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Severity Grading and Early Detection of Alzheimer's Disease through Transfer Learning

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Abstract: Alzheimer's disease (AD) is an illness affecting the neurological system in people commonly aged 65 years and older. It is one of the leading causes of dementia and, subsequently, the cause of death as it gradually affects and destroys brain cells. In recent years, the detection of AD has been examined in ways to mitigate its impacts while considering early detection through computer-aided diagnosis (CAD) tools. In this study, we developed deep learning models that focus on early detection and classifying each case, non-demented, moderate-demented, mild-demented, and very-mild-demented, accordingly through transfer learning (TL); an AlexNet, ResNet-50, GoogleNet (InceptionV3), and SqueezeNet by utilizing magnetic resonance images (MRI) and the use of image augmentation. The acquired images, a total of 12,800 images and four classifications, had to go through a pre-processing phase to be balanced and fit the criteria of each model. Each of these proposed models split the data into 80% training and 20% testing. AlexNet performed an average accuracy of 98.05%, GoogleNet (InceptionV3) performed an average accuracy of 97.80%, and ResNet-50 had an average performing accuracy of 91.11%. The transfer learning approach assists when there is not adequate data to train a network from the start, which aids in tackling one of the major challenges faced when working with deep learning.

Keywords: Alzheimer's disease; transfer learning; CNN; convolutional neural network; MRI; dementia; machine learning; deep learning; GoogleNet; AlexNet

Citation: Alqahtani, S.; Alqahtani, A.; Zohdy, M.A.; Alsulami, A.A.; Ganesan, S. Severity Grading and Early Detection of Alzheimer's Disease through Transfer Learning. *Information* **2023**, *14*, 646. https://doi.org/10.3390/info14120646

Academic Editors: Danilo Avola and Yutong Xie

Received: 26 September 2023
Revised: 20 November 2023
Accepted: 30 November 2023
Published: 3 December 2023

1. Introduction

Alzheimer's disease (AD) is a disorder that affects the nervous system, particularly the human brain. It not only impairs a person's abilities to carry out basic memory, thinking, and social functions, but it is also chronic and irreversible. It is one of the most common forms of dementia. Early symptoms of Alzheimer's disease include difficulties with thinking, self-management of language skills, and memory loss [1]. AD gradually damages memory and impairs the ability to perform everyday tasks. As mental capacity gradually declines, patients face increasing barriers to leading an independent, normal life. Patients become more reliant on their immediate family and other caregivers for survival as the disease progresses.

Alzheimer's disease is among the most well-known varieties of dementia in people aged 65 and older. By 2050, it is anticipated that 1 out of every 85 people will be diagnosed with the disease, and in the following 20 years, that number will double. Alzheimer's Association report suggests that age is among the largest risk factors for Alzheimer's disease. The likelihood of AD affecting someone increases with age 65 to 74 years old, and risks increase by 5.0% to 13.1% for the age 75 to 84 years old and 33.2% for people

85 years old and over. According to the Alzheimer's Association, it is estimated that in 2022, 6.5 million people aged 65 and older in the United States had Alzheimer's disease [1].

Alzheimer's disease was formally recognized as the sixth predominant cause of death in the United States in 2019 and the seventh leading cause of death in 2020 and 2021. While Alzheimer's disease is still to be ranked the fifth leading cause of death for people 65 and older, the actual fatalities might be significantly higher than what official reports suggest. A person with Alzheimer's disease lives through harsh years as the disease advances, incapacitated, and ill health before passing away. The Alzheimer's Association report in 2022 indicates that 121,499 people have died from Alzheimer's disease in 2019 alone; conversely, the report also suggests these numbers underrepresent deaths from Alzheimer's disease due to inaccurate reporting of cause of death. Many injuries and diseases are linked to Alzheimer's disease, particularly in the elderly, such as pneumonia, since severe dementia could cause further complications such as swallowing disorders, immobility, and malnutrition, which results in higher chances of serious acute conditions and ultimately death (comorbidity). In 2021, About USD 290 billion was the expected total cost of dementia patients' long-term medical treatment [2]. Even though there is no cure for Alzheimer's disease known at this time, detecting it early could be beneficial since there are some treatments available to slow its progress [1]. Prior to clinical manifestation, early AD detection is essential for prompt treatment.

In order to recognize AD and its various stages from conventional controls, a multiclass decision system is necessary. Since AD can be detected without the help of any specialists or skills when it is too late for therapy, differentiating AD from MCI or normal people is crucial [3].

Though the causes of Alzheimer's disease are not completely understood, the disease occurs when irregularities in protein function cause damage to nerve cells, leading to a loss of connectivity. Two irregularities are required to diagnose AD—extracellular amyloid plaques and intracellular neurofibrillary tangles [3]. In the first irregularity, layers of amyloid plaque become deposited on the outside of neurons, disrupting their connectivity. In the second, neurofibrillary tangles composed of filamentous tau proteins further disrupt connectivity and are linked to neuronal death [4]. These plaques and tangles have been commonly used to aid in the diagnosis of AD [5].

