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Declaration of Authorship

This is to certify that the work presented in this thesis is the outcome of the analysis and experiments carried out by under the supervision of Tareque Mohmud Chowdhury ,Assistant Professor of the Department of Computer Science and Engineering (CSE), Islamic University of Technology (IUT), Dhaka, Bangladesh. It is also declared that neither of this thesis nor any part of this thesis has been submitted anywhere else for any degree or diploma. Information derived from the published and unpublished work of others has been acknowledged in the text and a list of references is given.

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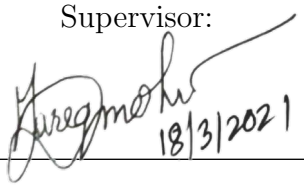

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Abstract

In this study we propose a deep learning based model for the detection of glioblastoma(an aggressive type of cancer that can occur in the brain or spinal cord) based on their origin in brain . The deep learnig based model will be obtained from the comparative analysis of the mdoels resnet,vgg16 , inception-net,alexnet .We also attempt to overcome the shortcoming of the above paper(Identification of Glioma from MR Images Using Convolutional Neural Network) [1] which is some astrocytomas and oligodendrocytomas are misidentified as GBM and do a comparative analysis between the implemented model.We conducted our experiment using the datasets TCGA and LGG1p19q Depletion from Cancerarchieve,Medpix,BraTS2020 consisting of samples over more than 12,000 patients. The experiments using Glioma images from the Brats2020 shows that we obtain 86% average classification accuracy for the network .

Keywords: *Glioblastoma, resnet,Vgg16 , Inceptionnet,Alexnet*

Contents

1 Introduction

1.1 Overview and motivation

The domain of our research study is bioinformatics. Here the research area where we are focusing on is detection of glioblastoma using resnet,vgg16 , inceptionnet,alexnet and do their comparative analysis. Glioblastoma is an aggressive type of cancer that can occur in the brain or spinal cord [2]. The types of glioblastoma are actrocytoma, oligodendroglioma and glioblastoma multiiforme (GBM).Among them type 1 and 2 are low grade glioblastoma(LGG) and 3 high grade glioblastoma(HGG). Detection of this disease is basically an image classification problem .In previous papers this disease classification were done using cnn(convolutional neural network). But this faced many problems so in modern time for image classification much advanced models has been developed like resnet, resnet,inceptionnet,vggnet. Since no other paper implemented theses advance models, we ought to implement theses models for a better classification accuracy and also to determine which model performs better by showing the comparative analysis and try to overcome the shortcomings of previous research in this domain.

1.2 Problem Statement

We propose a deep learning based model for the detection of glioblastoma based on their origin in brain . The deep learnig based model will be obtained from the comparative analysis of the mdoels resnet,vgg16 , inceptionnet,alexnet .We also attempt to overcome the shortcoming of the above paper(Identification of Glioma from MR Images Using Convolutional Neural Network[1]) which is some astrocytomas and oligodendrocytomas are misidentified as GBM and do a comparative analysis between the implemented model.

1.3 Research Challenges

For low grade glioblastoma we have total number of samples 258,702 from the datasets TCGA[3] and LGG1p1q [4]Depletion from Cancerarchieve,from Medpix we have LGG-HGG samples of around 12,000 patients and from BraTS2020[5] consisting of samples of over 7000 patients.For this huge number of samples we need to do a lot of data preprocessing which is a challenge. Also different datasets have different modalities . A first fundamental challenge is learning how to represent and summarize multimodal data in a way that exploits the complementarity and redundancy of multiple modalities. A second challenge addresses how to translate (map) data from one modality to another. Not only is the data heterogeneous, but the relationship between modalities is often open-ended or subjective. A third challenge is to identify the direct relations between (sub)elements from two or more different modalities. A fourth challenge is to join information from two or more modalities to perform a prediction.

1.4 Thesis Outline

In Section 1, we have discussed the overview of what we intend to do and why so, in a precise and concise manner. Section 2 deals with the necessary literature review for our study and there development so far. In Section 3, we have stated the skeleton of our proposed dataset, proposed methodology to extract information for the dataset, implementation process to construct the dataset and also our progress so far. Section 4 shows the Result analysis after a successful implementation of our proposed method. The final section of this study contains all the references and credits used.

