Detection and Stagewise Classification of Alzheimer Disease Using Deep Learning Methods

B.R. Pushpa, P.S. Amal, Nayana.P.Kamal

Abstract--- Alzheimer disease is a neuro degenerative disease that affects memory, thinking and cognitive behavior. It is one of the leading disease all over the world. AD leads to death of neurons in various brain regions like hippocampus, enlarged ventricles, entorhinal cortex, temporal and parietal lobes. Currently there is no medicine that can cure the disease but it can slower or stops neural damage. The diagnosis of AD involves heterogeneous clinical assessment such as patient medical history, neuropsychological test, family history, blood test etc. are conducted. Diagnosis of AD is important and challenging, with the early prediction of AD the treatment can be efficiently introduced in the early stages. The proposed work begins noise removal of MRI brain images which includes denoising using Median filtering and DnCNN.Further brain tissue are segmented based on voxel based that is white matter and grey matter and cerebrospinal fluid and region based segmentation and finally a deep convolutional neural network for classifying the different phases of AD

Keywords--- Alzheimer's Disease (AD), Deep Leaning, MRI Images.

I. INTRODUCTION

Neurodegenerative disease leads to progressive loss of neurons in brain that includes Parkinson's disease, Huntington's, AD and Amyotrophic lateral sclerosis etc [16]. Among which Alzheimer's disease (AD) is the most generally recognized type of dementia around the world. Alzheimer's disease (AD) is a neurodegenerative disorder that affects the functionalities of the brain which is an important part of central nervous system. AD normally affects people of age group 65 and above resulting in atrophy of brain region that causes the decline in memory, thinking, language and learning capacity[15] The main cause for the memory loss is due death of neurons that causes brain atrophy due to the formation of Plagues and tangles in the brain region. Once the symptoms of AD noticed a patient can survive for a period of 8- 20 years based on the severity of the disease. The drugs available for AD can control or slow the progression of AD. A very few cases will result in actual recognize with probable dementia but not the early prediction of AD. Hence it is important to develop techniques and methods to predict early diagnosis of the disease that can help people with dementia to take decisions on their future and also to undergo medication that improves cognition and quality of life.

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Brain imaging like CT, PET, SPECT and MRI biomarkers are used widely in diagnosing the AD. Structural MRI that adds positive prediction of disease. Since it has high resolution and provides good contrast for the soft tissues. It is used in evaluating the atrophy of parietal lobe, temporal lobe (Barnes et al., 2004; Wahlund et al., 2005), hippocampus, entorhinal cortex and ventricles that increases the diagnosis accuracy. Manually measuring these structures are time consuming and full pattern of atrophy cannot be captured.

The most common symptom pattern begins mild cognitive problems with gradually worsening complexity in learning, remembering new things, loss of identity as the disruption of neurons atrophy, symptoms projects as the regions involved informing new memories are affected.

Some of the symptoms of AD are-

- Memory loss that disrupts daily life
- Challenges in planning or solving problems
- Difficulty completing familiar tasks at home, work, or leisure
- Confusion with time or place
- Trouble understanding visual images and spatial relationships
- New problems with words in speaking or writing

Figure 1 represents MRI coronal anatomy of normal and AD brain that highlights major brain regions affected by Alzheimer disease. (Yellow - Cortex, Blue - Ventricle, Purple –Hippocampus volume reduced)

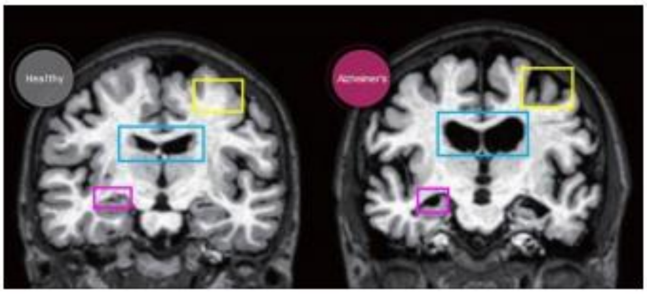

Fig. 1: MRI image of healthy brain (left) and an Alzheimer's brain (right).

