A Deep Convolutional Neural Network(CNN) design for pathology detection of COVID-19 in chest

X-Ray Images

*Anindya Sil, Balaji Kagiti, Krishna Kumar S, Ramanathan NB, VasanthaKumara SB*

**14-May-2020**

# Synopsis

## Problem definition

**Covid-19 (Corona Virus December– 2019) :** COVID-19 is caused by a new type of coronavirus which was previously named 2019-nCoV by the World Health Organization (WHO). It is the seventh member of the coronavirus family, together with MERSnCoV and SARS-nCoV, that can spread to humans. The symptoms of the infection include fever, cough, shortness of breath, and diarrhoea. In more severe cases, COVID-19 can cause pneumonia and even death. As on mid-May 2020, more than 4 million people across 180 countries in the globe have been infected with COVID-19 virus with 280,000 deaths.

The COVID-19 pandemic continues to have a devastating effect on the health and well-being of the global population. A critical step in the ﬁght against COVID-19 is effective screening of infected patients.

**PCR Testing :** The main screening method used for detecting COVID-19 cases is polymerase chain reaction (PCR) testing, which can detect SARSCoV-2 RNA from respiratory specimens (collected through a variety of means such as nasopharyngeal or oropharyngeal swabs). While PCR testing is the gold standard as it is highly sensitive, it is a very time-consuming, laborious, and complicated manual process that is in short supply. This is also a very risky procedure since the health care fraternity could come in direct contact with infected people and get infected themselves.

**Alternative methods :** It was found in early studies that patients present abnormalities in chest radiography images that are characteristic of those infected with COVID-19. Hence, an alternative screening method that has also been utilized for COVID-19 screening has been radiography examination, where chest radiography imaging (e.g., X-ray or computed tomography (CT) imaging) is conducted and analysed by radiologists to look for visual indicators associated with SARS-CoV-2 viral infection.

Motivated by this, a number of artiﬁcial intelligence (AI) systems based on deep learning have been proposed and results have been shown to be quite promising in terms of accuracy in detecting patients infected with COVID-19 using chest radiography images. These developed AI systems have been closed source and unavailable to the research community for deeper understanding and extension, and unavailable for public access and use.

While radiography examination can be conducted faster and have greater availability given the prevalence of chest radiology imaging systems in modern healthcare systems, making them a good complement to PCR testing (in some cases, even exhibiting higher sensitivity), one of the biggest bottlenecks faced is the need for expert radiologists to interpret the radiography images, since the visual indicators can be subtle. As such, AI based diagnostic systems that can aid radiologists to more rapidly and accurately interpret radiography images to detect COVID-19 cases is highly desired. This method is also cost effective and contactless. Hence reduces the risk of infection of health care fraternity.

Goals :

1. We would like to develop CNN based solution which will classify the X-Ray images into : Normal, Pneumonia or COVID-19
2. Our goal would be to develop a model with, COVID-19 sensitivity >= 80% and specificity >=80%.

