

Automatic Detection of Alzheimer's Disease with Transfer Learning and Image Processing Techniques

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by

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I, **Atlay Yeşilada**, declare that this thesis titled **Automatic Detection of Alzheimer's Disease with Transfer Learning and Image Processing Techniques** and the work presented in it are my own. I confirm that:

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- Where I have consulted the published work of others, this is always clearly attributed.
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Automatic Detection of Alzheimer's Disease with Transfer Learning and Image Processing Techniques

Abstract

Alzheimer's disease continues to be a serious public health issue. Alzheimer's disease affects generally old people, and it is a neurological disorder. The most significant sign of Alzheimer's disease is memory loss, which becomes worse over time. Therefore, early identification of Alzheimer's illness can aid in diseased getting the proper care. One of the aims of this thesis is to automate the early detection of Alzheimer's disease and create a self-improving system by utilising previous experiences each time it is detected automatically. In this way, the bad effects of the disease due to the late diagnosis can be protected at an early stage. Thanks to artificial intelligence and image processing algorithms, successful results can be achieved with brain MRI data used by transfer learning and deep learning models. In this thesis, a deep learning method with transfer learning based on brain MRI images for the detection of Alzheimer's disease has been proposed. In the experimental work, different convolutional neural network architectures and transfer learning techniques have been examined. The results show that the detection of Alzheimer's disease can be detected with remarkable accuracy with the transfer learning and data augmentation techniques.

Keywords: Alzheimer's Disease, Brain MRI, Deep Learning, Transfer Learning, Convolutional Neural Networks, InceptionV3

Transfer Öğrenme ve Görüntü İşleme Teknikleri ile Alzheimer Hastalığının Otomatik Tespiti

ÖZ

Alzheimer hastalığı günümüzde hala önemli bir sağlık problemi olmayı sürdürmektedir. Alzheimer hastalığı genellikle yaşlıları etkilemektedir ve nörolojik bir hastalıktır. Hastalığın en belirgin belirtisi ise zamanla kötüleşen hafıza kaybıdır. Bu nedenle Alzheimer hastalığının erken teşhisi, hastaların uygun ve doğru tedaviyi almasına yardımcı olmaktadır. Bu tezin amaçlarından biri, Alzheimer hastalığının erken teşhisini otomatik bir hale getirmek ve otomatik tespit yapılırken her defasında önceki deneyimlerden yararlanılarak kendini geliştiren bir sistem yaratabilmektir. Bu sayede, geç yapılan bir teşhiste karşılaşılabilecek kötü etkilerden hasta erken dönemde korunabilmektedir. Yapay zeka ve görüntü işleme algoritmaları sayesinde, transfer öğrenme teknikleri ile derin öğrenme modellerinin kullandığı beyin MRI verileri ile başarılı sonuçlar alınabilmektedir. Bu tezde, Alzheimer hastalığının otomatik olarak tespiti için beyin MRI görüntülerine dayalı transfer öğrenme ile derin öğrenme yöntemi önerilmektedir. Deneysel çalışma bölümünde, farklı evrimsel sinir ağı mimarileri ve transfer öğrenme yöntemleri incelenmektedir. Elde edilen sonuçlar, Alzheimer hastalığının transfer öğrenme ve veri artırımı yöntemleri ile dikkate değer bir doğrulukla otomatik olarak tespit edilebileceğini göstermektedir.

Anahtar Kelimeler: Alzheimer Hastalığı, Beyin MRI, Derin Öğrenme, Transfer Öğrenme, Evrimsel Sinir Ağları, InceptionV3

I would like to dedicate my thesis to my late grandmother, who once struggled with Alzheimer's disease and did a lot of work on me.

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List of Abbreviations

AD	Alzheimer's Disease
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
DTI	Diffusion Tensor Image
VOI	Volume of Interest
AI	Artificial Intelligence
CNN	Convolutional Neural Network
GCNN	Graph Convolutional Neural Network
DNN	Deep Neural Networks
ROC	Receiver Operator Characteristic
AUC	Area Under the ROC Curve
ReLU	The Rectified Linear Unit

Chapter 1

Introduction

Alzheimer's disease (AD) is a worldwide neurodegenerative illness that occurs in the human brain and significantly affects the patient's quality of life [1]. According to reports, one in every 85 people will be affected by the disease by the year 2050, and the number of patients affected globally is predicted to double in that time [2]. Each year, there are 7.7 million new dementia cases reported worldwide [3]. One of the most well-known sufferers of dementia among the elderly is Alzheimer's disease. The following are some of the key signs of this dementia: difficulty in communicating, memory issues, and different disabilities that make the patient's everyday life exceedingly challenging [4]. Besides that, Alzheimer's sufferers are troubled by lack of comprehension, difficulty in learning new situations, speech and language challenges, poor motivation, and other complications [5]. Early and accurate diagnosing of Alzheimer's disease can greatly benefit its treatment. Alzheimer's disease is typically diagnosed in clinics after a clinical evaluation and the completion of a questionnaire by patients and their loved ones. Due to the lack of knowledge regarding disease-related brain regions and known symptoms such as brain shrinkage, it is a challenging undertaking [6]. For several types of brain scans, including magnetic resonance imaging (MRI), well-known machine learning classification techniques have been used. Due to the complexity of medical imaging, this topic is still challenging. With the aid of ongoing and upcoming research in this area, we can better understand the course of the disease and create new treatments. Deep learning, a subclass of machine learning and deep learning, has been used for intelligent systems in many fields, particularly in the processing of medical pictures, and it can handle difficult decision-making tasks. For the diagnosis of illnesses and the segmentation of organs, convolutional neural networks have demonstrated promising results [7]. CNNs

combine the three key phases of a classification job, namely feature extraction, feature selection, and classification, in contrast to conventional machine learning approaches. In automated medical image analysis, convolutional neural networks have achieved major advancements. Transfer learning is among the most important techniques for training deeper networks without overfitting when the amount of data is smaller [8]. A pre-trained network is the foundation of transfer learning. The transfer learning strategy can take advantage of the generic feature mappings and concentrate on learning the problem-specific ones for the problem of interest rather than training a specialized CNN from beginning. Transfer learning reduces training time and requires small data. Additionally, since the model has already been trained, good results can be obtained with small training data.

In this thesis, we developed a deep learning method that automatically detects Alzheimer's disease by making tunings over a pre-trained model using the transfer learning method and applying data augmentation. In the thesis, different data augmentation techniques such as rotation, flip, translation, shearing, scaling, and cropping are mentioned. We employed pre-trained networks that use different architectures such as InceptionV3, ResNet50V2, and Xception. We calculated and compared the AUC values of all these base models over their performances. An experimental work demonstrated that, as a base model, InceptionV3 can be used for the automatic detection of Alzheimer's disease and can be operated by the transfer learning method.

The rest of this work is organized in the following manner. The literature work chapter reviews the existing methods and research in the literature related to Alzheimer's illness detection and classification. In the next section, an overview of the entire methodology of this thesis such as the used dataset and how it was obtained, deep learning, and transfer learning techniques and how they were used were explained. Implementation details, results, and evaluation are discussed in the next section. Conclusions and final thoughts are mentioned in the last part of our thesis.

Chapter 2

Literature Review

In this chapter, a review of the literature on prior research and studies has been made on Alzheimer's disease.

In recent years, many different methods have been proposed for disease prediction in medical fields. Recent developments in the field of computer vision have focused on establishing models for the identification and categorization of Alzheimer's disease as well as extracting usable characteristics using a machine learning approach. Since the 1980s, brain imaging tools such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Diffusion Tensor Image (DTI) have been used for the diagnosis and classification of Alzheimer's disease [9].

For the segmentation of the gray matter, Nair and Mohan employed the Gaussian Mixing Model [10]. Both the conventional classification problem and the difficulty of calculating the density are addressed by this paradigm. Then, features were retrieved using the Partial Least Squares approach, and the Support Vector Machine technique was employed for classification. In addition to these studies, a classification method built on level-set segmentation is presented [11]. It begins by determining which of the four learning examples is closest to the new input using four distances in this investigation. A different approach has also been suggested, and Mufidah et al. used 3D masking to isolate the Volume of Interest (VOI) region using voxel-based morphometry for feature extraction [12]. Besides, the segmentation of images was used based on voxel morphometry to collect the 3 brain tissues (the white matter, the gray matter, and cerebrospinal fluid) in [13]. Different methods used deep learning architecture especially CNN to detect and classify Alzheimer's disease. A graph convolutional neural network (GCNN) classifier was employed by Song et al. [14].

This network's eleven layers (nine convolutional layers and two fully connected layers) enable the division of Alzheimer's disease patients into four classes.

The work that used a 2D CNN with one convolutional layer, a max-pooling layer, and ultimately a neural network with a single hidden layer for classification is one of the earliest investigations of a transfer learning strategy for Alzheimer's disease diagnosis utilizing deep learning [15]. This study showed that the auto-classification encoder's performance in the subsequent layers can be improved by using real-world photos to train it. Later on, a different transfer learning technique was also put out, wherein three 2D CNNs with two convolutional layers were trained using only three slices from the middle of the MRI images of the hippocampal region [16]. The impact of transfer learning when used for medical image classification was demonstrated in one of the subsequent studies [17]. According to a study on several modalities, the results of the fine-tuning processes performed are superior. In addition, a transfer learning technique that uses ultrasound scans to locate plans and can transfer information on fewer layers is proposed [18].

