Lung Nodules Classification Using Convolutional Neural Network with Transfer Learning

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Abstract. Healthcare industry plays a vital role in improving daily life. Machine learning and deep neural networks have contributed a lot to benefit various industries nowadays. Agriculture, healthcare, machinery, aviation, management, and even education have all benefited from the development and implementation of machine learning. Deep neural networks provide insight and assistance in improving daily activities. Convolutional neural network (CNN), one of the deep neural network methods, has had a significant impact in the field of computer vision. CNN has long been known for its ability to improve detection and classification in images. With the implementation of deep learning, more deep knowledge can be gathered and help healthcare workers to know more about a patient's disease. Deep neural networks and machine learning are increasingly being used in healthcare. The benefit they provide in terms of improved detection and classification has a positive impact on healthcare. CNNs are widely used in the detection and classification of imaging tasks like CT and MRI scans. Although CNN has advantages in this industry, the algorithm must be trained with a large number of data sets in order to achieve high accuracy and performance. Large medical datasets are always unavailable due to a variety of factors such as ethical concerns, a scarcity of expert explanatory notes and labelled data, and a general scarcity of disease images. In this paper, lung nodules classification using CNN with transfer learning is proposed to help in classifying benign and malignant lung nodules from CT scan images. The objectives of this study are to pre-process lung nodules data, develop a CNN with transfer learning algorithm, and analyse the effectiveness of CNN with transfer learning compared to standard of other methods. According to the findings of this study, CNN with transfer learning outperformed standard CNN without transfer learning.

Keywords: Deep learning, Convolutional Neural Network, Lung nodules, CT scan

1 Introduction

Lung cancer is a well-known disease with a significant mortality rate in the modern era. It starts in the lungs, where cancer cells can move to lymph nodes or other organs such as the brain [1]. In 2018, lung cancer had the highest percentage of new cases and deaths worldwide by 11.6% [2]. According to the statistics by World Health Organization, lung cancer has the second highest rate of cases in Malaysia in 2018 after breast cancer [2]. About 16.6% of the patients are male while 5.4% are female. Based on The Malaysia National Cancer Registry Report 2012-2016, lung cancer stands as the third highest cancer detected among Malaysians which affects male more than females [3]. Deep learning is no longer a strange concept in the field of medical image analysis[4-7]. It is a growing trend, and there is a growing demand for the use of deep learning to achieve accurate and precise outcomes [8]. Deep learning involves imitating how the human brain works in dealing with data and recognizing patterns for the decision-making process. With the emergence of technology and better algorithms, more and more machines give high rates of accuracy and reliability for medical analysis. Detection of cancerous or malignant cells are crucial for treatment of lung cancer. Applications of image analysis deep learning on computed tomography (CT) scan images help to detect malignant cells early before they develop and become lethal [9, 10]. Deep learning has been proven to have significant performance in image processing especially in object detection and localization [11]. Deep learning, specifically CNN, is known to have a high success rate if a large amount of data is implied [12]. CNN requires a large amount of well-labeled training data, such as ImageNet, to perform well, which medical images lack. Large datasets are not always available due to several factors such as the costly expert explanatory notes, ethical issues, and shortage of disease images [12]. Models with large number of parameters fail to learn the patterns if supplied with small datasets and can easily cause overfitting [13]. Most traditional CNN architectures' performance is heavily dependent on the size of the data because they initially have a large number of parameters, and state-of-the-art CNN models trained with large datasets such as ImageNet are unsuitable for datasets with hundreds or thousands of instances [14]. This is a challenge that researchers must address in order to improve model performance while working with a large amount of labelled data. However, standard CNN is unsuitable for medical imaging processes with small datasets (hundreds to thousands number of data). A comprehensive review of various types of CNN for pulmonary nodules detection, false positive reduction and classification has been done in [15-18]. Table 1, on the other hand, focuses on CNN with advanced implementation approaches rather than conventional methods or traditional CNN.

