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Article

An Explainable Hybrid Deep Learning Framework for Multi-Class Alzheimer's Disease Classification from Brain MRI Using MobileNetV3–ResNet50 Feature Fusion

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Abstract: Early diagnosis of Alzheimer disease (AD) is a progressive neurodegenerative disorder is key to initiating timely therapeutic interventions. This paper proposes a deep learning model for four-class AD classification using brain MRI. We use a two pre-trained networks (MobileNetV3 and ResNet50) fusion with a final classifier of Multi-Layer Perceptron (MLP). The model obtained F1 scores of 0.88, 0.85, 0.87, and 0.93 for the NonDemented, VeryMildDemented, MildDemented and ModerateDemented classes respectively and had a perfect recall rate of 100% for the ModerateDemented class. Grad-CAM visualizations which represented the framework's ability to provide high prediction confidence as well as a pathologically relevant brain region identification, were able to correctly predict the class with 98.6% accuracy.
Keywords: Alzheimer Disease (AD), MobileNetV3, ResNet50, Multi-Layer Perceptron (MLP)

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that slowly damages brain function and causes the progressive deterioration of memory, thinking, language and mental function. This is the top cause of dementia in the world and is most common in older people gradually it affects the way people act, think and can carry out daily tasks. The irreversible damage of neurons that occurs in Alzheimer's is why early diagnosis is crucial in slowing the disease process and improving patient outcomes. Mild Cognitive Impairment (MCI) is the initial stage of AD and is defined as a level of cognitive decline that rises above what is usually seen with age but doesn't significantly interfere with everyday life. People in this stage often find it hard to remember things that happened in recent times, loose items and repeat conversations and have trouble with problem solving and decision making. This can slowly progress to more advanced stages of dementia if not treated properly. As the disease progresses to moderate stages of dementia, neurological illness spreads throughout the body. Memory problems become more severe, speech becomes impaired and people who are affected may not be able to tell who they are or what they are looking for. At this stage judgement, planning and independent living are significantly affected and medical supervision and care from others is required on a day-to-day basis.

Classical diagnosis of AD relies on clinical evaluation and the expertise of interpreters of neuroimaging. Radiologists assess changes of structure that can be seen in MRI and PET scans to identify indicators of brain shrinkage and abnormalities in metabolism, associated with Alzheimer's disease progression. The neurologist uses cognitive testing, behavioral testing, memory testing and standardized clinical rating scales to complement imaging analysis in order to characterize the severity and progression of the disease. These techniques are still clinically relevant but manual interpretation is time-consuming and could also have inter-observer variability. The advent of

artificial intelligence (AI) specifically deep learning (DL) techniques has transformed the landscape of medical image analysis facilitating automated extraction of features from complex neuroimaging data. Medical image analysis has seen a revolution in recent years with the advent of artificial intelligence (AI) and in deep learning methodologies which are enabling the automated extraction of features from complex neuroimaging data. Deep learning architectures learn hierarchical representations directly from MRI and PET scans, learning the features without requiring the human engineer to design them. Conventional machine learning methods rely on manually engineered features, whereas deep learning architectures learn the features directly from MRI and PET scans. These models have been trained using detailed annotated data sets and show ability in identifying healthy controls from those in the stages of Mild Cognitive Impairment and dementia. AI-powered diagnostic tools therefore hold potential to aid clinicians towards earlier diagnosis and consistency of diagnosis which would allow timely therapeutic interventions and better long-term outcomes for the patient before significant and permanent neurodegeneration starts to become evident**.**

In this study an easy-to-implement deep-learning system for automatically staging Alzheimer's disease using brain MRI scans is proposed with a transparent and efficient strategy. The model starts by fusing feature representations from two pre-trained networks, MobileNetV3 and ResNet50 and then passes the fused features through a Multi-Layer Perceptron (MLP) for classification. In order to provide clinical interpretability Grad-CAM visualizations are included to emphasize the brain areas that are most important in the model's decision making. Experimental results indicate that the system performs well for all the categories and successfully recalls the Moderate Demented group and can be confidently used to detect the early stages of dementia. The Grad-CAM outputs show that the model attends to clinically relevant areas. In general the results indicate that the incorporation of dual-CNN features together with a simple MLP classifier is a computationally efficient and interpretable approach for early Alzheimer's diagnosis.

