Highlights of the Article

- A simultaneous deep learning computer-aided diagnosis (CAD) based on the YOLO predictor is proposed to detect and diagnose COVID-19 lung disease from the entire chest X-ray images.
- The COVID-19 lung disease is automatically detected and classified end-to-end with overall detection and classification accuracies of 96.31% and 97.40%, respectively.
- The proposed deep learning CAD system is able to detect and classify COVID-19 or other lung diseases in a single X-ray image within 0.009 seconds.
- The presented CAD system is able to predict 108 frames per second (FPS) at the real-time of prediction.
Fast Deep Learning Computer-Aided Diagnosis against the Novel COVID-19 pandemic from Digital Chest X-ray Images

Abstract

Background and Objective: The novel coronavirus 2019 (COVID-19) is a harmful lung disease that rapidly attacks people worldwide. At the end of 2019, COVID-19 was discovered as mysterious lung disease in Wuhan, Hubei province of China. World health organization (WHO) declared the coronavirus outbreak a pandemic in the second week of March 2020. Simultaneous deep learning detection and classification of COVID-19 from the entire digital X-ray images is the key to efficiently assist patients and physicians for a fast and accurate diagnosis.

Methods: In this paper, a deep learning computer-aided diagnosis (CAD) based on the YOLO predictor is proposed to simultaneously detect and diagnose COVID-19 among the other eight lung diseases: Atelectasis, Infiltration, Pneumothorax, Mass, Effusion, Pneumonia, Cardiomegaly, and Nodule. The proposed CAD system is assessed via five-fold tests for multi-class prediction problem using two different databases of chest X-ray images: COVID-19 and ChestX-ray8. The proposed CAD system is trained using an annotated training set of 50,490 chest X-ray images.

Results: The suspicious regions of COVID-19 from the entire X-ray images are simultaneously detected and classified end-to-end via the proposed CAD predictor achieving overall detection and classification accuracies of 96.31% and 97.40%, respectively. The most testing images of COVID-19 and other lung diseases are correctly predicted achieving intersection over union (IoU) with their GTs greater than 90%. Applying deep learning regularizers of data balancing and augmentation improve the diagnostic performance by 6.64% and 12.17% in terms of overall accuracy and F1-score, respectively. Meanwhile, the proposed CAD system presents its feasibility to diagnose the individual chest X-ray image within 0.009 second. Thus, the presented CAD system could predict 108 frames/second (FPS) at the realtime of prediction.

Conclusion: The proposed deep learning CAD system shows its capability and reliability to achieve promising COVID-19 diagnostic performance among all other lung diseases. The proposed deep learning model seems reliable to assist health care systems, patients, and physicians in their practical validations.

Keywords: COVID-19; Coronavirus 2 (SARS-CoV-2); Lung Diseases; Artificial Intelligence (AI); Deep Learning; Diagnosis.

1. Introduction

Coronavirus 2019 (COVID-19) has recently become an unprecedented public health crisis worldwide [1]. At the end of December 2019, the positive cases of COVID-19 were discovered with unknown lung disease in Wuhan, Hubei province of China [2]. In the 25th of January 2020, at least 1,975 patients have been positively reported with COVID-19 since the first case was hospitalized on the 12th of December 2019. This new pandemic is caused by a new coronavirus named severe acute respiratory syndrome coronavirus 2 (SARA-CoV-2) [3,2]. The typical symptoms of COVID-19 include fever, shortness in breath, dizziness, cough, headache, throat, fatigue, and muscle pain [3,4,2]. After discovering the first positive case of COVID-19 in
Wuhan, the virus is rapidly spread to more than 200 countries in the world by passengers who carry the virus but in the early stage of its life cycle [1]. The pandemic of COVID-19 has caused a huge strain on the public health systems, health infrastructure, and economies of most countries in the world [5]. Because the total number of infected people by COVID-19 goes up rapidly, the capacity of healthcare systems (i.e., beds, ventilators, care providers, masks, … etc.) is extremely required to help people. Due to the rapid transmissible of COVID-19 from person to person, millions of people have been infected, more than four billion people are staying at home, and many people lost their jobs [1,2,5]. In fact, the severe acute respiratory syndrome of COVID-19 has caused death in humans worldwide [6]. As reported by the world health organization (WHO) on June 12, 2020 [6], the number of confirmed, recovered, and death cases affected globally by COVID-19 have been reached 7,596,987, 3,841,493, and 423,844, respectively. Moreover, the regular education systems in schools and universities have been negatively affected by COVID-19 and converted to remote education systems.

Up to date, the most widely screening tool used to detect and diagnose COVID-19 is a real-time reverse transcription-polymerase chain reaction (RT-PCR) [7]. The radiological imaging techniques such as chest digital X-ray (CXR) and computed tomography (CT) are the standard screening tools used to early detect and diagnose chest lung diseases including COVID-19 [1,8]. Due to the low sensitivity of the RT-PCR, the symptoms of lung diseases can be detected also by examining the radiological images as well. Although the scanning tool of CT is the gold standard, the primary chest digital X-ray systems are still useful because they are faster, lower dose, cheaper, and more widespread [8,4]. Indeed, the scanning routine of CT or X-ray imaging should to be effectively used beside the RT-PCR for improving the diagnosis accuracy of the COVID-19 [8]. In contrast, the huge number of patients who positively tested with COVID-19 makes the regular screening methods a daily challenge for physicians. Thus, the white house of America, on March 16, 2020, announced and encouraged the experts and researchers to employ artificial intelligence (AI) techniques to fight the novel pandemic of COVID-19 [1]. Nowadays, the experts start using machine learning and deep learning technologies for developing CAD systems to help and assist the physicians for a more accurate diagnosis of COVID-19 [1,8]. In the last few years, the applications of deep learning methods have been earned much interest to become an adjunct screening tool for physicians. Deep learning CAD systems proved their reliability and capability achieving a promising diagnostic performance using the entire image without user intervention [9,10]. The use of a deep learning CAD system shall to assist and improve the physician’s decision for COVID-19 [1]. Deep learning CAD systems have been successfully applied to predict different medical problems such as breast cancer [9,10], skin cancer [11,12], brain disease [13], funds image disease [14], and lung disease from digital X-ray images [8]. The rapid spread of the novel COVID-19 pandemic to kill humans in the world raises the necessity to use and apply deep learning technologies for developing CAD systems aiming to improve the diagnostic performance. This has increased the interest and inspired us to develop a deep learning CAD system to simultaneously predict COVID-19 from the entire digital X-ray images.

