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Glioblastomas Brain Tumor Segmentation Using Optimized Three-Dimensional (3DU-Net) Model

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***Abstract*—Automated segmentation is a computerized technique that helps to find tumor location, size, and shape. Human segmentation is error prone, time consuming, and needs an expert radiologist. In our study, we developed a customized 3D U-Net model that processes 3D volumetric images for multiclass tumor segmentation. This framework is modified in such a way that the gradient flow is better for finding accurate output. The BraTS 2020 dataset is used to train this network with end-to-end learning strategy followed by defining the proper skip connection from encoder to decoder. In model evaluation, binary cross-entropy with Dice loss functions is utilized. Testing samples are predicted and classified into three regions: whole tumor (WT), tumor core (TC), and enhancing tumor (ET). Model performance is evaluated through Dice coefficient metrics for each class.**

On the basis of this model, experiments were carried out on the BraTS 2020 dataset which could be considered as a validated benchmark. The segmentation's obtained results have been validated with ground truth references by computing the Dice Metric parameter. Our clinical partners have attested that the proposed tool could achieve great performances. The aim of this research is to make an advanced tool which could help radiologists to make a more accurate diagnosis. It could also assist clinicians in the early detection of brain tumors.

Keywords— Resonance Imaging (MRI); Deep Learning (DL) Segmentation;Gliomas, Brats dataset; 3D U-Net

1. INTRODUCTION

Gioblastomas brain tumors are among the most aggressive primary brain tumors arising from glial cells which cover almost 80 % of malignant brain tumors and 30 % of all Central Nervous System (CNS) tumors [1]. According to the World Health Organization (WHO), Gliomas can be characterized based on their grade, into High-Grade Gliomas (grades III and IV) and Low-Grade Gliomas (grades I and II).The early detection and accurate clinical diagnostics have significance for patients 'recovery.

Magnetic Resonance Imaging (MRI) is considered the most invasive technique for Glioblastomas tumors characterization and exploration since it provides highly detailed images about the shape, size, and location of such brain tumors. Moreover, multimodal MRI protocols can produce crucial complementary information that yields a valuable diagnosis.Manual segmentation is time-consuming and depends on the level of human experts thus accurate and automatic segmentation has a great significance for diagnosis and treatment planning by providing the exact localization of tumor sub-regions and by monitoring of the tumor growth progression by precisely quantifying their volume. Even the recent developing of sophisticated segmentationalgorithms thathave been proposed recently in the literature, such machine-learning and deep-learning based-approaches, in fully automated and reliable segmentation of Glioblastomas (GBM) there are often more complicated situations where the tumors 'intensity may overlap with intensities of other pathologies or healthy tissues. Furthermore, clinical MRI scans are usually acquired with different scanned technologies and acquisition algorithms causing asymmetrical noise effects, inadequate Signal-to-Noise-Ratio (SNR) and data heterogeneity that may also affect the final segmentation accuracy.

The segmentation is consisting of partitioning the image into several regions, to make it easier and more meaningful to interpret. In the context of brain MRIs, segmentation makes it possible to characterize the different structures of the brain and brain tumors, namely gray matter, white matter, cerebrospinal fluid. In clinical practice, the accuracy of the data, manipulated by the practitioners, is very important for a reliable diagnosis. In terms of image analysis, it is necessary for the segmentation to be precise.

In our research work, we propose to place ourselves in a more general framework and to develop a method capable of segmenting "more delicate" tumours, that is to say inhomogeneous, uncircumscribed tumours, which can propagate in a infiltrating towards the different anatomical structures such as the case of glioblastomas. These tumors are particularly characterized by ill-defined and imprecise borders. Given the nature of these tumours, the classic segmentation methods reported in the literature may have several limitations. Recently, a particular attention is paid to the use of deep learning to improve the performance of MRI image segmentation.

