CNN-LSTM: Cascaded Framework For Brain Tumour Classification

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***Abstract*— Glioma is common type of brain tumour in adults originating from glia cell. Despite advances in medical image analysis and gliomas research, accuarte diagnosis remains a challenge. Gliomas can be in general classifed into High Grade (HG) and Low Grade (LG). The exact classification of glioma helps in evaluating the disease progression and selection of the treatment strategy. Whilst medical image classification using a Convolutional Neural Networks (CNNs) has achieved remarkable success, but it is still difficult task for CNNs to accurately classify 3D medical images. One of the major limitation is the fact that CNNs are difficult to optimize in 3D volumetric classification. In current work, we addressed this challenge by introducing a cascade of CNN with Long Short Term Memory (LSTM) Network for classification of 3D brain tumor MR images into HG and LG glioma. Features from pre-trained VGG-16 were extracted and fed into LSTM network for learning high-level feature representations to classify the 3D brain tumour volumes into HG and LG glioma. The results showed that the features extracted from VGG-16 gave better classification accuracy as compared to the features extracted from AlexNet and ResNet.**

Keywords—Glioma, CNNs, classification, LSTM, VGG-16

I. INTRODUCTION

Abnormal growth of cells in the brain results in a mass, which pushes on the normal structures in the brain. This abnormal mass grows quickly and creates a mass of abnormal cells called a tumour. Brain tumours vary in shape, size and severity level. They are heterogeneous in nature i.e. they can occur anywhere in the Central Nervous System (CNS) and have different Image Intensities. The most frequent brain tumours in adults are gliomas. The abnormal growth of the glial cell in the brain that surrounds the neurons results in the formation of gliomas[1]. There are different types and grades of gliomas and to specify the type and grade of a tumour a microscopic study is carried out that is called histology. The two main grades of gliomas are Low Grade (LG) and High Grade (HG) gliomas. This grading is based upon how the tumour cells look under the microscope [2]. The histological study shows the slow division of cells in LG glioma under a microscope. Low grade gliomas can cause a problem by pressing on the normal structures in the brain, even if they are not cancerous. High grade gliomas have more aggressive growth as compared to low grade gliomas. World Health Organisation (WHO) has established a criterion for defining the grades of gliomas. The WHO criterion is modified in 2016 [3] and classification is done on the basis of molecular and genetic appearances. The diagnosis of a brain tumour is initially performed on neural imaging modalities mainly Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). CT scan uses X-rays to take a series of brain images at different angles. Sometime dye is injected in veins to improve the contrast of the pictures. Once the abnormal growth of cells has been identified through CT then the patient is referred for an MRI scan. MRI is non-ionizing and non-invasive Imaging modality with high spatial resolution as compared to CT. In structural MRI, the gliomas usually have a characteristic appearance. Usually, HG gliomas do not have clear edges and have the heterogeneous appearance and they also have the swollen area around a tumour. LG gliomas have clear and well circumscribed boundaries with little swelling and cystic areas in a tumour[4]. Tumours are characterized by a hyperintense lesion in contrast enhanced T1-w images and hyper intensity on FLAIR and T2-w images. Fig. 1 and 2 show the appearance of HG and LG gliomas on multi-sequence MRI from Brain Tumour Segmentation Challenge (BRATS) 2015 training dataset [5]. The gold standard in deciding the type of a tumour is through the examination of the tumour cells under a microscope. The surgical procedure called biopsy is carried out to isolate a small region of cancerous brain cells for examination. However, it is a painful process and in some cases, a tumour is located in the brain region where surgery causes more problem[6]. In such cases classification of a tumour is based on an evaluation of MRI results and treatment of the patient is planned accordingly. The exact classification of tumours may help in designing the rational therapies for tumours. Thus, there is a need for developing a new computer aided analysis tool that is more objective than the human reader and can provide more reliable tumour diagnostic procedures. The objective of this work is to design an automated tool that helps in evaluating brain MR images by distinguishing between HG and LG gliomas.

