

# **ALZHEIMERS DISEASE PREDICTION A TOOL FOR PREDICTING ALZHEIMER**

**A MINI PROJECT REPORT**

*Submitted by*

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*in partial fulfillment for the award of the degree*

*of*

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**IN**

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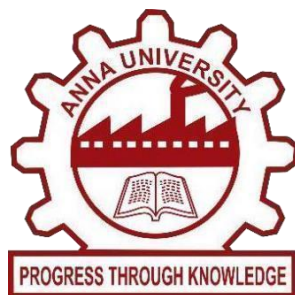
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Certified that this mini project report “**ALZHEIMERS DISEASE PREDICTION A TOOL FOR PREDICTING ALZHEIMER**” is the bonafide work of **SIVA SANKAR G (312321205156)** and **SURYA R (312321205171)** who carried out the mini project under my supervision, for the partial fulfillment of the requirements for the award of the degree of Bachelor of Technology in Information Technology.

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## ABSTRACT

Alzheimer's disease (AD) is the most common cause of dementia globally. It steadily worsens from mild to severe, impairing one's ability to complete any work without assistance. It begins to outstrip due to the population ages and diagnosis timeline. For classifying cases, existing approaches incorporate medical history, neuropsychological testing, and Magnetic Resonance Imaging (MRI), but efficient procedures remain inconsistent due to lack of sensitivity and precision. The Convolutional Neural Network (CNN) is utilized to create a framework that can be used to detect specific Alzheimer's disease characteristics from MRI images. By considering four stages of dementia and conducting a particular diagnosis, the proposed model generates high-resolution disease probability maps from the local brain structure to a multilayer perceptron and provides accurate, intuitive visualizations of individual Alzheimer's disease risk. To avoid the problem of class imbalance, the samples should be evenly distributed among four types of MRI images Mild Demented, Moderate Demented, Non-Demented, Very Mild Demented the classes DenseNet169 algorithm classification. The obtained MRI image dataset from Kaggle has a major class imbalance problem. A DenseNet169 algorithm classification is proposed to detect the dementia stages from MRI. Which is superior to existing methods, we also used the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset to predict AD classes in order to assess the efficacy of the proposed model. The objective of this work is to bring some useful information in simpler form in front of the users, especially for the medical staff treating the patient. The aim of this work is to define an algorithm that will result in an extracted image of the tumor from the MRI brain image.

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## LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ML	Machine Learning
MRI	Magnetic Resonance Imaging
AD	Alzheimer Disease
ADNI	Alzheimer's Disease Neuro Initiative
CNN	Convolutional Neural Network
DL	Deep Learning
CT	Computed Tomography
CAD	Computer Aided Diagnostics
DEMET	Dementia Network
APOE	Apolipoprotein E
AUC	Area Under Curve
FCM	Fuzzy C Mean
WM	White Matter
CSF	Cerebral Spinal Fluid
GM	Grey Matter
OASIS	Open Access Series of Imaging Studies
CDR	Call Detail Record
SVM	Support Vector Machine
MCI	Mild Cognitive Impaired
PET	Positron Emission Tomography
NC	Normal Cognitive
UML	Unified Modelling Language
CCF	Convolutional Channel Feature
BOLD	Blood Oxygen Level Dependent
CBF	Cerebral Blood Flow
CSV	Comma Separated Value
CNTK	Microsoft Cognitive Toolkit
VGG	Visual Geometry Group



# **CHAPTER 1**

## **INTRODUCTION**

Translational applications of computational neuro scientific approaches have been proven exceptionally beneficial in comprehensive mental health trials. This multidisciplinary field of study can help model the biological processes governing the healthy and diseased states of the human brain and map these processes into observable clinical presentations. In the past decade, the rapid increase in high-volume biomedical datasets (neuroimaging and related biological data), concurrent with the advances in machine learning (ML), has opened new avenues for the diagnosis and prognosis of neurodegenerative and neuropsychiatric disorders. The use of automatic systems capable of differentiating pathological cases from normal cases based on their magnetic resonance imaging (MRI) scans (i.e., no past hypotheses are needed) will contribute immensely to the initial diagnosis of AD. In this study, we review relevant studies that examine AD and use MRI data, ML and Deep Learning (DL) techniques with various AD datasets.

### **1.1 OVERVIEW**

Early detection of this disorder is being researched to slow down the abnormal degeneration of the brain, reduce medical care cost reduction, and ensure improved treatment. The recent failures in Alzheimer's disease research studies may suggest that early intervention and diagnosis could be crucial to the effectiveness of treatment. A wide variety of neuroimaging methods are becoming increasingly dependent on the diagnosis of dementia, and this is reflected in many new diagnostic criteria. Neuroimaging increases diagnosis accuracy for various subtypes of dementia using machine learning. Specific pre-processing steps are needed to implement machine learning algorithms. Extraction and selection of features, reduction of feature dimensionality and classifier algorithm are all phases of the machine learning-based classification process. Such techniques need advanced knowledge and several optimization steps, which can be time consuming.

## 1.2 PROBLEM STATEMENT

Our study deals with automated Alzheimer disease detection and classification. Normally the anatomy of the brain is analyzed by MRI scans or CT scans. The aim of the paper is Alzheimer disease identification in brain MR images. The main reason for detection of AD is to provide aid to clinical diagnosis. The aim is to provide an algorithm that guarantees the presence of a dementia by combining several procedures to provide a fool proof method of AD detection in MRI brain images. The focus of this project is MR brain images AD extraction and its representation in simpler form such that it is understandable by everyone. The objective of this work is to bring some useful information in simpler form in front of the users, especially for the medical staff treating the patient. The aim of this work is to define an algorithm that will result in an extracted image of the tumor from the MR brain image. The resultant image will be able to provide information like size, dimension, and boundary provides us with information related to the ad that can prove useful for various cases, which will provide a better base for the staff to decide the curing procedure. Finally, we detect whether the given MR brain image has tumor or not using Convolution Neural Network.

In addition to tumor detection, our study also emphasizes the importance of early detection and classification of Alzheimer's disease (AD) through MRI brain images. By incorporating advanced machine learning techniques, such as convolutional neural networks (CNNs), we aim to develop a robust algorithm capable of accurately identifying AD-related patterns in brain scans. Early detection of AD is crucial for initiating timely interventions and providing appropriate medical care to patients. Furthermore, our algorithm will not only aid in the diagnosis process but also facilitate the monitoring of disease progression over time. By extracting pertinent features from MRI images and presenting them in an interpretable format, our methodology aims to empower medical professionals with valuable insights for making informed treatment decisions and improving patient outcomes.

## CHAPTER 2

### LITERATURE REVIEW

**Helene Amieva, et.al (2021) [1] “Alzheimer disease” “DOI: <https://doi.org/10.1038/s41572-021-00269-y>”** proposed Alzheimer disease (AD) is biologically defined by the presence of  $\beta$ -amyloid-containing plaques and tau-containing neurofibrillary tangles. AD is a genetic and sporadic neurodegenerative disease that causes an amnesic cognitive impairment in its prototypical presentation and non-amnesic cognitive impairment in its less common variants. AD is a common cause of cognitive impairment acquired in midlife and late-life but its clinical impact is modified by other neurodegenerative and cerebrovascular conditions. This Primer conceives of AD biology as the brain disorder that results from a complex interplay of loss of synaptic homeostasis and dysfunction in the highly interrelated endosomal/lysosomal clearance pathways in which the precursors, aggregated species and post-translationally modified products of A $\beta$  and tau play important roles. Therapeutic endeavors are still struggling to find targets within this framework that substantially change the clinical course in persons with AD.

**Sean Knox, et.al (2021) [2] proposed “Diagnosis of Early Alzheimer’s Disease: Clinical Practice in 2021” “DOI: <https://doi.org/10.14283/jpad.2021.23>”** Alzheimer’s disease is a progressive, irreversible neurodegenerative disease impacting cognition, function, and behavior. Recently, clinicians have been encouraged to diagnose Alzheimer’s earlier, before patients have progressed to Alzheimer’s disease dementia. The early and accurate detection of Alzheimer’s disease-associated symptoms and underlying disease pathology by clinicians is fundamental for the screening, diagnosis, and subsequent management of Alzheimer’s disease patients. Unfortunately, detecting early-stage Alzheimer’s disease in clinical practice can be challenging and is hindered by several barriers including constraints on clinicians’ time, difficulty accurately diagnosing Alzheimer’s pathology, and that patients and healthcare providers often dismiss symptoms as part of the normal aging process. This review summarizes the importance of establishing an early diagnosis of Alzheimer’s disease, related practical ‘how-to’ guidance and considerations, and tools that can be used by healthcare providers throughout the diagnostic journey.

**Aydin Akan, et.al (2021) [3] proposed “Classification of Alzheimers’ Dementia by Using Various Signal Decomposition Methods” “DOI: 10.1109/TIPTEKNO53239.2021.9633007”**

Neurological disorders may spring from any disorder in the brain or the central and autonomic nervous systems. Among the neurological disorders, while Alzheimer’s disease and other dementias are the fourth-largest contributors of disability-adjusted life years, they are the second largest contributor of deaths. In the proposed study, various signal decomposition methods such as EMD, EEMD, and DWT are presented to classify EEG segments of control subjects and Alzheimer’ dementia patients. Time-domain features are calculated using selected 7 IMFs and 5 detail and approximation coefficients of DWT. Various classification techniques namely Decision Tree (DT), Support Vector Machine (SVM), k-Nearest Neighbor (kNN), and Random Forest (RF) are utilized to distinguish two groups. Simulation results demonstrate that the proposed approaches achieve outstanding validation accuracy rates.

**Allan I. Levey, et.al (2021) [4] proposed “Progress with Treatments for Alzheimer’s Disease” “DOI: 10.1056/NEJMe2103722”** An estimated 50 million people worldwide have dementia, mostly due to Alzheimer’s disease. The inexorable progression of Alzheimer’s disease exerts a huge toll on patients, families, and society, costing approximately \$1 trillion annually, an amount that is likely to increase with the growing number of elderly people. It is no surprise that Alzheimer’s disease is among the most feared diseases of aging. Hence, there is widespread interest as new clinical trial results are reported, but also much angst given all the trial failures to date. This issue of the Journal provides some tentative hope with the results of TRAILBLAZER-ALZ, evaluated the efficacy and safety of a promising new medication designed to target the underlying mechanisms of the disease. The results reveal encouraging findings, suggesting a potential breakthrough in Alzheimer's treatment. While further research is needed to confirm these initial results and address any potential long-term effects, the outcomes of TRAILBLAZER-ALZ offer a glimmer of hope for patients and their families grappling with the devastating impact of this condition. This abstract sets the stage for a detailed exploration of the trial methodology, results, and implications in the following articles of this journal issue.

**Yamini T, et.al (2022) [5] “Alzheimer’s Disease Detection Using Different Machine Learning Algorithms” DOI:10.22214/IJRASET** proposed Alzheimer’s disease is the most common form of dementia affecting the brain’s parts. A broad term used to describe illnesses and conditions that causes a deterioration in memory, language, and other cognitive abilities severe enough to interface with daily life is “dementia”. According to estimates, this disease affects 6.2 million Americans and 5 million people in India aged 65 and older. In 2019, the most recent year for which data are available, official death certificates reported 121,499 deaths from AD, making Alzheimer’s the “sixth leading cause of death in the country and the fifth leading cause of death for people 65 and older”. In this paper, we suggest several machine Learning algorithms like Decision trees, SVM, Logistic regression, and Naive Bayes identify AD at an early stage. The Alzheimer’s Disease Neuroimaging Initiative (ADNI) and the Open Access Series of Imaging Investigations (OASIS) provide data sets white used to detect the disease in its early stage. The datasets consist of longitudinal MRI data (age, gender, mini mental status, CDR) By taking into account many factors in each method, such as precision, F1 Score, Recall, and specificity are calculated. The results obtained 93.7% of maximum accuracy for the Decision Tree Algorithm.

**Kavitha C, et.al (2022) [6] “Early-Stage Alzheimer's Disease Prediction Using Machine Learning Models” “DOI:10.3389/fpubh.2022.853294”** proposed Alzheimer's disease (AD) is the leading cause of dementia in older adults. There is currently a lot of interest in applying machine learning to find out metabolic diseases like Alzheimer's and Diabetes that affect a large population of people around the world. Their incidence rates are increasing at an alarming rate every year. In Alzheimer's disease, the brain is affected by neurodegenerative changes. As our aging population increases, more and more individuals, their families, and healthcare will experience diseases that affect memory and functioning. These effects will be profound on the social, financial, and economic fronts. In its early stages, Alzheimer's disease is hard to predict. A treatment given at an early stage of AD is more effective, and it causes fewer minor damage than a treatment done at a later stage. Several techniques such as Decision Tree, Random Forest, Support Vector Machine, Gradient Boosting, and Voting classifiers have been employed to identify the best parameters for Alzheimer's disease prediction. Predictions of Alzheimer's disease is based on Open Access Series of Imaging Studies (OASIS) data, and performance is measured with parameters like Precision, Recall, Accuracy, and F1-score for ML models. The proposed classification scheme can be used by clinicians to make diagnoses of these diseases. The proposed work shows better results with the best validation average accuracy of 83% on the test data of AD. This test accuracy score is significantly higher in comparison with existing works.

**Vijeeta patil, et.al (2022) [7] “Early prediction of Alzheimer's disease using convolutional neural network:a review” “DOI:<https://doi.org/10.1186/s41983-022-00571-w>”** proposed a comprehensive review on Alzheimer's disease (AD) is carried out, and an exploration of the two-machine learning (ML) methods that help to identify the disease in its initial stages. Alzheimer's disease is a neurocognitive disorder occurring in people in their early onset. This disease causes the person to suffer from memory loss, unusual behavior, and language problems. Early detection is essential for developing more advanced treatments for AD. Machine learning (ML), a subfield of Artificial Intelligence (AI), uses various probabilistic and optimization techniques to help computers learn from huge and complicated data sets. To diagnose AD in its early stages, researchers generally use machine learning. The survey provides a broad overview of current research in this field and analyses the classification methods used by researchers working with ADNI data sets. It discusses essential research topics such as the data sets used, the evaluation measures employed, and the machine learning methods used. Our presentation suggests a model that helps better understand current work and highlights the challenges and opportunities for innovative and useful research. The study shows which machine learning method holds best for the ADNI data set. The work also contributes to the use of the ADNI data set, where the classification of training and testing samples is divided with such a number that brings the highest accuracy achieved with 18-layer CNN.