AD progression can be categorized into three important stages- Mild, Moderate and severe stages. Predicting AD in mild stage is burdensome as the MRI images of normal aged brain and AD patient brain appears similar that cannot be visualized and analyzed normally.it is also observed that disease get noticed when the patient reaches to moderate or severe stage where the patient requires round the clock

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assistance with day to day activities, loss of awareness about the environment and recent activities and forgetting one's own information and also physical changes.

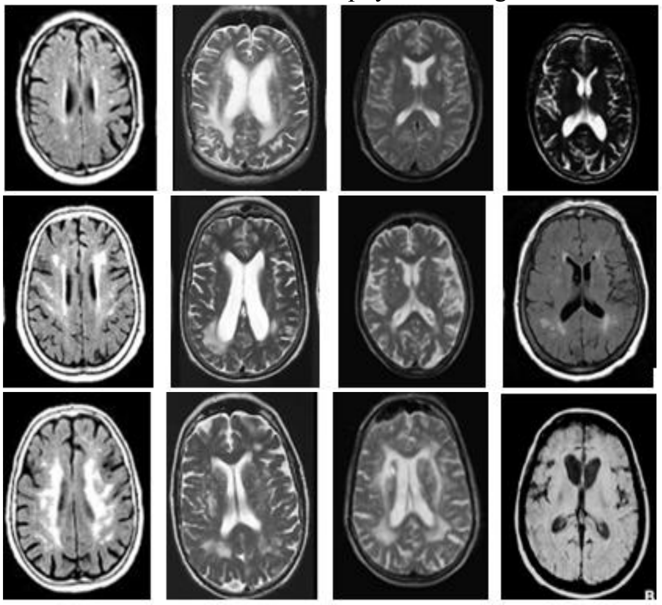

Fig. 2: Different stages of AD (a) Mild (b) Moderate (c) Severe

II. Dataset

Harvard is a research university in Cambridge, Massachusetts. The Harvard Dataverse is a warehouse for sharing, citing, monitoring and to analyze research data and it is open data repository for all researchers across the worldwide. The MRI structural images used in this paper are obtained from Harvard Dataverse.

Data were also collected from the Alzheimer's ADNI database. The ADNI is a multi-center study assessing neuroimaging for diagnosis and longitudinal monitoring. The ADNI was launched in 2003, and its principal objective is to assess the Alzheimers disease progression and MCI through various biological markers such as MRI, PET, clinical and neuropsychological assessment.

For more data we used Open Access Series of Imaging Studies (OASIS) data set, it is an scientific community aimed to provide neuroimaging datasets to avail freely.

III. LITERATURE SURVEY

Tao Chen et al[1] proposed a novel method for denoising image using Median Filter, a nonlinear filter called Tri-State Median (TSM).The input image get processed with Standard Median(SM) filter and Center Weighted Median (CWM) filter and hence output noise detected using impulse detector which compares to find the origin value to make a decision for tri-state. Tri-state decision technique effectively reduces the impulse noise without losing image details. The proposed technique presents stable performance for a wide range of images.

Chunwei Tian et al [2] introduced an approach for segmenting the digital image using deep learning. The segmentation is done with a technique called DnCNN (Denoising Convolutional Neural Network) which is a pertained or inbuilt method. The experimental results show that few segmentation method increases the computational cost and manual settings is required to enhance the performance and procedures incorporated to overcome segmentation problem.

Yoko Hirata et al [3] proposed a method for region based segmentation using Voxel Based Morphometry (VBM) applied on T1 MRI image for early diagnosis of Alzheimer disease. They have randomly taken the MRI images for VBM accuracy determination. VBM Z-Score map is used to determine the MCI and the normal healthy images and obtained the accuracy of 87.8%.

