Automated Semantic Segmentation of Brain Tumors using Modified UNet Architecture

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Abstract: There are various categories of tumors found in the human brain at different localities, each owning its features or characteristics (i.e. Sizes, shapes, and contrast) at different intervals of time. The intervention of medical images (especially brain MRI images) greatly assists in the identification and categorization of these tumors. Delicate analysis and precise segmentation of these lesions are crucial for the proper diagnosis of this life-threatening disease. A lot of time and effort is required to perform this task manually, which may also be error prone. A plethora of work has been done in the near past, for the automation of this task by employing image processing, machine and deep learning-based methods. Due to high performance, deep learning-based methods have diverted the focus of the research community towards neural networks and their variants. In our study, we have employed generative deep learning-based encoder and decoder structure for the multi-class semantic segmentation of brain tumors. The proposed architecture is trained over a publically available BRATS-2015 multi-modality brain MRI image dataset. To reduce the computational cost, the largest-shortest bounding box has been extracted, which removes unused background area. The anticipated architecture has out-performed state-of-the-art semantic segmentation UNet architecture, while achieved a DICE score of 86.45%.

Keywords: Automated Brain Tumor Segmentation, UNet, Deep Learning

1. INTRODUCTION

Brain cancer is the most prevalent forms of cancer that causes many deaths, worldwide [1]. These tumors are caused by the superfluous growth of brain tissues that turned into different forms of brain abnormalities (i.e. benign and malignant tumors). These tumors are further characterized into primary and secondary brain tumors based on their location of origination i.e. tumors that originate in the brain are known as primary tumors, while others are known as secondary tumors. Gliomas and lymphomas are the two most ubiquitous categories of primary brain tumors, while 80% of malignant brain tumors are caused by gliomas [2]. Based on the severity, gliomas tumors are classified into two categories i.e. Low-Grade Gliomas (LGG) and High-Grade Gliomas (HGG) [3].

To inspect the progression of the disease, medical images of different modalities play a vital role. For the diagnosis of tumors like brain tumor, MRI is the most widely used and considered to be a standard imaging modality [4], due to its ability to depict different categories of tissue contrast and various structures of interest [5]. Utilization of a single MRI sequence for the delineation and complete dissection of tumors into their subregions is not enough; therefore different MRI sequences are being combined, which includes 1) T2-weighted MRI (T2) 2) T2-weighted MRI with fluid-attenuated inversion recovery (T2FLAIR), 3) T1-weighted MRI (T1) and 4) T1-weighted MRI with contrast enhancement (T1c) [5]. All of these MRI sequences have their consequences over image features i.e. T1-weighted sequence is mostly being employed for the structural assessment of tumor; the boundary of the lesion could be more prominently visualized in T1c images, edema region (i.e. area around the tumor) is more evident in T2 weighted MRI, while T2FLAIR assists in detaching edema from cerebrospinal fluid (CSF) [5].

Manual segmentation of brain tumors (i.e. by radiologists) is a laborious and time-consuming task as it requires slice-by-slice delineation followed by segmentation procedure, which needs a high level of operator's expertise to avoid subjective results [6]. The variations in features of brain tumors (i.e. shape, size, and localization) among different patients make the segmentation process more challenging. To tackle these issues, automated AI-based brain tumor segmentation is a promising solution that assists in saving expert medical practitioners time, while providing precise and reproducible semantic segmentation results [7], which also supports physicians in proficient diagnosis, treatment, and surgical planning's. A general ML pipeline to perform classification and segmentation tasks automatically has been depicted in Fig 1.