**Fan Wu, et.al (2022) [8] “Deep Learning-Based Diagnosis of Alzheimer’s Disease” “DOI: [10.3390/jpm12050815](https://doi.org/10.3390/jpm12050815)”** proposed Alzheimer’s disease (AD), the most familiar type of dementia, is a severe concern in modern healthcare. Around 5.5 million people aged 65 and above have AD, and it is the sixth leading cause of mortality in the US. AD is an irreversible, degenerative brain disorder characterized by a loss of cognitive function and has no proven cure. Deep learning techniques have gained popularity in recent years, particularly in the domains of natural language processing and computer vision. Since 2014, these techniques have begun to achieve substantial consideration in AD diagnosis research, and the number of papers published in this arena is rising drastically. Deep learning techniques have been reported to be more accurate for AD diagnosis in comparison to conventional machine learning models. Motivated to explore the potential of deep learning in AD diagnosis, this study reviews the current state-of-the-art in AD diagnosis using deep learning. We summarize the most recent trends and findings using a thorough literature review. The study also explores the different biomarkers and datasets for AD diagnosis. Even though deep learning has shown promise in AD diagnosis, there are still several challenges that need to be addressed.

**Mir Jafkul Alam, et.al (2023) [9] “A Novel Approach Utilizing Machine Learning for the Early Diagnosis of Alzheimer's Disease” “DOI: <https://doi.org/10.1007/s44174-023-00078-9>”** proposed Alzheimer's disease (AD) is one of the leading causes of dementia among older people. In addition, a considerable portion of the world's population suffers from metabolic problems, such as Alzheimer's disease and diabetes. Alzheimer's disease affects the brain in a degenerative manner. As the elderly population grows, this illness can cause more people to become inactive by impairing their memory and physical functionality. This might impact their family members and the financial, economic, and social spheres. Researchers have recently investigated different machine learning and deep learning approaches to detect such diseases at an earlier stage. Early diagnosis and treatment of AD help patients to recover from it successfully and with the least harm. This paper proposes a machine learning model that comprises GaussianNB, Decision Tree, Random Forest, XGBoost, Voting Classifier, and GradientBoost to predict Alzheimer's disease. The model is trained using the open access series of imaging studies (OASIS) dataset to evaluate the performance in terms of accuracy, precision, recall, and F1 score. Our findings showed that the voting classifier attained the highest validation accuracy of 96% for the AD dataset. Therefore, ML algorithms have the potential to drastically lower Alzheimer's disease annual mortality rates through accurate detection.

**Prasun Chakarabart, et.al (2023) [10] “A systematic review on machine learning and deep learning techniques in the effective diagnosis of Alzheimer’s disease” “DOI: [10.1186/s40708-023-00195-7](https://doi.org/10.1186/s40708-023-00195-7)”** proposed Alzheimer’s disease (AD) is a brain-related disease in which the condition of the patient gets worse with time. As not all MCI patients will suffer from AD, it is required to accurately diagnose whether a mild cognitive impaired (MCI) patient will convert to AD (namely MCI converter MCI-C) or not (namely MCI non-converter MCI-NC), during early diagnosis. There are two modalities, positron emission tomography (PET) and magnetic resonance image (MRI), used by a physician for the diagnosis of Alzheimer’s disease. Machine learning and deep learning perform exceptionally well in the field of computer vision where there is a requirement to extract information from high-dimensional data. Researchers use deep learning models in the field of medicine for diagnosis, prognosis, and even to predict the future health of the patient under medication. This study is a systematic review of publications using machine learning and deep learning methods for early classification of normal cognitive (NC) and Alzheimer’s disease (AD). This study is an effort to provide the details of the two most commonly used modalities PET and MRI for the identification of AD, and to evaluate the performance of both modalities while working with different classifiers.

**Javed Rahebi, et.al (2023) [11] “Alzheimer’s Disease Diagnosis Using Machine Learning: A Survey” “DOI: <https://doi.org/10.3390/app13148298>”** proposed Alzheimer’s is a neurodegenerative disorder affecting the central nervous system and cognitive processes, explicitly impairing detailed mental analysis. Throughout this condition, the affected individual’s cognitive abilities to process and analyze information gradually deteriorate, resulting in mental decline. In recent years, there has been a notable increase in endeavors aimed at identifying Alzheimer’s disease and addressing its progression. Research studies have demonstrated the significant involvement of genetic factors, stress, and nutrition in developing this condition. The utilization of computer-aided analysis models based on machine learning and artificial intelligence has the potential to significantly enhance the exploration of various neuroimaging methods and non-image biomarkers. This study conducts a comparative assessment of more than 80 publications that have been published since 2017. Alzheimer’s disease detection is facilitated by utilizing fundamental machine learning architectures such as support vector machines, decision trees, and ensemble models. Furthermore, around 50 papers that utilized a specific architectural or design approach concerning Alzheimer’s disease were examined. The body of literature under consideration has been categorized and elucidated through the utilization of data-related, methodology-related, and medical-fostering components to illustrate the underlying challenges. The conclusion section of our study encompasses a discussion of prospective avenues for further investigation and furnishes recommendations for future research activities on the diagnosis of Alzheimer’s disease.



## **CHAPTER 3**

### **SYSTEM ANALYSIS**

#### **3.1 EXISTING SYSTEM**

The conventional MRI-based AD diagnosis methods usually partition the entire MR image into multiple regions with different scales for better feature extraction of local abnormal brain structural changes. Based on the partition with different scales, most of the existing MRI-based studies can be roughly divided into three categories, including 1) voxel-level, 2) region-level, and 3) patch-level. In voxel-level methods, the tissue features (e.g., gray matter densities) extracted from MRI scans composes high-dimensional voxel-wise structural features for AD diagnosis. However, compared with the dimensionality of features, the number of training images for AD classification is too small, which often leads to the curse of dimensionality. To alleviate this problem, region-level methods are proposed to identify the AD patients from normal controls with the handcrafted features (e.g. gray matter, cerebrospinal fluid and cortical thickness) derived from segmented regions of interest (ROIs). However, these methods are resource-intensive for segmenting ROIs. In contrast, patch-level (an intermediate scale between voxel-level and region-level) feature representations are proposed for more effectively characterizing the local structural changes in MR images. Specifically, the centers of patches can be located by certain anatomical landmark detectors or statistics methods. However, how to combine the local patches into a global feature representation for the whole brain structure is still a challenge in patch-level methods.

## 3.2 PROPOSED SYSTEM

A relation-induced multi-modal shared representation learning framework for AD diagnosis correspond to the training stage, relational regularizes and test stage, respectively. At training stage, the framework first obtains shared representations by learning a bi-directional mapping between original space and shared space. For one thing, it is hope to learn latent discriminative representations from multi-modal data by introducing the projection matrix which conducts original-to-shared transformation. And for another, it is also expected the shared representations can preserve original information as much as possible, and thus the reconstruction matrix is utilized to achieve shared-to-original conversion. Further the project shared the representations into target space by weight matrix, whose elements stand for the importance of the corresponding feature vectors for type's dataset in deep learning MRI images Mild Demented, Moderate Demented, Non-Demented, Very Mild Demented the class's final DenseNet169 algorithm classification AD diagnosis. Thus, representation learning (from original space to shared space) and classifier modeling (from shared space to label space) are integrated into the unified framework and can be optimized simultaneously. The Advantage of the proposed System the correction of image geometry enhances image information which makes the image more useful for any analysis process, Vanishing Gradient problem is alleviated by Dense-net, Feature Propagation is strengthened, Reusability of feature is enhanced, Number of the parameter is reduced, making use of all these we built this project to achieve high accuracy.

### 3.2.1 Materials and Methods

#### a. Dataset:

The datasets we used in this study are open-source and freely available on Kaggle. The data includes all four classes of mild, very mild, moderate and, non-dementia images from multiple domains. The dataset contains MRI images of all four classes. MRI and Clinical information on all the cases of collected dataset in a cross-sectional and longitudinal study design are collected. This dataset provides Morphometric data which gives the volumes of brain areas mostly affected by AD.

## **b. Libraries and System Configuration:**

In order to perform this classification, you need the basic Data Scientist starter pack (sklearn, pandas, NumPy, matplotlib, seaborn) plus some specific libraries like TensorFlow or flow, Tfidf Transformer, feature extraction, linear model, selection, pre-processing, accuracy score, train\_test\_split, Pipeline. Hardware system configuration are Processor – i3, i5, i7 Amd Processor, RAM -Above 4 Gb, Hard Disk - 260 GB.

## **c. Data Acquisition:**

The first step is to acquire images. To produce a classification model, the computer needs to learn by example. The computer needs to view many images to recognize an object. Other types of data, such as time series data and voice data, can also be used to train deep learning models. In the context of the work surveyed in this project, the relevant data required to detect Alzheimer disease will be images. The output of this step is images that will later be used to train the model.

## **d. Training:**

In this project, we are using transfer learning algorithms such as Densenet169, and vgg16. Densenet169: It predicts the output of a categorical dependent variable. VGG16: Transfer learning that process the image input and gives the output. The data preprocessing was done using Jupyter Notebook and Desktop Application was Implemented using python IDLE. The programming language which was used is python and deep learning Sklearn was used to build the model using transfer learning algorithm like Densenet169, VGG16 which gives the results in the next stage.

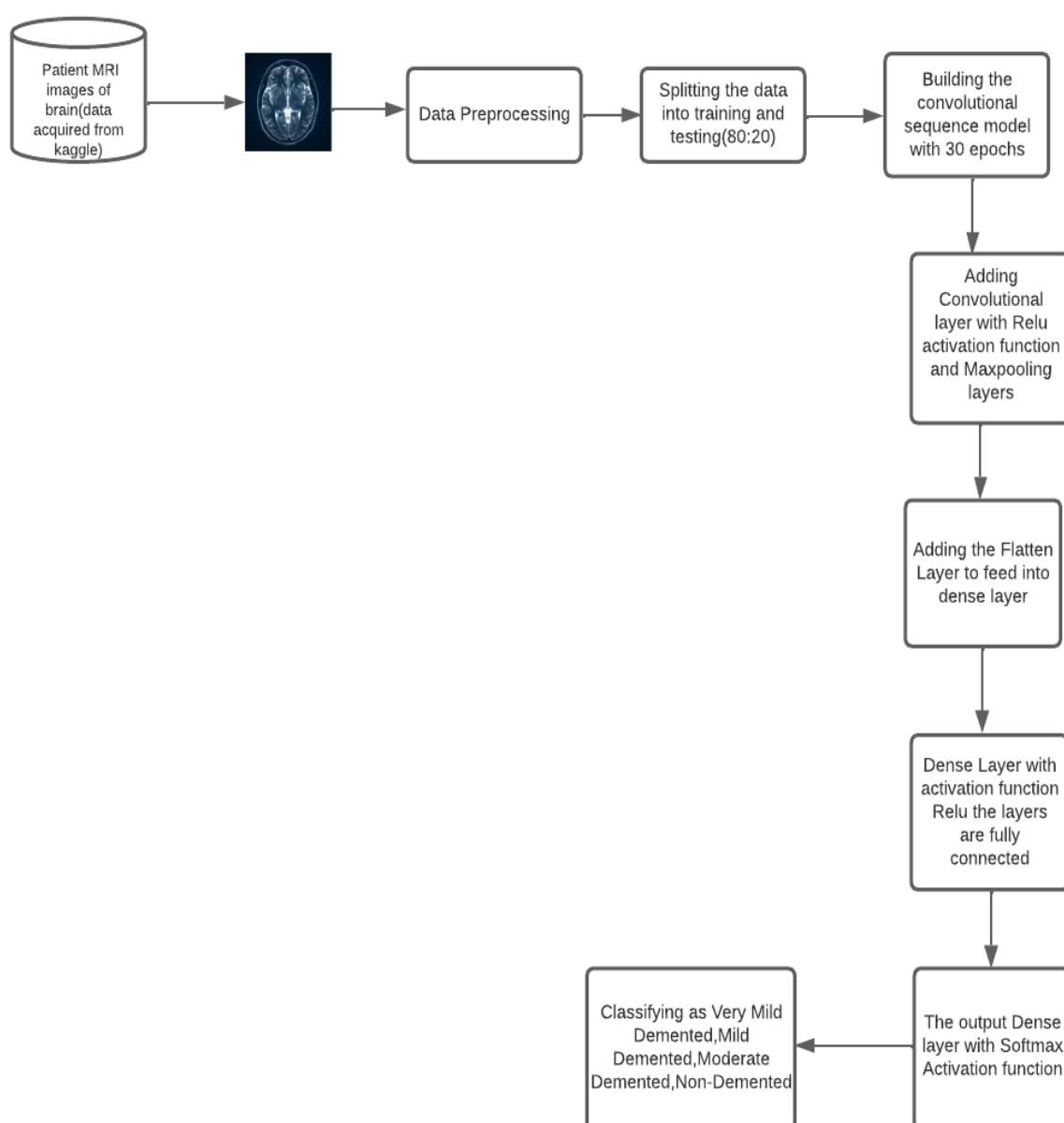
## **e. Classification Metrics:**

There are many classification approaches in the literature that can be used to extract relevant features with high discriminatory power. However, choosing the appropriate approach is a challenging step, requiring a careful study and good knowledge of the existing techniques. In the present study, popular and widely used transfer learning classification algorithms for analyzing medical diagnoses in the context of a multiple classification problems, as case-control studies. Thereby, we rely on two main classification approaches from which we select popular transfer learning classification algorithms, appropriate for decision-making problems.

## CHAPTER 4

### SYSTEM DESIGN

In this chapter, the System Architecture for the Alzheimer Disease Prediction using CNN Model is represented and the modules are explained.



**Fig 4.1 System Architecture Design**

## 4.1 ARCHITECTURE

Here we explore DL Algorithms to identify Alzheimer disease in the Medical Industry in this model. It uses two deep learning Algorithms for detecting the convolutional channel feature (CCF). However, in this model we choose the convolutional neural network (CNN) model and its layers to determine the mild, very mild, moderate and non demented stage of the disease.