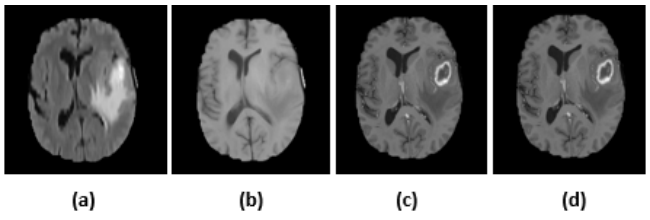

Fig. 1: (a) FLAIR (b) T1-w (c) T1-w contrast enhanced (d) T2-w MRI brain Images with HG glioma collected from BRATS 2015 dataset [5].

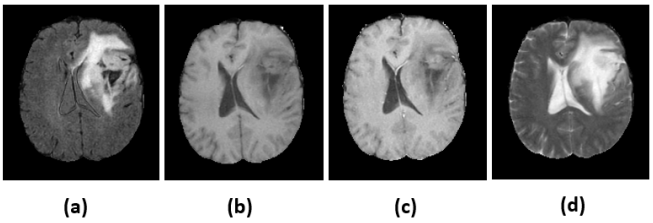

Fig. 2**:** (a) FLAIR (b) T1-w (c) T1-w contrast enhanced (d) T2-w MRI brain Images with LG glioma collected from BRATS 2015 dataset [5].

In this work, we have designed fully automatic frame work for classifying the gliomas into LG and HG using a cascaded Neural Network made up of Convolutional Neural Network (CNN) and Long Short Term Memory Network (LSTM).

II. Related Work

Various techniques have been proposed for classification and segmentation of brain lesions. Different categories of brain tumours can be separated from each other by studying the underlying features. Therefore, feature extraction techniques play an important role in classifying medical images into different categories based upon the extracted features. Related work includes the use of Support Vector Machine (SVM) and Random Forests [7-9]. Over the past few years, deep learning (DL) has been extensively used for medical image analysis. Convolutional Neural Networks (CNN) automatically learn the representation needed for classification or feature detection from raw data. CNNs has been broadly used in classification [10, 11], detection [12, 13] and segmentation [14] of medical Images. CNN architecture used for medical image classification are broadly classified based on interconnected operating modules [15-17]. Single path architectures [18] follow a unique flow of information from convolutional, pooling and non-linearity layer. The extracted feature maps thus extracted are passed onto the fully connected (FC) layer which is then used for predicating the classification labels. On the other hand, the cascaded architectures [17] have the advantage of processing the features at multiple levels. The feature maps from the last layer of the first network are extracted and used as input for the second network (classification). The cascaded CNN thus process features at multiple levels and is able to detect the subtle spatial information for increased classification accuracy. In previous work, Recurrent Neural Networks (RNNs) are cascaded with CNN for multi-level feature processing [19]. However, RNN suffers from vanishing gradient problem when input feature vector dimension is very high. Long short term memory Recurrent neural network (LSTM) has been recently used in a variety of task including natural language processing [20], speech recognition [21], EGG [22] and natural image processing [19]. LSTM is able to overcome the vanishing gradient problem by freeing up the memory [22]. The previous work in literature for glioma classification [9, 23-25] has mainly focused on machine learning techniques (ML) while in proposed method feature extraction for classification of HG and LG glioma is performed used DL techniques and is able to classify the 3D medical imaging volumes.

III. Materials & Methods

For volumetric MRI brain tumour image classification into HG and LG glioma, our method consists of two components, a pre-trained VGG-16 [26] for feature extraction and LSTM of classification of glioma into LG and HG.

A. VGG-16 for feature extraction:

Presently there are many CNN models with improved performance and deeper architecture. Table 1 presents some of the common architectures with their specifications. However, the deeper networks are difficult to train because they require a huge amount of data and millions of parameters for training. For the more accurate and generalizable models, the presence of large-scale precisely labelled dataset is very crucial. But in medical imaging problem, there is no large-scale labelled dataset available. To overcome this problem the technique of the transfer learning is used where the model is first pre-trained on large-scale natural image dataset e.g. ImageNet and then fine-tuned for the problem at hand [27]. In this work VGG-16 network pre-trained on ImageNet is used for feature extraction. These features are then used as Input signal for LSTM. VGGNet consists of 16 convolutional layers with 3×3 filters with a stride of 1 in the convolutional layer and 3 fully connected (FC) layers. VGG-16 has multiple stacked small size kernels in filters that increase the depth of the network which enables the network to extract more complex features at lower cost. In this work comparison of VGG-16 as feature extractor is performed with AlexNet [28] and ResNet [29].

