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Identifying cardiomegaly in chest X-rays: a cross-sectional study of evaluation and comparison between different transfer learning methods

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Abstract

Background: Cardiomegaly is a relatively common incidental finding on chest X-rays; if left untreated, it can result in significant complications. Using Artificial Intelligence for diagnosing cardiomegaly could be beneficial, as this pathology may be underreported, or overlooked, especially in busy or under-staffed settings.

Purpose: To explore the feasibility of applying four different transfer learning methods to identify the presence of cardiomegaly in chest X-rays and to compare their diagnostic performance using the radiologists' report as the gold standard.

Material and Methods: Two thousand chest X-rays were utilized in the current study: 1000 were normal and 1000 had confirmed cardiomegaly. Of these exams, 80% were used for training and 20% as a holdout test dataset. A total of 2048 deep features were extracted using Google's Inception V3, VGG16, VGG19, and SqueezeNet networks. A logistic regression algorithm optimized in regularization terms was used to classify chest X-rays into those with presence or absence of cardiomegaly.

Results: Diagnostic accuracy is reported by means of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), with the VGG19 network providing the best values of sensitivity (84%), specificity (83%), PPV (83%), NPV (84%), and overall accuracy (84,5%). The other networks presented sensitivity at 64.1%–82%, specificity at 77.1%–81.1%, PPV at 74%–81.4%, NPV at 68%–82%, and overall accuracy at 71%–81.3%.

Conclusion: Deep learning using transfer learning methods based on VGG19 network can be used for the automatic detection of cardiomegaly on chest X-ray images. However, further validation and training of each method is required before application to clinical cases.

Keywords
Artificial Intelligence, deep learning, transfer learning, cardiomegaly, validation

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Introduction

Background

Cardiomegaly is a condition defined by the enlargement of the heart, while it is thought to be associated with other diseases such as hypertension, coronary artery disease, kidney disease, and cardiomyopathy (1,2). Cardiomegaly can be present in various genetic and acquired cardiomyopathies. The prevalence of hypertrophic cardiomyopathy (HCM) is in the range of 1/250–1/500 in adults, while the prevalence of dilated cardiomyopathy (DCM) seems to be twofold. In children, HCM

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is uncommon, while DCM is more likely to occur in the first year of life (3). Cardiomegaly can originate from various abnormalities, such as hypertension, thyroid disorders, or heart valve or coronary artery disease. Early detection is important to ensure a modified diet or exercise regime is in place to reduce further complications.

Plain chest X-rays have been established as a standard imaging method to detect cardiomegaly, using the Cardio-Thoracic Ratio (CTR) as the parameter to evaluate, quantify and diagnose this pathology (4). The CTR is calculated as the ratio of the transverse diameter of the heart to the maximum diameter of the internal thoracic cavity. Specifically, the maximum diameter of the internal thoracic cavity is calculated by measuring the diameter from the medial border of the ribs (4). Usually, this measurement is performed on the level of the dome of the right hemidiaphragm. The transverse diameter of the heart is calculated after measurement of the right and left most borders of the heart, horizontally (Fig. 1). A CTR of 50% is thought to be the upper normal limit, although 45% has been also suggested (4,5). Although novel imaging techniques are nowadays available, plain chest X-rays are still the most cost-effective and accessible method to detect enlargement of the cardiac silhouette, while the specificity of this method when using CTR as the measurement parameter has proved to be high (84.5%) (6). Therefore, early and accurate detection of cardiomegaly on plain chest X-rays is considered to be very important and may also help reduce the costs associated with more expensive imaging methods. In this study, Transfer Learning (TL) methods were employed and evaluated to facilitate the detection of cardiomegaly on plain chest X-rays. The aim of the present study was to explore the feasibility of applying four different transfer learning methods, to identify the presence of cardiomegaly in chest X-rays, and to compare their diagnostic performance using the radiologists' report as the gold standard.

