

CHAPTER 6

Diagnosis of COVID-19 from 3D Medical Images using Deep Learning Approaches

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Introduction

Coronavirus, which started in China in 2019, has affected the whole world. The widespread impact of this virus worldwide has been referred to as a pandemic and has resulted in the deaths of many people. Many countries have allocated resources for early and accurate diagnosis as well as treatment of the disease. Various methods are used for the diagnosis of the disease, including antibody tests, RT-PCR, and Computed Tomography (CT). Based on some studies, it has been observed that the accuracy rates of antibody tests and RT-PCR may not be sufficient. Among the methods used, the CT scan provides the highest accuracy. Most individuals diagnosed with COVID-19 exhibit characteristic radiographic findings on CT scans, for example ground-glass opacities, multifocal patchy consolidations (Zhu et al., 2020). However, the expertise of a radiologist is needed to interpret CT images and differentiate them from other lung diseases.

In the contemporary, artificial intelligence (AI) has been increasingly employed across diverse domains that were traditionally exclusive to experts. AI has become increasingly popular and has been prominent since Alan Turing's work in the 1950s, with various studies and approaches in AI. AI approaches are also commonly used to diagnose many diseases in the healthcare field. AI techniques such as segmentation and classification are used in the diagnosis of diseases. Various studies have been conducted using AI techniques for COVID-19 diagnosis as well. In the literature, it has been shown that using AI, it is possible to decide whether a person has COVID-19, has different lung diseases or is healthy according to their CT scan without the need for a radiologist's expertise.

The classification problem is a common type of problem encountered in many areas, including the field of healthcare. Problems such as disease classification from blood test results, disease detection from images, and various other problems can be considered classification problems. Classification is defined as determining which predefined class each item in a dataset belongs to. Machine learning (ML) is included of artificial intelligence and includes various classification methods.

Deep learning approaches can also be expressed as deep neural networks and is a subfield of ML science. Deep learning approaches are one of the classification methods under the umbrella of ml. It is essentially a system that emulates the cognitive processes

of the human brain and has emerged as a successful approach for working with large-scale datasets (Singh et al., 2020). Deep learning approaches excel in self-feature extraction from data. The increasing availability of images and advancements in technology, along with the introduction of the ImageNet dataset in 2012, has contributed to the growing popularity of deep learning as a research field.

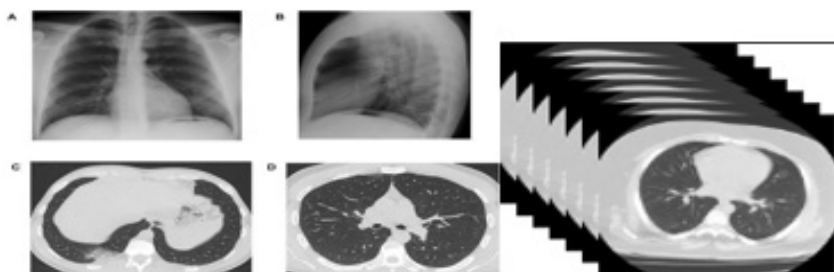
Deep learning methods consist of architectures with different characteristics for example Convolutional Neural Networks (CNNs) for images, standard Artificial Neural Networks, Recurrent Neural Networks (RNNs) commonly used in natural language processing problems, and Generative Adversarial Networks (GANs) used in areas for example generating new images. CNNs, a subfield of deep learning, are widely employed for image classification tasks. The architecture of CNNs encompasses convolution process layer, pooling process and fully connected layers. In the convolution process, the image features are extracted. The main purpose of the pooling layer added between different convolutional layers is to reduce dimensionality. In the fully connected process, the classification is performed. AlexNet, LeNet, GoogleNet, VGG-Net, ResNet, and DenseNet are some of the commonly used CNN architectures for classification and pattern recognition tasks.

Deep learning methods are able to classify images without the need for expert feature extraction, making them a valuable tool for rapid diagnosis in the medical field. Recent advancements in deep learning have enabled the development of computer vision models that can assist doctors in diagnosing various diseases. Studies in this field have shown promising results (Esteva et al., 2017; Litjens et al., 2017).