Numerous AI-based approaches have been introduced in past years to automate the whole task of brain tumor segmentation and diagnosis, which includes traditional machine learning-based approaches and advanced deep learning or artificial neural networks-based approaches [8]. The traditional ML-based methods achieved notable

performance in segmentation and classification tasks; however major limitation in conventional ML approaches is that they are specific to the training dataset (i.e. give efficient results over dataset related to training examples), these algorithms are not easily generalizable [8], while handcrafted features need to be extracted manually for the training of these algorithms. However, a plethora of new studies published in the last few years have exploited different categories of ANN architectures i.e. convolutional neural networks, fully connected networks, LSTM based networks, and auto-encoders, etc. In contrast to traditional ML-based methods, modern CNNs are not dependent on a limited number of hand-crafted features; instead, they could automatically extract a large number of complex (i.e. high level and low level) features. Numerous recent studies have demonstrated the exceptional performance of deep CNNs in automated brain tumor segmentation tasks using BRATS datasets [9-11]. It has been observed that most of the recent studies have utilized discriminative deep learning-based methods to perform this task [11].

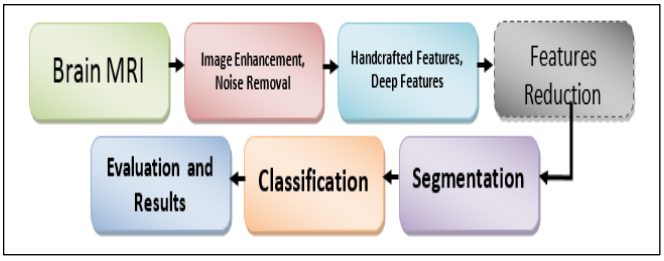

Figure 1. General Machine Learning Pipeline

In this study, we have proposed a generative deep learning-based encoder-decoder architecture for automated detection of brain lesions. The proposed architecture has outperformed state-of-the-art semantic segmentation U-Net architecture and has achieved significant performance.

The rest of the article is structured as follows: in section 2 related studies have been described, the description of the dataset that has been utilized in our study has been given in section 2.1, the proposed methodology and algorithm is mentioned in section 3, the detail of training hyperparameters has been given in section 4, while conclusion and future work is written in Section 6.

2. LITERATURE REVIEW

Numerous machine learning and deep learning-based methods have been exploited by different participants of BraTS-2012 to BraTS-2019 to get more and more precise predictions [12]. In our study, we have assessed the merits and demerits of some of these studies.

In BraTS 2012 & 2013, the majority of the proposed techniques are based upon statistical ML-based classifier, which includes: Markov Random Field (MRF), Random Forest (RF), and logistic regression [13] i.e. in one of the top-ranked technique in BraTS-2012 [14], the author has utilized random field regularization integrated with random forest classifier to perform automated segmentation of brain tumor and has achieved a Dice score of 0.59 and 0.73 over edema and tumor region. The top scorer of BraTS-2013 [14-16] has exploited a sequence of concatenated RF classifiers. In their proposed approach, a sequence of feature images is first generated from MR images, which are then fed to RF for the generation of probability maps. The extracted probability maps are then fed to succeeding RF, while to refine the resultant labels binary morphological processing is applied. The proposed approach has achieved a Dice score of 0.88 over the complete tumor, 0.76 over the core, and 0.55 over the enhanced tumor. The author has utilized a statistical classifier-based approach i.e. random forest; however, utilization of deep learning-based approaches could significantly improve the performance of the proposed technique.

In BraTS-2014, several researchers have employed deep CNNs in addition to Random Forest-based techniques for the semantic segmentation of brain tumor i.e. one of the top scorer [15-17] of BraTS-2014 has exploited a 3D CNN (i.e. consisted upon 3 convolutional layers) trained over 3D patches extracted from the provided multimodal brain MRI imagining dataset. The output layer of the proposed network incorporates 6-convolutional filters corresponding to 6 tumor classes to be predicted, while from the final prediction largest connected component is selected for false positives reduction. Similarly, another top scorer of this challenge [17,18] has adapted a 2D-CNN trained upon 19*19 2D-patches extracted from multi-model brain MRI imaging dataset. Images of the dataset are first down-sampled (i.e. before feeding into the network) using nearest-neighbor interpolation. The proposed methodology has achieved a dice score of 69.0±24.9, 73.6±25.6, and 83.7±9.4 over enhanced, core, and complete tumors respectively. The authors in these studies have utilized, patch-based approaches that need extra computation for patch extraction and reassembling, however utilization of generative deep learning-based models could assist in tackling this problem.

