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Research Article

Lungs Malignancy evaluation of the pulmonary nodules using deep learning

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Abstract: Detection of pulmonary nodules is a dangerous kind of lung cancer that is responsible for majority of deaths every year. Early diagnosis and proper treatment of Pulmonary Nodules significantly improves the patient's survival rate. In this study, we propose a multi-view convolutional network for pulmonary nodule detection. The main objective of our work is to establish a method that can automatically pre-process, localize and then segment the pulmonary nodules precisely and improve its accuracy. In our proposed method single shot multi-box detector (SSD) precisely localizes the nodules area in the form of bounding boxes and eliminates some clinical artifacts. The proposed approach was evaluated on LUNA 2016 dataset to show the robustness of our work which achieved a sensitivity and precision of 97.47 and 0.97 respectively. The results of the segmented image are also compared with the state-of-the-art methods to demonstrate the performance superiority of the proposed approach.

Keywords: Pulmonary nodules, Lung malignancy, Single shot detector (SSD), LUNA16, Deep learning.

1. INTRODUCTION

Lung cancer is a heterogeneous disease and the most aggressive cancer that can metastasis to other parts of body like brain, through blood circulation. Therefore, there is a dire need to diagnose lungs cancer at earlier stage to save the life of patient. Like blood cancer, liver cancer, breast cancer, and other types of cancer, lung cancer therapy also requires chemotherapy and radiotherapy when metastasis state begins to occur. In order to avoid these expensive and dreadful methods, early diagnosis is very important that becomes an effective way of cost reduction as earlier stages demand simple treatments another factor delay in earlier diagnosis is due to the inexperienced and limited availability of medical assistance. The diagnostic procedures need consideration of medical assistance, the workload, regular monitoring of the cancer and shortage of personnel eventually exceed the current screening capabilities. Therefore, there is a dire need to develop automatic diagnosis methods that may assist doctors in timely detection of Lung cancer to reduce the morality rate. By automating the analysis procedure, more patients can be screened; hence the doctors have more time for patients that require their attention. Many existing CAD systems are available that are still far from the excellence due to the challenges and requires more improvement in performance of Lung Cancer detection and segmentation [1, 2]. Our model is robust to identify tumor without defining region of interest, where other methods detect nodules by detecting lungs.

Jacobs et al. [1] proposed a Computer Aided detection system for the subsolid nodules in order to optimize the performance. Along with the shape and

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texture features, context features are also introduced. Experiments gave promising results by using these features with a sensitivity of 80% and average of 1.0 FP detections per scan. Van et al. 2010; and Firmino et al. 2014 [2, 3] proposed a framework ANODE09 for impartial evaluation of nodule detection systems. The results of six algorithms are compared and the final evaluation shows a substantial performance difference between algorithms. Previous study reported similar methods by using multilayer neural network, trained with back propagation algorithm [4, 5, and 6]. These systems are designed to deal with 2D shapes, and they are composed of multiple modules including segmentation, recognition and field extraction. Ginneken and his co-authors in 2015 used CNN features to train the object detection from natural images for nodule detection. The LIDC data set images are read by four thoracic radiologists and then features are extracted and classify with linear support vector machine. The studies conclude that the CNN has greater potential to be used for the detection frameworks [7]. In 2014 and 2015, Manos and his co-workers and Wille and co-authors used a technique called Lung Reporting and Data System to classify the nodules having high malignancy risk. When the malignancy risk increases, Lung Reporting and Data System level also increases [8, 9]. As compared to the state-of-the-art framework, these models improve communication between the patients and clinicians and provide a framework to facilitate evaluation and radiologists training. A system for the detection of pulmonary cancerous cells was proposed by [10]. A three-dimensional lung segmentation algorithm is used for the morphological processing and then thres-holding is applied to obtain the nodule candidates and morphological operations are used to detect the candidates which are either small or large. A computer aided detection system was proposed by using the CNN in order categorize features of the respiratory nodules erudite from the training data. The study showed that the proposed method is highly suitable for the reduction of false positive rate in Computer Aided Systems [11]. In 2013, a novel detection method was proposed based on hierarchical block classification. First the three-dimensional block images are obtained from tomography images and then classify the candidate images into nodules and non-nodules [13]. Feature vectors are taken out from the blocks and then they are classified by the support vector machines. Huang et al. (2017) proposed a new computer-aided detection system that uses 3D convolutional neural networks (CNN) for detecting lung nodules. nodule candidates are generated using a local geometric-model-based filter. Data augmentation techniques are used to generate many training examples and apply regularization to avoid over-fitting [14].