In this paper, our contributions to spontaneously diagnose COVID-19 from digital X-ray images are addressed as follows. First, a simultaneous deep learning CAD system via YOLO predictor is adopted and used to detect and diagnose COVID-19 against other lung diseases. Second, the COVID-19 is diagnosed against eight lung diseases in a multi-class recognition problem. Third, deep learning regularizations of data balancing, augmentation, and transfer learning are also applied aiming to improve the overall diagnostic performance of COVID-19
against other diseases. Finally, our proposed CAD system is trained and assisted using five-fold tests from two digital X-ray datasets, COVID-19 \cite{15,16} and ChestX-ray8 \cite{17}. The outcomes of this study should guide other researchers for developing a novel deep learning CAD frameworks to accurately diagnose the pandemic of COVID-19.

The objective of this work is to provide a practical and feasible CAD system based on AI to help physicians for faster and more accurate diagnosis of COVID-19.

The rest of this paper is organized as follows. The literature review of the latest works is presented in Section 2. The technical methodology of deep learning CAD-based YOLO system is detailed in Section 3. The results of the experimental study of COVID-19 are reported and discussed in Sections 4 and 5, respectively. Finally, the most important findings from this work are concluded in Section 6.

2. Related Works

Starting the year 2020 after discovering a novel COVID-19, some artificial intelligence (AI) systems based on deep learning have been employed for detecting the COVID-19 pandemic from digital images of X-ray and CT. Ozturk et al. \cite{8} proposed a deep learning DarkCovidNet to automatically detect the COVID-19 from digital chest X-ray images. They developed their model using 17 convolutional layers aiming to perform diagnosis of the binary (i.e., COVID-19 and No-finding) and multi-class (i.e., COVID-19, No-finding, and pneumonia) problems. They achieved overall classification accuracies of 98.08% and 87.02% for binary and multi-class classification problems, respectively. In May 2020, L. Wang et al. \cite{18} proposed a COVID-Net based on deep learning model to recognize COVID-19 against normal and pneumonia lung diseases from the digital X-ray images. The classification of their model was compared with the performances of VGG-19 and ResNet-50 using the same database of digital X-ray images \cite{18}. They concluded that COVID-Net outperformed VGG-16 and ResNet-50 achieving positive predictive values (PPV) of 90.50%, 91.30%, and 98.9% for normal, pneumonia, and COVID-19 cases, respectively. E. Hamdan et al. \cite{19} presented a deep learning COVIDX-Net model to classify COVID-19 against normal cases from 50 digital chest X-ray images. They used seven well-established deep networks as feature extractors and compared their classification results. They concluded that VGG-19 and DensNet201 achieved the highest diagnostic performance with 90% comparing other deep learning models. Apostolopoulos et al. \cite{20} tested five well-established deep learning networks to detect COVID-19 from digital X-ray images. They classified three lung diseases of normal, pneumonia, and COVID-19 and they achieved the best overall classification accuracy of 93.48% using VGG-19. Also, they tested all five deep learning models for a binary classification problem (i.e., COVID-19 against None-COVID-19) and they achieved the highest accuracy of 98.75% using VGG-19. Khan et al. \cite{21} proposed a deep learning convolutional neural network (i.e., CoroNet) to diagnose COVID-19 in multi-class problem from the whole chest X-ray images. They achieved overall accuracy of 89.6% for COVID-19 against pneumonia bacterial, pneumonia viral, and normal cases. Narin et al. \cite{22} compared the classification performances from three different deep learning convolutional neural networks (i.e., ResNet-50, InceptionV3, and InceptionResNetV2) using chest X-ray images. They evaluated these three models for detecting COVID-19 against normal cases and they achieved the best classification accuracy of 98% using ResNet-50. Sethy and Behera \cite{23} also employed well-established nine deep learning models with a support vector machine (SVM) to diagnose COVID-19 from digital X-ray images. They concluded that the deep learning model of ResNet-50 coupled with the SVM classifier achieved the best
diagnostic performance with 95.38%. Pereira et al. [7] presented a classification scheme based on the well-known texture descriptors and convolutional neural network (CNN). They used the resampling algorithm to balance the training dataset for a multi-class classification problem. Their model achieved an average F1-score of 65%. Such deep learning methods are employed to diagnose the novel COVID-19 cases from the whole input X-ray images. This is due to the lack of annotated X-ray images for the suspicious regions of the lung diseases. Indeed, the recognition of the whole X-ray image cannot provide a proper practical solution for reliable diagnosis of COVID-19 [24]. Thus, the detection of most mistrustful regions involving only the lung diseases is a key for more accurate diagnosis since it helps to derive more representative deep features of abnormalities. Based on our knowledge, this is the first time to develop a regional convolutional deep learning CAD system to simultaneously detect and classify the COVID-19 among all other different lung diseases from the entire chest X-ray images. The automatic detection of COVID-19 is a big challenge for researchers. Our previous promising diagnostic results from the breast cancer diagnosis CAD system using the YOLO predictor [9,10] have encouraged us to employ it for detecting and classifying COVID-19 aiming to enhance the diagnostic performance of the COVID-19.