Lung X-Ray is a method that allows for quick imaging of the lungs using radiation beams passing through the front of the chest. CT, on the other hand, provides more detailed images and clearer 3D images. Compared to chest radiography and chest ultrasound, CT scans are the most popular approach for chest imaging. CT has gained popularity by providing high-resolution 3D chest scans. Figure 1 shows CT images and X-Ray. Images that need to be classified using deep learning methods can be 2D or 3D. For example, X-Ray images can be considered as 2D images, while CT images can be considered as 3D images. 2D images are single-channel images consisting of RGB (red, blue, green) channels. 3D images, on the other hand, are stacks of multi-channel images obtained sequentially. CNN architecture works similarly on 2D and 3D images. In the case of having 3D images, the convolution and pooling layers employ filters and masks with a channel count matching that of the image.

Figure 1

X-ray ve BT images (Cellina et al., 2020)



Scientific investigations conducted during the COVID-19 pandemic have demonstrated that CT scans are faster and more accurate in detecting COVID-19 lesions compared to rRT-PCR testing (Ai et al., 2020). COVID-19 findings on CT scans are associated with ground-glass opacities, which can be labor-intensive and subjective for radiologists to label. Artificial intelligence models, on the other hand, can perform

these tasks quickly and reliably based on learned rules (Wang et al., 2021). There are numerous studies on lung diseases using CT scans, and these studies demonstrate that deep learning yields highly effective results in this field. (Angelini et al., 2019; Walsh et al., 2020; Wang et al., 2017). Numerous models have been proposed using deep learning approaches for COVID-19, including studies that utilize X-ray and CT scans in the literature.

Informed by relevant literature that employed CT images for COVID-19 prediction, experimental studies were conducted on a publicly available dataset using some traditional CNN architectures to aim for COVID-19 prediction. In this binary classification problem for COVID-19, classification was performed as positive or negative. Widely used CNN architectures, such as DenseNet and ResNet, were employed in the study. Results obtained with the standard settings of these architectures from the literature without any fine-tuning showed that ResNet architecture achieved good performance with an accuracy rate of 86%.

COVID-19

A novel virus called coronavirus (COVID-19) was discovered in 2019. This virus causes rapid lung involvement and lung damage, making early diagnosis and treatment crucial. The widespread of COVID-19 in many countries led to its classification as a pandemic, and most countries faced medical resource shortages. Many countries started utilizing the majority of their resources towards diagnosing this disease, preventing further spread, and finding necessary treatment methods. Therefore, early diagnosis, identification of high-risk patients, and optimization of medical resources have become of great importance.

During the pandemic, early diagnosis and high accuracy have been crucial in the fight against COVID-19. Various methods have been used for the diagnosis of the disease, including antibody tests, RT-PCR, and CT scans. Some studies in the literature reveal that antibodies and PT-PCR tests do not give the desired level of accuracy and their reliability is reduced. (Fang et al., 2020). In addition, the limited availability of test kits for performing RT-PCR tests in some countries has contributed to the spread of the pandemic and made early diagnosis more difficult. The highest accuracy in COVID-19 diagnosis has been achieved with CT scans (Xie et al., 2020; Ai et al., 2020). However, in addition to achieving high accuracy for diagnosis, the interpretation of CT scans requires evaluation by a radiology specialist in order to distinguish COVID-19 lesions from those of other lung diseases.

Deep Learning

Artificial intelligence can be defined as the imitation of human abilities by a system or machine. Nowadays, examples of artificial intelligence can be found in many fields, such as virtual assistants, intelligent disease diagnosis systems, banking applications, autonomous vehicles, etc. Machine learning, a subfield of artificial intelligence, involves machines learning from a dataset and producing appropriate outputs when encountering similar situations that are not included in the dataset.

Deep learning within machine learning is a field of study that works like a human brain to process data and can process larger data sets compared to traditional machine learning methods. It allows us to train artificial intelligence to predict outputs based on a given dataset. Deep learning requires more powerful computers to handle larger datasets. Unlike feature selection in machine learning methods, where features are taught to the system due to the advantage of having fewer data, deep learning approaches should

perform feature extraction processes by themselves (LeCun et al., 2015). In summary, deep learning methods do not require preprocessing steps, which sets them apart from many other machine learning methods (Li et al., 2018).

