False Positive Reduction in Lung Nodule Detection using Patch based Convolution Neural Networks

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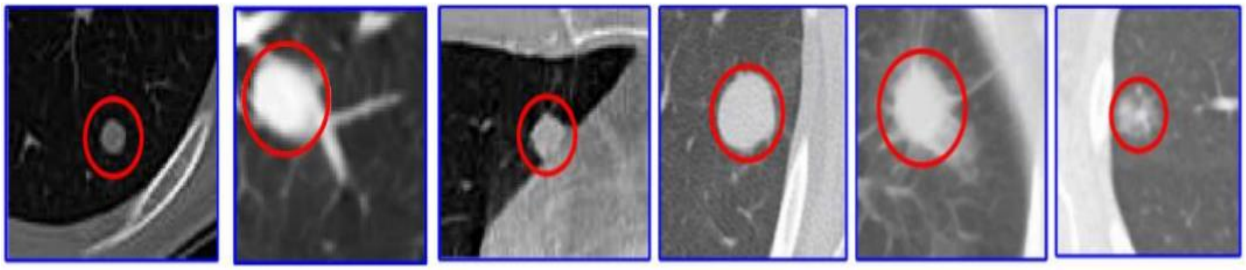
ABSTRACT

Lung cancer is the most prevalent form of cancer worldwide. Early prognostication and detection of lung cancer will enhance the survival rate of the afflicted patients. Hence, in this study, we introduced a highly effective Computer-Aided Diagnosis (CADe) system designed to automatically identify pulmonary nodules and minimize the occurrence of incorrect positive results per scan using lung Computed Tomography (CT) images. The design of the CADe system involves several key phases. These include preprocessing the lung slice using Riesz filter banks, segmenting the picture using iterative thresholding techniques, and detecting nodules using morphological operators. The primary difficulty in designing the CADe system lies in minimizing the number of false positives detected per scan. A unique patch-based Convolutional Neural Network (CNN) is constructed, consisting of three Convolution Layers with 32, 64, and 128 filters respectively, as well as two maximum pooling layers. The Leaky ReLu activation function is employed to enhance the convergence process during training. The ultimate Fully-Connected (FC) layer generates two outputs, one for nodules and one for non-nodules. The process involves the identification of pulmonary nodules, followed by the creation of 64x64 patches. These patches are then used as inputs for the Convolutional Neural Network (CNN). The proposed technique is assessed using the widely accessible and extensive LIDC-IDRI database. Among the 1018 cases examined in our study, we identified 888 scans that included a total of 1186 nodules. The outcomes of our proposed Computer-Aided Design (CAD) system demonstrate a biased performance, with a sensitivity of 94.8% and a false positive rate of 2.8 per scan, when compared to the current leading technology.
Index Terms- Computer-Aided Diagnosis (CADe) system, Computed Tomography, Lung Nodule, Convolutional Neural Networks (CNN), False Positive Reduction.

1. INTRODUCTION

Cancer is a significant general medical issue overall [1]. Lung malignancy is the main source of disease passing with the most noteworthy grimness and mortality among the people in China [3]. Both males and females but more in males who undergo smoking eventually majorly affect it. It will start first in the lungs and even spread to the other organs of the body. According to the survey made by the American Cancer Society (ACS), 78% of the people are dying because of the failure of the prediction of Lung cancer in the early stages and the survival rate improved if we predict five years earlier [4]. Early symptoms include are shortness of breath, cough, chest pain, and weight loss. Many diagnosis tools in the real-time processing of lung cancer are Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Positron Emission Tomography (PET). Among these Computed Tomography (CT) imaging is widely used because of its cost-effectiveness and also the mortality of Lung Cancer decreased by 20%. The early prediction of Lung Cancer dependent on low dose Computed Tomography (CT) imaging gives good results for further treatment of the lung cancer affected patient.

Pulmonary Nodule also called Rounded Opacity has a diameter up to 3cm when measured on Chest [6]. Pulmonary Nodules are classified based on internal texture as solid, part-solid, and non-solid, based on location as juxta-pleural, juxta-vascular, and well-circumscribed as shown in Fig. 1.



