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# Lung Nodule Detection in Computed Tomography: A Review

Youngseob Seo\*

Department of Medical Physics, University of Science and Technology, Daejeon, Republic of Korea

\*Corresponding author: Youngseob Seo, Department of Medical Physics, University of Science and Technology, Daejeon, Republic of Korea, Tel: +82-42-868-5479; E-mail: yseo@kriss.re.kr

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## Abstract

Lung cancer is becoming the major cause of cancer-related deaths in human worldwide. Detection of potentially malignant lung nodules is essential for the diagnosis and clinical management of lung cancer. In clinical practice, interpretation of computed tomography (CT) images is challenging for radiologists due to the large number of cases. There are higher rates of false positives in the manual findings. Computer-aided detection (CADe) and computer-aided diagnosis (CADx) systems enhance the radiologists in accurately delineating the lung nodules. It is extremely important task to analyze CADe and CADx for lung nodule detection. Therefore, it is necessary to review the various techniques in different CADe and CADx proposed and implemented by various researchers. This study aims at analyzing the recent application of various concepts in computer science to each stage of CADe and CADx. This review paper is special in its own kind because it analyses the various techniques proposed by different eminent researchers in noise removal, contrast enhancement, thorax removal, lung segmentation, bone suppression, segmentation of trachea, classification of nodule and non-nodule and finally classification of benign and malignant nodules. A comparison of performance of different techniques implemented by various researchers for the classification of nodule and non-nodule has been specified in the paper. The findings of this review paper will definitely prove to be useful to the research community working on automation of lung nodule detection.

**Keywords:** Lung cancer; Lung nodule detection; Computed tomography; Computer-aided detection; Computer-aided diagnosis

**Abbreviations:** AHE: Adaptive Histogram Equalization; ANN: Artificial Neural Network; BPBHE: Brightness Preserving Bi-histogram Equalization Method; CADe: Computer Aided detection; CADx: Computer Aided Diagnosis; CLAHE: Contrast Limited Adaptive Histogram Equalization; CT: Computed Tomography; DHE: Dynamic Histogram Equalization; ELCAP: Early Lung Cancer Action Program; FCM: Fuzzy C-Means; FLDA: Fisher Linear Discriminant Analysis; GLCM: Gray Level Co-Occurrence Matrix; HE: Histogram Equalization; IBSF: Intensity Based

Statistical Features; IRDI: Infectious Disease Research Institute; LDCT: Low-Dose Computed Tomography; LIDC: Lung Image Database Consortium; MAHE: Multi-Scale Adaptive Histogram Equalization; MCHOG: Multi-Coordinate Histogram of Gradient; MDT: Metal Deletion Technique; ResNet: Deep Residual Network; ROI: Region of Interest; SBGF: Selective Binary Gaussian Filtering; SNR: Signal-to-Noise Ratio; SVM: Support vector machine; WHO: World Health Organization

## Introduction

The statistics from World Health Organization (WHO) provides valuable information that 8.8 million deaths were caused worldwide due to cancer in 2015 [1]. Lung cancer, also known as bronchogenic carcinoma, is the most common cause of cancer in men and the 6th most frequent cancer in women, accounting for 1.69 million deaths in 2015 [1]. The discovery of lung cancer at a much later stage in patients makes the prognosis worse. If detected at an earlier stage the chances of survival increases. The recommended methods of screening for lung cancer are radiography, CT scan, sputum cytology or biopsy. CT scan is one of the common methods and the latest technology adopted in screening is low-dose computed tomography (LDCT). Although the introduction of LDCT in lung cancer screening protocols was found effective in detecting lung nodules at an early stage, it has negative influence on the visibility of low-contrast lesion due to increased noise and low spatial resolution under low-dose imaging. This poses a challenge to radiologists in finding and interpreting small nodules. Unfortunately, the interpretation of LDCT images is also challenging for radiologists to distinguish between benign and malignant lung nodules. Repeated CT scanning can increase the risk of developing cancer in older patients. As an attempt to reduce repeated CT screening, computer-aided detection (CADe) and computer-aided diagnosis (CADx) systems were developed to increase the sensitivity and reduce false positive findings. However, no efforts have been taken to review the effectiveness of the techniques discussed in this time period. This encouraged us to analyze the repository of this literature to identify the different techniques employed at different stages of image processing and compare their performance in terms of sensitivity, specificity and accuracy. The findings of this review will determine the most efficient

techniques in each stage of nodule detection and increase the accuracy of system for identifying the lung nodules.