In BraTS challenge 2015 [13] most of the proposed techniques are based upon CNN. The study that has achieved top performance in this challenge has proposed a two-pathway patch-based Input Cascade CNN trained over dataset provided by BRATs-2013. The proposed architecture focused upon both local and contextual features by employing two parallel CNNs. The features extracted from the two parallel systems are then concatenated and passed to the fully connected layer. The proposed architecture has accomplished a DICE score of 0.73, 0.79, and 0.88 over enhanced, essential and whole tumors respectively.

Like BraTS-2015, the center of attention for most of the researchers who have participated in BraTS-2016 [19] is deep CNNs. One of the top scorers of this challenge has

presented an 11-layered 3D-CNN namely Deep Medic [9,10] for the patch-based classification of image pixels (i.e. to perform semantic segmentation). The proposed network incorporates two parallel CNNs, each dealing with patches of different scales, while also having residual connections between convolutional layers. The final feature maps extracted from two pathways are concatenated for further processing. The proposed approach has achieved a DICE score of 0.72, 0.76, and 0.89 over enhancing tumor, core, and whole tumor over dataset provided by BraTS-2015. Similarly, another participant [20] has utilized 3D-UNet architecture trained over a dataset provided by BraTS-2016 to perform automated segmentation of brain tumors. Each input volume is first normalized before feeding into the network, while to deal with the class imbalance problem, loss function (i.e. cross-entropy) is weighted by utilizing class distribution. The proposed approach has achieved significant DICE scores for Core and Whole tumors (i.e. 0.76 and 0.89), while achieved comparatively poor results overactive class tumors (i.e. 0.37).

In BraTS-2017, out of 50 participating teams, authors of 42 different studies have exploited deep CNNs for automation of brain tumor segmentation. The performance of these models mainly relies upon the choice of the loss function (i.e. DICE loss, weighted cross-entropy, etc) [12]. In addition to these, the selection of appropriate hyper-parameters i.e. regularization technique, training optimizer, and the learning rate is challenging, while greatly impacts the performance of deep models. Moreover, to improve the predictive performance of segmentation models, ensemble learning is a preferable alternative and is being utilized in recent studies i.e. the winner of BraTS-2017 [4] has presented an ensemble of multiple models and architecture (EMMA) (i.e. including U-Net, two variations of DeepMedic model and two different fully convolutional networks). The proposed ensemble is trained over a dataset provided by BraTS-2017, while the final predictions of the proposed ensemble are obtained by averaging predictions of all models. The proposed architecture has achieved the complete finest performance in a challenge founded on Hausdorff distance and DICE score i.e. achieved DICE score of 0.75, 0.82, and 0.90 over attractive, core and entire tumor respectively.

Similar to the previous year challenges, CNNs have outperformed other ML-based techniques in BraTS-2018, while up to 50 diverse proposed techniques were CNN based [12] i.e. the participant [7] who has achieved the best performance in BraTS-2018 has proposed an encoder-decoder deep CNN for semantic segmentation of brain tumors. The encoder of the proposed architecture is comparatively larger than the decoder, while a virtual auto-encoder (VAE) branch has also been embedded in the proposed model to regularize the encoder part, due to the scarcity of training data. Dropout, L2-Normalization, and data augmentation are applied to avoid the model's over-fitting. The proposed approach has achieved a final DICE score of 0.82, 0.86, and 0.91 over enhancing, core and whole tumors respectively, by using an ensemble of 10 proposed models.

