Pvt.Ltd, Puthiyara, Calicut	200 images- 164 trainig set (82 LG, 82HG), 36 testing set (18 LG, 18HG)	T2w	[82]	2011
Brain web tumor repository Harvard medical school Pakistan Institute of Medical Sciences	25 patients with gliomas	T1w, T2w, PDw	[83]	2013

*<http://www.med.harvard.edu/aanlib/>

**<https://www.med.upenn.edu/sbia/brats2017/data.html>; <http://www.brain tumor segmentation.org/>

***<https://www.nitrc.org/projects/ibsr/>

ground truth. And it can be accomplished by either comparing each voxel in each lesion (voxel-to-voxel), or using the whole detected lesion (lesion-to-lesion). The voxels and lesions can be classified as a true positive (TP), false positive (FP), true negative (TN) or false negative (FN). The objective is to obtain the maximum of TPs and TNs, and at the same time reduce FPs and FNs. In practice, we must find the best trade-off between these values. In fact, there is permanent debate about the best method to evaluate

performance of results. Table 6 summarizes the most common measures used to evaluate the MS lesion segmentation algorithms [11, 19]. Table 7 summarizes some evaluation results in the MS lesion segmentation algorithms.

Discussion

Critical review

In this review, we gave an overview of the state of

Table 6 Summary of the most common measures used to evaluate the MS lesion segmentation algorithms

Categories	Metrics	Symbols	Calculation	Description
Overlap based metrics	Sensitivity, Overlap fraction, Recall, True positive rate.	SEN, TPR	$\frac{TP}{FN + TP}$	TP: True positive. FN: False negative. TN: True negative. FP: False positive.
	Specificity, True negative rate.	SPE, TNR	$\frac{TN}{FP + TN}$	
	Accuracy	ACC	$\frac{TP + TN}{FP + FN + TP + TN}$	
	Dice similarity coefficient, F1 score	DSC, Dice	$\frac{2TP}{FP + FN + 2TP}$	
	Positive predictive value, Precision, Reliability.	PPV	$\frac{TP}{FP + TP}$	
	Fallout, False positive rate, False alarm ratio.	FALL, FPR	$\frac{FP}{FP + TN} = 1 - SEN$	
Jaccard index, tanimoto	JI, JAC	$\frac{TP}{FP + FN + TP}$		
Volume based metrics	Volume difference	VD	$\frac{FN - FP}{FP + FN + 2TP}$	x_i : Volume of ground truth. y_i : Volume of automatic segmentation. \bar{x}, \bar{y} : Means of respective volumes. N: Number of time points.
	Pearson's r coefficient	PRC	$\frac{\sum_{i=1}^N (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^N (x_i - \bar{x})^2} \sqrt{\sum_{i=1}^N (y_i - \bar{y})^2}}$	
Pair counting based metrics	Rand index	RI	$\frac{a + b}{a + b + c + d}$	For each tuple (x_i, y_i) of the volume. Sa: Automatique segmentation. Sg: Ground truth. a: The number (x_i, y_i) that are in the same class by Sa and in the same class in Sg. b: The number (x_i, y_i) that are in the different class by Sa and in the different class by Sg. c: The number (x_i, y_i) that are in the same class by Sa and in the different class by Sg. d: The number (x_i, y_i) that are in the different class by Sa and in the same class by Sg.
	Adjusted rand index	ARI	$\frac{2(ad - bc)}{c^2 + b^2 + 2ad + (a + d)(b + c)}$	
Information theoretic based metrics	Mutual information	MI	$H(Sa) + H(Sg) - H(Sg, Sa)$	$H(Sa)$: Marginal entropy of automatique segmentation. $H(Sg)$: Marginal entropy of ground truth. $H(Sg, SA)$: Joint entropy.
	Variation of information	VOI	$H(Sa) + H(Sg) - 2 MI(Sg, Sa)$	
Probabilistic metrics	Intra-Class correlation	ICC	$\frac{\sigma_s^2}{\sigma_s^2 + \sigma_e^2}$	σ_s^2 : Variance of differences between the segmentations. σ_e^2 : Variance of differences between the points in the segmentations.
Spatial distance based metrics	Hausdorf distance	HD(A,B)	$\max(h(A, B), h(B, A))$	$h(A, B) = \max_{a \in A} \min_{b \in B} \ a - b\ $ $d(A, B) = \frac{1}{N} \sum_{a \in A} \min_{b \in B} \ a - b\ $ A,B: Two finite sets. $\ a - b\ $: The euclidean distance. N: Number of elements of the finite sets.
	Average distance	AD(A,B)	$\max(d(A, B), d(B, A))$	

the art in the MRI-based medical image analysis for brain tumor studies. The focus was on segmentation methods. The first attempts in this field were made almost two decades ago, but it can be observed that in recent years, the methods are becoming mature and an increase of their use in clinical practice is expected.