By utilizing the ADNI dataset, they proposed a transfer learning approach for the binary class Alzheimer's disease prediction. For Alzheimer's disease, they achieved 99.4% accuracy [19]. A transfer learning strategy was put forth by Maqsood et al. for the multi-class classification of Alzheimer's disease using pre-trained AlexNet. With regard to their findings on unsegmented images, they achieved 92.85% accuracy [20]. They demonstrated the effectiveness of using pre-trained models as the foundation for other networks. They didn't train the network from scratch; instead, they used GoogleNet and Inception-ResNet. These networks are trained on non-medical datasets, but the final layers are refined using samples from the relevant problem [21]. The ImageNet was used as the source domain in another piece of work. With the exception of the final fully connected layers, all the layers were initialized with the pre-trained model. The methodology used produced an overall Alzheimer's disease accuracy of 83.5% [22].

According to the literature, there are many methods for categorizing Alzheimer's disease. However, there are some restrictions, such as not addressing the class imbalance issue in multi-class Alzheimer's disease classification, which must be taken into account for Alzheimer's disease classification to be effective. Insufficient data

samples are another major obstacle for researchers to overcome in order to produce the best results. We put forth a framework based on transfer learning with data augmentation to overcome these specific limitations and produce accurate results for multi-class Alzheimer's disease classification. According to literature reviews, transfer learning models can reach an accuracy equal to or greater than that of a 3D-CNN model trained from the beginning which means scratch. As in related previous studies, instead of creating something new from scratch, high accuracy values can be obtained and studies can become more efficient by transferring similar features with transfer learning, much easier.

In recent years, as shown in Figure 2.1, interest in how artificial intelligence may be applied to medical imaging has increased exponentially. This interest is reflected in the rapid rise in publications in artificial intelligence from 200 peer-reviewed publications in 2010 to about 1000 in 2019 [23].

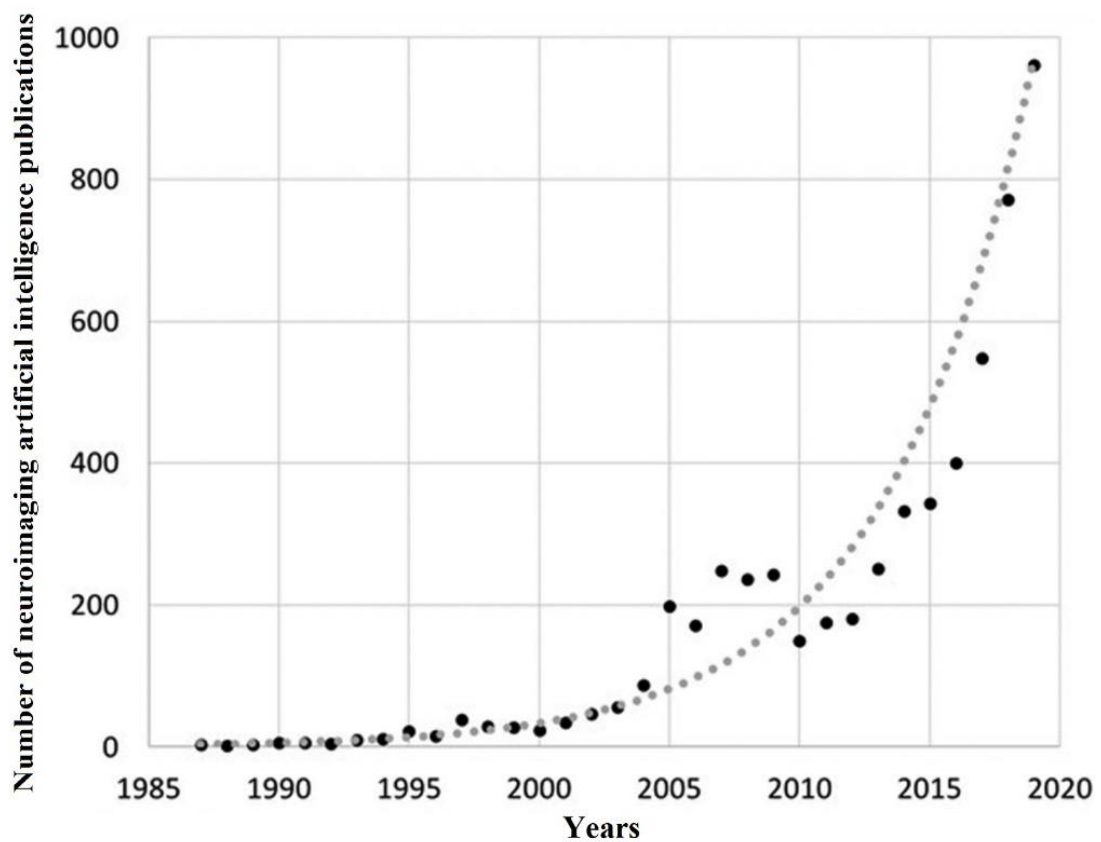


Figure 2.1: The number of neuroimaging artificial intelligence publications [23]

Chapter 3

Methodology

3.1 Image Classification

Image classification is a worldwide hot topic that is used to assign a label or class to an entire image [24]. The classification system's primary goal is to map input images into output classes for improved representation of image data [25]. Image classification technology, in particular, has provided valuable support for the diagnosis of numerous diseases, from preliminary theoretical study to clinical diagnosis [26]. This thesis focuses on image classification using deep neural networks (DNNs), also referred to as deep learning, the TensorFlow framework and transfer learning methods. With the growth of data in various industries, including e-commerce, automotive, healthcare, and gaming, image classification has recently gained popularity among technology developers [27].

Deep neural networks (DNNs) are also used in the framework for image classification, an example of which is shown in Figure 3.1. This process has four phases. Deep neural networks (DNNs) are then used to continue the process of gathering some of the input images, and finally, all of the input images are categorized into their respective groups [27].



Figure 3.1: The block diagram of image classification [27]

The image classification flowchart that will be used with TensorFlow is shown in Figure 3.2. The flowchart demonstrates how the systems will begin by gathering images. Deep neural networks (DNNs) are then used to train the model after that. Once the output is assigned to the appropriate image type, the process is complete. Inserting sets of images as input for this research is where the flowchart begins [27].

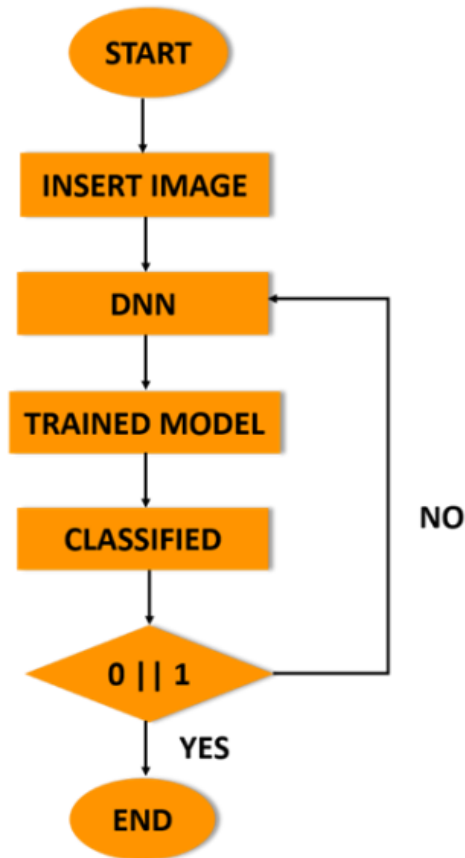


Figure 3.2: The flowchart of image classification system [27]

3.2 Deep Learning

Deep learning is an interdisciplinary field of work developed on designing systems that require data, algorithms, and hardware knowledge, aiming to solve complex problems that humans can solve. Although there are different deep learning models used today, they vary according to the field of study and data. Convolutional neural networks are used for image data. Deep learning has approached the human level in image classification, voice recognition, and the ability to answer questions.

The deep learning computing paradigm has recently been acknowledged as the industry standard by the machine learning group. It has also steadily gained popularity as the most widely used computational approach in the field of machine learning, producing outstanding results on a variety of difficult cognitive tasks that are on par with or even superior to human performance. Deep learning has the advantage of allowing for the learning of enormous amounts of data. Recent years have seen a rapid

expansion of the deep learning field, which has successfully been used for a variety of conventional applications. In many fields, including cybersecurity, natural language processing, bioinformatics, robotics and control, and the processing of medical information, deep learning has outperformed well-known machine learning techniques [28]. Deep learning uses a lot of data to map the input to specific labels rather than any rules created by humans in order to function. Multiple layers of artificial neural networks are used in the design of deep learning, and each layer offers a unique interpretation of the data fed to it [29].

Figure 3.3 depicts a subset of machine learning called deep learning that takes its cues from how the human brain processes information [28].