TABLE I. Comparison Of Different CNN Architectures

Architecture	**AlexNet**	**VGGNet**	**GoogleNet**	**ResNet**
Layers	8	19	22	152
Input Image dimensions	227×227×3	224×224×3	224×224×3	224×224×3
Parameters	60M	138M	4M	21-60M
% Error	15.3	7.3	5.5	3.6

B. LSTM for classification:

Recurrent Neural Network (RNN) is a type of neural network that can model the temporal dependencies. There is a direct cyclic connection between the units of RNN that can store its internal hidden state and thus help to model the dynamic temporal behaviour.

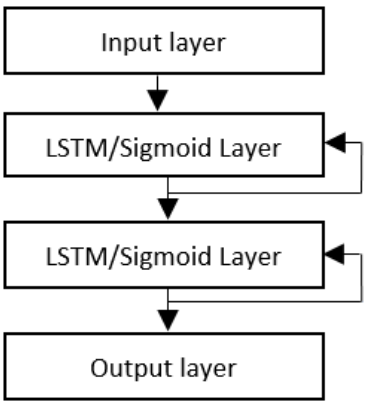

Fig. 3: Two layer stacked architecture of LSTM

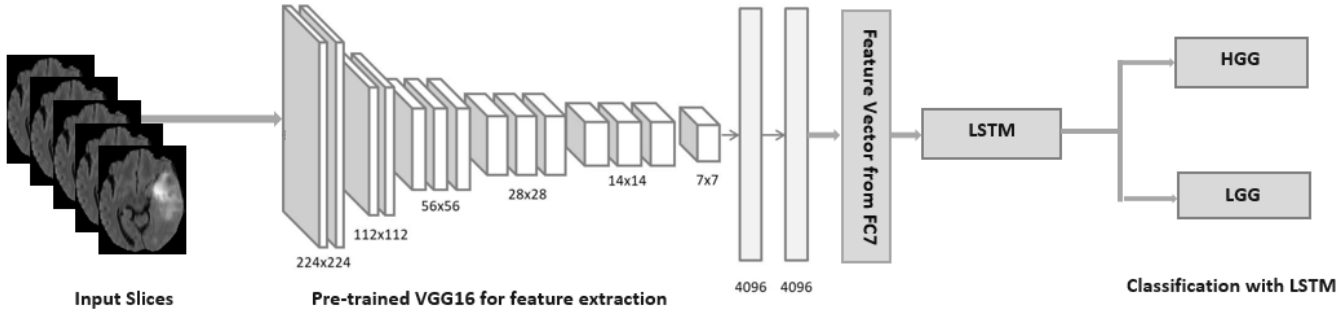

Fig. 4: Cascaded CNN-LSTM network architecture for brain tumour classification into Low Grade (LG) and High Grade (HG) glioma. Pre-trained VGG-16 is used for feature extraction by using transfer learning technique for training. Features from FC7 are then used as input to two layer LSTM for classification of volumetric 3D MRI brain tumour data.

TABLE II. GLIOMA CLASSIFICATION RESULTS OF THE PROPOSED AND STATE-OF-THE-ART METHODS

Method	Technique	Classifier	Training volumes	Training/Testing	Accuracy (%)
Li et al. [9]	ML	SVM	280	Leave-one-out	85
Citak-Er et al. [25]	ML	SVM	48	10 fold cross validation	93
Zollner et al. [24]	ML	SVM	101	Leave-one-out	87
Gupta et al. [23]	ML	SVM	200	Leave-one-out	88
Proposed Method	DL	Softmax	60	Hold-out	84

LSTM is an extended version of RNN with three gates namely an input gate, output gate and forget gate. It is two hidden layers neural network with 100 nodes in each layer. The stacked architecture of LSTM is shown in Fig 3. LSTM learns the long terms dependencies in temporal direction with these gates. LSTM is easier to optimize because these gates enable the input features to propagate through the hidden layer without effecting the output. LSTM also able to effectively deal with vanishing gradient problem because it frees up those memory locations in a temporal dimension that are not helpful in predicting the final classification labels. In this work input to LSTM are the features from the volumetric MRI data of HG and LG. The temporal direction of LSTM is occupied by the slices from each subject's volume.