## Methodology for Lung Nodule Detection

### Preprocessing

Preprocessing is an essential stage in lung nodule detection as medical images suffer from poor contrast [2]. This stage enhances the images improving the visibility of small nodule structures distinguishing them from other tissues and vessels in the lung in human body. There are a variety of techniques developed by different research personnel for the lung nodule detection. In the reviewed papers the authors have adopted the following two steps of noise removal and contrast enhancement to improve the image quality.

**Noise removal:** LDCT images have blurring, visual noise and artifacts. Blurring limits visibility of small objects in the CT images. Blurring can be caused at scanning stage or image reconstruction stage. Noise is affected by the size of focal spot and radiation detector. Blurring occurs when the ray is wider than the object under scanning. The size of the focal spot and radiation detector can be adjusted to reduce blurring [3]. In the image reconstruction stage the blurring can be reduced by increasing the voxel size [4]. However, reduction in the size of the focal spot and detector can cause an undesirable effect of visual noise. Thus balance should be maintained. Artifacts undoubtedly affect the image quality. They may occur during machine calibration process, scanning and reconstruction of images. These artifacts that commonly occur are ring, noise, metal, scatter, cone beam, helical, and pseudo enhancement. Ring artifacts can be corrected by recalibrating the detector. The noise and beam hardening can be reduced by iterative reconstruction. Metal deletion technique (MDT) can reduce metal artifacts [5]. Noise is affected by number of photon reaching the detector. Noise is one of the main issues affecting image quality and can be improved by using large voxels, or increasing radiation dose which is not advisable. Another useful method is to use a smoothing filter. Streaks are found in the images due to scatter artifacts. Wei et al. [6] proposed a correction algorithm for cone beam CT. Streaks in images are also caused due to motion and edge effects. Motion is due to voluntary or involuntary movement of patients. Noise is the main issue in case of CT images under low dose protocol [7]. Most of the studies that are under consideration reveal the fact that noise are Gaussian [8]. The Gaussian filter was used to remove noise in the lung CT images [9]. However, the Gaussian filtering method is very poor at accurately visualizing the edges. Gaussian kernel was adopted for the smoothing of image with Gaussian noise in the preprocessing step [10]. 3D coherence enhancing diffusion filter was proposed to be more appropriate for pulmonary nodule detection [11]. Sharma and Jindal [12] proposed a lung nodule detection system where white and pepper noise in the converted grey images was removed by Wiener filter. A new technique in Tetrolet transform was adopted for removing the Gaussian noise [13].

Green et al. [14] proposed a locally consistent non local means algorithm for removing Poisson noise.

**Contrast enhancement:** A challenging problem faced by radiologist in reading medical images is visibility of minute structures in the images. Contrast enhancement improves the visibility of the minute structures by enhancing the brightness difference between objects and background. Contrast enhancement methods can be broadly classified as linear and non-linear methods [15]. Linear contrast highlights the subtle variations within the images. Javaid et al. [16] performed contrast stretching or normalization as a contrast enhancement technique for improving the contrast and the visibility of the small nodules. Histogram equalization (HE) method was done by reallocating the pixels in the image for nonlinear contrast enhancement [17]. Adaptive histogram equalization (AHE) was performed by subdividing the images and then applying equalization to each sub image [18]. Brightness preserving bi-histogram equalization (BPBHE) method was implemented to enhance lung CT images [18]. Dynamic histogram equalization (DHE) method was developed to preserve the mean brightness [19]. Jin et al. [20] proposed multi-scale adaptive histogram equalization (MAHE) which provides better results than conventional methods of contrast enhancement. Contrast limited adaptive histogram equalization (CLAHE) was proposed for contrast enhancement of the CT images for the lung nodule detection [21,22]. Contrast enhancement in the lung CT images was performed using a novel method background suppressed fuzzy contrast enhancement method [23].

### Region of Interest (ROI) extraction

ROI extraction is performed to extract the most important and relevant features that may be useful in accurate delineation of the lung nodules. This is an important step in reducing an erroneous diagnosis and increasing the accuracy of nodule detection in CADe or CADx.

### Thorax removal

As the most common method for thorax removal, John and Mini proposed an iterative global threshold method which was based on the concept of density differences and morphological filling operation [24].

