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CURRENT TRENDS AND CHALLENGES OF PULMONARY NODULE DETECTION TECHNIQUES IN CT IMAGES.

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ABSTRACT

Lung cancer is one of the deadliest cancers worldwide with high mortality rate. The survival rate can be increased if the cancer is diagnosed at early stages. Computer aided detection (CAD) system act as a secondary opinion to the radiologist for the early detection of lung nodules in Computed Tomography (CT) images. This paper provides a comprehensive review of the recent existing automated methods of identifying lung nodules from CT scans. Current detection algorithms appear to report many false positives with high sensitivity rate. Therefore, false positive reduction plays an important role in classification process. It has been analyzed that the nodule classification based on deep learning with Convolutional neural networks (CNN) is dominant due to its excellent performance.

KEYWORDS: Computed Tomography (CT), Lung nodules, Deep CNN, Computer aided detection (CAD).

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I. INTRODUCTION :

Cancer is the uncontrolled growth of abnormal cells which can invade the adjoining parts of body and spread to other organs which later is referred to as metastases. According to WHO 2018 survey,lung cancer is the most common type of cancer in men and third most in women [18]. It has been reported that lung cancer is responsible for 1 in 5 cancer death worldwide. Usage of tobacco is the most important risk factor for cancer deaths. Lung cancer five year survival rate is 18.6% which is lower than all other cancer types. Only 16% of lung cancer cases are diagnosed at an early stage [18]. Mortality rate of cancer can be reduced if they are detected and treated early. Lung Screening test is an effective method for early detection. Sputum cytology chest radiography and Computed Tomography (CT) are the most commonly accepted screening measures. Early detection by low dose CT screening can decrease the mortality rate to 20 % [19]. Advancement in CT technology has resulted in faster acquisition and clearer images. Manual analysis of these images by radiologist is a tedious and time-consuming process. To solve this difficulty computer aided system can be used to improve the diagnosis and to make the interpretation of the images easier by the radiologist. Extensive research is taking place in the area of lung nodule detection. A pulmonary nodule is a small round or oval shaped growth in the lung which is smaller than 3 cms in diameter. Nodules larger than 3cm is called a pulmonary mass. Pulmonary nodules can be benign and malignant. Computer aided detection system can aid in discriminating malignant from benign modules. According to the location and connection with the surrounding pulmonary structure lung nodules can be classified into well circumscribed, juxta-vascular, juxtapleural and pleural tail nodules. Of all these nodules detection of juxta vascular and juxta pleural nodules are challenging as the attachment of these nodules with the branches alter the shape of nodule in appearance. Figure 1 shows the different types of nodules present in CT images [25]

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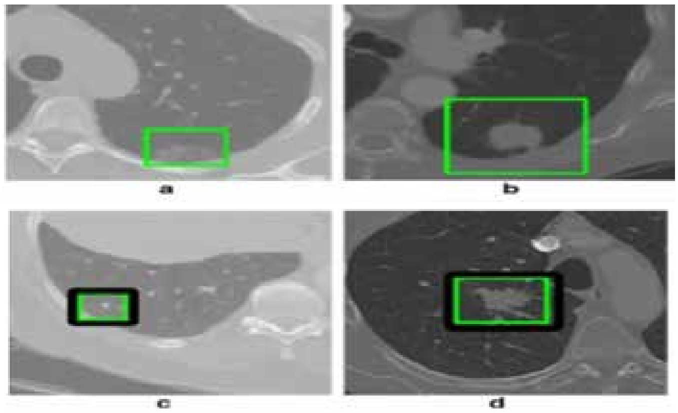

Fig.1 Nodule types: a) Ground glass b) Juxta-pleural c) well circumscribed d) Juxta-vascular

The available CAD systems results in large number of false positive rates which makes it difficult to use it in clinical applications. In addition to this some of the nodules remain undetected in CT images. Therefore, the techniques to detect lesions from broad spectrum of appearances are needed to improve the performance of CAD systems [1]. Recently machine learning algorithms especially deep learning algorithms are gaining importance in the field of image processing such as segmentation and classification. Machine learning algorithms required structured data whereas deep learning depends on layers of artificial neural networks (ANN). Deep learning algorithms gives excellent performance on the huge amount of data. Figure 2 illustrates the difference between machine and deep learning. Deep Convolutional neural network (CNN) can be used for nodule classification as it has auto learning capability and has a strong generalization ability.