The objective is therefore to propose an accurate and reliable method of segmentation of brain tumors based on deep learning and to detect mainly the entire tumor area,

i.e. to isolate it from the main brain structures such as the edema, necrosis, tumor core and enhanced tumor [7].

The remainder of this paper is organized as follows: Section 2 presents the related works, section 3 presents the proposed method for brain tumor segmentation, section 4 explored the experimental results and comparative study with existing segmentation methods and section 5 concludes the paper

2. Related work

Several studies have been proposed in the state-of literature for MRI gliomas brain tumors segmentations based on Machine Learning (ML) and Deep Learning (DL).

In 2020, R. A. Zeineldin et al. [3], residual neural network, dense convolutional network, and NASNet have been utilized in this study to build a fully programmed brain tumor recognition and segmentation, this deep learning architectures have been evaluated online based MRI datasets of brain tumor segmentation BraTS 2019, the lack of this study was that false positives (FP) indicated was high values of both recall and specificity, which might not precisely reflect the actual performance.

In 2020, X. Feng et al. [4] produced a 3D U-Net ensemble for brain tumour segmentation, multimodal brain tumor segmentation (BraTS 2018) challenge has been used in the study, the limitation of this structure , it hard to pick of the best model and/or hyper-parameter set because of that most models perform similarly. It is indeed one disadvantage of DCNN as the "black-box" nature of the network makes it challenging to analyze the effect of network structure and parameter except from the final performance. In 2021, T.Sadad et al. [5] developed U-Net with ResNet50 architecture for segmentation of tumours utilizing the Figshare dataset .

In 2021, F. Isensee et al. [6], nnU-Net utilized,nnU-Net pipeline's segmentation performance has been demonstrated to be greatly enhanced by the addition of BraTS specific characteristics such as postprocessing, data augmentation, and region-based training. For the BraTS challenge 2020 segmentation problem, excellent results have been obtained using the nnU-Net configuration's baseline setup, however, one limitation of this approach is the lack spans a small number of the modifications and lacks sufficiently extensive experimental validation thereof.

In 2019 Li Sun et al. produced a the framework for brain tumor segmentation and survival prediction using multimodal MRI scans using the 2018 MICCAI BraTS training set then applied the trained model for prediction on the validation and test set. compared the segmentation result of the ensemble model with the individual model on the validation set .The reslts have been obtained demonstrates that the ensemble model performs better than individual models in enhancing tumor and whole tumor, while CA-CNN performs marginally better on the tumor core.[19]

In 2019 Adel Kermi et al presents a fully automated and efficient brain tumor segmentation method based on 2D Deep Convolutional Neural Networks (DNNs) which automatically extracts the whole tumor and intra-tumor regions, including enhancing tumor, edema and necrosis, from pre-operative multimodal 3D-MRI. The network architecture was inspired by U-net and has been modified to increase brain tumor segmentation performance. Among applied modifications, Weighted Cross Entropy (WCE) and Generalized Dice Loss (GDL) were employed as a loss function to address the class imbalance problem in the brain tumor data. The proposed segmentation system has been tested and evaluated on both, BraTS'2018 training and validation datasets, which include a total of 351 multimodal MRI volumes of different patients with HGG and LGG tumors representing different shapes, giving promising and objective results close to manual segmentation performances obtained by experienced neuro-radiologists. On the challenge validation dataset, system achieved a mean enhancing tumor, whole tumor [20].

In 2021, has been trained multiple U-net like neural networks (Théophraste Henry et al.), mainly with deep supervision and stochastic weight averaging, on the Multimodal Brain Tumor Segmentation Challenge (BraTS) 2020 training dataset. Two independent ensembles of models from two different training pipelines were trained, and each produced a brain tumor segmentation map. These two labelmaps per patient were then merged, taking into account the performance of each ensemble for specific tumor subregions. More complicated training schemes and neural network architectures were investigated without significant performance gain at the cost of greatly increased training time. Overall, theirs approach yielded good and balanced performance for each tumor subregion[21].

