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Helping the Healthcare Providers to Differentiate Coronavirus Disease 2019 Pneumonias by Analyzing Digital Chest X-Rays: Role of Artificial Intelligence in Healthcare Practice

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Key Points:

- The major strength of this study is that it has developed a technology-based tool which can precisely detect COVID - 19 at an early stage and immediately isolate infected patients from the healthy population.
- This next generation test can be accessed by the healthcare providers remotely and therefore pose a prospect of convenience.
- The main limitation is that this tool may confuse with other Pneumonias if the quality of chest image is too low. Moreover, it focuses only on detecting whether or not it is COVID - 19, but not the severity of the disease.

Keywords: COVID - 19, Detection, Chest X-Ray, Artificial Intelligence, Bangladesh.

Abstract

Background: Detecting the Coronavirus Disease 2019 pneumonia, and differentiating it from other Community Acquired Pneumonias has been has been a challenging task for the healthcare providers since the pandemic begun. We therefore aim to develop and evaluate a simple, non-invasive tool to accurately detect COVID – 19 by using digital chest X-rays.

Methods: This is a retrospective, multi-center study where deep learning frameworks were used to develop the system architecture of the diagnostic tool. The tool was trained and validated by using data from the Github database and two hospitals in Bangladesh. Python programming was used to calculate all statistical estimates. Ethical approval was obtained, and administrative permission taken from the participating hospitals.

Results: This study revealed that the artificial intelligence- based diagnostic tool was able to detect COVID - 19 accurately by examining the chest X-rays. During the testing phase, the tool could interpret chest X-rays with precision of 0.98, recall/sensitivity 0.97 and F1 score 0.97 for COVID 19. The study evaluated the performance of the tool with real-life data from two hospitals in Bangladesh. The results showed high sensitivity (90%) and specificity (92%) in detecting COVID - 19. The AUC values for COVID - 19 and Pneumonia were 0.91 and 0.87 respectively.

Conclusions: This Artificial Intelligence- based diagnostic tool can offer the healthcare providers an effective means to detect and differentiate COVID – 19 from other forms of pneumonias, thus contributing to reducing the long-term impact of this deadly disease.

Background

The novel coronavirus, known as severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2, is responsible for coronavirus disease 2019 (COVID – 19) that primarily causes respiratory illnesses of varying severity ranging from common cold to fatal pneumonia [1-3]. The virus is highly transmissible which has ravaged the world since it was first identified in late 2019. So far it has affected millions of people, causing global pandemic and incapacitating the healthcare systems [2-5]. Although the SARS-CoV-2 potentially affects multiple organs of the human body, it mainly infiltrates the lower respiratory system triggering inflammatory changes in the lung tissue. Most of these infected patients commonly present with mild fever and dry cough, however, about one-fifth of all infected patients progress to severe pneumonia or even death [1,4-6].

Detecting COVID - 19 throughout the pandemic has been challenging and daunting task because of shortage of diagnostic tools in many countries. The detection was mostly dependent on a molecular technique called Polymerase Chain Reaction or PCR, which has been the most preferred testing procedure since the beginning of this pandemic. However, as the transmission of COVID - 19 escalated, the health systems of most countries struggled to provide the testing services to its entire population due to diverse technical, financial and logistical barriers [6-8]. Moreover, due to similarities of clinical presentations of COVID – 19 with other pneumonias, establishing correct diagnosis poses greater challenges to the health care providers. Accordingly, major medical societies in multiple countries recommended to use chest radiography to diagnose COVID – 19 pneumonia and also to differentiate from other community acquired pneumonias (CAP) [6]. In some cases, computed tomography (CT) scan has also been successfully used to detect COVID – 19 even with a negative PCR test or in patients without symptoms.

In almost all healthcare practices, clinicians use X-ray images to diagnose pneumonias and other lung diseases. Now a days, digital imaging machines – both static and mobile - are available in all hospitals and diagnostic centers; thus, digital X-rays are widely used for diagnostic purposes. However, the main challenge with the interpretation of the chest X-rays is that it requires a radiologist or a specialist doctor to do the analysis, and thereby can be time-consuming, and logistically inconvenient [6,7]. Moreover, it can become burdensome to the already stretched health system as more and more people are getting sick due to new COVID – 19 variants.