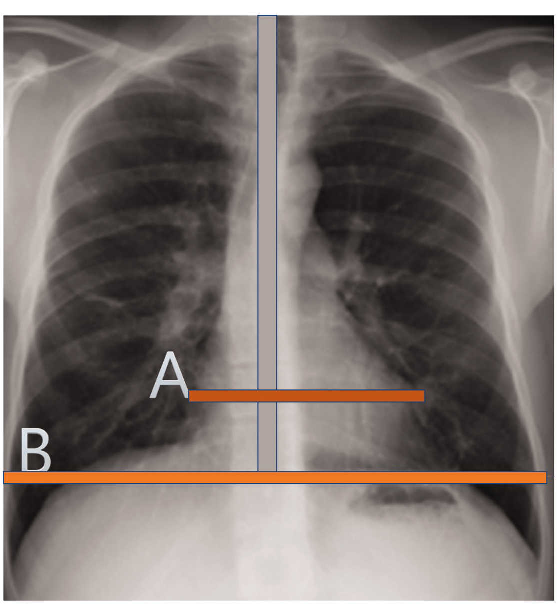

Fig. 1. The standard measurements for calculating the CTR measurement.

Introduction to TL networks

The recent technological advancements have brought Artificial Intelligence (AI) to the forefront of medicine and radiology.

The most widely used branch of AI in medicine is Machine Learning (ML), a statistical process to generate knowledge by training models with data, and fitting models to data (7). With ML, we can now provide systems with the ability to undertake complex tasks with high accuracy without even being explicitly programmed by identifying patterns in streams of input data (8). Deep Learning (DL), a fast-growing branch of ML since 2010s, attempts the abstraction of features directly from raw data, using multi-layered deep neural networks (DNNs) (Fig. 2) (9).

DL can be categorized into supervised, semi-supervised, and unsupervised (Fig. 2) (10). DL is thought to be a powerful tool for use within healthcare; however, it is commonly accepted that it is generally limited by issues such as low quality, low volume, and high sparsity of input data, which may limit the performance of DL methods (11). DL learning methods include the use of convolutional neural networks (CNNs) and recurrent neural networks (RNNs), two different types of learning methods. Many CNN-based models are used for classification of free-text reports, of mammograms, assessment of skeletal bone age, organ segmentation during MRI-guided radiotherapies (12–15). However, one of the most important problem of machine learning that we encounter after we have trained our model is when the model matches the training data almost perfectly but performs poorly in validation of new data. This is widely known as overfitting. Overfitting could be avoided by down sampled operations on the input maps, which reduces the dimension of the data.

TL refers to a method of reusing pre-trained models or knowledge for solving another related task avoiding using training from scratch. As it is widely known, training a model from scratch requires a vast amount of data in order to accomplish a high prediction level. Using TL enables us to use the weights of an already trained model such ImageNet which consists of a dataset of about 1.2 million images for training, 50,000 for validation, and 100,000 for testing, belonging to 1000

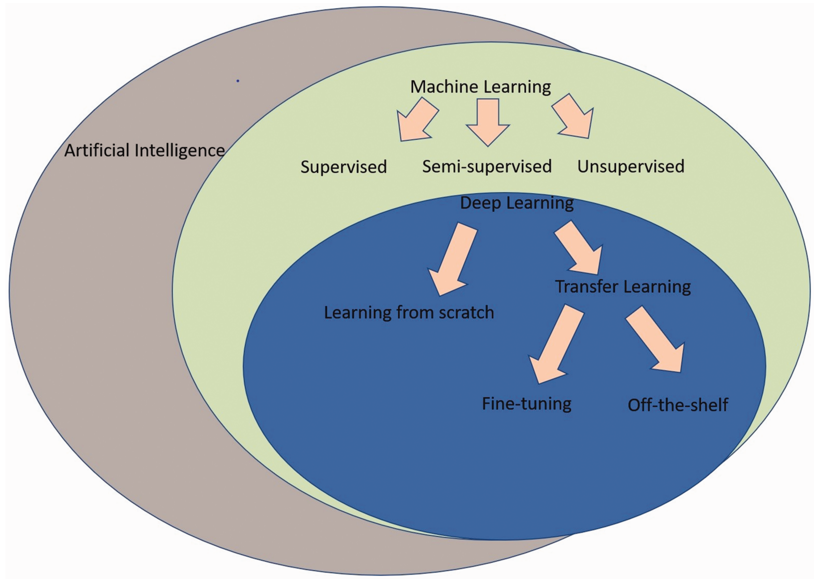

Fig. 2. The hierarchy of Artificial Intelligence and its main branches.

