Innovative Approach for Alzheimer's Disease Detection

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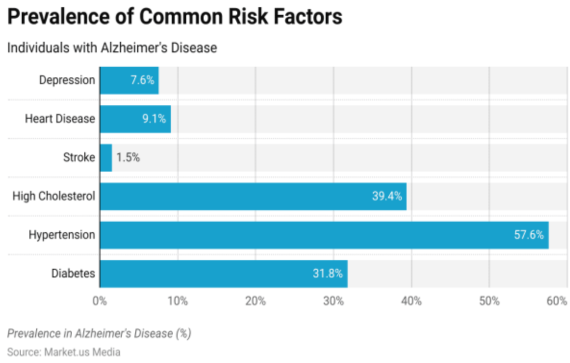
Alzheimer's disease (AD) presents a pressing global health challenge, with its prevalence expected to rise in the coming years. Early detection and management becomes crucial to improve the health of the patient. However, current diagnostic methods face limitations, including the reliance on manual interpretation of MRI images and the lack of comprehensive tools for disease management. To address these challenges, this research paper proposes a holistic approach to AD detection and management. Leveraging deep learning techniques, particularly transfer learning. Building upon existing literature the research study focuses on the key challenges faced during detection of the disease. This is followed by developing the Alzheimer's detection system using transfer learning approach, observing the output and its performance impact using AUC approach, respective learning rate along with the batch size that has been considered. The algorithm is further modified using hyper tuning parameters and data augmentation . The best algorithm between inceptionv3 with additional capacity and modified inceptionv3 is determined. The paper concludes by paving a path for utilizing different state of art technologies for Alzheimer's detection.

INTRODUCTION

Healthcare is considered to be one of the most critical factors in the life of every human being. The entire health care system comprises of understanding the parameters affecting the health, identifying and detecting the most prominent factors. Once detected the ailment has to be properly treated, monitored and evaluated for better health parameter results. All this is possible in cases of non coinciding parameters of different ailments .But ailments such as dementia, as said to be an advanced stage of Alzheimer's, is worrisome, especially when affecting the elderly people. There is a fine line between both diseases and it is difficult to distinguish between the completion of one and onset of the other. Alzheimer’s disease is a grave health concern that impacts every individual, their families and society at large.
The major causes of Alzheimer disease is found to be due to the aging population, the economic and societal burden of Alzheimer’s is substantial. Therefore there is a need to provide support services, develop public awareness to improve diagnosis, treatment, and care for individuals with Alzheimer’s and their caregivers. This paper thus focuses on accurately identifying individuals with ailments such as Alzheimer's or Mild Cognitive Impairment (MCI) ailment, track their progress and further assist in providing personalized recovery measures through use of advanced technologies. According to Mayo Clinic survey, Dementia is a term used to specify a set of symptoms that affect the memory, thinking capabilities and social abilities. One of the disease that can cause dementia is said to be Alzheimer's which is the most prevalent in the elderly. The elderly as well as the population with co morbidities have become more prone to Alzheimer's disease post COVID. The major factors that has aggravated dementia risk are diabetes, hypertension and cardiovascular diseases along with increase in aggression and restlessness among people.



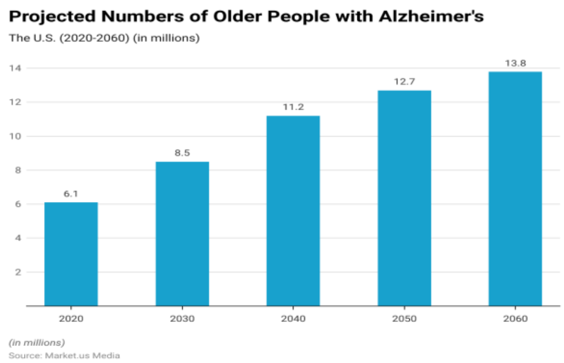


Fig.1 Common factors affecting Alzheimer's disease. **Fig 2 Statistics of Alzheimer's patients across USA**
source: https://media.market.us/alzheimers-disease-statistics/

]This increase in Alzheimer's is quite evident from figure 1. As projected in figure 2, million people worldwide would be suffering from this dreaded dementia ailment. By the year 2060, USA itself would have around 14 million cases of Alzheimer's patients while 139 million cases of dementia could occur across the globe by the year 2050 as shown in figure 3.