2 Background study

Glioblastoma forms from cells called astrocytes that support nerve cells. Glioblastoma can occur at any age, but tends to occur more often in older adults. Initially, signs and symptoms of glioblastoma are nonspecific. They may include headaches, personality changes, nausea and symptoms similar to those of a stroke. They can either start from normal brain cells or develop from an existing low-grade astrocytoma.The diagnosis typically is made by a combination of a CT scan, MRI scan and tissue biopsy. Treatment usually involves surgery, after which chemotherapy and radiation therapy are used. The typical duration of survival following diagnosis is 12 to 15 months, It most often begins around 64 years of age and occurs more commonly in males than females. glioblastoma have long been assumed to originate from glial-type cells. More recent studies suggest that astrocytes, oligodendrocyte progenitor cells, and neural stem cells could all serve as the cell of origin. When viewed with MRI, glioblastomas often appear as ring-enhancing lesions.[6]

Over 80% of secondary glioblastomas carry a mutation in IDH1, whereas this mutation is rare in primary glioblastoma (5–10%). Thus, IDH1 mutations are a useful tool to distinguish primary and secondary glioblastomas. About three per 100,000 people develop the disease a year, It is the second-most common central nervous system cancer after meningioma. In adults, GBM occurs most often in the cerebral hemispheres, especially in the frontal and temporal lobes of the brain. GBM has an incidence of two to three per 100,000 adults per year, and accounts for 52 percent of all primary brain tumors. Overall, GBM accounts for about 17 percent of all tumors of the brain.[6]

3 Literature review

- In the paper Identification of Glioma from MR Images Using Convolutional Neural Network[1] published in 18 October 2018, a novel approach of classifying the type of glioma using convolutional neural network (CNN) on 2D MR images was presented. Glioma, most common type of malignant brain tumor, and can be classified according to the type of glial cells affected. The types of gliomas are, namely, actrocytoma, oligodendroglioma and glioblastoma multiiforme (GBM). In medical domain, segmentation is the technique

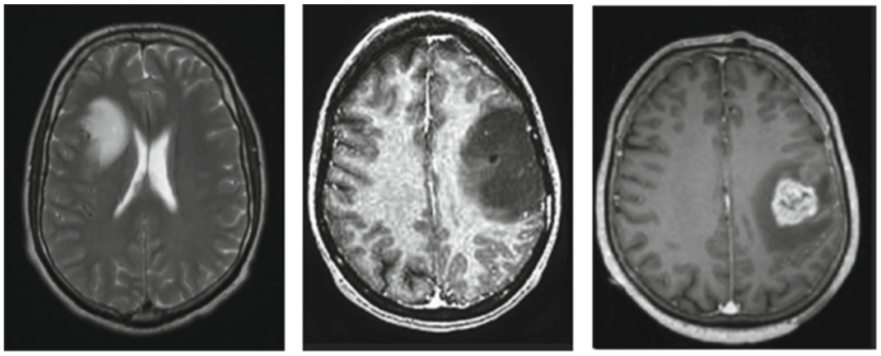


Fig. 1. MR scans of types of gliomas: a. Astrocytoma, b. Olidendroglioma and c. Glioblastoma multiform or GBM.

for detection and separation of a part from medical image (can be a lesion or an organ) that can be used for further diagnosis. Their work focuses on developing Hamiltonian Mechanics 591 a heuristic algorithm to segment the tumor region from 2D brain MRI images. Initially, preprocessing is done which enhances the tumor region in MR scans followed by multi-level thresholding to segment the lesion. Then accuracy is calculated on different slices of MR images, which is above 95% for all types of MRI slices.

- Deep learning can also be applied for segmentation of lesion and detection of cancer from modalities like Computed Tomography (CT) scan, ultrasound and MRI. Farnaz et al. [7], trained a deep convolutional neural network

(DCNN) for segmentation of lesions in brain from MR images. The proposed model was 6 layers deep (5 convolution layers and 1 FC layer) showed that the DICE similarity coefficient matric was 0.90 for complete, 0.85 for core and 0.84 for enhancing regions on BRATS 2016 dataset.

- Mingxia et al. [8] proposed an anatomical landmark based feature representation which automatically extracts features in brain MR images for the purpose of disease diagnosis.

- Experimental results showed that the proposed method improves the performance of disease classification. An approach to find the severity of tumor is to first segment tumor region from the scan then classify it as malignant or benign. Deckota et al.[9] proposed a system which identifies the cancerous nodule from the lung CT scan images using watershed segmentation for detection and support vector machine (SVM) for classification of nodule as malignant or benign. 6 stages: image pre-processing, segmentation of the pre-processed image, feature extraction, feature reduction using PCA, classification using SVM and evaluation of the classification. The model detects cancer with 92% accuracy classifier has accuracy of 86.6%.

