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Brain Tumor Augmentation Using the U-Net Architecture

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***Abstract*— Studies have found out that tumors in brain are one of the fiercest diseases which can ultimately lead to death. Gliomas are the most commonly found primary tumors that are very hard to predict and can be found anywhere in the brain. It is prime objective to differentiate the different tumor tissues such as enhancing tissues, edema, from healthy ones. To do this task, two types of segmentation techniques come into existent i.e. manual and automatic. The automation methods of brain tumor segmentation have gained ground over manual segmentation algorithms and further its estimation is very closer to clinical results. In this paper we propose a comprehensive U-NET architecture with modification in their layers for 2D slices segmentation as a major contribution to BRATS 2015 challenge.. Then we enlisted different datasets that are available publicly i.e. BRATS and DICOM. Further, we present a robust framework inspired from U-NET model with addition and modification of layers and image pre-processing methodology such as contrast enhancement for visible input and output details. In this way our approach achieves highest dice score 0.92 on the publicly available BRATS 2015 dataset and with better time constraint i.e. training time decreases to 80-90 minute instead of previously 2 to 3 days.**

Keywords*— Brain Tumor, Segmentation, U-NET, Gliomas, BRATS 2015

I. INTRODUCTION

Brain tumor is an irregularity of brain tissues with different degrees of aggressiveness, leadings to severe damages to cognitive ability of human's mind and ultimately lead to death. Due to their rapid development and numerous inhomogeneous divisions of sub-regions, such as necrotic, edematous cells, active and non-enhancing core, and gliomas. Among all, gliomas are the most common and threatening brain tumors with the highest recorded mortality rate.[1, 2] Further, these primary tumors named as gliomas are generally developed near the white tissues, but have the ability to spread anywhere in the brain. This creates a real problems in the process of predicting and detecting. Presently, malignant brain tumors are becoming more common, which have a significant effect on people and society [3]. According to World Health Organization (WHO) gliomas tumors are of four grades.. The low grade gliomas (LGG) include first two grades, and the high grade gliomas (HGG) contain last two grades. Furthermore, HGG are commonly known as glioblastoma multiform (GBM), and have decreased human's life cycle to less than one year. Timely Surgery, chemotherapy and other therapies are all options for gliomas treatment. Grade II tumor also named as LGG can increase life expectancy if it detects and cures on time [4].

Magnetic resonance imaging (MRI) is most accepted mechanism for brain tumor identification and recognition. Various MRI modalities make it more useful over other provided frameworks such as computed tomography (CT), positron emission tomography (PET) and magnetic resonance spectroscopy (MRS). Further, MRI image segmentation is a pivotal in order to monitor the irregular shapes of tumors and it performs well in differentiating between healthy tissues and abnormal tissues. Moreover, gliomas complexity and subtle differences in MRI analysis create insurmountable challenges for radiologist expert. This is so, because they cannot easily diagnose by visual inspection of MRI modalities. Automation approach of brain tumor segmentation is mostly adopted mechanism for brain tumor segmentation. While, using these segmentation techniques for brain tumor, first, MRI 3D images converted into 2D slices then further it is divided into the classes for the ease of use [11]. Multi-modal images are created by combining MRI modalities, which provide more detail about irregularly formed tumors that are difficult to locate with a single modality. There are some modalities named as T1 (MRI), T1C (MRI with contrast improvement), T2 MRI, and T2-weighted MRI with fluid attenuated inversion recovery (T2) (T2-Flair) [9]. These comprehensive modalities of data provide brief description about tumor segmentation and also help out in segmentation efficiency significantly.

White matter (WM), grey matter (GM), and cerebrospinal fluid (CSF) are the three building blocks of human brain .In surrounding of white matter (WM) tumor regions with unbounded boundaries are created and make difficulties while segmenting these regions. The swelling around the brain are created due to extreme tumors effectiveness with their sub categories i.e. necrotic center, active tumor region, and edema. A precisely segmented tumor region is of paramount importance in medical identifying and cure planning.

