Fast COVID-19 diagnosis with deep learning and chest X-rays: from toy datasets to clinical applications

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ABSTRACT

Accurate diagnosis of COVID-19 infection is a crucial tool to identify and control the spread of the disease. Current frontline technology, based on Reverse Transcription Polymerase Chain Reaction (RT-PCR), can depend on getting an adequate sample from the patient. If the sample collected does not have enough viral material on it, either because of the collection method or because of the stage of the infection, it can affect the result. RT-PCR also requires well equipped laboratories and specialized human resources. The technology being proposed uses Artificial Intelligence (AI) to analyze Chest X-Rays (CXR) to identify signs of disease at a very early stage and to monitor disease progression. The technology has multiple uses, from hospital settings to large public health screenings. It also has the potential to be applied to other pathologies.

Keywords: Sars-Cov-2, COVID-19, Artificial Intelligence, Deep Learning, Diagnosis, chest X-ray

1 INTRODUCTION

The rapid increase of new COVID-19 infections in many countries, in particular Western and Far Eastern countries, has led to national, state and local authorities to introduce emergency measures including special containment, mask mandates and contact tracing. With sustained transmission from the community, real-time RT-PCR of viral nucleic acid, the assumed gold standard to diagnose COVID-19, can be supported by more versatile diagnostic tools. New tools can help mitigate false-negative and false-positive results and the length of time to obtain a result. The search for complementary diagnostic and screening techniques is imperative not only for patients, but also for health care providers and broader health care systems. For hospital systems it would allow faster and safer triage of patients, it would improve safety for health care workers and would save the hospital systems considerable sums of money due to streamlining of processes and efficiency gains. Radiologic data, mostly from China, has suggested that chest radio-imaging could play a role in investigating COVID-19 cases. Early studies suggested that chest Computed Tomography (CT) in particular may yield positive results when the RT-PCR is a negative test. CT has been understood as a prime means of diagnosis and the diagnostic criteria in China originally included CT, driven by a significant number of daily cases and certainly because of equipment availability [1]. However, CT has important disadvantages relative to Chest Radiography (CXR), another radio-imaging technology capable of diagnosing lung abnormalities. Noteworthy is the need for effective infection control when transporting patients to the CT rooms, the need for extensive room and CT equipment decontamination, and lack of CT availability in parts of the world. CXR imaging is often performed as part of standard procedure for patients with respiratory symptomatology [2]. Jacobi *et al.* published a lengthy review article illustrating how CXR can be used in a clinical setting to diagnose COVID-19 [3].

This paper describes FastNET, our deep learning system to diagnose COVID-19 from CXRs. FastNET has also recently been extended to other medical pathologies reliant on medical imaging, in particular to the diagnosis of breast cancer through mammograms.

2 RADIOIMAGING TO DIAGNOSE COVID-19

Early studies from February 2020 have shown that abnormalities in CT images can be identified prior to detection by RT-PCR in symptomatic and asymptomatic patients who subsequently test positive by RT-PCR [4-7]. Two of these studies specifically compared the performance of CT with RT-PCR. Ai *et al.* [6] reported CT to have a diagnostic sensitivity of 0.97, positive predictive value of 0.65, and negative predictive value of 0.83 in a cohort of slightly over 1000 cases. CT was reported abnormal in 308 (75%) of 413 patients who tested negative by RT-PCR, but were clinically assessed as likely to have (147 [48%] patients) or probably did have (103 [33%] patients) COVID-19 infection. In a smaller cohort of 51 patients, Fang *et al.* found a similar CT sensitivity of 0.98 (vs 0.71 for RT-PCR; $p<0{\cdot}001$). In this study 15 ([29%] patients) tested negative on the initial RT-PCR [7]. There were, however, reports where patients with positive results by RT-PCR had clear CT scans. One such study by Bernheim and colleagues indicated that in 36 patients tested in the first 2 days of symptoms, CT was normal in 56% of cases (20/36), although the majority (> 90%) of the patients tested positive by RT-PCR [8]. This was attributed to very early infection. A few longitudinal studies have also been reported. Pan *et al.*, used CT scans to evaluate the time evolution of radiological features of 21 patients with confirmed mild to moderate infection who were discharged after hospitalization. The peak in radiological abnormalities occurred around day 10 and it was followed by a gradual regression, starting 2 weeks after the onset of symptoms [9]. In another study, Ai *et al.* reported that in 57 patients recovering from COVID-19 infection, 24 (42%) had shown radiological improvement before negative RT-PCR testing [6]. In June 2020 the WHO issued a rapid advice guide on the use of chest imaging in COVID-19 (WHO 2020b). Important recommendations are: 1) for asymptomatic contacts of patients with COVID-19, chest imaging should not be used for the diagnosis of COVID-19 due to lack of published evidence; 2) for symptomatic patients with suspected COVID-19 it is suggested to use chest imaging when RT-PCR testing is not available or when the initial RT-PCR testing is negative, but there is a high clinical suspicion of COVID-19 [10]. A recent Cochrane review evaluated the diagnostic accuracy of thoracic imaging for the COVID-19, including CT and CXR [11]. The findings indicate CT to be sensitive and moderately specific, while CXR is moderately sensitive and moderately specific. Thus, the authors suggest that radio-imaging may have a more prominent role in excluding SARS-CoV-2 infection rather than differentiating it from other causes of respiratory illness.

