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Detection of COVID-19 Using a Pre-trained CNN Model Over Chest X-ray Images

Mohammadreza Behnia[a], Touba Torabipour[b], Safieh Siadat*[c]

[a] Department of Computer Engineering and Information Technology, International Azad University Iran; qeshm,mbhnia@gmail.com

[b, c] Department of Computer Engineering and Information Technology, Payame Noor University (PNU), Tehran, Iran; s.torabi25@gmail.com[b], siadat@pnu.ac.ir[c]

ABSTRACT

Lung infection is the most dangerous sign of Covid 19. X-ray images are the most effective means of diagnosing this virus. In order to detect this disease, deep learning algorithms and machine vision are widely used by computer scientists. Convolutional neural networks (CNN), DenseNet121, Resnet50, and VGG16 were used in this study for the detection of Covid-19 in X-ray images. In the current study, 1341 chest radiographs from the COVID-19 dataset were used to detect COVID-19 including infected and Healthy classes using a modified pre-trained CNN (train and test accuracy of 99.75% and 99.63%, respectively). The DENSENET121 model has a training accuracy of 43.89% and a test accuracy of 57.89%, respectively. The train and test accuracy of ResNet-50 are, respectively, 89.43% and 90%. Additionally, the CNN model has test and train accuracy of 98.13% and 96.73%, respectively. The suggested model has COVID-19 detection accuracy that is at least 1% higher than all other models.

Keywords— Convolutional Neural Network, Deep Learning, Chest x-ray, COVID-19

1. Introduction

The coronavirus and Covid-19 virus were first identified in Wuhan, China, in November 2019. A month later, The World Health Organization (WHO) reported that the virus manifests as cough, fever, and pneumonia in clinical settings. Despite having its beginnings in China, the epidemic quickly spread around the world [1]. Since 2019, many techniques, including the nucleic acid (NAT) test, chest x-ray, and lung CT scan, have been utilized to diagnose Covid-19. Chest X-rays (CXR) are among the least expensive and most efficient COVID-19 detection techniques, even though diagnostic kits are successful in doing so [2].

since 2019, many studies were done by computer scientists on the diagnosis of covid19 with chest x-ray images, they used deep learning architectures, such as CNN with three to five hidden layers.and CNN architectures include DenseNet121, Resnet50, and VGG16. but the real challenge is how to build a useful model with an accuracy of over 98% to diagnose covid19 .for solving this challenge we propose a modified pre-trained CNN model with VGG16 architecture for diagnosis covid19. In Sections 2, 3, 4, and 5, respectively, the research background, methods, test and simulation findings, and conclusions will be provided.

2. Research Background

Unfortunately, early commercial CAD systems did not considerably enhance the effectiveness of breast cancer screening systems or provide radiologists with any assistance throughout the 1990s, according to the findings of prior studies. As a result, more than ten years after their inception, there was no advancement in this sector [3]. Since 2000, however, there has been a rise in research on illness detection by medical image diagnosis. Nevertheless, Block [4] was the first to employ CXRs and CT scans to diagnose the COVID-19 epidemic, although PCR tests provide superior results than CXRs or CT scans.

Tao [5] thought that clinical studies required the collection of patient samples, but the use of CXRs or CT scans, which are available even in distant locations, facilitates diagnosis.

Nine COVID-19 patients' CXRs or CT scans were examined by two radiologists for Meden Yi [6] in this study. The CT scan pictures with abnormal X-ray results were assessed. According to the data, there were 82.4%, 83.6%, and 33%, respectively, of non-SARS, non-M ERS, and non-o-covid-19 individuals in the first radiography findings.

In contrast, eight of the patients had double lung involvement as shown in the images. To put it another way, out of the nine patients, CXR images may not be the best model to identify Coved-19, but one weakness of their research was the sparse collection of images and test materials.

According to Fang et al. [7], CT scans have a substantially larger diagnostic impact than CXR pictures. This suggests that in regions with high incidence rates, CT scans should be the main imaging source for Covid-19 identification.