In our proposed approach we extracted meaningful data from LUNA16 dataset in 2D format, then those images were trained through single shot detection (SSD) network by varying the backbone networks i.e. MobilenetV1, MobilenetV2, InceptionV2 and resnet50 and resnet101. We proposed 2D DCNN which improves computational efficiency unlike other 3D DCNN-based frameworks. SSD detects the object in just one shot, unlike other approaches such as R-CNN which needs two shots i.e. one for region proposal generation and other one for detecting the object in proposed regions. Our proposed framework abridged the false positive rate and attains the sensitivity of 97.47%. We also did comparison with other state-of-the-art methods and our proposed framework outperforms all other methods with low computational complexity and improved results.

2. MATERIALS AND METHODS

In our proposed approach pre-processing is the primary step to convert the 4D images to 2D images. Patient images are pre-processed and only 3 axial slices are extracted per patient, which are meaningful data as the center CT scans are having maximum amount of information. Moreover, our preprocessing step is significant to use entire dataset; initially LUNA16 dataset is of 66.3GB size which can be downloaded from official website of LUNA16 challenge and after pre-processing it become 347MB. After pre-processing, localization of lung cancer lesion was employed through SSD network. We have evaluated the performance of SSD by varying the backbone network to estimate the most suitable network for Lungs nodule detection. We have used following convolutional networks as backbone network, MobilenetV1, MobilenetV2, InceptionV2 and resnet50 and resnet101. The architecture of the proposed methodology is shown in Fig. 1.

