

A Transfer Learning Approach For Deep Learning Based Brain Tumor Segmentation

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Abstract: Magnetic resonance imaging (MRI) is amongst the prevalent and widely used medical imaging techniques in visualizing and observing the internal organs of the human body. MRI provides a detailed analysis and guidance towards patient's health condition including the detection of anomalies such as brain tumor. Since manual analysis and detection of tumor is highly time-consuming process and providing medical assistance in critical cases is a biggest challenge for the medical practitioners. An accurate, efficient and advanced computational method is heavily in need for most deadly diseases like brain tumor. This proposed work addresses deep learning coupled with small kernels and handles the obstacles in brain tumor segmentation techniques. This research work is incorporating all the dimensions available as MRI images of brain, constituted and analyzed using convolutional neural network (CNN). It needs high level of computational capacity. The work presented in this paper addresses these concerns using deep learning coupled with small kernels. The model presented in this paper is effectively trained over 150 images in the dataset. The proposed work has attained comparative better results with respect to the dice score coefficient such as (0.78, 0.74, 0.74) for whole tumor, core tumor and active tumor respectively.

Keywords: Convolutional Neural Networks, Segmentation Algorithm, Transfer Learning, Deep Learning, Brain Tumor segmentation.

1. Introduction

Intracranial neoplasm or in common a brain tumor occurs due to abnormal cells that exist within the brain. As the amount of time required for manual segmentation of MRI images is high and as compared to the diagnostic time required for the patients detected with such type of tumor is very limited, automated techniques are quite essential as less time is consumed for assessment of the disease. Amongst the automated techniques, deep learning plays a vital role in segmenting these tumors efficiently. Convolutional Neural Network (CNN) is one of the most effectively used deep learning technique for brain tumor segmentation [1]. It is a feed-forward neural network, which is mostly utilized for image recognition and processing.

Gliomas are very common and most aggressive types of tumors in brain [2]. The sub-regions of a brain tumor are dead part termed necrosis, and swelling due to tumor called edema, enhancing, non-enhancing. Brain tumors are represented digitally using 5 levels i.e necrosis, edema, non-enhancing tumor, enhancing tumor and normal tissues [3][4]. The necrosis, edema, non-enhancing and enhancing part of the tumor as a whole known as the complete tumor [5][6]. Whereas the non-enhancing and the enhancing part of the tumor as a whole is known as the core tumor.

MRI provides a good contrast for soft tissues as compared to other imaging techniques available. In addition, there are no known health hazards from temporary exposure to MR environment. Therefore, MRI is a good technique for accessing brain tumor in human beings. Different imaging techniques with modalities are being utilized for mapping the tumor induced changes including T1, T1c, T2 and Flair MRI differentiated using contrast and brightness of images[7][8]. These MRI modalities are very sensitive due to the changes affected by inflammatory and these changes are associated directly to the pathology [9]. One of the most common types of modality is T1, used for differentiating healthy tissues and for structural analysis. Among various primary tumors, Gliomas is the most prominent tumor that possesses the highest mortality rate [10] presented an enhanced brain tumor segmentation technique to detect diverse tumor cells for both high grade and low grade gliomas in MRI images based on the gradient and the context-sensitive attributes [2]. The glioblastoma in the T1c are enhanced from borders. Among all others, the above modality is mostly utilized and supported for differentiating the part that is active among the glioblastoma from the other parts of necrotic. The edema portion in the T2 appears much brighter [11]. Utilizing Flair, we can identify the whole tumor structure. In the dataset, for each patient, images from different sequences namely: R1, T2-contrasted, T2 and FLAIR (Fluid Attenuated Inversion Recovery)

acquired. Each of these sequences exploits the distinct characteristics of the tissues as explained above which results in contrast among the images. Different MRI sequences exploit distinct characteristics of the tissues, which result in contrast between the images, which help for better segmentation. As shown in the figure below, the whole tumor is visible clearly in the sequence Flair figure 1-D. The core of the tumor is visible in the sequence T2 and the enhancing tumor structure is visible in the figure 1-C. Due to this, we need MR images from different sequences so that we can identify/classify the intra-tumor structure precisely [12][13].