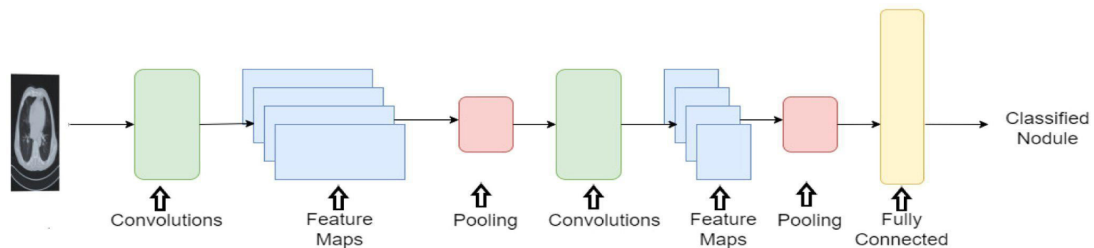
Deep learning is a widely adopted approach across various application domains, including biomedical, translators, chatbots and service robots, image enhancement and colorization, facial and voice recognition systems, object detection, object tracking, cyber threat analysis, natural language processing, recommendation systems, autonomous vehicles, virtual assistants, alarm systems, and many more.

What is CNN?

The CNN, a subfield of deep learning, is a frequently used architecture for image classification problems. CNN has layers for different functions such as convolution, pooling and fully connected. CNNs are widely employed for analyzing visual images. Due to their ability to extract features using filters on images, they are popular in image processing studies. (Modak et al., 2023). The convolutional layer performs feature extraction by running filters over the input data. The pooling layer, commonly used between convolutional layers, reduces the dimensionality of the output from the convolutional layer. Following the convolutional and pooling layers, the input data is flattened into a 1D vector and then forwarded to the fully connected layer for classification utilizing a multi-layer artificial neural network. The layers that constitute a 2D CNN architecture and the basic structure of the architecture are presented in Figure 2.

Figure 2

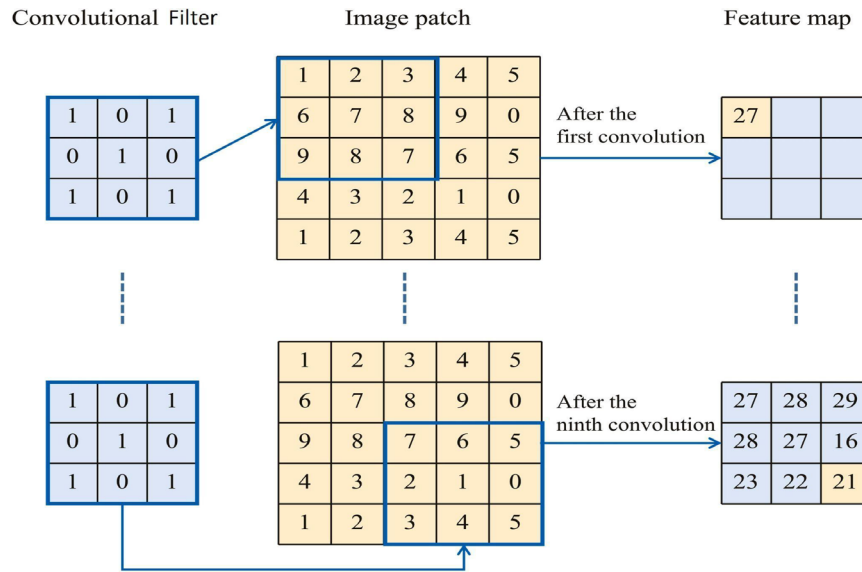
2D CNN architecture (Modak et al., 2023)



Usually, the images worked on are in the form of 2D $M \times N$ matrices. The fundamental expectation in performing convolution operation on an image is for the deep learning model to extract the features of the input image. In this layer, where features are extracted, uses filters, which are weights designed to detect the desired features. The filters move step by step over the image for feature extraction. The convolution in CNN involves convolving the image with filters, which enables the automatic extraction of features from the image. These filters' weights are updated through backpropagation during the training process of the CNN. High values are obtained in regions where the searched feature is present, while low values are obtained in regions where the searched feature is absent. The 2D convolution process is shown in Figure 3. The result matrix obtained from the filter is then subjected to an activation function before passing it to the next layer. Examples of these functions are Relu, Leaky Relu, Softmax, and tan H.