The Convolutional Neural Networks (CNN) technique [22] is well-suited for the segmentation of heterogeneous information without parametric distribution hypothesis. Havaei et al. [23] built a cascade of two sub-networks with different input patch size. The feature maps extracted from sub-network with larger input patches are concatenated with smaller patches as the input data of the other sub-network, thus bringing in more global contextual information simultaneously. Pereira et al. [24] investigated the potential of using deep architectures with 3×3×3 convolutional kernels for segmentation in MR images after intensity normalization. Kamnitsas et al.[25] utilized a dual pathway, 11-layers deep, three-dimensional CNN model named DeepMedic to classify various tissues in MR images. Kleesiek et al.[26] applied 3D filters to take advantage of structural information at the cost of the computational load increment. The vibration of prediction caused by imbalanced distribution of brain tissues even deteriorates in 3D models, methods [27]–[28] used to address the same issue of ordinary images are unsuitable for MR images due to the latter's innate structural features. Fausto Milletari et al.[29] proposed a 3D V-net model with a novel object function based on Dice coefficient, namely dice loss, which achieved better performance in the imbalanced distribution. Regard to strong imbalanced

distribution, Tsung-Yi Lin el al.[30] proposed another object function, namely focal loss, to address the extreme foreground-background class imbalance during dense object detection [32] .
The main Contribution part of our proposed model

- ✓ We adopted a three-dimensional model that exploits the volumetric MR images to generate a highly detailed features map and to incorporate the global and local features;
- ✓ We optimized the performance of classical 3D-Unet model as follows: we adopted the adaptive moment estimator (Adam) [29] to improve the convergence speed and to find a better minimum for the loss function. In general, Adam utilizes the first and second moments of gradients for updating and correcting the moving average of the current gradients. The parameters of our Adam optimizer were set as learning rate = 0.0000001and the maximum batch size = 32.
- ✓ We adopted dataset Generators from the Keras backend instead to fit the data into our proposed model. thus, could optimize the network performance and accelerate the leaning process and reduce the computational and memory requirement.
- ✓ To deal the huge memory and computational requirement issues of such three-dimensional models as (3D-Net) we resized the size of input MR images dataset from 244*244*155 to 128*128*3. Furthermore, we exploited small 3D small kernel's size.
- ✓ The performance evaluation of the proposed model using an open-access benchmark dataset confirms that the proposed model could produce refined and detailed segmentation results outperforming several studies from state-of-the-art. For instance our model reached 0.99 for Enhanced Tumor (ET) sub-regions segmentation;

3. PROPOSED METHOD

In this work, an efficient lightweight implementation of 3D U-Net deep networks is proposed with the goal of providing accurate real-time segmentation. This has been accomplished by altering the input layer of 3D U-Net to accept lower sizes of input images. The results have been quite promising. Instead of working with the default size of input images in the original version of 3D U-Net, which was 572 by 572 pixels, we have utilized images of smaller sizes, including 32 by 32 pixels. In addition, we have incorporated a more extensive and deeper stack of convolutional layers into the proposed architecture. This has assisted us in obtaining more precise information from the input images while also reducing the amount of compression.

A. Network architecture

The architecture of the proposed 3D U-Net model is shown in Fig.1, has the advantage of combining both the contextual information from the up-sampling path and the location information from the down-sampling path to finally generate a powerful segmentation map combining localization and context features , which emphases the segmentation accuracy.
Our network is illustrated based on auto encoder architecture consists of a encoding path (left-side) to analyze the input image then generate features map and a decoding path (right-side) to reconstruct the original resolution [7]