C. Tsai et al [4] proposed a technique on automated segmentation of brain MRI image using adaptive histogram analysis, morphological operations and knowledge based rules to accurately classify various regions. Morphological operators are used to extract the cerebrum region, adaptive thresholding applied to mark ventricular and extra ventricular regions, finally classifies the MRI into gray and white matter to detect the abnormalities.

Resmi et al. [5] proposed a novel method using voxel based method to extract abnormal regions in the brain by making use of MRI images. The pathological features are extracted using spatial filtering domain. The results obtained are compared with manually segmented images and efficiently gained the results.

Tong Sun et al.[6] presented a paper which describes a switching scheme for median filtering which is suitable for data compression and edge detection and it is used to eliminate impulse noises from digital images with less signal distortion and also they are applied different noise removal operations to get filtered image and finds the accuracy is less when compared with median filtering.

G. Evelin Sujji et al [7] introduced several methods for segmentation using thresholding and recorded different thresholding methods such as Global Thresholding, Local Thresholding, Adaptive Thresholding and selection like Iterative based, histogram based and Otsu's method and clustering. With this approach only two classes are generated and it cannot be used for multi-channel image.

Paul M. Thompson et al[8] proposed an approach that maps the hippocampus and ventricular region atrophy in AD affected patients. They developed a surface-based anatomical modeling method to map the dynamic changes occurred in the hippocampus and ventricular regions. Brain maps identify the abnormalities which disassociate with the healthy individuals. The method which had been proposed helps to identify the earlier changes in brain images and detect abnormalities.

Hae-Yeoun Lee et al [9] had proposed a paper related to the segmentation of the ventricular region of the brain tissue using iterative thresholding and active counter model. Iterative thresholding is used initially to recognize the endocardial border and estimate the blood and myocardium signal, and the algorithm they have proposed increases the accuracy and clearly segmenting the left ventricular region of the tissue.

Rigel Mahmood et al[10] presented a novel approach for determines the severity of Alzheimer disease detection using the Feature extraction and classification.

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PCA implemented for feature extraction and reduction and classification is achieved through feed forward multi-layer neural network. and they obtained an accuracy of 89.22%.

Alexandre Savio et al[11] proposed artificial neural network and Support Vector Machine(SVM) methods for classification of Alzheimer Disease. Features are extracted using Voxel based Morphometry(VBM).The feature are selected from the gray matter segmentation .The experiments evaluates the performance of each method to analyze their accuracy.

Jyothi Islam[12] have contributed a Deep Learning neuroimaging study on the early diagnosis of Alzheimer Disease and classify the stages of AD. from MRI images The algorithm proposed has been trained from a small dataset that resulted in high performance and deep convolutional neural network used for classification.

Zhang et al[13] introduced a method early detection using a deep convolution neural network, which efficiently performs early detection of AD using MRI images. Their proposed network grasp from a small dataset and still demonstrate superior performance for AD detection with the accuracy of 87%. Gunawardena et al[14] proposed Convolutional Neural Network for Alzheimer's Disease pre-detection from MRI data. Their study mainly constitute of two experiments, with an assumption that AD detection method can be successfully applied in AD pre-detection also. SVM classification is incorporated experiment and gained 95.3% sensitivity, 71.4% specificity and 84.41% accuracy and for second experiment they have proposed CNN model and obtained accuracy around 96%, sensitivity 96% and specificity 98%.

Karl Backstron et al[15]had proposed a Alzheimer Disease detection algorithm using Deep Convolutional Neural Network based on the features from MRI scanned images. The algorithm had been tested and trained using the 3D Convolutional Network (3D ConvNet) with five layer of Feature Extraction. The technique used a Deep Learning model for the detection of AD and also classify whether AD exists or not. It adapts the deep learning model for detection of AD and increases the accuracy.B. S. Mahanand et al.[16] proposed a method for AD diagnosis using MRI images. Voxel based method employed for feature extraction, PCA approach for feature selection and SRAN for classification. Main highlights of their work is the figure of samples are reduced by using SRAN classifier provides enhanced performance when compared with other classifiers and minimized computational effort.