We collect datasets from an open-source website called Kaggle. The dataset holds MRI images of the AD affected person. There were 400 images in total where 200 images of each category is taken and analyzed. Resizing the MRI image into 200X200.

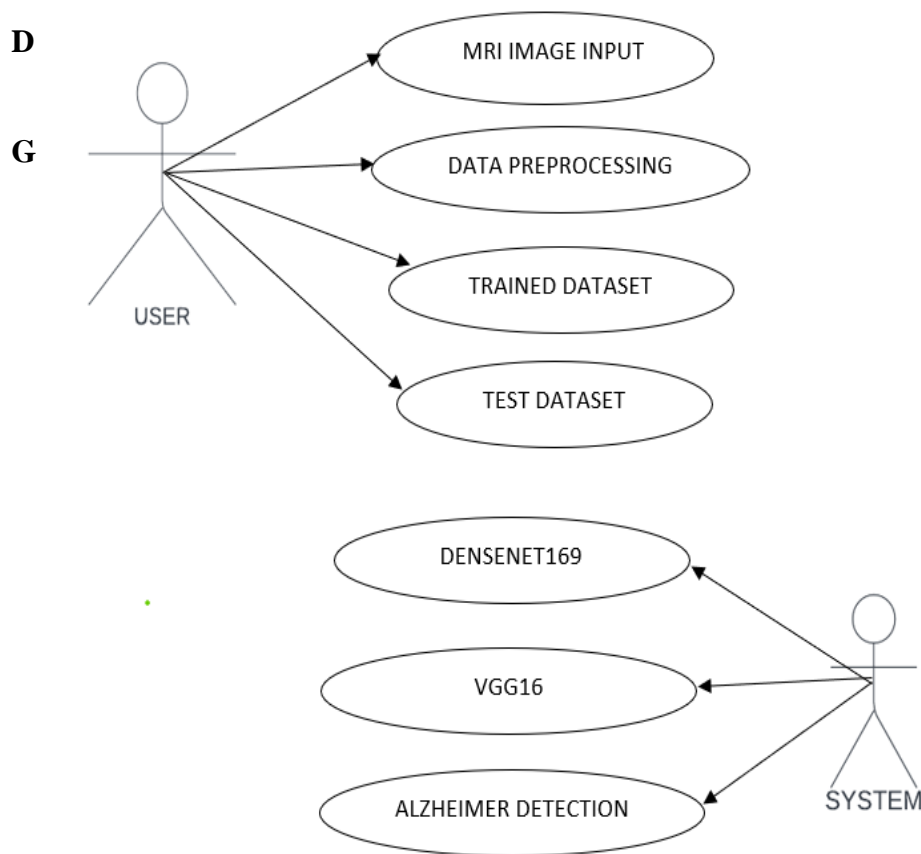
As per the Figure 4.1, after the dataset collection and pre-processing methods, we apply the following machine and ensemble learning algorithm. The Dense Net and VGG16 are the transfer learning method is a neural network for classification and feature learning. It can be used with one or a multilayer of unseen nodes. Parameters of unseen nodes are tuned. We are building a convolutional sequence model of 30 epochs. Where Convolutional sequence is approach to sequence-to-sequence learning that maps an input sequence to a variable length output sequence via recurrent neural networks. Then subsequently convolutional layer, Flatten layer, and Dense Layer. The convolutional layer is a set of filters, Parameters of which are to be Learned throughout the training. Flatten Layer collapses the facial dimension of the input into the channel dimension. Dense layer helps in changing the dimensionality of the output from the preceding layer. In this process relu and SoftMax Activation function are used. Relu activation function is most commonly used activation function in neural networks, especially in Convolutional Neural Networks (CNNs) & Multilayer perceptron.

## 4.2 SYSTEM FLOW:

The system flow of the Alzheimer's Disease Prediction tool is a structured process that begins with Data Acquisition, where MRI images are collected to train the model. The next step is Data Preprocessing, which involves image classification tasks and the application of Convolutional Neural Networks (CNNs) to prepare the data for analysis. Feature Extraction follows, utilizing DenseNet and VGG16 algorithms to analyze the images and extract relevant features. The DenseNet169 algorithm, in particular, is employed to address the class imbalance problem in the dataset and to detect the stages of dementia from the MRI images. The System Architecture is designed to utilize two deep learning algorithms for detecting convolutional channel features (CCFs). The architecture includes layers such as convolutional, max pooling, flatten, and dense layers, with activation functions like Relu and SoftMax. The Training phase involves building a convolutional sequence model over 30 epochs to learn from the data effectively. Finally, the Implementation phase sees the project come to life in Jupyter Notebook, where the functionalities required for the application are coded in Python. The implementation uses a variety of libraries and tools, including TensorFlow, Keras, and sklearn, to build and refine the model. The result is a system capable of classifying MRI images into categories such as Mild Demented, Moderate Demented, Non-Demented, and Very Mild Demented, providing valuable support for medical staff in diagnosing and treating Alzheimer's Disease. This system flow represents a comprehensive approach to leveraging machine learning for medical diagnostics.

### 4.3 USE CASE DIAGRAM:

Use case diagrams are considered for high level requirement analysis of a system. So, when the requirements of a system are analyzed, the functionalities are captured in use cases. So, it can be said that uses cases are nothing but the system functionalities written in an organized manner. Now the second things which are relevant to the use cases are the actors. Actors can be defined as something that interacts with the system. The actors can be human user, some internal applications or may be some external applications Use case diagrams are used to gather the requirements of a system including internal and external influences. These requirements are mostly 18 design requirements.

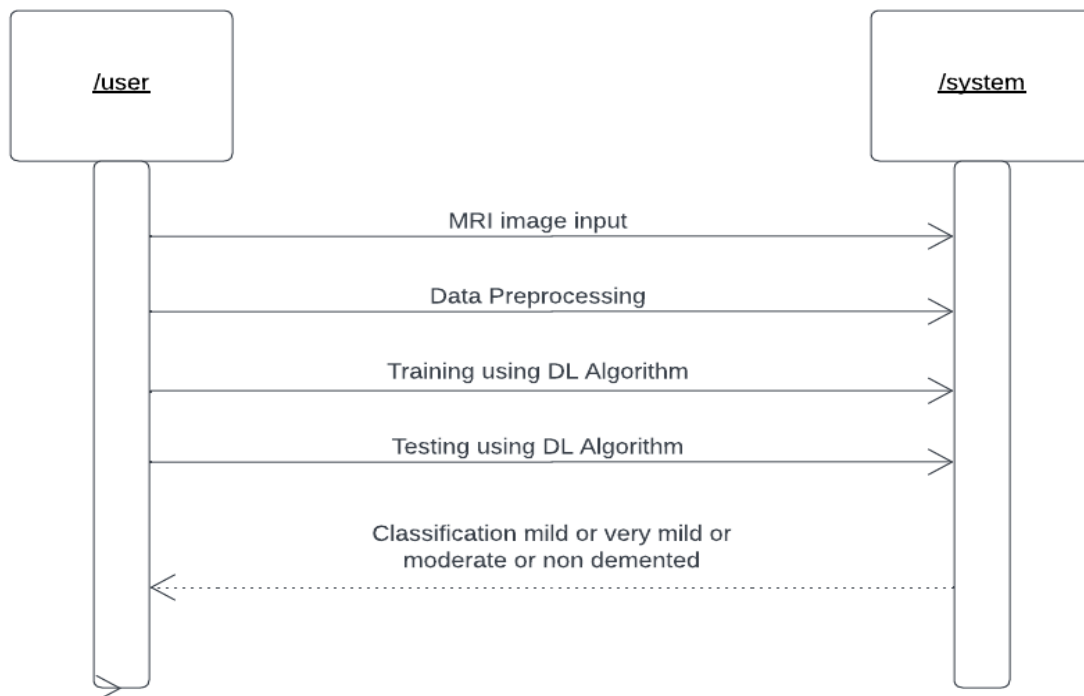


**FIG 4.2 USE CASE DIAGRAM OF ALZHEIMERS DISEASE PREDICTION**

Figure 4.2 shows that the functionalities are to be represented as a use case in the representation. Each and every use case is a function in which the user or the server can have the access on it. The names of the use cases are given in such a way that the functionalities are preformed, because the main purpose of the functionalities is to identify the requirements. To add some extra notes that should be clarified to the user, the notes kind of structure is added to the use case diagram. Only the main relationships between the actors and the functionalities are shown because all the representation may collapse the diagram.

#### 4.4 SEQUENCE DIAGRAM:

A sequence diagram represents the flow of messages in a system. It helps in envisioning several dynamic scenarios. It depicts the processes involved and the sequence of messages exchanged between the processes needed to carry out the functionality. It portrays the communication between any two lifelines as a time-oriented sequence of events, such that these lifelines took part at the runtime.

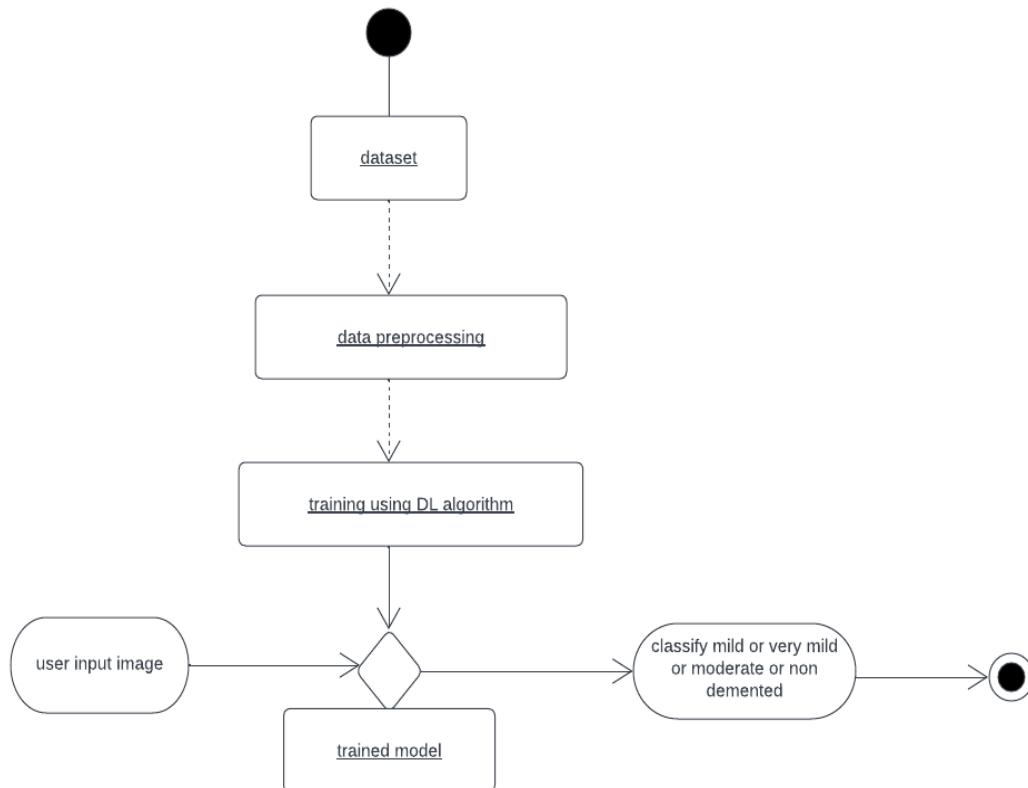


**FIG 4.3 SEQUENCE DIAGRAM FOR ALZHEIMERS DISEASE PREDICTION**



## 4.5 ACTIVITY DIAGRAM:

An activity diagram is a flowchart to represent the flow from one activity to another activity. The activity can be described as an operation of the system. The control flow is drawn from one operation to another. This flow can be sequential, branched, or concurrent. Activity diagrams deal with all type of flow control by using different elements such as fork, join, etc.

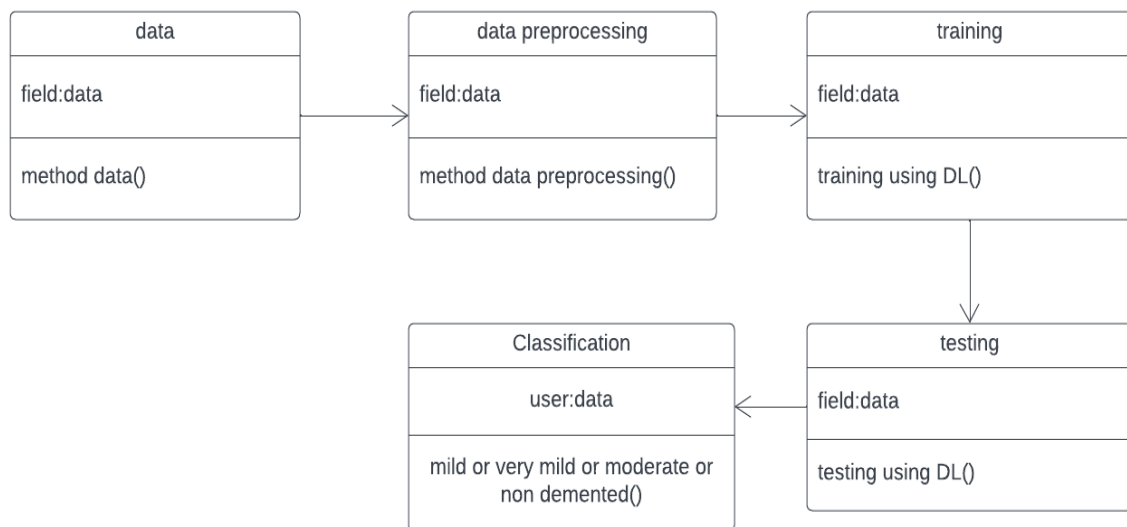


**FIG 4.4 ACTIVITY DIAGRAM FOR ALZHEIMERS DISEASE PREDICTION**

Figure 4.4 represents the activity diagram of the Alzheimer Disease Prediction system. The figure represents five activities that take place sequentially. Activities are a network of nodes connected by edges. There can be action nodes, control nodes, or object nodes. Action nodes represent some action. Control nodes represent the control flow of an activity. Object nodes are used to describe objects used inside an activity. Edges are used to show a path or a flow of execution. Activities start at an initial node and terminate at a final node.