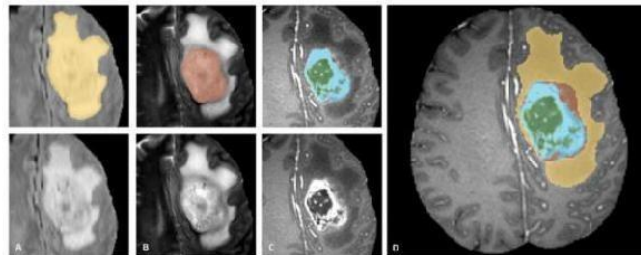


Figure 1: Different MRI sequences

In deep learning, feature extraction from the complex features is directly done from the data with increasing hierarchy. Therefore, instead of going in regular way our objective should be in developing architectures rather than working on handcrafted features. In addition, to achieve this may need a specialized knowledge. This is one of the major reasons of using deep learning for solving problems, as feature extraction is a complicated procedure when done manually.

Identification of tumor is a very challenging and intuitive task. The location, shape and the structure of tumor varies significantly from patient to patient which makes the segmentation a very challenging task [14]. In the figure below, we have shown some images of the same brain slice from different patients, which clearly reflect the variation of tumor. We can clearly see that the location of tumor is different in all the eight images or patients shown below. To make it worse, the shape and the intra-tumor structure is also different from all the eight images [fig 3]. In fact, there can be more than one region of tumor as seen from the images below [15][16]. This indeed reflects the complexity of automatic segmentation.

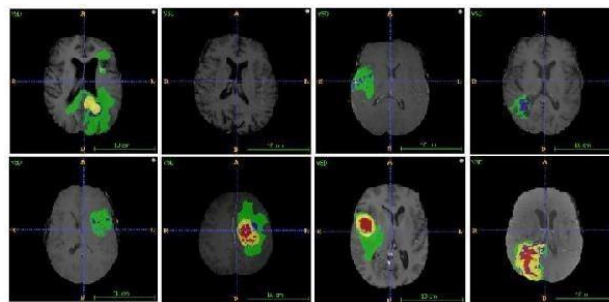


Figure 2: Tumor in different patients for the same brain slice

Dice score is the evaluation of the segmentation technique or algorithm, done by calculating the DSC i.e. Dice Similarity Coefficient [2], which measure the overlap between the automatic and the manual segmentation.

$$DSC = \frac{2TP}{(FP+2TP+FN)} \quad (i)$$

Here, TP represents True Positive, FP represents False Positive and FN represents False Negative [2][17].

This paper discusses some of the essential concepts of multilayer perception in convolutional neural network (CNN) [18][19]. One of the major challenges in evaluating the segmentation algorithms of brain tumor is with understanding Dice Score [22][23].

The remainder of this paper is organized as follows. In section II, literature survey is discussed briefly. Section III focusses on the proposed methodology In section IV, the evaluated best results on parameters such as similarity index, dice coefficient, peak signal to noise ratio are shared. This section also includes the comparative analysis of the proposed model. The paper has been concluded in section V.

2. Related Works

Based on the research papers surveyed in this work, this section provides a formal summary and classification of the deep learning models, systems and designs. All these algorithms briefly described in the following section.

2.1 Auto encoder's and stacked auto-encoders (deep AEs or SAE): In these networks, the auto encoder layers are inserted in the form of stack [24]. These layers are trained independently for fine-tuned prediction using supervised learning. These networks are simple networks and are directed by a weight matrix W as well as bias B extracted from input along with parallel bias from hidden layer processed to hidden state for the reconstruction. Hidden activation is calculated by a nonlinear function:

Equation 1: Hidden Activation Function

$$H_l = \sigma(W_{i,h}i + B_{i,h}) \quad (1)$$

A method was proposed for generating a noise free input to avoid the model from adapting an insignificant solution [25].

2.2 Deep Belief Networks: In these networks, neurons are densely connected that helps in rapid and accurate learning of a good set of parameters. Since the learning is difficult in these nets with many hidden layers, a fast and greedy algorithm is proposed for deep belief nets [26][27].