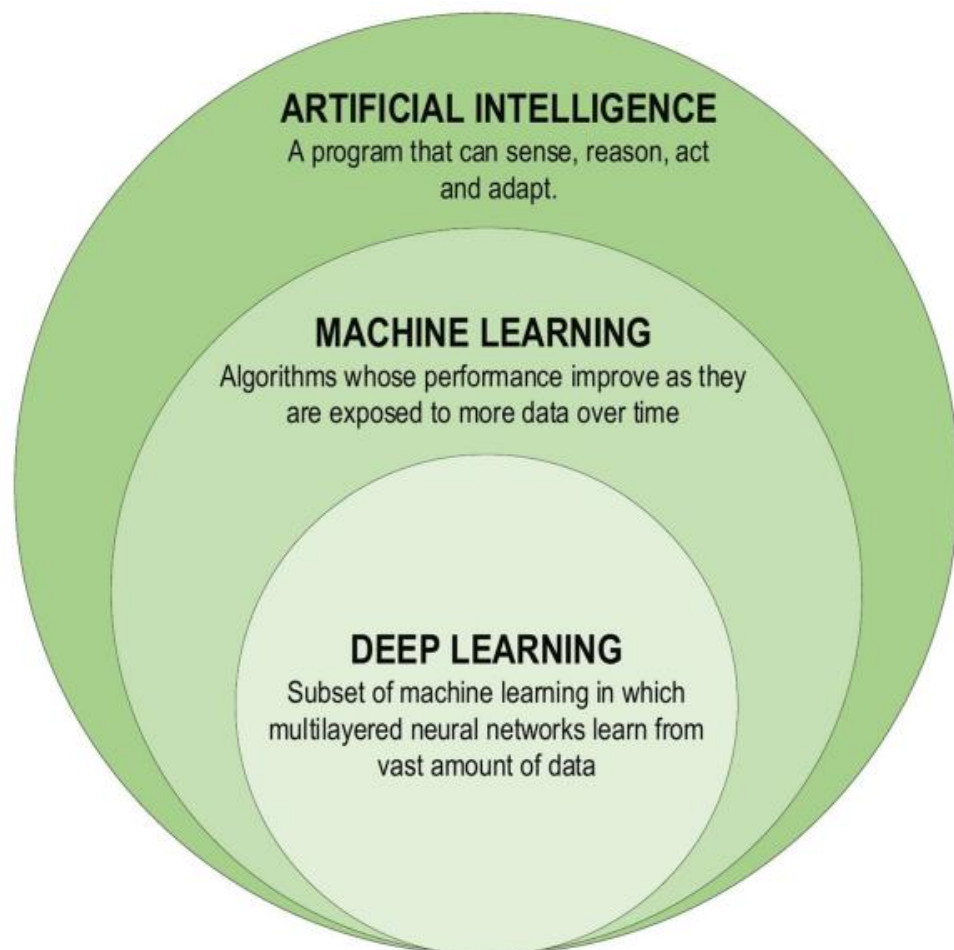


Figure 3.3: Relations among AI subclasses [28]

3.2.1 Convolutional Neural Network (CNN)

In order to process data with a grid pattern, such as images, convolutional neural network is a type of deep learning model. Convolutional neural network (CNN) was created with the animal visual cortex in mind and is intended to learn the spatial hierarchies of features automatically and adaptively, from low-level to high-level patterns [30]. Convolutional neural network (CNN) is used by deep learning in many fields, including the processing of medical images. In order to perform ROI detection and early diagnosis, these models are frequently used to classify images, signs, and medical records [31].

Convolution, pooling, and fully connected layers are the three types of layers that make up typical convolutional neural networks. Convolution and pooling layers, the first two, extract features, while a fully connected layer, the third, maps the extracted features into the final output, such as classification [32]. The convolutional layer is the first layer in deep learning models. With the filter size that was specified, the convolution layer wraps around the image and passes the result to the following layer. Deep feature maps produced by convolutional layers summarize the most significant deep features in an input. Each convolutional layer completes a particular function. As an example, the first layer focuses on displaying the edges, while the second layer displays the geometrical complexity of an image. The subsequent layer is then concerned with displaying shapes, colors, and so on. The three most crucial hyperparameters that influence a convolutional layer's performance are filter size, zero paddings, and stride. The Rectified Linear Unit (ReLU) layer follows the convolutional layer and passes positive data while blocking negative data and converting it to zero. The Rectified Linear Unit is a non-linear activation function used in deep neural networks or multi-layer neural networks. The main advantage of the ReLU function, which is often used in CNN, is that it does not activate all neurons at the same time. So if a neuron produces a negative value, it means that it will not be activated. Following the convolutional layer, pooling layers are used in deep learning techniques. Millions of parameters are produced by the convolutional layer. As a result, deep feature maps' dimensions are reduced by the pooling layer. Due to this, there are fewer parameters, which in turn reduces the computational complexity. The max and average pooling layers are the two types of pooling layers. The maximum

element of the max pooling layer chooses the deep feature map that is specified by the filter's filter. The max pooling layer produces a low-dimensional feature map that contains the most components from the previous feature map. The average pooling layer averages the feature map elements that the filter specifies. The average pooling layer produces a low-dimensional feature map that averages the earlier feature map elements. The fully connected layer feeds the neural networks forward as each layer connects to the one before it. The feature map is sent from the pooling or convolutional layer to the network's bottom layer. The feature maps are then flattened by putting them all on a single vector. Following that, these data are fed to the fully connected layer. The softmax activation function, which is the network's final layer, produces neurons according to the number of classes entered after receiving feature maps from fully connected layers [31]. Convolutional neural networks architecture can be observed in the Figure 3.4 below.

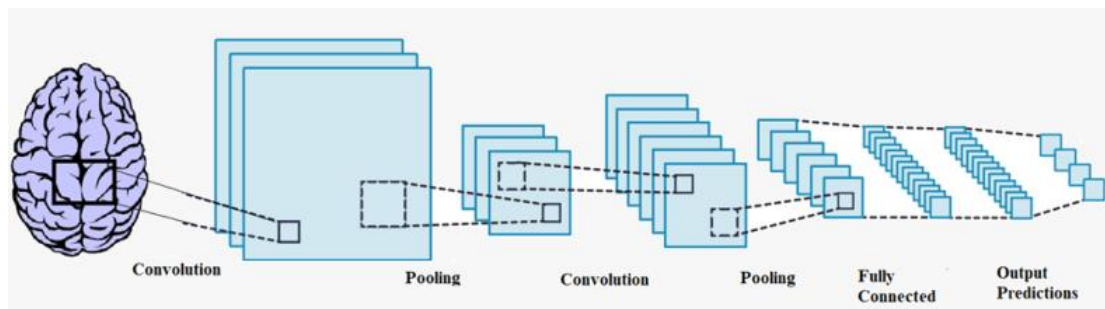


Figure 3.4: Convolutional neural network structure [33]

Convolutional neural network is a multilayered network structure that was developed using the multilayer perceptron, which is the standard neural network architecture. It is designed for object detection and it finds its use in image classification, segmentation, pattern recognition, etc. Due to its autonomous style of operation, convolutional neural network has become a crucial tool for machine vision and artificial intelligence.

Over the past ten years, convolutional neural networks have produced ground-breaking results in a range of pattern recognition-related fields, including voice and image

processing. The reduction in the number of parameters in artificial neural networks is the main advantage of convolutional neural networks. The only thing that matters is finding them, regardless of where they are in the provided images. Another important feature of convolutional neural networks is their ability to acquire abstract features as input propagates to deeper layers. For instance, in the first layer of image classification, the edge might be found, followed by the second layer's simpler shapes, and finally the third layer's higher-level features, like faces [34].

3.3 Data Augmentation

Data augmentation is a method that supports deep neural networks to develop their generalization capabilities while also indirectly regularizing networks [35]. It is crucial to getting results, particularly in medical studies where there is a shortage of data and getting new samples is expensive and time-consuming [36]. The geometric qualities of images are preserved by current data reproduction techniques. However, these processes have an impact on the values of image pixel densities. In medical data analysis, it is desired to produce the appearance of obtaining data with different gradients or saturations from various devices using pixel-level data duplication. For this, random or zero-mean Gaussian noise is added to the images to change the pixel intensities. By shifting or scaling the brightness of the image and applying gamma correction, sharpening, and blurring, it is possible to replicate medical images [37]. Because there wasn't enough data during the training phase, overfitting will develop if the data augmentation technique is not applied, which will result in subpar diagnostic outcomes. Furthermore, failing to apply this method when dealing with an unbalanced data set results in a poor level of diagnostic precision in general [31]. As shown in Figure 3.5, rotation, flip, transformation, shearing, scaling, noising and adjusting brightness processes are showed.

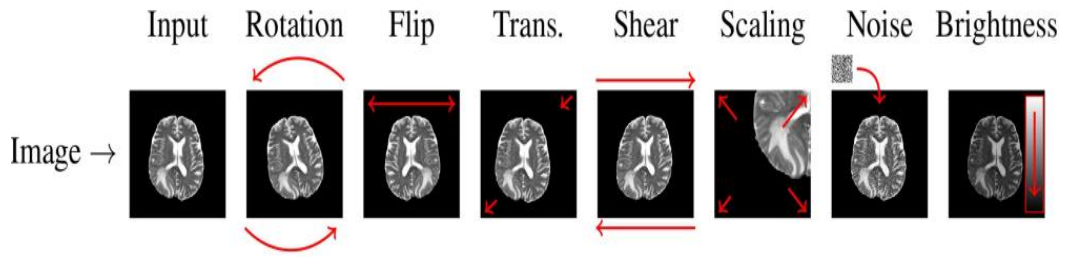


Figure 3.5: Brain-tumor data augmentation [35]

3.3.1 Rotation and Flip

A mirror reflection of the original image is produced by random flipping along one or more chosen axes. The horizontal axis of natural images can typically be flipped, but the vertical axis cannot always be done so because the up and down parts of an image are not always interchangeable. The left hemisphere and the right hemisphere are switched when the body is rotated along the horizontal axis. This can make a variety of deep classifiers position-invariant with respect to their location within the brain, which would otherwise be challenging for training sets that are not representative, especially those that benefit from the contextual tumor information. The same can be said for rotating an image by an angle around the central pixel. After this operation, the original image size is appropriately interpolated to fit [38].