3. Material and Methods
Deep learning computer-aided diagnosis (CAD) based on YOLO predictor is presented to simultaneously detect and classify the pandemic of COVID-19 against other eight lung diseases: Atelectasis, Infiltration, Pneumothorax, Mass, Effusion, Pneumonia, Cardiomegaly, and Nodule. The presented CAD system is validated and verified to simultaneously detect and

![Figure 1. Schematic diagram of the proposed deep learning CAD system based on the YOLO predictor.](image-url)
classify COVID-19 in a unique deep learning framework structure. **Figure 1** depicts the conceptual diagram of the proposed CAD system.

### 3.1. Digital X-ray Images Dataset

To achieve this work, we use two different digital chest X-ray databases namely, COVID-19 [15,16] and ChestX-ray8 [17]. The data distribution for both datasets is shown in **Figure 2**.

**Figure 2.** Data distribution over all nine classes of lung diseases. Dataset per each class is randomly split into 70%, 20%, and 10% for training, testing, and validation, respectively.

#### 3.1.1. COVID-19 Dataset

In this study, the COVID-19 dataset is collected from two different publically sources. First, we use the digital X-ray COVID-19 images collected by Cohen et al. from different public sources as well as through indirect collection from hospitals and radiologists [15]. These images are publically available to help expert researchers for developing AI based on deep learning approaches to improve the prediction and understand the crisis of COVID-19. The researchers from different countries try constantly to update and add more X-ray images to enlarge the size of this dataset. At present, we use all available COVID-19 X-ray images acquired from 125 positive patients (i.e., 82 males and 43 females). Unfortunately, a complete metadata of these patients is not available for all cases yet. The feature of age information is only provided for 26 patients with an average of 55 years old. Second, we use the digital X-ray COVID-19 images that collected by a researcher team from Qatar university [16]. All these images are publically available in portable network graphic (png) file format with the size of 1024×1024 pixels. This dataset is publically provided for researchers to develop useful and impactful AI models to tackle the crisis of COVID-19. Also, the metadata of all positive patients is not provided yet. In this study, we use all digital X-ray COVID-19 images available at present composing of 201 positive cases (i.e., patients). Thus, a total of 326 chest X-ray imagers are collected and used to develop the proposed CAD system. Unfortunately, the information of the GT localization from both datasets are not available yet. Thus, we asked radiologist experts in hospital to manually annotate the localization of COVID-19 diseases. Then, the rectangle bound box to surround the localization of COVID-19 is generated representing the GT information. **Figure 3** shows some examples of positive COVID-19 cases with their GT information.

#### 3.1.2. ChestX-ray8

The ChestX-ray8 [17] dataset is the most frequent and commonly accessible medical imaging examinations available for diagnosis of different eight lung diseases: Atelectasis, Infiltration,
Pneumothorax, Mass, Effusion, Pneumonia, Cardiomegaly, and Nodule. In this study, we use all X-ray images having ground truth (GT) information involving the disease class label and the information of the disease localization as a labeled bounding box. The information of GT bounding box for each image is publically available in XML file [17]. As shown in Figure 2, a total of 984 frontal views of X-ray images are used covering all eight different lung diseases. These images are accurately converted from DICOM format into ‘.png’ file format with the size of 1024×1024 pixels. Figure 4 shows an example of X-ray image for each class with their GT information.

3.2. Data Preparation: Training, Validation, and Testing
To fine-tune and evaluate the proposed CAD system, COVID-19 [15,16] and ChestX-ray8 [17] datasets are used. As shown in Figure 2, the chest X-ray images per class are randomly divided into 70% for learning, 20% for evaluation, and 10% for validation [9,10]. The hyper trainable
parameters of the proposed deep learning system are selected via the training process with using training-validation sets [25]. After that, the final performance of the proposed CAD system is assessed using testing set [26,27]. Figure 5 shows our strategy to train and test the proposed deep learning CAD system. Meanwhile, our proposed CAD system is assessed using five-fold tests for training, validation, and testing datasets. These sets are generated by stratified partitioning to equally test each X-ray image and to avoid system bias error [25,9,10]. Figure 6 shows the strategy of five-fold cross-validation used in this study. Indeed, using k-fold cross-validation is an important procedure to develop a robust, reliable, and efficient CAD system especially with the small size of the medical dataset [9,11,10]. In addition, to prevent the proposed prediction model during the learning process for any potential bias that may occur due to the unbalancing training set, we use some other remedies as follows. First, the training set per each mini-batch is automatically shuffled [28]. Second, a weighted cross-entropy is used as a loss function to optimize the deep learning trainable parameters [28],[29].

**Figure 5.** Training-testing strategy for the proposed CAD system for each fold test.
3.2.1. Balancing and Augmentation Strategies for Training Dataset
Data balancing and augmentation strategies are applied to enlarge the size of the training datasets, avoid overfitting, and speed-up the learning process [9,10]. These practical solutions are successfully applied to address the challenge of the small annotated medical images [9,10]. In the training time, the mini-batch should involve almost equal number of digital X-ray images per each class [30,31]. This is to revoke the overfitting and to prevent the deep learning model performance to be biased towards the majority class that has the largest number of instances (i.e., COVID-19). To balance training sets for matching the majority images of COVID-19, training image sets from ChestX-ray8 eight classes are flipped twice (i.e., left-right and up-down) generating 1,378 chest X-ray images. Thus, the total number of training images of all classes after balancing is 2,295 (i.e., 917: original images from all classes including COVID-19 and 1,378: balanced images from ChestX-ray8 for eight classes).