2.3 Restricted Boltzmann's Machine: These networks are type of markov random fields consisting of input layer, hidden layer that outputs hidden feature representation. There are bidirectional connections between the nodes, so latent feature representation extracted from an input vector and vice versa. An energy function is defined for a specific state of input and hidden units.

Equation 2: Energy Function

$$E(i, h) = h^T W i - c^T i + B^T i \quad (2)$$

where c and B are bias terms. The probability $p(i, h)$ of the state of the system is calculated as follows:

Equation 3: Probability of System state

$$p(i, h) = \frac{1}{P} \exp \{-E(i, h)\} \quad (3)$$

Figuring the partition function P is generally inflexible. However, restricted inference of calculating trained on or vice versa is flexible and results as follows:

Equation 4: Conditional Inference

$$P(h_j | i) = \frac{1}{1 + \exp\{-b_j - W_j i\}} \quad (4)$$

The major difference between DBNs [28] and SAEs are that in DBN's auto encoder layers are substituted by RBMs.

2.4 Convolutional Neural Networks: The convolution operation is performed with a set of N kernels with weights and added biases individually creating a new feature map on the input image at each layer. These features forced to an element by element nonlinear transform for every convolutional layer l :

Equation 5: Non-Linear Transform

$$F_N^l = \sigma(W_N^{l-1} * F^{l-1} + B_N^{l-1}) \quad (5)$$

A 6-layered 3D CNN proposed to perform striatum segmentation that included dropout function for reducing overfitting and learning more robust features [29]. In this T1 weighted MRI images are fed to the global CNN, which determines the approximate location of stratum. The volume of striatum is extracted from global CNN and fed to the local CNN, which predicts the accurate label of all boxes. The proposed algorithm obtained higher dice similarity coefficient and precision score.

A multi modal 2D CNN's is proposed for MRI segmentation in iso-intense stage where T1, T2 images are fed as input to the CNN and segmentation maps are received as output [30]. Highly nonlinear mappings are captured via intermediate layers of CNN that are convolution, pooling, local response normalization of features at the same spatial location for different feature maps, and other operations such as dropout function. This method gives better results for infant brain segmentation.

A multi scale late fusion CNN with convolution layer, max pooling layer and Rectified Linear Unit (ReLU), along with random walker as multi scale, CNN was not able to smoothly capture discriminative features from MRI due to the multifaceted background in brain images [29]. This method led to better and efficient segmentation quality.

A deep voxelwise residual network VoxResNet proposed for tissue segmentation combining features from different layers [3]. It incorporates the appearance features of an image at a low level, integral shape information and high-level context together for refining the volumetric segmentation performance.

A multi scale, CNN was proposed for lesion segmentation on non-uniform area to incorporate anatomical location information into the network. This method was used for segmentation of white matter intensities. In continuation to this work [32][33] FCN along with 3D CNN was proposed for candidate segmentation that reduced false positives for lacunae detection.

A 3D fully convolutional neural network is proposed for brain extraction on multimodal input [34]. This method was able to work for both enhanced contrast and non-enhanced contrast images. Hence providing the average dice score, high specificity and average sensitivity.

Hough-voting was proposed to plot from CNN structures for full patch segmentations that has attained robust, flexible and efficient results for multi-modal segmentation [35][36].

A CNN trained on multiple patch sizes was proposed in which dice coefficient based novel objective function optimized during training to deal with the strong disparity between the foreground and background voxels [37]. A CNN based Tumor segmentation proposed for input from multiple modalities that acquires multiscale information about each voxel by using multiple patch and kernel sizes [38]. A fully convolutional network trailed by Markov random fields is proposed along with Alpha-expansion to achieve imprecise inference imposing dimensional volumetric homogeneity to the CNN [39].

For pixel-wise classification, a multiscale CNN with late fusion architecture was proposed for tumor segmentation [40]. 2D CNN with self-learning feature selection method was proposed for tumor patch classification [41]. A 3D FCN trailed with 3D CNN is proposed for candidate segmentation for reduction in false positives. It also utilizes spatial information for extraction of high level features hence achieve much better detection accuracy [42] [43].