3.3.2 Translation

The translation operation shifts the entire image by a certain number of pixels in the desired direction after padding has been appropriately applied. It allows the network to avoid becoming focused on features that are only present in those regions, rather than forcing the model to learn features that are exclusive to those spatial regions. Due to the fact that the MRI scans of different patients that are available in training sets are frequently not co-registered, an image can be translated by a specific number of pixels along a selected axis or axes to produce usable and viable images. The inherent spatial invariance of convolutions and pooling operations is utilized by convolutional neural networks [39].

3.3.3 Shearing

Every point in an image is moved in a specific direction by the shear transformation. Because we frequently want to preserve original shape characteristics, even though this operation can deform shapes, it is rarely used to enhance medical image data [40].

3.3.4 Scaling and Cropping

By including scaled versions of the original images in the training set, the deep network can learn beneficial deep features independent of the original scale. Because brain MRIs come in different sizes, scaling can add useful augmented images to a training set. Scaling and cropping are frequently used in conjunction to maintain the original image dimensions because different deep architectures demand constant-sized images. These examples of augmented brains could show traits at different scales. Furthermore, cropping can limit the field of view to only the most important portions of the image [41].

3.4 Transfer Learning

One of the most well-known machine learning techniques for image categorization and detection is transfer learning. It enables the application of previously learned expertise from a highly accurate architecture to new issues [37]. Instead of rebuilding the models from scratch, transfer learning could use the model and the learned information to identify the images in the dataset containing brain MRI data. In our thesis, we use the InceptionV3 structure of the convolutional neural network as a base model in our research. CNN is typically not optimized, despite the fact that training a CNN from scratch has been done in many experiments. In general, starting from scratch requires a lot of computing power, and there aren't always enough samples [42].

Deep convolutional neural network models must be trained on very large data sets, which can take days or even weeks. Reusing model weights from pre-trained models created for popular test computer vision datasets is one way to enhance this stage. The top-scoring models may be downloaded and used immediately or incorporated into a new model for our own image processing tasks. Transfer learning is a method that

occasionally applies a model that has been trained on one task to another. A neural network model is first trained on a task that is similar to another one in a process known as transfer learning. The trained model is then applied to one or more layers of other models. Transfer learning has the benefit of shortening a convolution neural network model's training time and may help avoid overfitting [43]. The Figure 3.6 below shows the learning stage of the transfer learning operation.

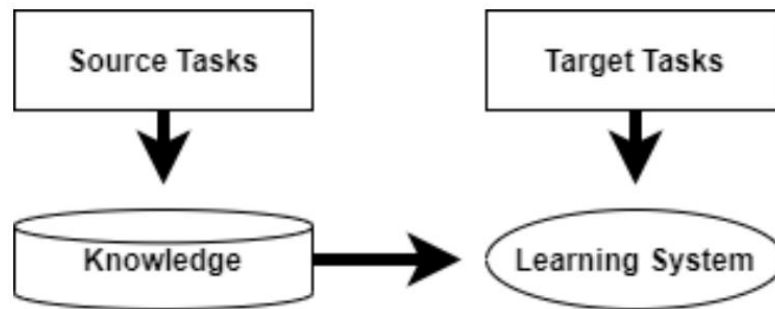


Figure 3.6: Learning phase of transfer learning [43]

In other learning methods, you must create a model from scratch. Transfer learning provides better starting points and some degree of task completion without even training. Transfer learning provides a higher learning rate during training because the problem has already received training for a similar task. Transfer learning enables a machine learning model to converge at a higher performance level, producing output that is more accurate thanks to a better starting point and faster learning rate. Because it uses a pre-trained model, the learning can achieve the desired performance quicker than traditional learning methods. Transfer learning might not outperform more traditional learning models, though. It is not possible to assess the effect of transfer learning until the target model is created.

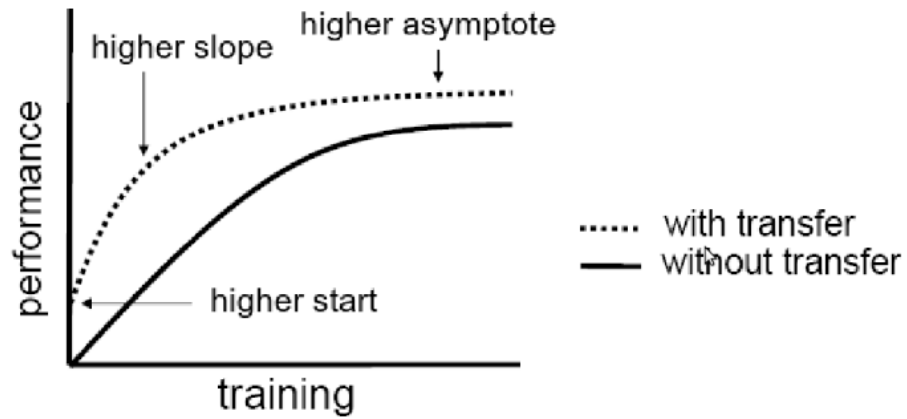


Figure 3.7: Performance difference of transfer learning [44]

The difference in the performance of using and not using transfer learning during training can be seen in Figure 3.7 above. On the other hand, Figure 3.8 demonstrates how transfer learning generally proceeds.

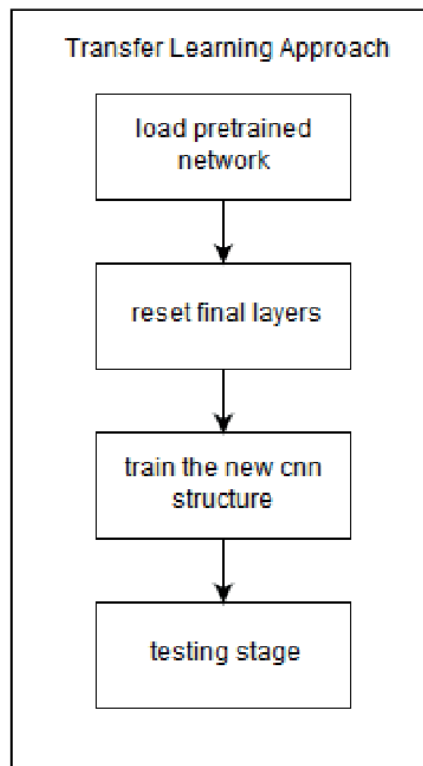


Figure 3.8: Transfer learning approach [45]

Chapter 4

Experimental Work

In this section, the dataset having brain MRI images, data preparation and preprocessing steps, pre-trained models, parameter settings, and mathematical metrics are discussed. In addition, the base model we implemented and the experimental results are explained.

4.1 Experimental Setup

4.1.1 Dataset

The dataset used in this thesis is an open database on the Kaggle website¹. The dataset consists of train and test folders containing a total of 6400 images. In this dataset, there are four classes of MRI images: "Mild Demented", "Moderate Demented", "Non-Demented", and "Very Mild Demented".

The main purpose of this dataset is to help researchers improve a model with high accuracy to detect and classify the phase of Alzheimer's disease. In Figure 4.1 shows a sample for each of the four classes in the dataset, which are, respectively, "Very Mild Demented", "Mild Demented", "Moderate Demented", and "Non-Demented".

¹ Alzheimer's Dataset, <https://www.kaggle.com/datasets/tourist55/alzheimers-dataset-4-class-of-images>

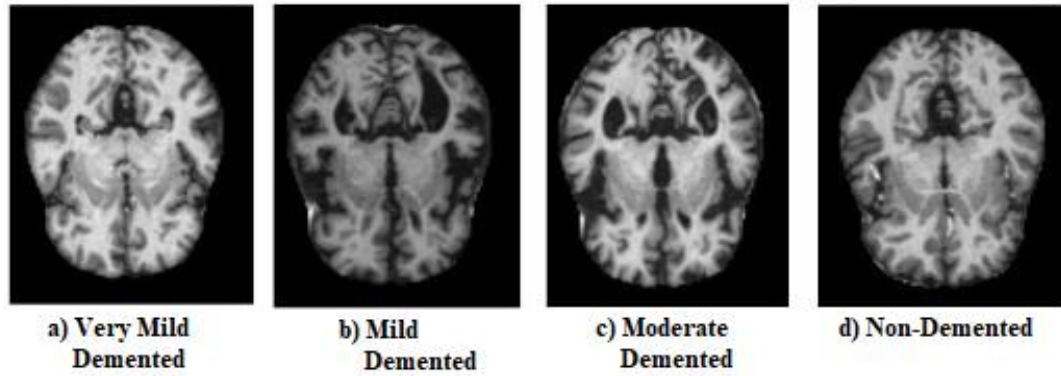


Figure 4.1: Example of four classes of dataset

4.1.2 Data Preparation

Data preparation is a collection of methods that properly initialize the data for use as input in deep learning models [46]. In the data preparation phase, libraries such as Tensorflow, Matplotlib, NumPy, and Pandas were installed and used. Afterward, paths to the images were identified and constants and seeds were determined for reproducibility. Then, the dataset was split into %80 train and %20 test batches consisting of four classes and determined the number of images for each class was. Images were copied and resampled from the train folder and split randomly with equal proportions in each class for the validation folder. In Table 4.1 below, it can be observed how much data each of the four classes in the Alzheimer's dataset contains after splitting them into train, validation, and test.