Table 1 A comprehensive review of various types of CNN for pulmonary nodules detection

	Ref.	Model	Data sets	Key Points
Hybrid CNN	[12]	2D LeNet + 2D AlexNet	LIDC/IDRI	Layers of LeNet settings are combined with AlexNet parameter settings to create a model for malignancy prediction
Transfer Learning Based System	[19]	2D CNN, SVM, MLP, KNN, RF, Naïve Bayes	LIDC/IDRI	Eleven 2D CNN models are used for features extraction. The models are Xception, VGG16, Inception-ResNet-V2, VGG19, DenseNEt201, MobileNet, InceptionV3, DenseNet169, ResNet50, NASNetLarge and NASNetMobile. SVM, MLP, KNN, RF, and Naïve Bayes are trained separately with collected features.
	[20]	VGG16	LIDC/IDRI Private Data set	Comparison of DCNN models for features extraction, features engineering based model and transfer learning model.
Multiscale Feature with Transfer Learning	[21]	3D U-Net CNN, Transfer learning	TIANCHI17 LUNA16	Using 3D U-Net structure for feature extraction. Transfer learning is introduced and fine-tuning the structure helps to extract features from image input. Experimental results showed that layer by layer transfer training method improved the accuracy of image detection under condition of small samples.
Advanced Off-The-Shelf CNNs	[22]	3D CNN	LUNA16	Pioneer application of reinforcement learning to medical image analysis for detecting pulmonary nodules in CT scan images.
	[23]	3D U-Net and 3D DenseNet	LUNA 16	2D U-Net, 3D DenseNet and Region Proposal Network (RPN) is employed for automatic detection of pulmonary nodules by utilizing multitask residual learning and online hard negative example mining approaches. 3D U-Net is for nodule candidates' generation and 3D DenseNet is mainly for false positive reduction.
	[24]	3D Faster R-CNN and 3D DCNN	Tianchi AI competition	Two-phased framework for nodules identification and false positive reduction. 3D Faster RCNN is employed to create nodule samples and 3D DCNN model identified nodules candidates.

Despite numerous studies attempting to improve the accuracy of early detection of lung cancer using deep learning, there remains a gap in detection and implementation of these algorithms in the real medical field. CNN deep learning system with transfer learning approach was proposed in this study to classify malignant and non-cancerous nodules. The proposed method is compared to a conventional CNN model that does not employ transfer learning.

2 Materials and methods

This study focuses on classification of benign cells at its early-stage manifestation in the form of pulmonary nodules using CNN with transfer learning on a subset of LIDC-IDRI data set, the LUNA16 data set. Data can be found in [25]. According to [26], screening of CT scans has been proven to be effective in diagnosing lung cancer by analyzing the pulmonary nodules present which decreasing mortality rate.

In implementing CNN, a huge number of parameters is required to be estimated and some hardware and software are required to use. Data collection and analysis are critical for achieving higher accuracy and better results for CNN algorithms. This study focuses on increasing the accuracy and lower the loss model for CNN with transfer learning and prove that CNN model with transfer learning is better to tackle data set with small amount and gives out better results than standard CNN without transfer learning. This study makes use of a commonly used lung cancer CT image data set. The Lung Nodules Analysis 2016 (LUNA16) dataset is a subset of the LIDC-IDRI Data Set. The LUNA16 dataset is a subset of the LIDC-IDRI dataset, with the heterogeneous scans filtered using different factors. Since pulmonary nodules can be very small, a thin slice should be chosen. Therefore, scans with a slice thickness greater than 2.5 mm were discarded. Furthermore, scans with inconsistent slice spacing or missing slices were also excluded. This led to 888 CT scans, with a total of 36,378 annotations by radiologists. In this dataset, only the annotations categorized as nodules ≥ 3 mm are considered relevant, as the other annotations (nodules ≤ 3 mm and non-nodules) are not considered relevant for lung cancer screening protocols. Nodules found by different readers that were closer than the sum of their radii were merged. In this case, positions and diameters of these merged annotations were averaged.

The files containing all the CT scan images have been divided into two subsets files. Subset1 files are for training the proposed model and subset2 is for testing the model. CT images are stored in MetaImage (mhd/raw) format in each subset and each mhd file is stored with a separate raw binary file for the pixeldata. Next, annotations csv file contains the annotations that are used as reference standard for nodule detection track. Each line holds SeriesInstanceUID of the scan, the location and position of x, y, and z in world coordinates and the diameter in mm. The file contains 1186 nodels. candidates_V2.csv file contains set of candidate locations in the CT scans for false positive reduction and lung segmentation is a directory containing lung segmentation of CT scan images computed using automatic algorithms [29]. The lung segmentation images are not intended to be used as the reference standard for any segmentation study. CT scan data has an alternative format which is stored in DICOM (. dcm) format. The original data set from LIDC-IDRI data set is in DICOM.