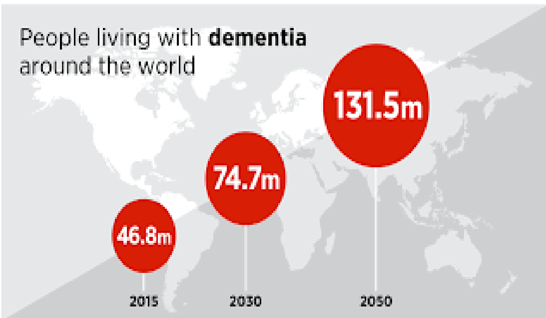


Fig. 3 Dementia Prevalence across the world
Source https://www.openaccessgovernment.org/dementia-become-trillion-dollar-disease-2018/26160/

Therefore, looking at the alarming situation, it is critical to have systems and policies in place to combat this high burden disorder.

LITERATURE SURVEY

The research work in this domain consisted of understanding the world wide scenario of the people undergoing the ailment and its projections for years ahead, as elaborated above through figures 1-3. Given the progressive nature of the disease, early detection and classification of Alzheimer's disease (AD) forms the critical area of research. Based on this, the survey was further carried out in the domain of Machine Learning techniques for Early Detection, Neuroimaging Biomarkers, Biomarkers in Cerebrospinal Fluid (CSF), Genetic Markers and working through Multimodal approaches. A number of research papers were further analyzed as elaborated below. The research paper by M. Talo et al [1] specified that early detection of the diseases can aid in providing timely best treatment. However, it was observed the diagnosis of brain abnormalities, when done through a manual approach is time-consuming. Minute changes in the MRI images , especially in the initial stages, are difficult to perceive. Therefore there is a need to automate the process of diagnosis through technologies of ML and deep learning . El Sappagh et al. [2] explored the prediction of Alzheimer's disease (AD) by incorporating various parameters such as patient co morbidities, cognitive scores, medication history, and demographics. The paper further elaborated on various machine learning algorithms. The authors identified that random forest model gave a better performance as compared to other methods. The authors De A et al. [3] introduced 3D Diffusion Tensor Imaging (DTI) approach to automate the classification process by using Convolution Neural Networks (CNNs) as well as using Random Forest Classifier. The prediction of determining severity of Alzheimer's Disease can be determined using acoustic and natural language features in spontaneous speech and their correlation with Alzheimer's diagnosis can be determined, expressed M. Rohanian et al. [4]. The proposed model utilized Long Short-Term Memory (LSTM) networks for text and audio data, combining their outputs with a gating mechanism for the final prediction [4]. Zheng, X et al.[5] employed a statistical likelihood-ratio approach for computer-assisted diagnosis in Alzheimer's disease based on signal detection theory that is derived from T1-weighted MRI images. The focus of the authors was on determining the sensitivity and specificity for the Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD) dataset. Shukla, A et al.[6] focussed on the disease detection methods, using automatic pipelines and machine learning techniques, Biomarker, Fusion and Registration. The challenges identified by the authors included performing multi class classification. The importance of multiple modalities of neuroimaging biomarkers for accurate AD classification was determined by Afzal et al. [7] . The research paper elaborated on using deep learning and Support Vector Machine classification methods on MRI, fMRI, PET, and amyloid-PET scans. Goenka et al [8] emphasized on the importance of neuroimaging biomarkers and deep learning models for accurate AD classification Early AD diagnosis can be determined using CNN for MRI images stated Salehi et al. [9]. The research paper authored by Basaia et al. [10] focused on utilizing CNNs for automated AD and Mild Cognitive Impairment (MCI) detection from MRI scans. Bandyopadhyay et al. [11] in their research paper compared ensemble learning and artificial neural networks (ANN) on the OASIS dataset during AD detection. Maringanti et al. [12] provided insights into the complexities and computational costs associated with machine learning as well as deep learning models for early-stage AD detection. Utilizing Diffusion Tensor Imaging (DTI) in 3D for AD diagnosis gave a better classification accuracy of 92.6% using a combination of Convolutional Neural Networks (CNNs) and Random Forest Classifier (RFC) mentioned Feng et al. [13]. Basaia and Agosta [14][15] also focussed on CNNs for automated AD and Mild Cognitive Impairment (MCI) detection from MRI scans.

CHALLENGES IN ALZHEIMER'S DISEASE DETECTION

Major challenges faced during working on Alzheimer's disease detection includes:-

1. **Limited data availability :-** There is a scarcity of publicly available large and labelled datasets. Overemphasis on a single biomarker as compared to integrating other biomarkers such as cerebrospinal fluid analysis (CSF) and Positron Emission Tomography (PET) imaging hampers the performance of the machine learning model incorporated.

2. Model applicability:- Determining the appropriate method for Alzheimer's detection is a challenge in itself. The lack of detailed model information, determining its architecture, training procedures, and imposing hyper parameter settings, results in increased complexity.