Table 4.1: Train, validation, test numbers for each of the four classes

Dataset Images	Very Mild Demented	Mild Demented	Moderate Demented	Non-Demented
Train	1434	574	42	2048
Validation	358	143	10	512
Test	448	179	12	640

4.1.3 Data Preprocessing

Data preprocessing is the operation of putting data into a simple format that makes it easier to use. All forms of data analysis, data science, and artificial intelligence development call for data preprocessing in order to produce accurate, precise, and reliable results. In the real world, data is unorganized and frequently produced, processed, and saved by a variety of people. This means that a data set could contain duplicate data, be incomplete, have manual input errors, or use different names to refer to the same thing. Humans can frequently find and correct these errors in the data that they use in their line of work, but data used to train artificial intelligence algorithms needs to be automatically preprocessed.

The performance of deep learning models can be improved using a technique called data preprocessing [46]. In order to reduce the size of the data, find relationships between the data, normalize the data, get rid of outliers, and extract features from the data, preprocessing is necessary [47]. Real-world data can occasionally be erroneous, inconsistent, redundant, and incomplete. The process of converting unprocessed data into a format that can be analyzed and understood is known as data preprocessing [48]. In our experiment, data were grayscale and they needed to be converted to RGB to use with pre-trained deep learning models. In the image transformation phase for data preprocessing, images were scaled. Convolutional neural networks can be trained using one of two general methods. One of them is to train a model with weights that were initially set at random. The second approach, known as "transfer learning," involves pre-training a model on a related task before applying it to the intended task. To avoid overfitting and produce cutting-edge results, the first method, also known as "training from scratch," typically calls for very large datasets. Transfer learning from a pre-trained model is a popular and effective method for medical image analysis because medical datasets are frequently very small as a result of privacy restrictions and the need for expert knowledge to generate ground truth. The ImageNet dataset, which contains more than 1.2 million labeled images, use to pre-train a number of publicly accessible models. The 1-channel grayscale images in our dataset must be converted to RGB and two additional channels added because the data in the ImageNet dataset has a 3-channel RGB structure and both natural images and trained models are used. It is necessary for our pre-trained models, InceptionV3, ResNet50V2, and

Xception. As shown in Figure 4.2, images are converted to RGB and set seed for reproducibility. Then, images were displayed in a grid of 9 images with their labels.

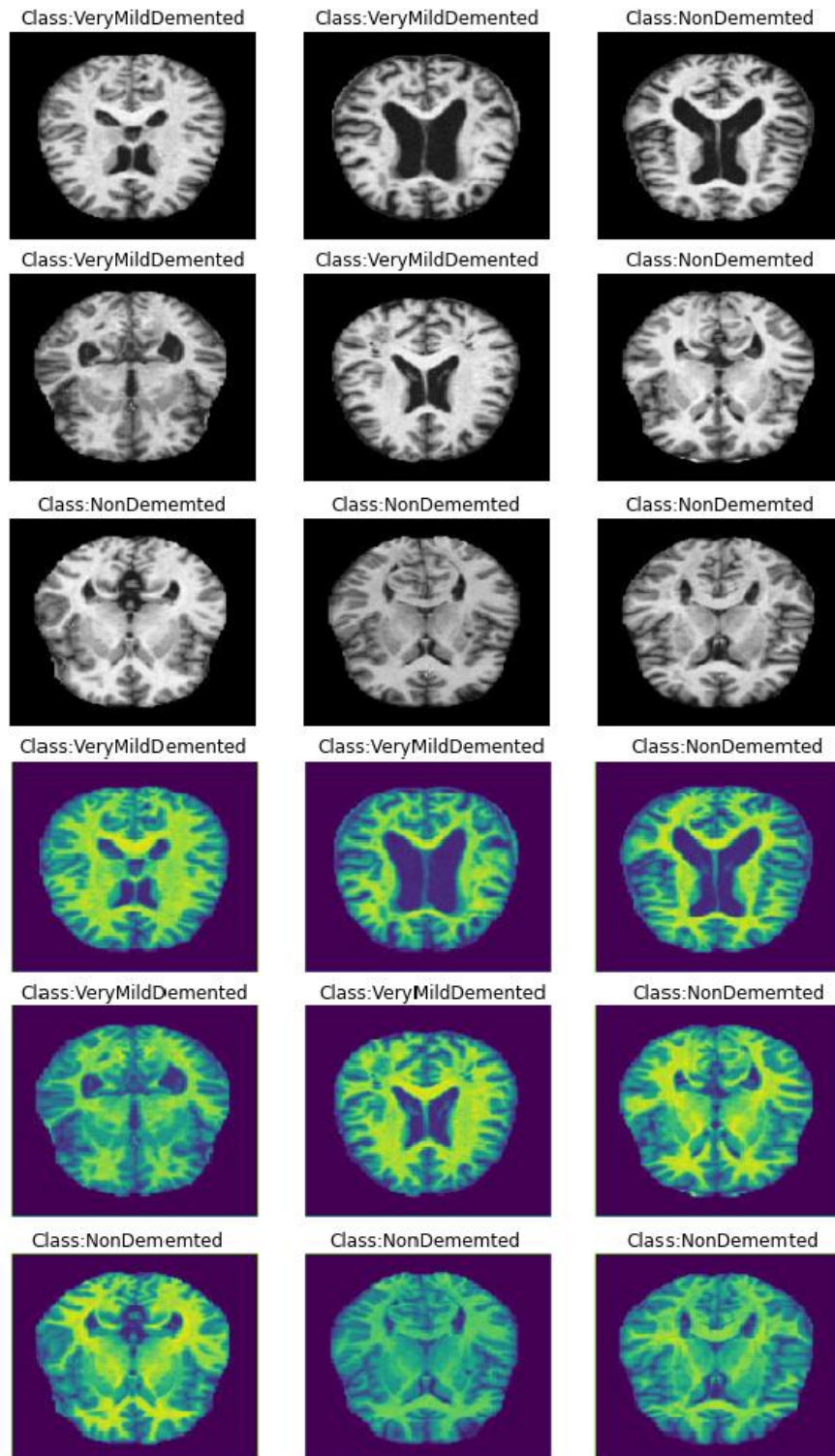


Figure 4.2: Brain MRI images with labels grayscale (up) and RGB (down)

4.1.4 Pre-trained Models

A pre-trained model is one that has already been created to address a similar issue. One can begin by using the model trained on another problem rather than starting from scratch to solve the same problem. In comparison to having to start from scratch, using a pre-trained model can save a significant amount of time and effort, even if it is not entirely accurate for the work.

4.1.4.1 InceptionV3

The InceptionV3 model is an advanced and powerful, highly engineered network that is regarded as a significant development in convolutional neural networks [49]. The third iteration of Google's Inception model is known as InceptionV3. It has between 42 and 48 layers, with both symmetric and asymmetric building blocks. These layers include convolutions, max pooling, average pooling, dropouts, and fully connected layers [50]. A module for GoogleNet, InceptionV3 is a convolutional neural network (CNN) that facilitates object detection and picture analysis. The goal of the Inception V3 design is to support deeper neural networks without letting the number of parameters balloon out of control. Compared to AlexNet's 60 million parameters, InceptionV3 has fewer than 25 million [51].

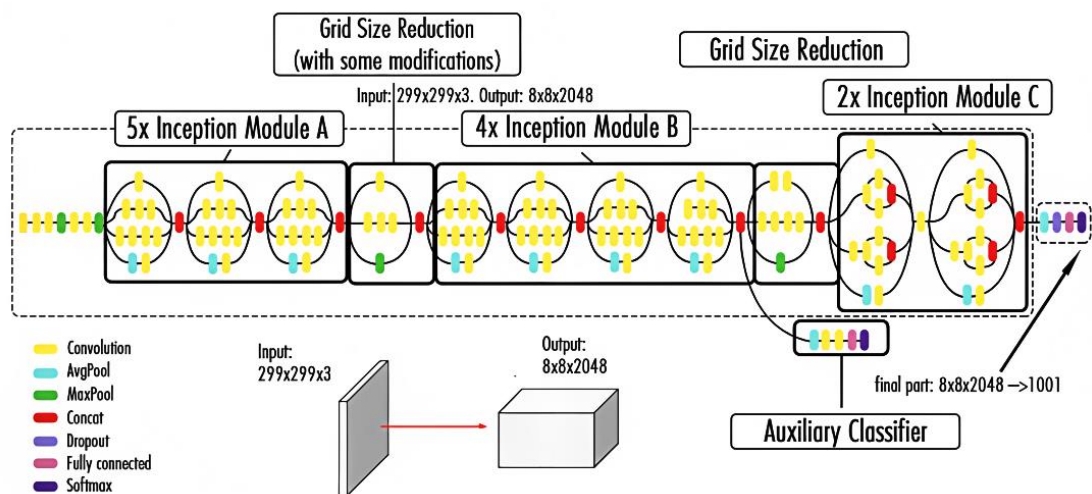


Figure 4.3: Architecture of InceptionV3 model [52]

The InceptionV3 model is made up of a combination of three major modules, as shown in Figure 4.3 above. The first module uses two fewer convolution layers in order to improve performance while lowering the computational cost. To create a less complicated network, Module B splits each convolution layer of $n \times n$ size into two layers of $1 \times n$ and $n \times 1$ dimensions. In order to avoid information loss, last module expands the filters to minimize the representational bottleneck. Thanks to its depth and the various kernel sizes used in the convolution operations, the InceptionV3 model collects more data without slowing down computation speed [52].