Figure 3

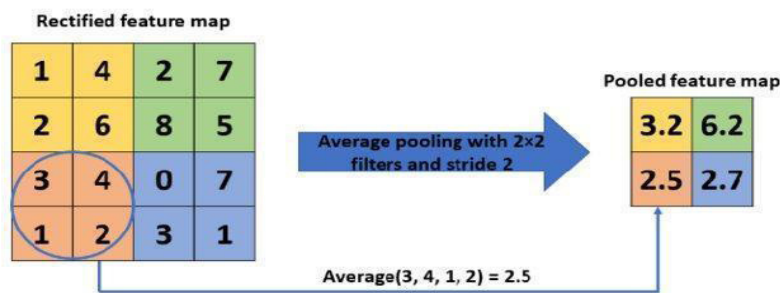
Convolution Layer (Gu et al., 2021)



Each convolutional layer in a CNN can have multiple filters. In this case, each filter captures different features, resulting in feature maps. Feature maps represent the features obtained from input images and include local features. Pooling layer is a down sampling layer added after the convolutional layer in a CNN, which represents a form of subsampling and reduces the dimensionality of the output feature map produced by the convolutional layer. In the deep learning phase, the size reduction method is used to reduce the computational cost. The pooling layer typically comes after the convolutional layer and serves as a connection with the fully connected layer. Max pooling and average pooling are pooling methods frequently used in the literature. Max pooling takes the maximum value within the pooled region of the input image, while average pooling takes the average of all values within the pooled region. An example is presented in Figure 4 to examine the average pooling process example.

Figure 4

Average Pooling (Gholamalinejad & Khosravi, 2020)



The data that is separated and dimensionality reduced in the convolutional and pooling layers is passed to a fully connected layer. In this layer, the classification is performed. This layer, called the fully connected layer, is the layer where the neural network structure is located. Before the fully connected layer, a flattening operation is performed on the data that has gone through the pooling process. This flattening operation converts the data into column vectors, which will be used as input to the fully connected layer. At each learning stage, backpropagation is performed, during which the weights and filters in the fully connected layer are updated, thus completing the learning process. The purpose of backpropagation is to determine important features in the input images during the learning process by propagating the error rate with labeled data.

What is 3D CNN?

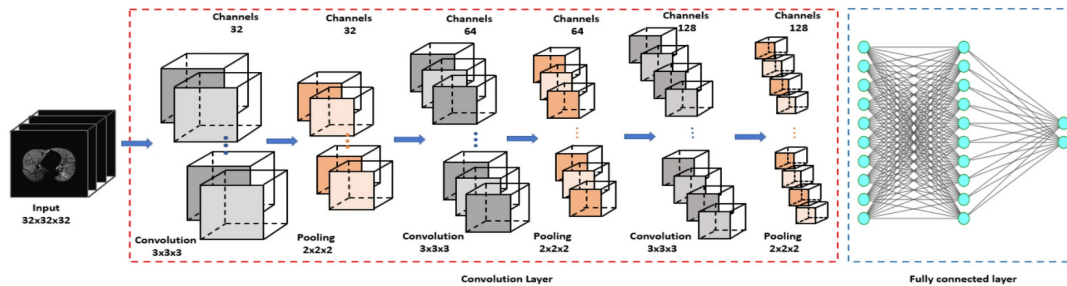
3D CNN is the CNN architecture used to 3D process data with temporal and/or motion information, such as videos, moving images, medical images, motion object detection, and activity recognition. It is an advanced version of the standard 2D CNN architecture.

With the increase in 3D datasets, deep learning studies on 3D datasets have gained momentum. 3D images can be thought of as a collection of 2D image slices or a sequence of consecutive frames in a video. If a 2D CNN is applied to a 3D image, separate predictions need to be made for each image slice, which increases the processing cost. 3D CNNs, which are based on performing convolution and pooling operations in a volumetric, are effective for processing 3D images. (Demir et al., 2023). In addition, 3D CNNs are more effective in processing 3D medical images compared to 2D CNNs. (Wang et al., 2023). The first way to process 3D images is to convert traditional 2D deep learning architectures into 3D. This way, the networks can be trained not only on images but also on the development and changes over temporal frames (Qiu et al., 2017).