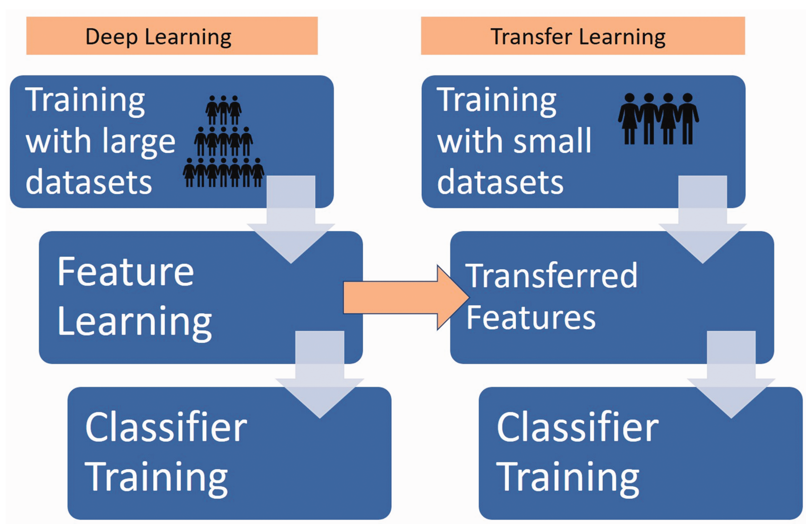

Fig. 3. Training procedure with Deep Learning and Transfer Learning.

categories, without its last fully connected layer as a feature extractor (16,17).

The advantage of TL is that the weights are already pre-trained, instead of using training from scratch (10). Therefore, these models are fine-tuned from pre-trained models, instead of using random Gaussian distributions or learning from scratch, without its final layer as a fixed feature extractor (Fig. 3). This fine-tuning process enables us to fine-tune all the kernels by means of back-propagation. TL is a method approach commonly used within DL applications, and it has proved to be very effective, especially with small training datasets (18). DL is very efficient in learning discriminative features and learn directly from the raw data (11). It can effectively extract learning patterns and data from large, complex data. DL-based algorithms are widely used in radiology, offering the ability of object recognition, classification, localization, and segmentation in medical images (9). When training a small network, a pre-trained large dataset is usually employed. In the present study, ImageNet was used as a pre-trained model, offering the advantages of containing 14 million images with 1000 classes, while it is also publicly accessible (19,20). TL strategies depend on various factors, but the most important ones are the size of the new dataset, and its similarity to the original one.

More detailed information on common strategies used in TL can be found in supplemental material.

Material and Methods

Study design

This is a retrospective quantitative research study, as it makes predictions based on the analysis of already acquired data (21). In this retrospective study, the pre-trained model approach was used to apply transfer learning (22). Ethics approval was not required as open-source data were used and readily available. No identifiable patient information was recovered. The STROBE cross-sectional reporting guidelines were used to write this article (23).

Databases used

Large-scale image classification dataset. ImageNet was chosen in this study as the large-scale object recognition dataset, on which the compared networks had been pre-trained. Its feasibility as a large-scale image recognition dataset is well-established within the literature (24). ImageNet provides more than 14 million of images with 1000 classes, more than 20,000 categories, and it has been widely used during TL applications within medical imaging (20,25).

Classification method. In the present study, off-the-shelf TL was used removing the last fully connected layer of the pre-trained models and replacing it with a logistic regression classifier optimized with regularization.

Logistic regression. Logistic regression is a supervised learning method that is usually preferred for binary classification problems (two class values), as in this study, and is used to model the probability of a certain class (normality vs. abnormality, in this case cardiomegaly). In terms of mathematics, a binary logistic model has a dependent variable with two possible values 0 or 1. To shorten the coefficients of the outcome of the classification, a regularization was used. As input variables were changed, the model's prediction changes a lot. Regression in terms of regularization reduces the variance of the model and the prediction rate is higher (26).