Recently a growing number in automation in brain segmentation approaches have been accepted widely inspired by deep neural networks. Presently, U-NET is one of the most influential deep neural network algorithms along with its encoding and decoding layers [5]. We present our contribution to the Brats 2015 challenge, which is focused on the well-known U-Net architecture. In brats 2015, major challenges are brain tumors have irregular shape size and

localities; MRI Scans come with noise problem, and multiple modalities are needed to segment tumor sub regions. We employ a comprehensive UNET architecture for segmentation and a Mask R-CNN approach for classification of exact brain tumor region. Although, our major focus was put on the segmentation part of the challenge, and minor on classification of brain tumor. Main innovations and paper contributions can be summarized as follows:

1) A modified U-NET with addition of hidden laayers have been proposed and implemented successfully.
2) The proposed novel framework of modified U-NET is validated successfully and obtained a dice score value of 0.91 on test images.
3) One of the main problems is high testing and training time which can be best overcome using this algorithem. For example, One training session takes about 12 hour while testing is almost immediate with about 1-2 minutes duration in our proposed methedlogy, while other Machine learning architectures takes up to 100 minutes to segment a complete brain.
4) We have tested our model generalization on another DICOM dataset, which again gives state of art performance as compared to previous work done on this dataset.

II. BACKGROUNDS

Various types of segmentations techniques of brain tumor i.e. semi-automatic, fully-automatic and manual segmentations have been introduced up till now. Fully automated methods based on neural network-based classification and image-based (semantic) segmentation-based methods performed exceptionally well in this study. Researchers have recently been enticed to use CNN for biological image segmentation due to the success of deep learning methods. Furthermore, when it came to semantic segmentation, CNN and fully convolutional neural network (FCNN) were the most effective. Encoder-decoder architectures are used in the majority of successful neural networks. Most prominent among all the encoder-decoder techniques are U-net and V-net. In the brain tumor segmentation method, preprocessing and data augmentation have been shown to be useful [6]. Few preprocessing operations, such as pixel intensity range standardization, are considered important due to the BRATS data format [7] fine-tuned their findings by using conditional random fields on the network's predictions. Approaches focused on hierarchical networks, such as multi-resolution based loss calculation, have yielded appropriate results [8]. Interactive methods, in addition to automated approaches, yield positive results and are currently being studied [9].

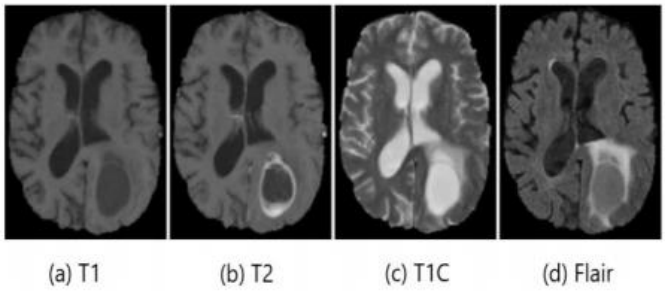

Fig. 1 MRI scans with four modalities [25]

On the BRATS dataset CNN used small (3×3) filters for deeper architecture to segment brain tumor in MRI and claimed segmentation accuracy of 0.88, 0.93, and 0.74 for whole tumor, core tumor, and active tumor, respectively [8]. On the other hand, used Cascaded Two-pathway CNNs for simultaneous local and global processing of brain tumor recognition and segmentation [10]. On the BRATS dataset, they achieved 0.88, 0.79, and 0.73 segmentation accuracy for whole tumor, core tumor, and active tumor, respectively. Finally, to segment the brain tumor in MRI, fused four CNNs, one for each modality, with their outputs concatenated as an input into an RF [11]. However, no outcomes have been published.