A Segnet named deep neural network introduced for automatic segmentation of Brain MRI. Segnet allocates each voxel to its equivalent anatomical region in an MR image of the brain. Non-linear registration of MRI is not required in this network [44].

A deep convolutional encoder neural network introduced for lesion segmentation from brain MRI [45]. This model integrates convolutional and de-convolutional layers to extract features and segmentation prediction in a single model. This model speeds up the training by acquiring features from entire images, which eradicates patch selection and redundant calculations at the intersection of neighboring patches.

A 11-layered deep, double-pathway, 3D Convolutional Neural Network, developed for the separation of brain lesions [46]. When multi modal 3D patch processes at multiple scales within the developed system, it fragments voxel-wise pathology. This network processes a 3D brain volume in 3 minutes. Conditional random fields was later added to the network for enhancing the results.

2D convolutional neural networks proposed for performing a volumetric segmentation of magnetic resonance images. The proposed network comprises of three networks such as full tumor segmentation, refined segmentation using grow cut method [47]. To conclude, sub-regions within the tumor segmented using an added group of networks trained for the task. Liyue Shen et. al. [48] proposed three CNN based architectures namely, baseline voxel-wise CNN, fully convolutional patch-wise CNN and full image fully convolutional CNN for glioma segmentation. The first two architectures performed well with a dice score of 0.84 and 0.86 respectively as compared to the third architecture.

According to the literature survey, deep CNN's can be evaluated base on following performance parameters such as dice similarity coefficient, sensitivity, similarity index and accuracy, precision [49].

3. Proposed Methodology

Figure 4 shows the overview of the proposed model. We will also present four different patch extraction methods proposed by us using the best method we will build a CNN for the patients, which will further be processed via transfer learning.

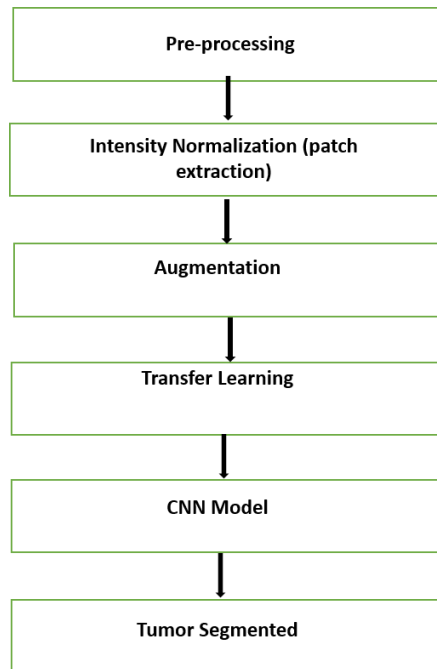


Figure 3: Overview of the Proposed Model Design

a.) Pre-processing is one of the challenging tasks in dealing with the MRI data, due to the facts that tumors produced either by inhomogeneity caused by various movements which are small during the scan time of a patient because of change in the magnetic fields [51]. Often a bias is present across the patients that make the segmentation difficult for an automatic segmenting model. Since bias field distortion alters the MR images, therefore the intensity of the same tissue may vary in a slice or image [51]. Therefore, we have applied N4Tk bias correction algorithm to correct this error. However, this is not enough for making the intensity of the same type of tissues similar across multiple patients [52][53]. Actually, the same tissue of the same patient can be in different intensity when taking the images/MRI at different times. So to make the intensity of the same tissue type more similar which is used and implemented by Nyul et al. [2][19].

b.) Intensity Normalization: Nyul et al. [2] [19] has proposed and implemented a two-step method for normalizing the images across multiple patients. The first step is the training step, executed only once for a given dataset and the second step is the transformation step, executed for each image in the dataset. Training, transformation, and patch extraction are three crucial stages to determine the intensity values corresponding to each landmark in the MRI locations, map the locations [54]. In transformation phase for any given image, the actual landmark locations obtained from the training phase are matched to several linear mappings from first to last and during patch extraction i.e. a sub-image of original image is obtained in image pixel ratio of 240x240 as shown below in figure 4.

