Review Article

Emergence of Convolutional Neural Network in Future Medicine: Why and How. A Review on Brain Tumor Segmentation

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Abstract

Manual analysis of brain tumors magnetic resonance images is usually accompanied by some problem. Several techniques have been proposed for the brain tumor segmentation. This study will be focused on searching popular databases for related studies, theoretical and practical aspects of Convolutional Neural Network surveyed in brain tumor segmentation. Based on our findings, details about related studies including the datasets used, evaluation parameters, preferred architectures and complementary steps analyzed. Deep learning as a revolutionary idea in image processing, achieved brilliant results in brain tumor segmentation too. This can be continuing until the next revolutionary idea emerging.

Key words: convolution neural network; brain tumor; segmentation; deep learning.

Introduction

The brain tumor is generated by abnormal growth of pathologic cells in the brain [1-3]. Due to the brain's role in the body, the people who are affected by tumors may have a serious dysfunction in sensation, movement, equilibrium, cognition [2, 4-6]. Brain tumors categorized into intra-axial and extra-axial in radiologic findings and benign and malignant types in pathologic findings. Based on International Cancer Research Center Report (2012), over 250000 people identified with primary brain tumor in the world which is about two percent of all the number of cancers [7]. Moreover, one quarter of deaths by cancers are caused by metastases to the brain [8,9]. The detection of the brain tumors is done by imaging. Different Imaging techniques used to show structural or functional abnormality, like CT scan, MRI, MRS, FMRI, SPECT and PET, and MRI is the most useful and common modality to show the tumors [10]. Manual analysis of brain tumors based on MR images is usually accompanied by numerous problems: different size, shape, texture and consistency of tumors can lead to different results in MR images analysis. Also, the large number of images in each study increases time of data acquisition and analysis [11]. All of the mentioned factors may cause wrong results and delay in decision making [1-4].

One of the most and recent techniques which are used by neurosurgeons or radiologists is extracting tumor's information to show of the tumors [17]. The segmentation of tumors includes extraction, measurement, visualization and presentation of the tumors [5-9]. Correct segmentation of brain tumors can be used for accurate brain modeling and pathologic atlases generation [23,24].

Several techniques have been proposed for the brain tumor segmentation [10,13,16,25-32]. Unfortunately the common practical techniques have some limitations. In recent years, the use of deep learning techniques in image processing application has grown significantly. This study will take a detailed review at the practical aspects of using the deep learning methods in brain tumor segmentation.

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Method

In this review, we searched IEEE, PubMed, arXiv and Google scholar databases for studies using the combinations of following search keywords: "Brain Tumor Segmentation", "brain tumor detection", "brain MRI segmentation" "deep learning" and "convolutional neural network". Publications in the English language were considered, but we did not impose study design or selection limitations. Review was conducted from relevant articles published between 2010 and 2016.

Brain tumor segmentation

Image segmentation in the field of computer science, is partitioning of one image into multiple segments to distinguish objects from background [10] This process is represented by sub-images, non-overlapped regions with two properties: Homogeneity within a region, Heterogeneity between the regions [11]. This method is used more meaningful and easier to analyze [12]. Based on various parameters should be considered in any image segmentation task, it has become a complex and multi objective problem [40,42]. Variation in tumor tissue characteristics like shape, size, gray level intensities and localization of tumor may affect on the results of processing [16, 33-36]. In addition, the complicated shape of brain tissues and the structures surrounding the tumor can make it much more sophisticated [37] The other great complexity is when we want to convert the visual information to meaningful regions as a level of semantic understanding of the image contents [43].

With correct brain tumor segmentation, the neurosurgeons are able to understand the location of tumor regions, active tumor tissues, necrotic tissue and edema therefore, it seems that it is a very relevant method for surgical planning. This technique is done by identifying abnormal areas of the brain when compared to normal tissues [13,14,38]. **Figure 1** shows some examples of brain tumor MR images with their ground truth segmentation (manually segmented by experts).