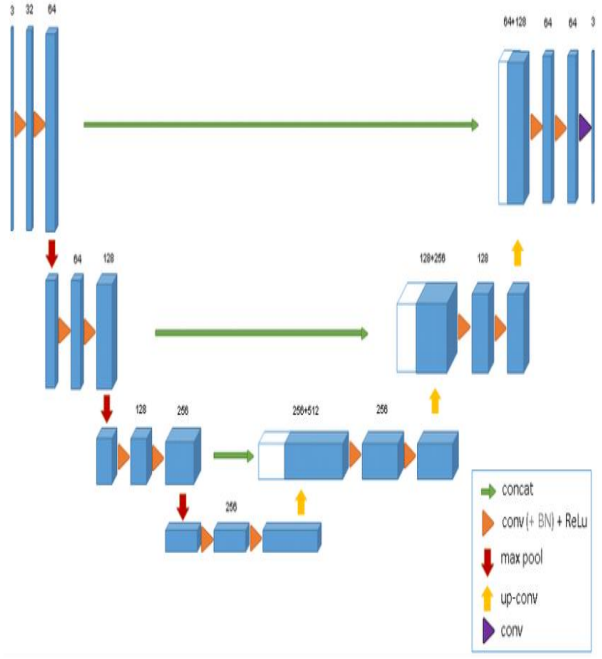

Fig 1 : 3D U-Net architecture [31]

Encoding part:
The encoding part also called the Down-sampling path consists of 4 convolutional blocks. Each block follows the typical architecture of a convolutional network, composed of:
- 3 x 3 x 3 Convolutional Layer, Relu as a activation function and same as a padding function
- 3 x 3 x 3 Convolutional Layer, Relu as a activation function and same as a padding function
- 2x2 x2 Max Pooling applied at the end of each block [7].

Decoding part:
The decoding part, also known as up-sampling path consists of 4 blocks, every block in the de-coding part expect the last block composed of :
- 3 x 3 x 3 De Convolutional Layer, Relu as a activation function and same as a padding function
- 3 x 3 x 3 De Convolutional Layer, Relu as a activation function and same as a padding function
- Concatenation layer with the corresponding cropped feature map from the encoding path

Finally, a 1×1×1 convolutional layer and Softmax

activation function in the last block [7] .

Skip connection:
Skip connection has shown its great performance for semantic segmentation of natural images, its performance could be more efficient for biomedical imaging. It aims to propagate relevant high-level spatial information at the same resolution from down-sampling into the up-sampling We introduced several skip connections in our proposed network for better intra-slice context exploration to produce a highly detailed segmentation[7] .

B. Preprocessing

Resize: we resized the size of Input volumetric MR images to handle 3D models since 3D models e very expensive in term of memory and computation requirement; we resized the size of input MR images dataset from 244*244*155 to 128*128*3 using open cv

Dataset split:we splitted our dataset as follows (80 % for training our model , 10 % for Validation and 10 % for testing). Fig.2 illustrates the dataset distribution

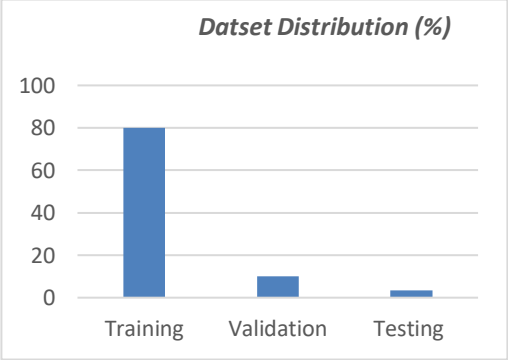

Fig 2: Dataset split ratio

Intensity-Normalization:MRI is usually affected by noise and artifacts especially during fast acquisition algorithms. Thus,could create non uniform intensity distribution between brain tissues, moreover for large scale medical image analysis, the data are very likely collected from different institutes with various hardware and protocols. These complicated data set always need complex preprocessing to correct the data heterogeneity, Hence, we applied data normalization for each t MRI scans by subtracting the mean of each MR images and dividing by its standard deviation across all training patches. Several studies attest that intensity normalization has a positive impact to increase the segmentation accuracy [7]**.**

C. Training process

In this section, we discussed the training parameters such as the optimizer. We adopted the adaptive moment estimator (Adam) [29] to improve the convergence speed and to find a better minimum for the loss function. In general, Adam utilizes the first and second moments of gradients for updating and correcting the moving average of the current gradients. The parameters of our Adam optimizer were set as learning rate = 0.0000001and the maximum batch size = 32.