However, in all the studies mentioned previously analysis of the radiographs was performed by skilled radiologists. There are, however, several limits in the perception of the human eye that may hinder human analysis. Medical radiography typically produces images containing between 12–16 bits/pixel, which corresponds to 4,096–65,536 shades of gray. The human eye is able to differentiate between 700 and 900 simultaneous shades of gray in optimal conditions. Therefore, with human reading there is no need for more than 10 bits of gray, or 1,024 shades of gray [12]. This raises the possibly of developing computer-based algorithms with better capabilities to assist the radiologist in identifying hidden features not visible to the best trained eyes. One such technology is the FastNET system developed by us. Next, we will describe the FastNET system followed by presentation of the most recent results and a final discussion.

3 THE FASTNET ALGORITHM

3.1 Technical details

The FastNET algorithm is a Convolutional Neural Network (CNN), with its configuration using transfer learning. The CNN system essentially summarizes repeated patterns in the data at different successive levels of abstraction, which in the end will represent a mathematical measure that quantifies whether the pixels of an image contain an anomaly, such as the opacity verified in COVID-19. The CNN is based on VGG16 which has been proposed by K. Simonyan and A. Zisserman [13]. The basic premise of transfer learning consists in using a model trained on a large dataset and transfer of its knowledge to the present dataset. FastNET also uses data augmentation. This technique is based on increasing the amount of data, in this case medical images, adding slightly modified or newly created synthetic copies from existing data. Data augmentation acts as an equalizer and helps reduce overfitting when training a model deep learning. FastNET is not, however, a simple reinterpretation of the VGG16 architecture. The FastNET technology initially segments the whole radiograph using a deep learning U-Net system. This way, it is possible to avoid the problem of recurring similar patterns between different images.

3.2 Training and Validation

FastNET was developed using two toy datasets, designated Dataset I and II. Dataset I Although the use of toy datasets has been questioned in the context of the use of AI in medicine [14], it is our believe that their use is still of great value[1]. Dataset I consisted of COVID-19 positive radiographs from an open GitHub repository[2], with data collected from public sources and indirectly from hospitals and physicians. Dataset II is from the BIMCV-COVID-19+ repository[3], consisted of radiographs from the Valencia region, Spain, representing more homogeneous conditions that are likely to be found in operational conditions. A subset of images from Dataset I was randomly selected to train the FastNET system (223 radiographs). The remaining images, still designated Dataset I, were used for validation. Dataset II was used exclusively for validation / testing. Images were selected from Dataset I for training purposes because of the greater diversity of the set. Datasets of radiographs of healthy individuals and patients of pneumonia were also included. Radiographs of pneumonia patients and of healthy individuals were selected from a Kaggle repository[4]. 500 radiographs of patients with pneumonia and 500 radiographs of healthy individuals were randomly selected to include the training set together with the COVID images. The remaining images were used in testing /validation and are designated “Pneumonia” and