2. LITERATURE SURVEY

One of the most pressing challenges of the current state of neuroscience is early diagnosis of Alzheimer's disease (AD), and recent years have seen a shift in paradigm toward computation based approaches exploiting the wealth of available patient data. Many papers in the literature have discussed that there is no single modality of data that "tells the whole story". This was a first step that was taken early on by K.P. Muhammed and his colleagues who showed that clinical and demographic data could be combined with the neuroimaging data to significantly improve diagnostic accuracy. They found that algorithms such as Support Vector Machines (SVM) and Convolutional Neural Networks (CNNs) made significant improvements when they were given both MRI and PET data and patient information such as age, gender, and medical history [1]. Nilanjana Pradhan and co-authors focused on incorporating further data sources incorporating even more diversity. Their study was a convincing one that showed how effective all 3 pieces of data structural MRI, Electronic Health Records (EHR) and Single Nucleotide Polymorphism (SNP) genetic data can be when combined. Authors used a Symmetrical CNN model to extract features from MRI images and used features extracted from EHRs to diagnose the disease. The global classification accuracy for MRI analysis was 95.44% and for EHR analysis it was 93.61% demonstrating the complementary nature of two data modalities [2]. The results indicate that there is no single diagnostic method that will be the cure-all for AD but rather an intelligent combination of several information streams.

In addition to the issue of what data to use researchers have been very busy optimizing the processing and analysis of that data. Rajasekhar Butta and others illustrate this trend towards methodological sophistication with their all-encompassing framework. They used a multi-stage pre-processing pipeline of histogram equalization, Gaussian filtering and skull stripping followed by a U-Net architecture optimized using Equestrian Ecosystem Optimization (EEO) algorithm for accurate brain segmentation. In addition to the hybrid feature selection strategy (HOA-AEO) Butta's work incorporated an ensemble classifier which combined an optimized Artificial Neural Network (ANN) Capsule CNN and Autoencoder. The ensemble approach yielded better performance than the traditional diagnostic techniques and the combination of several strengths of classifiers is beneficial [3]. An unusual comprehensive approach was taken by another study by Rahul Kumar & Others who combined bibliometric analysis with experimental evaluation. The bibliometric part characterized the intellectual structure of the research on AD by

analyzing the structure of publications and the networks of collaboration and the experimental part was a systematic evaluation of the performance of 20 classification algorithms on two benchmark datasets. Most importantly this study found that the use of the various feature selection methods always boosted diagnostic performance and also reduced the computational effort which could have practical implications for the clinical use of this work in case there is a resource constraint in real-world settings [4].

The deep learning revolution has had a significant impact on the field of AD research where many studies have been conducted comparing the different variants of the architecture in order to determine the optimal configuration. A. M. Anusha Bamini along her collaborators studied different ResNet variants (ResNet50, ResNet101, ResNet50V2, ResNet101V2) and its models with InceptionV3 for the classification of the AD stages and implemented various pre-processing and augmentation techniques to avoid overfitting and generalisation [5]. The evaluation by Akhilesh Deep Arya et al. based on ADNI, OASIS, and Kaggle datasets revealed that ResNet, VGG and DenseNet could attain as high as 99.4% accuracy which was well above the accuracy of Recurrent Neural Networks (91.2%) and traditional machine learning methods such as SVM (85.71%) and Random Forest (98%). Arya's work also continued the multimodal theme showing that the combination of MRI, PET and cognitive assessment scores yielded significant improvements in terms of diagnostic performance [6].