In spite of all these contributions, there are still some shortcoming in terms of low dice score, accuracy and computational complexities. Additionally, time consumption in training session is also one of the leading limitations. Conclusively, it can be said that to fill these loopholes there is dire need of some more accurate and less time consuming architectures.

IV. DATASETS

Various organizations have proposed various datasets to motivate researchers to take active participation in brain segmentation. Among these multiple datasets some are listed below i.e. ISBR (provided by Massachusetts General Hospital), DICOM (online accessible dataset with images and videos), and BRATS that are publicly available [12, 13]. The datasets mentioned below are used to conduct the majority of automated brain tumor segmentation methods since they allow for reproducibility and comparison of findings across studies.

A. BRATS DATASET

The BRATS dataset was introduced in 2012 with MRI scans consisting four different modalities. Aftermath, numerous segmentations and classifications approaches applied on BRATS challenges which quite producing splendid results. Dataset consisted of five major classes named as healthy brain's cells, non-enhancing brain tumor, edema, enhancing tissues of tumors and final is necrosis. On every passing year, training size of dataset has been growing continuously. There are two types of grades in dataset one is low grade other is high grade tumors. The BRATS dataset contains MRI scans with different modalities named as T1, T1 contrast-enhanced (T1C), T2 and T2 FLAIR. The dataset serves as a benchmark for analyzing the outcomes of different brain tumor segmentation techniques.

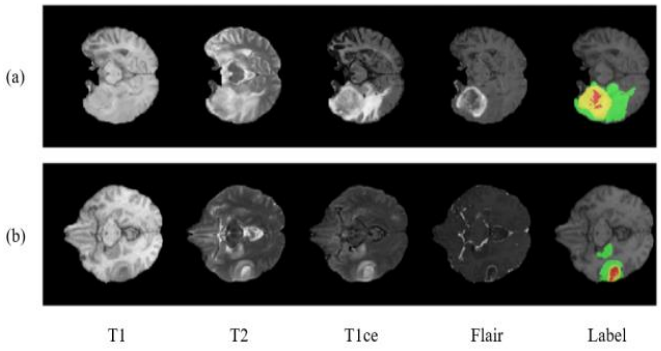

Fig. 2 a and b are two models. First four MRI scans are four MRI modalities and on the extreme right corner there is a ground truth.

V. MATERIALS AND METHODS

Manual, semi-automatic, and fully automatic are segmentations techniques that are widely depending on the human's interaction level[14]. Among these segmentation methods, manual segmentation uses prior information of the single patient with definite amount of human brain knowledge through past training and experience [15].In this section, we first discuss U-NET along with Relu activation filter segmentation of brain tumor on BRATS-2015 dataset. Then, proposed a Mask-RCNN for classification of brain tumor which resultantly gives better performance. Figure 3 shows the complete procedure of our designed methodology.

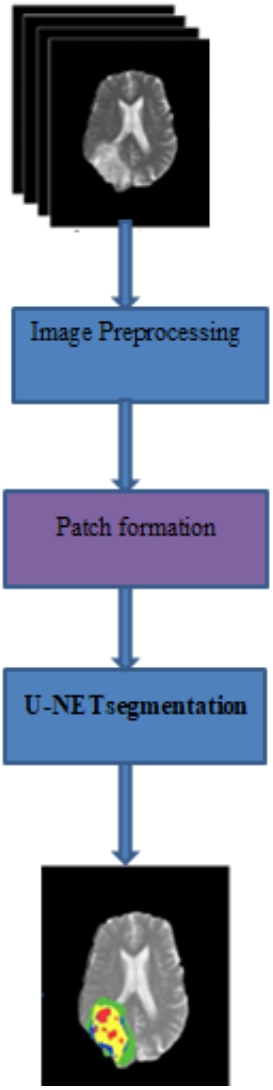

Fig. 3 Block diagram of our proposed model

B. Image Preprocessing

MRI images have noise problems because of heterogeneity and continuous in motion of images throughout image acquisition. These noises can cause an image's intensity level to change and consequently resulting in poor output. Two pre-processing techniques are applied to enhance our input images. Firstly, all images are homogenized using the N4ITK algorithm, which is a bias correction technique. The N41TK algorithm is capable of correcting MRI data's bias region. Furthermore, the intensities in the top 1% and bottom 1% are ignored. Secondly, each picture in our dataset was also subjected to intensity normalization. This process of normalization translates the image's pixel intensities into a functional collection. In this process we removed 1% top and bottom intensity values throughout the dataset which helps improving the learning process during training.

