Implementation of Cascaded CNN architecture for Fully automated Multiple modalities-based Brain tumour segmentation using selective overlapping patches.

MSc Research Project
MSc Data Analytics

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MSc Project Submission Sheet

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Abstract:

In this paper, the study aims to design & implement the fully automated High & low grade-based segmentation of glioblastomas brain tumors using Deep neural based CNN architecture. The proposed model utilized selective attention-based techniques which uses sizes of varying receptive field to identify the critical objects from the image in the successive layers of the CNN architecture. As a result, using the selective attention-based strategy in the CNN model provides us to extract the maximum number of appropriate features from the MRI images. The paper also addresses the two major challenges in the MRI images that is imbalance in class problems & identifying the spatial relationships amongst the patches in the images, for the foremost issue we suggested the uniform sampling method on Image patches(slice) & utilizing the class weighted based loss entropy function on the results of the segmentation for analysis. To address the second issue, we would be using the overlapping patches since it founds to be more effective in improving segmentation results against the adjacent patches as this would covers both the global and local features in the entire MRI images. The paper uses different modules of the CNN based architectures in order to maximize the feature extraction from the image with multiple skip connections with the modules. Further the results were evaluated on the basis of Dice score on different views and grades of tumor in the MRI image. The deep learning models were implemented using the BRATS 2018 datasets for the experimental analysis. The paper also utilizes the Unet architecture as an alternative methodology to segmentation process and compared with the proposed model in term of implementation time. Finally, the End-to-End automated deep learning-based CNN model shows the accurate and consistent segmentation results as compared to traditional methods which can be further utilized for the research proposed and clinical trials.

Keywords

CNN architecture, BRATS, class weighted, Overlapping patches, fully automated, Deep Learning model.

1. Introduction

1.1 Motivation

A brain tumor is a gradually developing unusual and untypical cell which is located in the middle of canal part of the brain (Young, R.J & Knopp, E.A, 2006). According to the survey of NBTS1, there could be more than 4.200 patient in the United Kingdom suffering with primary brain tumors (T. LogeswariT. & M. KarnanM, 2010). In United States of America around 1300 patient die with 2900 individual enduring from brain tumor-based disease (Singh, A, et al., 2012). Furthermore, depending on the age, and individual health condition a tumor can develop in any part of the brain.

With the expansion in the accessibility of significant quantity of data from the various medical devices such as Device recording, ultrasound, X-rays, MRI, and PET with the increase in the numbers of patients in the world this arise to introduce new innovative methods for treating patients. Glioma’s tumors are the most frequent type of original main brain tumors found in adults which accounts for 81% of the malignant brain tumors and 45% of remaining primary brain tumors (Schneider, T, et al., n.d.). Survival rates of this type of tumors in the patients ranges from 0.05% to 4.5% which contributes to the cause of death (Ostrom, Q.T, et al., 2014). Our paper proposed the technique which can segment the brain tumor of Glioblastomas type, which belongs to the category of gliomas tumor.

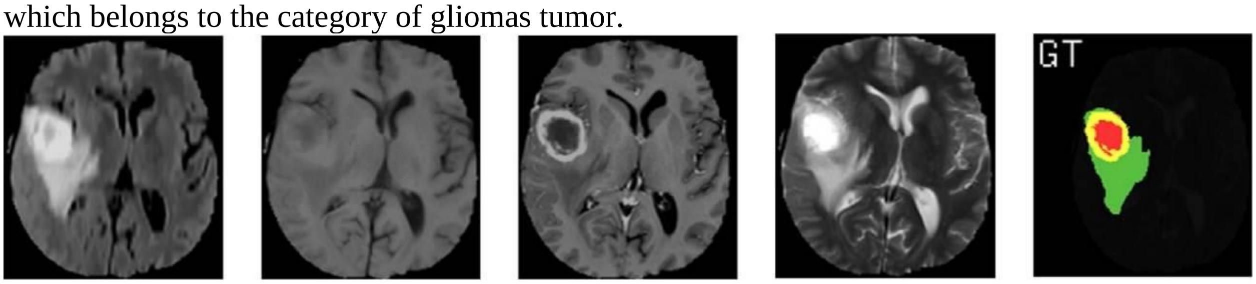


Fig 1.Different categories of Gliomas tumors modalities images

Radiologists utilize the MRI technique to generate the multimodal images to identify different regions of the tumors in the brain tissues (Anon., 2001). Furthermore, (Işin, A, et al., 29 August 2016) the radiologist developed 4 different MRI modalities pictures for Glioma’s tumors T2-weighted based attenuated inversion recovery (Flair), T1-weighted based contrast-enhanced (T1c), (T2) & (T1) weighted based for each individual patient. Then by performing pixel wise operation on very part of slice, corresponding regions of the Gliomas tumors needs to be segmented until the complete 3D images of the brain images gets separated into different significant locations as discussed in the ground truth information of the MRI image dataset (Fig.1). This generated segmentation map is then further used for the medical diagnosis procedures & clinal trials, pretreatment planning and to acquire the information about tumors whether it’s in growing or decaying stage. After the advancement in the field of computer vison in 2012, when Alex net had been developed by the team and the model was able to surpass the earlier traditional methods and could provide the best results in the areas of image recognitions. Many deep learning models has been put forward after 2014 in the study of brain tumor segmentation and varying architectures and model parameters (Havaei, M., et al., 1 January 2017) (Pereira, 2015).

The following table illustrates the different challenges involved in the paper during our experimental analysis, it also discusses how the challenges has been addressed in order to obtain the reliable and accurate prediction on the segmentation results. The tables summaries the goals of the paper which is to design and implement the fully automated End to End deep learning-based brain tumor segmentation model which is based on new convolutional methods. The proposed framework would be able to segment the Glioblastomas tumors of both low- and high-grade tumors.