There has been some research that has gone entirely new directions. Abebech Jenber Belay and collaborators presented a new quantum-enhanced ensemble approach which transcends the limits of classical computing. To improve the diversity and noise reduction authors used an adaptive Median filter to reduce noise and trained individual models using CNN get accuracy of 99.68% on OASIS, VGG16 get accuracy of 83.9% on ADNI and AlexNet get accuracy of 93.24%. Their ensemble model used the Quantum Support Vector Machine, ResNet50 and VGG16 which has a 5 qubit quantum feature map and was able to reach an accuracy of 99.89% [7]. These are impressive results but also important questions regarding the computational feasibility and clinical translatability. The transition to three-dimensional analysis there is a more short-term practical progress. Louise Bloch and her team used 3D DenseNet, EfficientNet and SE-Networks on ADNI, AIBL and OASIS MRI scans. What is even more interesting than the performance results of the similar models is the explainability analysis they did where the machine learning models focused on the inferior and middle temporal gyri while the deep learning models focused on regions such as the entorhinal cortex, cerebral vessels and optic chiasm. This apparent attention deficit indicates that there may be different model families emanating fundamentally different aspects of the disease which will have implications for clinical interpretation as well as model development [8]. One important issue that has been somewhat less studied is the categorization of Mild Cognitive Impairment (MCI) especially the differentiation of progressive versus stable MCI. In this four-class problem of cognitively normal, AD, progressive MCI and stable MCI when Lovepreet Singh Gill and others employed texture and statistical features (GLCM and FOS) the accuracy of Random Forest was 66.1%, while SVM and Decision Tree were performing well with 59.2% and 56.4% accuracy respectively [11]. These rather moderate outcomes were supported by the comparative study conducted by Vasco Sa Diogo et al. which also showed that the Random Forest model had a higher accuracy of 66.1% compared to SVM of 59.2% and Decision Tree of 56.4% [12]. These studies show that the performance gap between binary classification and prediction of progression to MCI is significant and more challenging to achieve than predicting the progression to AD.

There have been several research groups that have been working on more comprehensive predictions. Mingxia Liu and her colleagues developed a deep multitask learning model (DM2L) which simultaneously classifies the disease and predicts the clinical score using structural MRI and demographic information (age, gender and years of education). A multi task architecture has been extended to jointly learn multiple related clinical tasks and this approach has been validated on both the ADNI1 and MIRIAD datasets and has been shown to be efficient [14]. Nianyin Zeng and his colleagues created a prediction model with Principal Component Analysis to reduce features from 90 to 38 which captured around 95% of the original information and a new Multi-Task Feature Selection model to select the most discriminative features from MRI [15]. The genetic component has been also studied especially the ApoE ε4 gene which is a strong risk factor. In the multimodal investigation Haibing Guo and Yongjin Zhang combined the neuroimaging, genetic biomarkers and clinical data that examining the resting-state fMRI data to investigate links

between genetic variations and functional brain patterns. They performed comparative experiments and found that autoencoder models performed better than the other models showing the usefulness of deep learning for the predictive analysis of complex and multimodal medical data [16].

Mustafa Lateef Fadhil Jumaili and others proposed a deep ensemble learning framework for Alzheimer's disease (AD) prediction using MRI images. Their model integrates VGG16, VGG19, ResNet50, InceptionV3 and EfficientNetB7 through a voting-based ensemble to improve diagnostic performance. Evaluated on an Iraqi MRI dataset and validated using OASIS and ADNI datasets the framework achieved high accuracy and robustness. The authors also emphasized the importance of multimodal data integration and more diverse datasets to enhance the model's generalizability and clinical applicability [20].

Tazin Alam and others presented a comprehensive review of machine learning (ML) and deep learning (DL) approaches for Alzheimer's disease (AD) diagnosis. The study examined widely used datasets, including ADNI, OASIS, and AIBL, along with preprocessing techniques and advanced architectures such as CNNs, GNNs, and Vision Transformers. The authors also highlighted the role of explainable AI (XAI) in improving model interpretability and identified future research directions involving multimodal data integration, standardized datasets, and reliable clinical deployment.

The literature as a whole shows some salient points. Deep learning approaches in general outperform traditional machine learning in a binary classification task but for more complex clinical questions such as MCI progression prediction even highly complex models have a limited performance as shown by Gill [11] and Diogo [12]. There is an urgent need for explainability of such models that provide reasons for a prediction made by a model is essential for clinical use. Bloch et al. have done some important work in this area but there is still a great deal of research to be conducted [8].