## 4.6 CLASS DIAGRAM:

Figure 4.5 shows that class diagram is basically a graphical representation of the static view of the system and represents different aspects of the application. So, a collection of class diagrams represent the whole system. The name of the class diagram should be meaningful to describe the aspect of the system.

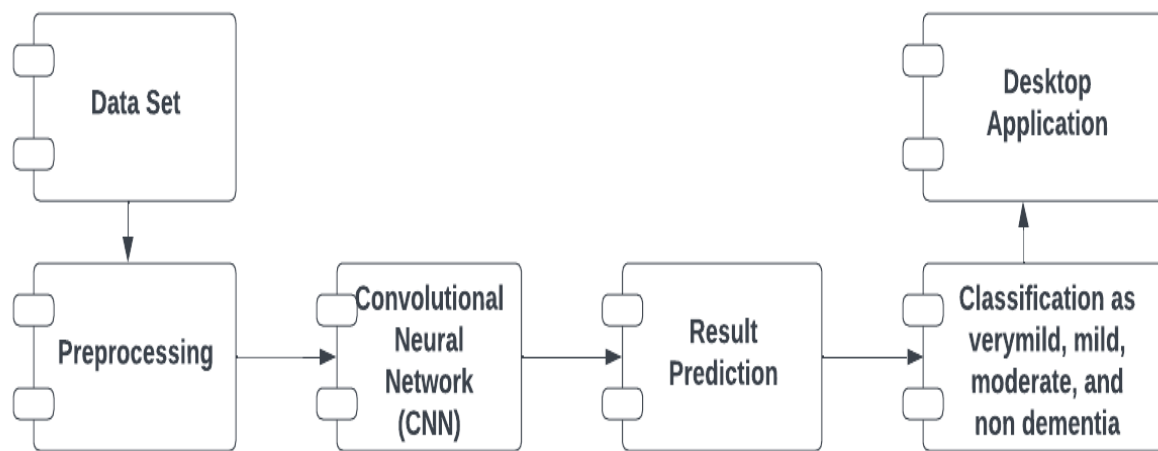


**FIG 4.5 CLASS DIAGRAM FOR ALZHEIMERS DISEASE PREDICTION**

Figure 4.5 shows the attributes, classes, functions, and relationships to give an overview of the software system. They are not only used to visualize the static view of the system but they are also used to construct the executable code for forward and reverse engineering of any system. In a class diagram, the classes are arranged in groups that share common characteristics. A class diagram resembles a flowchart in which classes are portrayed as boxes, each box having three rectangles inside which includes the name, attributes and methods used in each class.

## 4.7 COMPONENT DIAGRAM:

Component diagrams are used in modeling the physical aspects of object-oriented systems that are used for visualizing, specifying, and documenting component-based systems and also for constructing executable systems through forward and reverse engineering. Component diagrams are essentially class diagrams that focus on a system's components that are often used to model the static implementation view of a system.

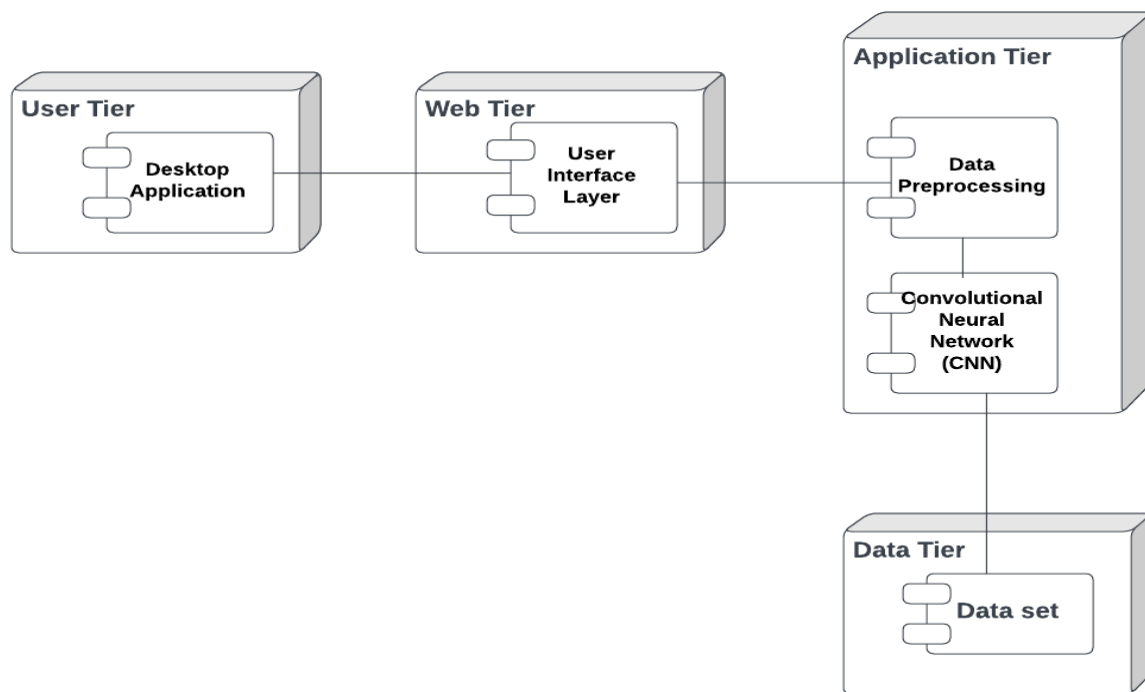


**FIG 4.6 COMPONENT DIAGRAM FOR ALZHEIMERS DISEASE PREDICTION**

Figure 4.6 depicts the component diagram of the Alzheimer Disease Prediction system. A component diagram breaks down the actual system under development into various high levels of functionality. Each component is responsible for one clear aim within the entire system and only interacts with other essential elements on a need-to-know basis. Since it is a special kind of a UML diagram, it holds distinct purposes. It describes all the individual components that are used to make the functionalities, but not the functionalities of the system. It visualizes the physical components inside the system. The components can be a library, packages, files, etc. The component diagram also describes the static view of a system, which includes the organization of components at a particular instant. The collection of component diagrams represents a whole system. The component diagram also describes the static view of a system, which includes the organization of components at a particular instant. The collection of component diagrams represents a whole system.

## 4.8 DEPLOYMENT DIAGRAM:

The deployment diagram visualizes the physical hardware on which the software will be deployed. It portrays the static deployment view of a system. It involves the nodes and their relationships. It ascertains how software is deployed on the hardware. It maps the software architecture created in design to the physical system architecture, where the software will be executed as a node. Since it involves many nodes, the relationship is shown by utilizing communication paths. Deployment diagram represents the deployment view of a system. It is related to the component diagram because the components are deployed using the deployment diagrams. A deployment diagram consists of nodes. Nodes are nothing but physical hardware used to deploy the application. Deployment diagrams are useful for system engineers. An efficient deployment diagram is very important as it controls parameters such as performance, scalability, maintainability, portability.



**FIG 4.7 DEPLOYMENT DIAGRAM FOR ALZHEIMERS DISEASE PREDICTION**

Figure 4.7 depicts the deployment diagram of the Alzheimer Disease Prediction system. The main purpose of the deployment diagram is to represent how software is installed on the hardware component. It depicts in what manner a software interacts with hardware to perform its execution.

## **CHAPTER 5**

### **SYSTEM IMPLEMENTATION**

In this chapter, the System Implementation for the Alzheimer Disease Prediction using Deep Learning is explained in detail.

#### **5.1 MODEL DESCRIPTION:**

##### **5.1.1 DATA ACQUISITION:**

The first step is to acquire images. To produce a classification model, the computer needs to learn by example. The computer needs to view many images to recognize an object. Other types of data, such as time series data and voice data, can also be used to train deep learning models. In the context of the work surveyed in this paper, the relevant data required to detect Alzheimer disease will be images. The output of this step is images that will later be used to train the model.

##### **5.1.2 DATA PREPROCESSING:**

An image classification task determines the category of a given input MRI image. It is a basic task in high-level image understanding and can be divided into binary- and multi classification tasks. After multiple convolution-and-pooling operations via a CNN, an image is classified in the output layer following the requirements. Activation function of the output layer is the only difference between binary and multi classification tasks. An image classification task for MRI image analysis easily identified and then necessary actions can be taken to which type of dementia, is a high performance in natural image classification, including Convolution neural network (CNNs) can be used in JPG/PNG image classification.

##### **5.1.3 FEATURE EXTRACTION:**

In this module, we are performing some more operation on segmented image. In this module we will perform feature extraction operation to get all detailed information about brain image. Feature Extraction and reduction has been playing a vital role for tumor region into their relevant categories in the field of computer vision and machine learning. The major issue behind feature extraction is to compute the most active or robust features for classification, which produced an efficient performance. The Feature extraction is used related to dimensionality reduction.

#### **5.1.4 MAGNETIC RESONANCE IMAGING CLASSIFICATION:**

This imaging technique utilizes radio waves and magnetic fields to generate high-quality and high-resolution 2D and 3D images of brain structures. No harmful radiations from X-rays or radioactive tracers are generated. The most commonly used MRI for AD cases is the structural MRI, which measures brain volumes in vivo to detect brain degeneration (loss of tissue, cells, neurons, etc.). Brain degeneration is an inevitable progressive component of AD. A structural MRI used to detect brain atrophy. Alternatively, Functional Magnetic Resonance Imaging (fMRI), a widely used method to measure human primary visual cortex and detect brain topography. fMRI provides useful information and data about the human brain's activity, i.e., how the brain functions. fMRI methods, such as brain imaging based on arterial Blood Oxygenation Level Dependent (BOLD) contrasts and spin-labelling, are sensitive to the cerebral metabolic rate of oxygen consumption and cerebral blood flow (CBF).

#### **5.1.5 CNN MODEL:**

Image classification involves the extraction of features from the image to observe some patterns in the dataset. Using an ANN for the purpose of image classification would end up being very costly in terms of computation since the trainable parameters become extremely large. For example, if we have a 50 X 50 image of a cat, and we want to train our traditional ANN on that image to classify it into a dog or a cat the trainable parameters become  $-(50*50) * 100$  image pixels multiplied by hidden layer + 100 bias +  $2 * 100$  output neurons + 2 bias = 2,50,30.

Examples of different filters and their effects Filters help us exploit the spatial locality of a particular image by enforcing a local connectivity pattern between neurons. Convolution basically means a pointwise multiplication of two functions to produce a third function. Here one function is our image pixels matrix and another is our filter. We slide the filter over the image and get the dot product of the two matrices. The resulting matrix is called an “Activation Map” or “Feature Map”.

### Step 1: Choose a Dataset

Choose a dataset of your interest or you can also create your own image dataset for solving your own image classification problem. An easy place to choose a dataset is on kaggle.com. This dataset contains 12,500 augmented images of blood cells (JPEG) with accompanying cell type labels (CSV). There are approximately 3,000 images for each of 4 different cell types grouped into 4 different folders (according to cell type). The cell types are Eosinophil, Lymphocyte, Monocyte, and Neutrophil. Here are all the libraries that we would require and the code for importing them.

### Step 2: Prepare Dataset for Training

Preparing our dataset for training will involve assigning paths and creating categories(labels), resizing our images. Resizing images into 200 X 200.

### Step 3: Create Training Data

Training is an array that will contain image pixel values and the index at which the image in the CATEGORIES list.

### Step 4: Shuffle the Dataset

### Step 5: Assigning Labels and Features

This shape of both the lists will be used in Classification using the NEURAL NETWORKS.

### Step 6: Normalizing X and converting labels to categorical data

### Step 7: Split X and Y for use in CNN

### Step 8: Define, compile and train the CNN Model

### Step 9: Accuracy and Score of models

```
function XCOMPRESSCU(*pCurCU)
M ← FastCUMope (PO, QP)
if M 4 SPLIT, then
C2n ←CHECKINTRA (pCurCU)
else
C2n ← ∞
end if
if M! = HOMO and Dcur < Dmax then
Cn ← 0
for i = 0 to 3 do
pSubCUi ← pointer to SubCUi
CN ← CN+ XCompressCU(pSubCUi) end for
else
```

```

    CN  $\leftarrow \infty$ 
  end if
  CHECKBESTMODE (C2N, CN)
end function

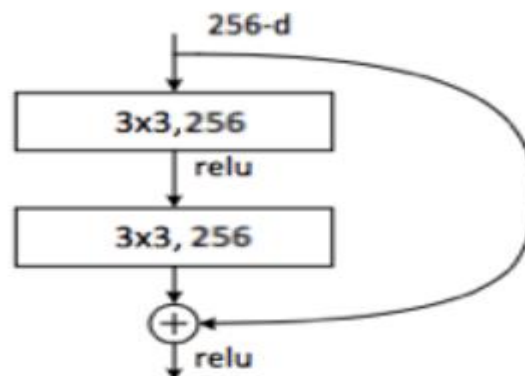
```

### a. Dense Networks (Dense Net)

Very deep neural networks are hard to train as they are more prone to vanishing or exploding gradients. To solve this problem, the activation unit from a layer could be fed directly to a deeper layer of the network, which is termed as a skip connection. This forms the basis of Dense networks or Dense Net. This post will introduce the basics of the residual networks before implementing one in Keras.

### Dense Block

A building block of a Dense Net is called a Dense block or identity block. A residual block is simply when the activation of a layer is fast-forwarded to a deeper layer in the neural network.



**FIG 5.1 DENSE BLOCK DIAGRAM**

Figure 5.1 represents the activation from a previous layer is being added to the activation of a deeper layer in the network. This simple tweak allows training much deeper neural networks. In theory, the training error should monotonically decrease as more layers are added to a neural network. In practice however, for a traditional neural network, it will reach a point where the training error will start increasing. Dense Nets do not suffer from this problem. The training error will keep decreasing as more layers are added to the network. In fact, Dense Nets have made it possible to train networks with more than 100 layers, even reaching 1000 layers. Building a Dense Net for image classification. Now, let's build a Dense Net with 50 layers for image classification using Keras. Keras is a high-level neural networks API, written in Python and capable of running on top of TensorFlow, CNTK, or Theano. It was developed with a focus on enabling fast experimentation.