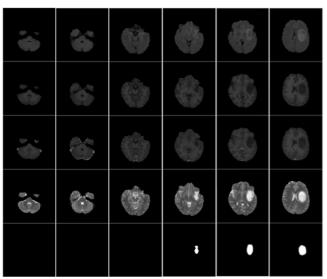


Figure 1. Brain Tumor MRI Scans: top to down: Flair, T1, T1 with contrast, T2 and ground truth (BRATS)

As we mentioned, the problems in manual analysis of brain tumor segmentation using of image processing techniques are growing [14-16]. Contemplation in the evolution of brain tumor segmentation techniques represent a series of efforts towards achieving the automatic and accurate methods. Meanwhile three generations of image segmentation algorithms have been introduced in the past decades to this goals [2,15,16, 26,27,45-54]. The first group of segmentation techniques consist of heuristic methods. Examples of such algorithms are the use of threshold level [17], area growth [18] and separation/merge edge detections [16,19]. The general feature of these techniques is the simplicity of their implementation, but the major challenge is the trouble in achieving the desired result when the test conditions have little change compared to their training setting.

The second group of techniques are based on probabilistic models and optimization methods such as: artificial neural networks [20,21], Bayesian models [22], fuzzy clustering [23] and support vector machines [24]. Also, techniques like Gaussian mixture models, linear and non-linear dynamic systems, conditional random fields, maximum entropy (MaxEnt) models, logistic regression, kernel regression and extreme learning machines are in this category [61-64]. These group of techniques are effective in solving simple or well-constrained problems, but their low modeling capacity cause problems when dealing with complex real-world issues involving natural signals and images processing [65].

The third group of methods seek to achieve the desired result based on the use of higher levels of knowledge. Such knowledge can be inferred from tacit information, rules, and models being created by human or patterns extracted from the bulky data sets. The sample of this generation include Atlasbased segmentation [25] and Deep Learning based methods [26] which is fascinatingly modeled based on the human vision system. Deep learning is a new window to the field of image processing and may revolutionize the medical image processing applications.

Deep Learning

The human brain's information processing mechanism uses deep architectures to extract complex patterns of information from rich sensor sources. For example, a sound processing and production system in humans is equipped with hierarchical layered structures to convert waveform information to verbal mode and vice versa [68-71]. Also the human vision system is naturally based on a hierarchical structure [72-74]. Modeling of the human brain as the best and most complete samples of natural processors, can guarantee that the most advanced mode of natural signal processing can be achieved by developing by hierarchical learning as in deep learning algorithms [65]. With this idea, deep learning is considered as a hierarchical model which designed to imitate the learning process of the brain's information processing system.

Deep learning is a hierarchical model, designed with the aim of mimicking the brain's learning process. The deep learning hypothesis is based on the fact that in order to represent a high level of data, a hierarchy of intermediate representations should be generated. Deep learning refers to the learning of multiple levels of representations in order to understand data such as images, audio and text. It includes a kind of machine learning techniques that use a large number of processing layers of linear and nonlinear transforms, with or without supervisor in order to feature extraction, pattern analysis and classification [75-79].

In Deep learning, the first level of representation can be Gabor-like filters, the second level involves identifying lines and angles and the higher levels are gradually moving towards objects and concepts recognition tasks [75-79]. The early idea of deep learning architecture dates back to the 1980s, but due to technical difficulties, their use in practical applications is restricted to the last decade. Some factors make them more popular such as:

- the existence of labeled training collections (some with a total of millions of educational samples);
- · more powerful processors along with new generation of GPUs with parallel processing;
- · optimized algorithms for training the models [65,76-79].

Deep learning algorithms are capable of learning low-level features and turning them into complex data representation in a hierarchical mode [80]. Unlike other machine learning techniques that feature engineering plays a fundamental role in their success, deep learning methods attempt to learn the hierarchy of features directly from raw data [81,82]. Various methods have been developed to implement the deep learning idea include convolution neural networks (CNN), deep belief networks and deep Boltzmann machine. Among these methods, the best technique for exploiting the benefits of multidimensional spatial data such as image, sound and time series is CNN [83].

CNNs are designed to work on multidimensional data, especially images and videos, and has shown its success in many image processing applications [27,80]. CNN idea in the field of deep learning, is based on some structural principles derived from a type of the artificial neural networks named multi-layered perceptron (MLP) [28,29]. The CNN functional idea, derived from time delayed neural networks, uses the idea of sharing intra-network weights in order to reduce the network computing time [30]. In this regard, CNN can be considered as a structure similar to multi-layered neural networks and functionally based on latency networks.

CNNs can be used on raw multidimensional data without preprocessing operations. The Convolutional Neural Network is able to learn the deep general features of multidimensional data such as the image through two basic operations: convolution and sampling.

Convolutional Neural Network (CNN) in brain tumor segmentation

The CNN structural idea is derived from the multilayered perceptron (MLP) because of the use of layered structure [84-86]. Also, the CNN functional idea is based on time delayed neural networks, which uses sharing the intra-network weights in order to reduce the network computations [87]. CNNs can be used on raw multi-dimensional data without preprocessing phase, with a variety of operations, such as convolution, sampling and rectified linear unit, it is able to extract a variety of features from raw data [83].