In imaging diagnosis, there are multiple types of imaging to diagnose AD accurately, such as structural and functional imaging. Single-photon emission computed tomography (SPECT) is an imaging technology used in AD diagnosis. PET and fMRI are examples of functional imaging, while MRI and CT are examples of structural imaging. A CT scan stands for computed tomography and uses multiple X-ray scans at once with different angles of the targeted organ, while MRI uses radio waves and electromagnetic fields to generate images of the targeted organ. On the other hand, positron emission tomography (PET) and functional MRI (fMRI) use molecular imaging, which targets radiotracers in order to spot chemical and cellular variations linked to a specific condition or disease. Considering the accessibility limitation of functional imaging and CT's limited capabilities, MRI has been ubiquitously used due to its availability and efficiency [1,2]. Compared to other procedures, MRI is far superior in its cost and effectiveness without the use of ionizing radiation. It could be used for all phases of Alzheimer's disease as well as to differentiate between healthy people and the ill. Additionally, MRI could be utilized for the detection of mild cognitive impairment (MCI) and Alzheimer's disease (AD), as well as the conversion from MCI to AD. It can also be used to distinguish between distinct forms of dementia, such as frontotemporal dementia and AD, which may exhibit similar clinical symptoms [6,7].

Computer-aided diagnosis based on artificial intelligence (AI) has emerged as a viable and well-liked instrument in medicine mainly because of its affordability and open decision-making process [8]. One artificial intelligence (AI) area is the deep neural networks machine learning algorithm (ML), where a computer learns about similarities and differences among a dataset to form a connecting relationship for decision-making without direct knowledge. The majority of development in machine learning algorithms was to exceed the abilities of humans, especially back in the late 1990s; however, it has not reached adequate functionality [9].

A convolution neural network (CNN) was developed with the inspiration of the human brain's visual processing [10]. Moreover, the development did not stop there; it continued to introduce deep convolution neural networks. The deep convolutional neural network has reached new and potent levels of learning abilities especially since it utilizes multiple feature extraction strategies that could instinctively learn patterns and unique features. In recent years, the advancement in computer capabilities has created more powerful processors, which has enabled the progress and enhancement in the research and development of convolutional neural networks. The hierarchical structure of CNN is one of its defining features. The CNN structure is made up of a combination of the layers: Convolution, Pooling, Activation, Normalization, and Fully Connected. The output of the convolution layer, also known as CONV, is computed by breaking the input image up into smaller blocks and convolving those blocks with weights. Concisely, CONV layers extract characteristics from the input images [9].

Deep learning lies within machine learning that consists of copious layers and parameters, and most deep learning utilizes neural network architecture. Any deep learning usually requires a large set of data. Once the dataset has been gathered and labeled properly, it can proceed to the deep learning process [11,12]. The most commonly used models of deep learning are Training from Scratch, Transfer Learning, and Feature Extraction. Training from scratch is the most unfavored among the three since it requires building the model with every minor and major detail in mind, but it is also excellent for new applications. Feature extraction is the second favored one, requiring some specialty to use the network as a feature extractor. After the extraction features process is completed, models such as support vector machines (SVM) could be used for classification. Finally, transfer learning is the most commonly used in deep learning applications, which involves pre-processing and fine-tuning to an already existing pre-trained network or model such as AlexNet and GoogleNet [13,14].

A pre-trained network is used regularly as it has many advantages; one of them stands out very much, which is the amount of data these networks have gone through to be very efficient and fairly accurate compared to other methods, especially for classification. These pre-trained networks could then be used again by other people to aid in the line of work, considering how much work, time, and accuracy they have once they are integrated [15]. Convolutional neural networks (CNN) are composed of layers that are capable of convolutionally extracting local information, such as edges from an input image. A small number of neurons with spatial connections connect each node in a convolutional layer. The connection weights are distributed among the convolutional layer nodes to look for the same local feature over the whole input image. A convolution kernel is the name given to each set of shared weights. Every series of convolution layers has a pooling layer after it to lessen computational complexity. The max pooling layer, known as the most common layer, minimizes the size of feature maps by choosing the highest possible feature response in nearby areas [16,17]. In this paper, we proposed a deep learning models approach that focuses on early detection and classifying each case accordingly through transfer learning (TL), AlexNet, ResNet-50, and GoogleNet (InceptionV3) by utilizing magnetic resonance images (MRI).

2. Related Work

There has been a substantial sum of work in Alzheimer's disease (AD) recently in early diagnosis, detection, and classifications, where most of the focus has been on techniques and approaches to achieve the goal of optimality and operationality in day-to-day clinics. Some techniques used different imaging formats, transfer learning with modified layers, added layers, and more data for training. These efforts have been very helpful in combating Alzheimer's disease, and in the age of artificial intelligence and transfer learning, recent and considerable related work has been analyzed and summarized in Table 1 below.