- Step 1: Define the identity block
- Step 2: Convolution block
- Step 3: Build the model
- Step 4: Training
- Step 5: Print the model summary

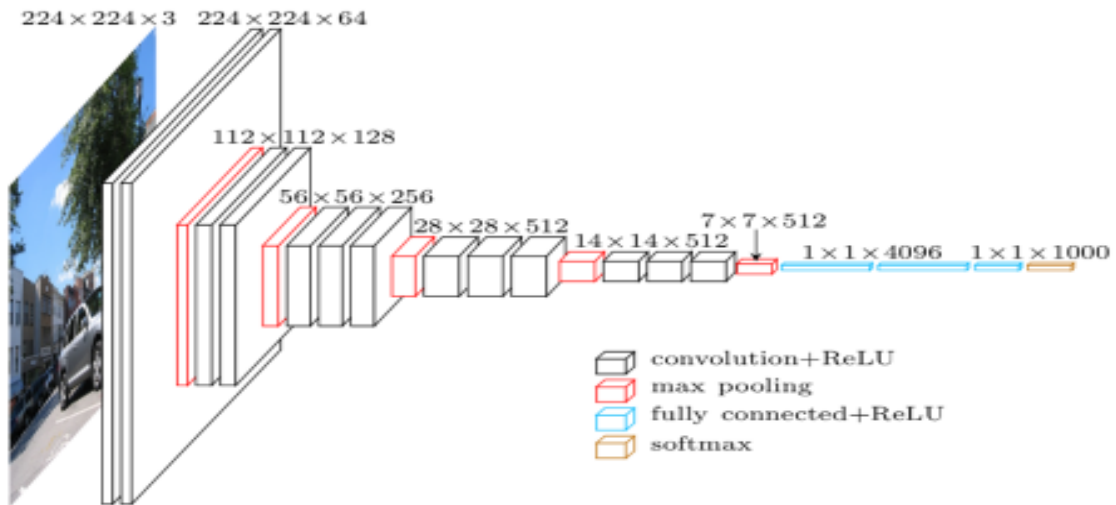
**Algorithm 2.** Pseudo code of the used preprocessing method.

<b>Input:</b> The raw 1D sensor signal ( $S$ ) with size of 5625
<b>Output:</b> Graylevel image ( $Im$ ) with size of 125 x 45
<pre> 1: <i>count</i> = 1; 2: <b>for</b> <math>i=1</math> to 125 <b>do</b> 3:   <b>for</b> <math>j=1</math> to 45 <b>do</b> 4:     <math>Im(i,j) = S(count)</math>; 5:     <math>count = count + 1</math>; 6:   <b>end for</b> <math>j</math> 7: <b>end for</b> <math>i</math> 8: Normalize <math>Im</math> by using min-max normalization.</pre>

**FIG 5.2 PSEUDOCODE OF THE PREPROCESSING MODEL**

## **b. VGG16 Implementation:**

VGG16 is a convolution neural net (CNN) architecture which was used to win ILSVR(ImageNet) competition in 2014. It is considered to be one of the excellent vision model architectures till date. Most unique thing about VGG16 is that instead of having a large number of hyper-parameters they focused on having convolution layers of 3x3 filter with a stride 1 and always used same padding and maxpool layer of 2x2 filter of stride 2. It follows this arrangement of convolution and max pool layers consistently throughout the whole architecture. In the end it has 2 FC (fully connected layers) followed by a SoftMax for output. The 16 in VGG16 refers to it has 16 layers that have weights. This network is a pretty large network and it has about 138 million (approx.) parameters.



**FIG 5.3 VGG16 IMPLEMENTATION DIAGRAM**

Here we first import all the libraries which will be need to implement VGG16. We will be using Sequential method as we are creating a sequential model. Sequential model means that all the layers of the model will be arranged in sequence. Here we have imported Image Data Generator from Keras preprocessing. The objective of Image Data Generator is to import data with labels easily into the model. It is a very useful class as it has many functions to rescale, rotate, zoom, flip etc. The most useful thing about this class is that it does not affect the data stored on the disk. This class alters the data on the go while passing it to the model.

Additionally, the VGG16 architecture has gained popularity not only for its performance but also for its simplicity and ease of understanding. Its consistent use of  $3 \times 3$  convolutional filters with a stride of 1 and same padding, along with  $2 \times 2$  max pooling layers with a stride of 2, makes it highly modular and adaptable to various image recognition tasks. This design philosophy, focusing on small filter sizes and deeper networks, has influenced subsequent convolutional neural network architectures, contributing to advancements in the field of computer vision. Furthermore, the VGG16 model's success in the ILSVRC competition demonstrated the effectiveness of deep learning approaches for image classification tasks and paved the way for further research and development in the field.

## 5.2 METHODOLOGIES:

**Data Acquisition:** The process of data acquisition for Alzheimer's disease detection involves several critical considerations beyond simply gathering images. Firstly, ensuring the ethical and legal compliance of data acquisition procedures is paramount, including obtaining appropriate consent from patients and adhering to data protection regulations. Secondly, the quality and consistency of the acquired data must be rigorously assessed to minimize biases and ensure the reliability of the trained models. This includes standardizing imaging protocols, calibrating equipment, and implementing quality control measures to address variations in image resolution, contrast, and artifacts. Moreover, the diversity and representativeness of the dataset play a crucial role in the model's generalization ability, necessitating the inclusion of images from diverse demographics, disease stages, and imaging modalities. Collaborating with healthcare institutions and research organizations can facilitate access to large-scale, annotated datasets, while data augmentation techniques, such as geometric transformations and intensity adjustments, can augment the dataset and enhance model robustness.

**Training with Transfer Learning Algorithms:** Transfer learning algorithms offer a powerful solution for leveraging pre-trained models' knowledge and adapting it to new tasks like Alzheimer's disease classification. However, successful implementation requires careful consideration of several factors, including model selection, architecture customization, and fine-tuning strategies. Model selection involves identifying pre-trained models with architectures and features suitable for the target task, considering factors such as computational efficiency, parameter complexity, and performance on similar tasks. Architecture customization involves modifying the pre-trained model's architecture to align with the input data's characteristics, such as resizing input images or adjusting the number of output classes. Fine-tuning strategies involve training the adapted model on the target dataset while adjusting hyperparameters, such as learning rate, batch size, and regularization techniques, to optimize performance and prevent overfitting. Additionally, transfer learning facilitates knowledge transfer across related tasks, such as other neurodegenerative diseases or medical imaging tasks, enabling the development of more versatile and robust classification models.

**Classification Metrics:** Evaluating the performance of Alzheimer's disease detection models requires a comprehensive understanding of classification metrics tailored to the specific characteristics of the dataset and the clinical context. In addition to traditional metrics such as accuracy, precision, recall, and F1-score, specialized metrics may be employed to address specific challenges in medical image analysis, such as class imbalance, uncertainty, and interpretability. For instance, sensitivity and specificity metrics assess the model's ability to detect true positive and true negative cases, respectively, while positive predictive value (PPV) and negative predictive value (NPV) measure the probability of correct predictions within positive and negative instances, respectively. Furthermore, domain-specific metrics, such as Cohen's kappa coefficient or Matthew's correlation coefficient (MCC), provide insights into the model's performance beyond simple accuracy measures, considering the agreement between predicted and observed classifications while accounting for chance.

**Convolutional Neural Network (CNN) Model:** The CNN model's architecture and training process are fundamental to its ability to extract meaningful features from medical images and classify them accurately. Beyond the basic structure of convolutional, pooling, and dense layers, several advanced techniques and optimizations can enhance the model's performance and efficiency. For instance, architectural innovations such as residual connections, attention mechanisms, and skip connections can improve information flow, gradient propagation, and feature reuse within the network, leading to better learning and generalization. Additionally, optimization techniques such as stochastic gradient descent (SGD) with momentum, adaptive learning rate schedulers, and gradient clipping can accelerate convergence, prevent vanishing gradients, and stabilize training dynamics. Regularization techniques, including dropout, L2 regularization, and batch normalization, help prevent overfitting by regularizing the model's parameters and promoting smoother optimization landscapes. Moreover, advancements in hardware acceleration, such as GPU parallelization and tensor processing units (TPUs), enable faster training and deployment of CNN models, making them more accessible and scalable for real-world applications in Alzheimer's disease diagnosis and beyond.

## **CHAPTER 6**

### **CONCLUSION AND FUTURESPECTIVE**

In this paper we proposed a simple and robust classification approach of MRI scans for Alzheimer's disease diagnosis. The approach is based on visual content description of anatomical structure of a brain region involved in AD ( hippocampal area). We proposed a late fusion of classification results on two biomarkers: hippocampus and CSF. The experiments showed that combining hippocampus features and CSF amount classification gave better accuracy especially when discriminating between AD and MCI than when using either visual features or CSF volume separately for discriminating between AD and MCI than using either visual features extraction or CSF volume computation separately. We also demonstrated that the proposed method provides better classification accuracy compared to other volumetric methods. In the perspective of this work, we plan to use multiple ROIs, but also multiple MRI modalities in the established classification framework.

Far greater expert optimism exists about breakthroughs in AD in the next 20 years than in the prior 20 years. In our assessment, 10 breakthroughs were judged as being at least 70% likely to occur by 2037, whereas in our 2001 study no breakthrough was judged as being even 50% likely by 2021. This optimism is reflected in the clinical pipeline for novel therapies, with a wide range of possibly disease-modifying biologics and small molecules now in Phase II and III clinical trials. However, challenges remain in delivering the predicted new AD therapies to patients, ranging from the use of appropriate cognitive screening tools to the preparedness of national healthcare systems to diagnose and treat large numbers of potentially eligible patients.

## APPENDICES

### APPENDIX 1

#### 6.1 Sample Code

##### **training.ipynb**

```
import numpy as np
import pandas as pd
import matplotlib.pyplot as plt
import skimage.io
import os
import tqdm
import glob
import tensorflow
from tqdm import tqdm
from sklearn.utils import shuffle
from sklearn.model_selection import train_test_split
from skimage.io import imread, imshow
from skimage.transform import resize
#from skimage.color import grey2rgb
from skimage.color import rgb2gray
from tensorflow.keras.preprocessing.image import ImageDataGenerator
from tensorflow.keras.models import Sequential
from tensorflow.keras.layers import InputLayer, BatchNormalization, Dropout, Flatten, Dense,
Activation, MaxPool2D, Conv2D
from keras.models import model_from_json
from tensorflow.keras.callbacks import EarlyStopping, ModelCheckpoint
from tensorflow.keras.applications.densenet import DenseNet169
from tensorflow.keras.preprocessing.image import load_img, img_to_array
batch_size = 32
# All images will be rescaled by 1./255
train_datagen = ImageDataGenerator(rescale=1/255)
```

```

# Flow training images in batches of 128 using train_datagen generator
train_generator = train_datagen.flow_from_directory(
    'alzheimer/training', # This is the source directory for training images
    target_size=(200, 200), # All images will be resized to 200 x 200
    batch_size=batch_size,
    # Specify the classes explicitly
    classes ['MildDemented','NonDemented','VeryMildDementedd','ModerateDemented'],
    # Since we use categorical_crossentropy loss, we need categorical labels
    class_mode='categorical')
valid_datagen = ImageDataGenerator(rescale = 1./255,
                                    validation_split = 0.2)
test_datagen = ImageDataGenerator(rescale = 1./255)
train_dataset=train_datagen.flow_from_directory(directory=r'C:/Users/admin/CODE-
ALZHEIMERDISEASEPREDICTION/alzheimer/training',
                                                target_size = (224,224),
                                                class_mode = 'categorical',
                                                subset = 'training',
                                                batch_size = 128)
valid_dataset=valid_datagen.flow_from_directory(directory=r'C:/Users/admin/CODE-
ALZHEIMERDISEASE PREDICTION/alzheimer/training',
                                                target_size = (224,224),
                                                class_mode = 'categorical',
                                                subset = 'validation',
                                                batch_size = 128)
fig, ax = plt.subplots(nrows = 1, ncols = 5, figsize=(20,20))
for i in tqdm(range(0,5)):
    rand1 = np.random.randint(len(train_dataset))
    rand2 = np.random.randint(50)
    ax[i].imshow(train_dataset[rand1][0][rand2])
    ax[i].axis('off')
    a = train_dataset[rand1][1][rand2]
    if a[0] == 1:
        ax[i].set_title('Mild Dementia')
    elif a[1] == 1:

```

```

    ax[i].set_title('Moderate Dementia')
elif a[2] == 1:
    ax[i].set_title('Non Demetia')
elif a[3] == 1:
    ax[i].set_title('Very Mild Dementia')
import tensorflow as tf
model = tf.keras.models.Sequential([
    # Note the input shape is the desired size of the image 200x 200 with 3 bytes color
    # The first convolution
    tf.keras.layers.Conv2D(16, (3,3), activation='relu', input_shape=(200, 200, 3)),
    tf.keras.layers.MaxPooling2D(2, 2),
    # The second convolution
    tf.keras.layers.Conv2D(32, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # The third convolution
    tf.keras.layers.Conv2D(64, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # The fourth convolution
    tf.keras.layers.Conv2D(64, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # The fifth convolution
    tf.keras.layers.Conv2D(64, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # Flatten the results to feed into a dense layer
    tf.keras.layers.Flatten(),
    # 128 neuron in the fully-connected layer
    tf.keras.layers.Dense(128, activation='relu'),
    # 5 output neurons for 5 classes with the softmax activation
    tf.keras.layers.Dense(4, activation='softmax')])
model.summary()
from tensorflow.keras.optimizers import RMSprop
model.compile(loss='categorical_crossentropy',
              optimizer=RMSprop(lr=0.001),
              metrics=['acc'])

```



```

total_sample=train_generator.n
n_epochs = 30
history = model.fit_generator(
    train_generator,
    steps_per_epoch=int(total_sample/batch_size),
    epochs=n_epochs, verbose=1)
model.save('model2.h5')
# Test Case 1: Non-Dementia
import numpy as np
from keras_preprocessing import image
import easygui
dic = test_dataset.class_indices
idc = {k:v for v, k in dic.items()}
img=load_img(r'C:/Users/admin/MultiClass-Image-Classification-
master/alzheimer/training/NonDemented/nonDem
18.jpg', target_size = (224,224,3))
img = img_to_array(img)
img = img/255
imshow(img)
plt.axis('off')
img = np.expand_dims(img,axis=0)
test_image=image.load_img(r'C:/Users/admin/MultiClass-Image-Classification-
master/alzheimer/training/NonDemented/nonDem18.jpg',target_size=(200,200))
test_image = np.expand_dims(test_image, axis=0)
result = model.predict(test_image)
if result[0][1] == 1:
    prediction = "NonDemented"
elif result[0][0] == 1:
    prediction = "MildDemented"
elif result[0][2] == 1:
    prediction = "VeryMildDementedd"
elif result[0][3] == 1:
    prediction = "ModerateDemented"
print(prediction)