3D CNNs allow the learning of local patterns and features in three-dimensional datasets, typically consisting of time, height, and width dimensions. The architecture of a 3D CNN can include different types of layers designed specifically for 3D data. The overall working mechanism of a 3D CNN architecture is presented in Figure 5 as an example.

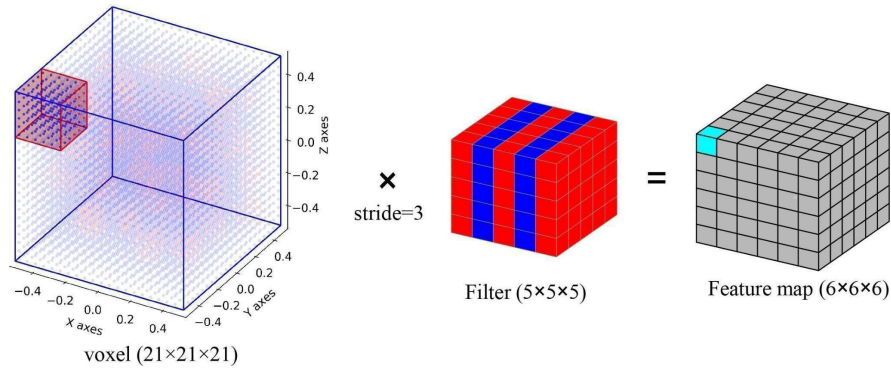
Figure 5

3D CNN architecture (Ho et al., 2021)



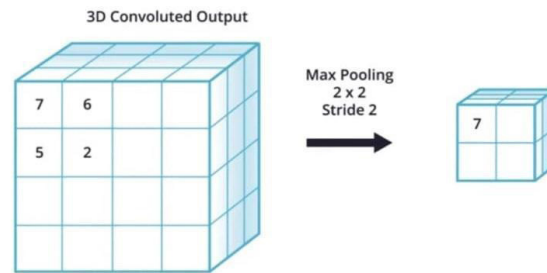
The 3D convolutional layer operates similarly to the 2D convolutional layer. However, the 3D convolutional layer differs in terms of input data structure, filter sizes, and hyperparameter numbers. The basic principle of the 3D convolutional layer is to use 3D filters to move across the data, focusing on specific regions at each step and detecting patterns in these regions to extract features. The 3D convolutional layer applies convolutional operations with a 3D filter to each pixel or voxel (3D pixel) in the input data. This filter is slid over the input data and applied to each region to extract features from that region. The 3D convolutional layer can capture 3D patterns in the input data (e.g., different structures of objects in time, depth, and width dimensions) and enable the learning of more complex features using these patterns. It is commonly used in applications that process 3D data, such as videos, medical images, and motion analytics. Figure 6 shows the 3D convolution layer.

Figure 6
3D Convolution Layer (Rao & Liu, 2020)



The pooling layer in 3D CNN architecture operates on the width, height, and depth (z-axis) dimension. Its fundamental principle is similar to the 2D pooling layer, but it is adapted for 3D data. The filters used in 3D pooling must also be 3D. In the 3D pooling process, the 3D pooling filter is applied volumetrically on the 3D image. Pooling methods, which are frequently used in 2D pooling, such as max pooling, average pooling, are also frequently used for 3d pooling. Maximum pooling selects the maximum value within the pooling region and uses that value, while average pooling takes the average of the values within the pooling region. The resulting value from the pooling process is placed at the center of the pooling region, thereby reducing the output data size. The 3D pooling operation, like in the 2D model, performs sampling and dimension reduction for the purpose of down sampling. Additionally, it reduces the computational burden of the network, resulting in faster operation. Therefore, the 3D pooling layer is an important component in 3D convolutional neural network architectures. Figure 7 shows the 3D pooling layer.

Figure 7
3D CNN Pooling Layer



In the same way as 2D CNN, After the convolutional and pooling layers, the outputs are flattened and used to generate predictions for classification, regression, or other tasks using fully connected layers. The flattened vector is then linked to the neurons. Each neuron is connected to all input data and uses weight and bias values to compute its outputs. The fully connected layer obtains the final outputs, which are then used to make predictions for classification, regression, or other tasks. The fully connected layer is located at the end of the network, producing the final outputs and enabling the model to make predictions for classification or other outputs. However, the use of fully connected layers in a 3D CNN structure can increase the complexity of the model and pose a risk of overfitting. Therefore, it is important to use properly configured and regularized fully connected layers.

