A Survey on Computer-Aided Diagnosis Systems for Lung Cancer Detection

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Abstract - Lung cancer is the most life threatening disease, the treatment of which must be the key goal through scientific research. The early detection of cancer can be supportive in curing the disease completely. There are several methods found in the literature for the detection of lung cancer. Several researchers have contributed their ideas for cancer detection. This paper mainly deals about existing lung cancer detection techniques that are available in the literature. A variety of methodologies have been found in the cancer detection approaches to improve the effectiveness of their detection. Different applications like neural networks, support vector machines, image processing techniques are widely used in Computer-Aided Diagnosing (CAD) systems for cancer detection.

Key Words: CAD system, Lung Cancer, Lung Nodule, LDA, ANN, SVM, Rule based classifier

1. INTRODUCTION

Lung cancer is leading cause of cancer-related deaths universal [1]. Identification of lung cancer in its initial stage is the only way to limit the death rate [2]. However, fining out the lung cancer in its initial stage is difficult and for which physician requests the patients to undergo several Computed Tomography (CT) images at regular intervals [3]. Even though CT imaging precisely captures the lung images; physician still finds it complicated to identify the cancerous nodules. The reason for this is due to the continuous cross-sectional images produced by the CT scanner and required to analyze the every cross-section. This demand for extra effort put by the radiologist to detecting the lung cancer and therefore high probability of error. The development of computer-aided diagnostic (CAD) system may help the physician and radiologist to accurately analyze the CT images to increase the accuracy of the cancerous nodule detection [4,5].

Commonly, nodules are the tiny mass inside the lung, which are the indicator for lung cancer. The nodules are classified into different types based on their location inside the lungs. They are juxta-pleural, well-circumscribed, pleural tail and vascularised [6]. Majority of lung nodules are non-cancerous (benign) but only about 40% of them are cancerous (malignant) [7,8]. Hence, cancerous nodules detection using CAD system is a real challenge for the researchers to quantify and detect the disease. Hence competent technique is required to detect the lung cancer in its early stage.

Lung cancer also can be detected through observed symptoms of patients. The common symptoms of lung cancer includes cough/persistent cough, weight loss, loss of appetite, shortness of breath, pain/persistent pain in the chest, cough up blood/blood in the sputum, fatigue/persistent fatigue and pain in the bone (back/hips)/shoulder/neck, etc. The stages of lung cancer are assigned a stage from I to IV, according to the seriousness of the disease. The staging of lung cancer refers to the severity (spread) of the disease in to the human body. Depending on the staging symptoms of cancer will differ.

2. LUNG CANCER DETECTION METHODS

Generally CAD systems are used for lung cancer detection. It can be detected based on the observed symptoms and analyzing Two Dimensional (2-D) Computed Tomography (CT) scan images of the patients. It can also be detected by Three Dimensional (3-D) analysis carried out for every segmented candidate nodules for the consecutive 2-D CT slices and 3-D visualization of stacks of 2-D CT slices.

2.1 Lung Cancer Detection from the Observed Symptoms

The development of CAD helps the physicians to diagnose the lung cancer from observed symptoms of the patients. Only very few studies have been reported in the literatures for detecting lung cancer based on the observed symptoms.
A detailed study on lung cancer diagnosis based on fuzzy rules was conducted by Durai and Iyengar (2010). The efficiency of their system was low, because of their simple algorithm. Later (2010), they developed a diagnostic model for the stage-wise lung cancer detection using improved fuzzy rules. In addition, it also suggests the type of treatment for the patients. The key characteristic of their latter system was easier modification and updation of database. Their later system efficiency was better than the former, could be used as medical diagnosis model for finding the stages of lung cancer patients.

A pre-diagnosis model developed by Abinav Vishwa and colleagues (2011) for the lung cancer detection, made use of artificial neural network (ANN). Their study concluded that, the developed model was designed with a smaller set of data (symptoms) and could be effective for lung cancer diagnosis.

Pre-diagnosing system for lung cancer based on supervised learning techniques was developed by Balachandran and Anitha (2011), utilized ANN model for making decisions. Statistical parameters, like symptoms and risk factors were used in their model and proved that, it can be an effective tool for pre-diagnosing lung cancer in comparison with clinical reports. Later (2014), they reported in their work that the ANN performance is superior to that of the simple statistical or rule based models.