3. Methods and Materials

In this study 4,000 brain magnetic resonance imaging scans were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database to build and test a deep learning model to predict Alzheimer's pathology. The dataset is divided into 80% for the Training of the model and 20% for the testing of the model. MRI is a non-invasive imaging technique with excellent soft tissue contrast and high resolution anatomical detail ideal for identifying structural abnormalities that are associated with progressive neurodegeneration. Based on these images quantitative features of relevance were extracted to successfully differentiate disease stages.

The sample was subdivided into four clinical groups: Non-Demented, Very Mild Demented, Mild Demented and Moderate Demented. The Non-Demented cohort consisted of scans from cognitively normal individuals who had no clinical or gross morphological abnormalities. The Very Mild Demented group represents the prodromal stage where there are already some obvious structural changes that can be detected although there may also be some subjective memory complaints but not necessarily obvious functional deficits.

Patients with images in the Mild Demented category had early well-defined clinical symptoms. In this stage short-term memory deficits are evident and there are some minor impairments in executive functioning. However the person usually can still live alone. The Moderate Demented group on the other hand is at a more advanced pathological stage corresponding to much more extensive shrinkage of the cortex and severe functional impairment. Individuals in this class often suffer from severe memory loss, impaired judgment and significant language problems and a high degree of dependence on others to help them with daily activities.

