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A Comparative study on classification performance of Emphysema with transfer learning methods in deep convolutional neural networks

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Abstract

Today Emphysema, which takes place among the top five diseases, is encountered in the western world in terms of rehabilitation and healthcare costs. Diagnosis of this type of respiratory tract disease with the help of computers is gradually increasing its importance. In this study, we aimed to classify it with the transfer learning method by using single labeled emphysema diagnosed data which is obtained from three large data sets. We classified the images that are obtained from ChestX-ray14, CheXpert, and PadChest databases by 95% of Area Under the Curve (AUC) with the fully connected layer model and DenseNet-121 pre-trained neural network and 90% of Area Under the Curve (AUC) with Xception pre-trained neural network. We evaluated this proposed deep learning-based model as an effective and practical diagnostic tool for emphysema alone, using x-ray data. Notably, transfer learning is a very functional approach in terms of differentiation between normal and patient in similar diseases that have just emerged in the pandemic period that we live in.

Keywords: Deep Learning, Transfer Learning, Convolutional Neural Networks, Medical Imaging, Emphysema Diagnosis.

MSC 2010: 68T10, 92C50, 92B20.

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1 Introduction

Emphysema is defined as the main type of lung condition known as a chronic obstructive pulmonary disease (COPD). The most important etiological factor of the disease is a smoking habit, the effects of which are expressed in various ways. In addition to smoking, other inhaled pollutants such as cadmium chloride, nitrogen oxides, and phosphagen are also identified as the main factors that cause this disease. Especially with the increase of smoking in the community, the increase in emphysema cases is important. In low- and middle-income countries, 90% of deaths occur due to emphysema and related COPD [1]. It is accepted that there are more than 200 million patients worldwide. However, the incidence of the disease is higher in industrialized settlements, where air pollution rates are high. Generally, the mild form of emphysema is quite common. The prevalence of individuals close to the age of 70 is quite high and it is more common in men. Although the pathogenesis (origin and development) of the disease is a complex process, there are two fundamental mechanisms. The first is structural fragility due to elastolysis (lack of elastic tissue) in the lungs, and the second is the loss of airway support.

As a result of the abnormal activity of proteolytic (protein-dissolving) enzymes, this disease causes irreversible destruction of alveolar walls in the lungs and expansion of distal air spaces. If it is defined in general, it can be called as airway obstruction. The symptoms that cause such morphological changes in the lungs mentioned here are difficult to detect with conventional radiographic imaging techniques [2] because the decrease in tissue density caused by emphysema can occur in very small sizes. Today, chest X-ray images are frequently used for this type of diagnosis for respiratory tract diseases. However, chest X-rays are known to be devoid of sensitivity in mild to moderate emphysema. The screening for emphysema detection is very often done today with the method called spirometric lung function test, which is based on numerically evaluating how much a patient breathes and how much of this breath can be extracted within a certain period of time. Of course, the cooperation of the patient is very important in this type of method. On the other hand, this screening method cannot be used to locate emphysematous changes in the lung. Determining the regional distribution of emphysema is very important for making clinical decisions if the patient will undergo lung volume reduction surgery.

New imaging techniques are helpful in the face of the difficulty of detecting the disease from these aspects. There are very good improvements in the detection of this disease with high-resolution computed tomography (HRCT) [3]. However, its use is limited to the high radiation dose applied to the patient. Some studies on this subject recommend using Magnetic Resonance Imaging (MRI) techniques as supplementary/complementary to Computed Tomography applications for the detection of emphysema. However, MRI applications are relatively expensive, difficult to access, and prone to breathing artifacts, preventing it from becoming a routine approach used in the diagnosis of this disease. It is an important issue to directly evaluate the microstructural damage in the alveolar network caused by emphysema, to see the course of the disease and the treatment results. However, in this case, histopathological interventional biopsy methods are still applied as a valid approach. Methods such as biopsy always pose a risk to the patient and burden time and cost.

Clinical X-ray imaging, which is frequently used in the medical world today, can be defined as the application of image creation depending on the X-Ray absorption properties of tissues and materials in the human body. Medical imaging is based on a physical phenomenon called photoelectric absorption. X-ray absorption is a variable that depends on approximately the fourth time the atomic number value of the atoms of a material or medium, denoted as Z [4]. Thanks to this feature, skin, bones, etc., it is ensured that the required image contrast is obtained between materials of different densities. The second feature that is effective in medical imaging is the depth of penetration. The depth of penetration of X-Rays corresponds approximately to the third times the photon energy for a given material. By adjusting the value of the photon energy, it is possible to obtain the appropriate penetration depth depending on the material being worked on.