Deep Learning Studies on Diagnosis of COVID-19

Many studies have been conducted in the literature on deep learning methods to assist in rapid detection and diagnosis throughout the COVID-19 pandemic. The main idea behind these studies is to classify images as COVID-19 positive or negative based on the findings in the images. In contrast to traditional X-ray approaches, since CT scans are 3-dimensional, they can provide a detailed image of the lungs. Studies using deep learning for COVID-19 classification have generally used specific classes. Some of those; healthy, normal, abnormal, other pneumonia, positive, negative, COVID, non-COVID.

In the conducted studies, it has been reported that in CT images, ground-glass opacities, patchy shadows, and diffuse ground-glass or scattered are most commonly identified indicators of COVID-19. Furthermore, the research revealed that COVID-19 infection findings may be present in CT images even if the PCR test is negative (Ai et al., 2020; Kovács et al., 2021; Xie et al., 2020).

Shan et al. proposed that demonstrating the potential of using deep learning methods for the detection of COVID-19 infections from CT scans, the segmentation process was performed in deep learning methods to predict the infection area to assist radiologists, using CT images of 300 COVID-19 patients (Shan et al., 2020).

Xuehait et al. their colleagues aimed to learn the distinguishing features of COVID-19 by using CT scans to classify it. They developed a self-supervised and transfer learning-based model for this purpose. The suggested model classifies CT scans as COVID Positive or Negative. As a part of this study, a publicly available dataset was created and published (He et al., 2020).

In another study that performed COVID-19 classification from CT images, lung regions were detected using a threshold segmentation value, followed by the classification process (Wu et al., 2020).

In a system based on the VGG-16 deep learning model, the classification process according to CT images is classified into 3 classes, namely Negative, Mild, and Severe cases. During the training of the system, lung images and clinical data were used. The output of the system was fed into a logistic regression to obtain the final prediction (Ning et al., 2020).

A multi-task self-attention learning model has been revealed for detection COVID-19 and the identification of different types of lung diseases other than COVID-19. The proposed model combines two different 3D CNN algorithms to perform different tasks (Wang et al., 2020).

In a study where the ResNet50V2 model was used as the base model to CT scans as either COVID-19 positive and negative. In this study, a feature pyramid network was applied to investigate various resolutions of input images, and it was observed that this addition significantly improved the classification performance (Rahimzadeh et al., 2021).

In another study that used a hybrid approach for COVID-19, the advantages of Transformer and CNN architectures were combined. The local feature extraction ability of CNN and the global feature extraction ability of the transformer were used together. The proposed model achieved an accuracy of 96.7%. In previous studies, using only CNN resulted in an accuracy of 95.2%, and using only the transformer resulted in an accuracy of 75.8%. Thus, it was clearly observed that the proposed hybrid model improved the accuracy performance (Fan et al., 2022).

In a study that used Fractional Fourier entropy (FrFE) for feature extraction, the deep learning method, Deep stacked sparse autoencoder (DSSAE), was used for

COVID-19 classification. The authors also used an improved data augmentation method to prevent overfitting. The performance of the proposed model was compared with different state-of-the-art models, and its COVID-19 classification accuracy was demonstrated (S.-H. Wang et al., 2021).

Various studies have been conducted on CT images using deep learning methods to distinguish between patients with and without COVID-19 (Mei et al., 2020; Zhang et al., 2020). Many of these studies classified cases into different categories, such as normal, non-COVID-19 pneumonia, or non-pneumonia during the classification stage (Song et al., 2020; S. Wang et al., 2021; Xu et al., 2020).

A U-Net with an attention mechanism was applied to CT images, which is an efficient tool for COVID-19 diagnosis, with the aim of assisting in diagnosis and patient monitoring. Experimental results evaluated on a COVID-19 segmentation dataset containing 473 CT slices showed that the proposed method could achieve accurate and fast segmentation results in COVID-19 cases (Zhou et al., 2021).

Application

An experimental study was conducted using a dataset obtained and made accessible in Moscow, for the classification of patients as COVID-19 positive or negative. The dataset consists of CT images of approximately 1100 patients from four classes. It includes CT scans of patients with COVID-19 findings, as well as scans without such findings (Morozov et al., 2020).