- Zakarakhi et al. [10] also proposed a scheme to classify brain tumor type and grade using MR images. The binary SVM classification accuracy,sensitivity and specificity were respectively 85%, 87% and 79% for discrimination of metastases from gliomas and 88%, 85% and 96% for discrimination of high-grade from low-grade neoplasms.

- From the paper Deep Radiomics for Brain Tumor Detection and Classification from Multi-Sequence MRI [11],They propose novel ConvNet models,which are trained from scratch, on MRI patches, slices, and multi-planar volumetric slices. The suitability of transfer learning for the task is next studied by applying two existing ConvNets models (VGGNet and ResNet) trained on ImageNet dataset, through fine-tuning of the last few layers. Leave-one-patient-out (LOPO) testing, and testing on the holdout dataset

are used to evaluate the performance of the ConvNets. the model is trained on the multi-planar volumetric dataset.Unlike conventional models, it obtains a testing accuracy of 95% for the low/high grade glioma classification problem. For the classification of low/high grade gliomas , the models were trained on the TCGA-GBM46 and TCGALGG47 datasets downloaded from The Cancer Imaging Archive (TCIA). The testing was on an independent set, i.e. brain tumor dataset from MICCAI BraTS 2017,containing images of low grade glioma (LGG) and high grade glioma(HGG). The TCGA GBM and LGG datasets consists of 262 and 199 samples respectively, whereas the BraTs 2017 database contains 210 HGG and 75 LGG samples.

- In the paper Hyperspectral Imaging for the Detection of Glioblastoma Tumor Cells in HE Slides Using Convolutional Neural Networks[12], They employed an HIS microscope, with a spectral range from 400 to 1000 nm, to collect 517 HS cubes from 13 GB patients using 20× magnification. Using a convolutional neural network (CNN), they were able to automatically detect GB within the pathological slides, achieving average sensitivity and specificity values of 88% and 77%, respectively, representing an improvement of 7% and 8% respectively, as compared to the results obtained using RGB (red, green, and blue) images. A custom 2D-CNN for the automatic detection of non-tumor and tumor patches was employed. Total of 32,878 patches from non-tumor tissue and 16,687 from tumor tissue were used. They used the TensorFlow implementation of the Keras Deep Learning API for the development of this network. . All convolutions and the dense layer were performed with ReLU (rectified linear unit) activation functions with a 10% dropout.

- In the paper Development of automatic glioma brain tumor detection system using deep convolutional neural networks[13], They used 3 × 3 kernels for designing in-depth architecture. the proposed work modeled various kinds of CNN architectures based on the variations of hyperparameter settings and estimated their performances using the internet real-time repositories such

as BraTS and whole brain atlas (WBA). Normal and tumorous images were randomly selected from BraTS2020 volumes to create a training set with 4500 images.

- In the paper . Automated glioma grading on conventional MRI images using deep convolutional neural networks[14], Three publicly available datasets have been used in the study. All these data are preoperative. The first one, denoted as Dataset1, is the BraTS 2018 data, which includes 210 HGG GBM and 75 LGG patients.26,31 All BraTS multimodal images are provided as NIfTI files with T1, T1-Gd, T2, and T2-FLAIR weighted volumes and were acquired with different clinical protocols and various scanners from different institutions. All images were resampled to size of 128 9 128 9 128 voxels due to the limitations of GPU memory and training time. Batch size was set as 1 and total training epochs 300. The network architecture is trained based on fine-tuning of a pretrained model (ResNet) on ImageNet dataset[12,15], which takes less time to achieve optimized network parameters. The base learning rate is set as 0.0025, and weight decay 0.0001. Learning rate can be decreased by a factor of 10 depending on the preset steps. The 3DConvNet tumor grading was implemented based on the NiftyNet,41 a deep-learning platform particularly for medical imaging. A single label file with NIfTI format was created with size of 1 9 1 9 1. Its value was set as 0 for LGG class, and 1 for HGG class. Cross entropy loss function was utilized, and learning rate was set as 0.0001.