Although a numerous works are achieved in the field of medical brain image processing to predict the AD. Most of the methods are simple and the satisfied accuracy is obtained. It is also observed that few of the works are focused on one particular feature extraction methods like voxel based , vertex based and region based and also classification performed to differentiate MCI(mild cognitive impairment), AD and NC (Normal controls) and also stage wise classification of AD is obsolete. Hence stage wise classification is essential and motivated us in proposing an computerized method for detection of classification of various stages of AD.

IV. PROPOSED METHODOLGY

The proposed methodology for detection and classification of Alzheimer disease into different stages is comprised of three important stages. Initially the approach starts with preprocessing of MRI structural images using median filter and DnCNN. Further the segmentation methods are implemented based on voxel based and region segmentation. And classification is carried out using deep convolution network. The block diagram representing the flow of proposed methodology is shown in Figure 3.

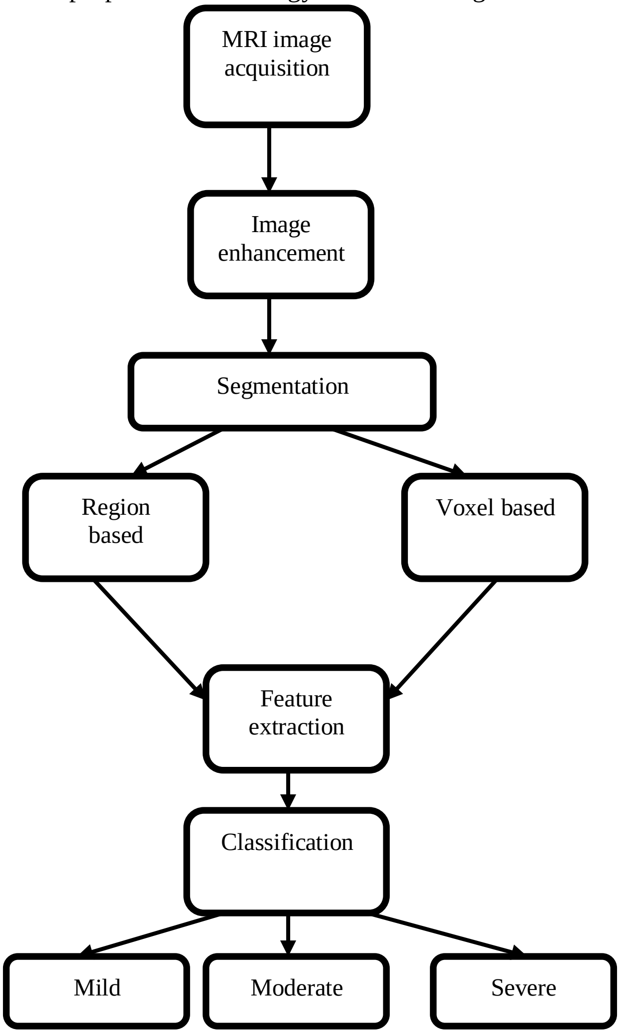

Fig 3: Block diagram of proposed methodology

Image enhancement

Image pre-processing begins with image enhancement that improves the quality of the image and to achieve more sensitivity by removing noise and redundancy without affecting the information of image, which is done related to the intensity values of the image. The main intend of pre-processing is enhancing the image by removing the unwanted particles or boost some of the important image features that is suitable for further processing. In this paper the input MRI image is preprocessed using two strategies:

1. Median filtering
2. DnCNN

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Median Filtering

The Median Filtering is a nonlinear computerized separating method that ejects noise from the given input image or signal. It was exceptionally utilized in digital image processing based on the fact that, under specific conditions it saves edges while expelling noise, additional applications of this method in the field of gesture processing. The median filter calculation replaces the pixel estimation with a median value of input image. Extracting the center value involves the following procedure.

First assemble the pixel points in mounting order then restore the pixel being calculated with the focal point pixel value.