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*Coressponding Author

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A network named Covid-net was developed by Wang and Wong [8] to identify specific anomalies in Covid-19 CHR pictures. They used Covid-19 as well as databases on bacterial and viral illnesses. In 600 instances, 10 CT scans were found to be positive. Their network obtained 80% sensitivity and 89.9% accuracy. The dataset's small amount of CT scan pictures might be seen as the biggest drawback to their work. To diagnose Covid-19 from CHR images, Narin et al. [9] presented three deep-learning models: InceptionV3, ResNet50, and Inception-ResNetV2. This research made use of the Covid-19 dataset and CHR images of pneumonia patients. In this database, there are 50 CHR photos of healthy individuals and 50 CHR photographs of those with Covid-19. They achieved 97% accuracy for the InceptionV3 model, 87% accuracy for the Inception-ResNetV2 model, and 98% accuracy for the ResNet50 model after running the three aforementioned models. Using CHR images, Zhang et al. [10] employed a model built on the ResNet architecture to diagnose Covid-19. To improve the accuracy of COVID-19 classification, this model does two tasks: it classifies COVID-19 and healthy cases and it looks for anomalies. The pictures utilized in this investigation were from 1008 CHRs from other patient cases and 70 CHRs of COVID-19 patients. The CHR-based detection method has sensitivity, specificity, and accuracy values of 0.96, 70.7%, and 95%, respectively. A CNN model was suggested by Iqbal et al. [11] for COVID-19 infection detection from CXRs. It was a CoroNet deep CNN model. They made use of a dataset made up of CXR pictures from COVID-19 and other databases. For COVID-19 and other examples, the suggested model has achieved an accuracy of 89.5% and recall rates of 97% and 100%, respectively. A Bayesian CNN was suggested by Ghoshal and Tucker [12] to assess the diagnostic uncertainty in COVID-19 prediction. These researchers produced typical pictures from CXRs of pneumonia using 70 CXRs from an available COVID-19 dataset. They increased classification accuracy using the ResNet50V2 architecture, which produced a >0.90% accuracy. A novel CNN architecture called STM-RENet was suggested by Khan et al. [13] to understand the radiographic patterns from X-ray pictures. A block-based CNN that uses split-transform merge in a novel manner is the proposed STM-RENet. Exploring region homogeneity, intensity inhomogeneity, and boundary-defining features are made easier by using convolutional procedures in conjunction with the region and edge implementations in a systematic way. They used the CoV-NonCoV-15k dataset and the usual CNNs. The CoV-NonCoV-15k dataset identification has a sensitivity, specificity, and accuracy of 0.97%, 96%, and 96.53%, respectively. To help medical professionals that use computer-aided detection (CADe), Banerjee et al. [14] suggested an ensemble technique for deep learning models to handle the problem of COVID-19 detection from chest X-rays (CXRs). To merge the decision scores utilizing the blending algorithm using a Random Forest (RF) meta-learner, they use the technique of decision-level fusion for Convolutional Neural Networks (CNNs), leveraging the method of transfer learning for CNNs. The suggested model has an accuracy, recall, precision, and F1-Score of 98.13%, 100%, 92.59%, and 96.15% on the substantial COVID-X dataset. The lack of a modified pre-trained CNN approach with VGG16 architecture to accurately diagnose COVID-19 was the key area of study that needed to be filled. Albahri et al. [15] performed a Review of machine learning applications to diagnose COVID-19. this paper used five databases, IEEE Xplore, Web of Science, PubMed, ScienceDirect, and Scopus containing the coronavirus between 2010 and 2020. They focused on reviewing papers for COVID detection algorithms based on machine learning.

Torabipour et al. [16] suggested Convolutional Neural Networks (CNNs) for the detection of chest disease from chest X-rays (CXRs). this model can diagnose 14 main diseases of the chest such as (cardiomegaly, emphysema, effusion, hernia, nodule, pneumothorax, atelectasis, pleural-thickening, mass, edema, integration, penetration, fibrosis, pneumonia(covid19)).

The suggested model has an accuracy, recall, precision, and F1-Score of 98.93%, 94.77%, 89.17%, and 92.26% on the NIH dataset.

Alamoudi et al. [17] offered a review of papers on the detection of COVID-19. They used IEEE Xplore, Web of Science, PubMed, and ScienceDirect.the stages of this review are Identification, Screening, Eligibility, and Included. they found 28 papers and the result of this review illustrates the current data do have not enough quality in the future for the detection of new kinds of covid19.

3. Methodology

A Covid-19 database was built to choose the data for the current study. Using Train pictures [18] and the COVID-19 CXRs [19] database for COVID-19 patients, we constructed a valid database (CXRs, Pneumonia) for healthy persons in the Normal Section. Additionally, we utilized 804 and 537 CXRs from the COVID-19 database for training and testing. Additionally, 224 × 224 × 3 inputs and valid CNN models were employed. The research methodology, As seen in Figure 1.

3.1. Methods of COVID-19 detection

Deep learning models have recently been demonstrated to complete numerous clinical trials in the diagnosis of various diseases. These models outperform conventional mathematical models in several areas, including medical image processing and machine vision issues [20].

A CNN typically consists of three main layers: fully connected layers, pooling, and convolution. Different layers operate in different ways, which results in learning in the end. Use this network alone or in combination with other networks to categorize data and diagnose diseases.

CXR features are used in the present study to accurately classify CHRs into both COVID-19 and normal classes. Recent years have seen the usage of deep learning models for illness diagnosis. Five layers, subsampling, completely connected, flattening, and batch normalizing are common components of convolution neural networks (CNNs). In our present study, we employ a CNN with a pre-trained VG G16 to diagnose Covid-19 illness using CXR pictures. Finally, we will have two classes: Covid-19 and healthy.COVID-19 patients are detected by applying the suggested CNN-based models based on the following stages:

a) *Feature Extraction:* CNN employs many convolution layers and one subsampling layer at this level to oversee and evaluate probable features.

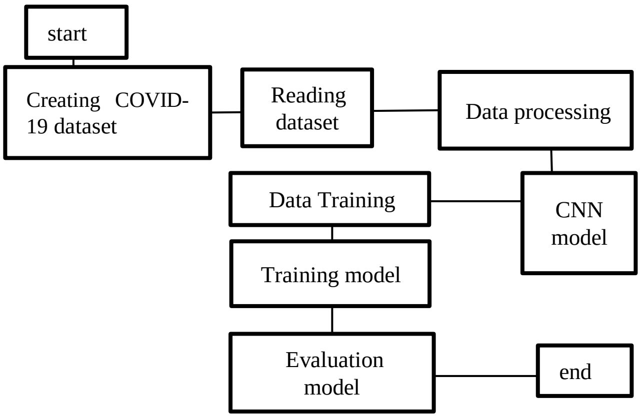

Figure. 1. The research methodology

Utilizing kernels or filters to extract good characteristics. To minimize the spatial dimensions, a max-pooling layer is then implemented. The issue of overfitting may be avoided by pooling characteristics. Then, we apply a subsampling layer with a window of size 2×2 and kernel size 2 (Figure 2).

To activate, we utilize a rectified linear activation (ReLU), which is a linear function and an output value between 0 (negative) and 1 (positive). This activation function is the default activation when developing many convolution layers because it's easier to train and often produces better results.

b) *Classification and Diagnosis:* The completely linked layers at this step classify the retrieved characteristics and determine the likelihood of illness. An activation function and a dropout () function are two functions that are used to build nonlinear connections and organize data. Finally, the fully linked layer created two classes to categorize the extracted attributes, separating sick from healthy people in both the COVID-19 and normal categories (Figure 3).