Pre-trained convolutional neural networks tested

Four different TL methods were evaluated and compared in this study. For this reason, four different pre-trained DL image recognition models with different amount of convolution layers were used. All of the models used in this study were trained on the ImageNet database. These models are Google's Inception V3, VGG16, VGG19, and SqueezeNet (27). The Inception V3 network is a widely used network, offering an accuracy $> 78.1\%$ on the ImageNet dataset, widely used within medical imaging, with very good results (28,29). The VGG19 is a CNN comprising 19 deep layers, it is trained on more than 1 million images on the ImageNet dataset, and it has shown promising results when applied to CNN-based methods within radiology (30,31). The third deep neural network used in this study was SqueezeNet, also trained on ImageNet database, consisting of 18 deep layers and having the ability to classify images into 1000 categories (32). Lastly, the VGG16 neural network was used in this study. This is a 16-layer network which has been widely used in similar studies, offering the advantage of an optimal performance during the Large-Scale Visual Recognition Challenge (24).

Data where TL methods were tested

A total of 2000 plain chest X-rays were retrospectively collected from the Picture Archival and Communications System (PACS). These images were categorized into two categories, based on the presence or absence of cardiomegaly. Images with poor quality or no clear anatomic presentation of the organ-target were excluded from the set. Among these X-rays, 1000 were normal (regarding the size of the cardiac silhouette) and 1000 of them depicted a confirmed cardiomegaly. A total of 1600 plain chest X-rays (80%) were used for training, while the remaining 400 (20%) images were used as test set; 2048 deep features were extracted from each plain chest X-ray image (Fig. 4). A logistic regression algorithm optimized in regularization terms was used to classify chest X-rays into presence or absence of cardiomegaly (normal or abnormal).

The selected plain chest X-rays were extracted from the viewer and converted into 384×384 pixel-sized images with a JPEG format. No further processing was applied to the images with regards to size and shape. Fig. 5 demonstrates an example of our data with a normal chest radiograph and a radiograph with cardiomegaly. It must be noted that there were cases in which the used networks failed to correctly identify the images as normal or abnormal, and such cases are demonstrated in Fig. 6.

Data analysis and evaluation of diagnostic performance indices

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were all calculated as part of evaluating overall diagnostic accuracy of each method (33,34). This method was preferred for

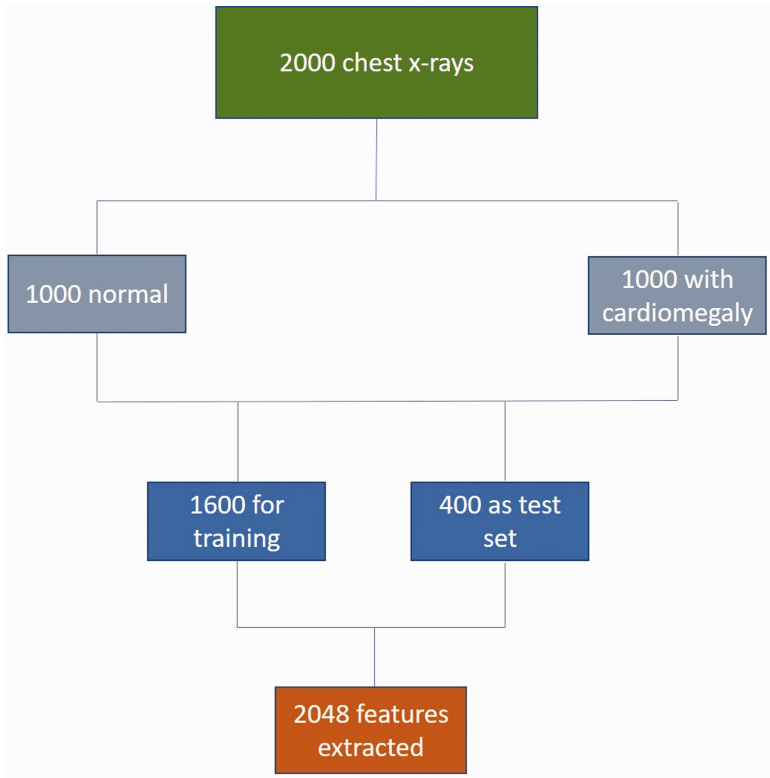

Fig. 4. Graphical depiction of the study's pipeline.