Use of artificial intelligence (AI) in the medical field is not new. Particularly deep learning method is being widely used in many healthcare settings due to its unique advantages in precisely detecting some complex health conditions, such as Tuberculosis and lung cancer [6-9]. Therefore, we hypothesized that an AI-based tool could be developed and trained to accurately detect COVID – 19 pneumonias and to differentiate them from other types of CAPs by using chest X-rays. In this paper, we present the system architecture of an innovative AI-based tool and the results of its validation and performance in differentiating the COVID – 19 from other forms pneumonias.

Methods

Development and Validation Data Sets

We trained our tool to distinguish X-rays of COVID – 19 from other CAPs. We also instructed the tool to isolate the chest radiology with no apparent abnormalities. Total 299 digital X-ray images were utilized to train this AI-based tool. Of them, 89 X-rays were COVID - 19 positive cases, 100 were diagnosed as Pneumonia cases, and 110 X-rays of 'normal' patients i.e. X-rays with no chest/lung diseases (Figure 1). The validation was carried out to evaluate the predicting power of the tool by using a sample of 24 chest X-rays of confirmed COVID - 19 patients, 234 images of CAPs, and 390 images of 'normal' patients.

Strict selection criteria were applied to select desired quality of chest X-rays. Only digital, Postero-anterior (PA) views of the images were used. For developing the tool, we used chest X-rays of confirmed COVID – 19 cases and the Community Acquired Pneumonias (CAP); and the X-rays of non-pneumonia or 'normal' cases. The X-rays of CAPs and 'normal' cases were selected randomly who fulfilled the inclusion criteria. Only confirmed SARS-CoV-2 cases were considered, who were anonymous but had a complete record ranging from the identification (ID) number, clinical history, and the final outcomes of treatment. Chest images from any unauthorized sources or of low resolution were discarded.

We have used chest X-rays from two hospitals in Bangladesh[1] and the COVID -19 X-ray images from the GitHub database [10]. Special attention was given to select X-ray images of

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those patients who had a complete trail of demographic and diagnostic history in the dataset. Although we used X-ray images of hospital patients, we had no direct contact with patients. All data were stored in a secure, encrypted database with strict security and privacy protocols in place.

(Place Figure 1 here)

Patient and public involvement

Although we have used the chest images from a known dataset, we did not directly involve patients or any other human participants. The study protocol was reviewed and approved by the university ethics committee and written permission was obtained from participating hospitals. Moreover, the data used was encrypted and anonymous.

Statistical analysis

In order to measure sensitivity and specificity, the AI-based tool was validated by randomly uploading data from the above-mentioned three data types. Rigorous statistical analysis was performed and the outputs of each round of validations were observed and recorded. These outputs were then compared with the WHO data set for accuracy and precision. The performance of the tool was analyzed and verified on the basis of standard measures such as sensitivity and specificity, and the receiver operating characteristic (ROC) curve and area under the curve (AUC). Python programming was used to calculate all statistical estimates. Furthermore, we have drawn a ROC curve which is the plot of sensitivity versus 1-Specificity. The AUC was also used for an effective measure of accuracy.

Results

In this section, we describe the system architecture of the AI-based tool and the results of the comparative performances of three deep learning image classifiers [11-13], which we experimented in this study.

Model architectures

For developing the system architecture, we examined different deep learning models which were derived from the field of artificial intelligence. These models are basically different architectures of Convolutional Neural Network (CNN) that has been a dominant method in computer vision tasks since the astonishing results were shared on the object recognition competition known as the ImageNet Large Scale Visual Recognition Competition (ILSVRC) in 2012. CNN uses multiple perceptrons that analyze image inputs and are able to segregate the images from one another. Another advantage of using CNN is that it leverages the use of local spatial coherence in the input images, which allow them to have fewer weights as some parameters are shared. This process is found to be efficient in terms of memory and complexity [14]. The basic building blocks of CNN are as follows:

Convolution layer

In the convolutional layer, a matrix named Kernel is passed over the input matrix to create a feature map for the next layer. We have performed a mathematical operation called convolution by sliding the Kernel matrix over the input matrix. At every location, an element wise matrix multiplication is performed and sums the result onto the feature map. Convolution is a specialized kind of linear operation which can be applied over more than 1 axis. If we have a 2- Dimensional image input, I, and a 2-Dimensional kernel filter, K, the convoluted image is calculated as follows:

$$S(i,j) = \sum_{m} \sum_{n} I(m,n)k(i-m,j-n)$$

Non-Linear activation functions

Activation function is a node that comes after the convolutional layer and the activation function is the nonlinear transformation that we do over the input signal. Different activations functions are:

a. ReLU: Rectified linear unit activation function (ReLU) is a piecewise linear function that will output the input if it is positive, otherwise it will output zero.

$$f(x)=max(0,x)$$

b. Leaky ReLU is a variant of ReLU. Instead of being 0 when $z<0$, a leaky ReLU allows a small, non-zero, constant gradient α (Normally, $\alpha=0.01$ $\alpha=0.01$)

$$R(z) = \{z \; when \; z > 0, z \; when \; z <= 0\}$$

c. Sigmoid takes a real value as input and outputs another value between 0 and 1. It's easy to work with and has all the nice properties of activation functions: it's nonlinear, continuously differentiable and it's used in the output layer when the classifier is binary.

$$S(Z) = \frac{1}{1 + e - z}$$

Pooling layer

A pooling layer is a new layer added after the convolutional layer, specifically, after a nonlinearity (e.g. ReLU) has been applied to the feature maps output by a convolutional layer. The drawback of the feature map output of a convolutional layer is that it records the precise position of features in the input. This means during cropping, rotation or any other minor changes to the input image will completely result in a different feature map. To counter this problem, we approached down sampling of convolutional layers. Down sampling was achieved by applying a pooling layer after nonlinearity layer. Pooling helped to make the representation become approximately invariant to small translations of the input. Invariance to translation means that if we translate the input by a small amount, the values of most of the pooled outputs do not change (Figure 2).

(Place Figure 2 here)

Fully Connected Layer

At the end of a convolutional neural network, the output of the last pooling layer acts as input to the Fully Connected Layer. There can be one or more of these layers. Fully connected means that every node in the first layer is connected to every node in the second layer.

Development of system architecture

In this study, we applied three different architectures of CNN such as: i) Visual Geometry Group Network 16 (VGG16), ii) Residual Networks 50 (ResNet50), and iii) Depthwise Convolution Neural Network (CNN) to assess their comparative performances in detecting COVID – 19 (Figure 3). The results of each of these tests were recorded.

Firstly, we studied the performance of VGG16 in distinguishing COVID – 19 and other Pneumonias. VGG16 is a convolutional neural network architecture. It was initially developed by the Oxford Robotics Institute's Karen Simonian and Andrew Zisserman which was first submitted to the 'ImageNet Large Scale Visual Recognition Challenge 2014 (ILSVRC2014)' where it performed very well and achieved 92.7% top-5 accuracy [15]. The first and second convolutional layers consist of 64 feature kernel filters and the size of the filter is 3×3. As the input image (RGB image with depth 3) passes into the first and second convolutional layer, dimensions change to 224x224x64. Then the resulting output is passed to the max pooling layer with a stride of 2. The third and fourth convolutional layers are of 124 feature kernel filters and size of filter is 3×3. These two layers are followed by a max pooling layer with stride 2 and the resulting output will be reduced to 56x56x128. The fifth, sixth and seventh layers are convolutional layers with kernel size 3×3. All three use 256 feature maps. These layers are followed by a max pooling layer with stride 2. Eighth to thirteen are two sets of convolutional layers with kernel size 3×3. All these sets of convolutional layers have 512 kernel filters. These layers are followed by a max pooling layer with stride of 1. Fourteen and fifteen layers are fully connected hidden layers of 4096 units followed by a softmax output layer (Sixteenth layer) of 1000 units.