### 2.2 Lung Cancer Detection from 2-D CT Scan Images

CT scan is generally preferred by the physicians to detect the lung cancer from the patients. CAD systems are most widely used in lung cancer detection schemes in 2-D CT scan images.

Commonly lung nodule detection using CAD systems for CT scan images involves four important steps: lung region segmentation, nodule candidate detection, feature extraction and classification. To extract the lung region from the CT scan images several methods were found in the literatures. The methods such as multiple thresholding, optimal thresholding and global thresholding were successfully implemented for lung region segmentation (Suzuki et al, 2003; Ye et al, 2009; Suarez-Cuenca et al, 2009). However, in these studies the threshold values were calculated manually by considering the pixel intensity of the CT scan images. Also morphological processing was performed on CT images to remove fat, bone and background noise of lung parenchyma in threshold based segmentation techniques. Since the threshold value is chosen based on the CT technology and X-ray dose, it varies from one CT machine to another CT machine. Hence this technique will not segment the lung region universally. Auto thresholding based algorithms were implemented in many literatures to overcome the difficulty of hard threshold segmentation.

After the segmentation of lung region, the nodule candidates were segmented. Various methods were successfully implemented in the literatures for the candidate nodule segmentation. It includes filtering based methods, active contour methods, shape-based methods and morphological approaches (Li et al, 2008; Kass et al, 1998; Pu et al, 2011; Kubota et al, 2011). The limitations of these methods were detection of more false positive nodules. The various thresholding techniques were proposed for the nodule candidate detection, however all the methods were based on the intensity values. These methods need human intervention to select the threshold value, hence not universal for all the CT machines. Template based matching were found in literatures to segment the nodule candidates’ detection (Jo et al, 2014; Lee et al, 2001). As the orientation of the image changes from one CT image to another CT image template matching segmentation fails. Hence this method is not reliable.

The suspected lung nodules from the segmented nodules candidate were successfully found in many of the literature in order to keep real malignant nodules for further analysis. Most of the papers in literatures used geometric features, gray level features, statistical features and gradient features for classification of the nodule candidate (C. Wook and C. Tae-Sun, 2014; Kuruvilla & Gunavathi, 2015). The final stage of the lung nodule detection in CAD scheme is the suspected nodule classification as either benign (non-cancerous) or malignant (cancerous). The various classifiers that have been most widely used in the CAD systems for the lung cancer detection were rule based classifier (Messay et al, 2010; Dehmeshki et al, 2007; Riccardi et al, 2011; Golosio et al, 2009; Gurcan et al, 2002), Linear Discriminant Analysis (LDA), genetic algorithm, Artificial Neural Network (ANN) and Support Vector Machine (SVM).

#### 2.2.1 Rule based Classifier in Lung Cancer Detection

Sharma et al (2011) described an automated CAD system for early detection of lung cancer for CT images using several steps. First, lung a region was extracted by image processing techniques, including bit image slicing, erosion, and Weiner filter. The CT image was converted into a binary image during the extraction process by bit plane slicing technique. After extraction of lung region, lungs and nodules were segmented by region growing segmentation. Then the set of features were extracted and fed to the rule based classifier for the final decision on the segmented nodules. The proposed system achieved the accuracy of 80%.

Kanazawa et al (2008) implemented a CAD system for lung cancer based on helical CT images at an early stage. This algorithm has two parts, namely, an analysis part and a diagnosis part. In analysis part, lung regions and pulmonary blood vessel regions were segmented and set of features of these regions are extracted by image processing techniques.
In diagnosis part, set of diagnosis rules were defined for the rule based classifier for nodule candidate classification based on the extracted features. The authors concluded in their study that, the proposed algorithm detects lung cancer candidates successfully. Latter, Kanazawa and his colleagues (2009) segmented the normal structures (vessels and bronchi) and nodules within the lung region using a fuzzy clustering method. They extracted a shape, a gray-level, and a position features for each candidate. Finally, a rule based classifier was used to combine these features for the detection of lung nodules.