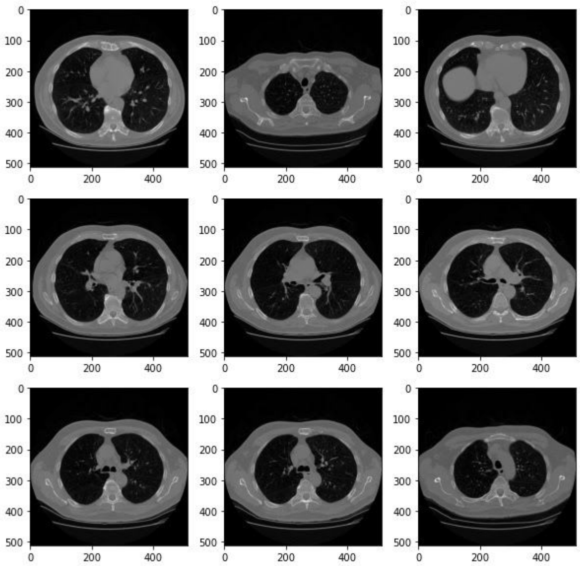

Fig. 1 Original CT scan DICOM slices from LUNA16 data set

These results in a set of 2290, 1602, 1186 and 777 nodules annotated by at least 1, 2, 3 or 4 radiologists, respectively. In Figure1, different slices from a LUNA16 CT scan.

There are four main phases conducted in this study: data set preparation, research design, application and implementation and performance analysis. LUNA16 data set is the input for the algorithm. CNN with transfer learning, the proposed algorithm, was trained and tested using Python programming language then evaluated using performance evaluation. Figure 2 shows the flow of research methodology of the study. Following the preparation of the data set, the data set was utilised to train and test the proposed algorithm. The results of the models are then analyzed and compared in terms of model performance. The proposed method has been processed using the same computer system with processor Intel ® Core™ i7-10750H CPU with 16GB of installed RAM. The proposed method is implemented using Python programming software as Python is most suitable for computational processes. The data sets used in models are divided into two groups: training set and testing set. Most of data set will be used for training and the rest of data set will be used for testing the models.

The training data is used to train the model and includes 711 patients out of 1595 total. The rest of the patients' CT scans are used for testing the proposed model.

Transfer learning is a popular approach where pre-trained models developed for a task is reused as starting point for another model on second task [27]. There are two common approaches for transfer learning which are develop model approach and pre-trained model approach[28, 29]. For this study, pre-trained VGG16 model that been trained with ImageNet which trained on 1.2 million natural images. Transfer learning is also proven to increase discriminatory power of a generic dataset which increase generalization ability to perform other tasks [19].

Phase 1: Data set Preparation

Data collection
Data pre-processing
Segmentation

Phase 2: Research Design

CNN with transfer learning

Phase 3: Implementation

Training
Testing

Phase 4: Evaluation

Performance Analysis Using Compute Metrics

Fig. 2 The flow of research methodology of the study

An overall framework for the proposed methods has been created. CNN algorithm has been used to leverage the use of data set. To propose intended method of classifying of lung nodules, the LUNA16 data set has been utilized in this study.