```

## **predict.py**

```
import tensorflow as tf
from keras_preprocessing.image import ImageDataGenerator
from keras_preprocessing import image
import numpy as np
import easygui
from keras.models import load_model
import os
import tkinter as tk
from tkinter import *
from tkinter import filedialog
from tkinter.filedialog import askopenfile
from PIL import Image, ImageTk
my_w = tk.Tk()
my_w.geometry('1244x829+0+10')
my_w.title('Alizheimer disease Prediction')
my_font1=('times', 18, 'bold')
        bg = ImageTk.PhotoImage(file='brain-tumorr.png')
bgLabel = Label(my_w, image=bg)
bgLabel.place(x=0, y=0)
l1=tk.Label(my_w,text='UploadFiles&getresults',width=30,font=my_font1,bg='#000080',fg='red',)
l1.place(x=550, y=190, width=300)
b1=tk.Button(my_w,text='UploadImages',width=20,command          =          lambda:result(),
activebackground='#000080', bg='green')
b1.place(x=590,y=500, width=230, height=40)
print(tf.__version__)
def close():
my_w.destroy()
titleLabel = Label(my_w, text=' ALIZHEIMER DISEASE PREDICTION', font=('italic', 22, 'bold '),
bg='black', fg='white', )
titleLabel.place(x=0, y=40, width=1350, height=50)
endbtn=Button(my_w,text="Exit",font='italic 14 bold',bg='black',fg='white',command=close)
```

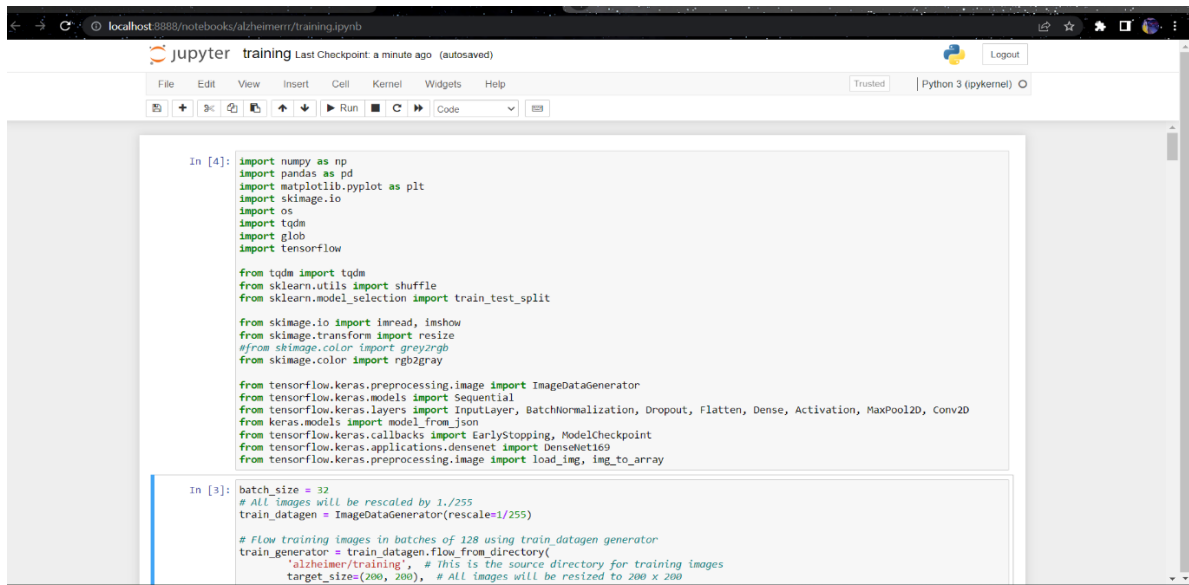
```

endbtn.place(x=670,y=600,width=50)
classifierLoad = tf.keras.models.load_model('model2.h5')
def result():
    filename =upload_file()
    test_image2 = image.load_img(filename, target_size = (200,200))
    test_image2 = image.img_to_array(test_image2)
    test_image2 = np.expand_dims(test_image2, axis = 0)
    # cnn prediction on the test image
    result = classifierLoad.predict(test_image2)
    print(result)
    if result[0][1] == 1:
        prediction2="NonDemented"
    elif result[0][0] == 1:
        prediction2="MildDemented"
    elif result[0][2] == 1:
        prediction2="VeryMildDementedd"
    elif result[0][3] == 1:
        prediction2="ModerateDemented"
    print(prediction2)
    prediction=prediction2
    l2=tk.Label(my_w,text="Result "+prediction,width=50,font=my_font1,bg='pink', fg='black',)
    l2.place(x=560, y=550, width=400)
    return filename
    def upload_file():
        filename = easygui.fileopenbox()
        img=Image.open(filename) # read the image file
        img=img.resize((200,140)) # new width & height
        img=ImageTk.PhotoImage(img)
        e1 =tk.Label(my_w)
        e1.place(x=590, y=240, width=240, height=250)
        e1.image = img
        e1['image']=img
        return filename
    my_w.mainloop()

```

## APPENDIX 2

### SCREENSHOTS



```
In [4]: import numpy as np
import pandas as pd
import matplotlib.pyplot as plt
import skimage.io
import os
import tqdm
import glob
import tensorflow

from tqdm import tqdm
from sklearn.utils import shuffle
from sklearn.model_selection import train_test_split

from skimage.io import imread, imshow
from skimage.transform import resize
# from skimage.color import grey2rgb
from skimage.color import rgb2gray

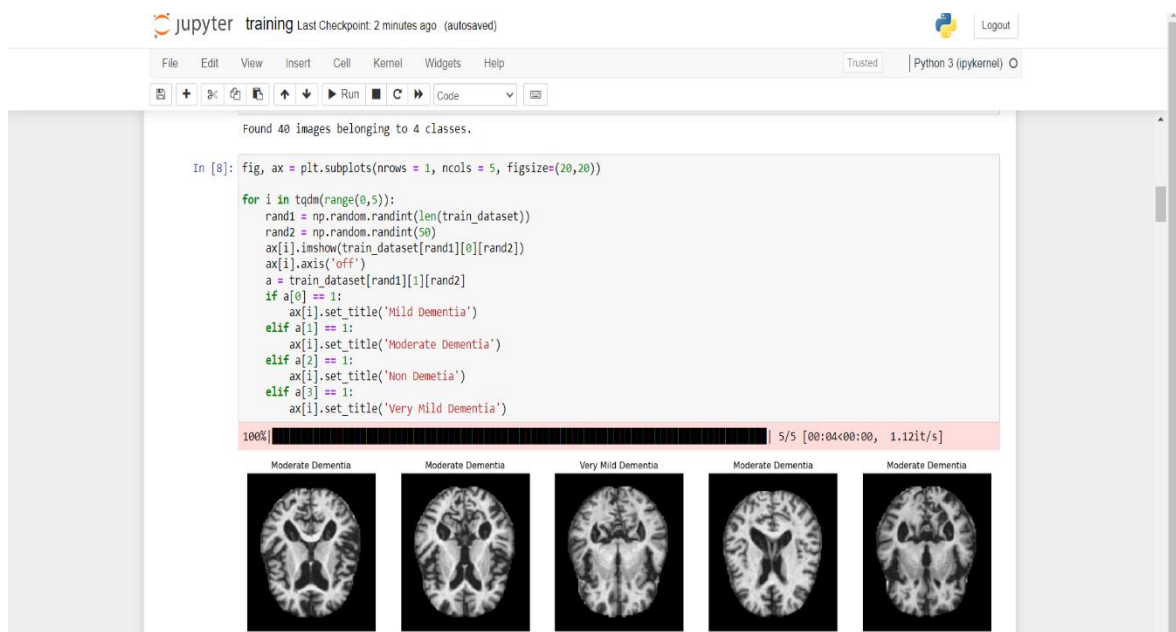
from tensorflow.keras.preprocessing.image import ImageDataGenerator
from tensorflow.keras.models import Sequential
from tensorflow.keras.layers import InputLayer, BatchNormalization, Dropout, Flatten, Dense, Activation, MaxPool2D, Conv2D
from keras.models import model_from_json
from tensorflow.keras.callbacks import EarlyStopping, ModelCheckpoint
from tensorflow.keras.applications.densenet import DenseNet169
from tensorflow.keras.preprocessing.image import load_img, img_to_array

In [3]: batch_size = 32
# All images will be rescaled by 1./255
train_datagen = ImageDataGenerator(rescale=1./255)

# Flow training images in batches of 128 using train_datagen generator
train_generator = train_datagen.flow_from_directory(
    'alzheimer/training', # This is the source directory for training images
    target_size=(200, 200), # All images will be resized to 200 x 200
```

**FIG 6.1 IMPORTING THE NECESSARY PACKAGES**

Figure 6.1 depicts importing of all the necessary packages like pandas, NumPy, sklearn, TensorFlow, Keras the predefined functions are used.



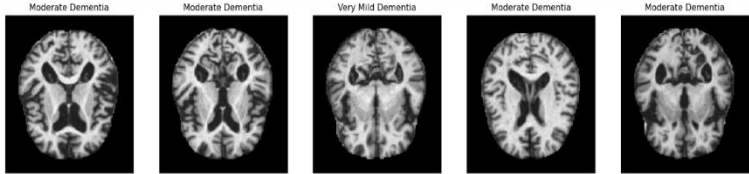
```
Found 40 images belonging to 4 classes.

In [8]: fig, ax = plt.subplots(nrows = 1, ncols = 5, figsize=(20,20))

for i in tqdm(range(0,5)):
    rand1 = np.random.randint(len(train_dataset))
    rand2 = np.random.randint(50)
    ax[i].imshow(train_dataset[rand1][0][rand2])
    ax[i].axis('off')
    a = train_dataset[rand1][1][rand2]
    if a[0] == 1:
        ax[i].set_title('Mild Dementia')
    elif a[1] == 1:
        ax[i].set_title('Moderate Dementia')
    elif a[2] == 1:
        ax[i].set_title('Non Dementia')
    elif a[3] == 1:
        ax[i].set_title('Very Mild Dementia')

100% | 5/5 [00:04<00:00, 1.12it/s]
```

Moderate Dementia   Moderate Dementia   Very Mild Dementia   Moderate Dementia   Moderate Dementia



**FIG 6.2 TRAINING THE DATASET**

Figure 6.2 depicts training the dataset where it uses the trained dataset of AD images and then assigned a random integer to the images. Specifying the looping conditions according to it.

```
In [9]: import tensorflow as tf

model = tf.keras.models.Sequential([
    # Note the input shape is the desired size of the image 200x 200 with 3 bytes color
    # The first convolution
    tf.keras.layers.Conv2D(16, (3,3), activation='relu', input_shape=(200, 200, 3)),
    tf.keras.layers.MaxPooling2D(2, 2),
    # The second convolution
    tf.keras.layers.Conv2D(32, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # The third convolution
    tf.keras.layers.Conv2D(64, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # The fourth convolution
    tf.keras.layers.Conv2D(64, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # The fifth convolution
    tf.keras.layers.Conv2D(64, (3,3), activation='relu'),
    tf.keras.layers.MaxPooling2D(2,2),
    # Flatten the results to feed into a dense layer
    tf.keras.layers.Flatten(),
    # 128 neuron in the fully-connected layer
    tf.keras.layers.Dense(128, activation='relu'),
    # 5 output neurons for 5 classes with the softmax activation
    tf.keras.layers.Dense(4, activation='softmax')
])
```

**FIG 6.3 REPRESENTATION OF DENSENET CODE**

Figure 6.3 Represents the coding part of the algorithm dense Net. where Convolutional, maxpooling at initial and for the 4 dense blocks and finally layers are flattened ,relu and SoftMax function is used.

```
In [21]: # Test Case 1: Non-Dementia
import numpy as np
from keras_preprocessing import image
import easygui

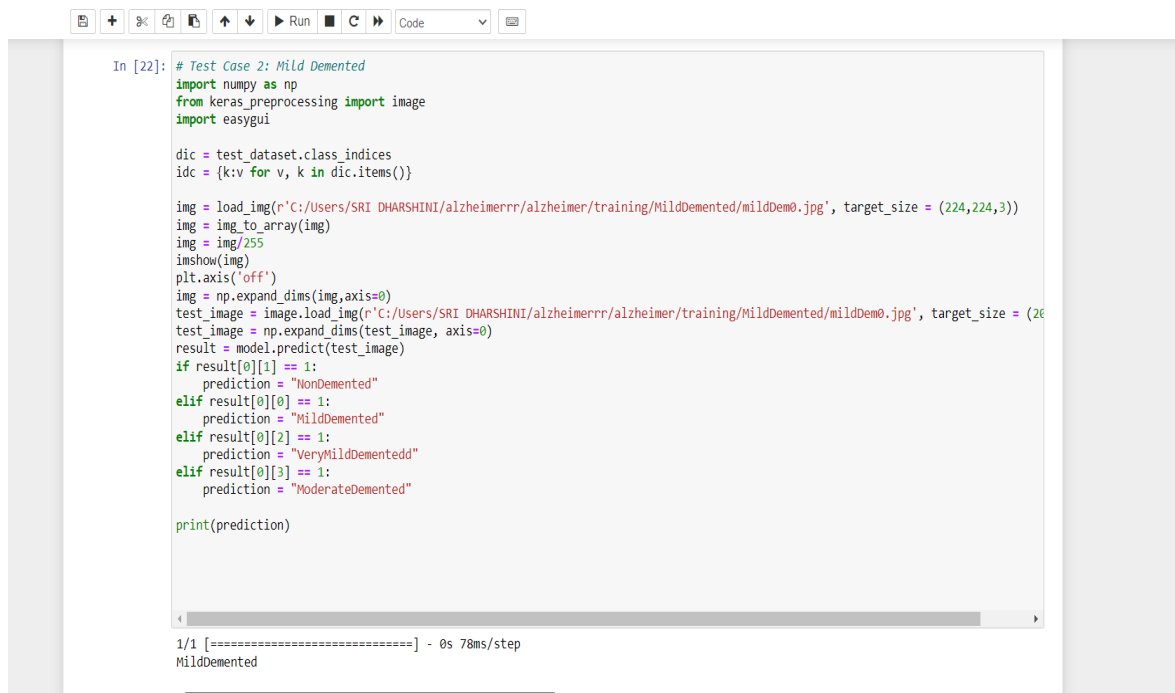
dic = test_dataset.class_indices
idc = {k:v for v, k in dic.items()}

img = load_img(r'C:/Users/SRI DHARSHINI/alzheimerrr/alzheimer/training/NonDemented/nonDem0.jpg', target_size = (224,224,3))
img = img_to_array(img)
img = img/255
imshow(img)
plt.axis('off')
img = np.expand_dims(img,axis=0)
test_image = image.load_img(r'C:/Users/SRI DHARSHINI/alzheimerrr/alzheimer/training/NonDemented/nonDem0.jpg', target_size = (200,
test_image = np.expand_dims(test_image, axis=0)
result = model.predict(test_image)
if result[0][1] == 1:
    prediction = "NonDemented"
elif result[0][0] == 1:
    prediction = "MildDemented"
elif result[0][2] == 1:
    prediction = "VeryMildDementedd"
elif result[0][3] == 1:
    prediction = "ModerateDemented"

print(prediction)
```