1.2 Research Attributes:

Sr. no	Research Challenges	Research Objectives/Contributions
1	Glioblastoma's tumors consist of three other sub regions along with the healthy tissues i.e., Peritumoral Edema, Necrotic & Non enhancing tumor along with Enhancing tumor. Both the tumors' Gliomas and Glioblastomas occupy the surrounding areas of the tissues instead of displacing it creating the indistinct and fuzzy boundaries, also in the MRI images Gliomas tumor looks pretty much similar to the blood spots, Gliosis, and inflammation. The paper proposes the CNN model which could address this issue by extracting he complete feature representation of the Glioblastomas tissues which helps the model to predict even the smaller, blur patches of the regions of the fuzzy boundaries	First aim of our paper is to propose the implementation of the Deep Learning models based on 3 different CNN based variant architecture which includes two phases of modules in each. The results provided from this CNN architecture would be more accurate and consistent in predicting the segmentation. This would address the solution for the first and second part of our research challenge.
2	The second challenge is common on the image's segmentation problems using CNN model which includes minimizing the features during the layers of convolution and pooling layers, to overcome this challenge we used multiple long and miniature skip connections within the modules of CNN, so while implementing, the model reuse the high-level features like objects, size, shapes and low-level features like borders and lines in the patch. This addition of both the features in the CNN architectures helps to better predict the frontier parts of locations.	
3	The third challenge in the deep neural based CNN architecture is that they won't perform well on the highly imbalanced datasets such as BRATS where 98% of the dataset include labels of healthy tissues i.e., non-tumorous regions of MRI. If we try to train the CNN Model with such imbalanced dataset the prediction may got bias towards the healthy class of tissue with low sensitivity. In Medical and neural science industry, sensitivity play an important critical role towards the decision of the clinal trail support system, thus, to address these issues we utilize multiple class weighted techniques with addition of the weight to the loss function. This would help jus to alter the contribution by adding specific weight to the outcome which proves to be efficient for segmenting image patches and overcome the imbalance problems in the medical datasets.	To address the issues of unbalanced in the datasets we would be implementing the class weight technique on the experimental analysis if the segmentation results. This involves providing the specific weights for 4 different sub regions which also include equal sampling of the patches. This would help us to overcome the third issues
4	The fourth challenge in the CNN architecture is that they won't consider the relationship amongst different patches of the Image which limits our image segmentation model to predict tumor more accurately. To address this challenge overlapping patches has been used to extract global features which includes the relationship amongst the patches along with their position and pixel intensity and label in the entire MRI images against the intersection of the patches at it adjacent.	With the utilization of the Overlapping patches though our CNN architecture provides better & accurate results, here the prediction is arrived using the output from its neighborhood for each pixel. So, the final prediction results from different patches prediction around same pixel image. Also, this would add the data augmentation of the datasets.

Table 1. Research attributes of the project

2. Related work

Primarily patter recognition and Artificial intelligence-based research paper were relied on the hand-crafted features i.e., feature engineering and models derived from mathematical estimation from period till 1990s in which the researcher utilized the training data in order to extract the input features. Further during 2000s much research conducted which shifted the trend from feature engineering to discriminative models which extract various feature from the large amount of data and utilize the classifier to differentiate better classes, those methods were based on approaches using threshold values (Gibbs, P, et al., November 1996), classification and clustering methods (Fletcher-Heath, L.M, et al., January 2001)(Bhandarkar, S.M & Nammalwar, P, 2001), region-based techniques (Anon., December 2005), and edge-based techniques (Lefohn, A.E., et al., 2003). These solutions are often ineffective, require frequent human intervention (e.g., region expanding), and are susceptible to noise (edge detector). Furthermore, these solutions compute a large number of features which are computationally highly overpriced and consumed more memory.

CNN based incremental Deep Learning model (Bennaceur, et al., November 2018) was developed to identify the glioblastomas tumor from the brain images. It utilized the combine method of ensemble and Deep learning to improve the error rate during the training time of model. Hyperparameter tuning has been utilized along with fixed threshold for the model using Brats 2017 datasets. The dice score evaluated by the model was 0.87 with no data augmentation and future processing. Using the images from the (Ziebart1, et al., 2021) CLE datasets for prediction of the tumor has been proposed, these datasets include 25 patients with distinguish tumor types and grades. Here the tissues were first analyzed prior to modelling and later used two phased CNN based Deep neural model for estimating the location of tumor. Around 13972 CLE images were taken using extraction process by model. Further the model was implemented using the prediction from two phase and were evaluated the performance, the model shows the accuracy of 90.4% on testing images with the AUC score of 0.92. The model shows the accuracy of 85.5% on the prediction of those testing datasets. The model utilizes the k=5 based cross validation method and with the final implementation, the model was able to score 0.94 confidence rate with accuracy performance of 98.6%.

Combined the deep learning and machine learning (Bal, et al., 29 June 2021) based feature engineering techniques were utilized to segment the boundaries of the brain tumor. Here first the CNN model was used to extract the feature using feature engineering on different tumor images. Later the output is fed with those extracted input in order to improve the segmentation performance. Three pathway-based CNN architecture were utilized to extract both the local and global features, this is to detect the high- and low-level feature like shapes and boundaries of the tumor regions using features extracted using feature engineering. handcrafted based. The model was implanted directly over 4 different image scans of tumors for extracting the features. The model performance was evaluated using dice score and sensitivity using BRATS 2018 datasets. Later the model is trained further augmentation and normalization of image has been performed.

In 2006 a distinct form of prediction technique defined by deep learning has introduced which utilized huge amount data to extract multiple low-level based features like lines and edge of images with varied rotations and then adding those via a similar way to developed high level-based features like shapes, boundaries & different object of the images, furthermore the deep learning-based approaches were used to for brain tumor segmentation research from 2014.

(Havaei, M, et al., 1 January 2017,) proposed an automated segmentation approach based on cascading of CNN architecture method for varied modalities-based brain tumor images which is more refined work of the earlier techniques (Axel, D, 2014) based on neural network. These cascaded based CNN network utilized two path technique which were then trained on different phase in order to extract both small local and large context based global features from the images. They also used 4 MRI patterns as the input channels along with input of 2D axial image patch and various input patches with varied input patches. Additionally, they suggested two training steps to overcome the class imbalanced issue as well as correcting the patches that are more skewed towards the healthy or wrong class of images. Further the connected components inside the skull were eliminated by employing the threshold method during post processing approach. While utilizing the GPU for the cascade implementation it took around 180 seconds for segmenting the complete brain image (Havaei, M, et al., 1 January 2017).

(Chang, 2016) constructed a CNN architecture which is based on two principles 1) fully connected CNN network which estimates the size of dense matrix output as employed in the original size to input (Long, 2015). 2) Features concatenation, in which concatenation of input MRI images is done at the concatenation layer before the output. This approach was employed by in their new variant CNN based implementation (Yang, S & Ramanan, D, 2015). Further the architecture also included 7 layers apart from up sampling & concatenation layer. Here four channels (T1, T2, T1c, Flair) of the MRI images are used as an input to the CNN design, this design used 0.93 seconds for the segmentation of entire brain image with GPU utilization.

(Ellwaa, A, et al., 2016) developed and adaptive approach using random forest tree-based method including 100 trees in each with a depth of 45 which uses 328 features extracted using MRI images, those features were based on gradient and different views-based features, 4 channels. This design takes 4 channels (T1, T2, T1c, Flair) of MRI as the input. This iterative based technique works by adding 5 patients to the training data during every iteration and then proceeding towards the random forest until the training phase get reached to at least 50 patients after which the iterative process gets terminated.