Table 1. Summary of all recent related work.

References	Computational Techniques	Study Objectives	Datasets	Results	Years
Brain MRI analysis for Alzheimer's disease diagnosis using an ensemble system of deep convolutional neural networks [18]	A deep convolutional neural network is proposed for early-stage Alzheimer's disease diagnosis using brain MRI data analysis, outperforming existing binary classification methods, and outperforming baselines in experiments.	The study offers a deep CNN capable of identifying and classifying Alzheimer's disease, demonstrating superiority and capability in performance on a small dataset, and efficiently approaching imbalanced data to train and learn.	Data obtained from Open Access Series of Imaging Studies OASIS.	The presented model achieves an accuracy rate of 93.18%, with precision of 94%, recall of 93%, and a f1-score of 92%.	2018
Transfer Learning With Intelligent Training Data Selection for Prediction of Alzheimer's Disease [16]	A transfer learning VGG, pre-processing the dataset includes images while applying image entropy to select the most relevant information.	Lowering the reliance on large data training while applying the layer-wise transfer learning to examine the training size impacts.	The dataset has been acquired by the benchmark dataset for deep learning based on Alzheimer's Disease Neuroimaging Initiative (ADNI).	Results technique has shown a 10–20 times smaller data size improvement in accuracy (4–7%) in classification problems involving AD vs. NC, AD vs. MCI, and MCI vs. NC.	2019
Neuroimaging and Machine Learning for Dementia Diagnosis: Recent Advancements and Future Prospects [19]	A comprehensive survey of automated diagnostic methods for dementia that utilizes medical image analysis through machine learning algorithms published in recent years.	To discuss the most recent neuroimaging procedures in the field of dementia diagnosis for clinical applications and Evaluating deep learning approaches in early-stage detection of dementia.	(ADNI), (OASIS), Australian Imaging, Biomarker and Lifestyle Flagship Study of Ageing (AIBL), and CAD Dementia, structural brain MRI scans.	Considering the current diagnostic approaches for AD using MRI scans, it is essential to work on diagnosing other types of dementia, such as FTD, VD, and PD. Deep learning techniques approaches outperform brain images obtained, rather than the conventional ML, in terms of accuracy and early diagnosis of dementia.	2019
Ensembles of Patch-Based Classifiers for Diagnosis of Alzheimer's Diseases [20]	Feature extractors and softmax cross-entropy (CNNs) classifier, while the addressed framework consists of three individual models for generating decisions.	Accuracy, overfitting issues, and proven brain landmarks for discernible AD diagnosis features on both the left and right hippocampus areas.	National Research Center for Dementia (GARD), Gwangju Alzheimer's and Related Dementia dataset	Achieving 90.05% accuracy compared to the other state-of-the-art models on the same dataset.	2019
A Data Augmentation-Based Framework to Handle Class Imbalance Problem for Alzheimer's Stage Detection [21]	TL using data augmentation for 3D Magnetic Resonance Imaging (MRI)	TL for multiclass AD with pre-trained AlexNet model. Two approaches for the brain and 3D brain MRI view while considering an extensive image augmentation to avoid overfitting issues.	From the publicly available dataset (OASIS).	The presented model's accuracy utilizing a 3D view of the brain MRI is 95.11%, whereas using a one-sided view is 98.41%.	2019

Table 1. *Cont.*

References	Computational Techniques	Study Objectives	Datasets	Results	Years
Optimized One vs One Approach in Multiclass Classification for Early Alzheimer's Disease and Mild Cognitive Impairment Diagnosis [22]	A pairwise *t*-test feature selection is employed to estimate selected features onto a Partial-Least-Squares multiclass subspace for one vs one output error correction.	To improve accuracy and reduce dependency on large data trained.	the data from the international challenge for automated prediction of MCI from MRI data to address the multiclass classification problem.	The proposed multiclass classification approach outperformed with 67% accuracy, illustrating the robustness towards small fluctuations.	2020
Spatial-Temporal Dependency Modeling and Network Hub Detection for Functional MRI Analysis via Convolutional-Recurrent Network [23]	An end-to-end deep learning Spatial-Temporal convolutional-recurrent neural Network (STNet) model	To predict Alzheimer's disease automatically considering the use of progression and network hub detection implying rs-fMRI time series.	The rs-fMRI time-series data collected from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database1 were studied in this paper.	Results from experiments conducted on 563 rs-fMRI images from the ADNI database show that the employed approach can both enhance classification performance when compared to cutting-edge techniques and offer new perspectives on the pathogenic cascade that underlies AD.	2020
Resting-State fMRI and Improved Deep Learning Algorithm for Earlier Detection of Alzheimer's Disease [24]	Using an Improved Deep Learning Algorithm (IDLA) which utilizes resting state fMRI along with important un-identifying information such as age and sex. It also utilizes autoencoder customization for the categorization of MCIs vs. NCs.	Detecting Early-stage Alzheimer's disease considers deep neural network data.	ADNI-2 fMRI data in the ADNI database	The methodology proposed increases diagnostic accuracy by approximately 25% compared with traditional approaches, which means combining the brain with improved deep learning is an excellent way to diagnose neurological disorders early.	2020
Diagnosing Alzheimer's Disease Based on Multiclass MRI Scans using Transfer Learning Techniques [25]	They used whole slide 2-dimension (2D) images to classify AD mild cognitive impairment and normal control subjects using state-of-the-art CNN base models. Also, they evaluated their effectiveness using an AD Neuroimaging Initiative dataset and demonstrated uniqueness using MR images.	Early Alzheimer's diagnosis and classification are crucial for preventing dementia progression in medical image analysis. Therefore, the primary objective was to use Deep learning techniques to detect early Alzheimer's disease.	The study uses the (ADNI) brain MR images.	Three models split data to 70:30 ration training and testing, respectively. The top result was shown by ResNet-101, with 98.37% accuracy and outstanding performance in multiclass classification, is the best out of the three.	2020