(a) (b) (c) (d) (e) (f)

Fig. 1 The visual aspect of different types of Pulmonary Nodules: From left to right Well Circumscribed, Juxta-Pleural, Juxta-Vascular, Solid, Part-Solid, and Non-Solid.

It is the task of the radiologists to determine the malignancy of the Lung based upon the shape, size, and texture of the Pulmonary nodule for further treatment. Even for trained radiologists, it is difficult to interpret when they are in heavy workload. As a result, a computer-aided diagnosis system is needed for the automatic detection and diagnosis of pulmonary nodules. Therefore, in this paper, we propose an efficient CADe system for the detection of the pulmonary nodules of type Solid, Sub-solid, and Large Solid nodules and false positive reduction using patch-based Convolution Neural Network (CNN).

2. RELATED WORK

Many CAD systems are designed for the detection and diagnosis of pulmonary nodules. In general, CAD systems are classified into two types: Computer-Aided Detection (CADe) systems and Computer-Aided Diagnosis (CADx) systems. CADe systems are used to detect nodules, segment, and reduce False Positives, whereas CADx systems are used to classify the lesion in to Benign or Malignant. In the present work, we focus on CADe systems for the early detection of the Pulmonary nodules and to reduce the False Positive (FP)/scan. The main steps include 1) Lung Slice Pre-processing, 2) Lung Segmentation, 3) Lung Nodule Detection, and 4) False Positive Reduction. Most of the preprocessing techniques include contrast stretching [22], Discrete Wavelet Transform (DWT) [25], masking and isotropic resampling [26], Hough transform [35], smoothing filter [31], median filter [33], morphological hole filling operator [31], erosion filter [24], linear transformation [15], and thresholding [17]. The most popular lung segmentation algorithms that yields better nodule detection include morphological filters [16,22,27], region growing [29], OTSU thresholding method [13,15], fuzzy C-means clustering [25], edge detection [30], active contour models [10,15,17]. Major stage of this work includes nodule detection, thresholding and clustering [19,26,28], statistical region merging [23], spatial fuzzy c-means(SFCM) [12], 3D detection box [23], CNN's [9,21]. The tough task is False Positive (FP) reduction, which includes assortment of different features extracted for better classification results. Based on types of the features intensity [13,22,26,27], geometry [13,26,27] and texture [34]. Recent works include gradient features [27], metabolic features [32], and spatial context [26]. Based on the classifier SVM [20,26,27,28], Rule-based method [22,27], ConvNet [19], and Particle Swarm Optimization (PSO) [2].

3. METHODS

Most of the medical images contain some redundant data at high-level frequencies during image acquisition that can be removed by proper processing techniques. In this section, we will discuss in detail the different stages of the CADe system as shown in Fig. 2.

Lung Slice pre-processing

The first stage after acquiring the lung Slice from the dataset is pre-processing. The Lung Computed Tomography (CT) image in general consists of some unwanted components along with the relevant data because various artifacts such as noise, motion, variations, shift, and non-uniform intensity affect the image quality. Hence preprocessing is the important step for removing unwanted components keeping useful data. Here in the present work Riesz filters [5], are used for the enhancement of lung boundaries.