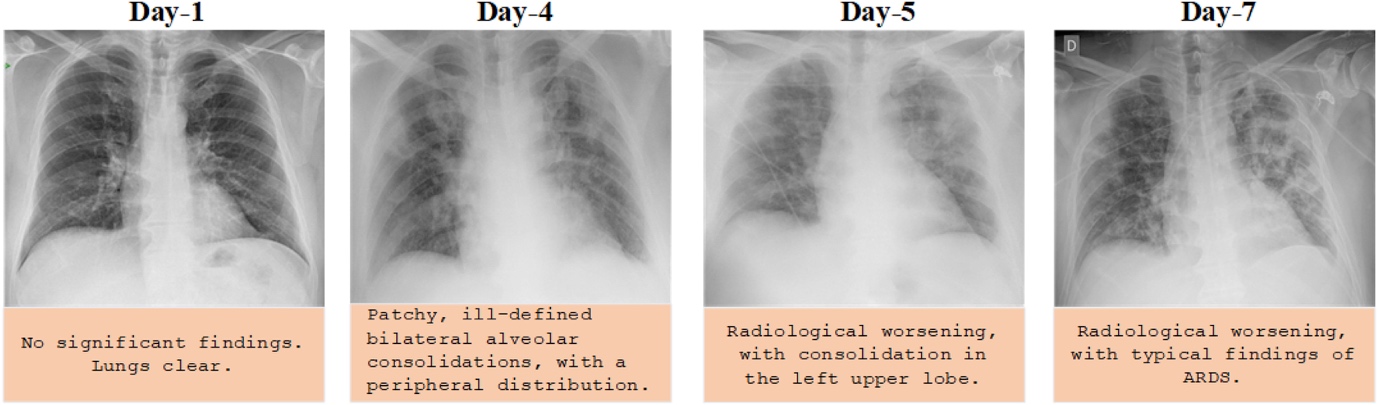
## Literature Survey

The below pictures shows the images of people with Normal chest x-ray, patients with Pneumonia and COVID-19 condition.

### A picture containing photo Description automatically generated

**Understanding the symptoms and Stages of Covid-19 using X-Ray**

The following pictures shows lung infection of COVID-19 disease from Day 1 to 7.



The following table lists various stages of COVID-19.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Stages | Day’s Range | Symptoms | X-Ray Findings of Lungs | Detect Covid-19 by X-Ray | Detect Covid-19 by PCR |
| Early | 0 – 4 | Mild - Fever, difficulty breathing and cough.  Some may not have any symptoms | Mild consolidation/Ground-Glass Opacities, partial crazy paving, lower number of involved lobes | No | No |
| Progressive | 5 – 8 | Gradually increase the above. Some patients may have aches and pains, nasal congestion, runny nose, sore throat or diarrhoea | Abnormalities (indicating infection), Extension of mild consolidation/Ground-Glass Opacities, Lung Opacity, increased crazy paving pattern | No | No |
| Peak | 10 – 13 | Severe symptoms of the above | Bilateral consolidation/Ground-Glass Opacities, Lung Opacity thickening of muscle | Positive | Positive |
| Absorption | >=14 |  | Gradual Resolution |  |  |

### **Chest Pathology detection using Convolutional Neural Networks(CNN) and Deep Neural Networks (DNN)**

Chest diseases can be shown in CXR images in the form of cavitations, consolidations, infiltrates, blunted costophrenic angles, and small broadly distributed nodules. By analysing the chest X-ray image, the radiologists can diagnose many conditions and diseases such as pleurisy, effusion, pneumonia, bronchitis, infiltration, nodule, atelectasis, pericarditis, cardiomegaly, pneumothorax, fractures, and many others.

Classifying the chest X-ray abnormalities is considered as a tedious task for radiologists; hence, many algorithms were proposed by researchers to accurately perform this task. Over the past decades, computer-aided diagnosis (CAD) systems have been developed to extract useful information from X-rays to help doctors in having a quantitative insight about an X-ray. However, these CAD systems could not achieve significance level to make decisions on the type of conditions of diseases in an X-ray.

A number of research works have been carried out on the diagnosis of chest diseases using artificial intelligence methodologies. Various deep learning methods have been used like : Multilayer, probabilistic, learning vector quantization, and generalized regression neural networks have been used for diagnosis chest diseases**[14]**. However, their performance was not as efficient as the deep networks in terms of accuracy, computation time, and minimum square error achieved. Deep learning-based systems have been applied to increase the accuracy of image classification. Most commonly used deep learning architecture is the convolutional neural network (CNN). CNN has been applied to various medical images classification due to its power of extracting different level features from images.

#### **Various architectures are used in chest X-ray image classification**

1. Well known CNN architectures like **AlexNet, VGG, Xception, Resnet, CifarNet** and **R-CNN** are used. There are currently three major techniques**[15]** that successfully employ CNNs to medical image classification:
2. Training the “CNN from scratch”
3. Using “off-the-shelf CNN” features (without retraining the CNN) as complementary information channels to existing hand-crafted image features
4. Performing unsupervised pretraining on natural or medical images and fine-tuning on medical target images using CNN or other types of deep learning models
5. In addition to the above, R-CNN ( with SVM) is also widely used for medical image classification.