(Kamnitsas, K., et al., 2016) created a 3D based CNN architecture-based model for segmenting the brain tumor relying on the CNN model performance. These 3D CNN design incudes 11 layers of dual path and the input to those models were the 3D MRI image with distinct patch size for each pathway, during post processing stage to remove the misclassified regions they introduce a conditional random field to the design which also provides spatial regularization. Furthermore, they included the residual connection to their network, however this new extended model won't provide significant performance over the original model. This 3D based CNN Model took around 24 hours for the training with the GPU implementation and 35secinds to segment the complete brain image during testing.

In contrast to (Zhao, X, et al., 1 January 2018,) who employed conditional random field during the post processing stage, developed a segmentation method which is based on adding the CRF and CNN layer in one network. The researcher used 3 MRI image type to create the three CNN design network with each using 3 pathways a similar to (Kamnitsas, K, et al., 1 February 2017), here each pathway is further trained on different image patches and slices from different views like coronal, sagittal and axial. The estimated results from three views are then merged in testing phase using a voting technique, furthermore these three networks took around 12 days for training utilizing the GPU implementation where individual model takes around 3 minutes of average time to segment the entire MRI brain image in individual view.

In the previous work suggested by (Rachida Saouli, et al., November 2018) implemented a fully automated based segmentation of brain tumor which is based on the techniques of incremented optimization i.e., at every cycle of model training a block is merged on the previous block automatically. The technique used in this tidy were based on two principles 1) Addition of layers improves the performance of segmentation 2) Two or three consecutive layers based Deep learning models provide better segmentation results. Automated machine learning (Barret Zoph, et al., 2018) is a new field of advanced machine learning (AI) which aims to create a model based on machine learning without any human interaction The suggested segmentation algorithms are trained on Axial view 2D based image Patches (32 x32). To distinguish the complete MRI image of brain tumor utilizing GPU implementation, the training period goes around five hours, and for the testing purpose the time was in the range of 19 - 21 seconds. The GPU memory is a restriction of this strategy; after a given amount of time of training, the memory is swamped by the additional newly blocks. To address such problem, we implemented a new idea called modules to replace the extra blocks in this study. The interconnection of the brain's regions respectively: retina, T1 V2, V1, V4. inspired these modules.

(Mlynarski, P, et al., April 2019) design an automated brain segmentation method based on 6 different CNN model, where each model consist of 3-5 CNN architecture and this each model were trained individually on the single MRI image. The suggested 3D based method is trained by concatenating features from different view of the brain image with two or three multimodal based tumor types. These approach of using additional features maps to the input of the architecture of other CNN model is utilized by (Havaei, 1 January 2017) to overcome two issues 1). Larger context information for this they used CNN architecture that extract the rich details of the image through enlarging the receptive field size. 2) Unbalanced data, for this they used loss function as weighted cross entropy.

(Kumar, et al., 2019) used the classification-based approach which was based on the technique of weight correlated based feature extraction which used the principles of Bayesian multivariate based Deep neural method to better the brain tumor based false alarm rate in diagnosis, here first the feature subsets were selected from the tumor image segmentation, and it uses the Bayesian based deep learning approach for estimating the error rate and further improving the segmentation accuracy of model. The above method was implement using the JAVA language and evaluated using parameter such as DDR. This gives the researchers new method of utilizing the classification base deep neural approach for image segmentation. (Zeineldin, et al., 05 May 2020) develop a classification based neural network which includes different BRATS dataset which were pretrained on the GAN s network, it is used learn and extract new features form the MRI images. Moreover, this newly learned and trained model replaced the existing CNN network to distinguish the tumor from the brain images. It utilized weighted parameter along with 6 different layers with the model further operation performed on the image includes augmentation and normalization process. The study utilizes the data of 233 patients each with 13 different images for modeling and used cross validation during evaluation. This model resulted in 93.5% accuracy. The input to the model is 64 x 64 size due to GAN network restriction.

Image processing (Mallick, et al., 15 March 2019) which includes the compression of the images was developed for the tumor segmentation, the paper uses the hybrid principles of wavelet encoder which includes feature reduction & image decomposition. This technique was utilized to know the feature size in order to improve the classification model. The model was able to achieve the accuracy of 96.2%. YOLOv3 (Hossain, et al., 04 June 2021) based new development deep learning algorithm were used for tumor detection. YOLOv3 is the advance image recognition method which uses the principle of antenna-based receiver. Using this technology, 50 image samples were built along with the post processing using delay x sum algorithm. The resultant images were further process to be used of the training and validation datasets. The datasets were divided into 80% for training purpose, 10% for testing and remaining 10% for validation of the model. The model implemented using YOLOv3 approach get the accuracy of 95.6% along with F1 score 94.3%. The accuracy obtained for the trained model were around 96.7%. This approach was found to be meaningful in the medical image analysis field.

Symmetricity of the MRI images was used (Qin, et al., June 2020) by the CNN model to enhance the quality of the feature extracted using the CNN model from MRI images. Here the CNN model attempt to detect the symmetry in the MRI images in the low- and high-level features of images near to tumor locations. Further, this symmetry feature was added within the CNN layers in order to detect the tumors in the image. This approach of segmenting obtained the dice similarity of 0.85 score.

Here the paper (Zhou, et al., 26 January 2019) uses the DenseNet approach in order to solve the issue of different size and shape of tumor and their locations in the brain image. The model extract feature based the axial view of the image(slice) and later were fed to the input of the model. This utilized 422 different MRI images of patients with variant tumor type each. DenseNet transforms the feature correlation within the images into 2D Tensors. This model was further evaluated and were able to get the accuracy near to 80-81% for each three types of tumors. Here the researcher employed LSTM built in memory approach for embedding the features.

2.1 Work related to unbalanced datasets & overlapping patches.

The referenced works, as a synopsis of related literature works by (Ellwaa, A, et al., 2016) (Mlynarski, P, et al., April 2019), tackle the core challenge of completely automatic brain tumor segmentation in various methods. These includes issues related to 1). Unbalanced data which was solved using two methods first is equal sampling and later using weighted cross entropy function 2) Context modelling of high-level features which includes different shapes and size of tumors in the brain location, to overcome this small 3d image patches has been used and feature were extracted. Thus, using this the CNN model could extract feature from low- and high-level features. Multiscale methods also used for image segmentation.

3. Methology

Our proposed End to End automated deep learning model-based segmentation pipeline include three working flow 1) Three pre-processing of images. 2) Segmentation operation of the overlapping patches in the MRI images using three variant CNN architecture. 3) Two post processing of the images.