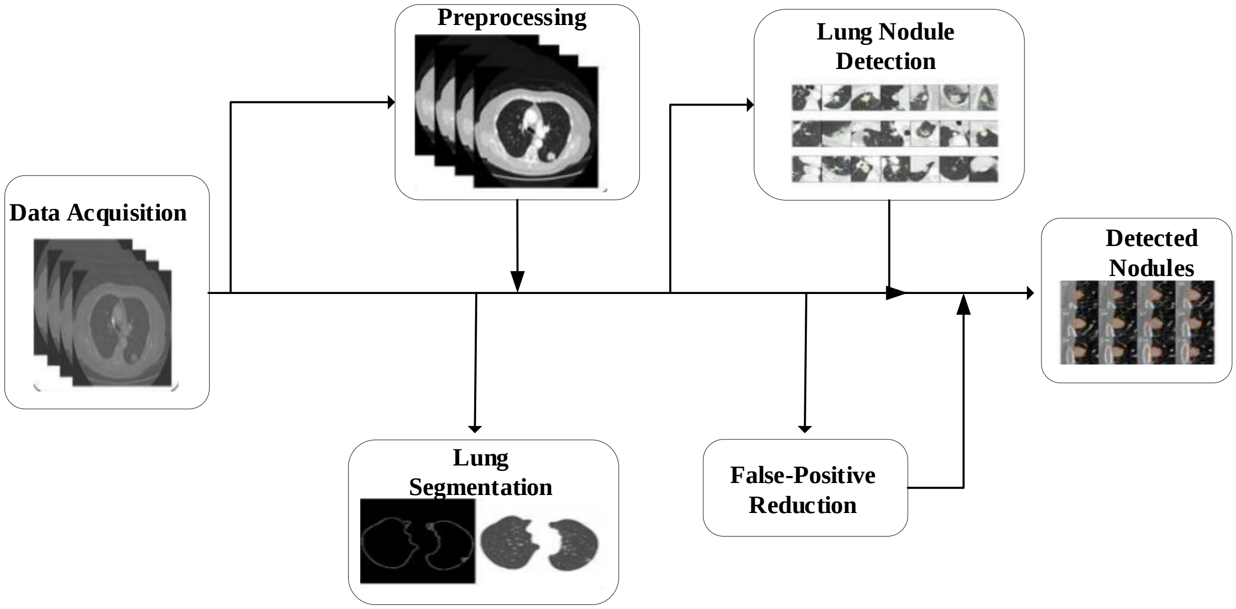


Fig. 2. Flow diagram of the proposed CADe system

Image Segmentation and Nodule Detection

The next stage followed by image preprocessing is image segmentation that consists of numerous methods in the literature. As shown in Fig. 3 the lung CT image consists of fat, bones, muscles, etc. To extract the lung region we have to select proper threshold value.

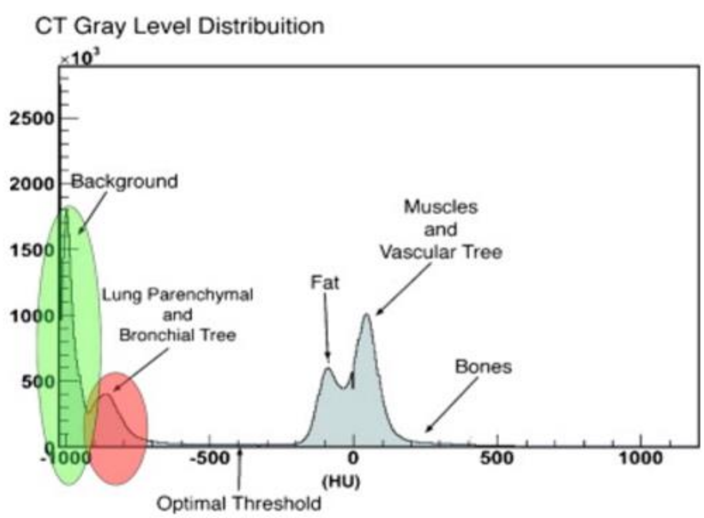


Fig. 3 Histogram of the Lung CT gray-level distribution

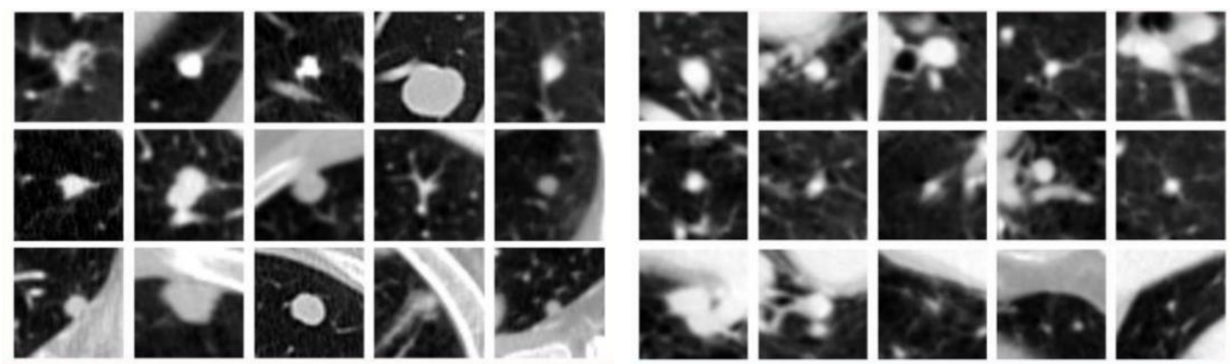
Clearly, from the histogram low-intensity values corresponds to lung region, and high-intensity values correspond to fat, muscle, bones, etc. To solve this problem an iterative threshold-based technique [10] is proposed in this paper. After thresholding, by using morphological closing operation nodules are detected.