If the nearest pixel of image which is regarded, include and even quantity of pixel, then it swap the pixel with average of two focal point pixel values. The mean filter can be determined as;

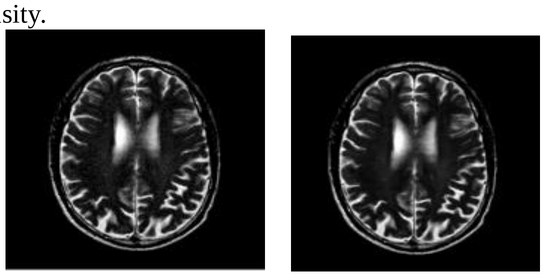
$$F\hat{}\,(p, s) = \text{median}\,\{g(x, y)\} \text{ where}(x, y) \in s_{ps}$$

When S_{ps} is a set of coordinates points in a rectangular sub image as the midpoint at (x, y) median filter analyze the median of the degraded image g (p, s) under the area S_{xy}. Here f^ (p, s) represent the restored image.

Median filter are most commonly used by researches because it's capability of robust out excellent noise reduction with less blurring effect of input noise values with extremely large magnitudes.

DnCNN

The DnCNN mesh is highly accomplished to discover the noise and other high wavelength image artifacts. For an illustration, we can prepare the DnCNN network to recover MRI image resolution or can remove JPEG density artifacts. Different layers in denoising Convolutional Neural Network are used in gray level images. In this work we capture one step ahead by examine the structure of feed-forward noise reduction convolution neural network to squeeze the evolution in extremely deep construction, learning algorithmic rule and regularization technique in image to perform noise reduction. The proposed DnCNN method is capable to grip Gaussian denoising with untried noise intensity.



a. b.

Fig 4: a) Input image b) Filtered image

Segmentation

Image segmentation is an important step that splits an image into different segments and representation of image can be more meaningful and easy to analyze. This is commonly used to distinguish objects or other data in digital images. There are a wide collection of approaches exists to segment images. To be significant and valuable for image examination and interpretation we have to emphatically identify the significant objects or highlights of features. In our work two types of segmentation methods are carried out based on region based and gray and white matter based.

Region based segmentation

Segmentation of MRI images is significant stage which is done without changing the information of an image. Several methods are derived for segmentation. We have been proposed a method for segmenting images by recognizing the most significant regions. It includes area inclusion and area exclusion. For our paper we utilized area exclusion, the entire image gets separated until each sub part is consistent. We constructed an anatomical mapping procedure for recognizing ventricular transform in Alzheimer Disease .Regional based brain changes can equally be identified with the evolution of psychosomatic impedance or genetic risk aspects. The learning has two objectives: first is to sketch out the ventricular transformation and to estimate them with AD.

Threshold based Image Segmentation

Thresholding technique for segmentation considers pixels with similar intensity to select a region. Thresholding provides boundaries in digital image that comprise hard things on a contrast backdrop. Thresholding is a method used for region-based segmentation. It is the most frequent image partitioning technique for extraction the searched details of the background image. The advantage of this technique is ease of implementation and its effectiveness in real-time system.

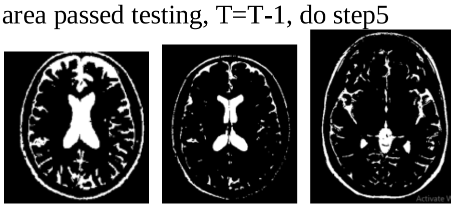
Adaptive Thresholding

In this work, Adaptive thresholding technique is incorporated that takes grayscale or color MRI as input and results in a binary output. For each pixel in an image the threshold is calculated, if this value is lesser than the threshold value, then this is set as the background image.

The existing pixel values will be compared with the threshold value T, and the change in the pixel values depends on the gradual shifting capacity whose position depends on the nearby neighboring measurements.