4. Proposed Methodology

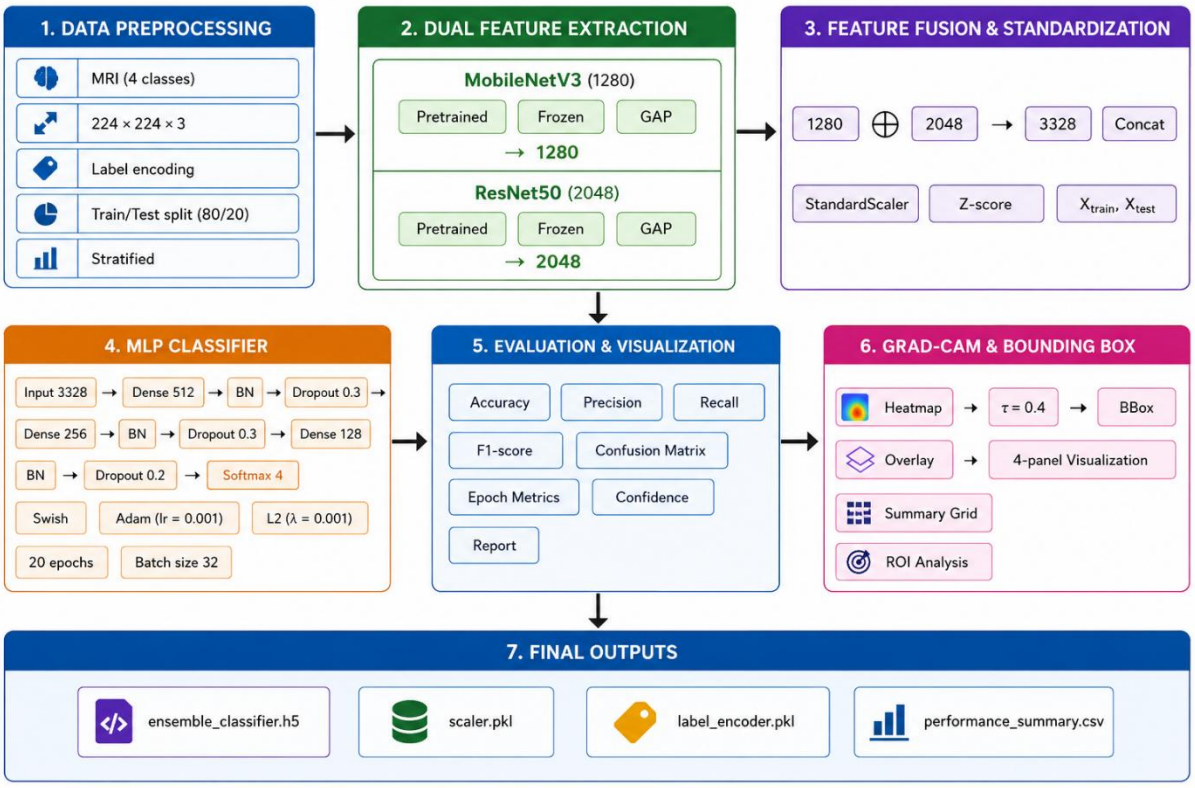

Figure 1: Proposed Methodology

The overall process of the proposed model to predict Alzheimer's disease is described in figure 1. The methodology consists of seven distinct steps, which build on each other, and make use of the complementary capabilities of two pre-trained convolutional neural networks. The first step, Data Preprocessing is to resize the MRI scan images from four diagnostic classes (NonDemented, VeryMildDemented, MildDemented, ModerateDemented) to 224×224×3 pixels. The classes are represented numerically and the data is divided into 80% training and 20% test sets, where the classes are split in a stratified manner to assure the same proportions of classes in each set. The Dual Feature Extraction stage uses two ImageNet-pretrained backbones (MobileNetV3 Small and ResNet50) each without its classification layer. Global average pooling is used on each one resulting in 1280 and 2048 dimensional feature vectors respectively. They are then stitched together into a 3328-dimensional vector in Feature Fusion & Standardization, which is then Z-Score normalized to centre and scale the data. There are three fully connected layers with 512, 256 and 128 neurons followed by Swish, BatchNorm and Dropout with 0.3, 0.3 and 0.2 respectively. Adam optimizer (learning rate = 0.001), L2 weight decay ($\lambda = 0.001$) are used to train for 20 epochs with a batch size of 32. The Evaluation & Visualization phase monitor performance using accuracy, precision, recall and F1-score matrices at epochs and confusion matrices. Lastly Grad-CAM and Bounding Box Generation (threshold = 0.4) generate heatmaps to show disease-relevant regions in models which aids in clinical evaluation.

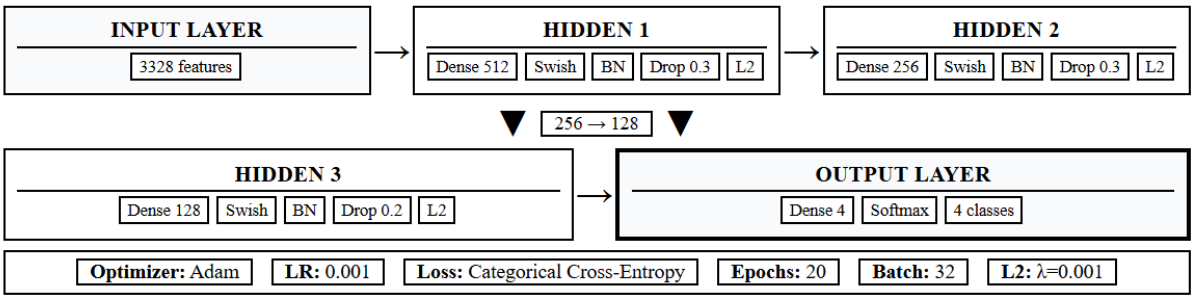

Figure 2: Multilayer Perceptron Architecture

The trainable part of the proposed framework is a Multi-Layer Perceptron (MLP) classifier consisting of three hidden layers that operate on the fused 3328 dimensional feature vector. The first hidden layer consists of 512 neurons with Swish activation and batch normalization as well as dropout regularization with a dropout rate of 0.3 to prevent overfitting. The second hidden layer is a dimensionality reduction layer with 256 neurons and the same activation normalization and dropout rate. The third hidden layer has 128 neurons and a lower dropout rate (0.2). L2 regularization is added to each dense layer with a weight of λ=0.001 to reduce the weights of the layer and make the model generalize better. The output layer has four neurons using the Softmax activation function, which result in probability distributions across the four categories of Alzheimer's disease. The network is optimized by Adam optimizer with a learning rate of 0.001 and trained with categorical cross entropy loss for 20 epochs and a batch size of 32. This architecture is a compromise between model capacity and regularization providing good classification results.