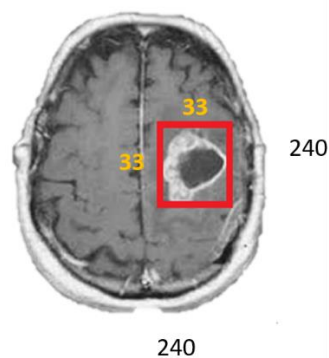


Figure 4: Patch extraction

We considered the size of each slice image is 240x240. If we train CNN over the complete slice, the number of parameters to train will be very large. Thus, we will need a very large amount of data. Nevertheless, since the dataset is not very large, so we train our model using patches. The class of any given voxel is highly dependent

on the class of its surrounding voxel. In the proposed model, patches are used for training purpose. At the testing stage, the patch size of 33x33 works fine with the dataset obtained.

c.) Augmentation: Data augmentation can increase the size of training set by 10 fold or even more. If the dataset is already very large then this technique may not be effective. We are doing rotation and flipping randomly in the training dataset at runtime to generate new dataset. Some samples (t) from the batch size of 128 selected randomly and amongst the three operations like rotation, horizontal and vertical flip, one of them applied randomly. Apart from this a random combination of the three operations to get 't' modified samples which are then merged with the remaining samples to get new batch of 128 samples which is used to train the model.

d.) Transfer learning is basically improving the learning curve with a new task through knowledge transferring from a task which is similar or related which is already trained and learned from process [55]. Take an example of knowledge obtained during the process of recognizing humans. This knowledge can be applied to learn and recognize different humans at various age levels [56][57]. This process is the learning process of machine, using external source of additional training information from one or more related tasks considering the basic training standardized data.

e.) CNN model: Convolution layer is the main building block of neural network. Consider the below image to look about working of the convolution layer.

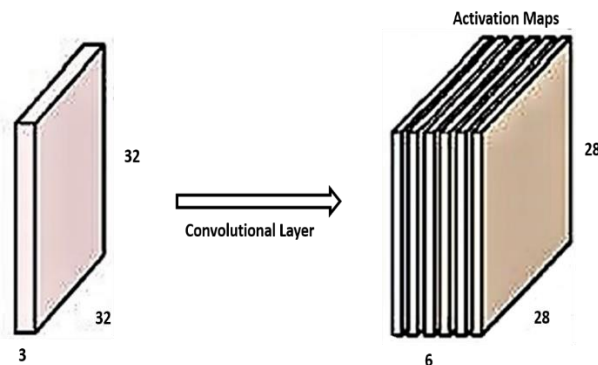


Figure 5: Convolution of image

Proposed Algorithm

Start:

Input: Image X

Step1: Bias Field Correction on X

Step 2: Intensity Normalization on X, patch extraction from X,

Obtain 240x 240 image

Step 3: Filter of Size 5x5x3 is selected and slid over the complete patch.

Step 4: Calculate Dot product between filter and image

-> new image generated.

Step 5: Max pooling on new generated image

Step 6: Convolve the filter and image-> generate an activation map of 28x28x1

Step 7: The convolved image is fed to the 11 layered CNN architecture.

Step 8: Output: Segmented Image -> 128 x 16x16

Step 9: Calculate dice similarity coefficient for the

output images.

End

A 5x5x3 filter layer every dot product taken, the result is scalar. Now to get a pixel of new image we do dot product. Usually a filter in our case 5x5x3 filter is slid over the image we considered and throughout the process, a dot product taken between image and filter to generate a new image. To extend the input volumes of filters in full depth are always used.

With convolving the overall image along filter, we get an output image called as the activation map. In the picture below considered an example of activation map of 28x28x1.

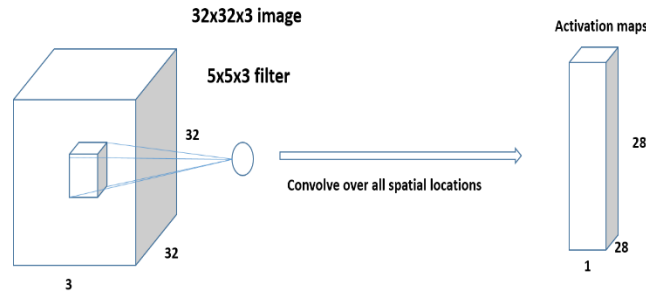


Figure 6: convolution with multiple filters

Above filters are randomly initialized or based upon our parameters.