Diagnosis and severity of pulmonary emphysema on chest radiographs are difficult, especially in the early stages of the disease. Conventional chest radiographs can visualize indirect signs of increased lung volume seen in emphysema, such as flattened diaphragm, widely spaced ribs, increased chest diameter, and increased retrosternal air space in lateral view. In conclusion, chest radiograms have been shown to be reasonably accurate for advanced emphysema, but to be moderately sensitive in mild to moderate emphysema with inter-observer variability [5-8].

In general, there are many publications in which different imaging techniques are used in the diagnosis of thoracic diseases. The approaches used in these publications can be divided into two groups. These two groups can be listed as chest x-ray and computed tomography. Artificial intelligence methodologies were frequently used in both of these groups. Especially in recent years, many methods have been tried using chest x-ray images. Convolutional Neural Networks (CNN) methods have yielded very successful results in this group. Some of the methods performed are as follows: classification of disease [9], determination of lungs by segmentation [9], and determination of pathological nodule and mass by localization [10]. Along with these methods, the methods of standardizing chest x-ray images and editing them with different approaches were also applied. These studies [11] in the ChestX-ray14 database are in the form of using the images in the database for the training of the artificial neural network. One of the most common problems encountered in the studies here is that the images in this archive are not uniform. There are many artifacts in the pictures, such as noise from medical equipment. Another problem is that pictures cannot be used in full resolution in artificial neural network training. Reducing the resolution brings the risk that small size and vital lesions will not be noticed. Successful researches have also been made to solve these two problems. In addition, the DenseNet [12, 13] neural network, which has been produced to solve these problems, has limited performance, although it also gives successful results. A remarkable study is the merging of two different artificial neural networks separated by the segmentation method using multiple tagging [14].

CheXpert, the database of Stanford University, is used in successful studies, especially in the diagnosis of pneumonia and lung cancer [15]. The best results obtained from this data set are listed on a website on a date basis and made available to researchers. Similarly, the PadChest is a preferred database by researchers for use in multi-label disease diagnosis. Here, there is a study on the production of labels for medical images with natural language processing methods [16]. Although the last two databases are not as popular as ChestX-ray14, they are often preferred in research.

In this study, we aimed to correctly identify emphysema patients by transfer learning method and analyzing chest X-ray data with the help of deep learning approaches. The first novelty here is the use of three large databases around the world. Secondly, Xception and DenseNet-121 pre-trained artificial neural networks were used to classify patients diagnosed with emphysema only in these databases.

2 Material and Methods

2.1 Data Sources

There are many respiratory system disorders such as bronchitis, pneumonia, asthma, pleural effusion (accumulation of water in the lung membrane), especially emphysema. Today, there are three data sets available to researchers worldwide for the detection of these diseases with machine learning methods. These data sets provide highly detailed X-ray images and diagnostic details for scientists who want to do research on this subject.

One of the data sets used in this study is the ChestX-ray14 [11] database provided by the National Institute of Health (NIH) in the United States. In this database, there are 112,120 anterior view chest x-rays of approximately 30,805 patients. The diagnostic information in this dataset includes 14 respiratory system diseases (thorax). The main ones can be listed as Pneumonia, Pneumothorax, Emphysema, Fibrosis, and Pleural Thickening. Another data set we used is the PadChest database of Alicante University in Spain [17]. In this database, there are 160,000 images of 67,000 patients. This set contains multi-labeled information on 19 different diagnoses. Images in the PadChest database were taken from six different angles. Finally, another data set we use is the CheXpert database provided by Stanford University [18]. In this database, there are 224,316 chest x-ray images of 65,240 patients. This set also includes diagnostic information for 14 different thoracic diseases such as ChestX-ray14.

The common feature of these databases is that there are cases in which the diagnosis of emphysema disease is alone, as well as data that have been diagnosed with other diseases. The diagnosis of emphysema, which is labeled multiple, is more than just a single labeled diagnosis. In this study, we used only data diagnosed with emphysema disease alone. In total, the number of data diagnosed with emphysema alone is 1,594. However, these images have been increased to 3,190 with augmentation to be used in the artificial neural network. The data sets and the information about the data numbers that we used are shown in Table 1.