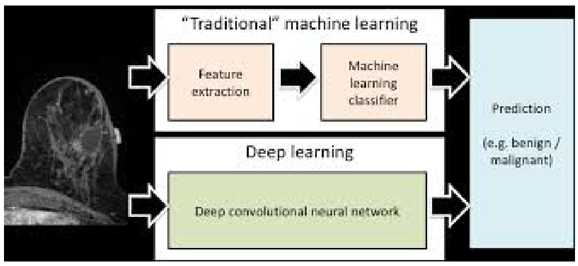

Fig 2: Machine learning vs Deep Learning [38]

This paper is organized as follows. Section 2 gives the materials and methods used in lung nodule detection system. Section 3 gives the performance measures and section 4 gives the conclusion and future challenges in the area of lung cancer detection.

II. MATERIALS AND METHODS :

The pulmonary nodule detection system consists of four main steps: Image Acquisition, Preprocessing, Lung/Nodule Segmentation and Nodule type Classification. This section explains each step with related works one by one. The process starts with the image acquisition where the available datasets are explained. Then image is enhanced by various preprocessing techniques. The lung nodule is then segmented out from the background and the features are extracted. Nodule types are finally determined during classification process. The performance of the classifier is estimated by means of various measures like sensitivity, accuracy and specificity.

IMAGE ACQUISITION

The process of retrieving images from an imaging modality is known as image acquisition. CT images are widely used for detecting lung nodules as it is faster and has higher resolution than MRI. CT scan images show better contrast difference among nodules and adjacent organs. Large number of publicly available datasets are present for nodule detection. Lung Image Database Consortium (LIDC-IDRI) is one of the largest datasets with 1018 cases from seven institutions. The reference standard is set by four radiologists through a two-phase image annotation process.In the first blinded reading phase each radiologists reviewed independently each CT scan and annotated lesions to one of the three categories as non-nodule, nodule<3mm or nodule≥3mm.In the second unblinded reading round all four radiologists reviewed the annotations and decided whether to accept or reject each annotation[2]. ANODE09 challenge provided a dataset of 55 CT scans in which each of them were annotated by two radiologists in a blinded fashion[3].The Early Lung Cancer Action Program (ELACP) database consisted of 50 low-dose documented whole-lung CT scans and 379 unduplicated lung nodule CT images [8].The percentages of nodule types in ELCAP were W-15%, V-16%, J-30%, and P-39%, respectively [7].The Kaggle Data Science Bowl (KDSB) 2017 challenge dataset comprised of labeled data for 2101 patients, where a label 0 is for the patient with no cancer and 1 is for the patient with cancer. In all these databases the images were in DICOM format with each CT scan imageof 512x512 pixels. The Lung nodule analysis 2016 (LUNA16) Challenge dataset comprises labeled data for 888 patients, where for each patient the data comprises of CT scan data and a nodule label (list of nodule center coordinates and diameter).The Lung Test Images from Motol Environment (Lung TIME) is another publicly available dataset of thoracic CT scanswith manuallyannotatedpulmonarynodules. It consisted of 157 CT scan dataset with 394 annotated nodules containing almost every nodule types such as pleura attached, vessel attached, solitary, regular and irregular with 2-10mm in diameter[4].Amongtheabovedatabases,LIDC-IDRIandELCAPwerethemostpopularones. TheLIDC-IDRI wasmostlyusedforthetwo-typenoduleclassification ofbenignandmalignant,whiletheELCAPwas mostly employed for the four-type nodule classification [6]. Apart from these databases researchers have also acquired databases from private hospitals also. The nodule detection algorithms were evaluated on public as well as private databases and the performance was calculated.

PRE-PROCESSING

Pre-processing helps to reduce the noise and other artifacts produced during image acquisition process. It improves the visualization of the image and makes the interpretation of nodules better. Median filtering is widely used in many of the works as it removes the salt and pepper noise present in CT images and also retains the sharpness of the image [9]. In median filtering each pixel value is replaced by the median value from the neighborhood pixels. Adaptive median filter eliminate the nonimpulsive noise and preserves the edge details of the image. Average filter removes the special noise in the digital images. Adaptive Histogram equalization was used to improve the quality and visual appearance of the image. Here each pixel is mapped to intensity proportional to its rank in the surrounding pixels [5]. Gaussian filter can also be used for smoothening and removing noise from CT image. Gabor filter is used especially for texture analysis due to its optimal localization properties in both spatial and frequency domain [10].