Table 1. *Cont.*

References	Computational Techniques	Study Objectives	Datasets	Results	Years
Deep Learning of Static and Dynamic Brain Functional Networks for Early MCI Detection [26]	CNN framework to simultaneously learn embedded features from BFNs for brain disease diagnosis.	To learn deeply embedded spatial patterns of the static and dynamic BFNs for eMCI diagnosis.	A rigorously collected, publicly accessible, multisite Alzheimer's Disease Neuroimaging Initiative 2 (ADNI2) dataset	Significant diagnostic performance improvement by almost 10%, including deep learning's efficiency in the preclinical diagnosis of Alzheimer's disease, according to the intricate and multidimensional voxel-wise spatiotemporal patterns of the brain's functional connectomics at rest.	2020
A 3D densely connected convolution neural network with connection-wise attention mechanism for Alzheimer's disease classification [27]	The paper introduces CAM-CNN, an enhanced densely connected network with a connection-wise attention mechanism From pre-processed images, it extracts multi-scale features and uses a connection-wise attention technique to integrate connections between layers. To distinguish AD, MCI converters, and non-converters, the approach was tested on 968 participants' baseline MRIs Using data from each 3D convolution layer.	The study proposes a deep learning method for efficient detection and prediction of Alzheimer's disease (AD) using a densely connected convolution neural network and connection-wise attention mechanism.	Collected from ADNI.	The proposed algorithm outperformed previous methods in distinguishing AD patients from healthy controls, with a 97.35% accuracy rate, MCI converters vs. Healthy subjects with 87.82%, MCI converters vs. non-converters with 78.79%.	2021
Deep learning-based pipelines for Alzheimer's disease diagnosis: A comparative study and a novel deep-ensemble method [17]	The study uses a deep learning approach to apply transfer learning techniques to CNN architectures pre-trained on Imagenet. The top three networks are AlexNet, Inception-ResNet-v2, ResNet-50, ResNet-101, and GoogLeNet. After fine-tuning, they are combined and classified using an ensemble bagged trees model.	This study presents an automated deep-ensemble approach for dementia-level classification from brain images, compares deep learning architectures, and evaluates robustness in detecting Alzheimer's disease and different dementia levels.	Data acquired from OASIS, KAGGLE, and ADNI.	The proposed strategy, tested on three MRI and one fMRI datasets, achieved an accuracy of 98.51% in binary classification (different levels of dementia recognition) and 98.67% in multiclass classification, surpassing cutting-edge methods.	2021