Table 1. The number of images and sources used during the study, which are only diagnosed with emphysema (with augmentation)

Dataset name	Diagnosis type count	Single labeled emphysema diagnosis
ChestX-ray14	14	1,046
CheXpert	14	1,018
PadChest	19	1,126
Total Emphysema		3,190
		Normal Labeled Images
Total Normal	-	2,617
General		5,807

Similarly, no disease was diagnosed in the same number in total from the same data sets, and we included the data in our study. The number of data we use for healthy patients is 2,617. As a result, we employed a total of 5,807 data to be used in the input layer of the model in the study. We used a distribution of 80% training, 15% verification, and 5% testing in our dataset. The rates of data distribution are shown in Figure 1.

Deep learning algorithms, especially convolutional neural networks (CNN), are a highly reliable approach that is often used to learn pre-

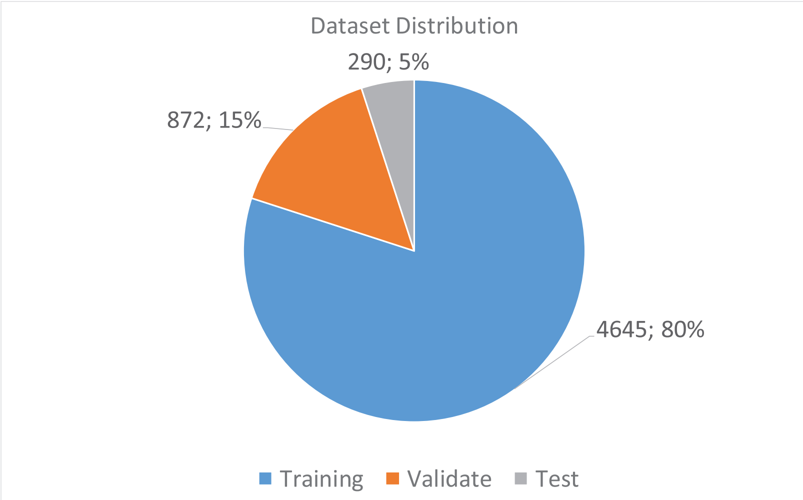

Figure 1. Distribution of data used in training our artificial neural network

dictive properties using visual data directly [19]. There are many deep CNN models for object detection and classification such as ResNet [20], InceptionV3 [21], and Xception [22], which are frequently used today. In 2015, the ResNet model succeeded in winning the ImageNet Large-Scale Visual Recognition Challenge with an error rate of %3.6 [23]. The Xception model we preferred in this study was derived from the Inception V3 model in 2016. Both models use the ImageNet dataset. CNN's are a frequently preferred method for classifying medical images, and new studies are constantly being conducted on them today. The basis of the performance of ESA is the provision of a large amount of data. However, if the data set to be studied is of small size, the success in training the artificial neural network decreases. At this stage, the transfer learning method offers a powerful option to avoid memorization during the learning of limited data [24].

The training of the artificial neural network in transfer learning is carried out in two stages. In the first step, using the fundamental weights of a pre-trained artificial neural network, fine-tuning is done for the data set being studied. Then, using the weights of the neural network that are obtained here is retrained with the layers of the new neural network added to the pre-trained neural network. Here the main reason for the approach is the relatively small size of the researched data set. However, the smallness of the data set in this study is to be able to classify the disease from the data of patients diagnosed with emphysema alone.

2.2 Preprocessing of X-ray Data

Many different methods and algorithms have been proposed for the classification of thoracic diseases by artificial intelligence. In this study, we aimed to classify images without any procedure, especially in images obtained and diagnosed with emphysema. However, when we examined the data sets, we realized that the images in the data set were not in the same standard. In addition to the image quality, the total number of images diagnosed with the disease remained below 2.000. Here, we used visual augmentation methods that are frequently preferred in CNN models. This augmentation process is used to prevent overfitting of the model. For this purpose, 28% magnification, 10% width shift range, 20% rotation operations were applied to the images. The pictures obtained from the data sets were reduced to 210 x 210 x 1 dimensions for use in the Xception and DenseNet-121 model. Moreover, the Contrast Limited Adaptive Histogram Equalization (CLAHE) filter, which is known to give good results in medical images, was applied to all images here. In this method, histogram equalization is performed by looking at the values of a central pixel in a local window [25]. The effect of the CLAHE filter in a sample image can be seen in Figure 2. This filter has greatly improved some images, especially in the PadChest dataset.