After data balancing, the augmentation strategy is applied for all nine classes as follows. First, the original chest X-ray images are randomly scaled and translated ten times. Second, the X-ray images per each class are rotated around the origin center via 0°, 45°, 90°, 135°, 180°, 225°, 270°, and 315°. Finally, the rotated X-ray images per each class with θ = 0° and 270° are flipped left-right and up-down. This means each X-ray image per each balanced class is augmented 22 times. Thus, in a total of 50,490 X-ray images are generated to train our proposed CAD system. For each k-fold test, the same strategy of data balancing and augmentation is utilized. In addition, the transfer learning is applied to initialize the trainable parameters using ImageNet [9,10]. Then, the deep learning CAD system is fine-tuned using our training chest X-ray images [32].

3.3. The Concept of Deep Learning CAD system
To simultaneously predict (detect and classify) COVID-19 among all other different lung diseases, a deep learning CAD system based on the YOLO predictor is developed. For object detection, the previous works are employed by using conventional image processing algorithms, machine learning classifiers, or complex deep learning pipelines [33-35,27]. In contrast, YOLO predictor is proposed as a regressor model to simultaneously detect the localization of the potential diseases and predict their corresponding class probabilities as well [10,36]. It has a robust functionality to learn the whole input X-ray image characteristics with its background.
simultaneously. Thus, it can predict the suspicious regions of lung diseases with fewer background errors comparing with other existing methods [37]. In addition, it has a unique deep learning structure allowing it to simultaneously optimize trainable parameters end-to-end for tuning the training weights for detection and classification tasks. Unlike Faster R-CNN [38] and sliding window [39] methods, YOLO inspects the suspicious disease regions directly from the entire chest X-ray images. The conceptual diagram of the CAD-based YOLO predictor is shown in Figure 1.

In fact, YOLO predictor starts to divide input X-ray image into N×N grid cells as shown in Figure 1. If the object (i.e., COVID-19 or any other lung diseases) center falls into any grid cell, that cell should be responsible to predict that disease. For each grid cell, five anchors (i.e., bounding boxes) are assigned and used to predict the object (i.e., COVID-19, Pneumonia, …etc). For each anchor, YOLO predicts the objects using five prediction parameters which are center location (x,y), width (w), height (h), and confidence score probability (Pr\text{conf}). The confidence score interprets the YOLO confidence in that predicted box contains a suspicious disease and how accurate it expects that box to represent the final output prediction.

During the training process, predicted confidence for each anchor is formulated as a multiplication of probability of the existing lung disease (i.e., object) and the value of the intersections over union (IoU) as follows,

$$\text{Confidence (Pr_{conf}) = Pr(Object) \times IoU_{GT}^{Pred}.}$$  

(1)

If the grid cell does not contain any lung disease, the confidence of all bounding boxes of that cell should be zeros. In contrast, if any suspicious disease falls in that grid cell, Pr(Object) should be greater than zero. Thus, the confidence of all bounding boxes of that cell should be greater than zero as well. However, the network is optimized to achieve the highest object probability as well as object confidence. Based on both object probability and IoU\text{GT}^{Pred}, the coordinates of all bounding boxes are simultaneously optimized and adjusted to fit the object that is falling in the specific grid cell. During the training process, each grid cell predicts the conditional class probabilities \(Pr(Class_i|Object)\) for all nine classes (i.e., COVID-19 and other lung diseases). During training, the confidence score for the detected bounding box is determined based on the conditional class probabilities as follows,

$$\text{Confidence Score} = \text{Pr(Class}_i\text{|Object}) \times \text{Confidence; } i = 1, 2, 3, \ldots, \text{and } 9 \quad (2)$$

where,

$$\text{Pr(Class}_i\text{|Object}) = \frac{\text{Pr(Class}_i)}{\text{Pr(Object)}}. \quad (3)$$

Then,

$$\text{Confidence Score} = \frac{\text{Pr(Class}_i)}{\text{Pr(Object)}} \times \text{Pr(Object)} \times \text{IoU}_{GT}^{Pred.} \quad (4)$$

At the testing time, to get the confidence score where there is no GT, the conditional class probability is multiplied by the individual box confidence value. The detected bounding boxes having the highest confidence represent that the COVID-19 or another lung disease is existed and should be considered as the final prediction output. However, the confidence score
probability for each detected bounding box encodes the probability of each class and how well this box fits the lung diseases. The confidence score for each box is computed as follows,

\[
\text{Confidence Score}_{\text{Box}_i} = \arg \max \{ \left( \Pr_{\text{conf}_1} \times \Pr(\text{class}_1|\text{object}) \right), \left( \Pr_{\text{conf}_2} \times \Pr(\text{class}_2|\text{object}) \right), \ldots, \left( \Pr_{\text{conf}_9} \times \Pr(\text{class}_9|\text{object}) \right) \}; \ i = 1, 2, 3, \ldots, 9.
\]

For each bounding box, only one class is predicted and assigned as COVID-19 or Pneumonia, Mass, … etc. As long as all bounding boxes are assigned to the same grid cell, the object type in these boxes should be same but they have different confidence and conditional probabilities. Finally, the detected box which has the maximum confidence probability should represent the final predicted output of the proposed CAD system. Moreover, all other detected bounding boxes having IoU_{\text{Pred.}} < 45% with lower confidence scores are suppressed using the algorithm of non-max suppression (NMS) [40,38,41].