4 Proposed Approach

4.1 Overview of the Experiment

Prior to train the model, we need to preprocess the data so that the features can be detected easily from the image samples. After that the dataset needs to be loaded split into training set testing set. Then according to the architecture, we need to construct the model fit the training samples to train the model. Then the hyperparameters need to be tuned. Finally, we'll have to evaluate the performance of the model in testing samples generate the result. versions of images in the dataset. Than we perform principle component analysis on the dataset. PCA is defined as an orthogonal linear transformation that transforms the data to a new coordinate system such that the greatest variance by some scalar projection of the data comes to lie on the first coordinate (called the first principal component), the second greatest variance on the second coordinate, and so on. Mathematically the transformation is defined by a set of size l of p dimensional vectors of weights or coefficients wk= (w1,. . . . . .wp)k that map each row vector xi of x to a new vector of principle component scores t(i)=(t1,. . . .tl)(i) given by Tk(i)=x(i).w(k) for i=1,. . . . . n k=1,. . . .,l In such a way that the individual variables t1,. . . .,tl of t considered over the data set successively inherit the maximum possible variance from X with each coefficient vector w constrained to be a unit vector. First component In order to maximize the variance , the first weight vector w(1) thus has to satisfy w(1) =arg max (t(1))2(i)=arg max (x(i) .w)2 Equivalently ,writing this in matrix form gives w(1) =arg max (X(w))2=arg maxwT XT Xw since w(1) has been defiend to be a unit vector , it equivalently also satisfies w(1) =arg max wT XT Xw/ wT w Dimensionality reduction The transformation T=XW maps a data vector x(i) from an optional space of p variables to a new space of p variables which are uncorrelated over the dataset. However not all the principal components need to be kept. Keeping only the first L principal components produced by using the first L eigenvectors, gives the truncated transformation T(l) = Xw(l) Where the matrix T(l) has rows but only the L columns , In the other words ,PCA learns

a linear transformation t= wT x, where the columns of p x L matrix W form an orthogonal basis for the L features .[15] As part of preprocessing , we have done the image thresholding, and we used binary thresholding. Here, any pixel having a value higher than the threshold will be considered as white otherwise black. This helps to detect the tumors from the image more clearly. Secondly, we have used dilation to dilate the noisy parts of the images. Then we have used eroding to erode the foreground boundary.

4.2 Loading data and Train Test set generation

After preprocessing, the samples in the dataset are loaded and then split into Training Testing set. Splitting ratio is important, because the model needs to be trained with sufficient training samples to yield a good accuracy in case of testing data. We have taken train-test ratio as 8:2, a standard ratio.