Adaptive thresholding procedure:

1) Binarize the MRI with a single threshold T
2) Thin the thresholded MRI
3) Eliminate all branchpoints in the thinned MRI.
4)After elimination the remaining endpoints are positioned in the queue, which is used as starting point for tracing
5) Trace the area with threshold T
6) If the area passed testing, T=T-1, do step5



(a)Severe AD (b) Moderate AD (c) Mild AD

Fig. 5: segmentation based on gray matter and white matter

Threshold Selection

In image segmentation we utilize the threshold selection method that decides in choosing the threshold point T. In the event of manual thresholding strategy, the threshold point T can be chosen by the client with the assistance of input image histogram. This strategy is commonly practiced by a device that enables the client to choose the threshold value T depends on their decision. And for the event programmed thresholding strategy, the estimation of T can be picked dependent on histogram, clustering, variance, means and so forth.

The Otsu's method and its variants

The objective of Otsu's thresholding is to calculate a best value for global thresholding. In this work, it is expected that an MRI has two-pixel classes. It selects the threshold to minimize the intra-class variance of white and black cluster pixels. The intra-class change could be defined using weighted equation of variances of each cluster which is showing in the following algorithm.

Algorithm

1. calculate histogram and expectation of each intensity stage
2. put up first $x_i(0)$ and $\mu_i(0)$
3. Step through all probable threshold T=1,…..maximum intensity
   I. Update wi and μi
   II. Compute $\sigma_c^2(T)$
4. preferred threshold corresponds to the highest $\sigma_c^2(T)$

(a)Severe AD (b) Moderate AD (c) Mild AD

Fig. 6: segmentation based on grey matter and white matter.

Classification

The intend of classification procedure is to categories all pixels of a digital representation into some limited figure of classes. This group of separated data may then be operating to make thematic representation of the data. Generally multispectral records are used to execute the classification and, in fact the spectral prototype present with the information of each and every pixel is used as the algebraic basis for categorization. The main intention of image classification is to identify and reveal as a unique gray level the features occurring in an image of the object, these features actually represented.

Convolution neural network

Convolutional Neural Networks is one of the classification approaches in Neural Networks that are built with neurons that have learnable weights and biases. Each neuron takes some inputs and then executes a dot product and alternatively tracks it by a non-linearity and provides some output. The entire network still reveals a distinct discernible score function from the input image pixels on one end to class scores at the other and have a loss function on the fully-connected layer.

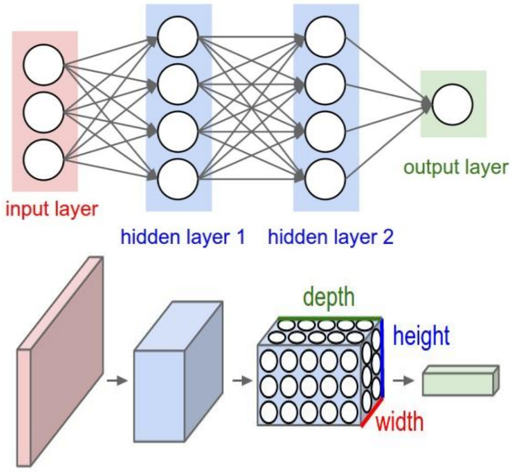


Fig. 7: Convolutional NN Architecture

Using CNN method the dataset is separated into both testing and training sets which is an important component of clustering. Most of the data is utilized for training and a few data is accounted for testing. By utilizing comparative dataset for testing and training, we can limit the impacts of data disparities and better comprehend the attributes of the model. After a model has been prepared by utilizing the preparation set, you test the model by making expectations against the test set. Science the dataset in the setting set as of now contains known qualities for the credit that you need to anticipate, it is anything but difficult to decide if the model's predictions are correct.

We trained the dataset using CNN and created a neural network, using that neural network the classification of Alzheimer's disease is done. CNN is an important deep learning technique that automatically classifies the images. The feature extraction and feature selection is done automatically in the CNN model. When dataset is inputted into a network it compares the features with the existing trained data and finally decides the stages of AD. The proposed method is experimented on 500 MRI images that includes mild , moderate and severe stages of AD.we have taken 200 images as training datasets and achieved accuracy of 88.89% and the results are shown below.