We will study the COVID-19 detection accuracy of the proposed model structure and other architectures, including Densenet121, Resnet50, and CNN.

3.2. Data Set

The dataset used Chest X-Ray Images (Pneumonia) collected for the Kaggle [18]. This dataset is organized into 3 folders (train, test, Val) and contains subfolders for each image category (Pneumonia/Normal). There are 5,863 X-Ray images (JPEG) and 2 categories (Pneumonia/Normal).

Chest X-ray images (anterior-posterior) were selected from retrospective cohorts of pediatric patients one to five years old from Guangzhou Women and Children's Medical Center, Guangzhou. All chest X-ray imaging was performed as part of the patient's routine clinical care.

For the analysis of chest x-ray images, all chest radiographs were initially screened for quality control by removing all low-quality or unreadable scans. The diagnoses for the images were then graded by two expert physicians before being cleared for training in the AI system. To account for any grading errors, the evaluation set was also checked by a third expert.

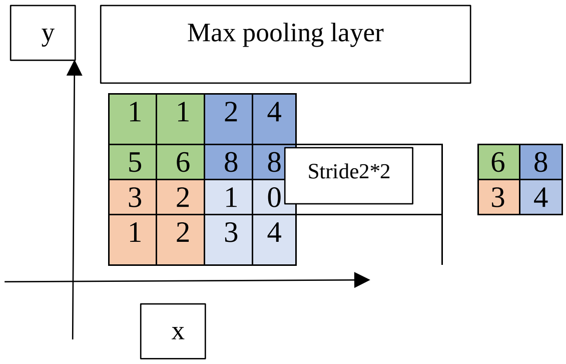

Figure. 2. Structure of 2x2 max pooling

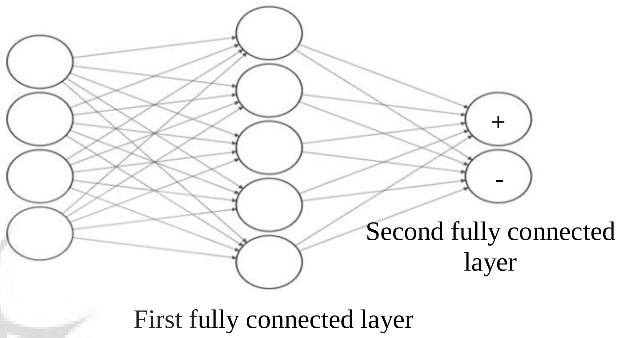

Figure. 3. Structure of classification covid-19 and normal.

The second dataset used in this work is COVID-19 X-ray images [19]. It includes COVID-19 cases as well as MERS, SARS, and ARDS.it has a metadata file with CSV format containing 16 features:

1. Patients (internal identifier, just for this dataset)
2. offset (number of days since the start of symptoms or hospitalization for each image, this is very important to have when there are multiple images for the same patient to track progression while being imaged. If a report says "after a few days" let's assume 5 days.)
3. Sex (M, F, or blank)
4. Age (age of the patient in years)
5. Finding (which pneumonia)
6. Survival (did they survive? Y or N)
7. View (for example, PA, AP, or L for X-rays and Axial or Coronal for CT scans)
8. Modality (CT, X-ray, or something else)
9. Date (the date the image was acquired)
10. Location (hospital name, city, state, country) importance from right to left.
11. Filename
12. DOI (DOI of the research article)
13. URL (URL of the paper or website where the image came from)
14. License

15. Clinical notes (about the radiograph in particular, not just the patient)
16. Other notes (e.g. credit) and 141 covid x-ray images.

4. Simulation

All models simulated in the present research used the Keras & TensorFlow library, The networks were designed in the Python simulation environment and then executed in the Spyder and Anaconda environments by applying the Keras library. Table 1 indicates Spyder hardware specifications.

The simulation's findings are shown step-by-step as follows:

4.1. Loading Dataset in Python

First, we load the dataset in python and display 25 CXRs in the Normal Section (Figure 4) and COVID-19 CXRs (Figure 5) as an example.

4.2. Proposed Model

Our Proposed model consists of several steps:

Pre-training Stage: We apply radiology images with a dimension of 224 * 224 * 3, and the data is pre-trained in the input layer with Vgg16 architecture.

Training Stage: The training phase itself is divided into several parts:

a) *Creating a COVID-19 dataset:* The valid database (CXRs, Pneumonia] was created for healthy people in the Normal Section using Train images and the COVID-19 CXRs database for COVID-19 patients. Based on the normal process for dataset creation, we now have 1,200 and 141 CXRs for healthy individuals and COVID-19 patients, respectively.

b) *Data processing:* In this part, the following four main and important actions are performed:

- Resizing and normalizing all CXRs
- Extracting all disease labels from the file name in the COVID-19 CXRs metadata helps us create the main classification classes.
- Creating two main classes, i.e., patient and COVID-19, according to the labels of Section 2.
- Data sharing: 60% for the training section and 40% for the testing section.

The training and testing data include 804 and 537 CXRs, each of which will be labeled.

c) *Creating the main CNN model:* It includes a convolution layer with three 3*3 filters to increase the number of output parameters from the pre-training stage.

- Size reduction: In this part, the output of the convolution layer goes to the classification section after applying a 2 *2 global average pool layer. There is a smoothing layer at the end.

Table 1. System hardware specifications

Hardware	*Description*
GPU	Intel(R) Iris(R) Plus Graphics
CPU	Intel, Corei7-1065G7
RAM	20.0GB
DISK	HS-SSD-E1000 256G

Figure. 4. CXRs of COVID-19 patients.