##### Challenges for translation of Chest X-Ray by AI systems to the Clinical settings :

There remain major challenges for the translation of chest x-ray algorithms to the clinical setting :

* First, the performance of deep learning chest x-ray algorithms, trained with mainly US-based chest x-ray datasets, on endemic and globally relevant diseases not commonly found in the US, such as tuberculosis (TB) is unknown.
* Second, most chest x-ray algorithms have been developed and validated on digital x-rays, while the vast majority of the world relies on film for X-ray interpretation, a barrier that denies these populations from the advancements of automated interpretation. In order to apply an interim digital solution, digital photographs of films for storage, interpretation, and consultation can be performed as a "workaround".
* Third, chest x-ray algorithms which are developed using the data from one institution have not shown sustained performance when externally validated in application data from a different unrelated institution, and instead, these models have been criticized as vulnerable to bias and non-medically relevant cues.

**Measures of Performance towards evaluating the model**

We have considered different measures of accuracy metrics generally used in various machine learning problems specific to medical diagnostics studies **[1].** It has been observed that ROC-AUC is a popular measure for model validation in the field of medical image classification after it has been first introduced in the medical field**[2].** The AUC indicates the model’s ability to separate out the diseased class from non-diseased class.

However, there are two issues related to multi-class classification which we need to consider while looking at this metric for our problem. ROC - AUC is generally used in binary classification. To overcome this challenge, we are planning to look at OVR (One vs. Rest) or OVO (One vs. One) macro average method to extend the concept in a multi-class setup. As we have class imbalance in COVID-19 cases, along with ROC-AUC, we will also look into PPV (Positive predictive value) so that we can reduce the False positive detection as much as possible. By reducing False positive we can reduce the overburden of doing confirmatory tests.

### **Evaluating predicted Class certainty and Model Explainability**

It is especially important to understand the model output and the features that play a pivotal role in discriminating the classes of interest in our prediction. In medical image analysis this is more of a requirement to boost the confidence of the medical fraternity. To achieve this, we are going to add two sections on model output that we consider a valuable addition for COVID or other respiratory ailments diagnostic procedure from chest x-rays.

#### **Confidence of class prediction by Model**

##### Probabilistic layers :

Generally, final layer of the CNN is a fully connected layer with a softmax function that produces the point estimates of the predicted classes. We are planning to add a dense Flipout layers instead of normal dense layer. This Flipout layer samples out weights from a certain distribution in each forward pass and by repeating the prediction of an image multiple times, it produces a probability distribution of each of the predicted class **[4]**. This distribution of an image belonging to a certain class can then be used as an additional supporting information by the Physicians to judge the uncertainty associated with the machine-driven approach and assist her in ruling out any pathology by investigating the x-ray image.

#### **Model Explainability :**

##### Gradient-weighted Class Activation Mapping (Grad-CAM) :

Grad-CAM will help to make the decision more transparent and explainable to the Physicians. This method extracts the gradients from the final convolutional layer of a CNN by using Global Average Pooling. The extracted gradients are then used to highlight the regions in the actual image that are most responsible to differentiate the predicted class. This is very useful in medical image classification as this gives the indication to the Physicians that the model is differentiating the classes based on the medical condition of the lungs only and not any of the surrounding areas in the chest x-ray image.

**Work accomplished by AI Researchers around the world on COVID-19 chest pathology until April-2020**

The AI researchers around the world have leveraged CNN / DNN which has been the trend for Image classification & recognition of pathologies using X-Ray / CT scan and MRI.

One particular subject in the CNN area, Transfer Learning has been experimented heavily due to numerous advantages like leveraging the learnings on similar such datasets and cutting down the time to learn about the new disease patterns using X-Ray image sets. The need also originates from the fact to provide a reliable and cost effective approach to detect the COVID-19 pathology to save lives across developed / developing nations from the pandemic.

In addition to the X-Ray imaging AI Research is also aiding in the development of the anti-viral drug by studying the gene protein sequencing of the COVID-19 virus. This topic is out of scope in this Synopsis.

We would be focusing mainly on the COVID-19 pneumonia detection in this synopsis.