C. Detail overview of patches

3-D MRI scans, as well as T1, T1c, T2, and FLAIR modalities, are included in BRATS-2015 collection. All these 3-D brain images are transformed into 2-D MRI slices having pixel size of 240 x 240. Further, patches are generated from these multiple slices and U-NET is trained on them. We tested on different size of patches to see which patch size give better results. After experimentation we choose patch size to be 33X33 throughout the dataset. Similarly, same step is repeated throughout the dataset.

D. U-NET framework for brain tumor segmentation

In our proposed work we address the problem of glioma brain tumor segmentation on U-NET architecture. We acquired images from BRATS 2015 dataset. The proposed methodology are divided into three main steps named as image preprecessing, patch formation and U-NET implementation architecture. These steps are described briefly following.

1) U-net architectural detail ;

Up till now, there is no single U-NET architecture which applied on BRATS-2015 dataset for better precision. Furthermore, in any of U-net architecture used until now there is no clear information between the layers and deep shallow. In our proposed work, we clearly defined each and every layer in encoding and decoding side of the architecture. Figure 4 shows the overall proposed U-net architecture which including encoding and decoding blocks. The Architecture below takes images of size 240 ×240 and generates output of the same size after implementation. The left side of the architecture acts as an encoder and the right side of the architecture acts as a decoder. In convolution layers activation functions such as soft-max and relu used for getting same sized of input and output images. Further, padding is used to get same sized input and output images.