Table 1. *Cont.*

References	Computational Techniques	Study Objectives	Datasets	Results	Years
Brain Asymmetry Detection and Machine Learning Classification for Diagnosis of Early Dementia [28]	The study introduces a new method for early dementia diagnosis using an asymmetry segmentation algorithm, allowing visualization of differences between brain hemispheres, simplifying feature engineering, and offering an advantage over existing methods.	The proposed pipeline offers a cost-effective solution for classifying dementia and possibly other brain degenerative disorders influenced by changes in brain asymmetries.	Acquired from the ADNI database	The C-SVM and Q-SVM showed the best performance among SVM variants. The C-SVM accuracy of EMCI vs. NC, AD vs. NC, and AD vs. EMCI was 92.5%, 93.0%, 93.0%, and 85.0%, respectively. The Q-SVM accuracy of EMCI vs. NC, AD vs. NC, and AD vs. EMCI was 92.5% and 92.5%, sensitivity and specificity, respectively. The CNN's prediction results are comparable to those of other classifiers.	2021
Differentiating Dementia with Lewy Bodies and Alzheimer's Disease by Deep Learning to Structural MRI [29]	ResNet was implemented due to its unique characteristics in preserving features in 3D images while performing similarly to other Convolutional Neural Networks.	This study explores the potential of a deep learning technique to distinguish between Alzheimer's Disease (AD) and Dementia with Lewy Bodies (DLB) through structural MRI data, compared to traditional voxel-based morphometry (VBM).	208 participants, 101 DLB, 69 AD, and 38 controls, which it was obtained from Wellcome Department of Imaging Neuroscience, University College London, UK, www.fil.ion.	Conventional statistical analysis showed no significant atrophy, but the deep learning method accurately distinguished DLB from AD with 79.15% accuracy and the conventional method with 68.41%, confirming fine differences that conventional methods may underestimate.	2021
Comparison Of Machine Learning approaches for enhancing Alzheimer's disease classification [30]	The study developed three machine learning-based MRI data classifiers to predict Alzheimer's disease (AD) and infer brain regions. They were compared to each other, SVM, VGGNet, and ResNet, and a transfer learning strategy was applied to improve performance and efficiency.	This study compares three models, one SVM-based and two deep learning algorithms, 3D-VGGNet and 3D-ResNet, for predicting Alzheimer's Disease (AD) and identifying brain regions contributing to disease progression.	A total of 560 images were acquired from ADNI; T1-weighted MR.	The ResNet model outperformed the other two classifiers in detecting Alzheimer's disease (AD) in elderly control subjects with an accuracy of 90% for SVM, 95% for VGGNet, and 95% for ResNet.	2021

Table 1. *Cont.*

References	Computational Techniques	Study Objectives	Datasets	Results	Years
Analysis of Features of Alzheimer's Disease: Detection of Early Stage from Functional Brain Changes in Magnetic Resonance Images Using a Fine-tuned ResNet18 Network [31]	proposed fine-tuning model uses ResNet-18, consisting of 3 × 3 filters, 1 × 1 filter, and a fully connected layer; last layer softmax layer. The model adapts pre-trained parameters to the new dataset by unfreezing all layers.	The paper shows a deep learning-based method for predicting MCI, early MCI, late MCI, and AD using hippocampal fMRI data from the ADNI database for early diagnosis.	Data from The ADNI; fMRI dataset. A total of 138 subjects were used for evaluation.	The proposed model performed exceptionally compared to other models with classification accuracy of 99 99.99%, 99.95%, and 99.95% on EMCI vs. AD, LMCI vs. AD and MCI vs. EMCI classification scenarios, respectively.	2021
An Intelligent System for Early Recognition of Alzheimer's Disease Using Neuroimaging [32]	Testing the AD multiclass classification's performance with ResNet18 and DenseNet201.	The study explores the challenge of using randomized concatenated deep features from two pre-trained models that extract discriminative features from MRI images of brain functional networks.	The data was acquired from the ADNI. A total of 138 MRI scans, 25 AD, 25 CN, 25 SMC, 25 EMCI, 13 MCI and 25 LMCI scans.	The proposed model achieved 98.86% accuracy, 98.94% precision, and 98.89% recall in multiclass classification, demonstrating its potential for predicting neurodegenerative brain diseases like Alzheimer's disease.	2022

3. Materials and Methods

Firstly, the data were acquired from Kaggle, which consists of combined MRI images from multiple sources such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), IEEE, Data.gov, and Cordis EU [33]. The data consisted of a large number of images in various stages that were found to be helpful to this study for generating a robust and accurate system. The dataset was made of 6400 MRI images and consisted of four classes: moderate demented, mild demented, very mild demented, and non-demented. The moderate demented had 64 images, the mild demented class had 896 images, the very mild demented had 2240 images, and the non-demented had 3200 images, as shown in Table 2. All of these MRI images were later pre-processed accordingly for training [25].

Table 2. Alzheimer's dataset—imbalanced.

Label	Count
Moderate Demented	64
Mild Demented	896
Very Mild Demented	2240
Non-Demented	3200

Part of the image pre-processing was to ensure we had balanced data, that is, the same number of images per class, to ensure the accuracy of the results. The data augmentation technique is one of many to evade overfitting or underfitting. The minority and the majority classes are another system of representation to which class is referred to that has the lowest number of data and the highest number of data; the minority class here would be the moderate demented class with 64 images followed by mild demented with 896 images, and very mild demented with 2240 images, respectively. The majority class would be the non-demented with 3200 images. Image augmentation was implemented to resolve the data imbalance between classes where all classes, except the non-demented, were augmented to reach 3200 images per class, which resulted in an equilibrium between all classes. Part of the imagining pre-processing phase was performed using Python image augmentation [5,34]. Table 2 shows the images' quantity per class before applying data augmentation. The image augmentation process started with configuring Microsoft Visual Studio Code to Python and installing the Python Augmentor library, then importing the dataset into the program. Then, the image augmentation parameters were customized, as illustrated in Table 3.

Table 3. Image augmentation.