Like other image processing applications, CNN has been successful in brain tumor segmentation too. **Table 1** summarized details of brain tumor segmentation using CNN-based techniques. Also method of deep learning, 2D/3D analysis, implementation tools, datasets, evaluation and important points related to each studies have been covered. In order to investigate the findings, the data in **Table 1** represented in distilled form in **Figure 1** (a-g).

Discussion

The details of implementing the CNN algorithms in the brain tumor segmentation presents some tips such as: implementation tools, architectures, input dimensionality, datasets and algorithm evaluation criterions.

The analysis of the tools mentioned in the studies for CNN implementation in brain tumor segmentation shows that the Caffe and the Pylearn's have the major contributions in the implementation. Caffe is implemented in C++ programming language, the Python and MATLAB wrappers are available too [34]. On the other hand, Pylearn is one of the most successful python libraries in the field of deep learning [35]. In addition, there are some platforms like Tensorflow that can be used with the both programming language and are gradually going popular in deep learning applications.

The dominant CNN architecture in the brain tumor segmentation is Fully Convolutional Network [FCN].

Fully convolutional network [FCN] is a successful model for image segmentation, which preserves the spatial structure of predictions [36]. In the FCN architecture, a combination of convolution, sampling and deconvolution are used. The point is the distinction between these two models. The first network uses some of the second networks with more limited layers. Indeed, FCN consists of convolution, de-convolution [37], or max-pooling in each layer.

With crossing the input data through the early layers of this architecture, convolution, deconvolution and sampling are used, which compresses information in large number of tiny-sized feature maps in the middle layers. Subsequently, using deconvolution and sampling, the intermediate feature maps combined together and rebuild the output, which is usually the same size as the input and in the segmented form.

Table 1. Techniques used in brain tumor MRI images automatic segmentation

	Author	Year	Method	2D/3D	Implementation	Dataset	Evaluation	Extra notes
1	Davy et al	2014	FCN		Pylearn2	BRATS	Dice 87% PPV 84% Sen 85%	N4ITK bias field correction
2	Zikic et al	2014	CNN with multi-channel convolutions	2D	Caffe	BRATS	Accuracy 83%	Inhomogeneity correction in each channel
3	Mikael Agn	2015	Convolutional Restricted Boltzman Machine + atlas-based probabilistic model	2D	MATLAB	BRATS	Dice 83%	Using atlas
4	Dvorak & Menze	2015	CNN	2D	Not-detected	BRATS	Dice 83%	Local structure prediction combined with standard prediction methods
5	Rao, Shari Sarabi, &Jaiswa	2015	CNN	2D	Caffe	BRATS	Accuracy 67%	ITK preprocessing
6	Lyksborg et al	2015	CNN	2D	Theano	BRATS	Dice 83%	Normalized the intensities + patch wised segmentation
7	Rewari	2015	CNN		caffe	BRATS	Accuracy 93%	N4ITK bias field correction
8	Y. Pan et al	2015	ANN vs CNN	2D		BRATS	Accuracy 66%	
9	L. Zhao & Jia	2015	Triplanar 2D CNN architecture for 3D voxel classification	3D	Not-Detected	BRATS	Dice 78%	
10	Havaei et al	2016	CNN	2D	Pylearn2	BRATS	Accuracy 81%	two-pathway architecture
11	Pereira et al	2016	CNN	2D	Theano	BRATS	Dice 78%	N4ITK bias field correction + Small 3*3 kernel
12	Ghafoorian et al	2016	CNN	3D	Not-Detected	MRI Scans Radboud University Nijmegen Diffusion tensor and Magnetic resonance imaging Cohort [RUN DMC]	Dice 79.1%	Bias field correction + Intensity normalization
13	Chen et al	2016	CNN	3D	Matlab and C++ based on Caffe library	BRATS	Dice 89%	Stacked residual modules
14	Yi et al	2016	CNN	3D	Not-Detected	BRATS	Dice 89%	a convolutional layer with pre-defined Difference- of-Gaussian [DoG] filters
15	Peter D Chang	2016	FCN	2D	Matlab	BRaTS	Dice 87%	fully convolutional residual neural network [FCR-NN]
16	Kamnitsas	2016	FCN	3D	Theano	BRATS	Dice 89%	A dual pathway, 11-layers deep, a 3D Fully Convolutional Conditional Random Field
17	Casamitjana, Puch, Aduriz, Sayrol, & Vilaplan	2016	FCN	3D	Not-Detected	BRATS	Dice 91.74%	standard normalization + two fully convolutional 3D CNN architectures inspired
18	X. Zhao et al	2016	FCN	2D	Caffe	BRATS	Dice 80%	N4ITK bias correction + fully convolutional network [FCN] and Conditional Random Fields [CRFs] in a unified framework
19	Tseng Kuan Lun	2016	FCN	2D	Not-Detected	BRATS	Dice 76%	Using pre-trained model as vgg-net
20	Balaji Pandian	2016	CNN	3D	Theano	BRATS	Dice 73%	N4ITK bias correction
21	Ramandeep Randhawa	2016	CNN	2D	Not-Detected	BRATS	Dice 87%	Use two-stage network training
22	Casamitjana	2016	CNN	3D	Not-Detected	BRATS	Dice 89%	Standard normalization