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.

Region-based techniques for brain tumor

Table 7 Evaluation of methods

Methods used	Paper	Year	Metrics (%) *							
			DSC, Dice	PPV	SEN, TPR	SPE, TNR	FALL, FPR**	ACC	Jaccard	HD
GA + SVM	[56]	2010			92	100		95		
Rule-based + Level set + SVM	[49]	2010	77							
GA + FCM	[87]	2010					75			
PSO + FCM							92			
SVM + Region growing	[66]	2011			95	100		97		
Fuzzy clustering and deformable model	[20]	2011							82	
GA - SVM	[57]	2011						92		
PCA + SVM	[88]	2012			89	84		95		
Content-based active contour	[21]	2012						87		5
MRF + Ant colony optimization (ACO)	[32]	2012	76							
ANN-controlled level-set	[58]	2012	49		75					
GA + Fuzzy ANN	[59]	2012			97	96		95		
PCA + ANN	[89]	2013						85		
Graph - cut	[90]	2013	84		87	83			74	
KNN + MRF	[40]	2014	75							
Back propagation neural network	[69]	2014						83		
particle swarm optimization + neural network	[80]	2014			98	95		99		
Random forest	[39]	2015	70		61	13				
Region growing and level set evolution	[23]	2015	81		82				70	
Competitive EM and graph cut	[31]	2015	70							
Convolutional neural networks	[37]	2015			73	73				
Intensity features of multimodality MRI	[75]	2015	77		85	98				
Self-organizing map + Fuzzy K means	[73]	2016	92		87	97			32	
Enhanced watershed segmentation	[81]	2016			97	86		96		
binary decision trees and random forest technique	[39]	2016	67							
Round Randomized Learning Vector Quantization	[41]	2016						86		
Improved Fuzzy c-Means	[45]	2016	89							82
Improved Watershed			93							89
Cell density patterns/tumor growth modeling	[25]	2017	75							
U-Net Based Fully Convolutional Networks	[42]	2017	86							
Watershed Technique and Self organizing Maps	[47]	2017	97		95	100		96		
K-means + Linear SVM	[72]	2017			95	89		93		
K-means + DWT + CA + Linear SVM						95	100		97	
Deep Neural Networks	[43]	2017	84		84	88				
Densely Connected 3D CNN	[44]	2018	79							
Fully Convolutional Neural Networks+ Conditional Random Fields	[67]	2018	82		83					
Random Forests + Multiscale Patch Driven Active Contour	[91]	2018	89		85	90				
Information theoretic rough sets	[92]	2018	70						59	

*The values given are obtained by calculating the averages of the results declared by the authors.

**Despite the fact that this measure exists, it is very rarely used.

segmentation are mainly used as refinement step for defining a connected boundary of the tumor. 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.

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 permits the use of vague concepts in the definition of clusters, and gives highly accurate results in cases of non-homogeneous tumors.

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. Segmenting tumors by making use of geometric deformable models or level sets, permits the development of fully automatic and highly accurate segmentation approaches. Unfortunately, these methods are still computationally expensive.

The majority of segmentation approaches operate on multi-sequence MRI data, employing classification methods using different features and taking spatial information in a local neighborhood into account. The trend is not to segment the tumor only, but also to delineate tumor sub-compartments and different healthy regions on images from standard clinical acquisition protocols. This provides the physician with a more comprehensive information on which diagnosis, tumor monitoring and therapy planning can be based. Apart from the evaluation of accuracy and robustness, an important criterion is the computation time.

Eventually, it would be useful to test any new method on a standard database of brain tumor images to allow for a fair comparison against the state of the art. The MICCAI BraTS dataset would be one candidate for such a database. It is also necessary to select some relevant measures that will be used as common evaluation measures to compare various methods.