LUNG/NODULE SEGMENTATION

The execution time of nodule detection methods can be reduced if the lungs are segmented initially from nearby structures. Various automatic and semiautomatic approaches have been used for lung or nodule segmentation. In a CT image the lungs appear as dark and the surrounding structures appear as bright. This contrast has inspired various threshold-based segmentation methods such as optimal thresholding and otsu thresholding [9]. The main drawback of thresholding is that the segmentation is depended on pixel information. Region growing approach can also be used to isolate lungs.It is a type of pixel-based segmentation which involves the selection of initial seed points. It examines the neighboring pixels of initial seed points and determines whether these pixels are within the target region.

Oluwakorede M. Oluyide et.al proposed an automatic lung segmentation based on Graph Cut using a distance-constrained energy function [DCE]. The globally optimal solutions are produced by modelling the image data and spatial relationship among the pixels. The DCE function penalizes the pixels based on their Euclidean distance from a coarsely estimated region containing the lungs. This term ensures that labels are assigned only to the pixels of the lung even in the presence of other anatomical regions with similar appearance model to the lung [11].

A novel segmentation lung segmentation method was introduced in [12] to detect the juxtra-pleural nodule precisely.Here it was assumed that the lung contour slightly and uniformly expanded or contracted over frames, while the juxta-pleural nodules showed a consistent appearance even though the lung contour pattern changes.Initially the lung contour was predicted using Bayesian approach and lung contour was updated over multiple frames. Then by comparing the results from the Bayesian approach and the CV model, the difference image was extracted. Each separated group in the difference image corresponds to a juxta-pleural nodule candidate.Concave point detection and circle/ellipse Hough transform was finally used to eliminate the false positives present in each separate group. In this method the irregular shaped nodules were filtered by hough transform. So, this approach suffered from the limitation that it cannot detect cancerous nodules which are irregular shaped.

MuzzamilJavaid et.al used intensity thresholding for segmenting lungs. Then histogram of CT image is done to select a suitable threshold value for better segmentation results.Morphological closing was done to include juxtapleural nodules in segmented lung regions. Nodules was then detected using K-means clustering. Segmented potential nodules were then divided into six groups on the basis of their thickness and percentage connectivity with lung walls and was then given for nodule classification [20].

Xiaojiao Xiao et.al also proposed a method based on Fractal Geometry and Convex Hull Algorithm for juxtrapleural segmentation. Initially a contour of lung parenchyma was constructed using automated threshold iteration method. The fractal geometry method was used to detect the concave boundary and convex hull algorithm was used to repair it, which resulted in accurate segmentation of juxtapleural nodules [13].Various optimization algorithms, namely, k-means clustering, k-median clustering [15], particle swarm optimization, inertia-weighted particle swarm optimization, and guaranteed convergence particle swarm optimization (GCPSO) have also been used to extract the tumor from the lung image [16].

To extract and learn the meaningful information from the huge amount of existing data as much as possible, deep learning technique including deep belief network (DBN) and CNN were introduced into nodule detection analysis.Hong yang Jiang et.al used multi-group 2D lung CT images for nodules detection. First, the distorted lung contours were repaired through a lung wall mending method. Second, vessel-like structures in lung CT images were eliminated through Frangi filters of adjustable parameters. Finally, deep learning convolution neural network (CNN) was employed for automatic lung nodule detection [14].

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NODULE TYPE CLASSIFICATION

Lung nodule are difficult to distinguish as they are low contrast tissues. Features from the nodules have to be extracted before classification process. It can be either 2D or 3D. Feature vectors are based on their shapes, texture, densities, intensity values, fractals, and deep features.

DiegoM. Peña et.al [17] extracted eight minimal characteristic features which include geometrical measurements (area, circularity, volume) and histogram measurement (mean intensity value, variation of intensity, skewness, kurtosis, sum of intensity) and classified into nodule and non-nodule by SVM classifier. The proposed approach could classify only those nodules of size greater than 4mm.

In [20] detected nodules are divided into 6 groups based on their thickness and connectivity with lung wall. Nodules in same group share similar features. Thus, false positives can be eliminated by providing distinct features for different groups. Intensity, geometric and statistical features of nodules were selected for different groups. Small sized nodules were classified by rule-based method and big nodules were classified by SVM classifier. This method could not detect ground glass nodules (GGO) with low intensity values.