4. RESULTS AND DISCUSSION:

In this section we will presents the obtained results and evaluate the performance and discuss the obtained results.

A. Implementation details

The proposed model was implemented using Tensor-flow and Keras backend and python as a developing environment. To train the model we used an Intel Core i7-CPU CPU occupied with an (16 GB) GPU NVIDIA GeForce GT-X 1060Ti.

B. Dataset

The Magnetic Resonance images used for the model training and evaluation are from the Multi-modal Brain tumour Segmentation Challenge (BraTS) 2020 [8, 9, 10, 11, 12]. The BraTS 2020 training dataset contains 494MR volumes of shape 240 × 240 × 155.
MRI is required to evaluate tumor heterogeneity. These MRI sequences are conventionally used for glioma detection: T1 weighted sequence(T1), T1-weighted contrast enhanced sequence using gadolinium contrast agents (T1Gd) (T1CE), T2 weighted sequence (T2), and Fluid attenuated inversion recovery (FLAIR) sequence. From these sequences, four distinct tumor sub-regions can be identified from MRI as: The Enhancing Tumor (ET) which corresponds to area of relative hyper-intensity in the T1CE with respect to the T1 sequence, Non Enhancing Tumor (NET), Necrotic Tumor (NCR) which are both hypo-intense in T1-Gd when compared to T1, Peritumoral Edema (ED) which is hyper-intense in FLAIR sequence.
TThese almost homogeneous sub-regions can be clustered together to compose three semantically meaningful tumor classes as, Enhancing Tumor (ET), addition of ET, NET and NCR represents the Tumor Core (TC) region and addition of ED to TC represents the Whole Tumor (WT). MRI sequences and ground truth map (the expert neuro-radiologist segmentation) with three classes [13] are shown in Fig. 3

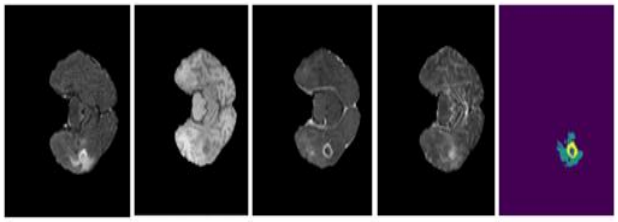

Fig 3 : Visual Analysis of BraTs 2020 Training Data. In the Ground Truth (GT) Mask, green, yellow and gray represent the peritumoral edema (ED), Enhancing Tumor (ET) and non-enhancing tumor/necrotic tumor (NET/NCR), respectively.

C. Evaluation Metrics

To evaluate the proposed method performance, several evaluation metrics have been used. The Dice Metric (DM), the Sensitivity, the Specificity and Accuracy have been selected to evaluate the segmentation's results.

Loss function

The Dice Metric (DM) and Iou Mtric have been used in this paper as Loss function

- Dice metric (DM)

This is essentially a measure of overlap between two samples. This measure ranges from 0 to 1 where a Dice coefficient of 1 denotes perfect and complete overlap. The Dice coefficient was originally developed for binary data, and can be calculated as:

$$Dice = \frac{2|X \cap Y|}{|X|+|Y|} \qquad \text{eq. 1}$$

- IOU metric

To compute the IoU score, divide the intersection point between the actual data (ground truth) and predicted segmentation by the point of union between the actual data (ground truth) mask and predicted segmentation mask." When assessing how much overlap there is between two masks or bounding boxes [14], it is a valuable statistic.

$$IoU = \frac{groundtruth \cap prediction}{groundtruth \cup prediction} \qquad \text{eq. 2}$$

- Sensitivity

The sensitivity (True Positive rate) measures th positives 'proportion that is correctly predicted by th segmentation method. It could be defined by the

$$Sensibilité = \frac{TP}{TP+FN} \qquad \text{eq. 3}$$

Where TP and FN represent respectively the true positive and the false negative.