2.3 Implementation of Model

In this study, we first based on the Xception pre-trained neural network for use in emphysema classification. Xception [22], is based on the assumption that the correlation between the input channels can be completely separated from the spatial correlation. Xception in particular extends the initial architecture by replacing the standard convolution

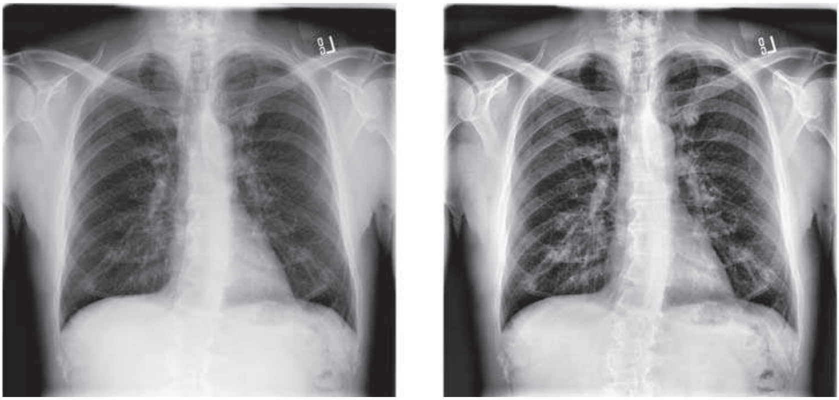

Figure 2. A sample x-ray image with a CLAHE filter applied

with a deeply independent convolution. Thus, this network is defined as a linear stack of deep collapsible layers with permanent connections. In visual classification studies, transfer learning or fine-tuning according to the size of the data set to be applied is a novel approach. The behavior pattern to be determined in the CNN training here is developed by considering the size and similarities of the data sets. If there is a small data set, learning transfer can be done depending on the fact that it is obtained from different and same sources, and fine-tuning can be done in case of having large data. However, these are not binding when it comes to research. Transfer learning (TL) is a method that transfers the pre-trained artificial neural network from the source area to the target area in order for the CNN model to have a better image recognition ability. In the studies conducted, it was revealed that the TL-CNN models have better generalizations, and their qualities in extracting strong image features, apart from the training data, were shown [26, 27]. However, since the TL needs the transfer of pre-trained weights and parameters, the TL-CNN models have a different working process and different efficiencies in training and testing compared to their prototypes.

The transfer learning method used in CNN is applied in two ways. The first of these is the method called a bottleneck. This method is based on training by replacing fully connected layers in the last part of a pre-trained artificial neural network (eg. ImageNet) with newly determined CNN layers. The important approach here is to obtain input weights by freezing the convolution layers of the first neural network while determining the bottleneck properties. Later, these frozen layers are activated and the values obtained in the previous step are transferred to the newly formed network. Another method is called the "Heating" method. In this method, the fully connected layers that we created in the model are determined randomly according to the Xception network which we have added. In the existing Xception neural network, there is a risk of losing the properties of the pre-trained neural network if the weights of these new fully bonded layers are not prevented from back-propagation. Normally, when an artificial neural network is being trained, the backpropagation process is stopped after fully connected layers. In this way, the artificial neural network enables feature extraction in the inversion layers. Unlike the bottleneck method, some parts of the network created in the fine-tuning process are excluded from the training, especially the entrance parts, and only fully connected layers are trained. Then the entire network is retrained with fully connected layers. The TL and fine-tuning approach that we have applied in this study is shown in Figure 3.

In this study, we have prepared the weights obtained with the Flatten layer after the Xception / DenseNet network, which is taken as the basis for the classification process, to be sent to two fully connected layers. The network model we have created has two Dense, that is, fully connected layers. Since we are using the last fully connected layer 2 class in our model, there are two inputs. For the transfer of learning, we first trained for frozen layers in the artificial neural network for 25 epochs. At this stage, the total number of parameters of the network is 21 million for Xception based model. Approximately 20 million of these parameters are non-trainable. In the next step, the neural network was trained for 100 epochs, together with the network structure designed by us. In this second stage, the total of untrained parameters is 8 million. We used the root mean square error method for optimization. In addition, we set the learning rate as 0.00001 at the beginning and the decreased value as 0.004.

