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Research Paper

Neuro-degenerative disease Identification using MRI 3D-Convolution Method

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Abstract: Alzheimer's disease (AD) is a perpetual neurological disorder primarily affecting the brain leading to cognitive deterioration, behavioral problems, and memory loss. Alzheimer's disease which poses a significant danger to individuals worldwide in accordance with the World Health Organization (WHO). According to a recent study, by the year 2060, 70% of the population would have this condition. With a prevalence rate of 60 to 80 percent among dementia cases globally, Alzheimer's disease emerges as the leading etiology. Researchers are diligently working on the development of advanced machine learning models to improve the accuracy of skull stripping, specifically for separating neural tissues from non-neural tissue in magnetic resonance imaging (MRI) scans and identifying affected patients. In this paper, we unveil a fresh perspective of modified 3D-UNet architecture for precise brain segmentation and 3D-CNN architecture for classification. We argue for a volumetric analysis of the whole brain instead of localization and context information-based approaches for disease classification. As the dataset possesses the time-series like nature, utilization of the long short-term memory-based LSTM architecture has been utilized for medical analysis using MRI data from multiple regular patients. It enhances disease diagnosis & treatment effectiveness. The proposed approach demonstrates segmentation accuracy of 97% and classification accuracy of 95%. These findings enlighten the potential of LSTM-based analysis for neuro-degenerative diseases like-AD.

Keywords: Brain Segmentation, 3D U-Net, Disease Classification, 3D CNN, Alzheimer's disease, MRI, LSTM

1. Introduction

Alzheimer's disease (AD) is a perpetual neurological disorder primarily affecting the brain, which is mainly seen in the population of age 65 and older. For prodromal state of AD it is known as Mild cognitive impairment (MCI) which can further be classified as stable MCI (sMCI) and progressive MCI (pMCI) [1]. A recent survey of World Health Organization (WHO) demarcated [2] that 70% of the population will be suffering from AD which is of major concern with respect to world metrics being measured. Further, automated detection of Alzheimer's disease using MRI concerning [3]. So far, no advanced treatment has been discovered for AD; however, early detection and treatment can significantly mitigate the progression of the disease. It is primarily based on a thorough assessment of medical history, cognitive tests, and evaluation of symptoms [4, 5]. Neuroimaging modalities, including magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, are used to rule out other causes and assess brain changes associated with the disease. An accurate diagnosis can only be achieved by conducting a post-mortem examination of brain tissue which is very time-consuming and costly. Ensuring detailed survey analysis over the nature of view of studies being approached with a highly efficient nature of data involved in the process [6].

Experts can manually execute segmentation procedures; however, this method is time-consuming and arbitrary for today's era where we have more and more patients. To drastically reduce the time required the MRI [7] portrays a novel field for identification of neuro-degenerative disease like-Alzheimer's disease (AD) based on 3D brain MR images with first-order statistical features. [8] To obtain optimal accuracy it was confirmed that coronal view of brain segmented images was used [9]. Another algorithm termed S3[10], trained upon supervised knowledge-based learning techniques employing adaptive intensity thresholding and morphological operations have been employed to improve the effectivity of the analysis. Using 3D convolution for proper segmentation requires consistency and reproducibility reducing inter-observer variability [11, 12]. As automatic skull stripping methods may not always achieve perfect results [13] due to the complexity of the algorithm and hyper-parameter tuning pose a major problem in the scenario of achieving optimal results, so the models proposed are compared with three most popular methods of brain segmentation working as a benchmark score for all other, namely, ROBEX(robust brain extraction), BSE(brain surface extractor), and BET(brain extraction tool), [14] have been developed utilizing brain anatomy and image intensity characteristics. Practical instances in the biometric analysis

using deep morphology helps in identifying deformed MRI having functional and structural characteristics ensuring hyperactivity disorder [15]. Challenges in handling heterogeneity in medical images, including MRI scans, often exhibit inter-patient and intra-patient anatomical variations, pathologies, and image artifacts [16]. Further analysis [17] in the domain of neuro-degenerative disease identification the model identifies various parts of the brain effectively using proper segmentation but are not capable of replacing the existing manual system [18]. Moreover, for validation and generalization of the algorithm performance it should be assessed on diverse data-sets, including different populations, image acquisition protocols, and scanner types, to ensure reliable and consistent results in clinical practice [19]. Investigation to detect the stability of 3D-CNN using transfer of information for AD classification [20]. Further shifting our concerns to proper classification of neuro-degenerative diseases like- Alzheimer's Disease [21]. Studying the nanoparticles as a contrasting agent in achieving the major threshold output to find out the accurate outcome [22, 23].
In this paper, we unveil a fresh perspective utilizing a modified 3D-Unet architecture for improved brain segmentation process moving further a Conv3D architecture for disease classification making it possible to utilize the utmost facilities of bio-medical image segmentation and disease classification. In earlier research studies [24] it is discussed why brain segmentation is an essential step in the study of medical imaging of neuro-degenerative diseases [25, 26]. Contrastive learning of the significant paper helps in better understanding [27, 28]