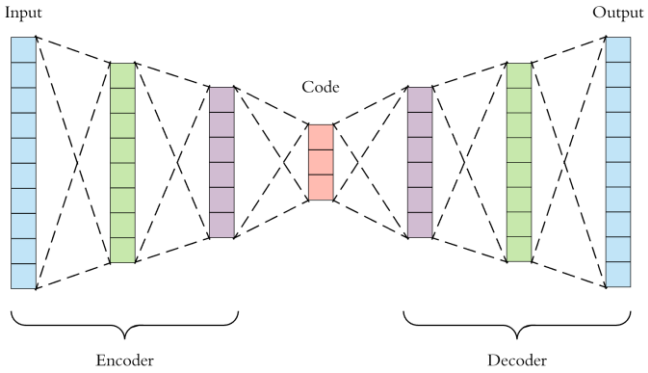

Fig. 4 U-NET block diagram

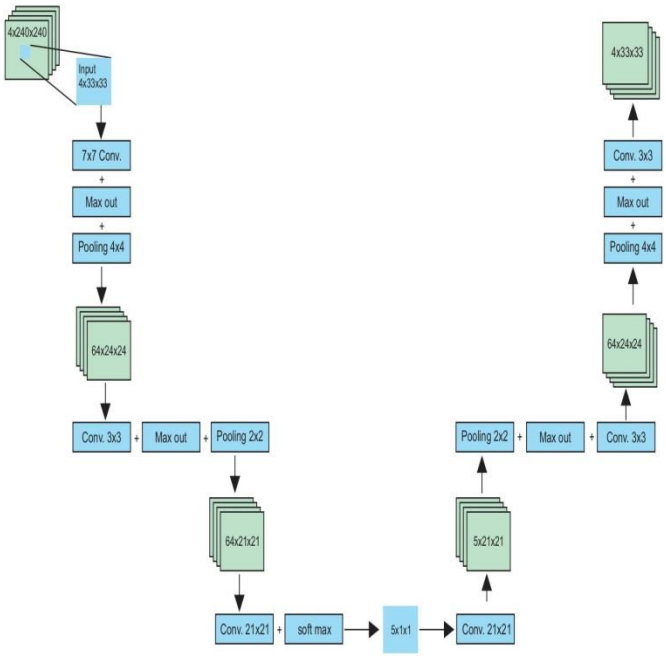

Fig. 5 U-NET architectural detail with encoding and decoding layers

a) Encoding side: left side of the architecture

The left side or encoding framework of the architecture each section comprises of convolution layer with max_out and a pooling function. For example in figure 4 input image of size four patches of 240 × 240 are indulged and extract four patches of 33 ×33 as a input. On this section 7 ×7 convolution filter is applied with couple of max_out activation function and a 4 ×4 pooling function. In the same way all the layers are working as described in the diagram. The last section of the encoder side is used activation function soft_max and output is 5 ×1 ×1 as final output on the encoder side of the architecture. Conclusively, it can be said that on the encode side of the architecture process of contraction is applied for better features learning. Further, details of all the layers is on the table 1.

TABLE 1: DETAIL OF ALL THE ENCODING LAYERS

Encoding Layers		
Layers	**Layer detail**	**Output Size**
Conv1_x	7×7, Pooling 4×4,Maxout	64×24×24
Conv2_x	3×3, Pooling 2×2,Maxout	64×21×21
Conv3_x	21×21, Soft-max	5×1×1

b) Decoding side of the architecture: right side

The right side of the architecture named as decoder side performs the expansion process. In this portion all the decoding layers work in a reverse order as compared to encoding layers. All the convolution layers show in table 2 of U-Net are followed by pooling layer and soft-max activation function. The mathematical representations of soft-max and ReLU function are as follow.

$$\text{ReLU(p)} = \begin{Bmatrix} 0, & if\ p \leq 0 \\ p, & otherwise \end{Bmatrix}$$

TABLE 2: DETAIL OF ALL THE DECODING LAYERS

Decoding Layers		
Layers	**Layer detail**	**Output Size**
Conv1_x	Convolution 21×21	64×21×21
Conv2_x	3×3, Pooling2×2,Maxout	64×24×24
Conv3_x	3×3, Soft-max	4×33×33

III. RESULT AND DISCUSSION

Out of all the datasets available for evaluating Gliomas brain tumor segmentation, the BRATS 2015 dataset is considered as the benchmark, we performed our proposed experimentations. In BRATS 2015 dataset there are two one is training set other is testing set. The training set consists of MRI images of 54 low grade gliomas (LGG) and 220 high grades gliomas (HGG) patients while the testing set consists of 220 images. It consists of four MRI modalities: T1, T1c, T2, and Flair MRI, each having its own ground truth image, as detailed in the dataset section. There are five classes named as edema (green), core (red), non-enhancing tumor (blue), healthy image and enhancing tumor (yellow) 0, I, II, III and IV respectively.

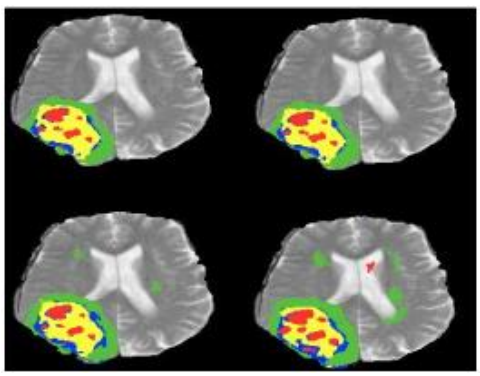

Fig. 6 Segmented results

We have carried out the segmentation on python most influential library named as KERAS which use tensor flow as back-up. On the input side there are four patches of 33 × 33 are indulged as input image in the network as showed in figure 4. Further, some parameters are being set for better precision of the results such as 0.001the learning rate, value of coefficient of momentum was adjusted at 0.9, value of decay is being set at 0.0001, and 0.3 dropout value has been set to drop weak features and reduce over fitting. In the figure 5 the segmented results showed of our proposed architecture.