3. Evaluation measures :- There is a need to resolve the issue of class imbalance, variations in the number of samples across different classes (AD, MCI, normal), and determine its impact on the performance and accuracy of machine learning algorithms incorporated is difficult.

4. Quality concerns :- The image quality used during the pre-processing phase impacts the accuracy of the output. Therefore, the omission of factors such as the gender, brain size and age corrections in brain volume calculations could impact diagnostic as well as model accuracy.

5. Cost factor :- Costs involved at every step of the feature extraction and detection process lead to determining the computational costs.

PROPOSED WORK

Before any treatment is applied, baseline assessment was proposed to determine the health of the cognitive functions and brain response through MRI and other scans as needed. This would then be followed by the intervention period focusing on the medication, cognitive training and lifestyle changes. Follow up at regular intervals would capture changes in brain structure, its function, as well as its cognitive abilities. The challenges in detection of the disease need careful insights into the input parameters or features. Therefore, feature extraction plays an important role in accurately predicting the disease. The features include measurements of brain regions, volumes, shapes, and textures and act as input to the machine learning model. This further requires careful consideration of other factors, such as the natural course of the disease and potential fluctuations in cognitive function. The machine learning model would be used to indicate changes in the individual's condition such as improvements, stabilization, or deterioration in brain health compared to the baseline, a positive prediction might suggest that the intervention is having a positive effect on the individual's brain health. Implementation of a CNN model for classification of brain MRI images is crucial for early detection of AD. Using the state of the art technology and proposing a transfer learning model for detection results in an increase in accuracy of the detection. At the same time , integration of the Mini-Mental State Examination (MMSE) test allows for regular cognitive assessment, providing healthcare providers with valuable insights into the progression of AD.

PROPOSED TRANSFER LEARNING APPROACH

Identification of the correct base model is crucial for accurate detection. With respect to that the proposed work focused on :-

1. **Selection of Transfer Learning (Base Models determination)**: Pre-trained models applied on large datasets(imageNet) such as DenseNet121, VGG19, InceptionV3, Xception, and ResNet101 were compared. These models were identified to act as starting points for transfer learning.
2. **Freezing Pre-Trained Weights**: For each selected base model, the pre-trained weights were frozen i.e. the layers of the base model were maintained without updating during the training process. This ensured that the learned features from the large datasets on which they were initially trained are retained when dealing with limited or unbalanced data.
3. **Adding a Single Dense Layer for Classification**: Once the base model was determined, a new dense layer was added to act as the classification head. This dense layer was responsible for making the final prediction based on the features extracted by the base transfer learning model. In order to perform multi-class classification, a softmax activation function was utilized. The number of classes in the dataset is represented by the respective neurons present in the dense layer.
4. **Incorporating Callbacks**: In order to prevent over fitting and to ensure that the model did not train longer than necessary, an early stopping callback was used based on the validation AUC, meaning that training would halt if even after a number of epochs the validation AUC did not improve.
5. **Using AUC as the Performance Metric**: Throughout the training process, AUC was used as the key metric for evaluating model performance. As it considers the true positive rate and false positive rate across all thresholds, it became helpful in case of class imbalance
6. **Training and Evaluation**: Each base model (DenseNet121, VGG19, InceptionV3, Xception, ResNet101) was trained on the same dataset and under identical conditions.
7. **Selection of the Best Base Model**: After training, the AUC for each model was determined and compared. The base model with the highest validation AUC was selected as the best model for transfer learning and was then used for further fine-tuning and deployment.

RESULTS

Once the proposed system is developed the output i.e. the results and diagnoses from the machine learning model can fall into several categories:

Positive Diagnosis (Alzheimer's Detected): The model predicts with high confidence that the person's MRI scan shows patterns consistent with Alzheimer's disease. This would prompt further clinical evaluation and intervention.

Negative Diagnosis (No Alzheimer's Detected): The model predicts with high confidence that the person's MRI scan does not exhibit patterns indicative of Alzheimer's disease.

Uncertain or Inconclusive: In some cases, the model might have difficulty making a confident prediction due to the complexity of the data or other factors. In such cases, further diagnostic tests or expert consultation would be recommended

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False Positive: The model might incorrectly predict Alzheimer's disease. This emphasizes the importance of combining machine learning predictions with clinical expertise.

False Negative: The model might fail to detect Alzheimer's disease in a person who actually has it. Again, this highlights the need for human oversight and validation.