4.1.4.2 ResNet50V2

ResNet50V2, a modified version of ResNet50, performs better on the ImageNet dataset than ResNet50 and ResNet101 [53]. The propagation formulation of the connections between blocks was modified in ResNet50V2. ResNet50V2 performs well on the ImageNet dataset as well [54]. A massive architecture called ResNet50V2 is a modern convolution neural network that uses the architecture's residual blocks to solve vanishing gradient problems. Multiple residual blocks are stacked on top of one another in a residual network. Each residual block is made up of connections that take shortcuts by skipping one or more layers. Weight layers are pre-activated in ResNet50V2. On the datasets, ResNet50V2 produces precise predictions [55].

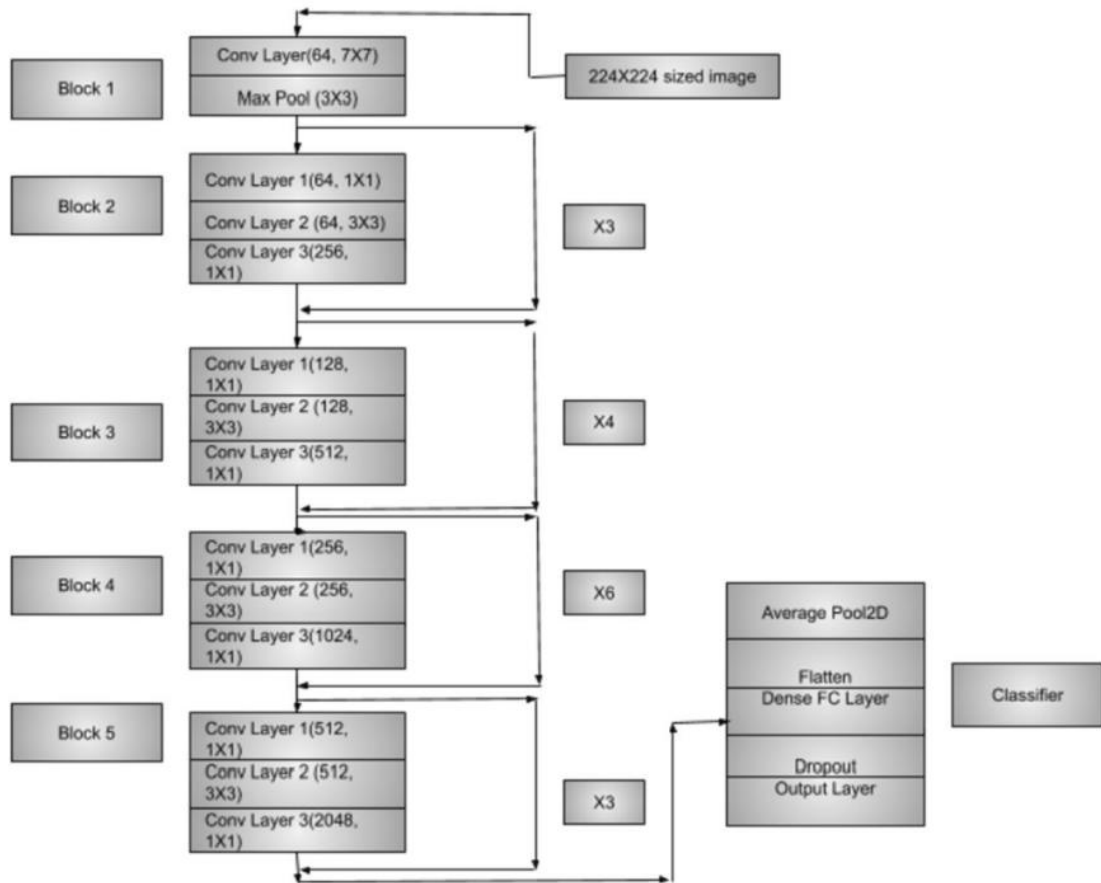


Figure 4.4: Architecture of ResNet50V2 model [55]

4.1.4.3 Xception

A Google product called Xception stands for an extreme version of Inception [56]. The model is an extension of the Inception architecture, using depthwise separable convolutions in place of the normal Inception architecture modules.

36 convolutional layers make up the network's feature extraction base in the Xception architecture. Except for the first and last modules, which are all surrounded by linear residual connections, the 36 convolutional layers are divided into 14 modules. A linear stack of depth-wise separable convolution layers with residual connections is, in essence, the Xception architecture. As a result, creating and changing the architecture is very easy [56].

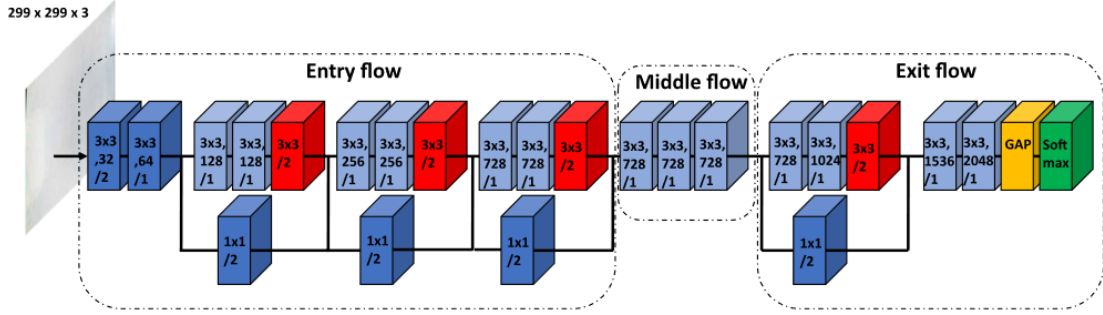


Figure 4.5: Detailed architecture of Xception model [57]

4.1.5 Parameter Settings

To increase the test AUC of the model, some experimental settings have been made with the transfer learning method in this thesis.

The function which builds the transfer model was tuned to add the additional layers. Also, additional convolution layers were added with dropout and batch normalization for regularization to increase the capacity of the model. In this way, it was given the additional capacity to the base model. At this stage, the epoch value was set to 50 and the learning rate was taken as 0.001.

Following this point, the training data revealed that the model was overfitting in the early epochs. Because of this, data augmentation was added to help generalize the model to new data. Changes have been made to the rescale, width shift range, rotation range, height shift range, and zoom range properties of images for data augmentation.

Finally, the model was re-trained with the tuned parameters using data augmentation and other techniques. In addition, early stopping was removed and the epochs were set to 150 to give the model as much time to train as possible without overfitting.

4.1.6 Metrics

The following metrics were used to evaluate the performance of the model described earlier. We calculated the three performance metrics accuracy (AC), F1-score (FS), and area under the curve (AUC) to evaluate the image classification process. The

confusion matrix shown in Figure 4.6 for binary or multi-class classification is used to calculate these performance metrics [58].

		Predicted value	
		Positive	Negative
Actual value	Positive	TP	FP
	Negative	FN	TN

Figure 4.6: Confusion matrix for metrics [58]

Instances that are both actually positive and expected to be positive are referred to as True Positive (TP). False Negative (FN) are occurrences that are positive despite being expected to be negative. Instances that are both actually negative and expected to be negative are referred to as True Negative (TN). False Positive (FP) are instances where a result is predicted to be positive but is actually negative [58].