- Specificity

The specificity (True Negative rate) measures the negatives' proportion that is correctly predicted. It could be defined by eq, where TN and FP represent respectively the true negative and the false positive.

$$Spécificité = \frac{TN}{TN+FP} \qquad \text{eq. 4}$$

- Accuracy

The Accuracy metric has been usually used to evaluate the classification model efficiency and is defined as follows:

$$\text{Accurcy} = \frac{\text{TP}}{\text{TP+FP}} \qquad \text{eq. 5}$$

Where TP, TN, FP and FN represent respectively the True Positive value, the True Negative value, The False Positive value and the False Negative value.

D. Segmentation Results

The evaluation of the proposed segmentation approach was carried out over the MICCAI 2020 challenge (BraTS 2020). Fig.4 present respectively segmentation result for three different cases from the Brats 2020 dataset. The first line of the figure illustrates the input images, the second line presents the Ground-truth MR images and the final line shows the segmentation results of our proposed method.

For segmentation results, we evaluate the following three parts: Whole Tumor (WT) regions involve all tumor four labels (1-4) or sub-regions including (Necrosis, edema, enhancing and non enhancing tumor, label) Tumor-Core (TC) involves all tumor sub-regions except edema(labels 1,3and 4) The Enhancing-Tumor (ET) include only label 4

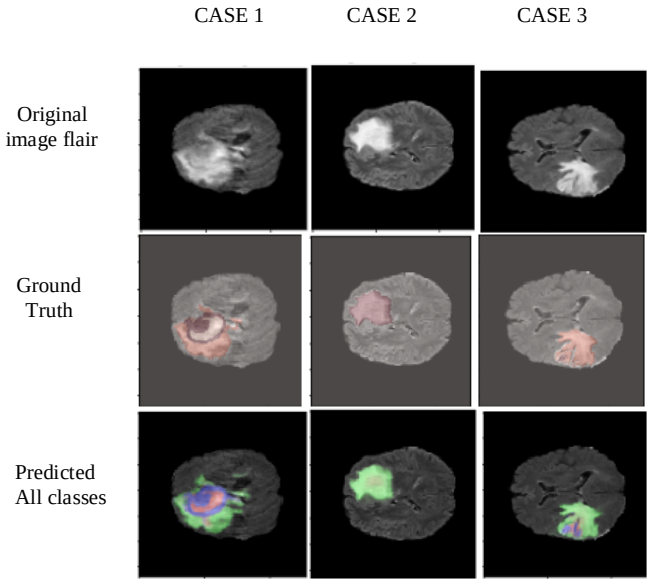

Fig.4: segmentation results of 3 subject-cases from the Brats-2020 dataset

Fig.5 shows the segmentation results of a Brats20 image from the validation database