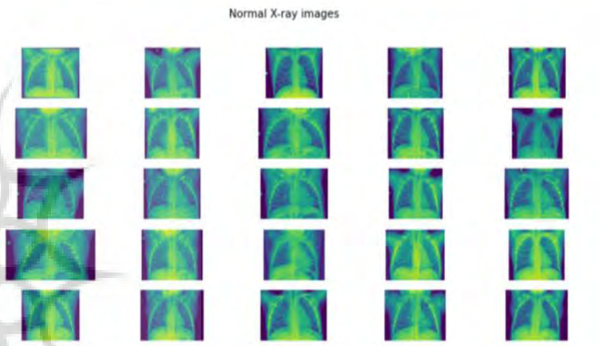

Figure. 5. Displaying 25 che.st X-rays of healthy people.

- Classification of classes: There are two fully connected layers and one dropout function (). The first fully linked layer has 64 neurons with the RELU activation function, whereas the second fully connected layer contains two neurons with the SOFTMAX activation function. For normalizing, we inserted a dropout () function between the two completely linked layers. At this point, the categorization is accomplished by completely interconnected layers, and we are left with two classes: COVID-19 and NORMAL.

Training data: At this point, the proposed CNN is trained with the needed 804 images using the proper weights. There are 10 iterations of this recursive step in the present research.

a) *Evaluating the model with testing data:* 537 CXRs are being tested at this time with the suggested CNN. There are two different sorts of classes in this project, COVID-19 patients and NORMAL, which eventually determine the type of class or sickness that is specified in the final result. The whole structure of the suggested model is shown in Figure 6.

The COVID-19-built datasets for this model included 804 CXRs (60%) and 537 CXRs (40%) for training and testing, respectively. Utilizes Relu activation function with Adam optimizer at Adam's learning rate. This network is trained ten times, and the data is categorized by a single digit. In the following, we need to introduce the VGG16 architecture:

VGG-16 is a deep learning model used in an article paper titled "Very Deep Convolutional Networks for Large-Scale Image Recognition." The “16” means that there are 16 convolution layers of the same weight [22].

The total number of parameters in our proposed model is 14,728,901, the number of learned parameters is 14,213, and the number of untrained parameters is 14,714,688.

4.3. Densenet121 Neural Network:

The DenseNet design begins with a convolution-pooling block, continues with a succession of dense block-transition layers, and concludes with a classification block consisting of a global medium pool layer, a fully linked block, and a global average pool layer. The input tensor undergoes a sequence of convolution operations with a given number of filters (k) in each dense block, and the output of each block is connected to the main tensor. Therefore, the number of input tensor feature maps increases by the number of convolution operations at each internal level of the dense block (k). The number of input tensor feature maps is cut in half in the transition layer [23]. There are the following layers in the classification block:

1. 7 × 7 global average pool layers
2. Fully connected layer with 1000 neurons

But DenseNet121 with the same structure consists of 121 convolution layers (Figure 7).

Out of 1341 CXRs employed in this model, 804 (60%) and 537 (40%) CXRs were used for training and testing, respectively, utilizing datasets integrated into COVID-19. The relu activation function and the adam optimizer were used with a learning rate of 0.0001. The data is separated into one-digit groups once this network has been trained ten times.

4.4. Resnet50 architecture:

Since taking first place in the 2015 ILSVRC, the Resnet50 architecture, a variety of CNN, has been widely used in computer vision. CNN dubbed the 152-layer architecture as its most complex. In contrast to deep CNNs, Deep ResNet runs the remaining connected layers between each layer and the output of the layer across from it. Each input feature for this procedure must use the data from its preceding two tiers. Two models are used to create the remaining connections from the standard neural network. The first model lessens the gradient; this issue is resolved by changing the gradient flow's course. The referenced functions are learned by the second model, which indicates that deeper or better layers are used or regarded as shallow layers [24]. The ResNet-50 network is used in this paper (Figure 8).

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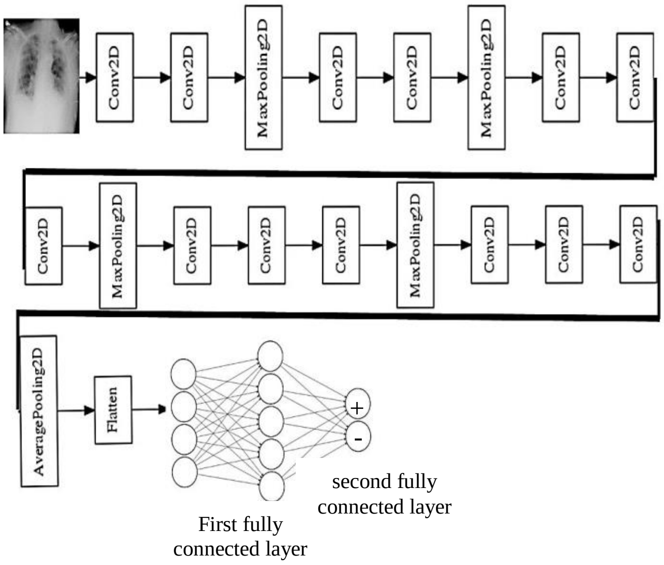


Figure. 6. Proposed model layers structure.