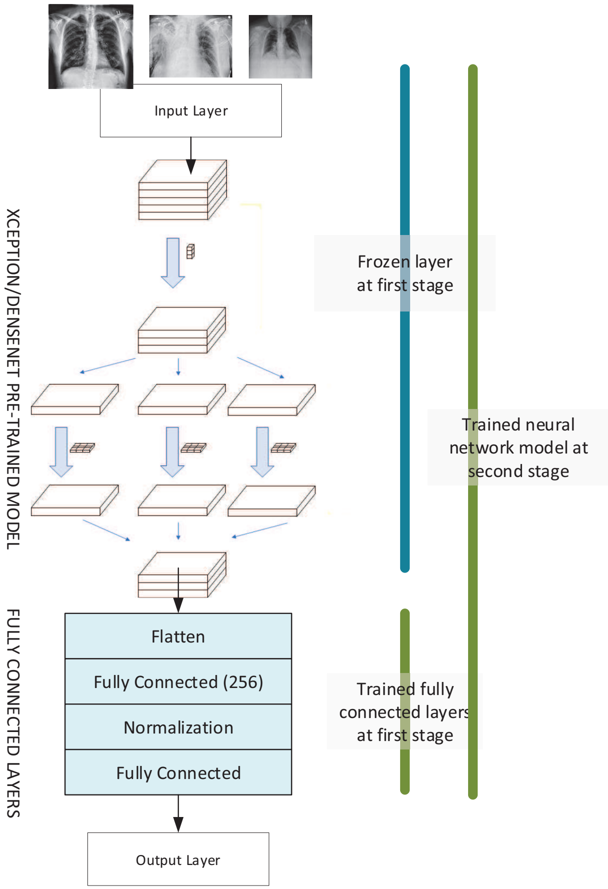

Figure 3. Artificial neural network model and training method with transfer learning

3 Results and Discussions

In this study, we tried to classify a total of 5,807 images obtained from three separate databases with only emphysema diagnosis. We developed the application and used it for classification using Python and Keras. We conducted our experiments using the Google Colab platform by serving our data on Google Drive. The training of the fully connected layers we used in our Xception Model took 1 hour 25 minutes and the training of the entire network took 5 hours 24 minutes. During our experiments, we tried to get the best results by testing various hyper-parameters. For the Xception pre-trained artificial neural network we could reach in this study, the highest Validate Accuracy was 86.44% and the highest AUC score was 90%. This value can be considered good when compared with many studies.

For the Xception model we created, the verification precision (val_acc) of the fully connected layers we first created resulted in 74.61%. Later, as a result of the training we conducted for the entire artificial neural network, we determined the accuracy of the verification as 86.44%. There are many respiratory system disease classification studies using the data sets we used in this study. As mentioned earlier in these studies, successful results have been obtained by using multiple classification methods and different deep learning models. As can be seen in these studies, the DenseNet pre-trained network gives very good results in the classification of x-ray images. However, there is limited work done with the Xception network in the literature. This paper yielded the best results compared to a small number of studies conducted using three different data sets and classifying only the diagnosis of emphysema. The values and comparisons of the results we obtained are shown in Table 2.

A distinctive feature in these studies is that auxiliary algorithms are also used in visual classification. For instance, in I. Allaouzi[28], firstly, the lung region in the data in the data set was separated by segmentation and the diagnosis classification was made accordingly. Studies with low AUC scores are directed towards the classification of X-ray data and special algorithms are not preferred. This raises the need for these data to be prepared according to certain standards be-

Table 2. Comparisons of previous studies and the proposed Xception based model

Author(s)	Dataset(s)	Label	AUC Score	F1 Score	Model
I.Allaouzi[28]	ChestX-ray14, CheX-pert	Multi	0.94-0.926	0.56-0.63	DenseNet
X. Wang et al.[11]	ChestX-ray14	Multi	0.833	0.95	ResNet
L. Yao et al.[29]	ChestX-ray14	Multi	0.842	Not Shared	DenseNet
S. Gündel et al.[12]	ChestX-ray14	Multi	0.895	Not Shared	DenseNet 121
L. Han et al.[14]	ChestX-ray14	Multi	0.921	Not Shared	DenseNet 121
C. Mao et al. [30]	ChestX-ray14	Multi	0.8823	Not Shared	DenseNet 169
H. Wang [31]	ChestX-ray14	Multi	0.8222	Not Shared	ChestNet
E. Çallı et al. [32]	ChestX-ray14	Single	0.854	Not Shared	ResNet5.0
P. Rajkupar et al.[33]	ChestX-ray14	Multi	0.9371	Not Shared	DenseNet 121
S. Rakshit et al.[34]	ChestX-ray14	Multi	0.9351	Not Shared	ResNet18
S. M. Sushavan et al.[35]	ChestX-ray14	Multi	0.52	Not Shared	Xception
Our Proposal	ChestX-ray14, CheX-pert, Padchest	Single	0.82	0.75	Xception

fore being subjected to excessive pre-processing. Apart from Table 3, Y. Wang et al. [36], in their study, stated the AUC score as 99.06% with ChesNet2, which they developed using DICOM visuals. However, in the mentioned study, no value was shared especially regarding emphysema.