In BraTS-2019, an author who has achieved the best performance in semantic segmentation of brain tumors using a dataset provided by BraTS-2019 has utilized a cascade of UNet architecture [21]. The author has presented a two-stage deep architecture i.e. in the first stage a simple encoder-decoder CNN has been utilized, where the decoder part is comparatively shallower than the encoder part, while in the second stage, the output of the primary stage is concatenated with the raw input images and fed to the second architecture. The second model incorporates one encoder and two decoders i.e. one used deconvolution while the other has utilized tri-linear interpolation for up-sampling. The second decoder has only been utilized in the training process to regularize the encoder. Data augmentation has also been applied to avoid over fitting, while the finest presentation in terms of DICE scores achieved by the proposed model is 0.887, 0.832, and 0.836 over the whole, enhancing and core tumors respectively by employing an ensemble of 12 proposed models.

3. PROPOSED METHODOLOGY

The proposed methodology relies upon three major steps, which include 1) Dataset preprocessing, 2) training of the proposed model, and 3) evaluation of the proposed model by testing over unseen data, as described below.

A. BRATS Dataset

In our study, we have utilized a dataset provided by the BraTS-2015 challenge, which mainly incorporates two categories of brain lesions (i.e. LGG and HGG). This dataset encompasses images of the BraTS-2012 and BraTS-2013 dataset together with cases of Cancer Imaging Archive (TCIA) collected for BeaTS-2014. A total of 54 LGG and 220 HGG cases are incorporated by the training dataset. Moreover, images of all 4-modalities (i.e. T1, T2, T1c, and FLAIR) and their corresponding masks are included in each case (Fig 2). The extent of each 3D image in the dataset is 155*240*240. Each voxel consists of 5 categories of tumors as mentioned in Table 1.

TABLE I. CATEGORIES OF TUMORS

Class	Numerical Representation
4	Edema
3	Enhancing core
2	Necrotic cystic
1	Enhancing
0	Normal and Background with Noise

The test dataset provided by the challenge encompasses 110 cases of mixed grades (i.e. HGG and LGG) [22]. The four distinct imaging modalities provided in the dataset endow with a different set of features that assists in finding tumor area and category of the tumor.

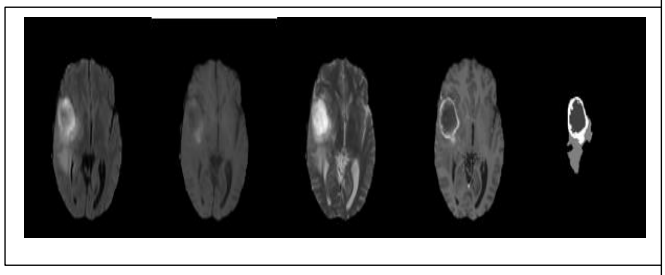

Figure 2: Sample images of BRATS-2015 dataset

B. *Preprocessing*

For the enhancement of input images, image preprocessing is a crucial task. It plays an important role in improving automated segmentation results. Various preprocessing techniques are there i.e. described in [23]. In our study, we have employed four different preprocessing techniques on input data before feeding them to the network i.e. described in Table 2.

TABLE II. *PREPROCESSING TECHNIQUES*

Preprocessing	Description
Pixel's intensity normalization	The pixel intensity ranges of input images do not lie in the standard range of 0-255. To make all the input images in the same intensity range, min-max normalization has been employed (i.e. to normalize pixels value in the range of [0,1])
2D slicing	3D images in .mha format have been provided in the challenge dataset. During preprocessing stage we have converted these 3D images into 2D NumPy arrays i.e. each 3D image of size 155*240*240 is altered into 155 NumPy arrays of sizes 240*240 each.
Concatenation	As four imaging modalities (i.e. T1, T2, T1c, and FLAIR) are available corresponding to each image, we have concatenated the corresponding slices i.e. images of size 4*240*240 are created.
Cropping	To reduce computational complexity and to make the training process faster, we have the computer the largest-shortest bounding box i.e. to crop the background pixels. The resultant images are of size ().