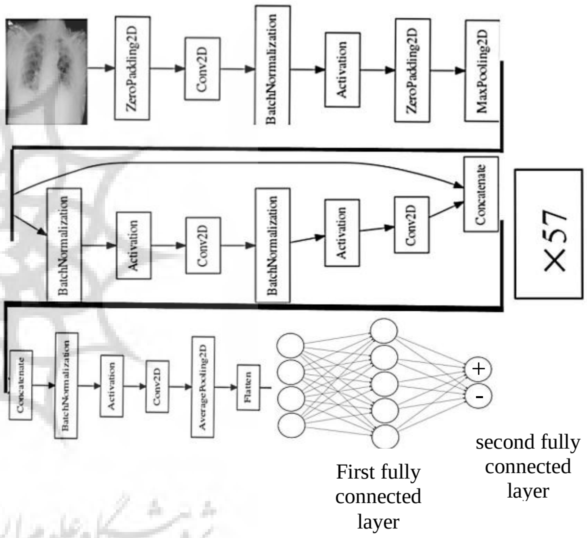


Figure. 7. Structure of dendenet121 architectural layers.

utilized the Adam optimizer and the relu activation function with a learning rate of 0.0001. The data is separated into one-digit groups once this network has been trained ten times.

4.5. CNN:

An example two-dimensional CNN with five hidden layers is shown in Figure 8. This network has a kernel of size 2 * 2, two convolution layers with 128 filters each, two convolution layers with 64 filters, two convolution layers with 32 filters, and two convolution layers with 16 filters. Convolutional networks are hierarchical neural networks in which two fully connected layers are joined by two convolutional layers that merge with alternating layers first (Figure 9). Ten convolutional layers and five pooling layers make up this network. Every layer that pools are a max-pooling layer with 2 * 2 steps. The smoothing layer must then transform the 2D output pooling layer into a 1D layer before sending it to fully linked layers. For all of the models utilized in the current investigation, the same padding was also used to fill the input data edges with comparable values in neighboring cells. Following the convolution layers, the data is divided into two categories: sick and healthy, using a fully connected layer with 128 neurons, a fully connected layer with 2 neurons, and a softmax activation function. The normalization layers and a dropout () function at 0.1 rates is taken into account after all convolutional layers to prevent overfitting. Relu is also the activation function used in this network's convolutional layers [25].

The total number of parameters in the CNN model is 402,946, trained parameters total 402,434, and untrained parameters total 512.

5. Evaluation

The objective of the present study was to categorize the CXRs of COVID-19 patients and healthy individuals. The categorization is assessed using the F1-score, precision, recall, and accuracy.

Accuracy, Equ. (1),is calculated by dividing the total number of instances by the number of successfully identified cases. A computed value's accuracy is how closely it resembles a genuine or natural value. This assessment criteria thus can measure a quantity whose precision can be assessed.

$$Accuracy = \frac{TP+TN}{TP+FP+TN+FN} \qquad (1)$$

Precision , Equ. (2),in deep learning architectures is calculated by dividing the number of properly labeled (labeled) things by the number of false-positive or true-positive ones.

$$\text{precision} = \frac{TP}{TP+FP} \qquad (2)$$

Recall , Equ.(3),refers to the number of correctly classified items to the total number of classified in a class.

$$\text{recall} = \frac{TP}{TP+FN} \qquad (3)$$

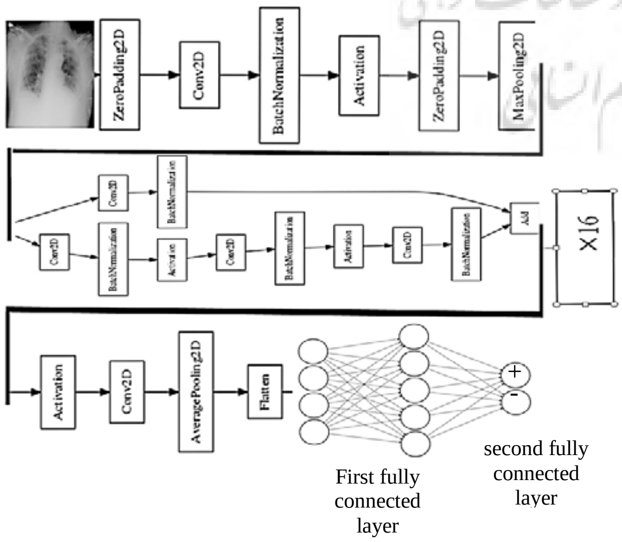


Figure. 8. Structure of Resnet50 architecture layer.

The F1-score value is computed using recall and precision calculations. The weighted average of recall and precision values is calculated using the F1-score as a criterion for classifying performance [22].

The classification algorithm's best and worst F1-score values are equal to 1 and 0, respectively.

5.1. Comparing the proposed method with other models

The outcomes of ResNet-50, DENSENET121, CNN, and the suggested model are shown in Table 2. The suggested model's training and test accuracies are 99.75% and 99.63%, respectively. The DENSENET121 has a training accuracy of 43.89% and a test accuracy of 57.89%, respectively. ResNet-50 has 89.43% train accuracy and 90% test accuracy, respectively. Additionally, the CNN model's training and test accuracies are 98.13% and 96.83%, respectively.

Figures 10-13 shows the results of comparing the accuracy, recall and precision, and F1 score values of studied models (Table 2).

Figure 14(a,b) shows the train and test accuracy and error analysis of the proposed model by observing the number of test rounds.

Figure 15(a,b) shows the train and test accuracy and error analysis of the densenet121 model by observing the number of test rounds.

Figure 16(a,b) shows the train and test accuracy and error analysis of the resnet50 model by observing the number of test rounds.

Figure 17(a,b) shows the train and test accuracy and error analysis of the CNN model by observing the number of test rounds.