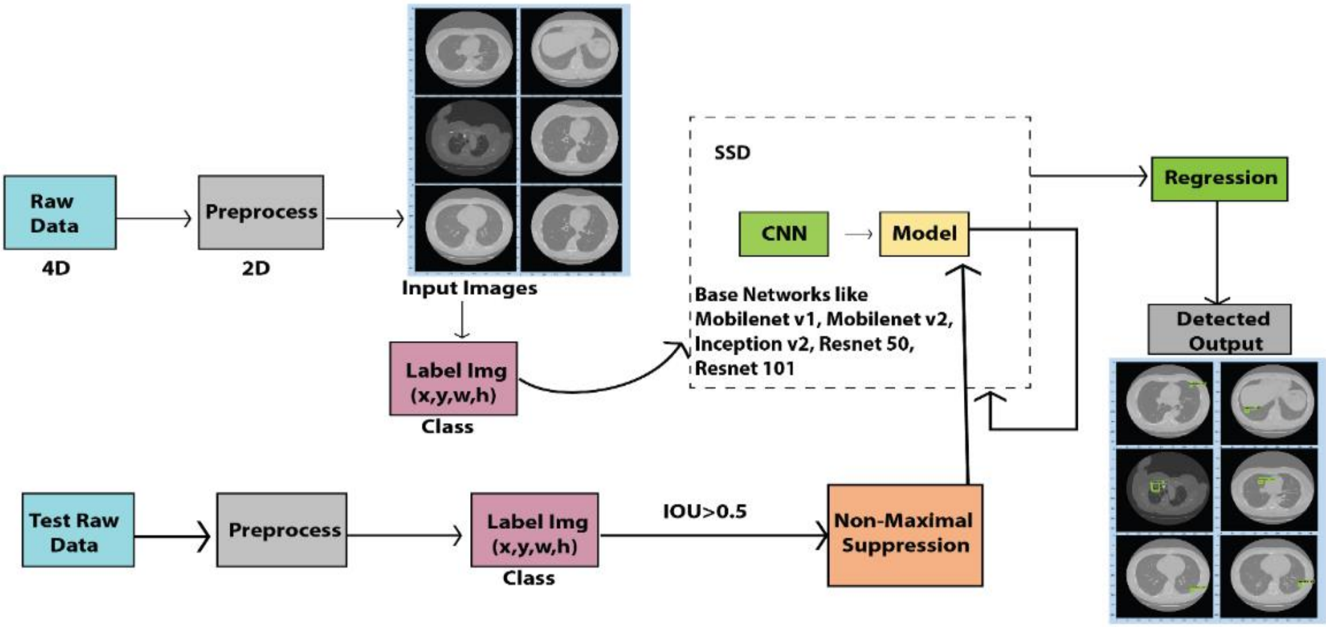

Fig. 1. An architecture of proposed methodology for detection of Lung Cancer

2.1 Pre-Processing

In the computerized analysis, LUNA16 challenge dataset was composed of patients CT scans and is in raw data format. In pre-processing step, processing of entire patient's information, we selected the 3 center slices of each patient scan. This selection of center slices is significant to reduce the size of data meaningfully as center axials slices hold significant amount of anatomical information. We pre-processed the data and converted the volumetric representation of 4D CT scan into 2D axial representation. Then the pre-processed input images are labeled and fed into the SSD. Test Raw data is also pre-processed, labeled and fed into SSD. The size of the nodules was obtained by the annotation's file provided by LUNA16 challenge for labeling purposes. The annotations file includes the estimated volume of nodules calculate by pathologists and provides the X, Y, Z coordinates as well as diameter of the nodule with patient name.

2.2 Nodule Detection using Single Shot Detection

For pulmonary nodule detection we employed the deep CNN based Single Shot Detection architecture that sum-up all computation in only one forward pass network. The main idea of SSD network is to make predictions from several feature maps, where each feature map is directed for detecting objects at multiple scales followed by non-maximum suppression to generate final detections. Unlike RCNN, Faster RCNN and other object detection models SSD network directly compute set of boundary boxes score and confidence score by eliminating region proposal stage. Consequently, as it does not require an intermediate region proposal step, so it achieves lower computation time and real-time processing for lung cancer detection. The architecture of the SSD is shown in Fig. 2.

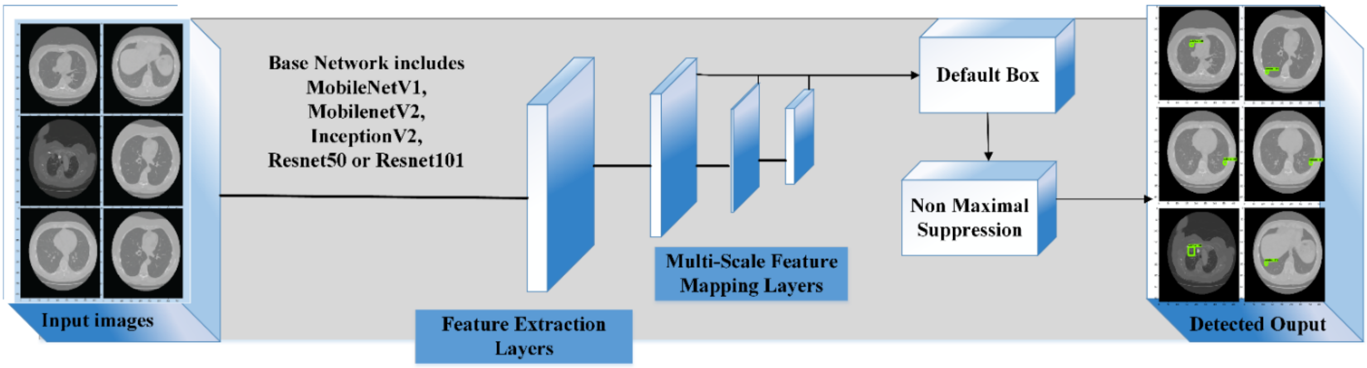

Fig.2. An architecture of Single Shot Detection (SSD).

2.2.1 Feature Extraction

In our SSD approach, an image is first passed through the CNN network to generate high level features. Feature selection methods are intended to reduce the number of input variables to those that are believed to be most useful to a model in order to predict the target variable. After the base network CNN feature layers are added that decreases the size of the feature maps, generated by base network, by 3×3 convolutions with stride 2 [15]. This allows the predictions at different scales. Consequently, the first feature map layers can detect the objects with small size whereas the latter layers can detect the larger objects. We have used 5 different base networks as feature extractors with SSD to evaluate the best performance. For the selection of features Filter feature selection methods are used in which statistical techniques to evaluate the relationship between each input variable and the target variable, and these scores are used as the basis to choose (filter) those input variables that will be used in the model.