C. Network design and Dataset:

Fig. 4 shows the network configuration for classifying the brain tumour data into LG and HG glioma. We have evaluated our system with the data from the 2015 BRATS dataset [5]. We have selected a total of 60 cases with an equal number of high grade (HG) and low grade (LG) glioma cases. For each subject, four MRI sequences are available, FLAIR, T1-w, T1-contrast enhanced and T2-w. However, in this work, only the FLAIR sequence is used for training and testing. The datasets have been pre-processed and provided as skull-stripped by the organizers, co-registered and resampled to isotropic 1mm^3 resolution. Dimensions of each volume are 240 ×240 ×155. 80% data is used for training and the rest of 20% is used for testing purpose using Hold-out scheme. Keeping in view the difficulty of getting big data in medical imaging, our focus was to develop a network that could classify with a minimum number of training and testing data. Our LSTM network has been trained by optimizing Stochastic Gradient Descent (SGD) as a cost function with an initial learning rate of 0.005 and dropout factor of 0.2. The number of units in each layer of LSTM were set to 100. The batch size was set to 27 with maximum epochs of 350. The model was implemented with MATLAB 2018b and the training took about two hours on NIVIDIA k4000 GPU machine.

IV. RESULTS & DISCUSSION

In the proposed method, the glioma classification is performed into Low Grade and High Grade based on feature extracted from FLAIR sequence MRI and percentage accuracy is used as a performance metric. Relevant method for glioma classification and the performance matrices are summarized in Table 2. Accuracy values achieved in previous work in literature for glioma classification are relatively high with the highest accuracy reported as 93%. However, our method has produced a comparable result with a small number of samples and has an accuracy of 84% with VGG-16. The accuracy may be increased by adjusting various hyper-parameters of network such as optimization technique, learning rate and a number of epochs. Moreover, classification accuracy may also be improved by exploiting the techniques that help to increase the amount of training data such as data augmentation [30] and generative adversarial networks [31]. These methods will be explored in future work. The proposed method is fully automatic as opposed to previous work in literature which relies on handcrafted feature extraction such as Region of Interest (ROI) extraction, therefore, requires manual interference by users. We have evaluated our method on three ImageNet pre-trained CNN architectures: AlexNet, ResNet, and VGGNet. The evaluation has demonstrated that VGGNet

achieves higher accuracy by more precise feature extraction. In the proposed binary class problem, we discriminate between the volumes with HG and LG glioma. As summarized in Table 3 the accuracy measurement for AlexNet and ResNet is 71% and for VGGNet is 84%.

TABLE III. GLIOMA CLASSIFICATION RESULTS OF THE PROPOSED-METHOD WITH DIFFERENT CNN ARCHITECTURES

Cascaded Model	Training/Testing	Accuracy (%)
AlexNet-LSTM	Hold-out (80.00-20.00%)	71%
ResNet-LSTM	Hold-out (80.00-20.00%)	71%
VGGNet-LSTM	Hold-out (80.00-20.00%)	84%

V. CONCLUSION & FUTURE WORK

In this work, we have proposed a cascaded CNN-LSTM model for volumetric classification of a brain tumour into High Grade and Low Grade glioma. Experimental results on the state of the art CNN architectures have shown that the VGG-16 model performs the best by extracting the high-level feature representations and thus enables the LSTM to effectively discriminate between HG and LG glioma. Another advantage of this method is that it is able to perform robustly on high dimensional 3D data. In future, we will extend this work for segmentation task by designing a model that can accurately predict the pixel labels for a brain tumour with a limited amount of training data.

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