Table 2. Results of 4 models

Architecture	*accuracy*	*precision*	*recall*	*F1-score*
Our model	0.99628	0.99632	0.99632	0.99632
DENSENET121	0.89572	0.89654	0.89654	0.89654
ResNet-50	0.896	0.90	0.90	0.90
CNN	0.96834	0.96875	0.96875	0.96875

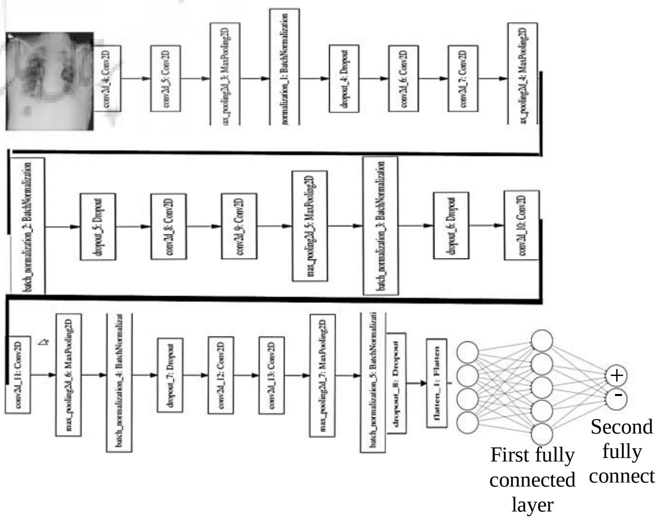


Figure. 9. CNN Structure Layer.

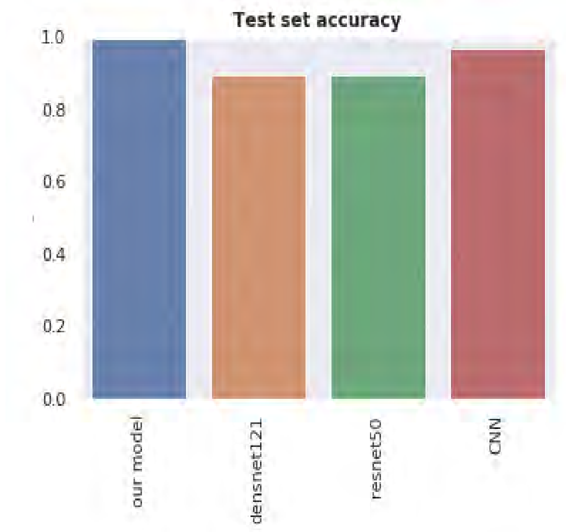


Figure. 10. The Accuracy values of the mentioned models.

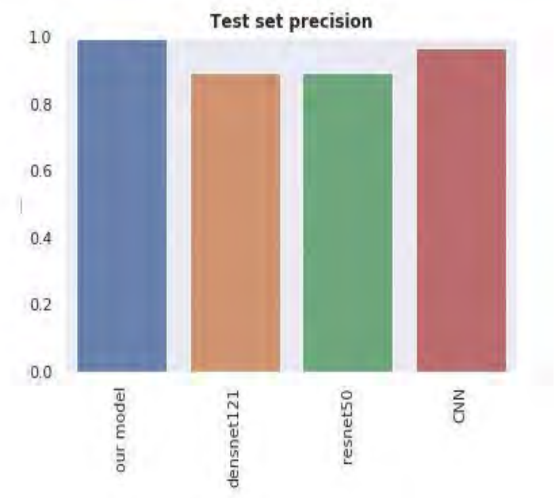


Figure. 12. The Precision values of the mentioned models.

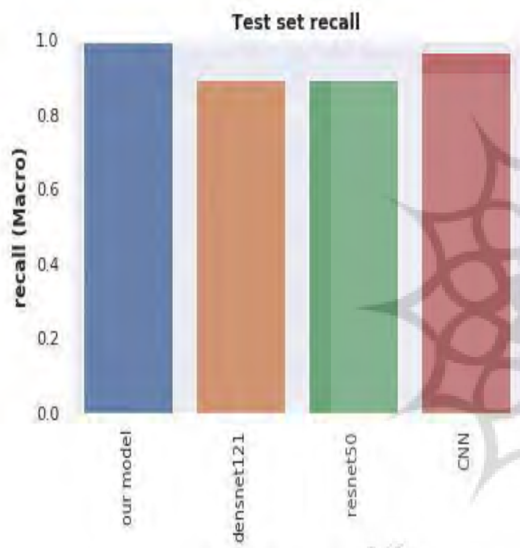


Figure. 11. The Recall values of the mentioned models.

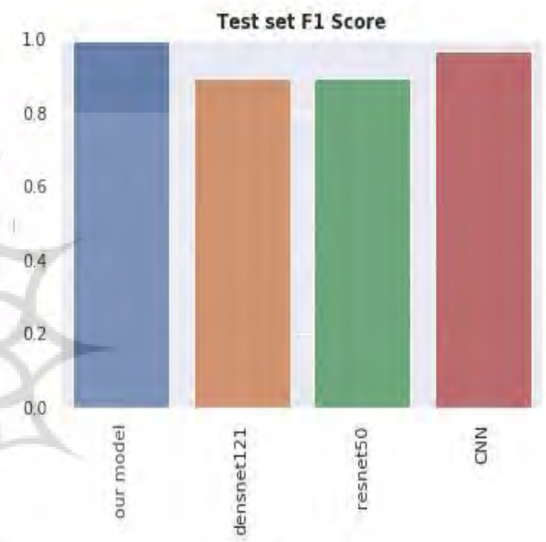


Figure. 13. The F1-score values of the mentioned models.

In medical research, it's crucial to reduce false-positive and false-negative outcomes throughout the modeling phase, particularly for COVID-19 disorders. Figures 18-21 displays the accuracy classification of all the previously described models as well as the false positive and negative effects as a confusion matrix.