2.2.2. Default Boxes and Aspect Ratio

For prediction task, at each location of these multi-scale feature maps of size MxN, 3×3 convolutional filters are applied. SSD generates total of (C+ 4) KMN predictions for K default boxes per location of feature map with size MxN and here C represents the number of classes. The idea of the default boxes applied in our SSD approach. SSD uses the K default boundary boxes over different scales and aspect ratio that discretizes the output space of the boundary boxes per feature map location.

2.2.3. Matching Strategy

Afterward, at the end of the SSD network, these predicted boundary boxes $bbox_{pt}$ are integrated and matched with ground truth boundary boxes $bbox_{gt}$ using IOU overlapping criteria. The IOU value is computed as shown in equation 1. For our pulmonary nodule detection model, we have chosen the IOU threshold value as 0.5 for precise detection. If the IOU score is greater than 0.5 then it detects the region as pulmonary nodule otherwise it is considered a healthy lung region.

$$IOU = \frac{bbox_{pt} \cap bbox_{gt}}{bbox_{pt} \cup bbox_{gt}} \qquad (1)$$

2.2.4 Non-Maximal Suppression

Finally, we obtained the nodules final detection results by using the non-maximal suppression (NMS) method [17, 18] that discards the repeated boundary box and the boundary boxes whose confidence score is less than a pre-defined threshold value. Let $bbox_{pt}$ is the set of predicted boundary boxes, and C_i is the confidence score of the i^{th} boundary box, then non-maximum suppression can be described as:

$$bbox = bbox_{\arg\max_i} C_i \qquad (2)$$

where *bbox* is the boundary box with the highest confidence score and it is chosen as the final nodule detection result.

3. RESULTS

Our proposed approach for nodule detection was trained and validated with the various kinds of nodules present in LUNA16 dataset having different features regarding texture, shape, and appearance. In section 3.4 we will discuss the results obtained on LUNA16 dataset in detail and Table [3] shows the detailed information about different backbone networks used and performance scores in terms of sensitivity, F1-score, recall and precision.

3.1 Dataset

LUNA16 dataset consists of 888 patients CT scans which are all in raw format, we preprocessed the dataset and extracted slices from those CT scans not only the middle ones but also the adjacent ones. After preprocessing, we got a set of 3531 images in total. We divided the images into 80:20 ratios for training and testing purpose. Sample size is shown in Table 1. Our training dataset consists of 2825 images and testing dataset consists of 706 images. We used SSD as main model with different base networks like Mobilenet V1, Mobilenet V2, Inception V2 and resnet 50 and resnet 10. For training we used the same batch size i.e. 64 for all base networks and input resolution of images is 430 x 418. Initial learning rate differs for base networks and the number of iterations and global training steps also differ for each base network. Number of classes is 1 i.e. Nodules and it is same for all base networks. Table [2] displays the information of training parameter in detail.

3.2 Performance Evaluation Parameters

After extensive training of each base network, we performed testing on 706 images and obtained confusion matrix for each base network which consist of true positives (TP), false positives (FP), false negatives (FN) and True Negatives (TN). We computed the Precision and Recall as our evaluation parameters and calculated F1-score using precision and recall values and also calculated sensitivity of our proposed method for each base network and below are the mathematical definitions:

$$\mathrm{Pr}\,ecision = \frac{TP}{TP + FP} \tag{3}$$

$$\mathrm{Re}\,call = \frac{TP}{TP + FN} \tag{4}$$

$$F1Score = 2 \cdot \frac{\mathrm{Pr}\,ecison \times \mathrm{Re}\,call}{\mathrm{Pr}\,ecison + \mathrm{Re}\,call} \tag{5}$$

$$Sensitivity = \frac{TP}{TP + FN} \cdot 100 \tag{6}$$

3.4. Performance Comparison

We evaluate the performances of our proposed approach, quantitatively as well as qualitatively. After obtaining results we then performed comparison and found out that MobileNet V1 is outperforming the other base networks with a sensitivity of 97.47 and precision of 0.97. The reason that MobilenetV1 is performing best as it is lightweight in its architecture and uses a depth wise separable convolution which significantly reduces the number of parameters. In MobileNetV1 the normal convolution is replaced by depth wise convolution followed by the pointwise convolution which then applies a 1×1 convolution to combine the outputs of the depth wise convolution. This factor reduces the model size and computation and performs best even for smaller objects. Resnet101 is performing worst among all other base networks as it contains a 3-layer block and converges faster but it’s better to use in Faster-RCNN architecture as it uses a proposed region. Table [3] shows the quantitative comparison of our proposed model having different base networks.