Images' Class	Pre Augmentation Quantity	Probability	Zoom Min Factor	Max Factor	Flip Top to Bottom	Sample	Post Augmentation Quantity
Mild Demented	896	0.3	0.8	1.5	0.4	2304	3200
Moderate Demented	64	0.3	0.8	1.5	0.4	3136	3200
Non-Demented	3200	0.3	0.8	1.5	0.4	None	3200
Very Mild Demented	2240	0.3	0.8	1.5	0.4	960	3200

After augmentation, all data, including non-demented, very mild demented, mild demented, and moderate demented, were 3200 images for each class. Training a deep learning model on an imbalanced dataset could potentially cause overfitting to the model, and to address this issue, this research balanced the dataset using an augmentation technique. Therefore, before applying the data augmentation technique, each class of the data had a significantly different number of images. On the other hand, Table 4 lists the number of images for each class after applying the data augmentation technique. Therefore, each class contains the exact number of images.

Table 4. Alzheimer's dataset—balanced.

Label	Count
Moderate Demented	3200
Mild Demented	3200
Very Mild Demented	3200
Non-Demented	3200

3.1. Transfer Learning

Transfer learning's foundation lies in the notion that knowledge that has already been learned may be applied effectively and efficiently to address new issues and challenges. Hence, transfer learning necessitates effective and reliable machine learning techniques that retain and recycle previously acquired knowledge [35]. Transfer learning is one of the very well-established methods in deep learning and is mostly used due to its high efficiency, where one would use a pre-existing trained network for their application. This method is vastly preferred due to its efficiency, and, in some cases, it yields the best results with proper fine-tuning. To employ transfer learning, there are two main ways to perform this: training the original network without any modifications or alterations to the layers and fine-tuning where adjustments would be applied to tailor-fit the chosen network for the job. Some examples of pre-existing transfer learning networks are ResNet-50, AlexNet, and VGG19 [36].

3.1.1. AlexNet

AlexNet has 25 layers and a depth of 8 and is considered among the most compact pre-trained networks for transfer learning. Convolution, normalizing, pooling, and a Rectified Linear Unit (ReLU) are fully linked layers in the order in which AlexNet's layers are arranged. AlexNet is a great example of a simple, small, and yet effective pre-existing network for its size [36,37].

3.1.2. ResNet-50

The residual network has multiple versions in which they are different mainly on how many layers each has, and ResNet-50 has 50 layers consisting of 1×1, 3×3, 7×7 convolution filters; 48 convolution, 1 average pool, and 1 MaxPooling layer. The Resnet-50 architecture propagates the added results of the convolution layer and input called residue. This lowers the overhead associated with the propagation of more characteristics. Thus, the over-fitting issue is diminished to enable quicker optimization of bigger networks [36,37].

3.1.3. GoogleNet (InceptionV3)

GoogleNet or VGG19 is another pre-trained network example that consists of 144 layers and works on input images of size $224 \times 244 \times 3$. The network depth layers are 22. The GoogleNet inception is created by combining the output of abundant simultaneous convolution layers with capricious filter sizes. As a result, the concatenated feature map comprises features from the same input attained using several filtering spaces. The auxiliary categorization output layers that result in a deeper network are another trait of GoogleNet [36,37].

3.1.4. SqueezeNet

SqueezeNet has 50 times less parameters in comparison with AlexNet and it was trained on over a million photos. The groundwork for this network is laid out as a fire model that comprises the squeeze layer and expand layer. Only 1×1 filters are used in the squeeze layer, which feeds into an expand layer that combines 1×1 and 3×3 convolution filters [37].

The diagram below in Figure 1 outlines the workflow of the system in detail, such as AlexNet, ResNet-50, and GoogleNet, since they were the main focus of the implantation.

Once the dataset has been balanced and augmented, using Python, the remaining process would be carried out in MATLAB.