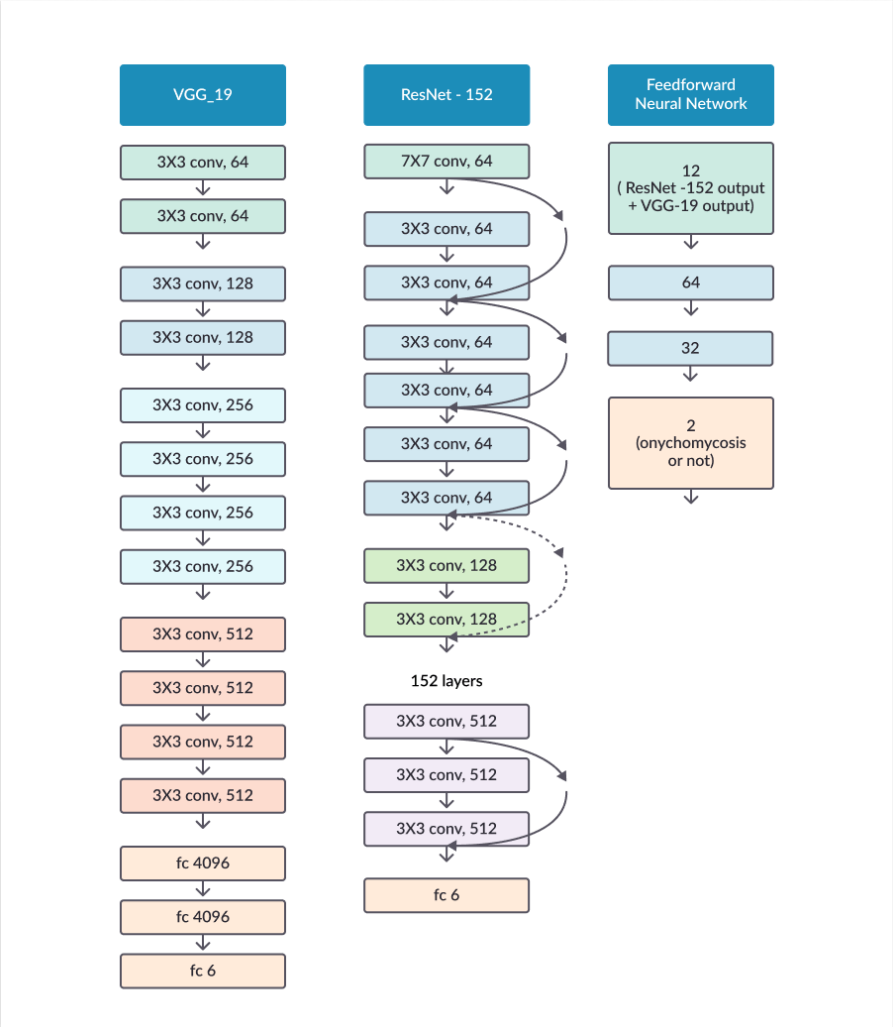
4.3 Implementation Details

Dataset used are LGG-1P19QDELETION:LOW GRADEGLIOMA TCGA-LGG:LOW GRADEGLIOMA,medpix, which consists of MR,CT , ,SEG,NIFTI scans of 12,358 patients suffering from glioma tumors of different types and at different stages. From this dataset, a total of 270,702 images,BraTS2020. We apply different models resnet,Alexnet ,inception,vgg16, and show their comparative analysis. The label 0 was astrocytoma, 1 was GBM and 2 was oligodendroglioma. The proposed models are implemented using tensorflow framework on a system with configuration as 4 CPU, 15 GB with 2 NVIDIA K80 GPUs.

4.4 Model creation with Resnet

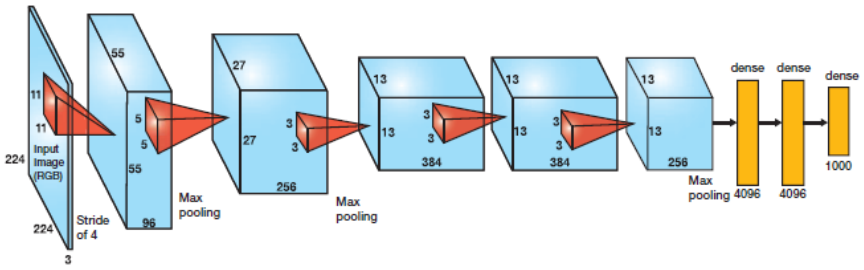
.Residual Network (ResNet) architecture was designed to enable hundreds or thousands of convolutional layers,it can add a large number of layers with strong performance.ResNet was an innovative solution to the “vanishing gradient” problem.The ResNet solution is “identity shortcut connections”as seen in the picture

it compresses the network into only a few layers, which enables faster learning. [16] Structure:



4.5 Model creation with AlexNet

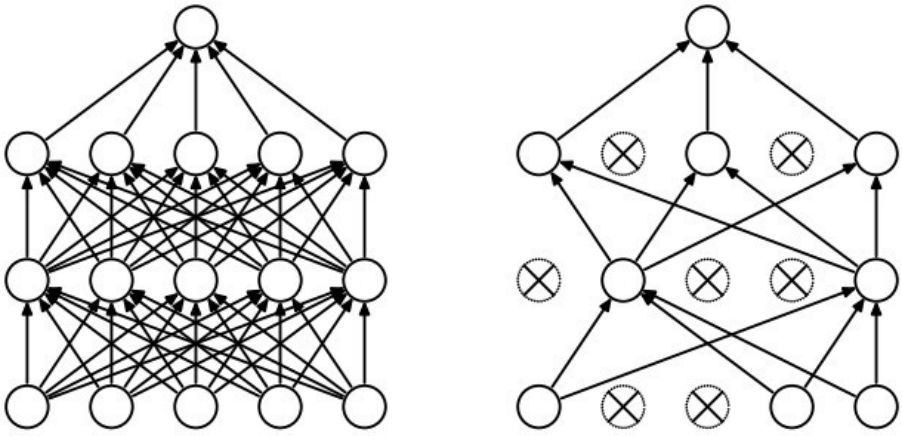
This architecture was one of the first deep networks to push ImageNet Classification accuracy by a significant stride in comparison to traditional methodologies. It is composed of 5 convolutional layers followed by 3 fully connected layers, as depicted in Figure-