3.3.1. Deep Learning Structure of the CAD System

The structure of the proposed CAD system involves convolutional layers, fully connected (FC) layers, and tensor of prediction (ToP) as shown in Figure 7. Deep high-level features are extracted utilizing twenty-three sequential convolutional layers (Conv.), while the coordinates of the detected bounding boxes and the output probabilities are predicted using two FC layers. The total number of derived deep feature maps depends mainly on the number of convolutional kernels that used for each convolutional layer. Moreover, the convolution reduction layers with the kernel size of 1×1 followed by 3×3 convolutional layers are added and utilized as shown in Figure 7. This is to reduce the size and compress the derived feature representations [9,10]. In addition, batch normalization (BN) layers are used after each convolutional layer to reduce the overfitting, speed-up the convergence, and stabilize the training of the deep network [9,10]. Down-sampling using max-pooling (MP) with a size of 2×2 is applied five-times after the convolutional layers to minimize the dimensionality of the derived deep feature maps and select the most proper deep features. The aggregated deep feature maps from the last convolutional layer are concatenated and flattened using global average pooling (GAP) to directly feed into the fully connected layers. The number of nodes or neurons for first and second dense layers is modified to be 512 and 4096, respectively. The final output of the proposed model called a tensor of prediction (ToP) where it contains the all detected predictors of the five anchors: coordinates \((x, y, w, \text{ and } h)\), confidence scores \((\Pr_{\text{conf}_i})\), and the conditional class probabilities of all nine classes \((\Pr_{\text{COVID-19}}, \Pr_{\text{Pneumonia}} \ldots \text{etc})\).

These predictors are encoded in the 3D matrix of ToP with the size of \(N \times N \times (5 \times B + C)\) where \(N, B, \text{ and } C\) represent the number of grid cells, number of anchors, and number of classes [42,10]. As mentioned above, the input X-ray image is divided into 7×7 non-overlapped grid cells where each grid cell should detect the object (i.e., COVID-19 or any other lung diseases) that shall be involved in that cell. Indeed, the size of 7×7 is chosen to achieve the best performance as investigated in our previous studies [43,9,10]. Meanwhile, five anchors or bounding boxes (i.e., \(B = 5\)) are used to detect the object in each grid cell. The proposed CAD system is built to detect and recognize nine classes of lung diseases (i.e., \(C = 9\)). Thus, the final output represents a 3D ToP with a size of 7×7×34. This means that the actual output layer of the fully connect has 7×7×34 or 1,666 neurons. Every 34 neurons, in the output FC layer, are responsible to predict all predictors for five bouncing boxes from each grid cell in the original chest X-ray image. Here, the key is that each grid cell can only make local predictions for its region from the input X-ray image. Due to that the proposed prediction model has the capability
to detect and classify the lung diseases faster comparing other recent detection methodologies [44]. Moreover, rectified activation function of linear leaky is utilized for all convolutional and fully connected layers [45,9,10], while the activation function of ReLU, $\phi(x) = max(0, x)$, is only utilized for the final dense layer [24]. The leaky activation function $\phi(\theta_i)$ is expressed the linear transformation of the input $\theta_i$ with a non-zero slope for the negative part of the activation function as follows,

$$\phi(\theta_i) = \begin{cases} \theta_i & \text{if } \theta_i > 0 \\ 0.1 \times \theta_i & \text{otherwise.} \end{cases}$$

3.4. Experimental Setting

The input digital X-ray images are normalized and scaled using the bilinear interpolation to the size of 448×448 pixels [9,10]. For training, the strategy of multi-scale training is used to learn prediction across different resolutions of the input X-ray images [42]. Since the proposed network downsamples the derived deep feature maps five-times, the network could choose randomly a new image dimension size in every 10 batches following multiplies of 32 (i.e., 320, 352, …, 608). Thus, the smallest input resolution is 320×320 and the largest input resolution is 608×608. Moreover, mini-batch size of 24 and number of epochs of 120 are utilized to train and validate the proposed CAD system.

3.5. Implementation Environment

To execute the experimental study, a PC with the following specifications is used. Intel® Core(TM) i7-6850K processor, RAM of 16.0 GB, 3.36 GHz, and four GPUs NVIDIA GeForce GTX1080.
3.6. Evaluation Strategy
The logic of our evaluation strategy follows two conditions to assign the detected bounding boxes as a final true detection. First, the overlapping ratio (i.e., $\text{IoU}_{\text{Pred}}^{GT}$) between the detected and its corresponding GT boxes should be equal or greater than a proper practical threshold. Second, the confidence score (i.e., $Pr_{\text{conf}}$) of the final detected box should be equal or greater than a proper threshold [46, 24]. Specifically, we always looking for a truly detected box that has a maximum confidence score [9, 10]. The high confidence score reflects the high accuracy of the object existing in the detected bounding box [9, 10].

For quantitative evaluation over each fold test, we use the weighted objective metrics including sensitivity (Sens.), specificity (Spec.), overall accuracy (Acc.), F1-score or Dice, Matthews correlation coefficient (Mcc.), positive predicted value (PPV), and negative predicted value (NPV) [9, 10]. To avoid the unbalancing testing sets from all nine classes, we use the weighted class strategy [24]. The weighted ratios for Atelectasis, Infiltration, Pneumothorax, Mass, Effusion, Pneumonia, Cardiomegaly, Nodule, and COVID-19 are recorded to be 0.14, 0.10, 0.08, 0.06, 0.12, 0.09, 0.11, 0.06, and 0.25, respectively. All evaluation indices are computed using multi-class confusion matrices over each fold test [9, 10].