3.1 Datasets

We have used BRATS 2018 datasets for our testing and evaluating experimental analysis which include real world patients' data. The training dataset includes the patient's data of 210 higher grade and 75 low grade tumor images. Each patients MRI sequence includes 5 scanning images (FLAIR, T1, T1c, T2, GT) and ground truth 4 segmentation labels. The ground truth labels are not included in the BRATS 2018 validation dataset, which includes 66 images of patients with undetermined grades.

Label 0: Background
Label 1: Necrotic and Non-Enhancing tumor
Label 2: Edema
Label 3: Enhancing tumor
Dataset source Link - *https://www.kaggle.com/sanglequang/brats2018*

3.3 Alternate Methology - Utilizing Unet for Brain tumor segmentation.

Here we have suggested an alternate method for segmenting the brain tumor which is based on the approach of utilizing the Unet model which is based on encoder and decoder-based CNN architecture. The 3DUnet based approach used one encoder and 2 decoders based fully connected CNN architecture in order to segment different brain tumor images. Below fig depicts the flow working of the layers involve in the architecture.

Drawback of this methodology – The implementation would require 8-9 hours to train the model using UNET based architecture using the GPU whereas our new approach would result in faster segmentation of brain with less time than this approach to segment the entire image.

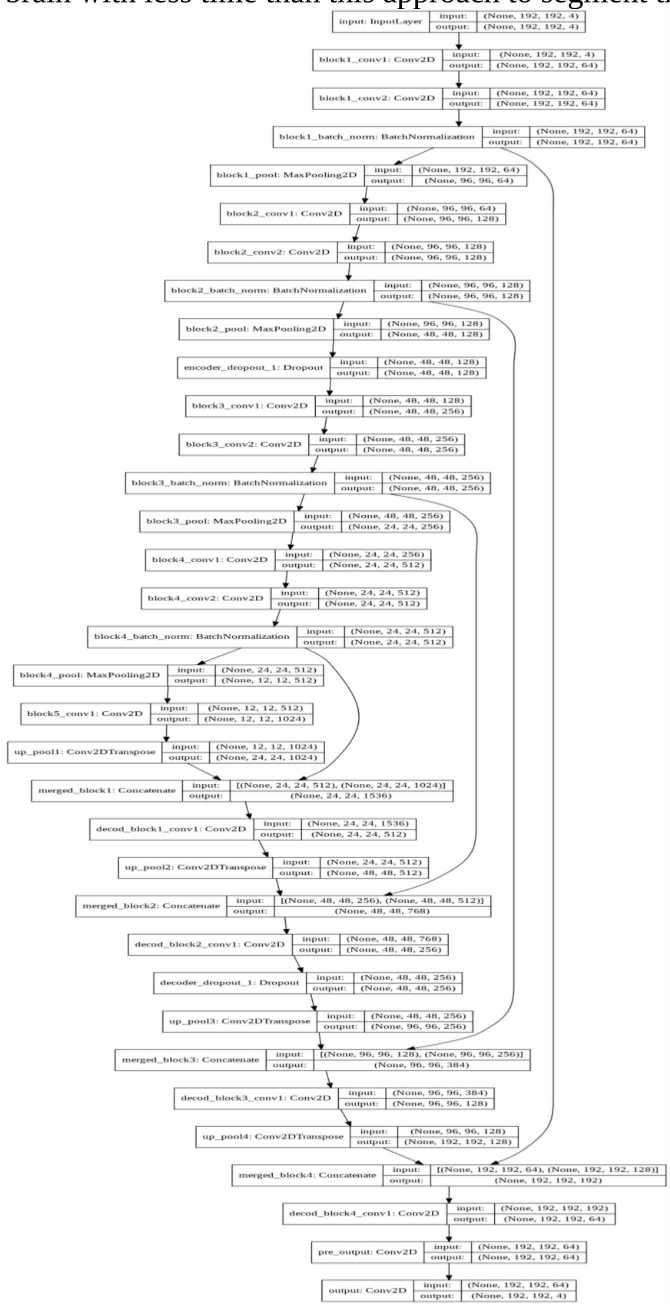


Fig 2.Unet CNN Architecture used for brain tumor segemnation with encoder & decorder

3.2 Core Methodology based- Pre-processing

The BRATS dataset includes MRI images which has been processed using different medical devices and protocols, thus we need to first enhance the quality of the images and remove the noise from the images. We would be employing 3 stage preprocessing technique in order to overcome the issue of varying intensity ranges in the MRI images. We would be applying three pre-processing steps. The normalization process of each slice (2D axial image) is stated below

1. Eliminating the 1% of lowest and highest-level intensities, this strategy would aid in eliminating the noise at the histogram tail. This method was used in earlier research papers which resulted in good results.
2. In the second step we subtract the mean and further divide it by the standard deviation of all channels with non-zero values, using this we are able to center and scale the data in same range. We attempt the bring the value of mean intensity and variance within the range of 1 & -1.
3. In the third step, we aim to separate the background (non- tumorous) with the tumors locations by setting the least value to -9, Using the integer ranges between -5 and -15 has fits our CNN architecture design. During the 2nd stage of preprocessing which resulted in the mean value within the span of [-1,1]. i.e., the locations which are healthy and non-tumorous part of brain intensities were put forward in the range of [-1,1]. Since in the MRI images the intensity of the background pixels of MRI image data is uniform to zero, we tend to normalize the histogram of the MRI image by proceeding towards the zero pixel to outside the range of [-1,1]. This strategy would allow us to segregate the zero pixels background (non-tumors regions) from other regions of brain MRI image. Accordingly, -9 bin found to be appropriate in training and testing phase with better results.

3.3 Overlapping patches

Our CNN architecture design is based on 2D image patches, in which the architectures aim to predicts the pixel which is the core of the 2D patch. Many studies employ the concept of Adjacent patches which involves utilizing patches (collection of pixels) that are adjacent to one another. However, the limitation of CNN employing adjacent patches is that CNN neglect the fact that the patches around the adjacent region's collectivity contribute the complete image. Thus, to address this issue and improve the accuracy of CNN architectures, we would be extracting the overlapping patches in order to support the model in covering the local and global features. CNN works by the convolution operation between each kernel with the image next equal match after which the kernel proceeds towards the next patch to make up the entire image. The CNN model would therefore aim to categorize these adjacent patches into distinct classes (four sub regions) during the learning phase resulting in a final segmented image with only one pixel prediction per patch. However, considering the Overlapping patches, the final predicted segmented image would be the summation of five prediction per patch, here the estimation from the other four pixel affects the first pixel prediction and vice versa. Thus, using Overlapping patches support to build the relationship amongst the patches. While using the approach of Overlapping patches, the CNN architecture would be able to predict and identify the larger global context while utilizing the smaller patches. Due to the fact that each pixel labels are predicted from its neighborhood. Overlapping patches give better accurate results then adjacent patches.