Secondly, we deployed ResNet-50 which is also a convolutional neural network[14] that is 50 layers deep as below:

- At first there is a convolution with a kernel size of 7 * 7 and 64 different kernels all with a stride of size 2 giving us 1 layer.
- Next we got max pooling with also a stride size of 2.
- In the next convolution, there was a 1 * 1,64 kernel following this a 3 * 3,64 kernel and at last a 1 * 1,256 kernels, These three layers were repeated in total 3 times so giving us 9 layers in this step.
- Next we saw kernel of 1 * 1,128 after that a kernel of 3 * 3,128 and at last a kernel of 1 * 1,512 this step was repeated 4 times so giving us 12 layers in this step.
- After that there was a kernel of 1 * 1,256 and two more kernels with 3 * 3,256 and 1 * 1,1024 and this is repeated 6 times giving us a total of 18 layers.
- And then again a 1 * 1,512 kernel with two more of 3 * 3,512 and 1 * 1,2048 and this was repeated 3 times giving us a total of 9 layers.
- After that we did an average pool and ended it with a fully connected layer containing 1000 nodes and at the end a softmax function so this gives us 1 layer.
- So totaling this it gave us a 1 + 9 + 12 + 18 + 9 + 1 = 50 layers Deep Convolutional network.

This network allowed us to load a pre-trained version of the network trained on more than a million images from the ImageNet database. As a result, the network has learned great feature representations for a wide range of images.

Thirdly, we examined the performance of Depthwise CNN which is another deep learning, artificial intelligence function that mimics the functioning of the human brain in processing data and creating models for decision-making use. The Depthwise convolution model is a 2D convolution which helps to reduce overfitting when the number of parameters is high. It deals not just with spatial dimension but with depth dimension as well as the number of channels. What we do here is apply a 2D depth filter at each depth level of input tensor in our dataset so that we have 3*4095*4095(input channels, max width, max height). The filter we have used to extract feature is 3*3*3. So the Depthwise convolution will break the image and filter into 3 different channels and then convolve the corresponding channel and then stack them back. After that we used 1*1 filter to cover the dimension. Here the amount of parameters is reduced by the number of input channels. The feature from Depthwise spatial convolutional model send to fully connected layers where the output layer consists of 3 nodes (Covid-19, CAP, and Normal)

(Place Figure 3 here)

Finalization of System Architecture

The comparative analysis showed that VGG16 performed better results among the three deep learning image classifiers used in this study (Figure 4). It was observed that the VGG16 was able to read Covid-19 images more accurately compared to ResNet50 and Depthwise CNN with precision of 0.98, recall/sensitivity 0.97 and F1 score 0.97 (Table 1). Once the tool was fully trained, the model was recalibrated and refined based on the outputs of the testing process. The whole process was random and was meticulously monitored and recorded. After several repetitions, the model was finally ready for validation.

Table 1: Comparison of used deep learning models

Type of Data	Sensitivity %	Specificity %	AUC
VGG 16	97	99	98
ResNet50	95	98	97
Depthwise CNN	96	97	97

(Place Figure 4 here)

Performance evaluation of the Tool

The age group of the study population and patients of data sources was between 20 and 90 years.

The tool was found to be very quick in processing any given X-ray image. On an average, it took 5.7 seconds to complete while we ran the tests through our server. It was also observed that the model was able to accurately detect COVID - 19 as the tool/model detected 96% of cases as true positive. On the other hand, it exhibited a high power of rejecting non COVID – 19 cases as specificity is approximately 98%. In addition, the results showed low false positives and false negatives, which gave us confidence about the accuracy of the model. Similarly, the model could also identify pneumonia and normal images fairly accurately (Table 2). It is important to note that the proposed model has achieved a low rate of false negatives, as a high rate of false negative diagnoses may have moral, ethical, financial and social implications.

Table 2: Validation results of the Tool

Type of Data	Sensitivity %	Specificity %	AUC
COVID – 19 (n=24)	90	92	91
Normal (n=234)	8	8	84
Pneumonia (n=390)	86	88	87

We have evaluated our AI-based tool for detecting COVID - 19 by using chest X-rays from confirmed Bangladeshi COVID - 19 cases. The evaluation results showed high sensitivity (90%) and specificity (92%) in detecting COVID - 19. The AUC values for COVID - 19 and Pneumonia were 0.91 and 0.87 respectively (Table 2).