**FIG 6.4 CASE 1**

Figure 6.4 Represents the coding logic of the non-Dementia stage of the Alzheimer disease affected person.



```

In [22]: # Test Case 2: Mild Demented
import numpy as np
from keras_preprocessing import image
import easygui

dic = test_dataset.class_indices
idc = {k:v for v, k in dic.items()}

img = load_img(r'C:/Users/SRI DHARSHINI/alzheimerr/alzheimer/training/MildDemented/mildDem0.jpg', target_size = (224,224,3))
img = img_to_array(img)
img = img/255
imshow(img)
plt.axis('off')
img = np.expand_dims(img,axis=0)
test_image = image.load_img(r'C:/Users/SRI DHARSHINI/alzheimerr/alzheimer/training/MildDemented/mildDem0.jpg', target_size = (224,224,3))
test_image = np.expand_dims(test_image, axis=0)
result = model.predict(test_image)
if result[0][1] == 1:
    prediction = "NonDemented"
elif result[0][0] == 1:
    prediction = "MildDemented"
elif result[0][2] == 1:
    prediction = "VeryMildDemented"
elif result[0][3] == 1:
    prediction = "ModerateDemented"

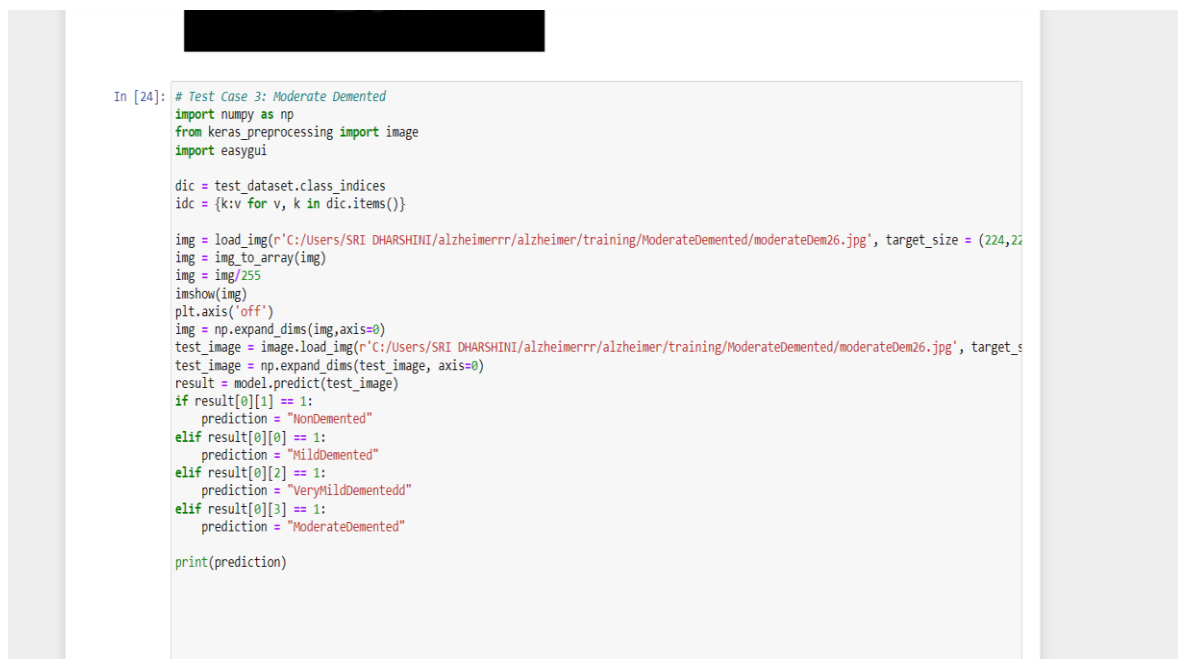
print(prediction)

1/1 [=====] - 0s 78ms/step
MildDemented

```

**FIG 6.5 CASE 2**

Figure 6.5 Represents the coding logic of the Mild Dementia stage of the Alzheimer disease affected person.



```

In [24]: # Test Case 3: Moderate Demented
import numpy as np
from keras_preprocessing import image
import easygui

dic = test_dataset.class_indices
idc = {k:v for v, k in dic.items()}

img = load_img(r'C:/Users/SRI DHARSHINI/alzheimerr/alzheimer/training/ModerateDemented/moderateDem26.jpg', target_size = (224,224,3))
img = img_to_array(img)
img = img/255
imshow(img)
plt.axis('off')
img = np.expand_dims(img,axis=0)
test_image = image.load_img(r'C:/Users/SRI DHARSHINI/alzheimerr/alzheimer/training/ModerateDemented/moderateDem26.jpg', target_size = (224,224,3))
test_image = np.expand_dims(test_image, axis=0)
result = model.predict(test_image)
if result[0][1] == 1:
    prediction = "NonDemented"
elif result[0][0] == 1:
    prediction = "MildDemented"
elif result[0][2] == 1:
    prediction = "VeryMildDemented"
elif result[0][3] == 1:
    prediction = "ModerateDemented"

print(prediction)

```

**FIG 6.6 CASE 3**

Figure 6.6 Represents the coding logic of the Moderate stage of the Alzheimer disease affected person.

```
# Test Case 4: Very Mild Demented
# Test Case 3: Moderate Demented
import numpy as np
from keras_preprocessing import image
import easygui

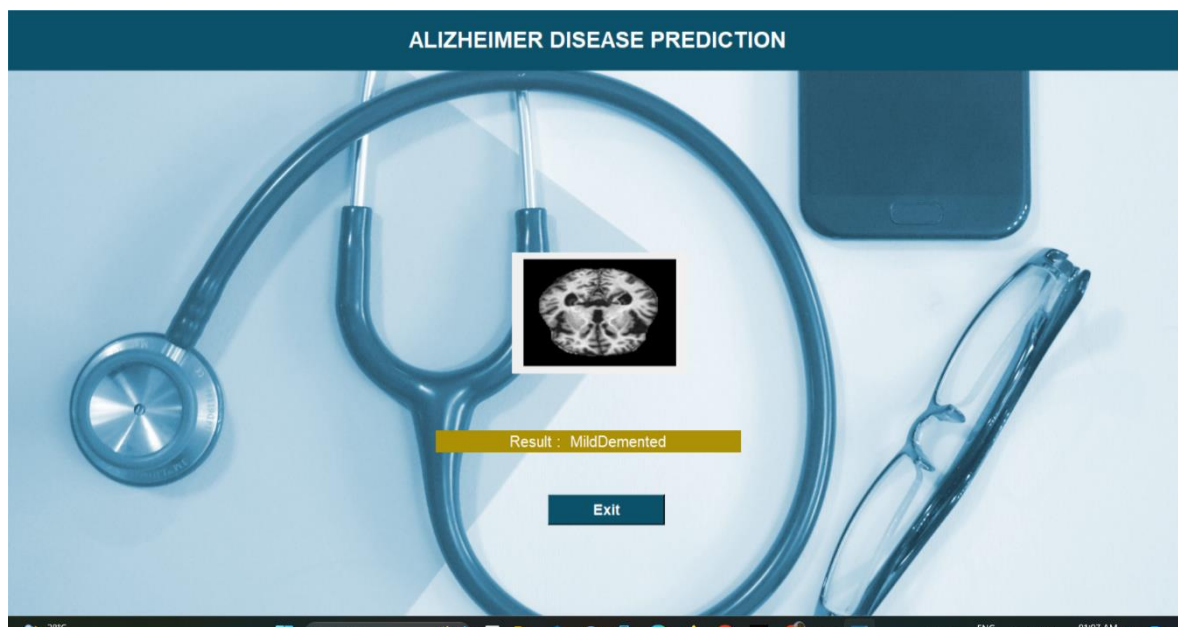
dic = test_dataset.class_indices
idc = {k:v for v, k in dic.items()}

img = load_img(r'C:/Users/SRI DHARSHINI/alzheimer/alzheimer/training/VeryMildDementedd/verymildDem1.jpg', target_size = (224,224))
img = img_to_array(img)
img = img/255
imshow(img)
plt.axis('off')
img = np.expand_dims(img,axis=0)
test_image = image.load_img(r'C:/Users/SRI DHARSHINI/alzheimer/alzheimer/training/VeryMildDementedd/verymildDem1.jpg', target_size = (224,224))
test_image = np.expand_dims(test_image, axis=0)
result = model.predict(test_image)
if result[0][1] == 1:
    prediction = "NonDemented"
elif result[0][0] == 1:
    prediction = "MildDemented"
elif result[0][2] == 1:
    prediction = "VeryMildDementedd"
elif result[0][3] == 1:
    prediction = "ModerateDemented"

print(prediction)
```

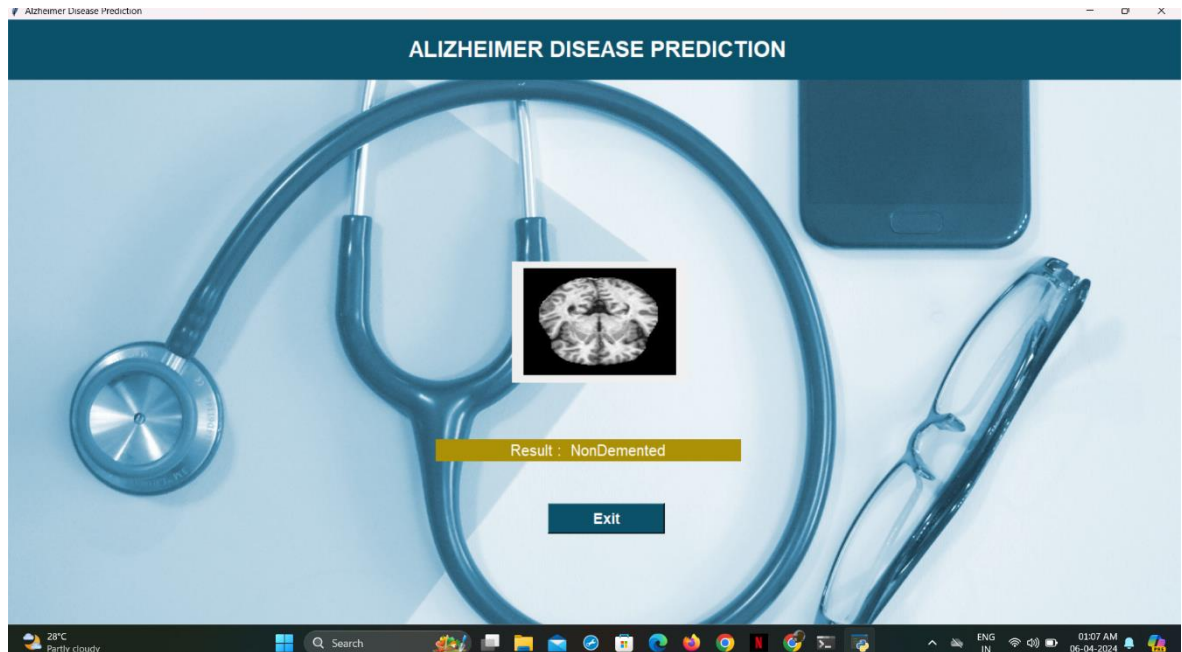
**FIG 6.7 CASE 4**

Figure 6.7 Represents the coding logic of the Very Mild Dementia stage of the Alzheimer disease affected person.



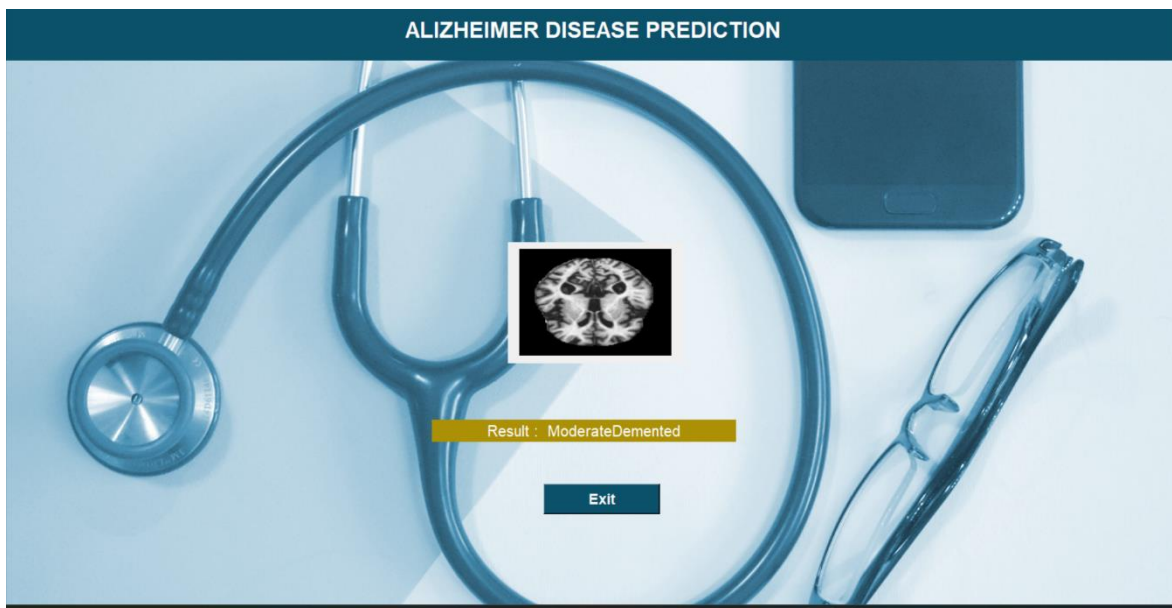
**FIG 6.8 REPRESENTATION OF MILD DEMENTIA**

Figure 6.8 Represents the output image of Mild dementia. The code analyses and recognizes the given image falls under the mild demented stage of the disease.