The following Transfer learning models have shown promising results in the detection of COVID-19 :

**COVID-Net[12], ResNet50, VGGNet, MobileNet[9], DarkNet[10], InceptionV3, InceptionResNetV2**

Most of these models are providing Specificity and Sensitivity significantly upwards of 80% in both binary and multi-class classification settings. Some of these models go a step further and even aid in the image localization aspects and share the areas of lung deterioration in the COVID-19 patients to the Radiologists and Doctors and aid in taking crucial decision making to save patient lives

There is also cutting edge research happening to detect the COVID-19 within a week of the onset of virus using lung X-Ray images.**[10]**.

COVID-Net is a deep convolutional neural network design tailored for the detection of COVID-19 cases from chest radiography images that is open source and available to the general public. The COVID-Net makes predictions using an explainability method in an attempt to gain deeper insights into critical factors associated with COVID cases, which can aid clinicians in improved screening.

In addition to the experimentation to use CNN to extract the features from the X-Ray images related to COVID-19 disease, a lot of research is also currently being carried out to suggest the AI researchers community, the ways to avoid bias creep-in to the models. New protocols are being designed and suggested while building models for COVID-19 detection. Some of the examples is non-inclusion of the meta data and Data Scientists being singularly focused on the image datasets, strict isolation of the training and test data sets to avoid overfit which will help in generalization of models. These are essentially model building practices which are being reminded to the AI research fraternity in order to build robust models required for critical health care area.**[6]**

Reducing bias errors in X-Ray images is also an area of interest. Ensembles of Transfer learning nets is also being experimented and suggested practice for the new development and deployment in real-life scenarios.

These machine learning / Data Science practices along with the application of sophisticated Transfer Learning nets will facilitate in robust model development which eventually could be deployed in the field.

## Sample data

1. The [NIH Chest X-ray dataset](https://nihcc.app.box.com/v/ChestXray-NIHCC) consists of 100,000 de-identified images of chest x-rays. The images are in PNG format. The data is provided by the NIH Clinical Center and is available through the NIH download site: <https://nihcc.app.box.com/v/ChestXray-NIHCC>
   1. The same is available in Kaggle as well : <https://www.kaggle.com/nih-chest-xrays/data>
2. Dataset from Cohen **[17]** - . [*https://github.com/ieee8023/covid-chestxray-dataset*](https://github.com/ieee8023/covid-chestxray-dataset)
3. COVID dataset in Kaggle - <https://www.kaggle.com/andrewmvd/convid19-X-rays>
4. Common bacterial-pneumonia x-ray scan images**[18]**

## Tentative list of algorithms

We will be using the Transfer Learning from the following CNN and build a custom CNN to perform multi-class classification of : Pneumonia, COVID-19 and Normal pathology in the X-Ray images :