Pooling layer is also an important layer used in CNN. To progressively reduce to spatial size, it is common to periodically use in between successive convolution layers to reduce the amount of parameters and computation to control over fitting.

Over fitting caused during training is a common problem in neural network [58]. If we consider an error occurred during training the image and the value is stored. The stored error value occurred during the training network is used to map with the new data obtained. Comparing both the cases, the error in both cases might vary and sometimes be large as well. This situation is called overfitting. The resulting network usually memorizes the training and model example outputs in over fitting, however in generalizing the results to learn new situations is a problem.

As compared with CNN, training a fully connected network is much larger when compared with the number of parameters [59]-[62]. Where CNN finds the relation and combination within the image between pixels and spaces, a fully connected neural network does not take in most of the images which are nearby and pixels are generally related.

The proposed model of CNN for segmentation is 11- layered architecture. The CNN model for the patients trained in the following way, where the last layer of the model is the new output layer. Then the best learned weights that we obtained and learned earlier for segmentation of tumor are loaded. Later all the training patches of the patients are passed through the model and a vector of size (128, 16, 16) is generated and stored for each patch. Once we have extracted vectors for all the training patches of the patients, we will then train the CNN for the other patients using those vectors.

Fig 7: Model using transfer learning

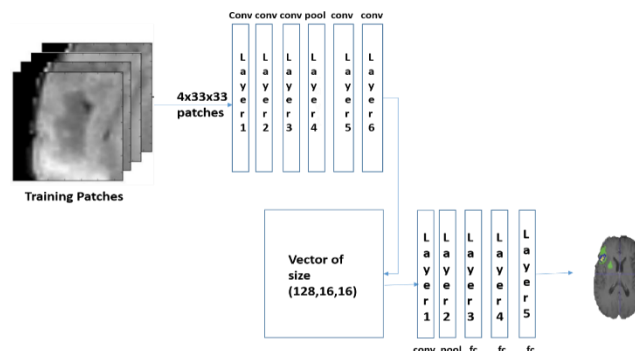


Figure 7: Model using transfer learning

Below is the CNN model comprising of the five layers such as convolutional layer, max-pooling layer and the three fully convolutional layer. A small kernel of 3x3 is used as a filter in convolutional and max-pooling layer.

Table 1: CNN model chart

Layers	Type	Input	Filter size	Stride	Filters	FC units
Layer 1	Convolutional	128x16x16	3x3	1x1	128	NR
Layer 2	Max-pooling	128x16x16	3x3	2x2	NR	NR
Layer 3	FC	6272	NR	NR	NR	256
Layer 4	FC	256	NR	NR	NR	256
Layer 5	FC	256	NR	NR </td <td>NR</td> <td>5</td>	NR	5

c.) Segmentation Layer

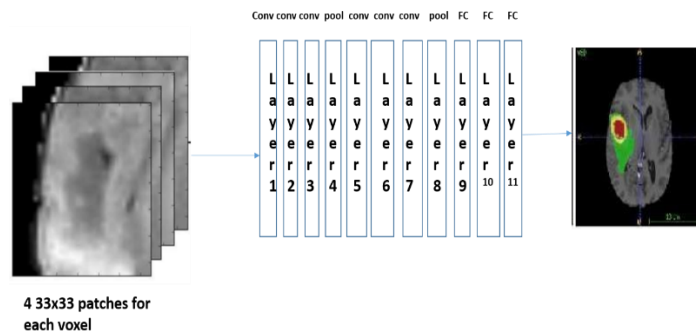


Figure 8: segmentation layer

Post processing is performed after segmentation. Hence, some of the clusters recognized are inaccurately reflected and categorized as tumors. To work with such cases, we have used volumetric constraints to remove such errors.

4. Results and Discussions

Below are some images showing the difference between automatic segmentation and the actual ground values. From the images shown below we can clearly see that the proposed model for patients could detect the location, shape, size quite precisely.