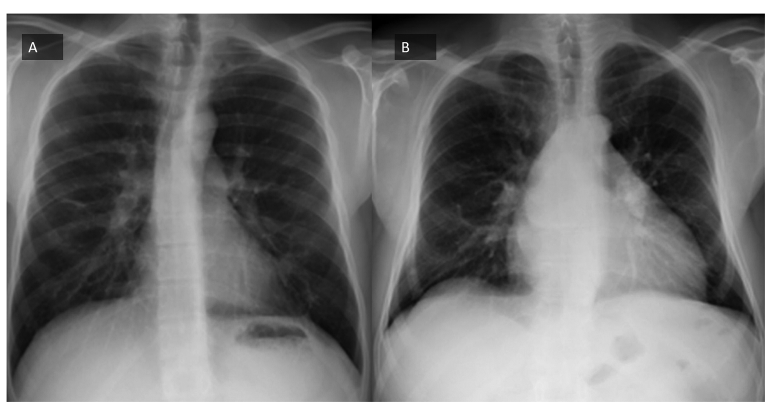

Fig. 5. Normal chest radiograph (a) and cardiomegaly (b) (32).

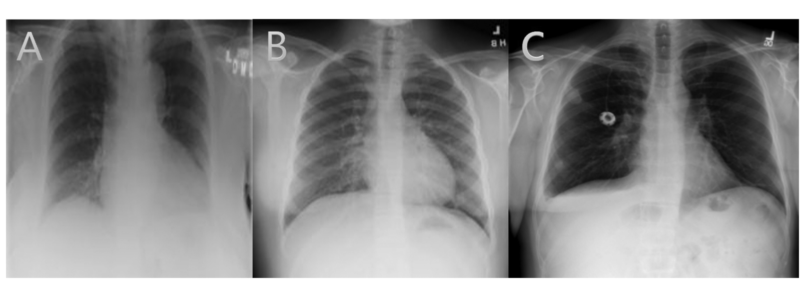

Fig. 6. Cases in which the networks failed to correctly identify cardiomegaly. (a) Normal result instead of cardiomegaly, due to suboptimal image quality. (b, c) Results of cardiomegaly despite the normal size of the heart silhouette, due to suboptimal image quality (b) and catheter insertion (c).

evaluation of the accuracy instead of receiver operating characteristic analysis, as it is more suitable for balanced data like the ones used for the present study.

Results

Using the remaining 400 plain chest X-rays of the test set, the performance of Google's Inception V3, VGG16, VGG19, and SqueezeNet neural networks was evaluated.

With regards to the sensitivity (the true positive rate) of the evaluated networks, Google's Inception V3 network achieved a sensitivity of 64.1%, while the VGG16 network had a sensitivity rate of 81%. Similarly, the sensitivity of SqueezeNet was reported at 82%. However, the sensitivity that the VGG19 network achieved was the highest among the tested networks, achieving a sensitivity rate of 84%. Consequently, the sensitivity of the tested networks achieved similar rates, in the range of 81%–84%, with the exception of Google's Inception V3, which yielded a significantly lower sensitivity rate. Fig. 7 and Table 1 depict the overall distributions of the tested networks regarding different accuracy indicators.

The measurements of the specificity of each of the tested networks showed that the networks achieved a more similar specificity compared to the sensitivity, as there is a greater uniformity among them. However, the lowest specificity rate was noted again for Google's Inception V3 network, achieving a rate of 77.1%. Similarly, the highest specificity rate was achieved by VGG19 network (83%), while VGG16 and SqueezeNet achieved 81.1% and 80%, respectively.

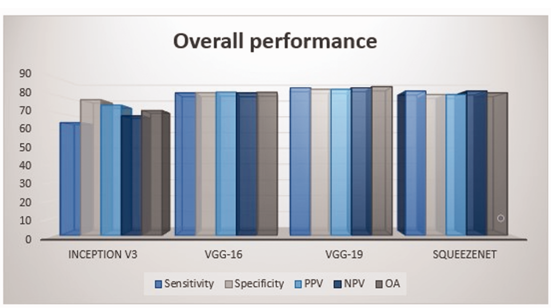

Fig. 7. Summary of overall performance of the tested networks.

The PPVs of each utilized network were assessed, and that indicated that again the VGG19 network achieved the highest PPV among all networks, giving a PPV of 83%. On the contrary, the lowest PPV was reported for Google's Inception V3 network (74%), while the VGG16 and SqueezeNet achieved a PPV of 81.4% and 80%, respectively.