Both ROC and AUC curves played a central role in evaluating diagnostic ability of tests to show the true state of disease condition, finding the optimal cut off values (close to sensitivity 100%), and AUC was close to 1. Figure 5 reveals that ROC and AUC as alternative diagnostic tasks performed well in this case.

(Place Figure 5 here)

(Note: Class 0 is covid-19, class 1 is Normal and class 2 is Pneumonia)

While evaluating the model, it has been observed that there is a strong relationship between pneumonia and having a COVID - 19 (figure 6). This may partly be explained by the fact that COVID - 19 causes serious pneumonia.

(Place Figure 6 here)

Operationalizing the Tool

We have developed a website to operationalize the AI-based tool (www.helpus.ai). The website can be accessed and used by health facilities or medical professionals both domestically and internationally, provided they have computer access. New users will need to register and have their account verified before they will be granted a login ID to access the website. A webmaster will monitor and manage the system in order to protect the system from unscrupulous use. A short online training program is included to enable new users to use the detection tool. The system is user-friendly and consists of a minimum interface. Authorized users can upload the digital X-ray image to be tested on the website. The program will detect if a valid chest X-Ray image (PAV) has been uploaded otherwise it will reject it. If a valid image has been submitted the results of the test will be displayed instantly. Our system is tuned to display “positive” or “negative” results along with a percentile probability of that image whether it is “COVID - 19”, “Pneumonia” or “Normal”. The entire process can take a few seconds to a couple of minutes, depending on the computer and connection speed of the user. The data provided by the users can be stored in our cloud-based server while maintaining security and privacy protocols. The data can be retrieved by users and are accessible by the research team for future analysis.

Discussion

The pace of transmission of different variants of COVID – 19 is so exponential that many health systems are facing an uphill battle to cope with the testing of COVID – 19 and detection of COVID – 19 induced pneumonias [1,6]. Traditionally, the chest X-ray is part of the routine check-up for patients with respiratory symptoms, and digital imaging is widely accessible even in resource-poor healthcare settings. Therefore, integrating the proposed AI-based tool to help the healthcare providers to analyse combination of chest radiography in their existing general practice. Our results provide evidence that this AI-based tool has the potential to improve the quality and accuracy of the radiologic interpretation of COVID - 19 pneumonias. We also believe that it can be acceptable to both healthcare workers and the patients, and can become relatively inexpensive compared to other diagnostic methods. Intensive efforts has been made in recent years to generate evidence which suggest that the examination of radiologic images was found to be an effective method for diagnosing COVID – 19. Others have demonstrated that AI technology was able to read chest X-rays and Computed Tomography (CT) scans to detect different lung diseases, especially pneumonias, lung cancers and Tuberculosis [6-9, 16-18]. However, the main challenges are either to get a radiologist to interpret the chest radiographs, or even inability to differentiate COVID – 19 pneumonias from other CAPs if the radiologist is not trained in reading the COVID – 19 radiographs. In our study, we demonstrated that a fully developed AI-based tool can read any chest radiographs with high precision. We have also operationalized the tool via a user-friendly software which instantly display the correct result once the chest X-ray is scanned. The software can be operated by any service provider having basic IT knowledge. During evaluation, our AI-based tool showed excellent performance with high sensitivity (90%) and specificity (92%) in detecting COVID – 19 pneumonias. The AUC values for COVID - 19 and Pneumonia were 0.91 and 0.87 respectively. Our result corroborates with the outcomes of other similar efforts where machine learning models were trained to diagnose COVID – 19. However, most of those studies were limited in their scope and dataset. Only couple of studies had relatively larger data set with varying degree of precision. Some studies also trained the machine learning tools to detect COVID - 19 by analyzing CT scans.

In Bangladesh, the digital imaging is available in almost everywhere, both in rural and urban clinics. Due to technological advancements, good quality digital imaging machines are also in good supply. Even there are mobile imaging units in the most remote areas of the country, which allows the clinicians to get the chest imaging done as and when they need. In our study, we systematically validated the tool by using the real-life data from two hospitals in Bangladesh. We also included a good number of chest X-rays of random patients with no know chest symptoms to train and test our tool to differentiate the non-pneumonia or 'normal' cases.