Patch Extraction

From the detected lung nodules 2-Dimensional image patches are extracted with a resolution of 0.78mm similar to the resolution of the CT lung slice. Initially, the image patches are drawn from 50×50 mm size and next converted into 64×64 pixels with intensity range rescaled to (0,1). To extract the patches a cube of size 50×50×50 is considered enclosing the nodule detected to the center of the cube. Nine patches are drawn in axial, sagittal, and coronal planes as in [7].

False-positive Reduction

It is a challenging step in any type of CAD system to reduce the false-positive rate. The true pulmonary lung nodules appear in different shapes and sizes whereas the false pulmonary lung nodules appear similarly as shown in Fig. 4. To solve this problem we provide a 2-dimensional Convolutional Neural Network (CNN) architecture for reducing the false positive rate.



(a) (b)

Fig. 4 Visual aspect of lung nodules a) True positive nodules b) False-positive nodules.

The input to the CNN is 64×64 patches drawn from the lung nodules detected in the previous step. The architecture for the assortment of features for the classification of pulmonary nodules as non-nodule and nodule is as shown in Fig. 5.

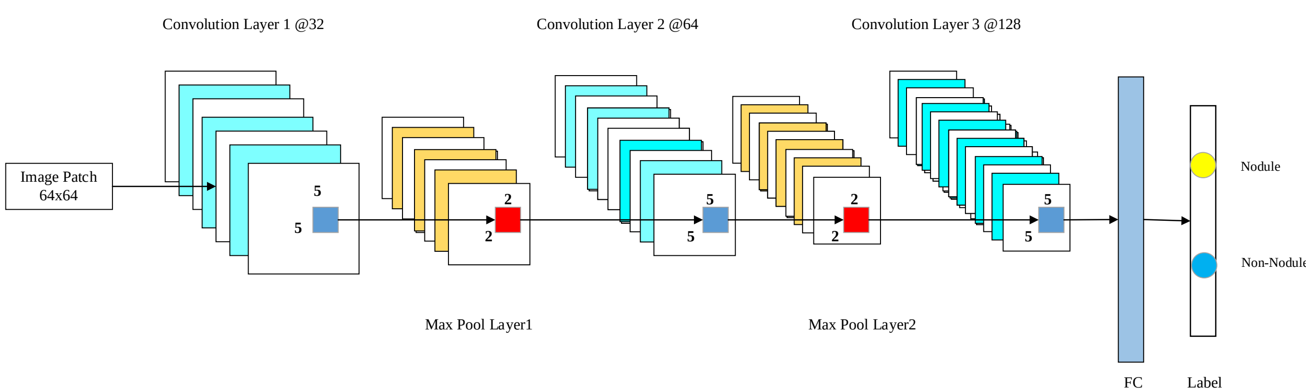


Fig. 5. Patch based CNN architecture for false-positive reduction

The architecture consists of three convolution layers with kernels of size 5×5 with stride 1, and the number of filters as 32, 64, and 128 respectively. The convolution layers are followed by a max-pooling layer with kernels of size 2×2 with stride as 2. For speeding the process of convergence during training Leaky ReLu activation layer is used. The output feature maps are connected to a softmax layer with a dropout of 0.5%. Data Augmentation using translation method is performed to only nodules patches, as they are fewer in number compared to non-nodules patches. The training of CNN is done by minimizing the loss function with Adam optimizer with zero bias, minimum batch size as 64, initial learning rate as 0.001, and the number of epochs as 20.