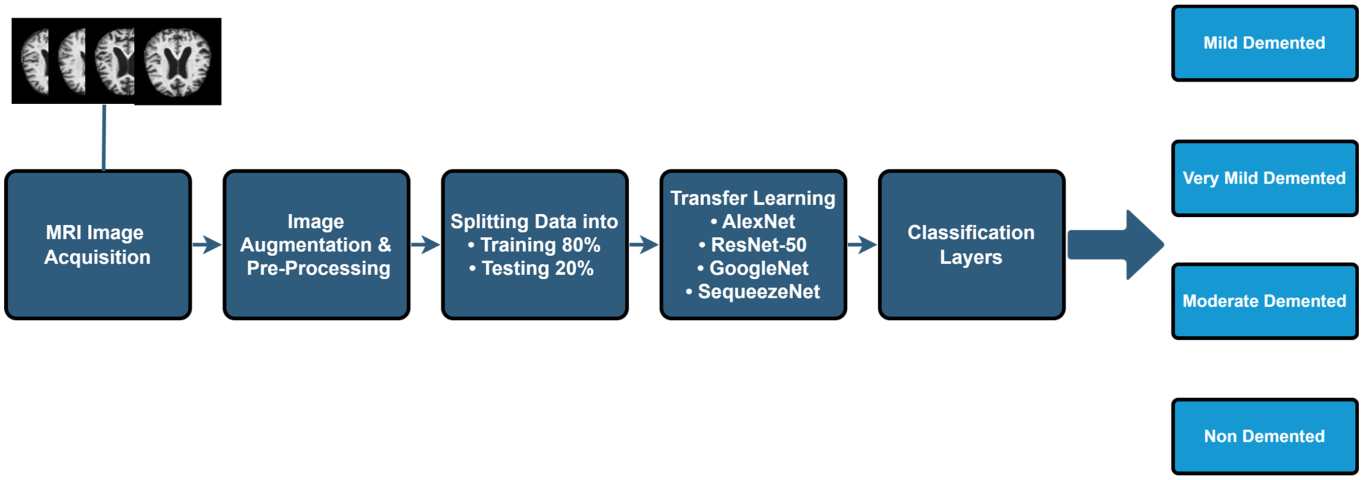

Figure 1. Detailed workflow for the proposed model.

After the first phase of image pre-processing was completed, the dataset was called Matlab, where it was stored and organized according to its labels. Then, the data were split randomly into a training set and a testing set, 80% training and 20% testing, for each category. The pre-processing continues to resize all images according to each pre-trained network input layer's specification, such as GoogleNet 224 $\times$ 224, and converting from grayscale to RGB, which concluded the pre-processing phase, thus deeming them ready to be injected into the pre-trained network after each pre-trained network has been fine-tuned.

4. Results

This section illustrates the experiment setup, result, and evaluation of this research. Pre-trained neural network classifiers, which are AlexNet, ResNet-50, and GoogleNet (InceptionV3), were employed. Each transfer learning model was trained to classify images into four categories: Mild Demented, Moderate Demented, Non-Demented, and Very Mild Demented. Each dataset class contains 3200 images; thus, the total images are 12,800.

Each pre-trained neural network classifier is evaluated using two types of evaluations: (1) k-Fold Cross-Validation and (2) Partitioning the Dataset into Training and Test Sets.

4.1. k-Fold Cross-Validation

K-fold cross-validation is a method used for evaluating the performance of machine learning and deep learning models. Specifically, we employed 10-fold cross-validation, in which each dataset is divided into 10 sets; 9 sets are applied for training, and the remaining set is used for testing. The process of training and testing is repeated k times, with k being 10 in our case [38]. We utilized a dataset of 12,800 images, employing the 10-fold cross-validation method for both training and testing purposes [38].

Tables 5–8 display the overall confusion matrix and the average accuracy of the 10-fold cross-validation. Table 5 presents the performance of the AlexNet model based on 10-fold cross-validation. The diagonal values represent the accuracy of correct predictions produced by the AlexNet model for each class of Alzheimer's disease. For example, the class Mild Demented is correctly predicted with 98.66% accuracy. Additionally, Moderate Demented is correctly predicted at 100.00%. Non-Demented and Very Mild Demented are correctly predicted with accuracies of 98.91% and 94.66%, respectively. The average accuracy is 91.63%. The same role is used for Tables 6–8 but for different pre-trained models. It is clear that the performance of the AlexNet model exceeded the other models.

Table 5. AlexNet 10-fold cross-validation.

	AlexNet Overall Confusion Matrix				**Average Accuracy**
Mild Demented	**98.66%**	0.34%	0.03%	0.97%	
Moderate Demented	0.00%	**100.00%**	0.00%	0.00%	
Non-Demented	0.03%	0.03%	**98.91%**	1.03%	98.05%
Very Mild Demented	4.13%	0.25%	0.97%	**94.66%**	
	Mild Demented	Moderate Demented	Non-Demented	Very Mild Demented	

Table 6. InceptionV3 10-fold cross-validation.

	InceptionV3 Overall Confusion Matrix				**Average Accuracy**
Mild Demented	**98.59%**	0.06%	0.09%	1.25%	
Moderate Demented	0.06%	**99.94%**	0.00%	0.00%	
Non-Demented	0.28%	0.00%	**98.44%**	1.28%	97.80%
Very Mild Demented	4.25%	0.06%	1.47%	**94.22%**	
	Mild Demented	Moderate Demented	Non-Demented	Very Mild Demented	

Table 7. ResNet-50 10-fold cross-validation.