However, this paper presents the segmentation procedure that seeks to find and measure disease-related alterations, which can help with diagnosis, tracking disease progression, and evaluating therapy effectively and reducing the wrong results in case of classification using the 3D-CNN architecture. [29] LSTM is used to analyze sequences of MRI scans taken over time from the same patients to detect patterns that may indicate the presence or progression of neuro-degenerative disease in the starting phase making it possible to track the effectiveness of treatment [30]. The proposed model offers a distinct value that lies in between the benchmark scores [31] but exhibits a consistent and linear output, showcasing its unique characteristics with segmentation accuracy of 98% and classification accuracy of 95%. Methods of volumetric analysis, which concurrently consider all three dimensions of the data, provide substantial advantages for the classification of diseases like Alzheimer's disease [32]. Early stages of disease identification strategy are helpful using MRI finely tuned with the ResNet18 network [33, 34]. Volumetric analysis [35] ensures a thorough investigation of the entire volume, in contrast to typical 2D models that concentrate on slices and could miss important information from the other two dimensions. Volumetric analysis offers more precise and reliable illness classification by capturing the entire spatial environment and keeping data across all dimensions [36]. This method reduces the possibility of overlooking crucial elements and improves the classification model's overall functionality and dependability. A multi parametric brain MRI using 3D CNN is helpful in analyzing different parts [17, 37]. Therefore, the use of volumetric analysis techniques shows a notable increase in the accuracy of disease classification and offers a greater awareness of the underlying pathology. The research was conducted to train a neural network to automatically detect brain tissue from MRI images and avoid overfitting [38], facilitating proper diagnosis and better understanding of the brain. From the above discussed context, 3-dimensional convolution of skull-stripping is better identification of locating diseases in a human brain cell [39, 40]. Disadvantages of Segmentation includes manual segmentation which is a time-restraining phenomenon that needs expertise and can be subject to inter-observer variability [41]. These algorithms may require substantial computational resources, including high-performing computing or specialized hardware. Multi class MRI classification of brain tumor cells using AI [42] and CNN (Convolution Neural Network) application is also a major concern in our project for better visibility [43, 44].
Rest of the paper is organized as follows: Section 2 outlines various measures employed for better accuracy and efficiency, Section 3 elaborates on the architecture and proposed algorithm for better results, Section 4 describes results and discussions based on scores, Section 5 concludes research work with future directions.

2. Theory

Skull-stripping, a crucial step in magnetic resonance imaging (MRI) analysis, involves the isolation of brain tissue., which contains non-neural tissues like the nose, neck, skull, etc. and is normally the first step in most neuro-imaging applications. This method not only increases efficiency by lowering the complexity of the image itself, but it also lowers the complexity of time and space. Due to its significant impact on subsequent operations conducted on anatomical MR images, the quality of skull-stripping results is of utmost importance [45]. Numerous methods for skull-stripping [46] have been proposed and incorporated into various software packages. Further, application of 3D CNN [47] to develop a prototype that will facilitate proper diagnosis and better understanding of the brain part using CNN-model of approach and further enhancing it using 3D convolution method [38].

$$it = \sigma\ (Xyiyt + Xgigt-1 + bi), \tag{1}$$

The forget gate is formulated as:

$$f_t = \sigma\ (X_{yf}y_t + X_{gf}g_{t-1} + b_f), \tag{2}$$

, The output gate regulates the retention of long-term memory in the current output, denoted as:

$$o_t = \sigma\ (X_{yo}y_t + X_{go}g_{t-1} + b_o), \tag{3}$$

, Ultimately, the output of the LSTM is determined by the interplay between the unit state and the output gate, resulting in the formulation:

$$gt = ot \odot \varphi(ct), \tag{4}$$

The Bi-LSTM calculates $\vec{h}$ and $\overleftarrow{h}$,ensuring forward hidden sequence and backward hidden sequence respectively:

$$\overrightarrow{g_t} = G(X_{\overrightarrow{y g}}y_t + X_{\overrightarrow{g g}}g_{\overrightarrow{t-1}} + \overrightarrow{b_g}) \tag{5}$$

$$\overleftarrow{g_t} = G(X_{\overleftarrow{g}}y_t + X_{\overleftarrow{g g}}g_{\overleftarrow{t-1}} + \overleftarrow{b_g}) \tag{6}$$

By combining $\overrightarrow{g_t}$ and $\overleftarrow{g_t}$, we generate the final output z_t:

$$z_t = G(X_{\overrightarrow{g_z}}\overrightarrow{g_t} + X_{\overleftarrow{g}}\overleftarrow{z g_t} + b_z) \tag{7}$$

Specification of System Used - 32 Thread Processor, 100GB Memory, 1TB SSD, 24GB NVIDIA Quadro RTX 6000.Time Taken for various processes.