4. MATERIALS

The proposed CAD system is executed on the publicly available Lung Image Database Consortium (LIDC-IDRI) database. In the database, 1018 cases are taken from four radiologists in two rounds. For the CT images, the slice thickness varies from 0.6mm to 5mm. The images are available in DICOM format with 512×512 size. A separate XML sheet is provided for the number of nodules annotated by the radiologists. In the blind round, the radiologists annotated the nodules as two categories: non-nodule for nodule < 3 mm and nodule > 3mm. In the database total number of lesions that received a "nodule >= 3mm" mark from at least one of the four LIDC radiologists is 2669 and the total number of lesions that received a "nodule < 3mm" mark from at least one of the four LIDC radiologists are 4702. In the present study, only 888 scans are considered containing 1186 nodules. To evaluate the proposed CADe system the performance metrics sensitivity and False Positive per scan are used. Sensitivity is defined as in equation (1).

Sensitivity: It is defined as the ratio of the correctly predicted cases per class to the total actual cases per class.

$$sensitivity = \frac{TP}{TP+FN} \quad (1)$$

Where TP- True Positive (Nodule is predicted correctly), FP- False Positive (Non-nodule predicted as Nodule), TN- True Negative (Non-Nodule is predicted correctly), and FN- False Negative (Missed Nodule) .

5. RESULTS AND DISCUSSIONS

The proposed CADe system is assessed on the LIDC-IDRI database considering 888 scans. The number of nodules is 1186 in the given scans. On fivefold validation, the system achieved a sensitivity of 94.8%, and the number of false positives per scan is 2.8.

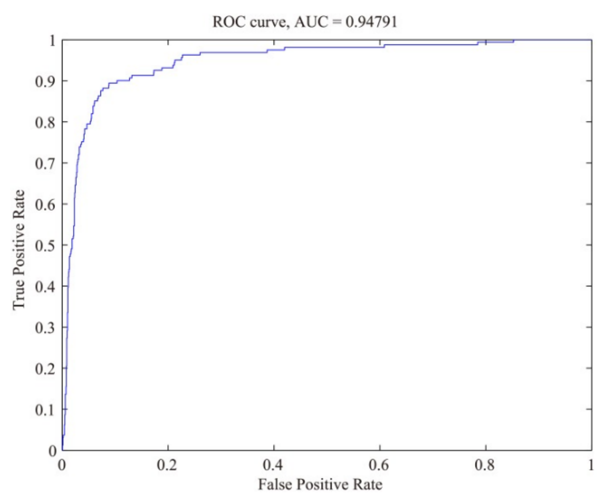


Fig. 6. ROC curve showing an AUC value of 0.94791.

The graph drawn between False Positive Rate and True Positive Rate is as shown in Fig. 6, it measures an AUC value of 0.94791. Fig. 7 shows nodules detected in a red circle using the proposed method.