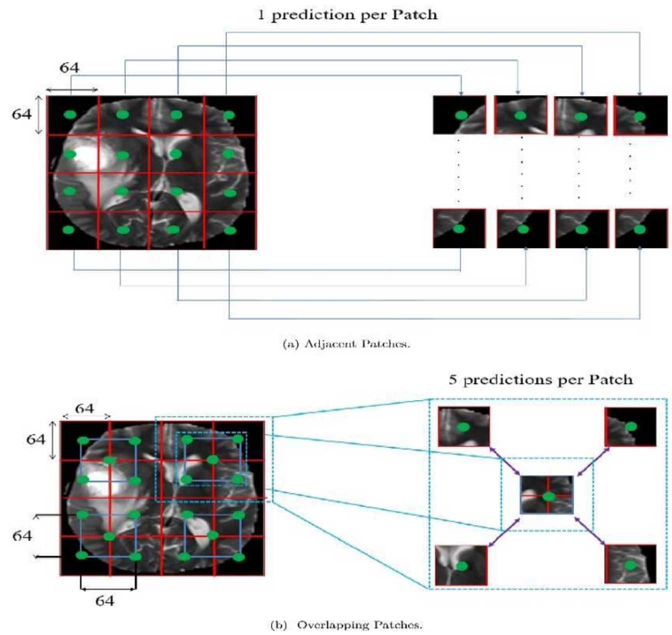


Fig 3. Feature extraction based on selecton of overlapping patches with adjacnet patches

3.4 Models & CNN architectures

The MRI images shows the contrast between the brain soft tissues; however, these images do not reveal the borders of the brain regions clearly making brain looks like a single monolithic mass. The proposed model is utilized to extract only the tumorous parts from the entire brain images, this requires the model to extract more feature related to tumors and healthy tissues. To overcome this problem, we would be proposing three variant CNN architecture which would maximize the feature representation i.e., extracting only the relevant feature form the image inside the model. These CNN models are based on the technique of Patch-wise approach. So, the CNNs models takes as an input patches with size 192 x 192 x 4, where 4 represents the four MRI sequences (i.e., T1, T1c, T2, FLAIR). Here three individual architectures would have 2 modules in each. Constructing 1st module which has six different phases of operational layers in it.

3.4.1 Module's architecture:

a) Building the 1st Module – Sparse Connection:

1st Phase – Take the input as 192 x 192 x 4 image size, where 4 represent the four MRI sequences (i.e., T1, T1c, T2, FLAIR).

2nd Phase – Here the convolutional operation has been performed to extract the different level of feature through the entire image, here trainable parameters has been used for the convolutional. We have proposed 2 convolutional layers of 3 x 3 kernel size for better performance using Relu as no linear activation function.

3rd Phase – In order to minimize the feature map, we would be utilizing the 2 x 2 Max pooling layer, Max pooling layer extract the maximum values form each non overlapping layers of the image of feature map.

4th Phase – Here we have again used the 2-convolution layer operation of filter size 32 in order to extract features form the output of Max pooling layer along with computing of features map.

5th Phase – Up sampling has been performed here in order to scale the image form lower resolution to higher resolution feature map, these works but adding the zero padding in the image as per the stride parameter. Up sampling is to scale the feature maps from phase 2 and phase 5 since both are not at equal scale.

6th phase – In this layer the concatenation has been performed from the extracted feature maps from 2nd Phase and 5th Phase of module has been concatenated.

The above 6 operational layers contribute the 1st module of our architecture which is also termed as sparse connection module. This module has 2 output one from the 6th phase and other output from the connection made as back propagation to the 1st Convolution layer.

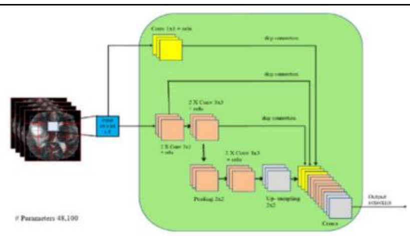
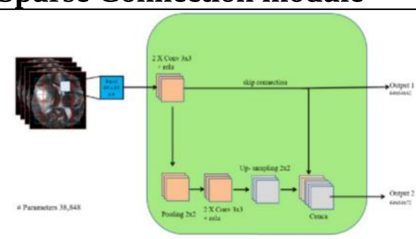
b) Building the 2nd Module Dense Connection:

Here, 3 x 3 Convolution layer with Relu activation function has been added along with the size of 1 x 1 Convolutional layer with SoftMax activation function, this is to classify the images into 4 sub classes i.e., 3 tumors and 1 healthy. This module contributes towards the dense connection has well as perfume concatenation of the low-level feature (lines, edges) with high level features (Shape and boundaries). Here for computing the real error for each class we have used parameters such as stochastic gradient descent optimizer with a learning rate 0.001 and momentum of 0.9 with cross entropy loss function.

Using these two modules the model would be able to extract the distinguish features from the input brain tumor BRAT image. Two modules which are used here are:

Sparse connection Module: This module applies the approach where the convolutional layer subset has been connected with each layer. The sparse module has 1 input and two output.

Dense connection Module: This module utilizes two approach 1) 1 x 1 convolution operation 2) Dense connectivity. This module is responsible for concatenation of all low-level features and high-level features of feature maps before the output in the concatenation layer.

Dense Connection module	**Sparse Connection module**
	

Tabel 2.Shwoing the Sparse anmd Dense Module CNN architecture

3.4.2 CNN architecture:

1st Architecture - Sparse Multi connection: This architecture consists of cascading of 2 modules of Sparse CNN connection with two outputs. The foremost module firsts output has been concatenated with the second module pre output concatenation and the output from the second module has been put has an additional input to the second part of sparse module. This model architecture includes 127,876 parameters

2nd Architecture - Input Sparse Multi Connection architecture: This architecture has the same implementation as above sparse Multi connections. Here the difference is only we have added the input directly as another feature maps to analyze the effect of directly adding the input. This architecture includes 130,180 parameters

3rd Architecture - Dense Multi Connection architecture: Here the first modules consist of three Convolutional layers along with the up sampling done at the output for scaling. Further the concatenation has been performed from all the three convolutional layers and output for the up-sampling layer to the final output. The second module has been implemented in the similar way. This architecture has 121, 181 parameters.