**FIG 6.9 REPRESENTATION OF NON-DEMENTIA**

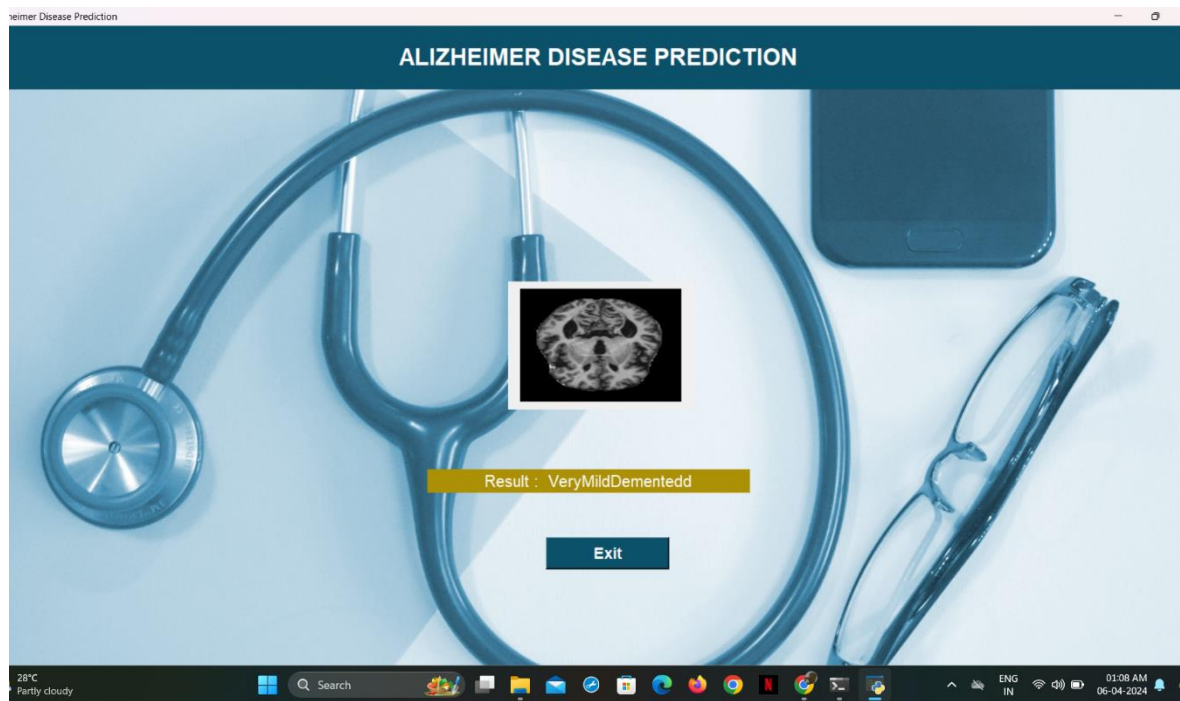
Figure 6.9 Represents the output image of Non dementia. The code analyses and recognizes the given image falls under the Non demented stage of the disease.



**FIG 6.10 REPRESENTATION OF MODERATE DEMENTIA**



Figure 6.10 Represents the output image of Moderate dementia. The code analyses and recognizes the given image falls under the Moderate demented stage of the disease.



**FIG 6.11 REPRESENTATION OF VERY MILD DEMENTIA**

Figure 6.11 Represents the output image of Very Mild dementia. The code analyses and recognizes the given image falls under the Very Mild.

## REFERENCES

- [1] Allan I. Levey, et al. "Progress with Treatments for Alzheimer's Disease" in *The NEW ENGLAND JOURNAL of MEDICINE*, (2021). DOI: 10.1056/NEJMe2103722
- [2] Arya, A. D., Verma, S. S., Chakarabarti, P., Chakrabarti, T., Elngar, A. A., Kamali, M., & Nami, M. (2023). A systematic review on machine learning and deep learning techniques in the effective diagnosis of Alzheimer's disease. *Brain Informatics*, 10(1). <https://doi.org/10.1186/s40708-023-00195-7>.
- [3] Bass, C., et al. (2023). ICAM-Reg: Interpretable Classification and Regression with Feature Attribution for Mapping Neurological Phenotypes in Individual Scans. *IEEE Transactions on Medical Imaging*, 42(4), 959-970. <https://doi.org/10.1109/TMI.2022.3221890>.
- [4] Bellenguez, C., Küçükali, F., Jansen, I. E., Klei, L., Amin, N., Naj, A. C., Andrade, V., Holmans, P. A., Boland, A., Damotte, V., J., S., Costa, M. R., Kuulasmaa, T., Yang, Q., De Rojas, I., Bis, J. C., Yaqub, A., Prokic, I., Chapuis, J., . . . Lambert, J. (2022). New insights into the genetic etiology of Alzheimer's disease and related dementias. *Nature Genetics*, 54(4), 412-436. <https://doi.org/10.1038/s41588-022-01024-z>.
- [5] Bogdanovic, B., Eftimov, T., & Simjanoska, M. (2022). In-depth insights into Alzheimer's disease by using explainable machine learning approach. *Scientific Reports*, 12(1), 1-26. <https://doi.org/10.1038/s41598-022-10202-2>.
- [6] Borovkova, M., et al. (2022). Screening of Alzheimer's Disease With Multiwavelength Stokes Polarimetry in a Mouse Model. *IEEE Transactions on Medical Imaging*, 41(4), 977-982. <https://doi.org/10.1109/TMI.2021.3129700>.
- [7] Cheung, C. Y., Ran, A. R., Wang, S., Chan, V. T. T., Sham, K., Hilal, S., ... & Wong, T. Y. (2022). A deep learning model for detection of Alzheimer's disease based on retinal photographs: a retrospective, multicenter case-control study. *ARTICLES*, 4(11), E806-E815. [https://doi.org/10.1016/S2589-7500\(22\)00169-8](https://doi.org/10.1016/S2589-7500(22)00169-8).
- [8] Cummings, J., Zhou, Y., Lee, G., Zhong, K., Fonseca, J., & Cheng, F. (2023). Alzheimer's disease drug development pipeline: 2023. *Alzheimer's & Dementia : Translational Research & Clinical Interventions*, 9(2). <https://doi.org/10.1002/trc2.12385>
- [9] Dara, O. A., Manuel, J., Raheem, H. I., Rahebi, J., & Zulueta, E. (2022). Alzheimer's Disease Diagnosis Using Machine Learning: A Survey. *Applied Sciences*, 13(14), 8298. <https://doi.org/10.3390/app13148298>.
- [10] Gupta, M., Kumar, R., & Abraham, A. (2024). Adversarial Network-Based Classification for Alzheimer's Disease Using Multimodal Brain Images: A Critical Analysis. *IEEE Access*, 12, 48366-48378. <https://doi.org/10.1109/ACCESS.2024.3381956>.
- [11] Helaly, H.A., Badawy, M. & Haikal, A.Y. et al. "Deep Learning Approach for Early Detection of Alzheimer's Disease" in Springer Link. *Cognitive Computing* 14, 1711–1727 (2022). <https://doi.org/10.1007/s12559-021-09946-2>.

- [12] Jeffrey Cummings, Garam Lee, Kate Zhong, Jorge Fonseca, “Alzheimer's disease drug development pipeline: 2021”, in Alzheimer's Association, vol. 7, <https://doi.org/10.1002/trc2.12179>, 2021.
- [13] Kavitha, C., Mani, Vinodhini, Srividhya, S. R., Khalaf, Osamah Ibrahim, et al. (2022). Early-Stage Alzheimer's Disease Prediction Using Machine Learning Models. *Frontiers in Public Health*, 10:853294. DOI: 10.3389/fpubh.2022.853294.
- [14] Knopman, D.S., Amieva, H., Petersen, R.C. et al. “Alzheimer disease”.in *Nature Reviews Disease Primers* 7, 33 (2021). <https://doi.org/10.1038/s41572-021-00269-y> .
- [15] Liao, S., & Hsieh, F. (2024). Unraveling Heterogeneity of ADNI's Time-to-Event Data Using Conditional Entropy—Part I: Cross-Sectional Study. *IEEE Access*, 12, 3292-3314. <https://doi.org/10.1109/ACCESS.2023.3344319>.
- [16] McCombe, N., et al. (2022). Practical Strategies for Extreme Missing Data Imputation in Dementia Diagnosis. *IEEE Journal of Biomedical and Health Informatics*, 26(2), 818-827. <https://doi.org/10.1109/JBHI.2021.3098511>.
- [17] O. K. Cura, G. C. Yilmaz, H. S. Ture and A. Akan, "Classification of Alzheimers' Dementia by Using Various Signal Decomposition Methods," in *IEEE Xplore 2021 Medical Technologies Congress (TIPTEKNO)*, Antalya, Turkey, 2021, pp. 1-4, doi: 10.1109/TIPTEKNO53239.2021.9633007.
- [18] Parag Parekh, Andrew A. Badachhape, Eric A. Tanifum, Ananth V. Annapragada, Ketan B. Ghaghada, *Advances in nanoprobe for molecular MRI of Alzheimer's disease*, *WIREs Nanomedicine and Nanobiotechnology*, 10.1002/wnan.1946, 16, 2, (2024).
- [19] Parag Parekh, Andrew A. Badachhape, Eric A. Tanifum, Ananth V. Annapragada, Ketan B. Ghaghada, *Advances in nanoprobe for molecular MRI of Alzheimer's disease*, *WIREs Nanomedicine and Nanobiotechnology*, 10.1002/wnan.1946, 16, 2, (2024).
- [20] Patil, V., Madgi, M., & Kiran, A. (2022). Early prediction of Alzheimer's disease using convolutional neural network: A review. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, 58(1), 1-10. <https://doi.org/10.1186/s41983-022-00571-w>.
- [21] Porsteinsson, A.P., Isaacson, R.S., Knox, S. et al. “Diagnosis of Early Alzheimer’s Disease: Clinical Practice in 2021”, in *Springer Nature J Prev Alzheimer’s Dis* 8, 371–386 (2021). <https://doi.org/10.14283/jpad.2021.23>.
- [22] Qiu, S., Miller, M. I., Joshi, P. S., Lee, J. C., Xue, C., Ni, Y., Wang, Y., Hwang, P. H., Cramer, J. A., Dwyer, B. C., Hao, H., Kaku, M. C., Kedar, S., Lee, P. H., Mian, A. Z., Murman, D. L., Paul, A. B., Alton Sartor, E., Saxena, A. R., Kolachalama, V. B. (2022). Multimodal deep learning for Alzheimer’s disease dementia assessment. *Nature Communications*, 13(1), 1-17. <https://doi.org/10.1038/s41467-022-31037-5>.
- [23] Saleem, T. J., Zahra, S. R., Wu, F., Alwakeel, A., Alwakeel, M., Jeribi, F., & Hijji, M. (2022). Deep Learning-Based Diagnosis of Alzheimer’s Disease. *Journal of Personalized Medicine*, 12(5). <https://doi.org/10.3390/jpm12050815>.

- [24] Self, W. K., & Holtzman, D. M. (2023). Emerging diagnostics and therapeutics for Alzheimer disease. *Nature Medicine*, 29(9), 2187-2199. <https://doi.org/10.1038/s41591-023-02505-2>.
- [25] S. Harika, T. Yamini, T. Nagasaikamesh, et al. "Alzheimer's Disease Detection Using Different Machine Learning Algorithms" in *iJRASET*. 2321-9653 (2022). <https://doi.org/10.22214/ijraset.2022.46937>.
- [26] Tsai, C. -F., et al. (2021). A Machine-Learning-Based Assessment Method for Early-Stage Neurocognitive Impairment by an Immersive Virtual Supermarket. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 29, 2124-2132. <https://doi.org/10.1109/TNSRE.2021.3118918>.
- [27] Uddin, K.M.M., Alam, M.J., Jannat-E-Anawar et al. A Novel Approach Utilizing Machine Learning for the Early Diagnosis of Alzheimer's Disease. *Biomedical Materials & Devices* 1, 882–898 (2023). <https://doi.org/10.1007/s44174-023-00078-9>.
- [28] van Bokhoven, P., de Wilde, A., Vermunt, L. et al. "The Alzheimer's disease drug development landscape". *Alzheimer's Research and Therapy* 13, 186 (2021). <https://doi.org/10.1186/s13195-021-00927-z>.
- [29] Yuan, S., Li, H., Wu, J., & Sun, X. (2021). Classification of Mild Cognitive Impairment With Multimodal Data Using Both Labeled and Unlabeled Samples. *IEEE/ACM Transactions on Computational Biology and Bioinformatics*, 18(6), 2281-2290. <https://doi.org/10.1109/TCBB.2021.3053061>.
- [30] Yu, Tien-Wei, Hsien-Yuan Lane, and Chieh-Hsin Lin. 2021. "Novel Therapeutic Approaches for Alzheimer's Disease: An Updated Review" *International Journal of Molecular Sciences* 22, no. 15: 8208. <https://doi.org/10.3390/ijms22158208>.
- [31] Yu, Tien-Wei, Hsien-Yuan Lane, and Chieh-Hsin Lin. 2021. "Novel Therapeutic Approaches for Alzheimer's Disease: An Updated Review" *International Journal of Molecular Sciences* 22, no. 15: 8208. <https://doi.org/10.3390/ijms22158208>.