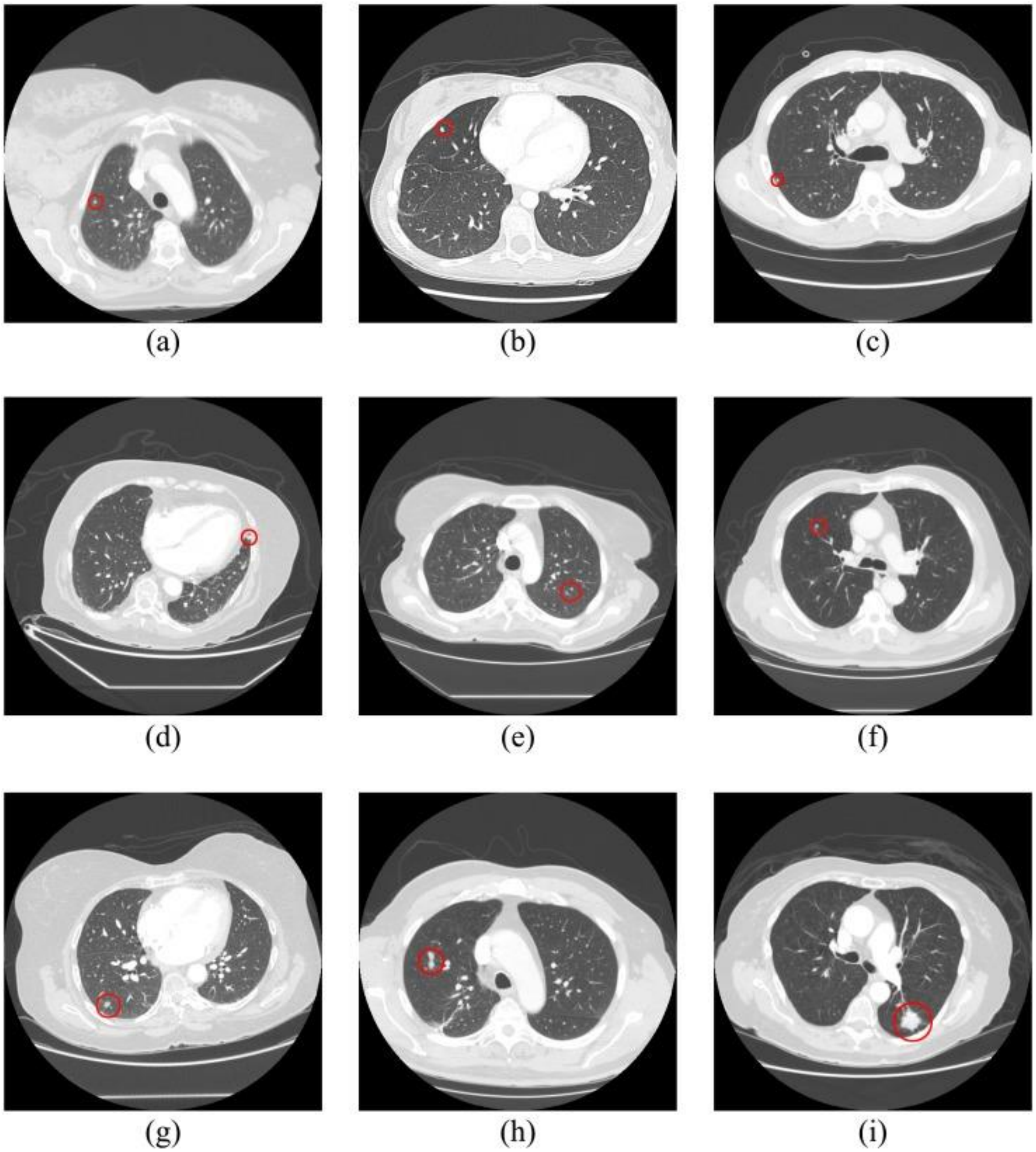


Fig. 7. Nodules detected using the proposed method.

Comparison with the recent handcraft techniques from the literature

In this section, we compare the proposed CAD system with the recent existing techniques in terms of Sensitivity, False Positives per scan, types of the database used, and the number of nodules as given in Table 1. Gong [13], detected nodules using multiscale 3D tensor filtering approach and extracted altogether 422 2D, 3D features. Out of which only 19 features are considered and given to random forest for classification. The system is evaluated on LUNA16, ANODE09, and attained a sensitivity of 79.3% and 84.62% respectively. Gupta [8], identified nodules based on multi-thresholding and morphological operation and extracted altogether 515 features and fed to the classifier to reduce false positives. This method attained a sensitivity of 85.6% when evaluated on the LIDC-IDRI database considering 1390 nodules.

Table 1. Comparison of the proposed method with recent handcraft techniques from literature

Author	Database	No. of Nodules	Sensitivity%	FP per scan
Gong [13]	LUNA16 ANODE09	1186	79.3 84.62	4 2.8
Gupta [8]	LIDC-IDRI	1390	85.6	8
Zhang [10]	LIDC-IDRI	168	89.3	2.1
Saien [14]	LIDC-IDRI	198	83.98	3.9
Liu [12]	LIDC	978	92.4	4.5
Proposed	**LIDC-IDRI**	**1186**	**94.8**	**2.4**

Zhang [10], segmented nodules using active contour model, nodules are detected using thresholding, and morphological operations, and extracted 3D skeletonization features that are given to the SVM classifier. When evaluated on the LIDC-IDRI database this method achieved a sensitivity of 89.3%. Saien [14], by assortment of 18 featues detected nodules. This method achieves a sensitivity of 83.98% when evaluated on the LIDC-IDRI database. Liu [12], detected nodules using Spatial Fuzzy C-Means (SFCM) method, assorted 22 features, and performed classification using unsupervised method random forest. This method gives a sensitivity of 92.4% when evaluated on the LIDC database.