Li et al (2008) described a computerized detection of lung nodules in thin-section CT images by selective enhancement filters and an automatic rule-based classifier. Their database has nodules of different sizes (4-28 mm, mean 10.2 mm), shapes, and patterns. This CAD scheme has five steps: lung segmentation, selective nodule enhancement, initial nodule detection, feature extraction, and classification. The key technique of their method is selective nodule enhancement filter for the significant enrichment of nodules and suppression of normal anatomic structures (blood vessels), which are the major sources of FP. Another key technique of their method is an automated rule-based classifier for reduction of FP. The experimental results indicated that their CAD scheme with its two key techniques minimizes overtraining effect and improved classification performance for nodules presenting large variations in size, shape, and pattern. Their CAD scheme achieved an overall sensitivity of 86% with 6.6 FP/patient.

Ye et al (2009) demonstrated a new method to optimize the detection of lung nodules in CAD systems. The authors utilized fuzzy thresholding, feature maps, adaptive thresholding rule-based classifier with SVM which segmented lungs, selection of candidate nodules, nodule segmentation and elimination of FPs, respectively. The implemented system achieved a sensitivity of 90.2% and 8.2 FP/patient which was validated with 220 nodules of sizes between 2mm and 20mm.

2.2.2 Linear Discriminant Analysis in Lung Cancer Detection

Negar Memarian et al (2006) developed a novel classification method called iterative LDA and used in addition with fuzzy c-means clustering segmentation for successful FP reduction. They concluded in their study that LDA classifier was superior over rule based classifier for FP reduction in detected candidate nodules.

Armato et al (2001) presented an automated detection of lung nodules in CT scans using rule based scheme and LDA classifier. Extracted nine 2-D features from thick-slice (10 mm) diagnostic CT scans of 43 patients with 171 nodules using LDA classifier result in sensitivity of 70% with 42.2 FPs.

Messay et al. (2010) described a new computationally efficient CAD system for pulmonary nodule detection by combining simple image processing techniques, such as intensity thresholding and morphological processing, to segment and detect structures that are lung nodule candidates. The lung nodule candidates are determined by extracting 245 features from the segmented lung CT image. Then, significant features are selected and fed to the LDA classifier. This method was able to detect 92.8% of the structures, which are nodule candidates.

Suarez et al (2011) demonstrated an automated detection of pulmonary nodules in CT for the FP reduction by combining multiple classifiers. Experimented classifiers are LDA, Quadratic Discriminant Analysis (QDL), ANN and SVM. They are applied independently and combined to the Lung Image Database Consortium (LIDC) using 85 images which has 110 cancerous nodules. The reported sensitivity is 80%, and the number of FPs/patient for each of the six classifiers is 6.1 for LDA, 19.9 for QDA, 8.6 for ANN and 17.0 for SVM. When the classifiers are used in combination, the number of FPs per patient is greatly reduced.

Iwano et al (2005) developed a computer-aided system which automatically classifies pulmonary nodules, detected on High Resolution Computed Tomography (HRCT), into different shape categories. The extracted nodules are classified into different shape categories based on quantitative measures of aspect ratio, circularity, and their second central moment from a series of 102 CT images without a prior diagnosis of malignancy. The results are compared with radiologists’ (subjective classification) results and reported that the proposed automated system accurately classifies the nodules. They concluded that their developed system has the potential to aid radiologists in classifying nodules as malignant or benign based on the correlation between certain shape categories. Later (2008), the same research group extended their work and achieved a sensitivity of 76.9% and a specificity of 80% with their system based on the LDA classifier (using circularity and second central moment) with 107 HRCT images comprising of 52 malignant and 55 benign nodules.

2.2.3 Genetic Algorithm in Lung Cancer Detection

Lee et al (2001), implemented a template matching technique for the detection of lung nodules in helical CT images. This technique was performed on both, inside the lungs and on the lung walls. Lung nodules inside the lungs were detected by Generic Algorithm Template Matching (GATM). Lung nodules at the walls were detected by Lung wall template matching (LWTM). The reported system accuracy was less because of more FPs. Using this system detection of nodules in low contrast CT images was difficult and which increased FPs.
Farag et al (2004) described an automatic detection and recognition of lung abnormalities in helical CT images using deformable templates. The proposed novel algorithm is based on four different types of deformable templates relating typical geometry and gray level distribution of lung nodules. They are 1. solid spherical model of large-size calcified and non-calcified nodules appearing in consecutive slices 2. hollow spherical model of large lung cavity nodules 3. circular model of small nodules appearing in only a single slice and 4. semicircular model of lung wall nodules. Every template has a particular gray level pattern which is analytically estimated in order to fit the available empirical data. Abnormality detection is based on the normalized cross-correlation template matching by genetic optimization and Bayesian post-classification. This method isolated the abnormalities which spread over several consecutive CT slices. Their result revealed that the technique can detect lung nodules more precisely based on the experiments conducted with 200 patients CT scans.