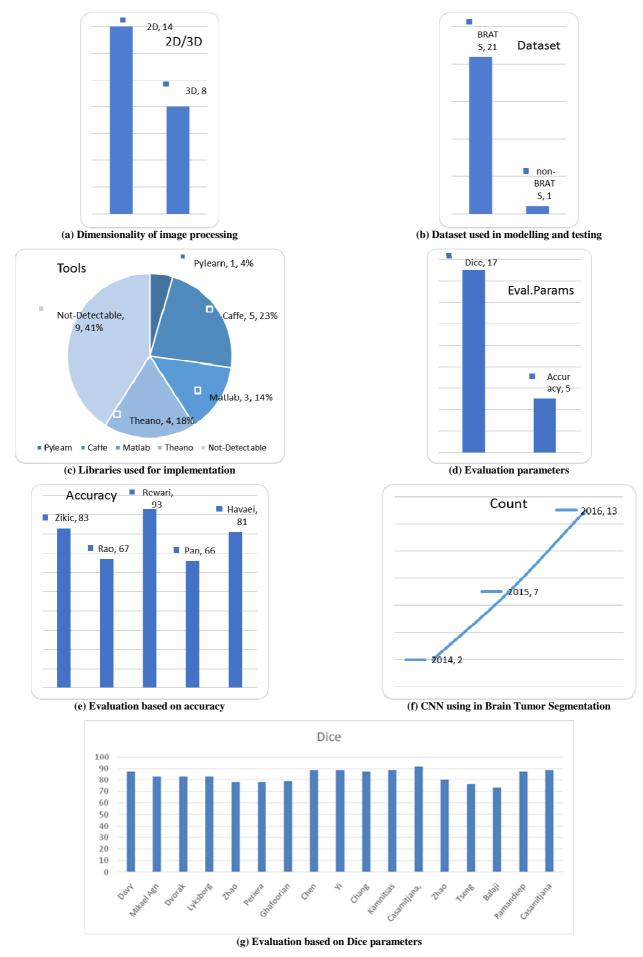


Figure 2. Results of review analysis

This architecture is very suitable for application such as segmentation and therefore has been used frequently in brain tumor segmentation. The studies with two-dimensional images analysis in the literature are more than 3D images ones. Considering that magnetic resonance imaging of the brain tumor is done in 3D form, 3D analysis of image is preferred and emphasized. However, it should be noted that the use of deep learning techniques requires a large number of input samples, in order to fulfill this requirement, each 3D image was converted into dozens of 2D images. Hence, more studies have been done to date on two-dimensional images.

BRATS as the major dataset used in the studies, is a collection of multi-modality brain tumor MR images (T1, T2, T1C and Flair) with their ground truth (manual segmented by experts) [106].

A variety of parameters can be suggested for evaluating segmentation models, and some of them, such as sensitivity, specificity, etc., are mentioned in some studies. But according to the study, the two parameters Dice and Accuracy are the most important parameters for the evaluation of segmentation models and have been used in most of studies in the area of brain tumor segmentation [38-43].

The parameters are calculated as follows. Dice in segmentation evaluation:

$$Dice = \frac{2*|S \cap G|}{|S| + |G|}$$
 Eq. 1

In the above relation, S is equal to the region segmented by the algorithm and G is equal to the reference segmentation region.

The Accuracy parameter in the evaluation of segmentation of brain tumor images defined as below:

$$Accuracy = \frac{Tp + Tn}{All \ pixels}$$
 Eq. 2

In the above relation, Tp is the number of tumor pixels identified by the algorithm correctly as a tumorous pixel, and Tn is the number of non-tumor pixels that are correctly identified by the algorithm as a non-tumorous pixel.