Table 1: Hyperparameter

Component	Hyperparameter	Value
Feature Extraction	Feature Dimension (MobileNetV3)	1280
	Feature Dimension (ResNet50)	2048
	Fused Feature Dimension	3328
Feature Standardization	Scaler	Standard Scaler
Hidden Layer 1	Neurons	512
	Activation	Swish
	Dropout rate	0.3
	L2 Regularization	0.001
Hidden Layer 2	Neurons	256
	Activation	Swish
	Dropout Rate	0.3
	L2 Regularization 0.001	0.001
Hidden Layer 3	Neurons	128
	Activation	Swish

	Dropout Rate	0.2
	L2 Regularization 0.001	0.001
Output Layer	Neurons	4
	Activation	Softmax
Training Configuration	Optimizer	Adam
	Learning Rate	0.001
	Number of Epoches	20
	Batch Size	32
Grad-Cam	Threshold	0.4

5. Result and Discussion

The experimental results are presented in this section and a thorough comparison with the existing leading methods is carried out. The main objective of this work is to validate the effectiveness of the proposed deep learning model for medical image classification tasks. The adopted methodology is based on transfer learning strategy which involves using ResNet50 and MobileNetV3 as backbone feature extractors followed by feature integration and then classification using multi-layer perceptron. To improve the transparency of the model visualizations based on Grad-CAM are used which produce heatmaps, bounding regions and confidence scores that identify diagnostically relevant areas. All the experimental procedures are implemented in Python and are run on Google Colab with a T4 GPU. Overall goal is to mainly test the performance and robustness of the proposed system with respect to Alzheimer's Disease identification.

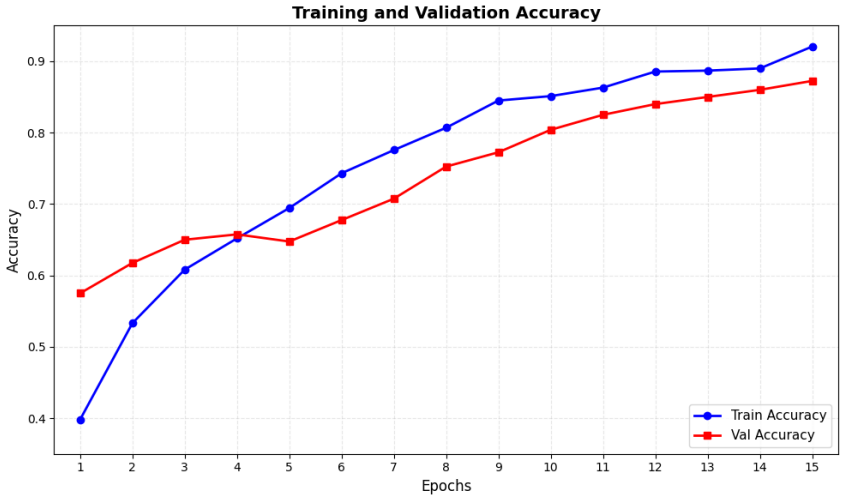

Figure 3: Training and Validation accuracy graph

In this section the accuracy progression curves presented in Figure 3 are analysed for the proposed model which shows the learning behaviour of the proposed model during the multi-class classification of Alzheimer's disease. The training accuracy curve starts high and rapidly rises in the early epochs indicating the network's ability to learn the relevant patterns from the MRI data. The validation accuracy curve closely follows the learning curve during training, indicating that the system will perform well on new data and it is not prone to overfitting. With continued training, both curves approach each other gradually, demonstrating stable optimization and a good learning of the parameters. The convergence pattern confirms the effectiveness of the hybrid feature representation generated by the

fusion of the outputs of MobileNetV3 and ResNet50 and passed to a Multi-Layer Perceptron for final classification over the four cognitive stages. The model also showed strong performance in validation, with an average accuracy of 98.9%, highlighting its potential as a valuable clinical aid for the diagnosis of neurodegenerative diseases.