4.1.6.1 Accuracy

A qualitative performance characteristic called accuracy expresses how closely a measurement result agrees with the value of the measurement. To determine the level of confidence that can be placed in a result and the dependability of the decisions based on that result, a quantitative estimate of the accuracy of the result is necessary [59]. Accuracy refers to the percentage of test samples that were successfully categorized. A general metric for assessing the efficiency and accuracy of learning classifiers is the accuracy rate. Using a test set that is separate from the training set, the accuracy is calculated. “tp+tn” represents all actual classifier examples, and “tp+fn + tn+fp” represents all instances across the entire dataset [58].

$$Accuracy = \frac{tp + tn}{tp + fn + tn + fp} \quad (4.1)$$

4.1.6.2 Precision

How many samples that were retrieved with positive class labels are actually positives is measured by precision performance metrics. When evaluating brittle classifiers, which are used to categorize every instance of the used dataset, the precision rate is helpful. Where "tp" stands for the total number of instances that are predicted to be positive and "tp+fp" stands for the total number of instances that are actually positive and that the classifier classified as positives. Precision shows how many of the values we estimated as positive are positive [58].

$$Precision = \frac{tp}{tp + fp} \quad (4.2)$$

4.1.6.3 Recall

Recall is a metric that shows how well we positively use our estimates. Recall measures a classifier's effectiveness and efficiency to estimate the proportion of instances with the correct class label. "tp" stands for the anticipated positive instances, while "tp+fn" refers to all of the actual positive instances in the dataset [58].

$$Recall = \frac{tp}{tp + fn} \quad (4.3)$$

4.1.6.4 F1-Score

F1-score helps to calculate the precision and recall using the confusion matrix. The harmonic mean of the precision rate and recall rate, known as the F1-Score or F-measure, provides a useful indication of the average. The F1-Score has a value between 0 and 1. It evaluates the robustness and accuracy of the used classifier. The effectiveness of the used classifier will improve as F1-Score rises. To achieve extremely accurate performance, the precision should be higher and the recall must be lower [58].

$$F1 - Score = \frac{2 * Precision * Recall}{Precision + Recall} \quad (4.4)$$

4.1.6.5 AUC

AUC is also a popular metric for assessing the effectiveness of a multi-class classification system is the area under the receiver operator characteristic (ROC) curve. A ROC curve is a graph that shows the true and false positive rates. The area under the curve (AUC), shown in gray in Figure 4.7, which represents the degree of separation between the two groups of data, is the commonly used metric for assessing the effectiveness of logistic classification models [60].

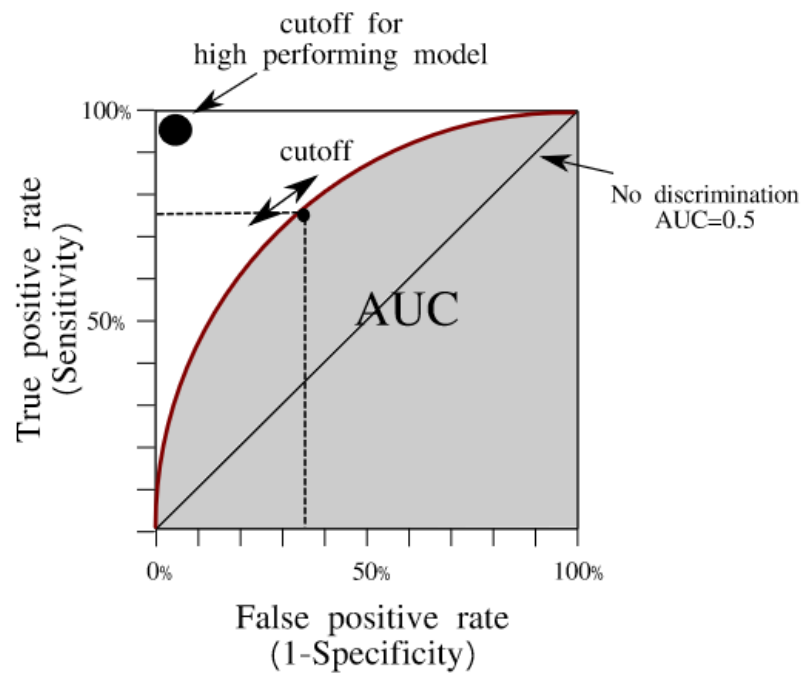


Figure 4.7: Area under the curve (AUC) [60]

The AUC can range from 0.5, which represents a random classification model with a diagonal ROC curve in the unit square, to $AUC = 1$, which relates to a perfect classification model. AUC indices of 0.5 to 0.7 are regarded as having poor discrimination, 0.7 to 0.8 are considered acceptable, and greater than that is regarded as excellent [61].

$$AUC = \frac{1}{2} \times \left(\frac{tp}{tp + fn} + \frac{tn}{tn + fp} \right) \times 100 \quad (4.4)$$

4.2 Base Model Selection

In this section, InceptionV3, ResNet50V2, and Xception models are used. AUC, F1-Score, and Accuracy metrics of all models have been calculated. As a result of all these calculations, the InceptionV3 model got 85.00%, and the ResNet50V2 model and the Xception model got 81.00% AUC. The model with the best AUC value was selected from the 3 models. That model was InceptionV3, with an AUC value of 85.00%. After this section, some improvements were applied to the InceptionV3 base model.

Table 4.2: Base model scores

Base Model Scores for Alzheimer's Disease	Accuracy	F1-Score	AUC
InceptionV3	0.65	0.49	%85.00
ResNet50V2	0.62	0.47	%81.00
Xception	0.57	0.49	%81.00

4.3 Results Evaluation

In this thesis, after the base transfer learning model was trained, the base model was tuned and different improvements were made to the model to get better results. In this section, the changes made to the model and the results obtained are shown in Table 4.3.

Table 4.3: Stages of the InceptionV3 model

Stages of the InceptionV3 model based on Transfer Learning	Accuracy	F1-Score	AUC
InceptionV3	0.65	0.49	%85.00
InceptionV3 + Additional Capacity	0.65	0.49	%86.00
InceptionV3 + Additional Capacity + Data Augmentation (only rescale)	0.63	0.49	%81.00
InceptionV3 + Additional Capacity + Data Augmentation (only rescale + width shift range)	0.78	0.47	%83.00
InceptionV3 + Additional Capacity + Data Augmentation (only rescale + width shift range + height shift range)	0.71	0.55	%86.00
InceptionV3 + Additional Capacity + Data Augmentation (only rescale + width shift range + height shift range + rotation)	0.59	0.49	%86.00
InceptionV3 + Additional Capacity + Data Augmentation (rescale + width shift range + height shift range + rotation + zoom)	0.70	0.48	%87.00

In figures 4.8, 4.9, and 4.10 below, confusion matrix and validation loss, validation AUC graphs of different periods can be observed, respectively, of the base model

InceptionV3, InceptionV3 with additional capacity, and later InceptionV3 models with both additional capacity and data augmentation.