Critical approach: Deep learning

More recently, deep learning techniques have been adopted in brain tumor segmentation studies following their success in general image analysis fields.

Convolutional neural networks (CNNs), an outstanding branch of deep learning applications to visual purposes, have earned major attention in the last years. With the time, large annotated training datasets and more powerful graphics processing units (GPUs) have been created, enabling researchers to continue working in the area. Nowadays, deep CNN architectures are widely used in brain MRI for preprocessing data, detecting and segmenting lesions and segmenting tumors. CNNs take patches extracted from the images as inputs and use trainable convolutional filters and local subsampling to extract a hierarchy of increasingly complex features. CNNs are the most popular machine learning algorithm in image processing. CNNs and recurrent neural networks (RNNs) are examples of supervised machine learning algorithms, which require significant amounts of training data. Unsupervised learning algorithms have also been studied for use in medical image analysis. These include autoencoders, restricted boltzmann machines (RBMs), deep belief networks (DBNs), and generative adversarial networks (GANs) [84-86].

Clinical applicability

Although a lot of research has been done in this field over the last few years, application in the clinics is still limited. Many tools developed so far are pure research tools, which are not easy to handle for clinicians. This is probably mostly due to a lack of communication between researchers and clinicians. So far, in most commercial workstations, only very simple methods have been implemented, for example, thresholding.

Recently, more researchers have tried to consider standard clinical acquisition protocols when developing their methods, instead of focusing on feasibility studies that employ pure research data as image material. This will hopefully aid in spreading the application more quickly. Another important aspect is the computation time: the real-time segmentation will be hard to achieve, but computation times which are beyond a few minutes are unacceptable in clinical routine.

In order to be able to make the best possible use of automatic methods for the medical image analysis, it is essential to have image data, which have been acquired according to a well-defined protocol across different clinical sites. We expect that such standardization would aid significantly in improving the applicability and spread the use of automatic.

Available toolboxes

Only very few implementations of the presented

methods are publicly available. This impedes a comparison of new methods to existing approaches and also hinders a large-scale evaluation with clinical data from different sites. To the best of our knowledge, at the moment, there are only three methods publicly available for download, which are dedicated to the analysis of brain tumor images:

- TumorSim: Software for the simulation of synthetic brain tumor images (www.nitrc.org/projects/tumorsim) [93];
- BraTumIA: Software dedicated to multimodal image analysis of brain tumor studies (http://www.istb.unibe.ch/research/medical_image_analysis/software) [94];
- GLISTR: Software package designed for simultaneously segmenting brain scans of glioma patients and registering these scans to a normal, healthy atlas (<http://www.med.upenn.edu/sbia/glistr.html>) [79, 80].

Future challenges

The first challenge is the acquisition of MRI data. In recent years, enriched MRI protocols have been developed. It is expected that their improvement will continue, in terms of standardization and optimization as well as the unification of the acquisition protocols.

The comparison of different automated MS lesions segmentation techniques, based on MRI data, faces objective difficulties. For starters, not all advanced approaches are publicly available to the world of research. In addition, many methodologies are tested on proprietary MRI databases, making their comparison unreliable. A common large-scale database for research, as well as the corresponding truth on the ground, would be a very positive addition to this burgeoning field.

Future segmentation techniques for MS lesions based on brain MRI should be hybrid. Combining the most promising individual strategies of the state of the art and exploiting their combined advantages should prove very useful in further improving the segmentation performance of MS lesions. In addition, it is also expected that, in the future, efforts will focus on unsupervised techniques to avoid the costly training process. Finally, in a more generic setting, robust segmentation techniques based on deep learning can be used. Future work must be based on the concept of real time in order to engineer the techniques into the computer-assisted processing process.

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. 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 or region growing techniques can be employed, other tumors can be identified by their shapes, so that a model-based technique can be applied for the segmentation.

Although the reported accuracy on brain tumor segmentation of the proposed automated methods is quite promising, these approaches 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 in 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.

After reviewing so many papers, we would expect to be able to distill the perfect method for brain tumor segmentation. Deep learning is now clearly the top performers in most medical image analysis competitions. Our point of view is also to try to group

the best performing methods into clinical applications, unify MRI image acquisition protocols, and use a single set of learning data like MICCAI.

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