NPV is a measure to assess the degree of the true negative results of a test, meaning that a negative prediction of the test is yielded and the true condition is also negative. The highest NPV was achieved by the VGG19 network (84%), while Google's Inception V3 was again the network with the lowest rate (68%). Similarly, VGG16 and SqueezeNet achieved similar results regarding NPV (81% and 82%, respectively), giving the conclusion that the overall performance related to NPV was similar to PPV.

Finally, the overall accuracy (OA) of the tested networks was evaluated. OA is the weighted average of a test's sensitivity and specificity (33). The evaluation of the OA of the tested neural networks showed that the VGG19 network achieved the highest OA among all the networks, giving an OA of 84.5%. On the contrary, Google's Inception V3 network achieved the lowest OA among the four tested networks (71%). Following the results of sensitivity and specificity, the VGG16 and SqueezeNet networks achieved similar rates of OA, reporting an OA of 81.3% and 81%, respectively.

Discussion

There is currently a wealth of academic literature underlining the feasibility and efficacy of TL approaches using CNNs for image recognition and classification (20,25,35).

Previous studies have used other deep learning methods, with variable results in detecting cardiomegaly but also using a smaller sample size (36–39). Another study has tested three TL algorithms, including Inception 3, but found out much lower accuracy levels than the ones we describe here (40). The results of the present study clearly indicate that a TL approach using CNNs can be reliably used for automatic detection of cardiomegaly on plain chest X-rays. Moreover, after evaluating the performance of four different

Table 1. Summary of overall performance of the tested networks.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	OA (%)
Inception V3	64.1	77.1	74	68	71
VGG-16	81	81.1	81.4	81	81.3
VGG-19	84	83	83	84	84.5
SqueezeNet	82	80	80	82	81

networks on the same dataset, the present study revealed that the VGG19 neural network has the highest diagnostic performance among these networks. The superiority of the VGG19 network has been already supported, with Shaha and Pawar (41) concluding that a fine-tuned VGG19 network achieves an overall higher performance compared to VGG16.

Our study reinforces published literature (37,42,43), indicating that automatic detection of cardiomegaly is now feasible when using pre-trained neural networks. These methods are very promising and already revolutionize feature exaction from medical images.

However, there are still some limitations:

- This study uses a pre-trained network, and this may differ from actual medical images in many different ways.
- We need not have access to prior medical images or other clinical data of these patients to be able to understand the clinical significance, correlations, or importance of these findings; this would be better suited to a prospective study.
- It also uses a relatively small dataset. Within the literature, it is a consensus that when applying CNN-based approaches to medical imaging, limited datasets can be a great drawback, and growing a well-annotated dataset is believed to be as crucial as developing new algorithms (17). However, using TL, small datasets can be used, taking a neural network, which has been pre-trained on a large dataset and adapt its knowledge to the specific task without over-fitting (44).
- Such models must be able to become generalizable to unseen data. To achieve this, over-fitting must be minimized. Over-fitting occurs when a model memorizes the noise instead of the signal on the image. Therefore, this over-fitted model will not perform well on a new dataset (20). Increasing the size of the dataset will result in decreased over-fitting.
- This method is able to differentiate between normal appearance of the cardiac silhouette and severe cardiomegaly. Further work must be done to ensure that discrimination of marginal cases of cardiomegaly would not be missed by the proposed network.

Although the results of the current study are very promising for the timely evaluation of cardiomegaly on plain chest X-rays using TL methods, future work with larger datasets and use of prospective studies with new clinical imaging data are needed in order to establish the optimal methods to be used. Moreover, either fine-tuning TL or using learning from scratch, would offer the ability to use larger datasets, compare the results and suggest the optimal methods for the diagnosis of cardiomegaly.

In conclusion, TL approaches using pre-trained CNNs have been well established for image classification, recognition, and segmentation. The results of the present study confirm the efficacy of these methods for automatic detection of cardiomegaly on plain chest X-rays and conclude that the pre-trained network VGG19 has superior performance compared to three other networks. Further research is needed using larger prospectively collected datasets for clinical validation of the model.

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Supplemental material

Supplemental material for this article is available online.

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