Final Step – Eventually after this architecture has been implemented using two modules (Sparse and Dense Connection). The addition of 1 x 1 x 4 twice consecutive convolution layer has been inserted before the final output to extract the merge features. This is implemented because we have multiple concatenated feature maps from various level of second modules as well as from the input patches which has raw pixels, so we have the diverseness of feature maps along with this raw input pixel which require to be merge along with the similar level before SoftMax function classify them into 4 classes.

3.5 Class Weighted Technique

Since most of the data acquired from the medical devices consist of imbalanced datasets which includes our BRATS dataset also which has almost tumorous regions of about 2% in the datasets and healthy tissues contributes to 98% of datasets which will create a bias towards majority class during training with such datasets, so to overcome this issue we would be using two techniques while implemented during training phase. 1) Using axial view randomly extracting the patches with individual class having an equal count of train patches. 2) By using class weighted approach we would be giving the specific weights to the output of each class.

3.6 Post Processing

Two post processing approach has been implemented in order to eliminate the non-tumorous parts form the segmentation results of our CNN architectures model.

1) ***Post processing 1*** - We would be using the threshold values within the range of 50 to 200 in order to remove the misclassified, smaller, no tumor regions from the architecture results. The pixel value of 110 found so be better threshold values with good results. Thus, the components found to be smaller than that pixel value of 110 would be removed from the architecture results.
2) ***Post processing 2*** – In this step we would be performing the morphological operation on the images. This includes operation which apply structuring element to the images and create a similar size output image.

4. Implementation

For the implementation of our End-to-End fully automated based deep learning model, we have used open-source python library keras which is used for high level deep learning projects and TensorFlow as the backend technology. The TensorFlow utilized the GPU optimization through the GPU in the Google colab pro software. For the computational, prediction and operations part we had utilized python environment on Windows based 64-bit Operating system with specification includes 8gbDR4 RAM, AMD Ryzen 5 3500U with Radeon Vega Mobile GFX 2.10 GHz processor and 2 GB of AMD Vega RADEON graphics utilization.

We have used Adam as an optimizer of our CNN architecture as this play a significant role in our training model with the learning rate of lr=1e-5. Since our BRATS dataset consist of 285 MRI image, hence, to overcome the problem of overfitting we had use the concept of overlapping patches which is used to balance between the training data with the other classes of 4 subregions of tumors. Furthermore, it also provides the data augmentation to the datasets.

While preparing for the training and validation datasets, we had split the training datasets into 80/20 and validation datasets into 75/25. This distribution found to be the best for training the model. The BRATS validation dataset consists of unknow grade MRI images of 66 patients.
Later, the data extraction is done we had further reshaped it and transform it into array using Simple Tk library and perform the transpose also before proceeding towards modeling so that all images would be of equal shape and size. For our implementation we have utilized packages from keras.

5. Design Specification

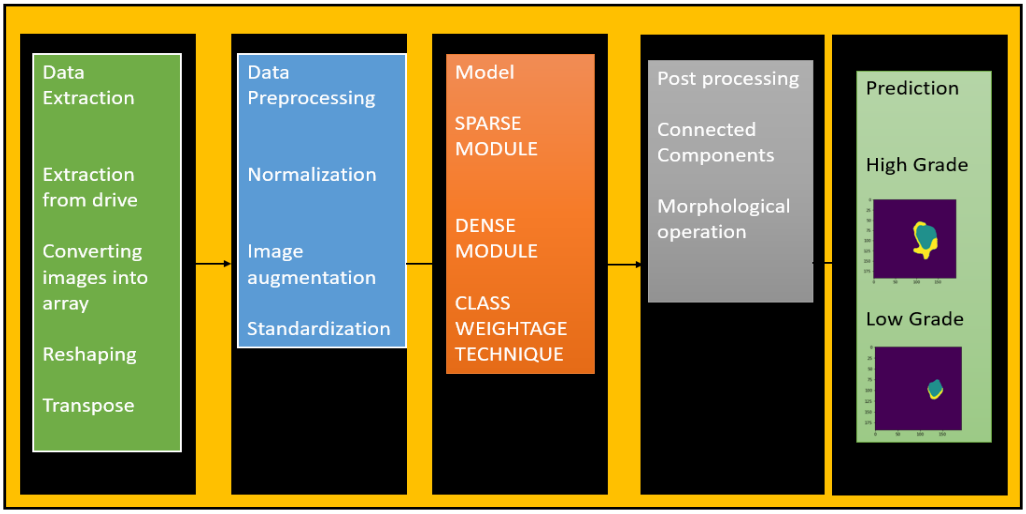


Fig 4.End to End Deep learning pipeline framework for segemnation.

The above fig.4 depicts the design overflow of our End to End deep learnimg based brain segmemntaoon model which starts from extracting the data from the drive & converting into array, Transpose and reshaping, second stage include preprocessing which does operation of image normalization and standardization along with image augumentation, then we build different model based on sparse and dense module and furthur, we finally prepare the image post processing which includes removing the small connected components from the image and performimng dialation and morphological operations. Last stage we import the saved model and run on our dataset using image with low garde, high grade and image wih no tumor and we plotted the loss and model score and evaluated our results through the dice and loss coefficent parameters.

6. Results

The model was evaluated using dice coefficient and loss parameters as stated below in the table at 16 Epoch. Dice coefficient index is used to find the accuracy of the similarity between two datasets.

Epoch	**Dice coefficient**	**Loss**
16	0.0092	0.9908
	Validation Dice coefficient	**Validation Loss**

	0.0092	0.9908

Table 3.Evaluation results of model.

Epoch cycles	Loss	Dice coef	Val Loss	Val Dice coef
1	0.032	0.967	0.0348	0.9652
2	0.03	0.97	0.0294	0.9706
3	0.0245	0.9755	0.0284	0.9116
4	0.0205	0.9795	0.0199	0.9805
5	0.0179	0.9821	0.018	0.9829
6	0.0163	0.9837	0.0161	0.98
7	0.0157	0.9849	0.0152	0.982
8	0.0141	0.9859	0.0142	0.9831
9	0.0131	0.9864	0.0132	0.9848
10	0.0124	0.9876	0.012	0.9858
11	0.0117	0.9883	0.0111	0.9868
12	0.0111	0.9896	0.0112	0.9889
13	0.0104	0.9889	0.0102	0.9888
14	0.0101	0.9899	0.0101	0.9899
15	0.0096	0.9904	0.0091	0.9907
16	0.0092	0.9908	0.0092	0.9908

Table 4.Score at each epoch cycles.