During the testing and validation, our AI-based tool performed very well to identify COVID - 19 by analyzing 2D chest radiology PA view. We have further evaluated the AI tool by using chest X-rays of COVID – 19 patients from two Bangladeshi hospitals. We demonstrated that our tool had high sensitivity and specificity which conforms to previous studies [6-9, 16-18]. However, the uniqueness of our model is that it is simple and is able to differentiate three scenarios – COVID – 19 pneumonias, CAPs, and those with no obvious abnormalities; by analyzing. readily available digital chest X-rays instead of CT scans which, in turn, could easily be integrated within the regular medical practice.

Although our AI-based tool was able to accurately detect COVID - 19, this research has some limitations. As COVID - 19 is caused by a type of coronavirus, it may produce similar changes in the chest imaging as of CAP. This tool may sometimes give incorrect results only if the image quality is too poor. However, during our validation process, it consistently produced highly accurate results for randomly selected X-ray images. Another limitation was that due to the limited availability of data, we were unable to extensively evaluate the tool with real-time Bangladeshi data. Lastly, the tool focuses only on detecting the existence of COVID - 19, not the severity of the disease.

Conclusion

In this study, we developed a simple, non-invasive AI based tool for the diagnosis of COVID – 19 pneumonias by using traditional chest X-rays, which can assist the government and the private healthcare workers who are attempting to triage both symptomatic and asymptomatic COVID – 19 patients. We demonstrated that our AI-based tool was effective to detect COVID - 19 and could differentiate COVID - 19 from other CAPs by analyzing the chest X-rays. Therefore, it gives a glimpse of hope to the policy-makers and service providers who are striving for an alternative diagnostic tool to screen, detect and triage the mass population for COVID - 19. However, further validation of this tool may be needed with larger datasets before operationalizing it nationwide.