What distinguishes these two parameters, is their power in evaluating the performance of segmentation technique, where Dice focuses specifically on the tumor area, and the Accuracy refers to the overall evaluation of the image. According to the study, some studies have selected the latter for assessing their technique, while the first has been used in most of the studies.

However, using these two parameters (especially Dice) to assess a segmentation technique provides the ability to compare the technique with other studies. As mentioned above, the two parameters are the most commonly used criteria for evaluating fragmentation of brain tumor images.

On the other hand, Dice, can be considered as an appropriate parameter to assess the overlapped areas in the images and can be used as a most useful parameters for evaluation of segmentation [107].

Despite the high interest towards the use of deep learning methods in image processing application, some challenges exist for using them, like:

- · Need for bulky datasets:
 - This challenge lies in the essence of deep learning, because the philosophy of these techniques depends on the repetition of the feature extraction process. So the analyzes provided by these techniques are generalizable if in the next step, the fine tuning applied on pre-trained networks. In order to solve this challenge, publicly available data sets are being expanded such as BRATS in the case of brain tumor segmentation.
- · High computing power required:
 - Like the previous challenge, this need is also based on the deep learning paradigm. However, with the advancement of technology in the development of faster hardware and the use of parallel processing architectures, this challenge has been largely overcome.

Conclusion

Using Dice parameter in future studies can provide a very good measurement for accurate and in detailed comparison of brain tumor segmentation techniques. However, some factors such as geography, race and other demographic parameters can affect practical use of models but BRATS dataset can be used in future studies.. In such situations using BRATS in initial training phase is preferred, then local dataset can be used for fine tuning for better results.

As mentioned earlier, the main feature of deep learning paradigm is independency from engineering processes which leads to extract images from raw data in automatic manner. However, it should be noted that the use of enhancing tools can increase the efficiency of deep learning based methods. As it was shown in the study, the use of preprocessing phase such as N4ITK for bias correction as well as the conditional random field in final processing stage in the CNN learning can enhance CNN performance in brain tumor segmentation. On the other hand, some strategies in the training of a CNN can increase the performance of the CNN, such as the using of pre-trained models and the use of multi-stage training.

Future perspective

Deep learning is a revolutionary idea that has created a new paradigm and has gradually shown its success in various image processing applications. The complexity of medical images is high and making decisions about them requires the use of high-level knowledge and complex feature engineering processes. In such a situation, the use of deep learning techniques will be increased due to their ability to automatic feature extraction. This will create a cycle of usage and success, and we hope in the future to see the application of the deep learning techniques, including the convolutional neural network, in a variety of image processing applications.

Executive summary

- · Over 250'000 people identified with primary brain tumor in the world which is about two percent of all the cancers, moreover, one quarter of deaths by cancers are caused by metastases to the brain.
- · BRATS as the major dataset used in the brain tumor segmentation studies, is a collection of multi-modality brain tumor MR images (T1, T2, T1C and Flair) with their ground truth (manual segmented by experts).
- The detection of brain tumors is done usually by imaging. MRI is the most useful and common modality to show the tumors in the brain MRI scans.
- The most important step of MR image processing is the segmentation of tumors which is used in extraction, measurement, visualization and presentation of the tumors.
- · Brain tumor segmentation is a difficult task due to variation in tumor tissue characteristics like shape, size, gray level intensities and location of tumor in the brain.
- · Surveying the techniques revealed that three generations of algorithms used in brain tumor segmentation: heuristic methods, probabilistic models and optimization methods and finally methods that use the higher levels of knowledge

- which can be inferred from tacit information, rules, and models being created by human or patterns extraction.
- · Deep learning is a hierarchical model, designed with the aim of mimicking the human brain's learning process and capable of learning low-level features and turning them into complex data representation in a hierarchical mode.
- · Convolutional neural network as one of the successful models of deep learning paradigm has been successful in brain tumor segmentation.
- The dominant CNN architecture in the brain tumor segmentation is Fully Convolutional Network [FCN]. In this architecture, a combination of convolution, sampling and deconvolution are used for segmentation.
- The analysis of the dimensions of the input images shows that the number of studies on two-dimensional images of brain scans are larger than 3D images studies.
- · Despite the high interest towards the use of deep learning methods in image processing application, some challenges faced for using them like: need for bulky datasets and high computing power.

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