4. Experimental Results
4.1. Detection Results
4.1.1. The Proper Threshold of IoU and Confidence Score
The presented CAD system is able to predict five anchors (i.e., bounding boxes) for each grid cell in the entire X-ray images. To suppress the undesired detected boxes having very small confidence scores, the non-max suppression (NMS) technique is used [42, 9]. This algorithm requires three consecutive stages during the testing phase. First, detected bounding boxes with confidence scores less than 0.005 are directly discarded [40]. Second, while there are any remaining boxes, the box with the highest confidence score (i.e., $Pr_{\text{conf}}$) is picked up to represent the final predicted bounding box [40]. Finally, any remaining boxes having $\text{IoU}_{\text{nms}} \geq 50\%$ with the final output predicted box in the second step are discard too. Figure 8(a) shows the potential predicted boxes after applying NMS. During the evaluation phase, the overlapping ratio of IoU between the final predicted box and its GT should be greater than a proper threshold to ensure the predicted box involves the object (i.e., lung diseases) with high confidence. Experimentally, we found that the proper threshold of $\text{IoU}_{\text{Pred}}^{GT}$ should be greater than 45% as shown in Figure 9(a). The majority of the final detected bounding boxes for the testing X-ray images possess the accuracy of IoU more than 90%. The final detected boxes having $\text{IoU}_{\text{Pred}}^{GT} < 45\%$ are considered to be false detection. Besides the controlling of IoU, we can also adjust the proper threshold of the confidence score to ignore the undesired detected boxes. Figures 8(b)-(d), show the detected bounding boxes according to different probability thresholds of the confidence score. Experimentally, we found that the proper confidence threshold should be greater than 10% as shown in Figure 9(b). This is to detect at least one suspicious region from each testing image for the diagnosis purpose.
4.1.2. Detection Results over 5-fold Cross-validation

The presented deep learning CAD system has the efficiency to automatically predict the suspicious regions of COVID-19 and other lung diseases from the whole input X-ray images. Table 1 shows the overall detection performance via 5-fold tests using the testing images from all nine classes. For each k-fold test, the same deep learning structure, training, and testing tunings of the presented CAD system are applied. The detected regions of interest (ROI) that involve the COVID-19 or other lung diseases are considered to be correctly detected if and only if \( \text{IoU}_{\text{Pred}} \geq 45\% \) with \( \text{Pr}_{\text{conf}} \geq 10\% \). Otherwise, they are considered to be false detection cases even if the \( \text{Pr}_{\text{conf}} \geq 10\% \). Indeed, the most correctly final detected bounding boxes possess the maximum IoU and confidence scores as well. As an average for 5-fold tests, the CAD-based YOLO presents its reliability and feasibility to reveal the COVID-19 with an overall detection accuracy of 96.31\%. Whereas, it fails to detect only 3.69\% of COVID-19 cases from all testing images. Generally, the presented CAD system has the capability to correctly detect lung diseases with an overall detection accuracy of 90.67\% from all nine classes. The true and false detection cases for the individual class over 5-fold test are presented in Table 1.
| Fold Test | Atelectasis | Infiltration | Pneumothorax | Mass | Effusion | Pneumonia | Cardiomegaly | Nodule | COVID-19 | Total Classes |
|-----------|-------------|--------------|--------------|------|----------|-----------|--------------|--------|----------|---------------|
| **Fold-1** | 32 True 4 False | 24 True 1 False | 15 False 2 True | 8 False 3 True | 12 False 3 True | 20 True 2 False | 62 True 3 False | 235 True 28 False |
| **Fold-2** | 31 True 5 False | 24 True 1 False | 16 False 1 True | 14 False 2 True | 20 True 2 False | 13 False 3 True | 26 True 4 False | 215 True 27 False |
| **Fold-3** | 31 True 5 False | 25 True 0 False | 16 False 1 True | 13 False 4 True | 22 False 2 True | 12 False 4 True | 63 True 2 False | 226 True 27 False |
| **Fold-4** | 33 True 3 False | 25 True 0 False | 15 False 5 True | 14 True 3 False | 20 True 4 False | 14 False 2 True | 63 True 2 False | 240 True 23 False |
| **Fold-5** | 33 True 3 False | 24 True 1 False | 16 False 5 True | 15 False 1 True | 30 False 1 True | 21 False 3 True | 64 True 1 False | 264 True 19 False |
| **Avg. (%)** | 88.89 | 11.11 | 97.60 | 2.40 | 71.50 | 28.50 | 90.59 | 9.41 | 91.61 | 8.39 | 86.67 | 13.33 | 97.24 | 2.76 | 78.75 | 21.25 | 96.31 | 3.69 | 90.67 | 9.33 |
For qualitative evaluating, Figure 10 shows examples of correctly detected suspicious lung diseases of COVID-19 and all other classes. The overlapping ratios (i.e., IoU) for the resulted bounding boxes beside their corresponding confidence scores from each case are presented as well. The detected boxes of these cases have acceptable ratios of IoU as well as high confidence scores to represent the detected objects. Figure 11 shows some other examples of the falsely detected cases from all nine classes. The final detected boxes of these cases have undesired overlapping ratios with their GTs. Due to that, they considered being wrongly detection cases even they satisfy the confidence score condition.