Training Model Time comparasion:

Model Comparison - Here I have used alternate methodology which is based on UNET architecture for segmenting brain tumors and later have compared it with my core model which is based on sparse and dense architecture based on the training time taken by the model and segmentation time. The former Unet based used 1 encoder and 2 decoder which took around 8 to 9 hours for training the model utilizing GPU and segmentation time was also more compared to our model where each model based on cascaded sparse and dense architecture (Sparse, Input Sparse and Dense models) took around 1 hours for training and the segmentation of entire brain image including low grade and high-grade tumor was also less. It was observed that using the concept of segmentation of the overlapping patches, using the small input patches feature maps and through use of skip connection in the architecture the inference time has been reduced to 8 times as compared to Unet architecture and its less than the methodology used as discussed in the literature review of the papers utilizing approach like CNet. The design used for the CNN architecture helps to reduce the overall inference and training time utilizing the GPU.

Model	**Time (hr.)**
Unet (Alternate Methodology Model)	9
Sparse Multiconnection Model	1
Input Sparse Multiconnection Model	1
Dense Multiconnection Model	1

Table 5.Time comparasion for implementation using GPU by different model

The following graph depicts the relationship between the model loss and dice coefficient of train and validation datasets of MRI images.

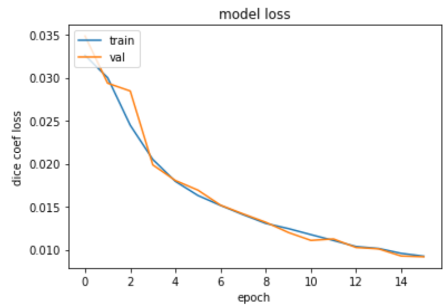


Fig 5.Graph of Model loss vs Epoch cycles

The following graph depicts the relationship between the model score and dice coefficient of train and validation datasets of MRI images.

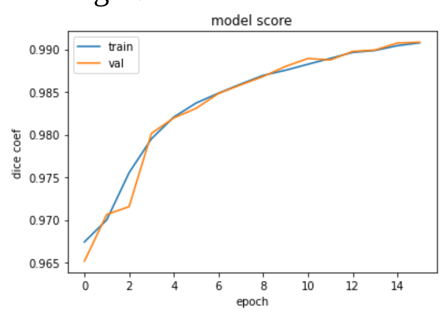
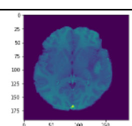
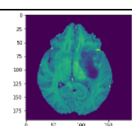
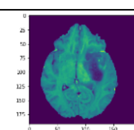
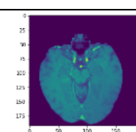
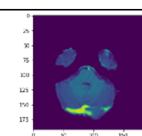
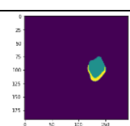
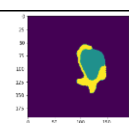
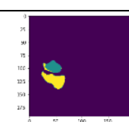
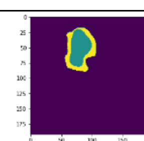
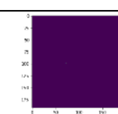
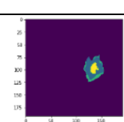
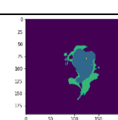
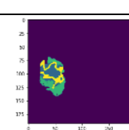
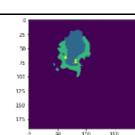
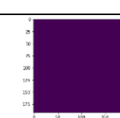
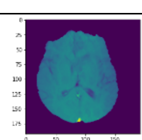
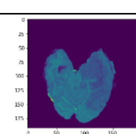
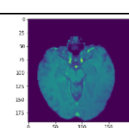
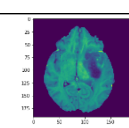
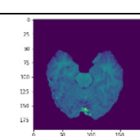


Fig 6. Graph of Model score vs Epoch cycles

Finally, we tested our trained model on the datasets with and without tumor, High grade and low-grade tumor images and the predicted image are shown in the below table with Test, actual image, and the predicted image.

Parameter	Low Grade	High Grade	Low Grade	High Grade	No tumor
Test image					
Actual					
Predicted					
Test Image					

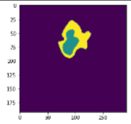
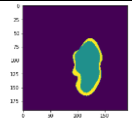
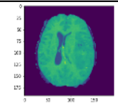
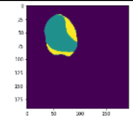
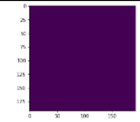
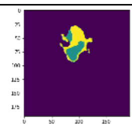
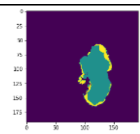
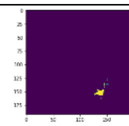
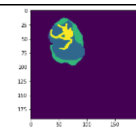
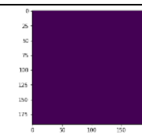
Actual					
Predicted					

Table 6. Results of predictoion with Low grade, High grade and no tumor brain MRI test images.

7. Discussion

In this paper, we design the fully automated framework with deep learning-based CNN model for segmenting the brain tumors from MRI images. Here, we developed 3 variant of CNN architecture along with Unet architecture as alternative approach and later compare the time required for implementation and segmentation performance using GPU. These architectures were used to segment both low- and high-grade brain tumor based on different modalities of MRI images. Here we started with the preprocessing of the images in order to enhance the quality of our images as a part of pour segmentation pipeline which include different approaches of the preprocess Further, we post process the image using two ways first by removing the small, connected region less than the value of 110-pixel threshold from the images and then performing the morphological operation on the image. Our three variant CNN architecture were build using 2D images patches where each patch has been equally sampled during training stage so that each class would consist of equal number of patches this approach along with the use of weight cross entropy function were implemented to overcome class imbalanced issue sin the datasets. Using the three CNN architecture we have applied the new strategy of using overlapping patches in the model so that we would be able to capture the features both locally and global context. Using this approach, we would be able to have prediction of results from both adjacent and overlapping patches. Our model of 3 CNN architecture were based upon the use of skip connections within modules. This would help to capture the missing details from each layer of Max pooling and convolution strides between modules and would eventually help in combing the low- and high-level feature representation.

8. Conclusion & Future work.

The paper aims to design the working model of fully automated brain tumor segmentation using the MRI images. The methodology starts with preprocessing of the images and further applying the three variant CNN architecture and finally post processing of the images. Here we are able the segment the brain tumor of both the high- and low-grade tumor images. Here the model uses the concept of extracting the features from both the adjacent and overlapping patches and later provided the final prediction. The resulted dice score and the inference time required for the implementation outperformed the earlier traditional methods & handcrafted based CNN model. For future work, we can study upon the 3D base overlapping patches on three different tumors view also we can design new CNN architecture which can overcome the problem of model performance degradation during modelling which is due to presence of heterogeneous data in the BRATS datasets. This would lead to the development of some synthetic type of data for model building.