The experimental study followed the classification of patients into four classes based on the extent of lung involvement: Class 1 includes patients with normal lung tissue, Class 2 includes patients with 25% lung involvement, Class 3 includes patients with 25-50% lung involvement, and Class 4 includes patients with over 75% lung involvement. Inspired by previous studies in the literature, for the experimental study, Class 1 patients, who do not have COVID-19, were considered as the first class, and Class 2 patients, who have 25-50% lung involvement, were combined with Class 3 patients, who have 25% lung involvement, to represent patients with COVID-19. This way, the classification problem was transformed into a binary classification problem. The study used a subset of the downloaded dataset, which included 100 COVID-19 patients and 100 patients with normal lung images who were classified as COVID-19 negative.

A 3D CNN was used to predict COVID-19 from CT scans. The data in Nifti format was read and then subjected to normalization to prepare it for input into the CNN. Normalization was performed using a threshold of -1000 and 400, which are commonly used in the literature. The data was resized to make it suitable for input into the CNN.

70% of the data set used in the experimental study is reserved for training. Half of the remaining 30% data set is reserved for validation and the other half for testing. Experiments were conducted using 3D versions of well-known CNN architectures such as ResNet and DenseNet (He et al., 2016; Huang et al., 2017). The original versions of these architectures were used without any fine-tuning. The experiments were conducted on Colab using TPU and GPU. A batch size of 2 and a learning rate of 0.0001 were set for each model. The sigmoid activation function was used for all models, and the Binary Cross Entropy loss function was used. The selected models were trained for 50 epochs, and the results obtained after training were evaluated.

The confusion matrix is a matrix used for evaluating classification performance in classification problems. It consists of four main elements based on the true class and predicted class values: True Positives (TP), False Positives (FP), True Negatives (TN), and False Negatives (FN). Performance metrics such as accuracy, recall, specificity, precision, and F-measure can be calculated using the confusion matrix. Accuracy represents the ratio of correctly classified examples to the total number of examples.

Recall shows the proportion of true positives that are correctly classified. Specificity shows the proportion of true negatives that are correctly classified. Precision shows the proportion of positive predictions that are truly correct. F-measure provides a summary of classification performance and measures the balance between precision and recall. The formulas for the basic evaluation metrics in the confusion matrix are presented in Table 1.

Table 1

The fundamental evaluation metrics and their formulas of the confusion matrix

Measure	Formula
Accuracy	$(TN+TP) / (TP+FP+TN+FN)$
Precision	$TP / (FP+TP)$
Recall	$TP / (FN+TP)$
Specificity	$TN / (FP+TN)$
F1-score	$2 * ((precision * recall) / (precision + recall))$

The results of the experimental study are presented in Table 2, showing the Recall values which represent the proportion of COVID-19 positive cases that were mistakenly predicted as negative by the model. A low Recall value indicates poor performance in correctly identifying positive cases. On the other hand, Precision value focuses on whether the cases predicted as positive by the model are truly positive. Striking a balance between Recall and Precision is important in this context. The Specificity metric indicates the proportion of COVID-19 negative cases that were correctly predicted as negative by the model. Based on these results, the highest accuracy rate was achieved with ResNet18 and ResNet50 architectures, with an accuracy rate of 86%. The F-measure values, which are a comprehensive metric that incorporates all error costs, were measured as 84% and 85% respectively for ResNet18 and ResNet50 architectures. Fine-tuning of the methods and expansion of the dataset can potentially lead to performance improvements.

Table 2

Experimental Study Results

Model	Accuracy	Recall	Specificity	Precision	F- Measure
DenseNet201	0,83	0,66	1	1	0,79
DenseNet169	0,8	0,6	1	1	0,75
ResNet18	0,86	0,73	1	1	0,84
ResNet50	0,86	0,8	0,93	0,92	0,85

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To Cite This Chapter:

Uymaz, S. & Uymaz, O & Kaya, E. (2023). Diagnosis of COVID-19 from 3D Medical Images using Deep Learning Approaches. In S.N. Guner, Y. Uzun & I. Cetin (Eds.), *Current Studies in Healthcare and Technology* (pp.73–87). ISRES Publishing.