4.2. Classification Results
The presented CAD-based YOLO predictor has the capability to simultaneously classify end-to-end the detected ROIs of COVID-19 and other lung diseases. As shown in Figures 10 and 11, the presented CAD system detects the final suspicious regions of lung diseases and classify them at the same time. In fact, this is the key that makes YOLO predictor faster and more accurate than other techniques such as Faster R-CNN [42,10,24]. All final detected bounding boxes are considered for the classification evaluation even if they are wrongly detected. For classification, we are always anxious to know the final status of each X-ray image (i.e., COVID-19 or another disease) since the GT label of the whole X-ray image is available. The classification evaluation results are derived based on the multi-class confusion matrices for all nine classes over each fold test. Figure 12, shows the confusion matrices for all classes from third and fifth testing folds. Indeed, most of the COVID-19 cases are correctly classified against other lung diseases. Due to the high similarity between the COVID-19 and other different lung
diseases, some cases of COVID-19 are misclassified as Pneumonia and vice versa. Meanwhile, the weighted recognition evaluation metrics via five-fold tests for all classes are reported in Table 2. Specifically, the classification evaluation results for each individual class as an average over five-fold tests are shown in Figure 13. It is clearly shown that the proposed CAD-based YOLO achieves average overall accuracy classification performance in between 94.60% for Pneumonia and 97.40% for COVID-19. The sensitivity of 91.69%, specificity of 98.79%, and Mcc. of 91.96% for classifying COVID-19 are achieved against all other lung diseases. The classification performance of the COVID-19 in term of F1-score is achieved to be 93.86%.

Our CAD system could achieve satisfactory and promising classification performance of the multi-class recognition problem of lung diseases.

4.3. The Affecting of the Regularization Strategies

To improve the diagnostic performance of COVID-19 against other lung diseases, data balancing and augmentation strategies are used. In this regard, the presented CAD system is trained and tuned over 5-fold tests using the original, balancing, or augmentation datasets in three separate scenarios. In each scenario, the same deep learning structure and learning settings are used. Figure 14, shows the weighted classification performance as an average of 5-fold tests for each scenario. The balancing strategy helps to improve the diagnosis performance by 3.43%, 1.47%, 2.79%, 3.35%, 3.86%, 3.28%, and 1.43% in terms of sens., spec., Acc., F1-score, Mcc., PPV, and NPV, respectively. The major improvement is achieved due to the use of data augmentation after the balancing strategy. After applying augmentation strategy, the classification performance is improved by 12.91%, 4.49%, 6.64%, 12.17%, 12.99%, 11.72%, and 3.56% in terms of sens., spec., Acc., F1-score, Mcc., PPV, and NPV, respectively.
Figure 12. The derived multi-class confusion matrices of the COVID-19 against other lung diseases from the testing sets over (a) Fold-3, and (b) Fold-5.
4.4. The Cost of the Prediction time

For training, the training time depends on the deep learning structure, training settings (i.e., number of epochs and mini-batch size), the number of training sets, and the specifications of used PC. For each fold test, the presented CAD system requires almost eighteen hours. For testing, to predict all testing images, the proposed CAD system requires 2.44 seconds. Since we have 263 testing images from all classes, the prediction time of an individual X-ray image is 0.0093 seconds. Our CAD system presents its reliability to predict 108 FPS at the real-time of prediction. The physicians are always suffering in the hospital regarding the rapid spread of COVID-19 worldwide. The accurate and fast inspection of COVID-19 from the entire chest X-ray image is intensify required to help physicians, patients, and health care systems.

Table 2: Weighted Classification Measurements (%) for the COVID-19 against all other Lung Diseases as an Average over 5-Fold Tests on the Testing Sets

| Fold Test | Sens. | Spec. | Acc. | F1-score | Mcc. | PPV  | NPV  |
|-----------|-------|-------|------|----------|------|------|------|
| Fold-1    | 88.25 | 99.16 | 97.59| 85.47    | 83.60| 86.0 | 98.90|
| Fold-2    | 84.47 | 99.09 | 97.37| 84.75    | 82.75| 85.33| 98.72|
| Fold-3    | 83.33 | 98.78 | 97.08| 83.63    | 81.50| 84.40| 98.68|
| Fold-4    | 85.25 | 99.16 | 97.59| 85.47    | 83.60| 86.0 | 98.90|
| Fold-5    | 84.47 | 99.09 | 97.37| 84.75    | 82.75| 85.33| 98.72|

Average (%)  

| Sens. | Spec. | Acc. | F1-score | Mcc. | PPV  | NPV  |
|-------|-------|------|----------|------|------|------|
| 85.15 | 99.056| 97.40| 84.81    | 82.84| 85.412| 98.784|

Figure 13. Classification evaluation measurements (%) for each individual class of lung diseases as an average over 5-Fold Tests on the testing sets.
5. Discussion

Recently, the researchers encouraged to apply artificial intelligence (AI) methodologies to help physicians and health care systems in the hospitals for diagnosing the COVID-19. Indeed, deep learning based on CNN presented their capabilities to achieve promising classification results for different applications. Up to now, a few studies based on machine learning and deep learning models are designed and presented. Such studies employed deep learning models to classify the whole input X-ray images. However, the diagnosis of a whole X-ray image cannot provide a reliable solution for more efficient and accurate predictions [24, 12]. Thus, the

| Reference            | Method                          | Prediction Classes: No. Of images                  | Diagnosis Accuracy (%) |
|----------------------|---------------------------------|---------------------------------------------------|------------------------|
| Ozturk et al. [8]    | DarkCovidNet                    | COVID-19: 125, Pneumonia: 500, and Normal: 500    | 87.02                  |
| L. Wang et al. [18]  | COVID-Net                       | COVID-19: 53, Pneumonia: 5526, and Normal: 8066   | 92.40                  |
| Apostolopoulos et al. [22] | VGG19, Mobile Net, Inception, Xception, and InceptionResNet v2 | COVID-19: 224, Pneumonia: 700, and Normal: 504 | 93.48 → for VGG19     |
| Khan et al. [21]     | CoroNet                         | COVID-19: 284, Pneumonia bacterial: 330, Pneumonia viral: 327, and Normal: 310 | 89.60                  |
| The Presented CAD    | CAD-based YOLO Predictor        | COVID-19: 326 and the number of images from other eight classes are shown in Figure 2. | Detection: 90.67       |
| system               |                                 |                                                   | Classification: 97.40  |

Figure 14. Effecting of the enlarging training set sizes using different strategies of deep learning regularization on the overall classification performance of the proposed CAD system. The evaluation results are derived as an average over 5-fold tests from the testing sets for all classes.