Table 2. Comparison with recent cnn architectures.

Author	Database	No. of Nodules	Sensitivity%	FP per scan
Jiang [16]	LIDC-IDRI	25723	80.06	4.7
Setio [19]	LIDC-IDRI	1186	85.4	1
Qi [11]	LUNA16	1186	87	4
Wang [18]	LIDC	893	92	NM
Li [9]	JSRT	NM	94	5
Proposed	**LIDC-IDRI**	**1186**	**94.8**	**2.4**

Where NM stands for Not Mentioned.

Comparison with the recent CNN techniques from the literature

Table 2 provides the comparison performance of the proposed CAD system with the popular CNN architectures used for lung nodule detection and false-positive reduction. Jiang [16], detected nodules based on patch-based deep learning architecture, multiscale Frangi filters are used for false-positive reduction. This approach when evaluated on the LIDC-IDRI database attained a sensitivity of 80.06% considering 25723 nodules from 1006 cases.

Setio [19], detected nodules using ConvNets. For false positive reduction, nine 2D patches were extracted and fed to ConvNets. When evaluated on the LIDC-IDRI dataset considering 1186 nodules from 888 scans a sensitivity of 85.4% was attained. Qi [11], proposed three different 3D CNN architectures and achieved 87% sensitivity when evaluated on the LUNA16 database. Wang [18], proposed a CF-CNN model for nodule detection and attained a sensitivity of 92% on the LIDC database. Li [9], designed three CNNs with input patches of size 12×12, 32×32, and 60×60 respectively. This method is assessed on the JSRT database giving 94% sensitivity. Figure 8 shows the performance of the proposed model with different false positive reduction schemes from the literature in terms of sensitivity and false-positive per scan. Figure 9 shows the types of features used by authors in the literature.