The receiver operating characteristic (ROC) curve is one of the models used to assess the effectiveness of binary categorization. Medical decision-making often uses ROC, which has lately gained a lot of traction in data mining and machine learning models. Plotting true positive rate (TPR) vs false positive rate shows the ROC (FPR). This suggests that the ideal position is when TPR = 1 and FPR = 0. Figures 22-25 display the ROC of the aforementioned models as well as Classes 1 and 0 for COVID-19 illness. The above figure displays the ideal point for Class 0 and Class 1. The maximum value (area = 1) is applied to calculate the area under ROC (AUC).

6. Conclusion and Future Studies

In this research, we proposed a method for the diagnosis of Covid19 in 2 classes of COVID-19 patients and NORMAL, proposed model uses a modified pre-trained CNN model with VGG16 architecture. This method can detect covid19 with four evaluation parameters

Accuracy of 99.62%, a precision of 99.63%, a recall of 99.63% and a 99.63%f1-score.

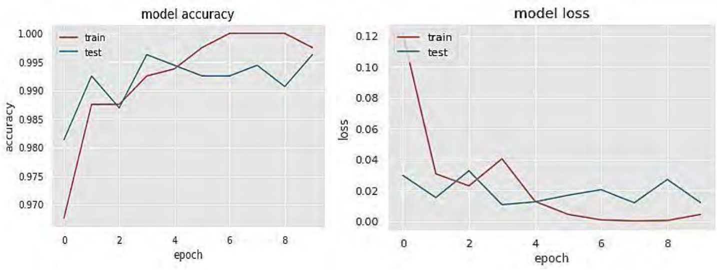
Compared to the proposed model with other models such as ResNet-50, DENSENET121, and CNN. the proposed model minimum of 1 percent better in accuracy, precision, recall, and an f1-score.

One of the distinctive features of this model compared to other deep learning architectures such as DenseNet121, and Resnet50, CNN reaches a maximum of 98% accuracy, although, using the proposed model reaches 99% accuracy.

Our proposed model can help in the fast detection of covid19 in deprived areas when we can't access physicians and just have cxray images.

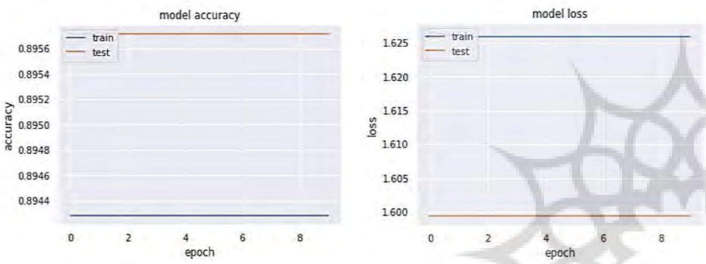
Atlast we suggesteing:

1. Using the proposed model for real big clinical data.
2. Developing the proposed model with maximum accuracy and minimum loss.
3. Build a web application to diagnose covid19 automatically.



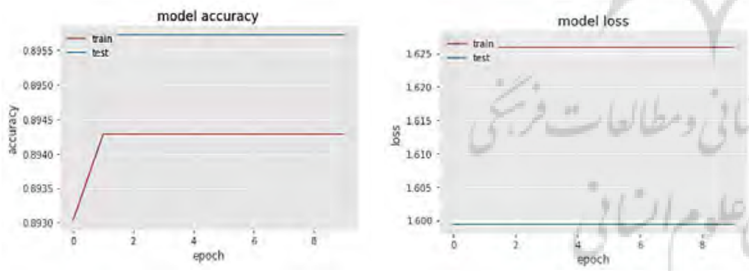
(a) (b)

Figure. 14. (a) The accuracy (b) The error of the proposed model.



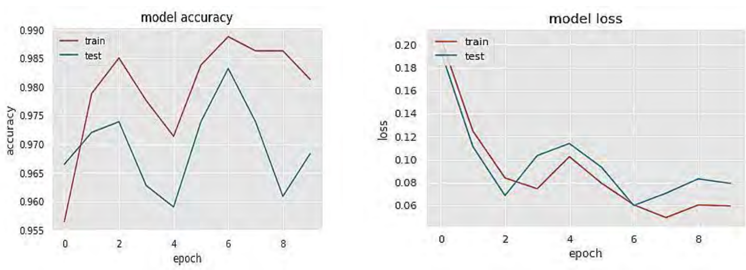
(a) (b)

Figure. 15. (a) The accuracy (b) The error of the densenet121 model.



(a) (b)

Figure. 16. (a) The accuracy (b) The error of the resnet50 model.



(a) (b)

Figure. 17. (a) The accuracy (b) The error of the CNN model.

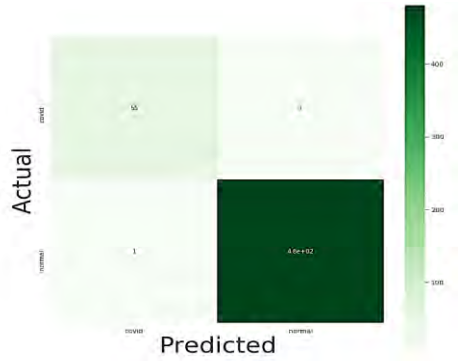


Figure. 18. The confusion matrix of the proposed model.

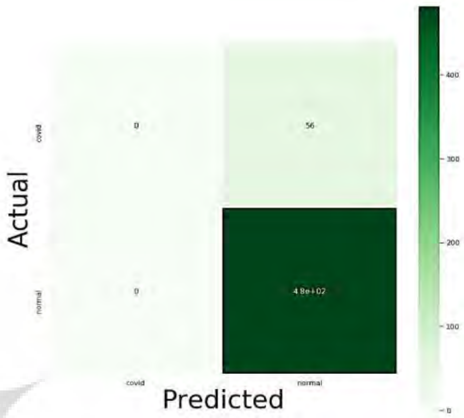


Figure. 19. The confusion matrix of the resnet50 model.