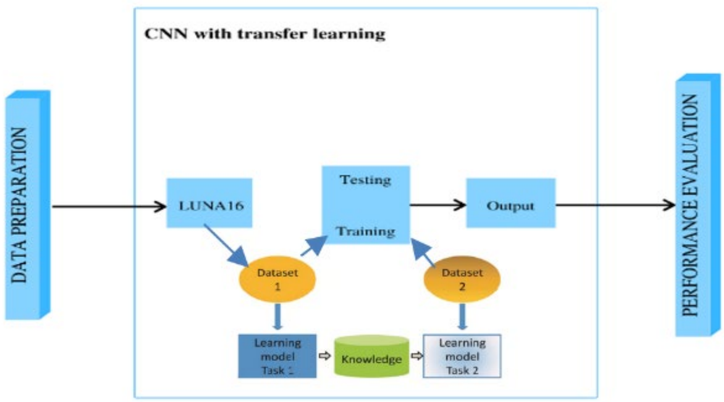

Fig. 3 The overall framework for the proposed methods

3 Findings and Discussion

Visualization of data set is using pydicom library to display the image array and metadata information stored in CT scan images. Images are stored in DICOM file and cannot use standard browser to access DICOM images. Figure 4 shows an example on metadata that is stored in the file.

```
-------------------------------------------------
(0008, 0005) Specific Character Set              CS: 'ISO_IR 100'
(0008, 0016) SOP Class UID                       UI: CT Image Storage
(0008, 0018) SOP Instance UID                    UI: 1.2.840.113654.2.55.247817952625791837963403492891187883824
(0008, 0060) Modality                            CS: 'CT'
(0008, 103e) Series Description                  LO: 'Axial'
(0010, 0010) Patient's Name                      PN: '00cba091fa4ad62cc3200a657aeb957e'
(0010, 0020) Patient ID                          LO: '00cba091fa4ad62cc3200a657aeb957e'
(0010, 0030) Patient's Birth Date                DA: '19000101'
(0018, 0060) KVP                                 DS: None
(0020, 000d) Study Instance UID                  UI: 2.25.86208730140539712382771890501772734277950692397709007305473
(0020, 000e) Series Instance UID                 UI: 2.25.11575877329635228925808596800269974740893519451784626046614
(0020, 0011) Series Number                       IS: "3"
(0020, 0012) Acquisition Number                  IS: "1"
(0020, 0013) Instance Number                     IS: "134"
(0020, 0020) Patient Orientation                 CS: ''
(0020, 0032) Image Position (Patient)            DS: [-145.500000, -158.199997, -356.200012]
(0020, 0037) Image Orientation (Patient)         DS: [1.000000, 0.000000, 0.000000, 0.000000, 1.000000, 0.000000]
(0020, 0052) Frame of Reference UID              UI: 2.25.83033509634441686385652073462983801840121916678417719669650
(0020, 1040) Position Reference Indicator        LO: 'SN'
(0020, 1041) Slice Location                      DS: "-356.200012"
(0028, 0002) Samples per Pixel                   US: 1
(0028, 0004) Photometric Interpretation          CS: 'MONOCHROME2'
(0028, 0010) Rows                                US: 512
(0028, 0011) Columns                             US: 512
(0028, 0030) Pixel Spacing                       DS: [0.597656, 0.597656]
(0028, 0100) Bits Allocated                      US: 16
(0028, 0101) Bits Stored                         US: 16
(0028, 0102) High Bit                            US: 15
(0028, 0103) Pixel Representation                US: 1
(0028, 0120) Pixel Padding Value                 US: 63536
(0028, 1050) Window Center                       DS: "40.0"
(0028, 1051) Window Width                        DS: "400.0"
(0028, 1052) Rescale Intercept                   DS: "-1024.0"
(0028, 1053) Rescale Slope                       DS: "1.0"
(7fe0, 0010) Pixel Data                          OW: Array of 524288 elements
```

Fig. 4 Metadata stored in a single DICOM file.

For segmentation of data set, watershed algorithm is used. The watershed is a classical algorithm used for segmentation and for separating different objects in an image. Watershed is a transformation defined on a grayscale image. The name refers metaphorically to a geological watershed, or drainage divide, which separates adjacent drainage basins. The watershed transformation treats the image as if it were a topographic map, with the brightness of each point representing its height, and finds the lines that run along the tops of ridges. “The topological watershed” was introduced by M. Couprie and G. Bertrand in 1997. Starting from user-defined markers, the watershed algorithm treats pixels’ values as a local topography (elevation) [30].

The algorithm floods basins from the markers until basins attributed to different markers meet on watershed lines. In many cases, markers are chosen as local minima of the image, from which basins are flooded. Watershed algorithm highlights the lung part and makes binary masks for lungs using semantic segmentation approach.

Firstly, internal and external markers from CT scan images are extracted with the help of binary dilations and add them with a complete dark image using watershed methods. It also removes image noise and provides a watershed marker of lungs and cancer cells.

As illustrated in Figure 5, External noise is removed by using a watershed marker and applies a binary mask on the image, black pixels in lungs represent cancer cells. For better segmentation, integrated sobel filter was applied to the with watershed algorithms to remove external layers of lungs.

After removing the outer layer, the internal marker is used, and outline created to generate lungfilter using bitwise_or operations of numpy. It also removes the heart from CT scan images. Next step is to close off the lung filter with morphological operations and morphological gradients. It provides better segmented lungs than the previous process.