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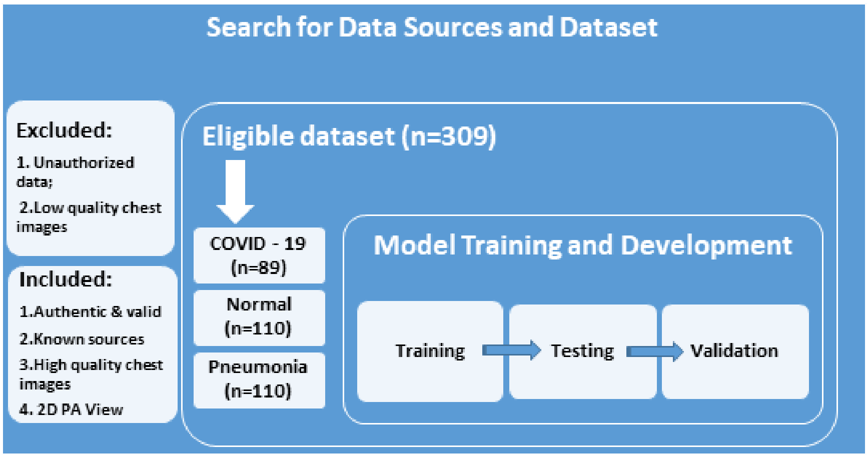
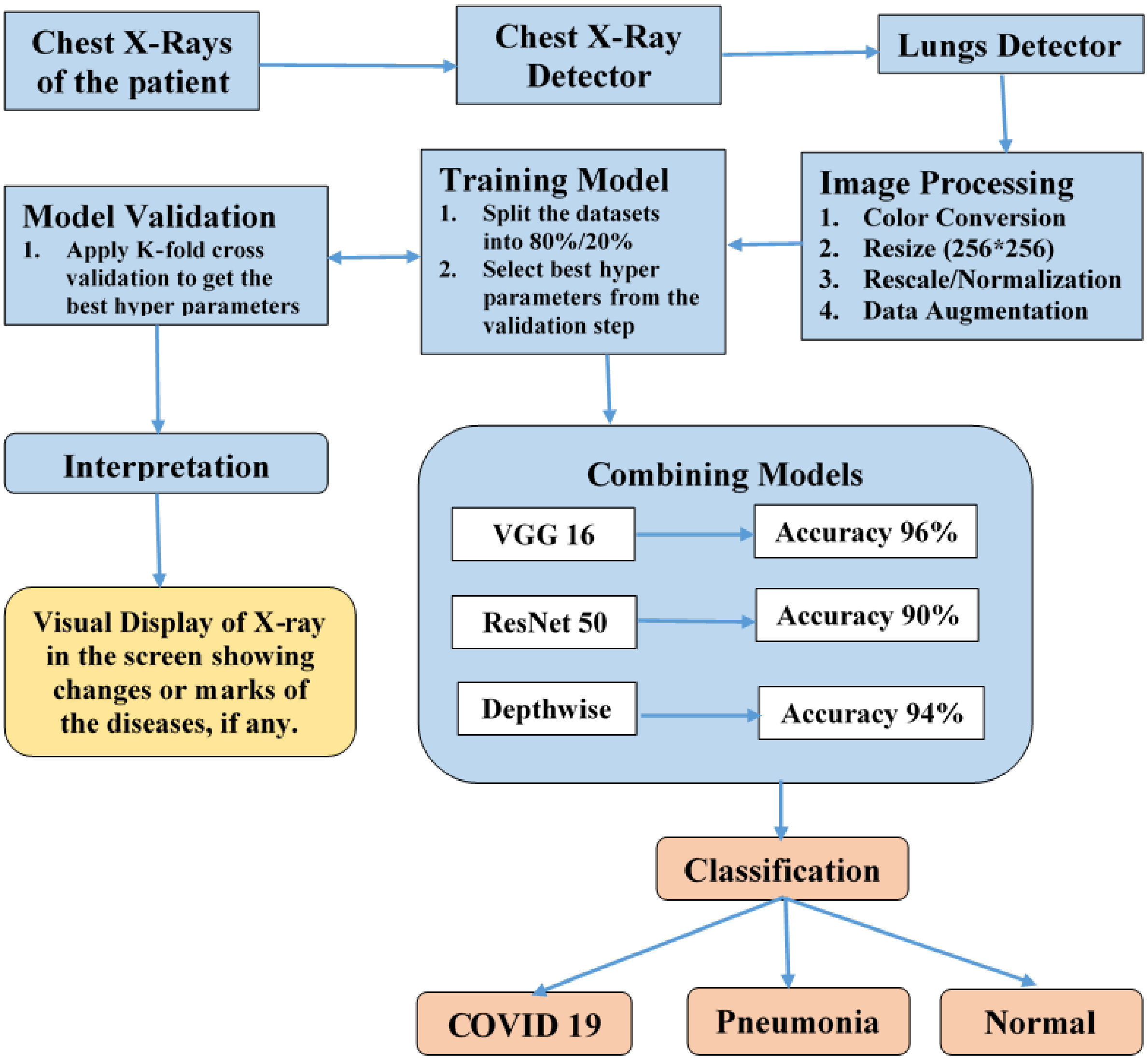
List of Figures:

1. Figure 1: Data used to train the model.

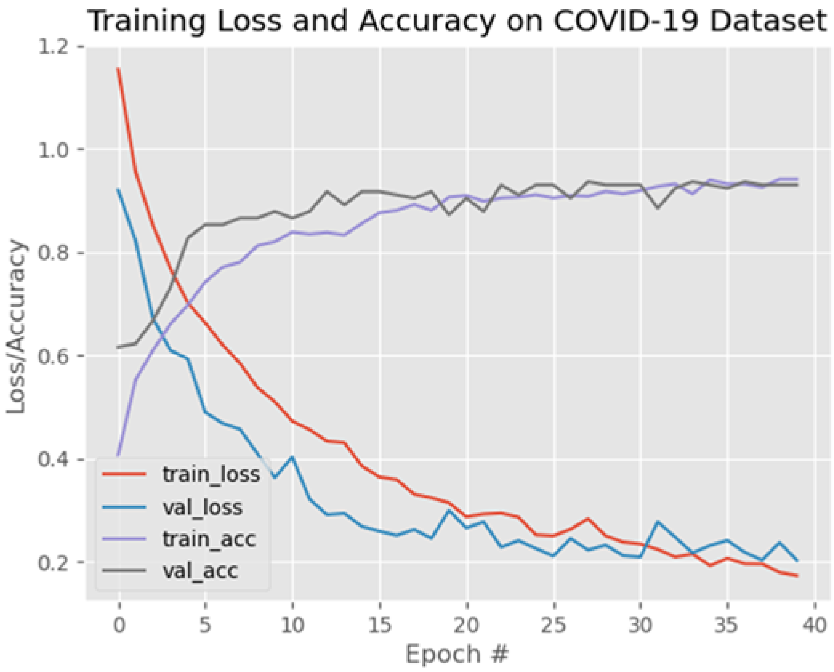


2. Figure 2: Types of pooling

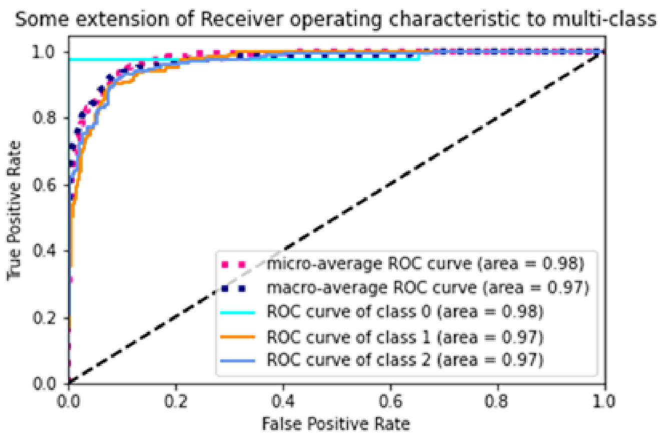
3. **Figure 3: System architecture.**



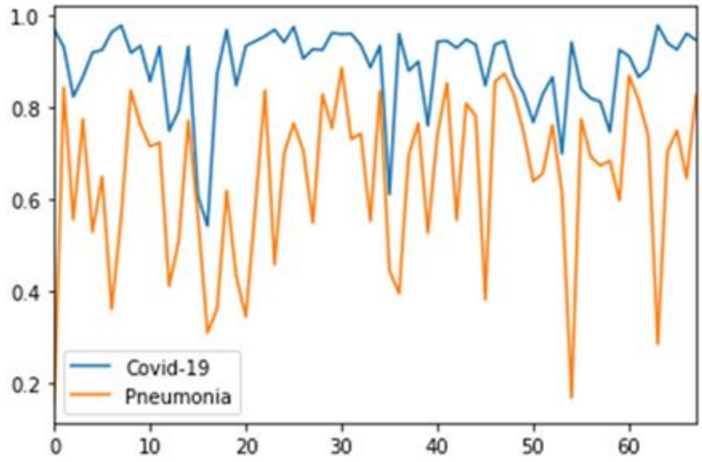
4. **Figure 4: Power of VGG16 in detecting COVID-19 images accurately.**



5. **Figure 5: ROC and AUC curves for the diagnostic tests.**



6. Figure 6: Relationship between Covid-19 and Pneumonia.



Declarations:

Ethical considerations

The research protocol has been approved by the Research Ethics Committee, Faculty of Allied Health Sciences, Daffodil International University (FAHS-REC, DIU) and participating hospitals. The ethics ID number is FAHS-REC/DIU/2020/1002. Only publicly available data were used, and no identifying participant information was obtained.

Data Availability Statement:

The data that support the findings of this study are openly available in Github at https://github.com/ieee8023/covid-chestxray-dataset. The local hospital data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors have declared no conflicts of interests.

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Author Contributions:

Abu Naser Zafar Ullah (ANZU) is responsible for the design, planning and leading the study. ANZU drafted the article, on which all authors made important contributions. Md. Habibur Rahman (HR), Shaikh Muhammad Allayear (SMA), Mohammed Liakwat Ali Khan (LAK) and Sheikh Md. Faysal (SMF) designed the system architecture and participated in collection, extraction, analysis and interpretation of the data. SMA contributed to the technical design of the software and revised the methods section of the article. NU participated in the collection and extraction of local data. Hafiz TA Khan (HTAK) and A B M Alauddin Chowdhury (AC) contributed to the methodology of the study especially in sampling and statistical analysis. ANZU led the process of analysis and interpretation of findings with active contribution from all authors. All authors have revised the article for important intellectual content, and approved the final version of the article for publication.

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