C. *Model's Architecture*

In our study, we have proposed encoder and decoder CNN structure for the semantic dissection of brain tumors. Our proposed architecture is inspired by the state-of-the-art deep semantic segmentation architectures i.e. U-Net [24]. Both encoder-decoder parts of the proposed model incorporate 4 sub-blocks, in which a combination of rectified linear unit (ReLU), pooling, and convolutional layers have been embedded. Motivated from the U-Net structure, skip acquaintances have been embedded amongst encoder and decoder parts of the proposed network. Moreover, residual connections are added in the encoder part of the network to avoid degradation issues [25]. Fig 3 depicts the structure of the proposed encoder-decoder CNN.

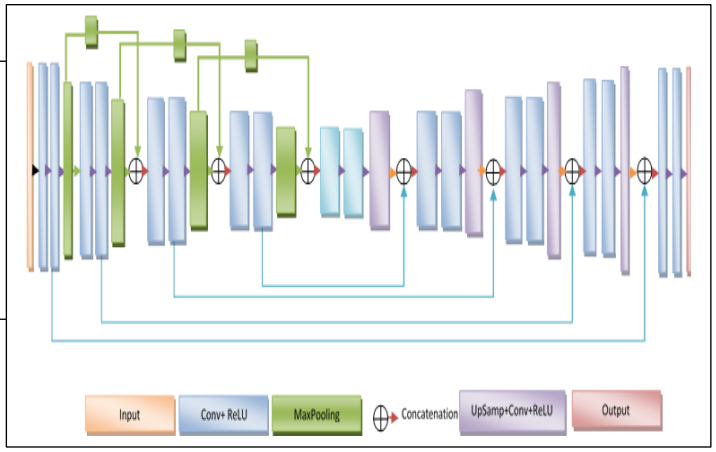

Figure 3. Proposed Deep Model Architecture

a) *Encoder*

As we have already discussed, the input dataset consists of brain MRI slices of size 240*240 of four different imaging modalities. Before feeding these images to the network slices of all 4 modalities are concatenated i.e. resulting in images of size 4*240*240. To reduce the memory and computational cost, the unnecessary background is cropped out from input images i.e. resultant images of size 4*176*144 are fed to the network. The encoder part of the network extracts complex features from input images i.e. by employing pair of frequent convolutional layers surveyed by batch stabilization and pooling layers. Each block of convolutional (3*3) and pooling layers (2*2) downsamples the extent of the input image into half, while the number of convolutional filters doubles up in each subsequent encoder block. To tackle with degradation issue, residual connections are embedded between pooling layers of subsequent blocks.

b) *Decoder*

The decoder of the proposed network is counter to the encoder or contracting path. Similar to the contracting path, the decoder also incorporates 4 blocks. The task of each decoder block is to up-sample the input features maps (i.e. by employing up-convolution) and to reduce the sum of input networks in half. Moreover, feature maps of expanding path blocks are concatenated with corresponding feature maps of encoder blocks using skip connections. The network outputs 4 feature maps of size 176*144 corresponding to each abnormal class (i.e. edema, core, ornamental, and cystic), while during testing of model final predictions are obtained by taking class with the highest probability i.e. by employing argmax function.

The detailed conformation of the anticipated network is depicted in Table 3.