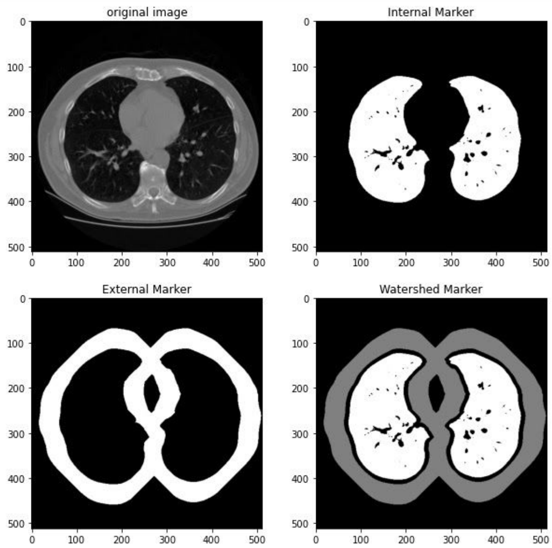

Fig. 5 Different markers extracted from watershed algorithm on the CT scan.

Figure 6 shows the segmented lungs after the application of sobel filter. In total generated 1002 images with related labels which includes almost 12 patients CT scan data in which there are almost the same number of cancer and non-cancer patients.

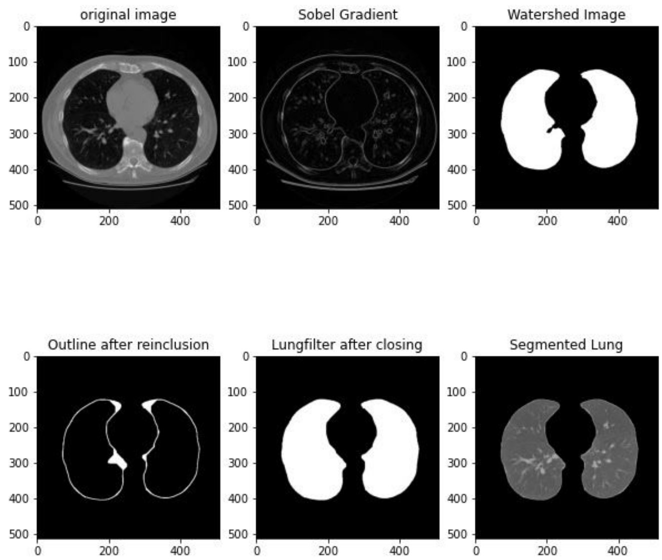

Fig. 6 Lungs segmentation visualization.

The proposed model is a CNN with transfer learning approach based on lung segmentation on CT scan images. Two different models of CNN are built for comparative study; the first model is a standard CNN model, and the proposed model is CNN with transfer learning algorithm. First model is the standard CNN without transfer learning is the basic simple approach of using the convolution layers, flatten fully connected layers, max pooling and dropout in the middle layers, which performs significantly well on the number classification problem. Table 2 shows the summary of the first model without transfer learning.

Furthermore, the proposed model approach is using transfer learning on pretrained model with changes in fully connected layers. Transfer learning on VGG-16 with some changes in the last three layers which are fully connected. This model gives appreciable results in object classification. Using Adam optimizer, learning rate applied on the model is 0.0001. Table 3 shows the summary of the proposed model.

After building the two models, without transfer learning and with transfer learning, the proposed model and comparison model are implemented and train models on segmented lungs with a batch size of 32 for image data generator and using 100 images in each epoch for 30 epochs with exception of 500 images in each epoch for CNN with transfer learning. Training images with the shape of (512,512,1) for the first model and the shape of (512,512,3) for proposed model.

For a better result data, augmentation is used to train models on different augmentations like shear range, zoom range, horizontal flip, rotation range, and center shift etc.

A single node for binary classification is used in the end layer to differentiate between cancer and non-cancer lungs. Moreover, callbacks from tensorflow keras are used to save the best accuracy model to run a complete 50 epoch training session to plot the comparison graphs.

Table 2 Model summary of standard CNN without transfer learning.

Model: "sequential_1"

Layer (type)	Output Shape	Param #
conv2d_1 (Conv2D)	(None, 510, 510, 32)	320
max_pooling2d_1 (MaxPooling2	(None, 255, 255, 32)	0
conv2d_2 (Conv2D)	(None, 253, 253, 32)	9248
max_pooling2d_2 (MaxPooling2	(None, 126, 126, 32)	0
conv2d_3 (Conv2D)	(None, 124, 124, 32)	9248
dropout_1 (Dropout)	(None, 124, 124, 32)	0
conv2d_4 (Conv2D)	(None, 122, 122, 32)	9248
flatten_1 (Flatten)	(None, 476288)	0
dense_1 (Dense)	(None, 128)	60964992
dropout_2 (Dropout)	(None, 128)	0
dense_2 (Dense)	(None, 128)	16512
dense_3 (Dense)	(None, 1)	129

Total params: 61,009,697
Trainable params: 61,009,697
Non-trainable params: 0

Table 3. Model summary of CNN with transfer learning.