AlexNet, uses ReLu(Rectified Linear Unit) for the non-linear part, instead of a Tanh or Sigmoid function which was the earlier standard for traditional neural networks. ReLu is given by f(x) = max(0,x) The advantage of the ReLu over sigmoid is that it trains much faster than the latter because the derivative of sigmoid becomes very small in the saturating region and therefore the updates to the weights almost vanish. This is called vanishing gradient problem. Another problem that this architecture solved was reducing the over-fitting by using a Dropout layer after every FC layer. Dropout layer has a probability,(p), associated with it and is applied at every neuron of the response map separately. It randomly switches off the activation with the probability p, as can be seen in figure- Another problem that this architecture solved was reducing the over-fitting by using a Dropout layer after every FC layer. Dropout layer has a probability,(p), associated with it and is applied at every neuron of the response map separately.[17]

4.6 Model creation with VGG16

It makes the improvement over AlexNet by replacing large kernel-sized filters(11 and 5 in the first and second convolutional layer, respectively) with multiple 3X3 kernel-sized filters one after another. With a given receptive field(the effective area size of input image on which output depends), multiple stacked smaller size



(a) Standard Neural Net (b) After applying dropout.

kernel is better than the one with a larger size kernel because multiple non-linear layers increases the depth of the network which enables it to learn more complex features, and that too at a lower cost. The VGG convolutional layers are followed by 3 fully connected layers. The width of the network starts at a small value of 64 and increases by a factor of 2 after every sub-sampling/pooling layer. It achieves the top-5 accuracy of 92.3 % on ImageNet.[17]

4.7 Model creation with GoogLeNet/Inception

GoogLeNet uses convolutions of different sizes to capture details at varied scales(5X5, 3X3, 1X1). GoogLeNet as an example which has 192 channels as input. It has just 128 filters of 3X3 kernel size and 32 filters of 5X5 size. The order of computation for 5X5 filters is 25X32X192 which can blow up as we go deeper into the network when the width of the network and the number of 5X5 filter further increases. In order to avoid this, the inception module uses 1X1 convolutions before applying larger sized kernels to reduce the dimension of the input channels, before feeding into those convolutions. So in the first inception module, the input to the module is first fed into 1X1 convolutions with just 16 filters before it is fed into 5X5 convolutions. This reduces the computations to 16X192 + 25X32X16. All these changes allow the network to have a large width and depth. We fit all these model to the training data and for each of the cases we determine the training accuracy,testing accuracy,precision ,recall,specificity and

do a comparative analysis.[17]

5 Result Analysis

5.1 Work Progress

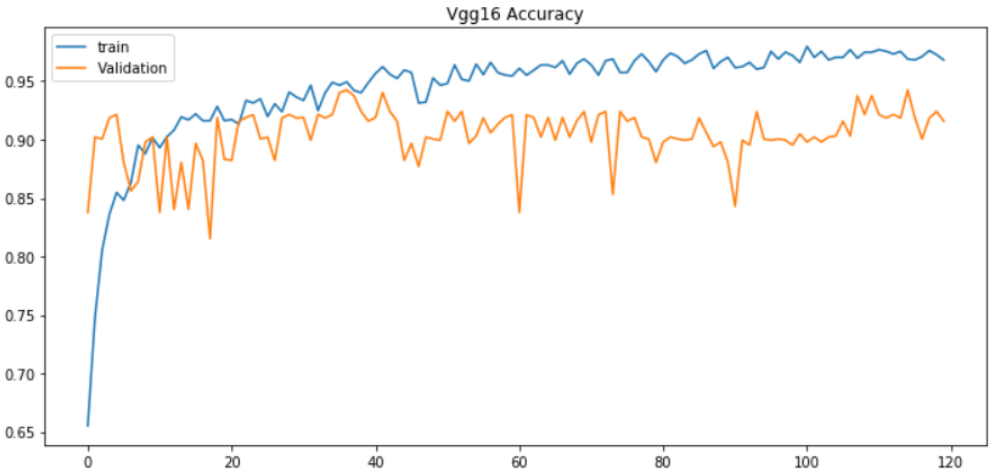
So far we have worked with BraTS20,at first we needed to converet the NIfTI files to png format and the original imagae size was 240, 240, 155 ,in the reprocessing we performed min-max scaling to convert the mri images to a standard format 128,128,128 after preprocessing-