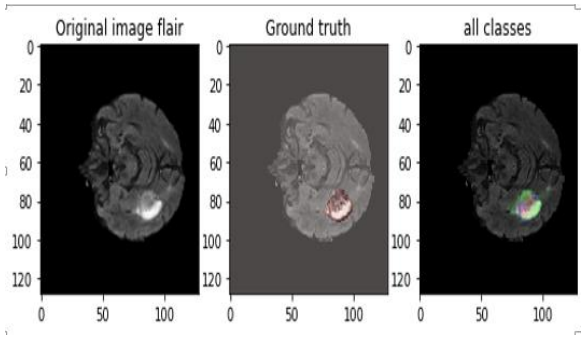

Figure 7 Original image, ground truth, all classes

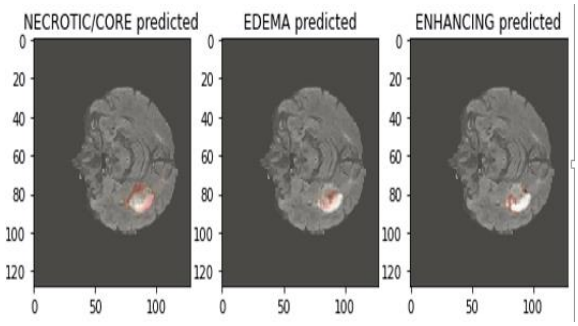

Figure 8 Segmented output

1) Achievements in term of better Dice score

The designed archuitecture as described in figure 4 perfomed extra ordinary well on BRATS 2015 challenges of high class imbalance and some others. Table 3 shows the high class imbalance problem which is main source of low accuracy and less dice score value.

TABLE 3: HIGH IMBALANCE OF CLASSES IN MRI SCANS.

Name of Class	*Area Occupied in percentage*
Benign cells	98.23
Edema	1.25
Non-Enhancing Tumor	0.31
Enhancing tumor	0.21

2) Better time constraints

All of the above testing was done on an Intel core I9 9TH generation processor with an 11GB NVidia RTX 2080 GPU and 64GB of RAM. One training session takes about 2-3 hour while testing is almost immediate with about 4-5 minutes duration. It can take up to 100 minutes for other machine learning architectures to segment a full brain.

To solve the issue that has been discussed above, U-NET architecture utilizes a combined loss function paradigm for better dice score. In our work, we divided output in three different areas named as specificity, sensitivity and dice score. Further, we have compared our results with all the state of the art architectures up till now and our result shows greater performance over all. Table 4 presents comparison of our output and provided all state of art architectures output. Last row of the table 4 shows our proposed U-NET architecture result which is better out of all the top table presented output.

TABLE 4:COMPARATIVE ANAYLSIS OF DIFFENRENT MODELS ON BRATS DATASET.

Architecture presented by	**Comparison of the top architectures on BRATS dataset.**		
	Dice score	***Sensitivity***	***Specificity***
Mohammad, et al. [9]	0.88	0.90	0.88
Kamnitsas [13]	0.90	0.92	0.87
D. Liu, H. Zhang[14]	0.88	0.85	0.88
Valverde [15]	0.87	0.85	0.90
Our U-Net model	**0.92**	**0.93**	**0.92**

IV. PERFORMANCE MATRICS

To compare and measure the accuracy of a model, various output measuring matrices are used. Table 3 shows sensitivity, specificity, dice score and accuracy which use multiple metrics, such as True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN), are used to measure results in these methods. Further, their mathematical expressions are listed in the table 3.