El-Baz et al (2013) developed a new algorithm for lung nodule detection using GATM. Their proposed algorithm was based on three steps: (i) Isolation of nodules, arteries, veins, bronchi and bronchioles from other anatomical structures (ii) Isolation of the nodules using deformable 3-D and 2-D templates and (iii) Elimination of the FPs. The algorithm was validated using private database which yielded 82.3% of sensitivity and 9.2% of FPs.

Ozekes (2007) developed a lung nodule detection scheme trained with genetic algorithm, in which lung segmentation was based on rules and template matching that produced 93.4% sensitivity and 0.594 FP/patient. Later, Ozekes et al (2008) reported that, adding cellular neural network and thresholding. The lungs were segmented using their approach, the CT scan images which were in gray scale was firstly converted to binary image using grey level thresholding technique. The blood vessels from the segmented images were removed by morphological operations. The Region of Interest (ROI) was extracted by region growing. Gray Level Co-occurrence Matrix (GLCM) and texture features were calculated and applied to the ANN. The implemented CAD system using ANN has achieved 86.3% accuracy.

Tariq et al (2013) developed a CAD method, in which median filter was used to remove noise content and the background was removed using gradient mean and variance. The lung region was segmented by optimal thresholding. Morphological operations were applied to remove the unwanted structures in the lungs. The ROI was extracted and texture features were computed. These extracted features formed as vectors and were given to the hybrid NN and fuzzy classifier. The disadvantage of this system was the large computational time for larger data set.

Kruvilla and Gunavathi (2014) described a system for the detection of lung cancer in CT scan images using ANN. In their approach, the CT scan images which were in gray scale was firstly converted to binary image using grey level thresholding. The lungs were segmented using morphological operation. Then the statistical parameters such as mean, standard deviation, skewness, kurtosis, fifth and sixth central moment were calculated. The classifications were done by feed forward and feed forward-back propagation networks. Their study concluded that the feed forward-back propagation network provided better classification results. The implemented ANN yielded the sensitivity of 82% and specificity of 90% with 0.5 FP/patient.

2.2.4 Artificial Neural Networks in Lung Cancer Detection

Lin et al (2005), presented an extension of NN based fuzzy model for the detection of lung nodules. Thresholding technique was applied to remove some part of the blood vessels or the large airways. Morphological closing and labeling was done to fill these areas. Three main features, area, brightness and circularity were calculated to discriminate lung nodules from other structures from the lung region. This NN based fuzzy model achieved classification accuracy of 89.3%. The main advantage of this system is that it is faster and no prior knowledge is required for the classification.

Henschke et al (2005) described a pattern classification approach for lung cancer detection in which pixel data was directly used as features for ANN classifier. Their system was tested with 14 benign nodules and 14 malignant nodules that produced an accuracy of 89%.

Vijay Anand (2010), demonstrated a CAD system in which different image processing techniques were combined with NN that applied on the CT images. The preprocessing technique was performed on the CT image for the noise removal. Lung region was segmented and converted into binary using optimal thresholding technique. The blood vessels from the segmented images were removed by morphological operations. The Region of Interest (ROI) was extracted by region growing. Gray Level Co-occurrence Matrix (GLCM) and texture features were calculated and applied to the ANN. The implemented CAD system using ANN has achieved 86.3% accuracy.
followed by a weighted SVM. Several steps were performed in order to detect the lung nodules. First, Lung region was segmented using fuzzy thresholding method. Then the nodules inside the lungs were enhanced by volumetric shape index map method. Adaptive thresholding and modified expectation-maximization methods were employed to segment probable nodule objects. Rule-based scheme was used to remove easily dismissible non-nodule objects. Finally, a weighted SVM classification was applied to further reduce the number of FP objects. The proposed method yielded a sensitivity of 90.2% with 8.2 FPs per patient in an independent test.