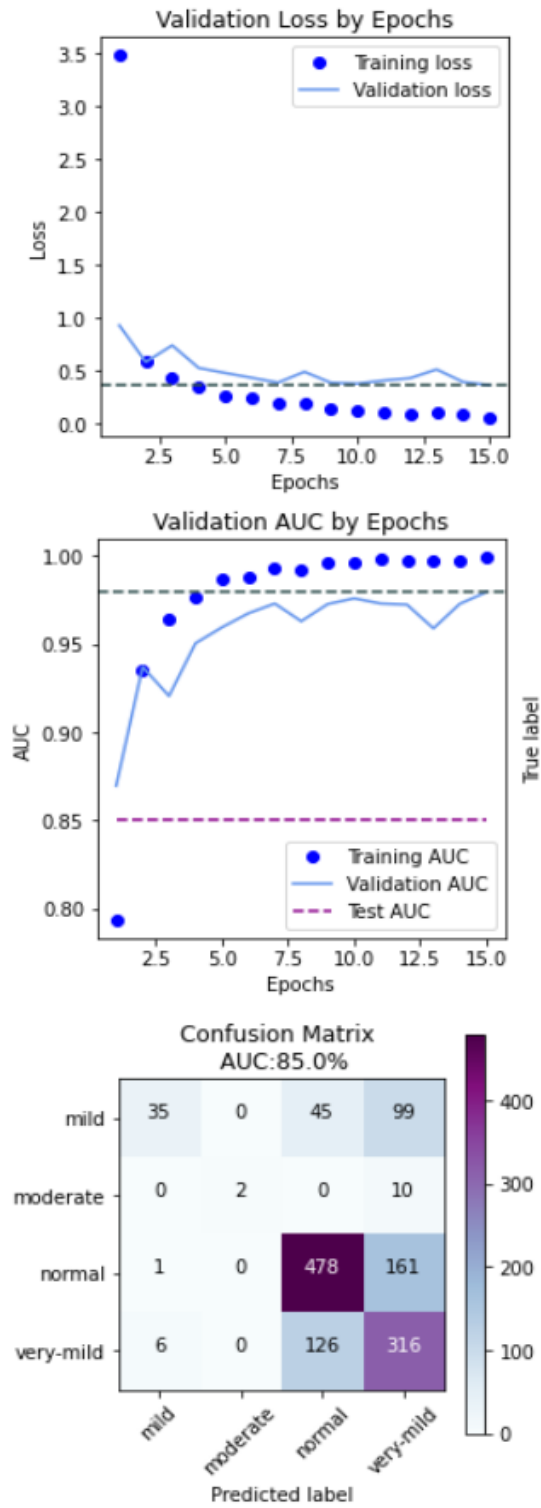


Figure 4.8: Base model InceptionV3

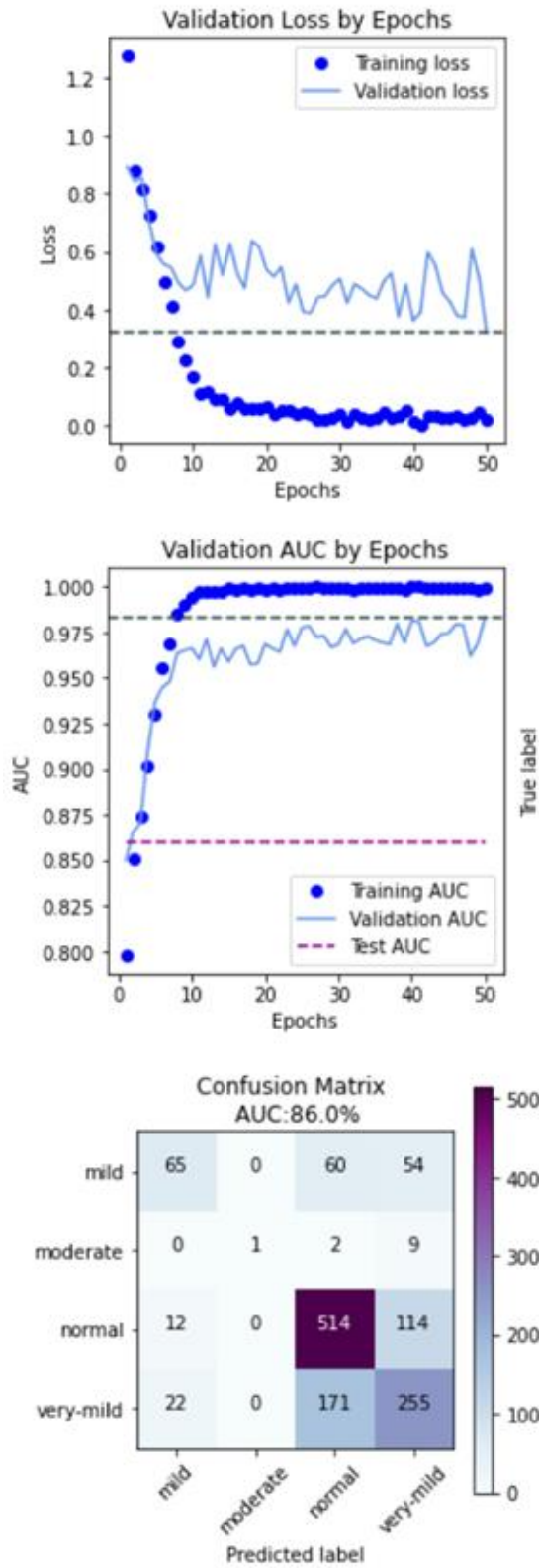


Figure 4.9: InceptionV3 + Additional Capacity

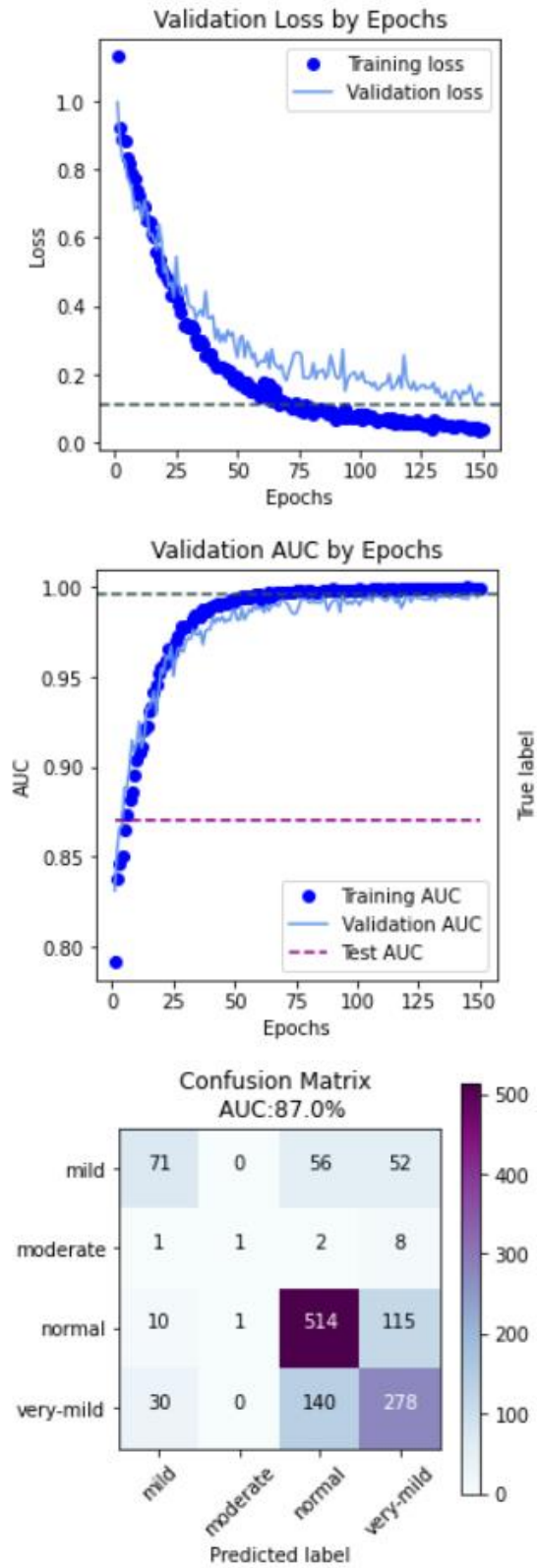


Figure 4.10: InceptionV3 + Additional Capacity + Data Augmentation

4.4 Experimental Comparison

In this section, we compare our AUC results with those of other studies in the literature using the Alzheimer's disease dataset that we used from Kaggle. The results of the comparative experiments are given in Table 4.4.

Table 4.4: Comparison between the AUC of the proposed method and others

Studies	Models	AUC
Ding et al., 2018 [62]	InceptionV3	%76.00
Wang, 2018 [63]	InceptionV3	%80.00
Bae et al., 2020 [64]	InceptionV4	%88.00
Suganthe et al., 2021 [65]	InceptionV3	%77.52
Dai et al., 2021 [66]	InceptionV3	%80.90
Hasan et al., 2021 [67]	InceptionV3	%80.95
Pradhan et al., 2021 [68]	DenseNet169	%82.00
Ahmed et al., 2022 [69]	Inception-ResnetV2	%81.90
Kujur et al., 2022 [70]	InceptionV3	%84.26
The proposed method	InceptionV3	%87.00

As shown in Table 4.4, we can compare our work to other studies since 2018 that have used the same dataset we used in our work and that have used various deep learning models and techniques to obtain different AUC values. Only one of the nine different studies in the table had results better than ours. The AUC results of the other eight studies in the table were lower as compared to those of our study. With InceptionV4, Bae et al., achieved better results, with an AUC score of 88.00% in 2020. In the previous years, the InceptionV3 deep learning model was used most frequently, while the InceptionV4, DenseNet169 and Inception-ResNetV2 deep learning models were also preferred. In conclusion, our proposed method significantly improves the AUC of Alzheimer's disease patients according to the experimental comparison.

Chapter 5

Conclusion

In this thesis, the task of Alzheimer's disease classification is evaluated using the Alzheimer's Disease dataset consisting of 4 classes from Kaggle. Since InceptionV3 has the best AUC among ResNet50V2, Xception, and InceptionV3 models, InceptionV3 was used as the base transfer learning model, and then applied some tunings on the InceptionV3.

Additional convolution layers were added to increase the capacity of the model and at this stage, the epoch value was set to 50 and the learning rate was taken as 0.001. After that process, the model was overfitting early in the epochs. Because of that problem, a data augmentation process was added to help generalize the model to new data. Some changes have been made to the rescale, width shift range, rotation range, height shift range, and zoom range properties of images for data augmentation. Finally, the model has trained again with the tuned parameters using data augmentation and additional convolution layers. During this process, the epoch value was set to 150 to give the model as much time to train as possible without overfitting.

It has been demonstrated that the proposed method, when combined with transfer learning and data augmentation techniques, can detect Alzheimer's disease up to a certain level. In the medical field, using pre-trained models rather than starting from scratch ensures noticeably better performance. Based on the data in the confusion matrix, it can be said that the model does best at identifying normal and very-mild MRIs and poorest at identifying moderate cases. Also, adding capacity to the model, searching for optimal hyperparameters, and adding data augmentation resulted in better performance on the test dataset.

In future work, different datasets can be used for this problem. Pradhan et al. achieved an AUC of 82.00% in 2021 using a different model, DenseNet169. In 2022, Kujur et al., obtained an AUC of 84.26% using the pre-trained InceptionV3 model. Bae et al., in 2020, used the same dataset and InceptionV4 instead of InceptionV3, and obtained an AUC of 88.00%. Likewise, the methods and models used in previous years have changed, and different results have been obtained. Changing the pre-trained models and adjusting various parameters over the next few years can yield remarkably different results. Different deep learning approaches and hybrid models may achieve a better outcomes.

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Appendices

Appendix A

Publications from the Thesis

Conference Papers

1. Yeşilada A, Gökalp O. Automatic detection of Alzheimer's disease with transfer learning and image processing techniques. In: 4th International Eurasian Conference on Science, Engineering and Technology (EURASIANSCIENTECH). Ankara, Türkiye. 2022. p 946-953.

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2016 – 2020 Space Camp Turkey – Counselor
2018 – 2018 Ege Serbest Bölgesi (ESBAŞ) – Test Automation Engineer Intern
2019 – 2019 Ege Serbest Bölgesi (ESBAŞ) – Frontend Developer Intern
2020 – 2023 Mayteks Örme Sanayi ve Ticaret A.Ş – IT Specialist

Publications (if any):

1. Yeşilada A, Gökalp O. Automatic detection of Alzheimer’s disease with transfer learning and image processing techniques. In: 4th International Eurasian Conference on Science, Engineering and Technology (EURASIANSCIENTECH). Ankara, Türkiye. 2022. p 946-953.