**AlexNet, VGGNet, ResNet****-50, Covid-Net****, Mobile-Net, DarkNet**

## References

1. Abdel Aziz Taha and Allan Hanbury. Metrics for evaluating 3D medical image segmentation: analysis, selection, and tool. BMC Medical Learning. DOI 10.1186/s12880-015-0068-x
2. James A. Hanley, Ph.D., Barbara J. McNeil, M.D., Ph.D. The Meaning and Use of the Area under a Receiver Operating Characteristic (ROC) Curve. DIAGNOSTIC RADIOLOGY. April 1982 Volume 143, Number 1
3. Mausner JS, Kramer S: Mausner and Bahn Epidemiology: An Introductory Text. Philadelphia, WB Saunders, 1985, p. 221
4. Wen et al. Flipout: Efficient Pseudo-Independent Weight Perturbations on Mini-Batches. arXiv:1803.04386v2 [cs.LG] 2 Apr 2018
5. Selvaraju et al. Grad-CAM:VisualExplanationsfromDeepNetworks viaGradient-basedLocalization. arXiv:1610.02391v4 [cs.CV] 3 Dec 2019
6. [G Maguolo](https://scholar.google.com/citations?user=Df9a1YkAAAAJ&hl=en&oi=sra), [L Nanni](https://scholar.google.com/citations?user=5NSGzcQAAAAJ&hl=en&oi=sra)  et al -A Critic Evaluation of Methods for COVID-19 Automatic Detection from X-Ray Images. arXiv preprint arXiv:2004.12823, 2020 - arxiv.org 27 Apr 2020. <https://arxiv.org/pdf/2004.12823>
7. [Ali Narin](https://arxiv.org/search/eess?searchtype=author&query=Narin%2C+A), [Ceren Kaya](https://arxiv.org/search/eess?searchtype=author&query=Kaya%2C+C), [Ziynet Pamuk](https://arxiv.org/search/eess?searchtype=author&query=Pamuk%2C+Z) et al. Automatic Detection of Coronavirus Disease (COVID-19) Using X-ray Images and Deep Convolutional Neural Networks. [arXiv:2004.12823](https://arxiv.org/abs/2004.12823) [eess.IV]
8. [Muhammad Ilyas](https://arxiv.org/search/eess?searchtype=author&query=Ilyas%2C+M), [Hina Rehman](https://arxiv.org/search/eess?searchtype=author&query=Rehman%2C+H), [Amine Nait-ali](https://arxiv.org/search/eess?searchtype=author&query=Nait-ali%2C+A) et al. Detection of Covid-19 From Chest X-ray Images Using Artificial Intelligence: An Early Review. arXiv:2004.05436v1 [eess.IV] 11 Apr 2020
9. Ioannis D. Apostolopoulos1  · Tzani A. Mpesiana2 Covid‑19: automatic detection from X‑ray images utilizing transfer learning with convolutional neural networks. <https://doi.org/10.1007/s13246-020-00865-4>
10. [Tulin Ozturka](https://www.sciencedirect.com/science/article/pii/S0010482520301621#!), [Muhammed Talo,](https://www.sciencedirect.com/science/article/pii/S0010482520301621#!) [Eylul Azra, Yildirim,](https://www.sciencedirect.com/science/article/pii/S0010482520301621#!) [Ulas Baran Baloglud](https://www.sciencedirect.com/science/article/pii/S0010482520301621" \l "!), [Ozal Yildirime](https://www.sciencedirect.com/science/article/pii/S0010482520301621#!), [U.Rajendra Achary.](https://www.sciencedirect.com/science/article/pii/S0010482520301621#!) Automated detection of COVID-19 cases using deep neural networks with X-ray images (NIH). <https://doi.org/10.1016/j.compbiomed.2020.103792>
11. [Joseph Paul Cohen](https://arxiv.org/search/eess?searchtype=author&query=Cohen%2C+J+P), [Paul Morrison](https://arxiv.org/search/eess?searchtype=author&query=Morrison%2C+P), [Lan Dao](https://arxiv.org/search/eess?searchtype=author&query=Dao%2C+L). COVID-19 Image Data Collection. [arXiv:2003.11597](https://arxiv.org/abs/2003.11597) [eess.IV]
12. [Linda Wang](https://arxiv.org/search/eess?searchtype=author&query=Wang%2C+L), [Alexander Wong](https://arxiv.org/search/eess?searchtype=author&query=Wong%2C+A). COVID-Net: A Tailored Deep Convolutional Neural Network Design for Detection of COVID-19 Cases from Chest X-Ray Images. [arXiv:2003.09871](https://arxiv.org/abs/2003.09871) [eess.IV]
13. NG Ming-Yen, LEE1 Elaine YP et. al. Imaging Profile of the COVID-19 Infection: Radiologic Findings and Literature Review. <https://doi.org/10.1148/ryct.2020200034>
14. Rahib H. et al. Deep Convolutional Neural Networks for Chest Diseases Detection. <https://doi.org/10.1155/2018/4168538>
15. Hoo-Chang Shin et al. Deep Convolutional Neural Networks for Computer-Aided Detection: CNN Architectures, Dataset Characteristics and Transfer Learning. IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 35, NO. 5, MAY 2016
16. Cohen. https://github.com/ieee8023/covid-chestxray-dataset, 2020. 2, 3
17. Kermany DS, Goldbaum M, Cai W et al (2018) Identifying medical diagnoses and treatable diseases by image-based deep learning. Cell 172:1122–1131.e9. https://doi.org/10.1016/j. cell.2018.02.010 7. Weiss K, Khoshgof