	ResNet-50 Overall Confusion Matrix				**Average Accuracy**
Mild Demented	**92.88%**	1.03%	0.63%	5.47%	
Moderate Demented	2.97%	**95.19%**	0.00%	1.84%	
Non-Demented	2.44%	0.47%	**93.16%**	3.94%	91.11%
Very Mild Demented	11.63%	1.25%	3.91%	**83.22%**	
	Mild Demented	Moderate Demented	Non-Demented	Very Mild Demented	

4.2. Partitioning the Dataset into Training and Test Sets

The dataset was split into 80:20 portions, so 80% of the images were used for training, and 20% were used for testing. For the training parameter, the initial learning rate is set to 0.0010, and the maximum number of epochs is set to 50. As for optimization measures, a stochastic gradient descent with momentum (SGDM) was applied. The experiment was performed on a machine with the following hardware: an Intel® Core™ i-7 processor and an NVIDIA GeForce RTX 2070 GPU. We utilized MATLAB R2023a.

Table 8. SeqeezNet10-fold cross-validation.

	ResNet-50 Overall Confusion Matrix				Average Accuracy
Mild Demented	**83.94%**	0.53%	2.19%	13.34%	
Moderate Demented	0.66%	**98.91%**	0.03%	0.41%	
Non-Demented	1.28%	0.00%	**88.13%**	10.59%	86.37%
Very Mild Demented	9.69%	0.22%	15.56%	**74.53%**	
	Mild Demented	Moderate Demented	Non-Demented	Very Mild Demented	

The classification accuracy, precision, recall, and F1 score were calculated to test and evaluate the experiment conducted in this study. The classification accuracy is shown in Equation (1). TP, TN, FP, and FN refer to true positive, true negative, false positive, and false negative, respectively. Precision is computed using Equation (2), recall using Equation (3), and F1-score using Equation (4) [39].

$$\text{Accuarcy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}} \tag{1}$$

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}} \tag{2}$$

$$\text{Recall} = \frac{\text{TP}}{\text{TP} + \text{FN}} \tag{3}$$

$$\text{F1} - \text{Score} = 2 * \frac{\text{Precision} \times \text{Recall}}{(\text{Precision} + \text{Recall})} \tag{4}$$

Table 9 illustrates the evaluation of this research work, which includes four different pre-trained neural networks. Each pre-network is responsible for performing multi-classification for Alzheimer's MRI Scans. According to Table 5, AlexNet is superior to other pre-trained networks. It is significant to mention that GoogLeNet (Inception V3) and ResNet-50 performed comparable performances with similar margins of accuracy (between 92% and 94.776%). SeqeezNet shows the lowest performance compared to other pre-trained neural networks.

Table 9. Transfer learning evaluation.

Model	Accuracy	Precision	Recall	F1-Score
AlexNet	96.616%	96.621%	96.619%	96.620%
GoogleNet (InceptionV3)	94.776%	94.784%	94.775%	94.779%
ResNet-50	94.363%	94.341%	94.363%	94.352%
SeqeezNet	91.602%	92.207%	91.601%	91.904%

5. Conclusions

In this paper, we performed Alzheimer's disease detection and classification into four classes using transfer learning (pre-trained networks) through AlexNet, ReNet-50, and GoogleNet (InceptionV3). The concept of using transfer learning in deep learning abolishes challenges faced with training networks with a small set of data. The previously mentioned models used 12,800 images for training and testing. These pre-trained networks' architectures were altered to fit the attained MRI images, 12,800 images, and classified into four categories: non-demented, mild demented, moderate demented, and very mild demented. The data were acquired from Kaggle and collected from different sources such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), IEEE, Data.gov, and Cordis EU. The performance of each model was evaluated with multi-classifications in mind. The performance of AlexNet was superior to all other pre-trained networks covered in this study, while it is worth mentioning that GoogleNet (InceptionV3) performed very closely to ResNet-50 with similar margins of accuracy (between 92% and 94.776%). In conclusion, while designated deep learning models for medical imaging detection could potentially yield different results, transfer learning promotes very promising results when dealing with limited data. One of the limitations that is worth mentioning is the limited dataset available as compared to other fields where deep learning is used. As for future direction, it is worth looking into Generative Adversarial Networks (GANs) and/or Self-Organizing Maps (SOMs) with or without CNN or the current model to be combined with another state-of-the-art model for a rigid system. Our study demonstrates the value of deep learning, particularly transfer learning, as a tool for medical advancement in AD detection from MRI imaging. Although such systems are not ready for practical use without medical personal supervision, it is not farfetched as these promising results could serve as an aid tool for medical professionals.

Author Contributions: Conceptualization, S.A., M.A.Z. and S.G.; methodology, S.A., M.A.Z. and A.A.; software, S.A., A.A.A. and A.A.; validation, S.A., M.A.Z., S.G., A.A. and A.A.A.; formal analysis, S.A., A.A. and M.A.Z.; investigation, S.A., A.A., S.G. and M.A.Z.; resources, S.A. and A.A.A.; writing—original draft preparation, S.A.; writing—review and editing, S.A., M.A.Z. and A.A.; visualization, S.A. and A.A.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Data are publicly available, as referenced in [33].

Conflicts of Interest: The authors declare no conflict of interest.

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