In our experiments, we created a model in the same way by using the similar TL method and DenseNet weights. In our DenseNet-121 application, we preferred not to change the hyper-parameters and optimization functions we created earlier. In our training, we obtained with this model the highest values as 93.75% accuracy and 95% AUC scores among the results of the studies that are shown in Table 3. Among these studies, the studies in which we reordered DenseNet users and their results are shown in Table 3.

The ROC graph of the model training we did with the DenseNet121 network during the study is shown in Figure 4.

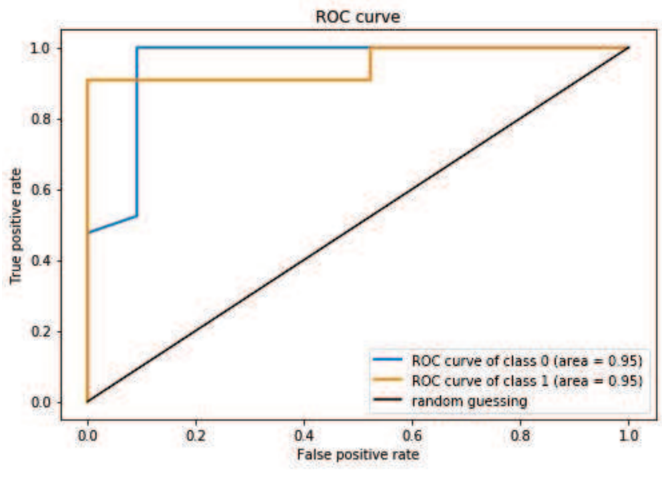

Figure 4. ROC curve of classification success of DenseNet-121 artificial neural network

The high AUC score we obtained in the experiments and evaluated the classification that we made was successful. Undoubtedly, we think that we will make great progress in the diagnosis of this disease with

Table 3. Comparison of previous studies and proposed model using DenseNet-121

Author(s)	Dataset(s)	Label	AUC Score	F1 Score	Model
I.Allaouzi[28]	ChestX-ray14, CheXpert	Multi	0.94-0.926	0.56-0.63	DenseNet
L. Yao et al.[29]	ChestX-ray14	Multi	0.842	Not Shared	DenseNet
S. Gündel et al.[12]	ChestX-ray14	Multi	0.895	Not Shared	DenseNet 121
L. Han et al.[14]	ChestX-ray14	Multi	0.921	Not Shared	DenseNet 121
C. Mao et al. [30]	ChestX-ray14	Multi	0.8823	Not Shared	DenseNet 169
Our Proposal	ChestX-ray14, CheXpert, Padchest	Single	0.95	0.94	DenseNet 121

new approaches to be produced by adding more original data obtained from different databases. In general, only one data set was used in studies in the literature. In addition, the diagnosis of emphysema disease is classified together with diagnoses seen with more than one thoracic disease. The records of patients diagnosed with emphysema alone, which we used in this study, are relatively few compared to patients diagnosed with more than one respiratory disease. In diagnoses related to the disease, it is difficult to determine it apart from other disease diagnoses, but it gives high results when it is classified together with very specific diseases such as pneumonia, requiring further research on whether it is a health classification. Especially, it may be a preferred method to detect respiratory system diseases that cause such micro damages by computed tomography rather than x-ray. It is clear that medical image classification studies will not be used in decision-making instead of the experts. However, it has a guiding feature in order to assist medical doctors in the diagnosis of these diseases.

In this study, we have shown that the transfer learning method is a successful method in such medical classification applications if the data sets are different and the number of data is low. Especially with the Covid-19 pandemic, we are experiencing today, it has once again revealed the importance of artificial intelligence applications in diagnosing with medical images. Since lung lesions caused by Covid-19 also cause damage to alveoli like emphysema, their detection is promising with the methodologies mentioned in this study. Especially in this disease, even if the blood tests are negative, the definitive diagnosis of this disease can be made with computer-aided tomography images. Image recognition models that will distinguish Covid-19 infection from standard pneumonia show high success. In addition, new methods are being developed to better show the situation in human tissues in standard X-ray images. With the advancing technology, artificial intelligence models that can classify these images as successfully as computed tomography images will be developed.

4 Additional Info

Data sets of the developed models and models of the study can be accessed at github.com/MachineLearningLessons/DenseNetEmphysema.

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