Riccardi et al (2011) described a heuristic approach for lung nodule detection, based on geometric features followed by an SVM classification. The implemented system produced a sensitivity of 71% with 6.5 FPs/patient in a 2-fold cross-validation test.

Hong et al (2012) demonstrated a detection approach for solitary pulmonary nodules based on CT images. They used Wiener for preprocessing and morphological filters with thresholding for the segmentation. Adaptive thresholding was used for detection of candidate nodules and SVM was used to eliminate FPs. Their proposed system had a sensitivity of 89.47% with 11.9 FP per/patient when tested with 44 solitary pulmonary nodules.

Orozco et al (2012) implemented lung nodule classification scheme in frequency domain using SVMs. In their work a computational alternative to classify lung nodules within CT thorax images in the frequency domain was presented. The ROI was manually segmented after the image acquisition. Then, the spectrums of 2-D Discrete Cosine Transform (DCT) and 2-D Fast Fourier Transform (2-D FFT) were computed. Then the histogram computed from the spectrum of each CT image for extracting the two statistical texture features. Finally, SVM with RBF as kernel was used as the classifier. Their implemented work showed 2 FPs and 10 False Negatives (FN) per patient cases with sensitivity and specificity of 96.15% and 52.17% respectively. Orozco and his colleagues (2013) later described a very simple but competent methodology for lung nodule classification without the using segmentation process. Based on the histogram analysis eight texture features were extracted and the Gray Level Co-occurrence Matrix (GLCM with four different angles) was computed after each CT image. SVM was utilized to classify the lung nodules into cancerous and non-cancerous categories. The better consistency results were shown with 90' and 135' of the GLCM.

Sivakumar et al (2013) proposed an effective lung nodule detection system for CT images by performing nodule segmentation through weighted fuzzy possibilistic based clustering approach. They demonstrated that Radial Basis Function (RBF) kernel based SVM classifier outperformed the linear and polynomial kernel based SVM classifier. The reported sensitivity and accuracy were 82.05% and 80.36%, respectively.

Choi et al (2014) demonstrated a lung nodule detection scheme for feature extraction and classification to reduce number of FPs. The 3-D shape based extracted feature vectors were analyzed by a SVM classifier. First, lung volume was segmented by optimal thresholding and 3-D connected component analysis. Then the nodule candidates are detected using multi-scale dot enhancement filtering in the segmented lung volume. Angular histogram of surface normals (AHSN) feature was described for the detected nodule candidates. Iterative wall elimination method was used to refine the AHSN feature descriptor. Finally, a support vector machine-based classifier is trained to classify malignant nodules and non nodules. This method achieved 97.5% sensitivity, with 6.76 false positives per scan.

2.3 3-D CT image analysis in Lung Cancer Detection

The 2-D lung image analysis was performed in many literatures in which the single slice of the CT scan was analysed for decision making on the cancerous nature of the lung. The 3-D analysis was normally carried out by analyzing the consecutive slices of CT images for every candidate nodule that was segmented using 2-D analysis. Usually the 2-D lung nodule analysis produced more false positives than the 3-D analysis; results in less accuracy. Hence 3-D analysis was carried out to reduce the false positives.

The work implemented by Ozekes et al (2008) using genetic and fuzzy rule based algorithm produced 100 percent sensitivity but with the cost of 13.4 FPs/patient. An Automated pulmonary nodule detection system for CT images using a hierarchical block classification approach was demonstrated by Wook-Jin and Tae-Sun (2013) which produced 2.27 FPs/patient. The work demonstrated by Alilou et al (2015) primarily focused on 3-D structural visualization of lung nodules which produced a 3.9 FPs/patient. The work implemented by Demirrad and Camurcu (2015) using texture 3-D model of lung nodules resulted in an FPs of 2.45/patient. The work described by Lu et al (2015) by a complex hybrid model for nodule segmentation and classification, yielded an FPs of 3.13/patient. Sousa et al (2010) described an automated lung nodules detection scheme which had six stages: thorax extraction (2-D region growing), lung extraction (2-D region growing), lung reconstruction (rolling-ball algorithm & mathematical morphology), structures extraction (thresholding process & region growing algorithm), tubular structures elimination (3-D skeletonization algorithm) and classification (SVM). Their implemented system achieved a sensitivity of 84.84% with FP/patient of 0.42.
2.4 3-D Visualization Systems for Lung Cancer Detection