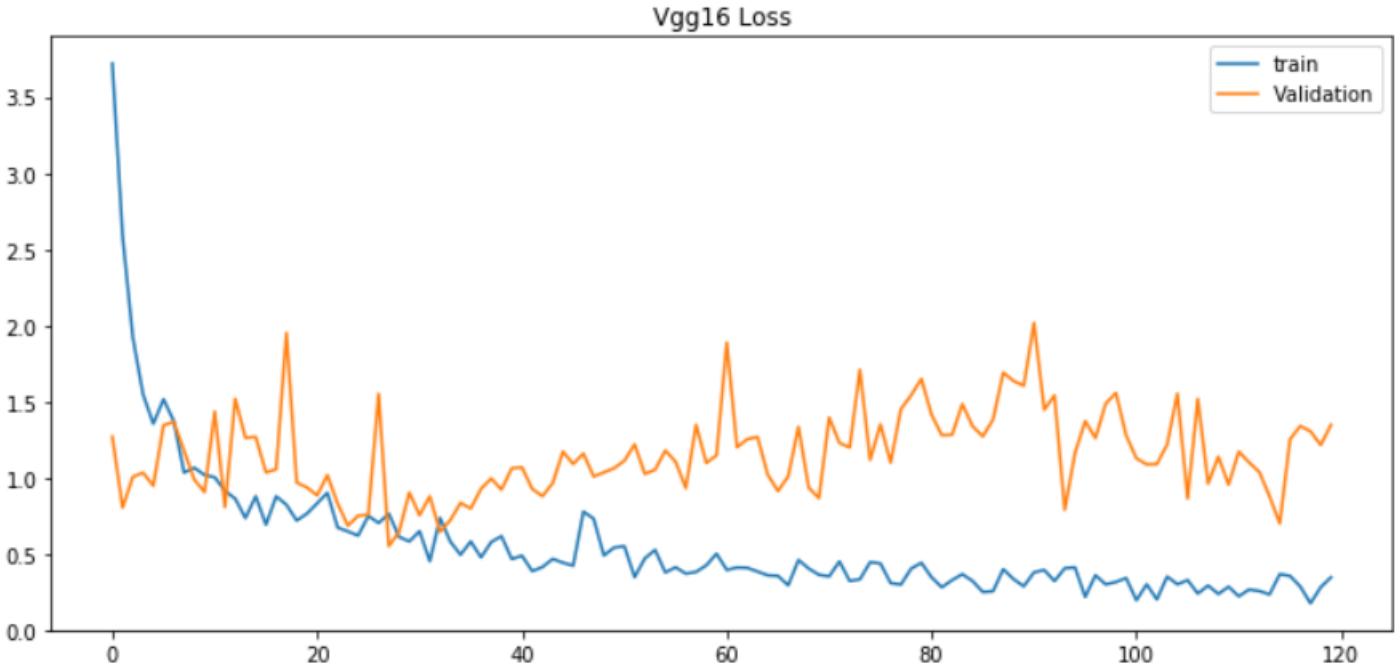
To prevent overfitting we performed data augmentation by randomly flipping along spatial axis,Splitted the datsest into 8:2 ratio(a standard ration)For each fold of the network in the training phase we performed stochastic gradient descent approach where number of epochs were 150 epochs learning rate of 1e-4,with Rmsprop optimizer and for the loss function we have chosen binary cross entropy loss.

5.2 Experimental Result

Inceptionnet gave training accuracy of 64%,Resnet- 86%,Alexnet- 62% Vgg16-91%,we achieved highest accuracy for vgg16 which was 91%,in the hidden layer we have 13 2D Convolutional Layer,4 Max Pooling Layers,2 Dropout Layers and 3 Dense Layer. the parameters that were taken was binary cross entropy as loss function,Rmsprop as optimizer with learning rate 0.0004,the metric was accuracy

As far the model performance vgg perfomed the best in the training phase with 91% accuracy so we applied this model in the testing phase and got accuracy 86%,precison 85% ,recall 85%


Vgg16 Accuracy
train
Validation
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0
20
40
60
80
100
120


Vgg16 Loss
train
Validation
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
20
40
60
80
100
120

6 Future Work

For future work we would like to use u-net classification model. We also ought to integrate other types of brain disease like alzheimer's disease and try to find the relationship between glioblastoma and alzheimer's disease and other types of brain cancers so that a single model can be used for multiple disease detection.

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