Figure 4 represents the training parameters used for the inception V3 algorithm. Based on the execution of the algorithm applied, various quantitative parameters such as precision , recall, f1-score and support were determined as indicated by figure 5. The training and validation loss were further determined on the Inception V3 algorithm as shown in figure 6 while figure 7 represents the confusion matrix developed on Inception V3

```
Model: "sequential"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
inception_v3 (Functional)    (None, 4, 5, 2048)        21802784
_________________________________________________________________
dropout (Dropout)            (None, 4, 5, 2048)        0
_________________________________________________________________
batch_normalization (BatchNo (None, 4, 5, 2048)        8192
_________________________________________________________________
flatten (Flatten)            (None, 40960)             0
_________________________________________________________________
dense (Dense)                (None, 512)               20972032
_________________________________________________________________
dense_1 (Dense)              (None, 4)                 2052
=================================================================
Total params: 42,785,060
Trainable params: 20,978,180
Non-trainable params: 21,806,880
```

Fig 4. InceptionV3 training parameters

	precision	recall	f1-score	support
mild	0.38	0.27	0.32	179
moderate	0.00	0.00	0.00	12
normal	0.57	0.93	0.71	640
very-mild	0.67	0.17	0.27	448
accuracy			0.56	1279
macro avg	0.41	0.34	0.32	1279
weighted avg	0.57	0.56	0.49	1279

Fig 5. Performance of InceptionV3 model

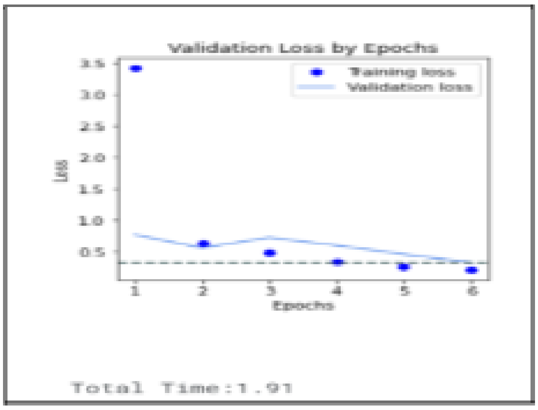


Fig 6. Validation loss by Epochs

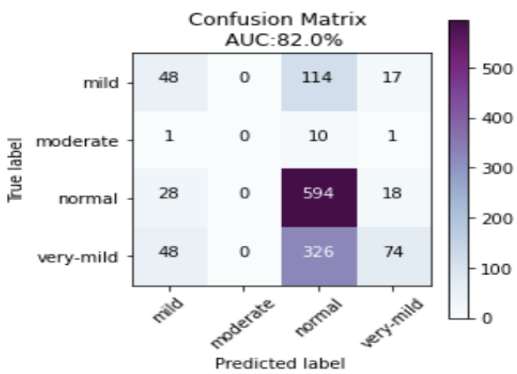
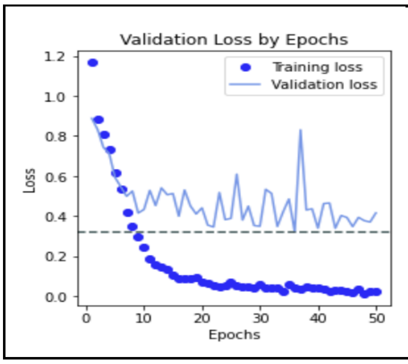
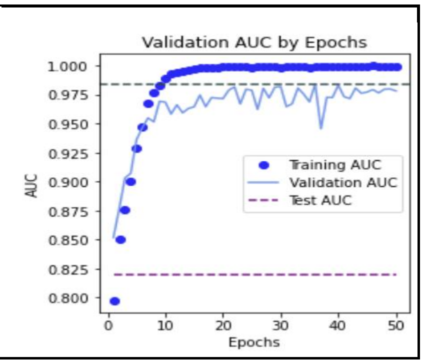


Figure 7 : Confusion matrix representing AUC coverage

To further enhance the model's performance and improve its generalization ability, additional convolution layers were added on top of the existing InceptionV3 architecture. These layers introduced more filters, which enabled the model to capture the intricate patterns and learn finer details from the input images. This led to improved feature extraction and better performance. Dropout was introduced to prevent over fitting, a common problem when adding more capacity to a model. Dropout layers were further inserted after some of the newly added convolution layers. Randomly, these layers, at the time of training, set a few of the input units to zero. This led to effectively forcing the model to learn redundant representations of the data. This regularization technique helped in mitigating the risk of over fitting by ensuring that the model does not depend on any single feature. This improves its ability to generalize the data that is unseen. Batch normalization layers were incorporated to normalize the input to each layer, ensuring that the mean output is close to zero and the output variance is close to one. This helps in maintaining the training process stability of the by mitigating issues like covariate shift and allows for higher learning rates, leading to faster convergence. The build_transfer_model function that worked with the simple dense layer on top of the InceptionV3 base was modified by varying filter sizes to capture different levels of feature granularity. After incorporating the additional layers, the model underwent fine-tuning.