Table 1: Step-Wise Time Taken

Step	Time Taken
Bias Correction (Segmentation)	2 hours
Resizing & Normalization (Segmentation)	10 mins.
Per Epoch (Segmentation)	17 sec.
Training (Segmentation)	7 min
Training (Classification)	3 hours

METHODOLOGY

The study encompasses the collection of datasets followed by the 2-fold model of architecture in which segmentation plays the first major role in the experimental process followed by accurate disease classification.

A. Segmentation

Here, modified Residual 3D U-net architecture with dense atrous convolution and Rmp block is used. Having a precise advantage over the traditional 2D model. The Residual U-net model introduces residual connections within the U-net architecture, enabling a direct information flow from the encoder to the decoder path. This incorporation of residual connections enhances the model's performance by facilitating efficient information propagation. In this case there are 4 encoders and 5 decoders. This helps in alleviating the vanishing gradient problem and enables the network to learn more effectively. The effect of skull stripping in ADNI data is clearly visible, forming computationally expensive 3D CNN [26]. The Rmp (Residual Multi-Path) block is a building block used within the Dense Atrous Convolution. The architecture comprises multiple parallel branches, each consisting of a sequence of convolutional layers. The outputs are subsequently concatenated to yield the final output of the block. This project was engaged with a dataset of 125 participants residing in the age-group of 21-45 years.

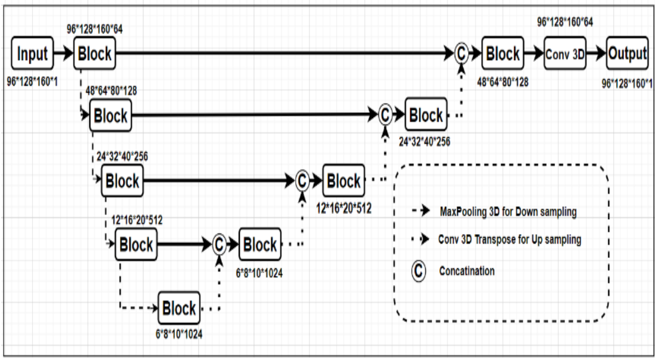

Fig. 1: 3D-Unet Architecture

B. Classification

Following the process of segmentation there comes the process of classification in which Skull stripping, ensures pre-processing of neuroimaging that aims to separate the brain neural tissue from the surrounding skull and non-neural structures in an image. The purpose of skull stripping is to obtain a clean representation of the brain for further analysis or visualization, without the confounding effects of extracranial tissues. Depending on the feature extraction process followed by adjusting kernel size, drop-out and batch normalization, resulting in hyperparameter tuning to make a compact outcome of the output with the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset having 819 subjects.

3. Experimental Method/Procedure/Design

After much thought and testing, we were able to determine the ideal mix of hidden layers and hyperparameters to create the most precise and high-quality brain images.

Table 2: Summary of Segmentation and Classification Results

Task	Dataset	Participants	Age Group	Dimensions	Accuracy
Segmentation	NFBS	125	to 45	256x256x192	97%
Classification	ADNI	819	to 90	256x256x166	95%

Table 3: Segmentation Results

Segmentation	
Model	Modified 3D-Unet
After Processing Dimension	96x128x160
Total Parameters	245
Trainable Parameters	221
Non-Trainable Parameters	24
Batch Size	4
Hidden Layers	24
Hyper-Parameters	4

Table 4: Classification Results

Classification	
Model	Conv3D
After Processing Dimension	256x256x166
Total Parameters	2,032,833
Trainable Parameters	2,031,745
Non-Trainable Parameters	1,088

A. Data Augmentation

Based on this observation, we decided to train CNN using the volumetric analysis having a detailed approach. With respect to the data-sets being trained there was found a shortcoming regarding the number of abnormal data-sets that results in the introduction of data augmentation to equalize the quantity of abnormal and normal data-sets using vertical and horizontal flipping. This was a random rotation at an angle performed in the three-dimensional space to acquire a precise number of data-sets being used.