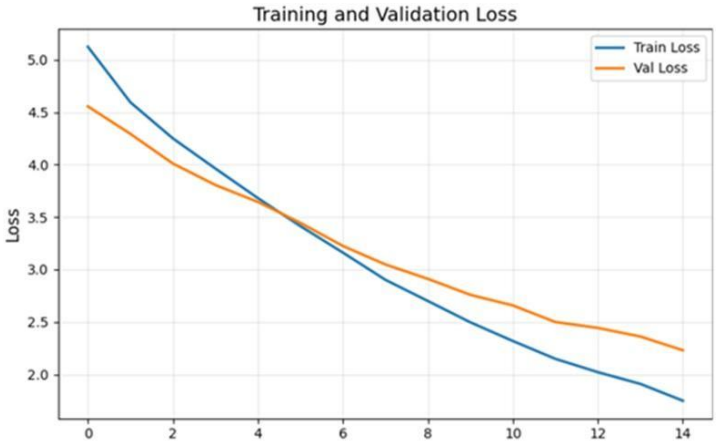

Figure 4: Training and Validation loss graph

The loss curves shown in figure 4 illustrates the optimization behaviour of the model during training for the multi-class classification of Alzheimer's disease. The trend of the training loss is decreasing steadily as the number of epochs increases, showing the system's increasing ability to minimize classification errors as it moves forward. The validation loss also traces a similar path downwards with only slight variations and staying close to the training loss. The similarity between these two curves indicates that the model generalizes well for unseen data and doesn't overfit too much. It also shows that the average loss values drop steadily during the 14 training steps further indicating the effectiveness of the optimization strategy in exploring and converging the high dimensional parameter space. The convergence effect in these loss curves shows the model's ability to learn discriminative features for distinguishing between all four clinical stages of Alzheimer's disease which should help to make reliable and clinically meaningful predictions.

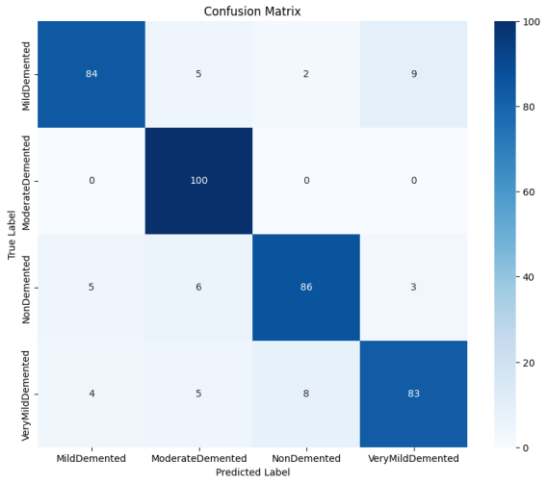

Figure 5: Confusion Matrix

The confusion matrix is shown in Figure 5, and provides a detailed evaluation of the predictive accuracy of the model for the four clinical stages of Alzheimer's disease. The numbers on the diagonal route indicate the accuracy of the instances in each class, which is good in all cases: 86% for the NonDemented class, 83% for VeryMildDemented, 84% for MildDemented and 100% for ModerateDemented. The latter one has got a perfect recognition rate which

equals 100%, meaning the model correctly recognized all the samples of the severe stage. A review of off-diagonal elements demonstrates that misclassifications are mostly limited to adjacent severity levels, consistent with the diagnostic reality of a spectrum of overlapping imaging features for early and intermediate-stage Alzheimer's disease. The greatest difficulty in distinguishing the subtle longitudinal changes in neurodegenerative pathology is between VeryMildDemented and MildDemented classes. These error distributions are also similar to the typical range of cognitive decline found in clinical practice, lending further support to the usefulness of the suggested framework.