TABLE III. *CONFIGURATION OF PROPOSED MODEL*

Encoder	**Input**	**Output**		**Size**
	Input	Input		4*176*144
	Input	Conv1+ReLU 1	2	64*176*144
	Conv1+ ReLU1	Pooling1		64*88*72
	Pooling1	Pooling1_1		64*44*36
	Pooling1	Conv2+ ReLU2	2	128*88*72
	Conv2+ ReLU2	Pooling2		128*44*36
	Pooling2	Pooling2_2		128*22*18
	Pooling1_1,Pooling2	Merge1		192*44*36
	Merge1	Conv3+ ReLU3	2	256*44*36
	Conv3+ ReLU3	Pooling3		256*22*18
	Pooling3	Pooling3_3		256*11*8
	Pooling2_2,Pooling3	Merge2		384*22*18
	Merge2	Conv4 +ReLU4	2	512*22*18
	Conv4 +ReLU4	Drop4		512*22*18
	Conv4 +ReLU4	Pooling4		512*11*9
	Pooling3_3,Pooling4	Merge3		768*11*9
	Merge3	Conv5 +ReLU5	2	512*11*9
	Conv5 +ReLU5	Drop5		512*11*9
Decoder	Drop5	Upsamp1+Conv6+ ReLU6		512*22*18
	(Upsamp1+Conv6+ ReLU6)(Drop 4)	Merge6		1024*22*18
	Merge6	Conv6 +ReLU6	2	512*22*18
	Conv6 +ReLU6	Upsamp2+Conv7+ ReLU7		256*44*36
	(Upsamp2+Conv7+ ReLU7)(Conv3)	Merge7		512*44*36
	Merge7	Conv7 +ReLU7	2	256*44*36
	Conv7 +ReLU7	Upsamp3+Conv8+ ReLU8		128*88*72
	(Upsamp3+Conv8+ ReLU8) (Conv2)	Merge8		256*88*72
	Merge8	Conv8 +ReLU8	2	128*88*72
	Conv8 +ReLU8	Upsamp4+Conv9+ ReLU9		64*176*144
	(Upsamp4+Conv9+ ReLU9) (Conv1)	Merge9		128*176*144
	Merge9	Conv9 +ReLU9		64*176*144
	Conv9 +ReLU9	Conv10		4*176*144

4. EXPERIMENTS AND RESULTS

In the experimental phase of our study, we have compared the performance of our proposed modified UNet architecture with state-of-the-art UNet architecture for the semantic segmentation of brain tumors using MRI images. The detailed description of tuned parameters together with the training and testing dataset description is mentioned below.

The proposed deep architecture is implemented in Tensorflow on NVIDIA GeForce RTX 2080 Ti GPU with 11GB memory size. Near about 48 hours are required to train the whole model over 20 epochs on training data, while near about 0.5ms are required to test an image over the trained model. We have trained the proposed model over the HGG tumor images provided in the dataset. Dataset is split into three parts i.e. 70%, 20%, and 10% for training validation and testing dataset. The detail of several examples in each split is provided in Table 4.

We have performed multiple experiments with different hyper-parameters to achieve the best performance results, while the final set of tuned parameters are mentioned below. The initial learning rate is set to 0.001, which is reduced after every 4 epochs by a factor of 0.9 if validation loss does not reduce. Adam optimizer has been utilized for updating network weights, while the Binary Cross-Entropy loss function has been employed during network training. Batch size provided to the model during training has also an impact on the performance of deep models. A mini-batch size of 20 has been used in our study.

TABLE IV. *DATASET SPLITTING PROPORTION*

Dataset	Split	No of Slices
Training	70%	23871
Validation	20%	6820
Testing	10%	3409

Results are evaluated for the whole tumor region, as required by the BRATS-2015 challenge. For the evaluation of similarity score over test data, DICE score, sensitivity, and specificity metrics have been calculated as mentioned in Table 5. The formulae for the calculation of these metrics have been mentioned below:

A. DICE Coefficient

Dice Coefficient is used to measure the similarity between two samples.

$$DICE = \frac{2TP}{FP+2TP+FN} \quad (1)$$

or

$$DICE = \frac{2(X \cap Y)}{(X \cup Y)} \quad (2)$$

B. Sensitivity & Specificity

Sensitivity is a measure to determine the true positives. Specificity is a measure to determine the true negatives.