[1] https://www.european-radiology.org/opinions/letter-to-the-editor-covid-19-ai-enthusiasts-and-toy-datasets-radiology-without-radiologists/

[2] https://github.com/ieee8023/covid-chestxray-dataset, accessed on April 12, 2021

[3] https://bimcv.cipf.es/bimcv-projects/bimcv-covid19/#1590857662078-c30d2790-05dc, accessed on April 12, 2021

[4] https://www.kaggle.com/nih-chest-xrays/data, accessed on April 12, 2021

"Healthy" in the text. In total 1223 radiographs were selected to train the deep learning system.

4 RESULTS: NOT ALL ALGRORITHMS ARE CREATED EQUAL

After training following the protocol above, the predictive performance of the FastNET system was evaluated using the 3 datasets described above. In Table 1 we compare the raw results for the three datasets. For dataset I we obtained a high sensitivity of 0.96 (95% CI 0.94 - 0.97), while for the dataset II the sensitivity was slightly higher at 0.980 (95% CI 0.97 - 0.98). The sensitivity with the dataset II was worse at 0.868 (95% CI 0.82 - 0.91). These results highlight the predictive power of FastNET. FastNET displays outstanding capabilities. For both datasets the sensitivity is very high, while scoring perfect sensitivity. For the whole set of radiographs from the Healthy and Pneumonia sets, with a total of 5232 images, no false-positives were identified by FastNET. These results are significantly better than previously published studies using deep learning algorithms within hospital settings. For example, Zhang *et al.* [15] reported a sensitivity of 0.88 (95% CI 0.87–0.89) and a sensitivity of 0.79 (95% CI 0.77–0.80) in a universe of 5869 images. Importantly, the AI system proved superior to the analysis of 3 experienced thoracic radiologists. Castiglioni *et al.* 2021 [16] reported a sensitivity of 0.78 (95% 0.74–0.81) and a specificity of 0.82 (95% 0.78–0.85) in 250 COVID-19 positive and 250 COVID-19 negative radiographs. Compared to the two literature reports FastNET is significantly better. The marginally better performance of the Castiglioni *et al.* algorithm, relative to the results of Zhang *et al.*, may be due to the homogeneity of the radiographs from the same region. The results of FastNET deserve deeper analysis. Surprisingly, results with Dataset II are slightly better than with the Dataset I, despite no radiographs from Dataset II had been included in the training dataset. This bluntly contradicts the recent results of DeGrave *et al.* [17]. DeGrave *et al.* analyzed the robustness of deep learning systems to accurately detect COVID-19 in chest radiographs, concluding that often the deep learning systems achieve their performance from confounding factors rather than the medical pathology, yielding poor transferability to datasets not included in the training of the algorithm. It is important to stretch that the study of DeGrave *et al.* [17] used the same datasets we used in this study. These results clearly stretch the robustness of FastNET. The design of the algorithm followed three main rules: (1) to use opensource libraries – Tensorflow[5]; (2) to use published algorithms, for example VGG16 [13] and (3) to include proprietary algorithms and protocols. With (1) and (2) FastNET is intrinsically upgradable and based on solid algorithms. The differentiating aspects of FastNET are, however, the proprietary algorithms and protocols that allow great adaptability when interpreting new radiographs.

[5] www.tensorflow.org

While DeGrave *et al.* [17] found significant problems of transferability between datasets from different sources, FastNET was able to improve the score from the training dataset. The superiority of FastNET is due to its design, in particular the focus analysis on disease related features in the radiographs and not possible confounding elements. This way, the homogeneity of Dataset II proved marginally beneficial because the set showed less variability compared to the training set.

Table 1: Raw performance of FastNET in diagnosing COVID-19 using CXR images from healthy individuals and individuals with pneumonia and COVID-19.