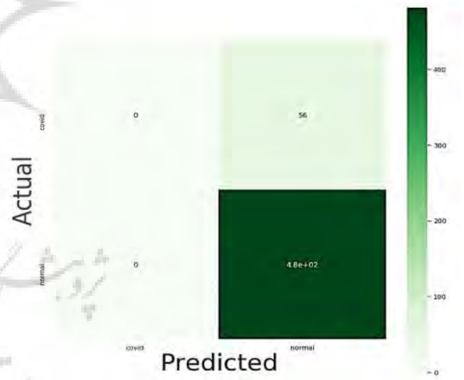


Figure. 20. The confusion matrix of the densenet121 model.

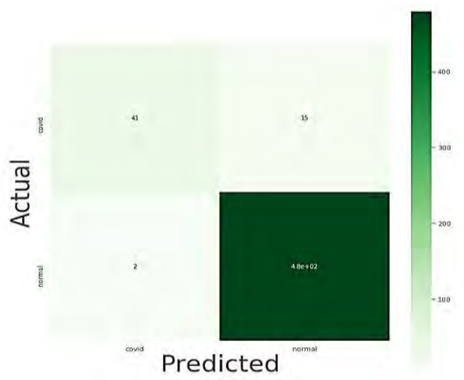


Figure. 21. The confusion matrix of the CNN model.

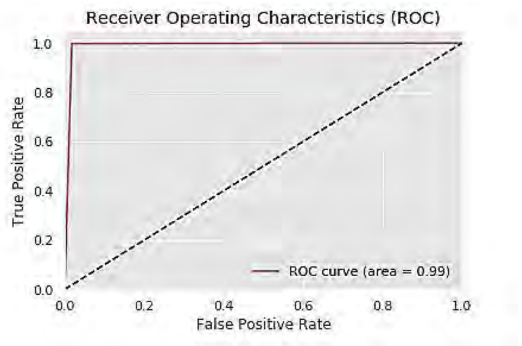


Figure. 22. The ROC curve of the proposed model.

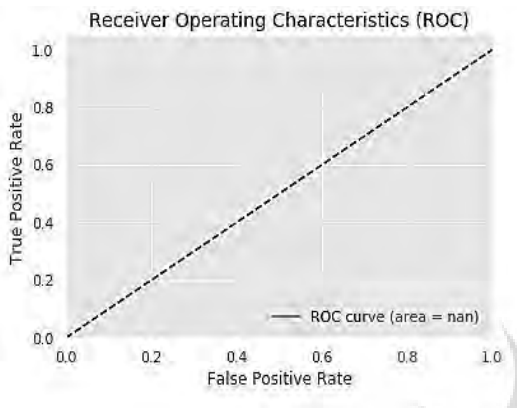


Figure. 23. The ROC curve of the densenet121 model.

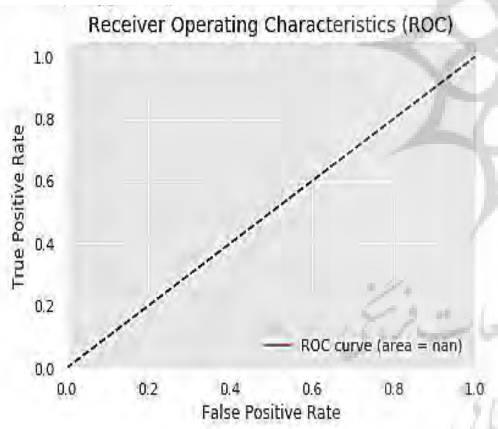


Figure. 24. The ROC curve of the resnet50 model.

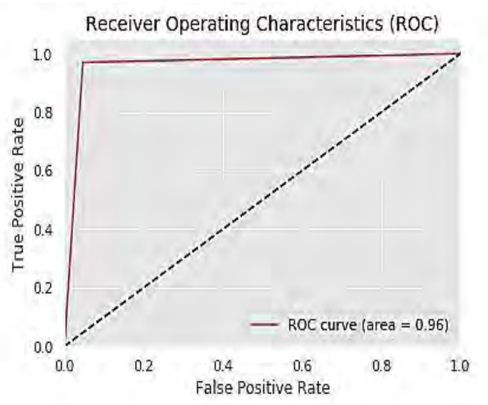


Figure. 25. The ROC curve of the CNN model.

Declarations

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Authors' contributions

MB: Study design, acquisition of data, interpretation of the results, statistical analysis, drafting the manuscript; TT: Study design, interpretation of the results, drafting the manuscript, revision of the manuscript; SS: Supervision, drafting the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

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Mohammad Reza Behnia completed his bachelor's degree in computer software engineering from Bandar Abbas Azad University in 2016, and he received a master's degree in the same field in 2021 at Qeshm Azad University, International Branch.

His field of activity is in the development of applications and the design of computer system architecture. He has designed several applications in these fields.

Touba Torabipour has a bachelor's degree, and a master's degree in computer engineering, majoring in software engineering. Her areas of interest include Deep learning, reinforcement learning, machine vision, artificial intelligence, and the Internet of Things. She has published more than 6 articles in prestigious Iranian and international journals and conferences.

Seyedeh Safieh Siadat, Assistant Professor, at Payame Noor University, has a bachelor's, master's, and doctoral degree in computer engineering majoring in software engineering. She has been a full-time faculty member at Payame Noor University since 1996. His areas of interest include the Internet of Things, game theory, machine learning, and cloud computing. She has published more than 42 articles in prestigious international journals and conferences