In medical tests, sensitivity mainly focuses on finding the people who are suffering from the disease, while specificity mainly focuses on measuring the people who do not have the disease.

$$Sensitivity = \frac{TP}{TP+FN} \quad (3)$$

$$Specificity = \frac{TN}{TN+FP} \quad (4)$$

In our study, we have tested both state-of-the-art UNet and our proposed modified deep architectures over the above-mentioned parameters, while results depict that our proposed architecture has outperformed UNet. We have also compared the testing results of our proposed model with several top-performing studies of BraTS-2015 as depicted in the table 5. The prediction results of our proposed network are depicted in Fig 4.

TABLE IV. *RESULT OF THE WHOLE TUMOR OVER TESTED DATASET*

Author	Dataset	Model	DICE	Sensitivity	Specificity
[21]	Test Split of BRaTS-2015 training Data	Modified UNET (Proposed Architecture)	**86.45%**	0.8078	0.9978
[22]	Test Split of BRaTS-2015 training Data	UNET	82.01	0.7697	0.998
[24]	BRaTS-2015 training data	Random Forest	84.%	---	---
[25]	BRaTS-2015 testing Data	Stacked Denoising Autoencoder	81.41%	---	---
[26]	BRaTS-2015 testing Data	Random Forest	80.%	---	---
[27]	BRaTS-2015 testing Data	Feed Forward Neural Network	73.15%	---	---

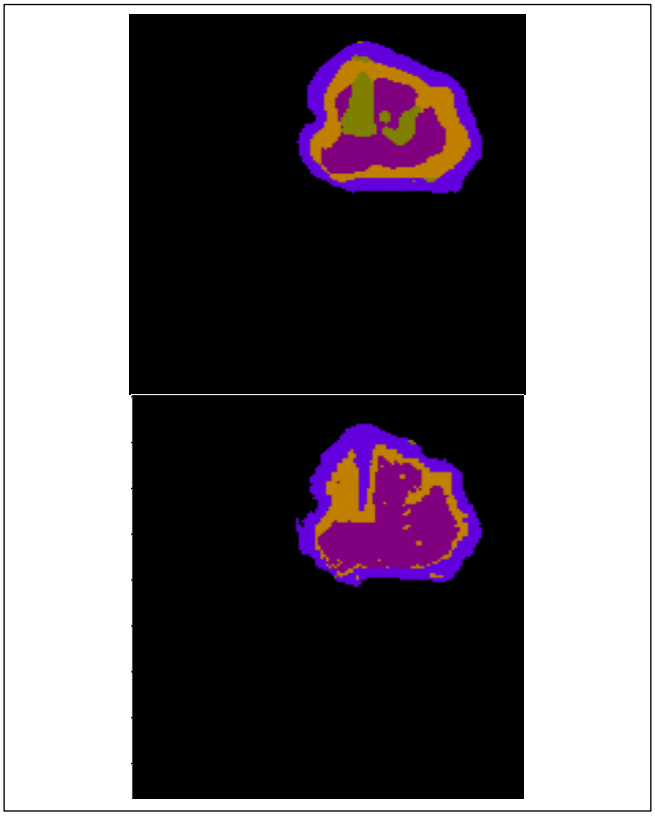

Figure 4. Proposed Network a) Ground-Truth b) Prediction

5. CONCLUSION AND FUTURE WORK

Traditionally most of the automated discriminative models proposed for the automated brain tumor segmentation are based on statistical machine learning-based methods (i.e. RF). The intervention of deep learning-based methods has significantly improved the performance of this task. In our study, we have presented an efficient deep learning-based semantic segmentation model that has achieved comparable performance over a multi-modality BRATS-2015 brain MRI imaging dataset. The results of the proposed architecture depict the impact of residual connections over the performance of semantic segmentation of tumors. The computational cost of the proposed methodology is reduced by removing an extra background region from the images. Our proposed deep model has outperformed state-of-the-art UNet architecture and several other deep learning and machine learning-based techniques (i.e. depicted in Table 5), while achieved a DICE score of 86.45%. As future work, we have planned to employ several preprocessing techniques on input images to enhance the quality of features.

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