	Number of images			
	COVID-19	Healthy	Pneumonia	Total
Dataset I	601	5	23	629
Dataset II	4046	19	62	4127
Healthy	0	1334	15	1349
Pneumonia	0	59	3824	3883

5 COVID-19 APPLICATIONS AND BEYOND

The FastNET CAD software is in the process of achieving CE certification. Concomitantly, FastCompChem wishes to perform the first clinical trial to establish FastNET as a state-of-the-art algorithm to diagnose COVID-19 infection. There are many applications of FastNET that conform with current WHO guidelines, in particular in resource poor settings and in specific circumstances. Besides use in resource poor developing countries, one potential application in developed economies is by the armed forces. Notable examples of military forces being incapacitated for significant periods of time due to COVID-19 outbreaks. For example, in 2020 the carrier Theodore Roosevelt remained sidelined in Guam for almost two months[6], while half of the Portuguese forces in the Central African Republic were also infected[7]. More recently, 247 sailors aboard a South Korean destroyer tested positive for COVID-19 infection[8]. In all these cases, the FastNET technology would be a valuable tool for fast and effective diagnosis of COVID-19. Another direct application of the current technology is in Emergency Rooms (ER). FastNET can be immediately deployed to perform rapid triage of patients arriving in ERs with symptomatology compatible with COVID-19 infection. This would allow hospital

[6] https://www.navytimes.com/news/your-navy/2020/05/19/carrier-theodore-roosevelt-sidelined-in-guam-by-coronavirus-heads-back-to-sea-this-week/, accessed on August 12, 2021

[7] https://www.publico.pt/2020/09/14/politica/noticia/covid19-88-militares-portugueses-infectados-republica-centroafricana-1931513, accessed on August 12, 2021

[8] https://www.japantimes.co.jp/news/2021/07/19/asia-pacific/south-korean-military-coronavirus-destroyer/, accessed on August 12, 2021

systems to rapidly process patients by sending them to the appropriate ward without delay.

The FastNET technology is powerful and can be extended beyond diagnosis. With the appropriate clinical partners, and after the relevant clinical trials are concluded, the technology can be extended to play a prognosis role. In this scenario the full automated system will be able to assess the expected outcomes and suggest the best treatments. The technology will have then a very important role in helping clinicians taking the best decisions with obvious improvements to patient outcomes and reduction of clinicians' workload. All this contributes to more efficient hospital systems and a reduction of costs. Furthermore, the general principles behind FastNET can be extended to other pathologies that rely of medical imaging for diagnosis. One such pathology is breast cancer through mammograms.

6 DISCUSSION AND CONCLUSIONS

More than one year into the COVID-19 pandemic, and despite massive vaccination efforts, the situation remains dire with governments and health authorities imposing lockdowns, travel restrictions and face mask mandates. The need for fast, accurate and cheap diagnosis tools for COVID-19 remains important in the fall of 2021 as in the beginning of the pandemic. Many efforts have been developed to use radio imagining techniques such as CT scans or CXR as diagnosis tools. The Sars-Cov-2 virus induces lung lesions that are detectable by radioimaging. However, radiologists often confound chest radiographs of individuals with symptoms of COVID-19 infection with those of individuals without symptoms. In this study we demonstrate that FastNET, our deep learning system to analyze medical images, can be trained and used to diagnose COVID-19. The system shows very high sensitivities, 0.96 and 0.98, using two publicly available datasets. The system also scored perfect specificity in both datasets, despite the significant number of healthy and pneumonia radiographs (5232). Our study had some limitations though. First, we only considered simple classifications: COVID-19, pneumonia and healthy. Importantly, our system does not seem to suffer from confounding issues when tested across different datasets, as was found by DeGrave *et al*. [17]. The system is currently undergoing CE marking and clinical trials are being though to validate the technology in real clinical conditions. No attempt in currently being made to have the algorithm differentiating specific categories of pneumonia such as bacterial and non–COVID-19 viral. Therefore, FastNET is currently better used in ruling out COVID-19. There are many situations where FastNET can have a significant impact in combating the pandemic. These include, for example, resource limited scenarios. In developed countries the armed forces would greatly benefit from having fast and accurate diagnosing tools to limit spread of possible outbreaks, for example aboard navy ships.

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[9] https://www.portugalventures.pt
[10] http://www.centro.portugal2020.pt/