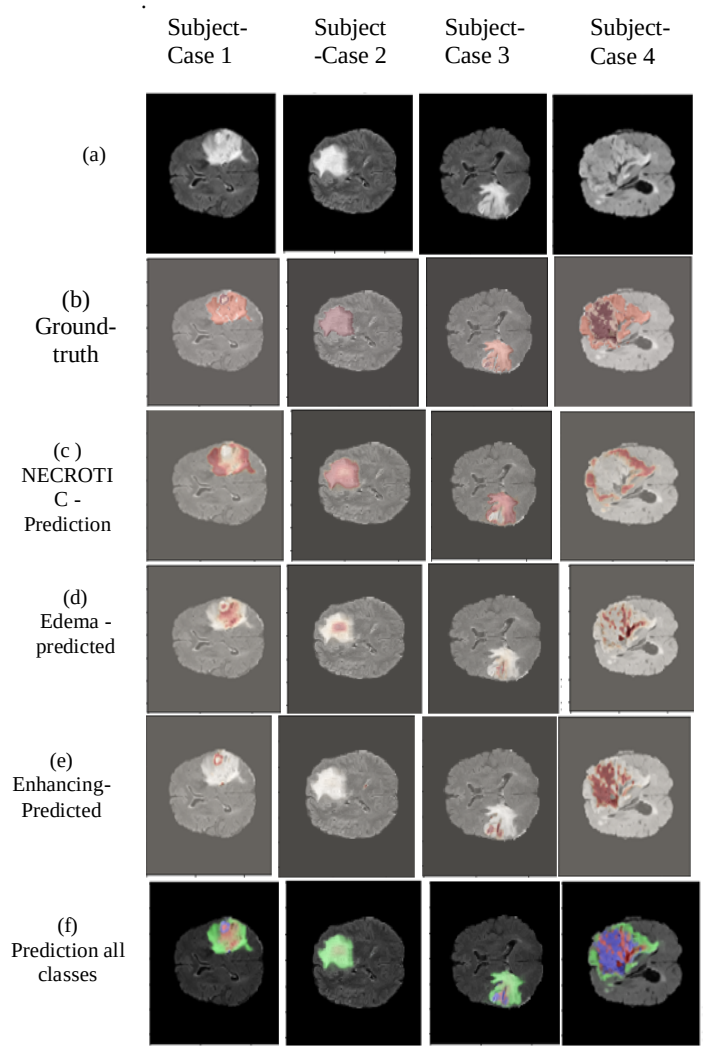

Fig.5: (5-a): Glioma segmentation results from the validation data base Input MR Image of the four subject-cases(1,2,3,4) ;Figure (5-b) ground truth of the four subject-cases(1,2,3,4) ;Figure (5-c) Necrotic predicted of the four subject-cases(1,2,3,4) ;Figure (5-d) Edema predicted of the four subject-cases(1,2,3,4) ;Figure (5-e) Enhancing predicted of the four subject-cases(1,2,3,4) ; Figure (4-f) Prediction of all classes

E. performance evaluation

Accuracy of segmentation is confirmed by visual assessments by physicians, and by quantitative comparison with manual segmentation by an expert. The reliability of the algorithm is confirmed by tests on images of variable quality, acquired on different machines and according to different protocols.

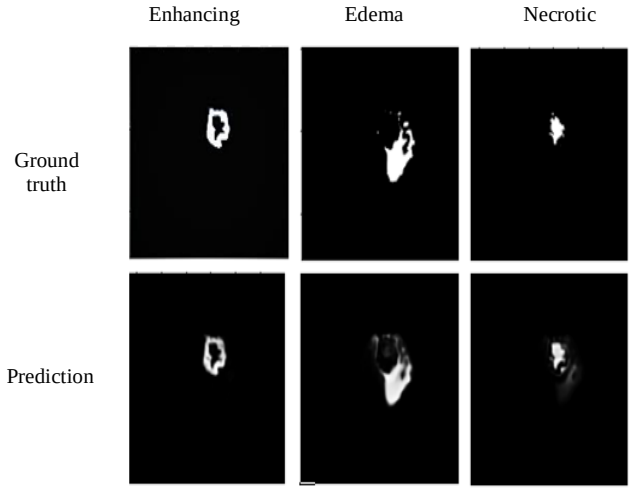

Fig.6: Training segmentation results

In Table 1, we provide the DM coefficients for the three regions (complete tumor (WT), tumor nucleus (TC) and enhanced tumor (ET)), the sensitivity, specificity, accuracy and precision obtained from which the results of segmentation are given respectively by fig.6.