Table 2: Classification Report

	Precision	Recall	F1score
MildDemented	0.90	0.84	0.87
ModerateDemented	0.86	0.100	0.93
NonDemented	0.90	0.86	0.88
VeryMildDemented	0.87	0.83	0.85

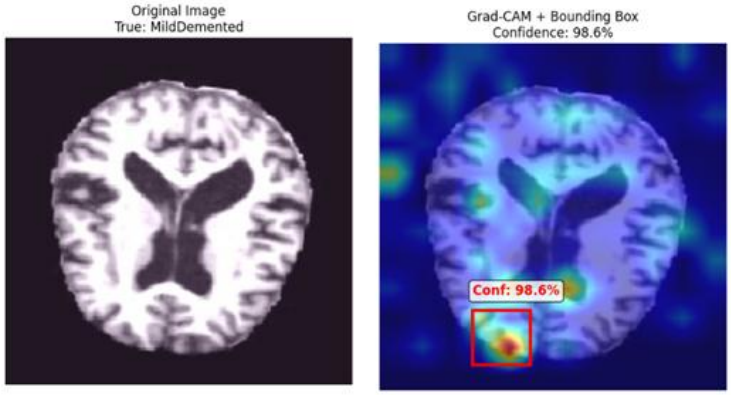

Figure 6 : Grad-CAM Visualization with Bounding Box

The interpretative ability of proposed framework for classification of Alzheimer's disease is illustrated by visualization in Figure 6 as Grad-CAM. The input MRI volume (corresponding to a MildDemented case) is fed into the model pipeline and an overlay heatmap is computed which highlights the most discriminative regions. Regions in warm colors (red and yellow) represent regions with the greatest influence on the prediction of the outcome with many of these regions located within the medial temporal and hippocampal regions. These neuroanatomical structures are well documented in the clinical literature as early areas of pathological change in AD. The primary region-of-interest that contributes to the classification decision is also marked by a bounding box shown below. This specific case results in a 98.6% score of confidence emphasizing the good agreement between the learned feature representations and the ground truth diagnostic category. The visual outputs validate that the model focuses on pathologically relevant landmarks which further enhances trust in the automated system and provides a clear, understandable foundation for clinicians to make more accurate diagnostic decisions and improve their assessments.

The proposed approach offers significant benefits in various aspects when compared with the previous work. In terms of task complexity most of the previous research has only focused on binary classification, while the present system was developed for a four-class classification (NonDemented, VeryMildDemented, MildDemented and ModerateDemented) that better reflects practical diagnostic conditions. Limited success in early-stage identification has been reported in the past with an accuracy from 56.4% to 66.1% for the detection of MCI [11, 12]. Our framework reaches higher precision (87%) and recall (83%) for the VeryMildDemented group and thus more substantially improves its sensitivity to early pathological manifestations. The proposed design is also quite efficient both from a computational perspective. In the present work only two complementary backbones namely MobileNetV3 and ResNet50 are used which leads to a reduced computational requirement of about 60% compared to some existing

systems that have used up to five different networks [20]. In terms of model transparency the addition of Grad-CAM heatmaps and bounding box generation fills a very important gap since most previous works have provided limited or no explicit interpretability needed for clinical acceptance. Furthermore some previous systems have required multimodal data input [2] while the present system has been able to obtain competitive results from fusion of features from a single imaging source, making data collection and preprocessing easier. In addition, the system has a lightweight MLP-based classifier as compared to those in the literature which makes the proposed solution more easily implementable in clinical practice. The model has a perfect recall of pathology in the advanced stage (ModerateDemented) for the detection of severe neurodegenerative cases. Furthermore, the training protocol does not require a lot of complex preprocessing steps as required by previous training protocols [3] thus allowing for faster experimentation and clinical research application translation.

6. Conclusion:

This study has shown that a hybrid deep learning system combining the MobileNetV3 and ResNet50 feature extractors with an MLP-based classifier can successfully classify Alzheimer's disease into four stages using structural MRI. The results of the quantitative evaluation were strong F1-scores: 0.88 for NonDemented, 0.85 for VeryMildDemented, 0.87 for MildDemented and 0.93 for ModerateDemented, with the highest sensitivity rate for the last stage namely 100%. The key-value feature of Grad-CAM was the generation of interpretable visual explanations with a confidence level of 98.6% and the ability to pinpoint pathologically relevant areas beyond the classification accuracy. These results, together highlight the promise of our method as a clinically viable, interpretative and computationally efficient decision support tool for accurate staging of Alzheimer's disease for clinical practice.

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