Layer (type)	Output Shape	Param #
input_3 (InputLayer)	(None, 224, 224, 3)	0
block1_conv1 (Conv2D)	(None, 224, 224, 64)	1792
block1_conv2 (Conv2D)	(None, 224, 224, 64)	36928
block1_pool (MaxPooling2D)	(None, 112, 112, 64)	0
block2_conv1 (Conv2D)	(None, 112, 112, 128)	73856
block2_conv2 (Conv2D)	(None, 112, 112, 128)	147584
block2_pool (MaxPooling2D)	(None, 56, 56, 128)	0
block3_conv1 (Conv2D)	(None, 56, 56, 256)	295168
block3_conv2 (Conv2D)	(None, 56, 56, 256)	590080
block3_conv3 (Conv2D)	(None, 56, 56, 256)	590080
block3_pool (MaxPooling2D)	(None, 28, 28, 256)	0
block4_conv1 (Conv2D)	(None, 28, 28, 512)	1180160
block4_conv2 (Conv2D)	(None, 28, 28, 512)	2359808
block4_conv3 (Conv2D)	(None, 28, 28, 512)	2359808
block4_pool (MaxPooling2D)	(None, 14, 14, 512)	0
block5_conv1 (Conv2D)	(None, 14, 14, 512)	2359808

Table 4 shows the comparison of model training accuracy and model testing accuracy.

Table 4 Summary of accuracy of the two models.

Models	Training accuracy	Testing accuracy
Standard Model	90.77%	81.19%
Proposed Model (with Transfer Learning)	99.84%	88.00%

The Proposed model with transfer learning achieved better results than the standard CNN without transfer learning. Due to overfitting, the standard model performed worse than the proposed model without achieving the desired testing accuracy. However, it can be used to solve a classification problem. The proposed model outperformed the original model, however it still need more improvements. There are numerous elements influencing the performance of the proposed model. To improve testing accuracy, for example, the number of epochs offered for training can be increased. Although it can be beneficial, it is also important to avoid overfitting the model, since this can reduce the model's performance and hence the accuracy attained. Next, data pre-processing is essential for the model's training phase. Although the watershed algorithm can aid in segmentation, alternative methods can be used in future research.

Proposed model with transfer learning achieved better result than the standard CNN without transfer learning. The proposed model's testing accuracy was lower than its training accuracy. This is owing to the restricted number of datasets available, as well as the overall scarcity of medical data sets. The study's key findings focus on the implementation of a pretrained model utilising transfer learning on CNN. It has been demonstrated that by incorporating transfer learning into a CNN model, better accuracy in classification problems can be attained when data sets are minimal.

Several challenges were encountered during the study's development, which had an impact on the study's outcomes and outputs. The data set used was in dmc format, which is different from standard image processing formats like jpg; this format stores all of the patient's information as well as a 3D CT-Scan image of the patient, which when converted into a 2D numpy image results in the shape of (n, m, m, 1), which is not supported by the models for transfer learning. Furthermore, it is in float64 data format, which is difficult to handle and process when using standard libraries like as CV2, skimage, and matplotlib.

Furthermore, when the data is converted to a 2D grayscale image, it is difficult to train it with the Tensorflow and Keras frameworks because they do not allow such shapes (n, m, m) during model creation. When the images are transformed back into RGB or BGR format using different libraries, some or many attributes that are useful in the classification process are lost.

4 Conclusion

The medical industry is critical to the improvement of daily life. Deep learning can be used to gather more deep knowledge and assist healthcare workers in learning more about a patient's disease. Deep neural networks and machine learning are becoming more popular in the healthcare industry. The benefit they provide in terms of improved detection and classification has a positive impact on healthcare. CNN is widely used in imaging detection and classification tasks such as CT and MRI scans. Although CNN has advantages in this industry, the algorithm must be trained with a large number of data sets in order to achieve high accuracy and performance. CNN with transfer learning was created to improve the classification of lung nodules. There is still space for improvement, but CNN combined with transfer learning can assist in more properly classifying data. To improve model accuracy, more efficient pre-processing and segmentation can be performed. In addition, new data processing, training, and classification methods and architecture based on other transfer learning methods and design might be considered to aid the models in more accurate data classification.

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