TABLE 5: EVAULTING PERFORMANCE OF THE MATRIX

Sr. No.	**Performance Evaluation Metrics**	
	Method	***Mathematical Expression***
1	Dice Coefficient	$\frac{2TP}{2\text{TP} + \text{FP} + \text{F}N}$
2	Sensitivity	$\frac{TP}{\text{TP} + \text{F}N}$
3	Specificity	$\frac{TN}{\text{TN} + \text{F}P}$
4	Accuracy	$\frac{TP + \text{T}N}{\text{TP} + \text{TN} + \text{FP} + \text{F}N}$

V. COMPARATIVE ANALYSIS

Table 4 presents a comprehensive comparative analysis on brain tumor segmentation of different techniques applied on BRATS dataset up till now. From year 2015 to 2021, we listed all the proposed methodology their results in term of

dice score and datasets they used. In the end we listed our proposed framework with highest achieved dice score.

VI. CONCLUSION

Due to high class imbalance of brain MRI images it is very difficult task to segment properly of brain tumor and aim is to predict tumors by segmenting the entire MRI images very carefully by adopting newly developed artificial intelligence. We proposed a novel framework named as U-NET with minor changes for glioma tumor segmentation and achieved better result over all other frameworks up till now. Further, we discussed in detail all the available dataset with their challenges and works on BRATS 2015 dataset challenge. Machine learning methods. In all of these methods, deep learning methods give better results with high time constraints and slow processing time.

We have introduced some performance metrics for evaluation of segmentation performance. As we discussed earlier that segmentation of brain tumors in term of identification of gliomas tumors is one of the most difficult task due to various diaspora conditions of the tumors. MRI images modalities type and their low brightness also one of the challenging issue in segmentation. To counter all these issues and challenges, however deep neural network with newly developed techniques performs well and improves efficiency to a greater extent.

To contribute the existing challenges and issues while in segmentation of brain tumors we proposed a U-NET novel architecture with minor changing in convolution layers such as adding pooling layers, activation function i.e. ReLU softmax for better precision in output layers. Further, we added image pre-processing session to increase the quality of the MRI images. Additionally, patch formation is also used for improving qualitative properties of the MRI input images. Each input image divided into multiples patch and these patches are extracted on the output side of the proposed architecture. After evaluation experimental results shows that our methodology works extraordinary well and achieve highest dice score on all the state-of-the-art frameworks present up till now.

As future directions, we should pay more attention by applying newly developed CNN models on different publicly available datasets and achieve better time constraint and high dice score. The filtration process in dataset can also be applied for betterment of result. Therefore, my research work paves the way towards new dimensions of the problem.

TABLE 6: COMPARATIVE ANALYSIS OF RESULTS 1

Sr. No	Writer of the paper	Architecture	Published in	Menu-driven interface	Dice score	Datasets	Reference
1	E. Abdel-Maksoud	Fuzzy c-mean and k-mean clustering	2015	Automatic	0.85	DICOM	[16]
2	N. J. Tustison	Conventional Machine Learning	2015	Automatic	0.86	BRATS 2013	[17]
4	I. Njeh, et al.	A Graphic matching approach	2015	Semi-auto	0.76	BRATS 2012	[18]
5	Pereira et al.	CNN architecture	2016	Automatic	0.88	BRATS 2015	[8]
5	Mohammad, et al	CNN two phase training architecture	2016	Automatic	0.88	BRATS 2013	[9]
6	Huber, T, et al	Conventional processing algorithms	2015	Semi-automatic	0.86	3-D MPRAGE-private	[19]
7	M. Soltaninejad	Super pixel based Classification	2017	Automatic	0.87	BRATS 2015	[20]
8	S. Amiri et al.	Support vector algorithms	2016	Automatic	0.84	BRATS 2012	[21]
9	J. Liu, et al.	Neural Network	2018	Automatic	0.88	3-D MPRAGE-private	[32]
10	D. Liu, H. Zhang.	Deep neural networks	2018	Automatic	0.88	BRATS 2015	[14]
11	**Proposed Mohsin jabbar**	**U-NET with modification**	**2021**	**Automatic**	**0.92**	**BRATS 2015**	

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