Apart from quantitative comparison we also did a qualitative comparison of proposed method and all base networks were successfully able to detect nodules on the images we used for validation. Again, Mobilenet V1 is outperforming other networks, a detailed qualitative comparison for nodules detection is shown in Fig. 3.

Table 1. Sample size and total dataset images

Categories	Total
Dataset images	3531
Training images	2825
Testing images	706

3.5. Performance Comparison with State-of-the-art Approaches

We have also compared our proposed work* with other state-of-the-art approaches as shown in Table 4. We have compared our results in terms of sensitivity with other methods and discussed the methods in detail in this section.

Pereira et al. (2019) proposed a method similar to our proposed method but the major difference is that

Table 2. LUNA16 dataset and training parameters

Main Model	Backbone Network Architecture	Batch size	Initial learning rate	Input resolution	Iterations
SSD	resnet101_v1	64	0.04	430x418	12.4K
	inception_v2	64	0.0001	430x418	61.4K
	mobilenet_v1	64	0.001	430x418	112.6K
	mobilenet_v2	64	0.004	430x418	109.9K
	resnet_50	64	0.04	430x418	16.5K

Table 3. Performance measurement of the proposed methods

Main Model	Backbone Network	TP	FP	FN	TN	Precision	Recall	F1-score	Sensitivity
SSD	resnet101_v1	387	319	36	0	0.91	0.55	0.69	91.48
	inception_v2	398	308	36	0	0.92	0.56	0.70	91.7
	mobilenet_v1	270	436	7	0	0.97	0.38	0.55	97.47
	mobilenet_v2	345	361	32	0	0.92	0.49	0.64	91.51
	resnet_50	316	390	13	0	0.96	0.45	0.61	96.04