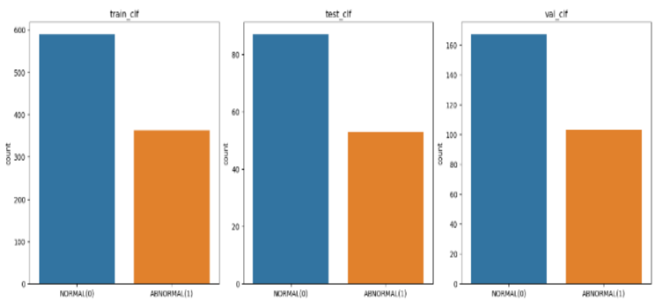

Fig. 2: Graphical representation of Train, Test & Val

This augmentation technique helped in tackling the issue the issue of biasness by tripling the number of datasets for abnormal subjects in classification further helping us improving the model accuracy and avoiding overfitting.

4. Results and Discussion

Our research paper successfully demonstrates significant advancements in processing brain MRI images, resulting in highly accurate and high-quality segmentation. The quality of our segmentation was evaluated using the Dice coefficient, achieving an impressive score of 95%. Additionally, our approach exhibited a specificity of 97% and sensitivity of 98%, enabling us to accurately classify patients having Alzheimer's disease. Notably, our methodology achieved an outstanding accuracy of 97% in brain segmentation and 95% in disease classification. These results underscore the effectiveness of our proposed approach and its potential to contribute to improved treatment in the field of Alzheimer's disease.

• The Jaccard index quantifies the level of agreement between the obtained result and the ground truth by assessing their overlap. Mathematically, it is defined as follows:

$$\mathrm{J} = \frac{\mathrm{TP}}{\mathrm{FP} + \mathrm{TP} + \mathrm{FN}} \tag{8}$$

• The Dice coefficient evaluates the overlapping, can be calculated in the following way:

$$D(A,B) = \frac{2.TP}{2(TP+FP+FN)} \tag{9}$$

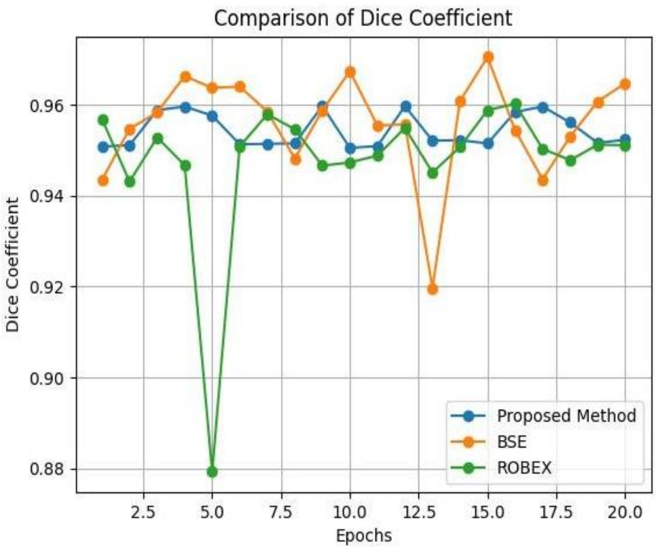

Fig. 3: Dice Coefficient

• The sensitivity, also known as the true positive value can be calculated in the following way:

$$SN = \frac{TP}{TP+FN} \tag{10}$$

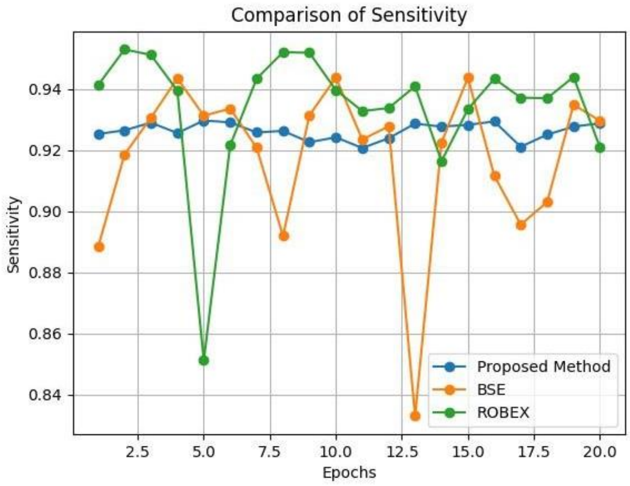

Fig. 4: Sensitivity

• The specificity evaluates the proportion containing pixels that are devoid of the region of interest and are correctly detected. The specificity can be calculated in the following way:

$$SP = \frac{TN}{TN+FP} \tag{11}$$

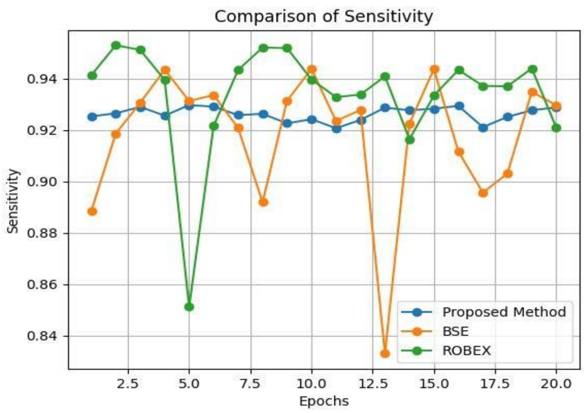

Fig. 5: Specificity

In case of brain segmentation by exploiting small convolutional kernels, we were able to achieve a deeper network which has fewer parameters and thus, making it less prone to overfitting. Total subjects - 125 in the age group of - 21 to 45 yrs. With the calculated total parameters of 245, Trainable parameters of 221, non-Trainable parameters of 24, Having batch size - 4.

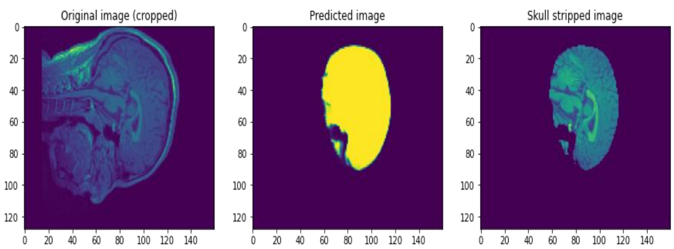

Fig. 6: Example of Segmented Brain

Volumetric analysis involves measuring changes in brain structure volume over time. Furthermore, in-case of classification approach we used a total of 819 subjects, 229 - CN, 398 - MCI, 192 - AD (approximately equal number of men and women) in the age group of - 55yrs to 90 yrs. Followed every 6 months for 24 months 1.5 Tesla MRI scan. With the calculated total parameters of 2,032,833, Trainable parameters of 2,031,745, non-trainable parameters of 1,088 dimensions -224*224 slices having train set N - 589, train set AB - 363, test set N - 87, test set AB - 53, valid set N - 167, valid set AB - 103, Having batch size – 16.

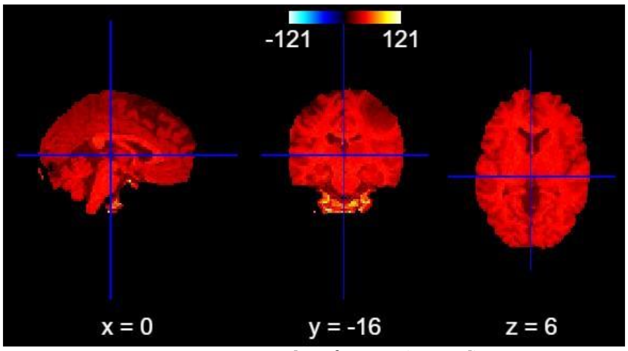

Fig. 7: Disease Classification (Normal)

5. Conclusion and Future Scope

This research introduces a novel framework that utilizes a modified 3D-Unet architecture for brain segmentation and conv3D combined with LSTM for disease classification. Our method focuses on preserving the features using bias correction and proving high resolution stripped brain. Using CNN for label identification, our strategy performs better as compared to other competing approaches. Through brain shielding experiments, we will experiment this algorithm on other image modalities to demonstrate the performance of the method.

Data Availability

The data presented in this study are available on request from the corresponding author.

Conflict of Interest

The authors report no conflicts of interest. The authors are solely responsible for the content and writing of this article.

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Authors' Contributions

Conceptualization, Aditya Kumar Singh, Sabbir Reza Tarafdar. Methodology, Suprava Saha, Sabbir Reza Tarafdar. Investigation, Suprava Saha, Deepika Das, Aditya Kumar Singh; Resources, Suprava Saha, Deepika Das, Aditya Kumar Singh. Writing— Suprava Saha, Deepika Das, Aditya Kumar Singh, Sabbir Reza Tarafdar and Tushnik Sarkar. Writing—review and editing, Sabbir Reza Tarafdar Tushnik Sarkar. Supervision, Tusnik Sarkar, Sabbir Reza Tarafdar.

All the authors have given their consent and concurrence to the final form of the manuscript.

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