Table1: Validation metrics for segmentation results

Method	**Dice score(%)**			**Sensitivity (%)**	**Specificity (%)**	**Accuracy (%)**	**Precision (%)**	**Mean_io_u(%)**
	ET	TC	WT					
3D U-NET	92.46	87.55	88.04	99.16	99.78	99.34	99.36	83.37

We tested the proposed approach on the whole ‘BraTS 2020’ training database. The quantitative evaluation of the segmentation results of the complete tumor, the enhanced tumor, and the tumor core, using the previously defined validation metrics, is given in Table 1. Fig.7 shows the dice loss and accuracy score recorded for each epoch for 3D U-Net

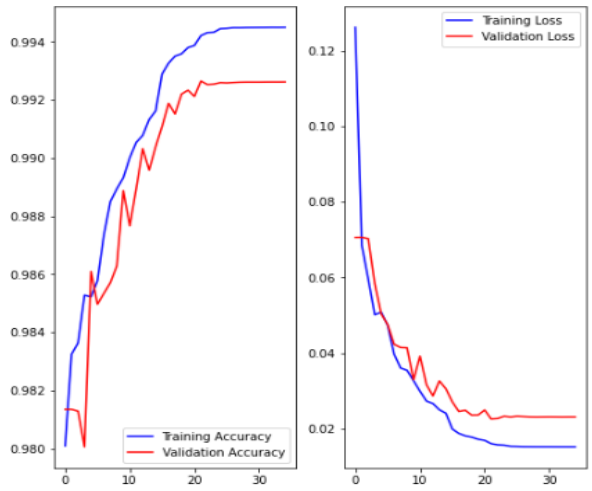

Fig.7:Dice Loss and Accurcay Graph of 3D U-Net

In this section, we are interested in performing a comparative performance study with the most recent approaches reported in the literature using the same training database. We calculated the mean value of the "DICE" similarity measure of the complete tumor, the enhanced tumor and the tumor core. The results are presented in Table 2. According to this comparative study, the results obtained confirm that the proposed segmentation approach outperforms the other methods. As indicated in several studies, the most difficult task in glioblastoma tumor segmentation is the extraction of enhanced tumor sub-regions (Enhancing-Tumor (ET). The proposed approach gives promising results on the extraction of different regions and outperforms comparative approaches.

The Dice scores of the 3D U-NET method in the three categories of ET, TC, and WT are 92.46%, 87.55%, and 88.04%, respectively. Compared with Attention U-Net, VTU-Net, SwinBTS, V-Net, Tran-BTS, U-Netr, 3D U-Net has obvious improvement. It also has a certain improvement compared with methods using transformer structures, such as Attention U-Net. We can also see that the improvement in the 3D U-Net model in Table 2 is relatively limited compared to the SwinBTS, Tran-BTS, U-Netr and VTU-Net model, so the standard deviation of the Dice score is compared, and it is found that the standard deviation of the 3D U-Net model is much lower, indicating that the model is in a large number of segmentation tasks. The model is much more stable and does not exhibit large deviations

5. CONCLUSION

Through this work, we have proposed a approach for a multimodal segmentation of brain tumors via MRI images. The proposed approach is based on the deep learning of a cascaded Auto-encoder type network inspired by the 3D U-Net architecture. Through this work we have unveiled the results obtained by our segmentation approach. Our approach has achieved a segmentation which is judged, according to the similarity measures used and the qualitative results observed, as very encouraging in view of the increased difficulty by the deformations of glial tumors. A comparative study with recent methods in the state of the art has been carried out at the end of this work

Table 2: Comparative study with state of art segmentation method

Method	Dice coef(%)		
	ET	TC	WT
AttentionU-Net (Brats2020) [15]	71.83	75.96	85.57
VTU-Net (Brats2020) [16]	76.45	80.39	88.73
SwinBTS(Brat2020) [17]	77.36	80.30	89.06
V-Net (Brats2020) [33]	68.97	77.90	86.11
Tran-BTS(Brats2020) [34]	76.31	80.36	88.78
U-Netr(Brat2020) [35]	71.18	75.85	88.30
Proposed 3D U-Net	**92.46**	**87.55**	**88.04**

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