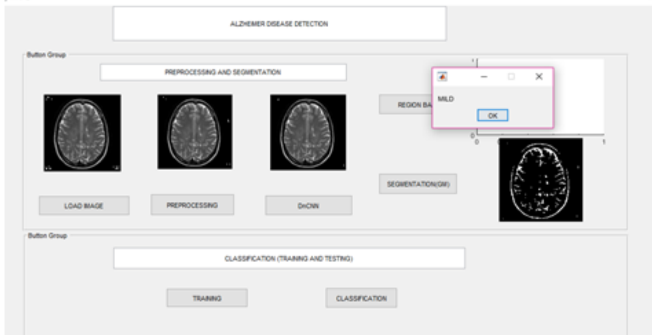


Fig. 8: Classification of MRI into Mild

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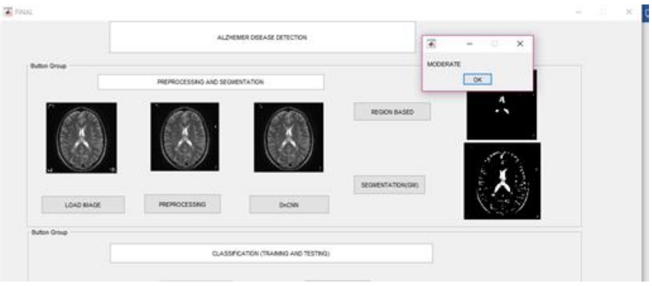

Fig. 9: Classification of MRI into Moderate

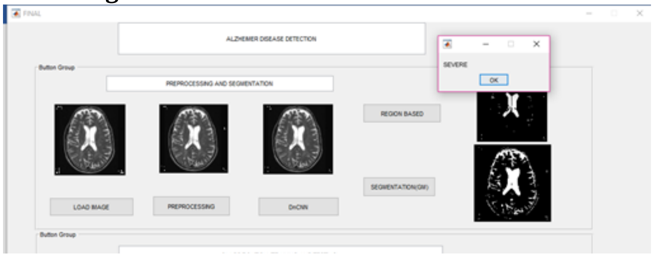

Fig. 10: Classification of MRI into Severe

V. EXPERIMENTAL ANALYSIS AND RESULTS

In this work different thresholding methods are employed to extract features of ventricle region, gray matter and white matter from the brain mri image and followed by CNN for classification of MRI images into different stages of AD i.e. mild, moderate and severe. The figure shows the result of training dataset for classifying the stages of AD.

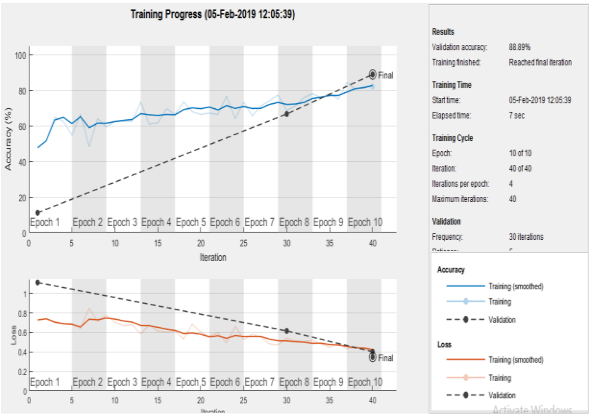

Fig 11: Training dataset

VI. CONCLUSION

Detection of Alzheimer disease in the mild stage is most significant for patient care and for research. In our proposed work segmentation have been done using different thresholding methods that efficiently segment the MRI images into ventricle region as well as gray matter which are helpful for identifying the stages of dementia. The classification approach is implemented with CNN alone considering a group of MRI images for training and remaining data for testing and achieved an accuracy of 88.89%.The work is focused on the stage wise classification of AD using MRI alone, further the work can be expanded by considering Multi modalities such as PET, fMRI in combination with the MRI to improve the accuracy.

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