Table 3. PREDICTION PERFORMANCE COMPARISON AGAINST THE LATEST DEEP LEARNING WORKS FOR THE COVID-19 DIAGNOSIS FROM CHEST X-RAY IMAGES
detection of the suspicious regions that containing a possible lung disease (i.e., COVID-19 or another disease) represents a crucial prerequisite for a more accurate diagnosis of the CAD system. **Table 3** presents the prediction compression performance of our proposed CAD system against the latest deep learning works. In [8], Ozturk et al. presented deep learning DarkCovidNet to diagnose COVID-19 against Pneumonia and normal cases. They achieved an overall diagnostic performance of 87.02%. L. Wand et al. developed COVID-Net deep learning model to also recognize COVID-19 against normal and Pneumonia diseases. They achieved an overall diagnosis performance of 92.40%. Meanwhile, Khan et al. [21] presented a deep learning CoroNet to diagnose the COVID-19 against Pneumonia bacterial, Pneumonia viral, and Normal diseases. The diagnostic performance of 89.60% is achieved for a multi-class recognition problem.

In this study, the proposed CAD system presents its efficiency to diagnose COVID-19 against the other eight lung diseases. The detection accuracies of all nine classes are achieved in the range between 71.50% for Pneumothorax and 97.60% for Infiltration. The overall detection performance of correctly detected suspicious regions is recorded with 90.67%. For COVID-19, the overall detection accuracy of 96.31% is achieved. The detection evaluation results for an individual class are reported in **Table 1**. Simultaneously, the proposed CAD system could predict the diagnostic status (i.e., COVID-19 or not) for each detected ROIs to represent the final diagnosis status of the input X-ray images. As presented in **Table 2**, promising classification performance is achieved recording 97.40% over 5-fold tests. The simultaneous detection and classification of COVID-19 or other lung diseases in only look once on the entire X-ray images is helpful for physicians especially with a huge number of patients. This will directly help and support the health care systems in the hospital as well. By controlling the confidence score threshold for the detected bounding boxes, we can determine the desired number of boxes shall be used for the final real-time diagnosis. As shown in **Figure 8(b)**, after adjusting the confidence threshold to be greater than 10%, two final detected boxes are assigned two different suspicious regions containing COVID-19. It represents also logic results since the COVID-19 can attack both right and left lungs for the same patient. Meanwhile, it is important to consider the final detected suspicious regions even they are wrongly detected. As shown in **Figure 11**, most false detected cases are truly classified. Also, it may help physicians to focus on other suspicious regions rather than those having GTs. **Figures 11(h-j)**, present false detected ROIs according to the annotated position of the GT, but the final diagnosis status are truly diagnosed. Meanwhile, deep learning regularizations of data balancing and augmentation are applied aiming to improve the final diagnosis performance of the proposed CAD system. As shown in **Figure 14**, these regularizers obviously improve the diagnostic performance in terms of all evaluation indices. As an average results for five-fold tests using the overlap class problem, the classification performance is increased from 90.76% to 97.40% and from 72.64% to 84.81% in terms of Acc. and F1-score, respectively. Generally, CAD systems could help physicians supporting them by a second opinion for the overall diagnosis decision. The fast and accurate diagnosis of COVID-19 from the entire X-ray images is key to help physicians, patients, and health care systems.

The proposed CAD system has some advantages as declared in the following. First, the promising prediction accuracy of the novel COVID-19 against other lung diseases is achieved. Second, the fast prediction of the COVID-19 and other lung diseases from the whole entire X-
ray images is achieved. Finally, the user interventions are not required for detecting and classifying COVID-19 since the proposed CAD system has a unique end-to-end deep learning structure.

Despite the encouragement of diagnostic performance and fast prediction of COVID-19, some drawbacks and limitations are addressed. The real digital X-ray annotated images of COVID-19 are still unavailable. The labeling process to localize the exact regions containing COVID-19 costs a lot of time and effort for physicians.

In the future, we plan to validate the presented CAD system since real chest X-ray images become available. For more reliability, we will use the CT images to detect COVID-19 to get more advantages from the proposed CAD system. Also, we have a plan to locally collect the digital X-ray and CT images for further validation. For more accurate pre-training of deep learning models, generative adversarial network (GAN) could be used for creating more synthesized images.

6. Conclusion
In this work, a deep learning CAD system is proposed to simultaneously detect and recognize the COVID-19 from chest X-ray images. Our presented deep learning system is built in a unique deep learning structure to rapidly predict the suspicious regions of COVID-19 from the entire X-ray images. The proposed CAD system is validated for a multi-class recognition problem achieving a promising diagnosis accuracy of 97.40% over 5-fold tests. The promising diagnostic performance as well as the rapid prediction time make the proposed CAD system reliable to apply for practical solutions assisting the physicians, patients, and health care systems.

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CONFLICTS OF INTEREST
None.

DECLARATIONS
Not applicable.
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