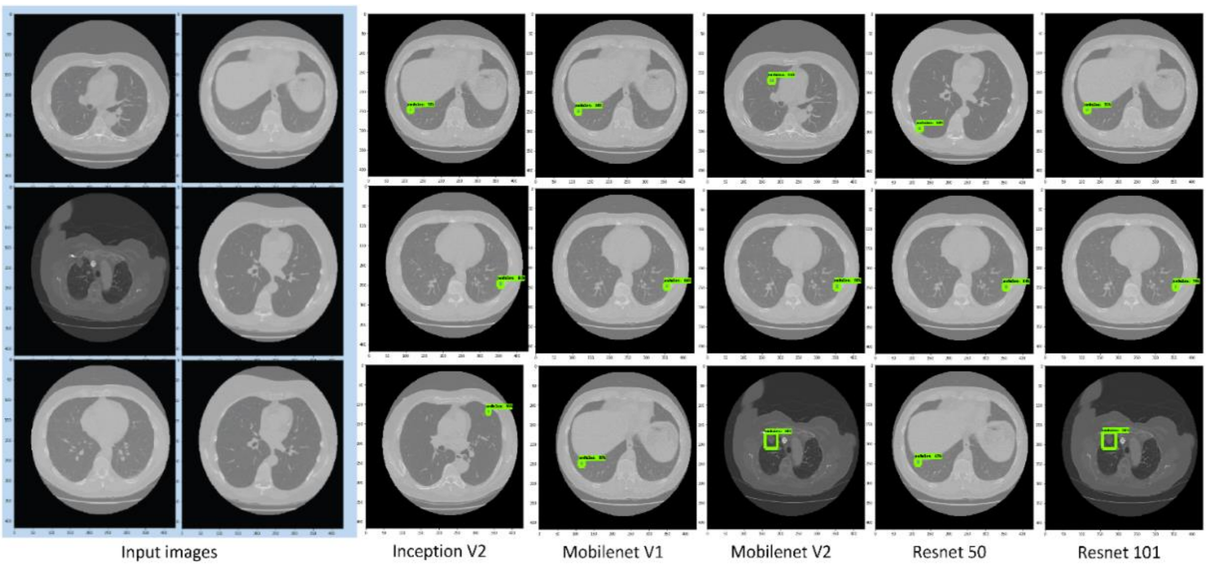

Fig.1. Detected outputs of different base networks

they used VGG16 as base network with SSD by grouping DCNN 2D candidates while we used 5 different base networks with SSD like Mobilenet V1, Mobilenet V2, Inception V2 and resnet 50 and resnet 101 [16]. By experimentation our model gave improved results with Mobilenet V1 as a base network. Duggan et al. (2015) presented their findings on lung nodule candidate detection which depends upon the applications based on filtering and mean curvature minimization. At first, CT scan is further subdivided into air and tissues, and then pursued by morphological strategies. In step two the mean curvature smoothing method was used to isolate connected nodules and then Merriman-Bence-Osher method is used for smoothing and for detection rule-based classifier is applied. The average detection rate observed for 16 candidates per scan is 96.0% [17]. An accurate exposure of pulmonary nodule using CDA technique based on DCCN by Ding et al. (2017); it consists of two various stages, in first stage Faster RCNN is applied for candidate detection and in second stage 3D DCNN is used for FP reduction. Experimental results show the candidate nodule detection susceptibility of 94.6% on average 15.0 Fps per scan and gained 0.8910 average FROC score [18]. Deep-Lung fully automated method for lung CT cancer detection was reported by Zhu et al in 2018; this system is the combination of neural network for nodule detection and the neural network for nodule classification. Experimental results show the candidate nodule detection susceptibility of 95.8% and gained 0.8420 average FROC score [20]. A two-step methodology based on nodule detection technique was reported in 2017 by Dou and co-authors; first step detection of candidate nodule was achieved by a 3D-FCN used in volumetric CT-Scans. Second step compromised of the hybrid-loss of 3D residual network by FP-reduction. Experimental results show the candidate nodule detection susceptibility of 97.1% on average 219.1 Fps per scan and gained 0.8390 average FROC score. Experimental results demonstrate superior performance of our proposed method compared with state-of-the-art approaches [21].

Table 4. Performance Comparison with state-of-the-art approaches

Work	**Technique used**	**Database**	**Patients Scans**	**Sensitivity**
Duggan et al., [17]	Merriman-Bence-Osher smoothing	LIDC	16	96.00%
Ding et al., [18]	Faster R-CNN , DCNN	LUNA16	888	94.60%
Zhu et al., [20]	Two Neural networks	LUNA16	888	95.80%
Dou et al., [21]	FCN , 3D residual network	LUNA16	888	97.10%
Fernando et al., [16]	Grouping DCNN 2D candidates	LUNA16	173	96.70%
Our proposed	(SSD with MobileNetV1)	LUNA16	888	97.47%

*Only compared our best performing base network result

4. DISCUSSION

The goal of this study is to establish a method that can automatically pre-process, localize and then segment the pulmonary nodules precisely and improve its accuracy. The proposed approach contains steps like, Pre-processing, annotations, training of model for detection of pulmonary nodules and then nodule prediction and location. A fully automatic CAD system for automatic detection of pulmonary nodules was described and extensively evaluated. The data set used in this work LUNA16. To show the robustness of our work we performed validation tests on LUNA16 as well as we can detect nodules on random images taken from different sources but resizing of those images is the primary step. For the selection of features Filter feature selection methods are used in which statistical techniques to evaluate the relationship between each input variable and the target variable. And for prediction task, at each location of these multi-scale feature maps of size MxN, 3×3 convolutional filters are applied. Our proposed approach for nodule detection was trained and validated with the various kinds of nodules present in LUNA16 dataset having different features regarding texture, shape, and appearance. It is hypothesized that results of the segmented image show superior performance as compared to other state of the art approaches.

5. CONCLUSIONS

In our work, we adopted a SSD with backbone CNN networks including, mobilenetv1, mobilenetv2, resnet50, resnet101, and inceptionv2; for automated pulmonary nodule detection by overcoming the LUNA16 dataset challenges present in images as to reduce false positives and the size of the nodules present in images exhibit different features in context of texture and shape. Our proposed approach contains these steps: Pre-processing and annotations, training of model for detection of pulmonary nodules and then nodule prediction and location. In comparison with the state-of-the-art object detection models, the SSD model is capable for multi box detections along with classification of more than one classes. Therefore, the SSD can detect several other lung diseases, at the same time, of same patient as well as different patients. To show the robustness of our work we performed validation tests on LUNA16 as well as we can detect nodules on random images taken from different sources but resizing of those images is the primary step. In future, we may perform the classification task by integrating our proposed nodule localization task.

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