Fangfang Han et.al used 2D (Haralick, Gabor and Linear binary pattern (LBP)) texture features to classify nodules into malignant and benign. Classification was performed by SVM classifier using RBF kernel. In this work uncertain nodules were not considered for classification [21].

Kuruvilla J. et.al presented an automated classification method based on artificial neural network. The statistical parameters calculated from segmented image include mean, standard deviation, skewness, kurtosis, fifth central moment and sixth central moment. The classification was done using feedforward and feed forward back propagation networks. The feed forward back propagation network [BPN} gave better classification and skewness gave maximum classification accuracy [23]. Nodule located near the pleural side of the lung was misclassified in this method. Two new training functions were proposed which provided better classification results when compared to already available training function in BPN network.

Krishnamurthy S. et.al [29] employed a histogram-based auto center seed k-means clustering to segment the nodule candidates. False nodule candidates were eliminated using shape and texture features (2D and 3D). The two-stage classifier in this work classified the malignant and benign nodules. In the first stage a rule-based classifier was used. Later a BPN based ANN classifier was used as the second-stage classifier which reduced the false positive rate. Features such as tissue deficit, tissue excess, isotropic factor and edge gradient were used as nodule growth predictive measure. This work was implemented with a smaller number of patient data.

WookJin Choi et.al proposed a novel method based on genetic programming-based classifier. Thresholding and 3D connected labelling was used for lung segmentation. Nodule candidates was extracted by multiple thresholding and rule-based pruning. Finally, a genetic based classifier was used to classify nodules and non-nodules [32].

Keshani et.al [31] used active contour modelling to segment lung. Masking technique was used to isolate nodules. Solid and cavity nodules were detected by SVM classifier using 2D stochastic and 3D anatomical features. In this method lung tissues were classified into four classes such as lung wall, lung parenchyma, bronchioles and nodules. This helped to distinguish nodules from lung wall from the one covered by parenchyma.

With the increase of the training datasets and the improvement of computational power, deep learning has achieved great success in the field of machine learning, especially in the field of image classification. In deep learning multilevel nonlinear processing units were cascaded to construct deep structures for feature extraction and representation. Here the parameters could be automatically adjusted. The input of deep CNN is ROI (Region of Interest) pixel data without feature extraction and selection. Deep learning models, such as CNNs, Auto-encoder, DBNs et al. were used in lung nodule image classification.

Qi Dou et.al proposed a method using 3D convolutional neural networks (CNNs) for false positive reduction from volumetric CT scans [22]. The 3D networks encode 3D spatial information and produce high discrimination capability. Here three 3D CNNs were used with each encoding specific level of contextual information. The final classification was obtained by fusing the probability prediction output of these networks. This method is time consuming and requires more memory usage.

Wei Li et.al [24] designed a deep convolutional neural network to classify three types of nodules such as solid, semisolid and ground glass opacity. The CNN architecture in this approach consisted of two convolution layers with down sampling layer in between. Fully connected layer was connected to the last down sampling layer. First convolutional layer contained 8 feature maps and the second has 16 ones. The Kernel size used for convolutional layer is 5x5 and that for down sampling layer is 2x2.The neural network was trained with large number of images than other methods and this approach showed more general characteristics of nodules with high accuracy.

III. PERFORMANCE MEASURES :

The performance of the classification algorithm is evaluated by the following measures.

$$\text{Sensitivity} = \frac{TP}{TP+FN} \quad \text{----------------(i)}$$

$$\text{Specificity} = \frac{TN}{TN+FP} \quad \text{--------------(ii)}$$

$$\text{Accuracy} = \frac{TN+TP}{TP+TN+FN+FP} \quad \text{------------(iii)}$$

Where TP (true positive) denotes the number of nodules that are correctly identified as cancerous. FN (false negative) represents the number of nodules classified as negative for the actual positive nodules. TN (true negative) denotes the number of nodules that are correctly classified as non-cancerous. FP(false positive)is the number of nodules classified as positive for the negativenodules.The performance of the classifier at various operating points was characterized using Sensitivity-specificity ROC curve. The area under the curve (AUC) is another indicator used to evaluate the performance of a classifier.