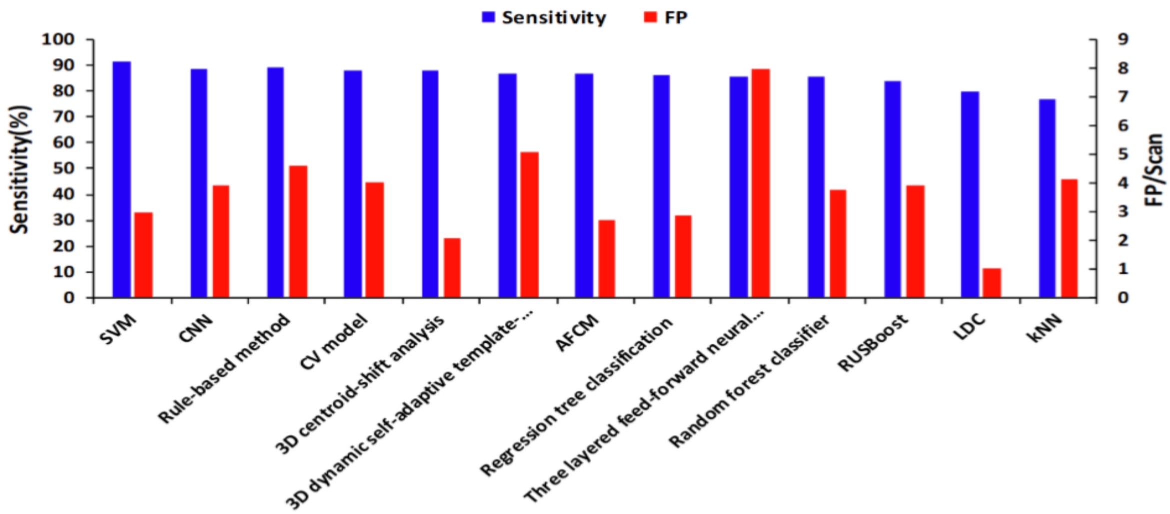


Fig. 8. Comparison with different false reduction schemes from the literature

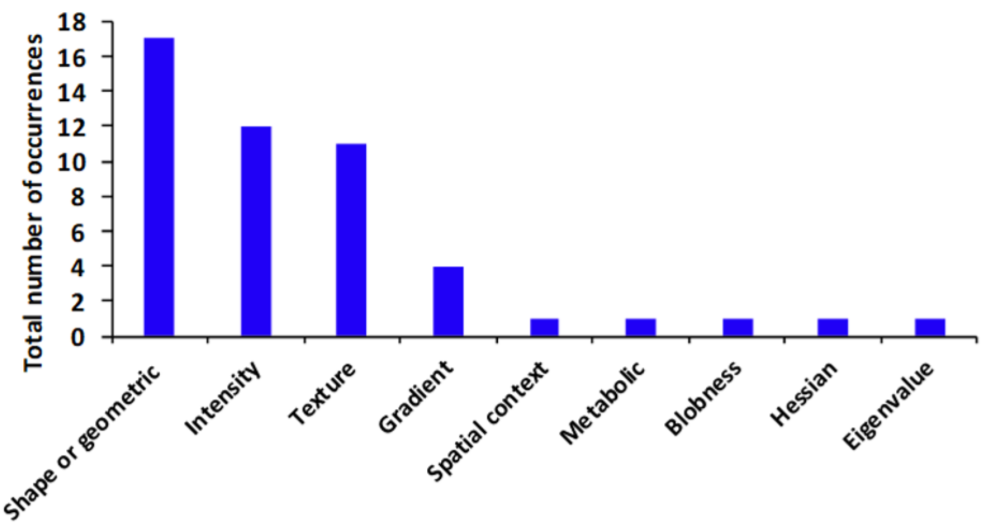
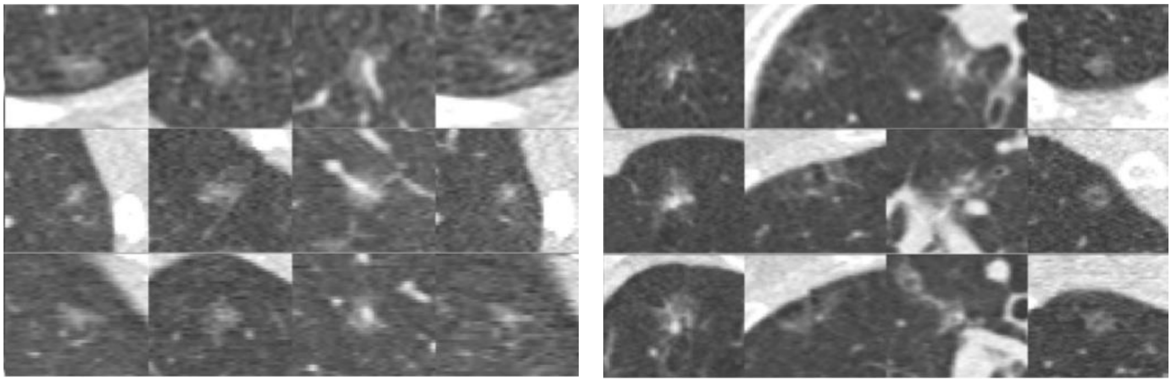


Fig. 9. Types of features used by different authors from the literature

Fig. 10 shows the nodules detected and missed by the proposed CADe system when operated 1FP/scan. The image patches are given in axial view (first row), sagittal image (second row), and coronal view (third row). The image patches are shown in 50×50 mm size with nodule centered.



(a) True Positives (b) False Positives

Fig. 10. Pulmonary Nodules detected representing a) True Positive nodules, and b) False Positive Nodules.

6. CONCLUSION

We proposed an efficient CADe system for the automatic detection of pulmonary nodules and the reduction of false positives (FP) per scan using patch-based Convolution Neural Networks (CNN). After detection of lung nodules, 64×64 image patches are drawn which are given as input to CNN. CNN is designed with three convolution layers, two maximum pooling layers and the last fully connected layer produces output such as nodule and non-nodule. The method when evaluated on the publicly available LIDC-IDRI database considering 888 scans with 1186 nodules, achieves 94.8% sensitivity, and 2.8 false positive (FP)/scan. The proposed CADe system shows promising results compared to recent techniques from the literature and proves CNN can be used for the early prediction of lung cancer. In the future, we will focus on 3D CNN's for the biopsy study of lung nodules.

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