### Lung segmentation and reconstruction

Lung segmentation is one of the important phases in ROI extraction because the nodules may be missed due to improper lung segmentation. These methods discussed here are after the year 2012 to recent date to the best of our knowledge. Cascio et al. [25] have developed the volume of interest segmentation algorithm to delineate the parenchyma and its adjacent regions with CADe for automatic detection of lung nodules in spiral CT images. The lung extraction performed by region growing algorithm is followed by the lung reconstruction using the rolling ball technique due to the elimination of the nodules in the thoracic wall during the lung extraction process. In 2013 Jang et al. [26] proposed the lung

volume segmentation system which is performed using the threshold values and 3D-connected component labeling. In CADx proposed by Iqbal et al. [27], density thresholding method was used to divide the lung region. The artifacts due to air in the lung were eliminated by employing the pixel connectivity concept. The reconstruction of lung boundaries was done using the technique of mathematical morphology followed by smoothing operation of morphologic similarities [27]. Than et al. [28] proposed an initial lung segmentation method based on grey-level threshold and morphological filtering. The proposed method has the disadvantage of merged appearance of right and left lobes of lungs. Orozco et al. [29] adopted Hough transform for ROI extraction which removed the areas outside the dotted circumference in order to depict the ROI clearly. The lung mask generated by the preprocessing step including threshold values and flood filling method is a boundary characterized by bidirectional differential chain encoding method to identify the areas with juxtapleural nodules in the lung [30]. Dai et al. [9] proposed a graph cut algorithm which is performed on adjacent graphs where every pixel in the image is represented as the vertex and the weighted edge is nothing but the difference in pixel intensities. The fuzzy soft membership function was used to segment the data into clusters. In the initial step the lung region was separated from the fat and muscle regions using cluster values computed independently. The pixels in the image were segmented by constructing a distance matrix which was fuzzified smoothly and stored independently. The image was subjected to Fuzzy rule based assignment with respect to the above fuzzified data. The segments were further refined iteratively. The opening morphology was performed on the segmented image. The lung parenchyma was finally separated by the operation performed on segmented image and original CT image [31]. In the method proposed by Gong et al. [32] thresholding and region growing algorithms were employed for segmentation and lung reconstruction boundary correction. Yet another proposal segmentation of the lung was performed for the first time by the optimal thresholding and connected component labeling [33]. In the model proposed by Nithya et al. the lung parenchyma was extracted by a new sign pressure force function in selective binary Gaussian filtering (SBGF) which is very efficient with weak edges [34]. Though the fuzzy classifier performance decreases considerably when the images are noisy, Fuzzy C-means (FCM) is popularly used as a classifier for lung segmentation [35]. A supervised pulmonary nodule segmentation algorithm was proposed in this method based on self-adaptive algorithm.

### Bone suppression

Bone shadow suppression method proposed by Berg et al. [36] was to convert the contour of the bone interfering with the lung to a straight line. The bone contour can be removed by subtracting all reconstructed bone shadows from the original image. Thus the bone contour is subsequently smoothed as well as reintegrated from the original image.

### Segmentation of trachea

Trachea is a membranous and cartilaginous tube which begins at larynx and branches into two primary bronchi; passage ways leading to the lung. Segmentation of the trachea and main bronchi was done by the 3D region growing algorithm [37]. Segmentation of the trachea was performed by 2D Hough transform [38]. Segmentation of the trachea can be done by implementing the two material decomposition approaches which are based on the concept of intensity differentiation between air and lung voxels. Thresholding operation followed by a connect component analysis clearly depicts the trachea. Identification of the trachea is done by Hough transform. By using the simple deletion process of the trachea region the resultant mask is obtained [10]. Vessels are also removed based on eccentricity and area criteria [39].

### Removal of vessel and bronchi

Dhara et al. suggested the accurate segmentation of nodules which could improve the efficiency of the CADe by vasculature pruning technique based on computing geodesic distance map [40]. The proposed method was the inevitable step in segmentation and removal of the blood vessels attached to the nodules. Liu et al. proposed a method of detection of lung nodules based on the concept of artificial neural network (ANN) [41]. The vessel regions were removed by 3D line filter which is based on eigenvalue analysis using Hessian matrix.