The top layers of InceptionV3, which were initially frozen, were partially unfrozen to allow for fine-tuning. Figure 8 below shows the validation losses when additional CNN layers are added.





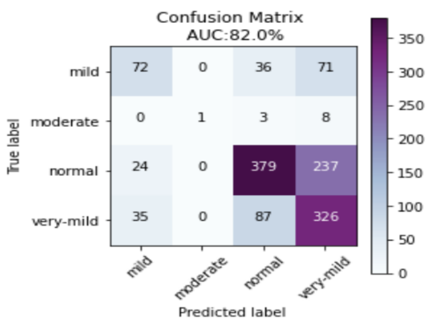


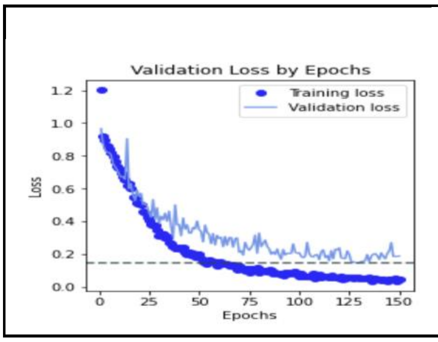
Fig 8. **Validation losses with additional CNN layer**

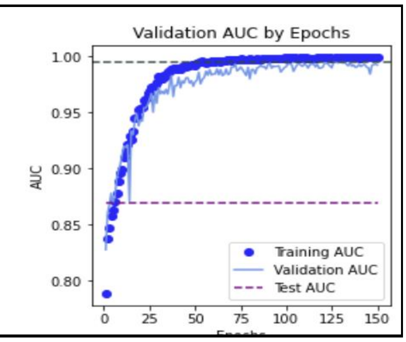
Fig 9. Validation AUC by epochs with additional CNN layer

Fig10. Confusion matrix with additional CNN layer

Validation losses occur when additional layers are incorporated in the CNN algorithm as indicated by figure 9. The effect on the confusion matrix with an additional layer of CNN is indicated by figure 10.

The focus was then on fine tuning the base InceptionV3 models performance .This was done by optimizing the hyper parameters that included its learning rate, size of the batch and the epoch count .The model was trained for 150 epochs to fully learn the complexities of the data. The longer training period was chosen to enable the model to reach its full potential without prematurely halting the training process. The batch size was optimized to strike a balance between memory efficiency and training stability. Data augmentation techniques such as random rotation , Random Flipping, Zooming and shifting were then applied to the images. This resulted in the model becoming invariant to the orientation of the objects, enhanced ability to recognize objects from various perspectives, focus on different levels of detail within the images and create variations in object positioning within the image. This helped in reducing over fitting. The model's ability to generalize to new, unseen data was also improved. Monitoring. of the performance on the validation set was continued even though early stopping criteria was removed. This ensured that the model worked well, and did not over fit. Figures 11 -13 represent the validation losses, validation AUC with epochs and confusion matrix developed with IV3 along with optimized parameters and data augmentation with additional CNN layers added.





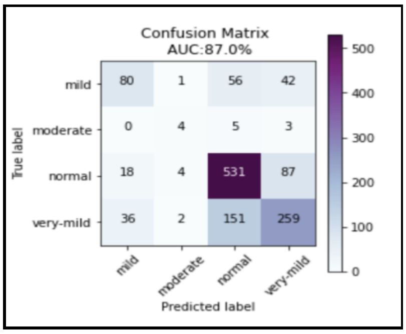


Fig 11. Validation losses with with optimized approach

Fig 12. Validation AUC with epochs with optimized approach

Fig 13. Confusion matrix with optimized approach

The above figure 13 using inception V3, optimized parameters and data augmentation showcases an AUC of 87.0% as compared to 82 % that was obtained by using inception v3 model having additional capacity.

CONCLUSION

This paper focuses on the healthcare domain and identifies the critical factors affecting Alzheimer's disease. It was observed that Alzheimer's disease is on the increase as evident from the statistics around the world. Generating awareness and developing an Alzheimer's disease detection system using state of the art technologies was the need of the hour. This paper further proposed a system using transfer learning, optimizing the various parameters and performing data augmentation. The performance was evaluated using AUC, rate of learning rate, size of the batch size as well as epoch count. The focus of this paper was developing an optimized disease detection system using transfer learning model. One of the paths that can further be explored is to use a multimodal approach to detect, classify and predict Alzheimer's disease.

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