Modern multi-slice high resolution CT (HRCT) scanners produce isotropic CT images, which has the slice thickness of 0.6 mm. These narrow slices could provide anatomical details of the lungs, similar to those available from gross pathological specimens (Meziane et al, 2008). A new CT scanner produces a complete scan of the lung cavity of an average person’s results in about 300 images. This large number exceeds the surgeon’s ability for handling the information. To reduce the work load of the surgeons, several isotropic CT images are combined to get a clinical 2.5-7.0 mm CT image, resulting in the loss of valuable information that could be used for more accurate surgical planning (Wei et al, 2009).

With the appearance of virtual reality techniques, the 3-D visualization of lung cavities is gaining popularity for surgical planning of treating lung cancer (Hu et al, 2006; Hemminger et al, 2005). In recent years, serious efforts have been made toward the advancement of CAD systems in three dimensional visualization of diagnostic radiology (Webb et al, 2001). In radiology, the CAD system supports the diagnosis made by a clinician (radiologist), who uses the output from a computerized analysis of medical images as a second opinion. Unlike conventional 2-D views, 3-D visualization provides views of the actual lung cavities in three dimensions, where there is no need for mental reconstruction. Recent studies revealed that the 3-D visualization of lung cavities outplayed conventional 2-D CT images for surgical planning.

To our knowledge, there have been only a very few 3-D CAD studies developed to reconstruct the CT lung images in 3-D environment. Delegacz et al (2000) has developed a 3-D visualization system to aid physicians observing the abnormalities in human lungs. This algorithm provides better visualization of internal lung structures like bronchi and possible cancer masses. However there were no supporting results for their work.

Hu (2006) investigated the role of 3-D visualization in the surgical planning of treating lung cancer, by utilizing the software AMIRA (Mercury Computer Systems Inc., France), the author calculated the planning time, workload experienced and accuracy of predicted respectability for surgical planning of treating lung cancer. However, no information was specified about the lung cancer location.

Liao et al (2006) described a medical color-enhanced 3-D visualization system for lung cancer detection, based on the volume rendering method. In their work, they identified lung tumor in a 3-D visualization environment, but sacrificed some visual effects to gain the rendering performance.

Aggarwal et al (2010) implemented an efficient visualization and segmentation system for early diagnosis of lung cancer for CT images. They utilized DICOM viewer YaDiV for detection of various lung tissues as well as for efficient visualization of lung images and MATLAB, based tool MATITK for segmentation of lung images. Their work provided a fully automatic method for visualizing the lungs in three-dimensional (3-D). For performance analysis, various lung data sets of NCI (National Cancer Institute) of NBIA (National Biomedical Imaging Archive) have been evaluated.

Wei et al (2009) developed a pipelined algorithm based on the modified adaptive fissure sweep and wavelet transform to segment the lung lobes in 2-D environment. In addition, the algorithm describes a procedure for visualizing lung lobes in three dimensions using AMIRA software. Their algorithm allows surgeons to segment the lung lobes in a 3-D environment but, there is no evidence about the cancerous nodule location and no information about its width, breadth, height and volume.

Filho et al (2013) described 3-D segmentation and visualization of lung its structures using CT images of thorax. Their work was based on two singularity methods, the 3-D region growing and the multi-thresholding algorithms, for the segmentation of the lungs and its internal structures. It aimed to assist medical diagnosis of pulmonary diseases through 3-D visualization and reconstruction from its 2-D CT slices. This facilitates the detection of lung cancer by the medical experts and reduces the bias of interpretation of the result. Their results were evaluated and validated by two medical pulmonologists.

3. CONCLUSION

This paper has given a brief review on recent developments in lung cancer detection methods. Various techniques have been used in the lung cancer detection methods to improve the efficiency of cancer detection. Each method has its own uniqueness, advantages and limitations. As it is of substantial significance to detect the cancer in its early stage, many researches are still being done. The popular classifiers used for lung nodule detection schemes are also presented.

REFERENCES


**BIOGRAPHIES**

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