IV. OBSERVATIONS :

A brief comparison of few recent techniques based on machine learning and deep learning is presented in table 1. The table comprises information regarding authors,classifiers employed, type and size of nodule correctly identified, and the results in terms of standard parameters sensitivity, specificity and accuracy. For small amount of data machine learning techniques gives high sensitivity rate with low false positives per scan. But its performance degrades for larger data. Figure4 depicts the performance comparison of deep learning networks. These networks give high sensitivity rate with low false positive rate. Among the deep learning networks 3D Dense CNN gives the highest sensitivity rate of 95.2% and false positive rate of 7%.

Table 1. Comparison of Existing Machine Learning and Deep Learning Techniques

AUTHOR	CLAS-SIFIER	TYPE OF NODULES	PERFOR-MANCE
Diego M. Pen et.al [17]	SVM	Nodules>4mm	94.23%-sensitivity 84.75%-specificity 89.19%- accuracy
Fangfang Han et.al [21]	SVM	Benign and malignant	AUC-92.70%
Muzzamil-Javaid et.al [20]	SVM	Juxtavascular, Juxtapleural nodules	91.65%-sensi-tivity 96.22%-accu-racy 3.19 FPs per case
Kuruvil-la.J. et.al [23]	Feed-forward Back-propa-gation Neural Network	Benign Malignant	91.4%-sensi-tivity 93.3%-accuracy 2 FPs per case
Krish-namurthy S. et.al [29]	BPN	All type of nodules ≥3mm	88.8%-sensi-tivity 83.3%-Speci-ficity 2.26 FPs per case
WookJin Choi et.al [32]	Genetic Pro-graming based classifier	Non-nodules and Nodules	94.7%-sensi-tivity 5.45 FPs per case

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Keshani et.al [30]	SVM	Solid,Non-sol-idand cavitary nodules>5mm	89%-Sensitivity 7.3 FPs per case
Messay et.al [31]	Fischer Linear Discrim-inant Classi-fier and Quadrat-ic Classi-fier	Nodules 3mm to 30mm.	82.66%-Sensi-tivity 3FPs per case
Liu,et. al[33]	Mul-tiscale CNNS	Solid, semi-solid, Ground Glass opacity.	92.3%-sensi-tivity
Al-Imam[36]	CNN and RNN	Benign and alignant	94%-sensitivity

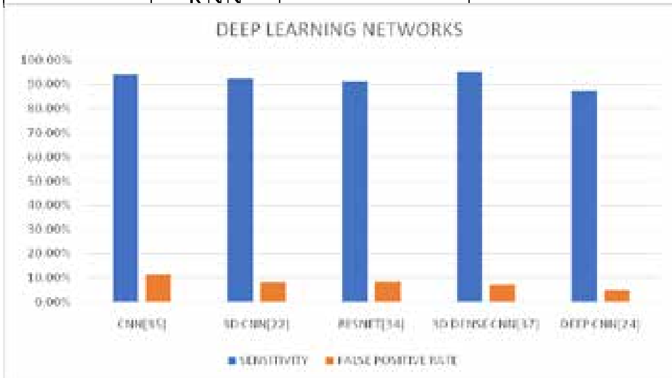

Fig 3.Performance comparison of deep learning networks

V. CONCLUSION AND FUTURE CHALLENGES :

Automated identification of the pulmonary nodules from CT scans is challenging task in computer-aided analysis as the nodules have large variations in sizes, shapes and locations. In addition to this the similarity in morphological appearance of some false positive candidates to that of true pulmonary nodules, further increases the difficulty in detection. This paper provided a review of the current nodule detection and characterization techniques in computed tomographic images. Among the detection process, the nodule classification based on deep learning is dominant due to its excellent performance. Even though the existing methods exhibited high detection rates, some of them do not yield satisfactory results when applied on nodules of assorted shapes and varying sizes such as juxta-pleural nodules. Additional enhancements are still needed to precisely discriminate such nodules from non-nodules. 3D feature-based method provides more information and make lung nodule representation more comprehensive. The malignant levels of nodules given in LIDC-IDRI was not balanced. The number of uncertain samples is larger than the number of certain samples. So, the future work must be directed to the efficient usage of uncertain data samples and grading of images based on the degree of the malignancy of pulmonary nodules. This type of work will be of valuable significance for the diagnosis and treatment of lung cancer in clinical applications A close relationship between researchers and clinicians is also needed for the better understanding and interpretation of pulmonary nodules.

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