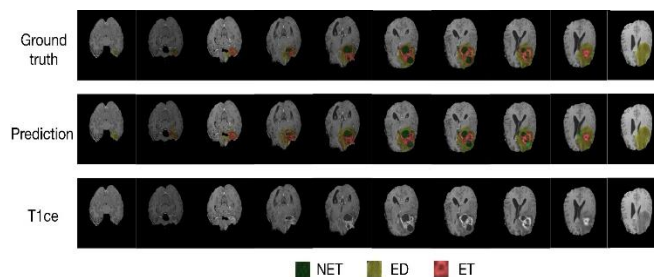


Figure 9: Ground Truth vs automated segmentation

Below table provides information about various performance properties or parameters like dice score, mean square error, peak signal to noise ratio, similarity index , and signal-to-noise ratio. From the dataset of 150 images, some of the best segmentation results are elaborated in the table below.

Table 2: Parameters for segmented tissues and its performance analysis

Images	Mean Square Error (MSE)	Peak Signal to Noise Ratio (PSNR)	Structured Similarity Index (SSIM)	Dice Score (DS)
Img1	1.857	55.45 dB	0.8849	0.820
Img2	0.610	67.91 dB	0.8990	0.860
Img3	4.900	57.12 dB	0.9658	0.815
Img4	5.090	59.61 dB	0.8086	0.910
Img5	1.310	59.64 dB	0.8920	0.780
Img6	3.620	56.25dB	0.9455	0.820
Img7	5.140	59.59 dB	0.8090	0.890

A comparison of the proposed model with the deep learning method for Pereira et. al. [49] is shown in the figure below. In this figure, dice coefficient values of low-grade gliomas and high-grade gliomas are calculated in three categories of tumor (whole tumor, core tumor and active tumor) along with various parametric sets both of high-grade and low-grade gliomas. The low-grade gliomas are usually not in active tumor state due to which there value is 0.00 in the figure 10.c.

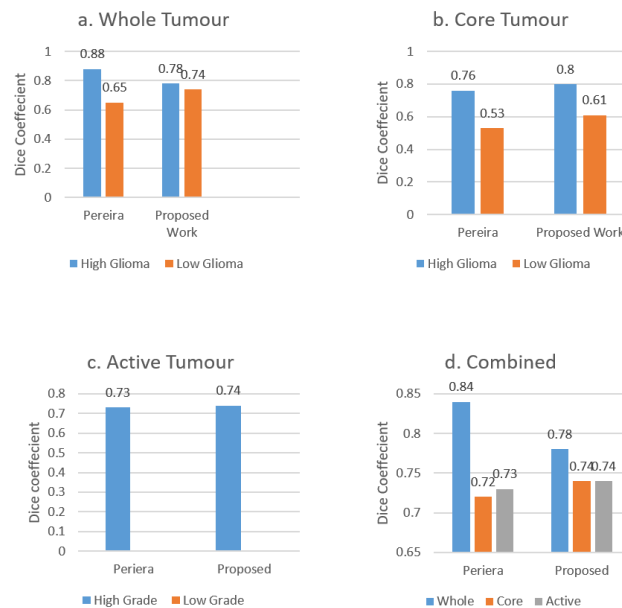


Figure 10: Comparative analysis of proposed model

5. Conclusion

In this research paper, have revised, implemented and observed the segmentation process of tumor from MR images and trained the CNN to perform automatic segmentation. The proposed model consists of 11 layered convolutional neural network that incorporates transfer learning. Due to the transfer learning, the model has achieved high dice score coefficient such as 0.78 in whole tumor, 0.74 in core tumor and 0.74 in active tumor. This paper mostly provides the proper insights, methods, necessity and problems involved in using the traditional methods and improve the efficiency using automated segmentation. We took our best of effort to improve the efficiency of the segmentation algorithms by considering the qualitative measures such as accuracy, sensitivity, precision using quantitative parameters such as similarity index, mean square error and peak signal to noise ratio evaluated for the complete dataset. This research focuses on implementing a new algorithm for improving the computational speed and efficiency of the current medical image segmentation in real time scenario and planning to process our idea further more and utilizing deep learning techniques.

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