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10. References

1. Zhou, Y. et al., 26 January 2019. Holistic Brain Tumor Screening and Classification Based on DenseNet and Recurrent Neural Network. In: *Brainlesion: Glioma, Multiple Sclerosis, Stroke and Traumatic Brain Injurie.* s.l.:Springer Link, pp. 208-217.
2. Anon., 2001. Segmentation of multispectral MR images using a hierarchical self-organizing map. *Proceedings of the IEEE Symposium on Computer-Based Medical Systems,* Issue 2001, pp. 294-299.
3. Anon., December 2005. Case study: An evaluation of user-assisted hierarchical watershed segmentation. *Medical Image Analysis,* 9(6, December 2005), pp. 566-578.
4. Axel, D, 2014. Brain Tumor Segmentation with Deep Neural Networks. In: Proceedings MICCAI-BRATS. Issue 2014, pp. 01-05.
5. Barret Zoph, Vijay Vasudevan, Jonathon Shlens & Quoc V. Le, 2018. Learning Transferable Architectures for Scalable Image Recognition. *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR),* Issue 2018, pp. 8697-8710.
6. Bhandarkar, S.M & Nammalwar, P, 2001. Segmentation of multispectral MR images using a hierarchical self-organizing map. *Proceedings of the IEEE Symposium on Computer-Based Medical Systems,* Issue 2001, pp. 294-299.
7. Chang, P., 2016. Fully convolutional neural networks with hyperlocal features for brain tumor segmentation. *Proceedings MICCAI-BRATS Workshop,* Issue 2016, pp. 4-9.
8. Ellwaa, A, et al., 2016. Brain tumor segmantation using random forest trained on iteratively selected patients. *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics),* 10154(2016), pp. 129-137.
9. Ellwaa, A, et al., 2016. *Brain tumor segmantation using random forest trained on iteratively selected patients.* Egypt, Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics).
10. Fletcher-Heath, L.M, Hall, L.O, Goldgof, D.B & Murtagh, F.R, January 2001. Automatic segmentation of non-enhancing brain tumors in magnetic resonance images(Article). *Artificial Intelligence in Medicine,* 21(January 2001), pp. 43-63.
11. Gibbs, P, Buckley, D.L, Blackband, S.J & Horsman, A, November 1996. Tumour volume determination from MR images by morphological segmentation. *Physics in Medicine and Biology,* 41(1996), pp. 2437-2446.
12. Havaei, M., et al., 1 January 2017. Brain tumor segmentation with Deep Neural Networks. *Medical Image Analysis,* 35(2018), pp. 18-31.
13. Havaei, M, et al., 1 January 2017,. Brain tumor segmentation with Deep Neural Networks(Article). *Medical Image Analysis,* 35(2017), pp. 18-31.
14. Havaei, M, et al., 1 January 2017. Brain tumor segmentation with Deep Neural Networks. *Medical Image Analysis,* 35(2017), pp. 18-31.
15. Havaei, M. D. A. W.-F. D. B. A. C. A. B. Y. P. C. J. P.-M. L. H., 1 January 2017. Brain tumor segmentation with Deep Neural Networks. *Medical Image Analysis,* 35(2017), pp. 18-31.
16. Işin, A, Direkoğlu, C & Şah, M, 29 August 2016. Review of MRI-based Brain Tumor Image Segmentation Using Deep Learning Methods. *Procedia Computer Science,* 102(2016), pp. 317-324.
17. Kamnitsas, K., et al., 2016. *DeepMedic for brain tumor segmentation.* London, United Kingdom, Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics).
18. Kamnitsas, K, et al., 1 February 2017. Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation. *Medical Image Analysis,* 36(2017), pp. 61-78.
19. Kumar, A. et al., 2019. A deep neural network based classifier for brain tumor diagnosis. *Applied Soft Computing,* 82(18 May 20).

20. Lefohn, A.E., Cates, J.E & Whitaker, R.T, 2003. Interactive, GPU-based level sets for 3D segmentation. *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*, 2878(2003), pp. 564-572.
21. Long, J. S. E. D. T., 2015. Fully Convolutional Networks for Semantic Segmentation. Issue 2015, pp. 3431-3440.
22. Mlynarski, P, Delingette, H, Criminisi, A & Ayache, N, April 2019. 3D convolutional neural networks for tumor segmentation using long-range 2D context. *Computerized Medical Imaging and Graphics*, 73(2019), pp. 60-72.
23. Mlynarski, P, Delingette, H, Criminisi, A & Ayache, N, April 2019. 3D convolutional neural networks for tumor segmentation using long-range 2D context. *Computerized Medical Imaging and Graphics*, 73(2019), pp. 60-72.
24. Ostrom, Q.T, et al., 2014. The epidemiology of glioma in adults: A state of the science review. *Neuro-Oncology*, 16(7, July 2014), pp. 896-913.
25. Pereira, S., 2015. Deep convolutional neural networks for the segmentation of gliomas in multi-sequence mri. *International Workshop on Brainlesion: Glioma, Multiple Sclerosis, Stroke and Traumatic Brain Injuries*, Issue 2015, pp. 131-143.
26. Rachida Saouli, Mohamed Akil & Rostom Kachouri, November 2018. Fully Automatic Brain Tumor Segmentation using End-To-End Incremental Deep Neural Networks in MRI images. *Computer Methods and Programs in Biomedicine*, 166(2018), pp. 39-49.
27. Schneider, T, et al., 12 November 2010. Gliomas in adults. 107(2010), pp. 799-808.
28. Singh, A, et al., 2012. Malignant brain tumor detection. *Scopus Review* , 4(6, 2012), pp. 1002-1006.
29. T. LogeswariT. & M. KarnanM, 2010. An improved implementation of brain tumor detection using segmentation based on soft computing. *CANCER RESEARCH AND EXPERIMENTAL ONCOLOGY*, 2(1)(31 March 2009), pp. 006-014.
30. Yang, S & Ramanan, D, 2015. *Multi-scale recognition with DAG-CNNs.* Sichuan University, China, Proceedings of the IEEE International Conference on Computer Vision ; Volume 2015 International Conference on Computer Vision, ICCV 2015, 17 February 2015, Article number 7410501, Pages 1215-1223..
31. Young, R.J & Knopp, E.A, 2006. Brain MRI: Tumor evaluation. *Magnetic Resonance Imaging*, 24(4, October 2006), pp. 709-724.
32. Zeineldin, R. A. et al., 05 May 2020. DeepSeg: deep neural network framework for automatic brain tumor segmentation using magnetic resonance FLAIR images. *International Journal of Computer Assisted Radiology and Surgery* , 15(June 2020), p. 909–920.
33. Zhao, X, et al., 1 January 2018,. A deep learning model integrating FCNNs and CRFs for brain tumor segmentation. *Medical Image Analysis*, 43(2018), pp. 98-111.