### Feature extraction

Feature extraction is an important step in the process of lung nodule detection as it eliminates false positives. Feature descriptor using multi-coordinate histogram of gradient (MCHOG) and intensity based statistical features (IBSF) were employed for gradient and intensity feature extraction [42]. ROI is represented by a set of texture-based features like gray level co-occurrence matrix (GLCM) moments, auto correlation coefficients, edge frequency, Gabor filter descriptor and combined texture feature [43]. The features like intensity, size, overlap value and compactness were calculated after the ROI extraction was performed [44]. The extraction of features was done by geometric features (Boyce-Clark radial shape index and spherical density) through texture measurements and histogram structures [17]. The features were extracted by the five-layer auto encoder where the fourth and fifth layers formed the basis for constructing the vector [45]. Concave, length and position features were used in CADe for the segmentation of both lung and juxtapleural nodules [30]. Shape feature was extracted from each of the two lungs and was fed into trained neural network for nodule detection in CADx [46]. In the method proposed by Shaukat et al. the shape, texture and intensity features were employed in feature extraction phase [33].

## Discussion

### Classification of nodules from non-nodules

The accurate identification of lung nodule has a direct effect on the false positive rate and subsequently affects the specificity of the CADe or CADx. Initially 3D dynamic self-adaptive template matching was used to detect the nodules in the extracted ROI followed by Fisher linear discriminant analysis (FLDA) classifier which reduces false positive [32]. Classification of lung nodule was performed with the support vector machine (SVM) concepts in the method proposed by Filho et al. [47]. Before the feature extraction and classification the six regions of rings and spheres with constantly reducing sizes of radii were built for each candidate nodule to analyze the texture-behavior patterns. The feature extraction was done by constructing a phylogenetic tree with leaves representing voxels ranging from 0 to 65536 intensity values. The two values (taxonomic diversity and distinctness) identify the relationship between any two chosen leaf nodes in the tree. Classification is done by extracting 14 features for candidate nodules in three scenarios: two features (taxonomic diversity and distinctness index) from scenario 1, six more features from indexes in annular region from scenario 2 and six features from indexes in spherical region in scenario 3. In the method proposed by Froz et al. [48] nodules were delineated with the texture feature by employing the methods of artificial crawlers as well as Rose Diagram [49]. The classification was done by SVM and accuracy of 94%, sensitivity of 91% and specificity of 94% was achieved [50]. Classification of nodules from non-nodules can be done by bootstrap aggregating or bagging. Bagging employs several base classifiers on selected instances of datasets rather than a single classifier on single data. The positive point is that it is more efficient method when inducers are not stable [42]. Cao et al. employed two feature selection algorithms - spectral feature selection which belongs to unsupervised category and relief feature selection which belongs to supervised category of feature selection algorithm. These algorithms together with the multiple kernel learning method can be employed for feature selection and classification [49].

### Classification of lung nodules - Benign and malignant

Shape-, texture- and margin-based features were used for classification of nodules as benign or malignant with SVM [50]. Many attempts have been made from last decades to improve the efficiency of CADx of predicting malignant lung nodules. One of these attempts was made using the concept of deep residual network (ResNet) proposed by Nibali et al. [51]. There were some modifications to the ResNet like the initial convolution layer accepting 64×64 pixel greyscales and allowing 3 column networks to fit in GPU memory [51]. In terms of the method proposed by Yuan et al. [52], the classification of lung nodules was based on a hybrid feature of statistics and geometry. In this method sampling was done to make data isotropic and then icosahedron was used to divide

and sample the nodule volume in multiple views followed by sorting the views. After that, the convolutional neural network (CNN) was trained by image data which was constructed by radii calculation and sorted views. These data with scale-invariant feature transform (SIFT) calculation was used for Fisher vector (FV) encodings [52].

## Conclusion

This review paper exhibits an extensive study of various techniques in each phase of CADe and CADx. The pros and cons of diverse methods are also discussed. This paper specifies the different noises corrupting the lung images and the suitable filters to denoise them. It also represents the categories of contrast enhancement methods and lung segmentation methods. This paper summarizes the details of the dataset, nodule description, techniques and the performance for the various methods proposed by researchers with respect to CADe and CADx for lung nodules detection, and also throws light on the different techniques specifically for sub-stages in ROI extraction. In conclusion, the area of research dealing with algorithms and techniques for classification of a lung nodule to be benign or malignant has more scope for future work.

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