Feature based analyses of lung nodules from computed tomography (CT) images

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Abstract. Among various lung image modalities, CT (computed tomography) images have been found most suitable and widely used for detection of small lung nodules. Although an expert radiologist can analyse these images quite perfectly, however an efficient CADe (computer-aided detection ) system capable of detecting pulmonary nodules automatically may be of great help considering the large number of CT images, a radiologist needs to analyse a day in recent years. A few CADe systems have already been tested within lung cancer screening trial which have enjoyed mixed results. So, the field has enough voids to be filled and research towards development of novel and efficient CADe systems has become an interesting, but challenging field of research. We too have been trying to develop CADe systems that can analyse CT images to detect and identify various lung nodules. In the process, we are reporting herein one of our development for the same. Our CADe system has maintained its 81.25% accuracy in detecting malignant nodules. Hand-crafted features of the selected lung CT images were used in the study. The study is emphasised on developing efficient CADe systems capable of detecting solid nodules (size > 2 mm) at different locations, whether isolated, juxtapleural or juxtavascular nodules. While MATLAB was used to carry out pre-processing, segmentation and nodule detection, testing of datasets was done by a MLP (multilayer perceptron) network by using WEKA (Waikato Environment for Knowledge Analysis) software.

1. Introduction

Lung cancer or lung carcinoma is reported as the deadliest among all the cancers when death toll related to cancer worldwide in last couple of decades are considered [1]. L. Garfinkel et al. in their report in 1991 made a special remark that fatalities in women due to lung cancer had surpassed that caused by breast cancer in the United States in the year 1987 [2]. It is one of the most aggressive kinds of cancers as only 10-16% of the patients are found to be reported to survive for 5-years [3]. The prime reason behind this low value of survival rate is the diagnosis of patients in advance stages of their disease. Reports suggest that the rate could be increased up to 70% by diagnosis of lung cancer in early stages [4,5]. So, a successful clinical treatment of lung cancer relies on procedures and techniques which are capable of accurate detection of lung nodules in early days of the disease. Due to its high structural imaging ability, computed tomography (CT) has become the most suitable and widely used imaging technique for the detection of small lung nodules.

The National Lung Screening Trial (NLST) carried out during the period August 2002 to September 2007 revealed the effectiveness of low-dose computed tomography LDCT images in comparison to chest radiography. Mortality rate in 7 years could be reduced to 20% by screening high
risk patients thrice in a year with the former in comparison to the later [6]. This result evolved a genuine hope of changing the scenario of late diagnosis by conducting lung-cancer monitoring programs using LDCT particularly for risk groups such as smokers. U.S. has already implemented such programs while many other countries are likely to follow soon [7]. Indian government too launched national cancer screening program for three types of cancers (cervical, breast & oral) in people more than 30 years of ages in 100 districts [8]. However, we have not found any record of extending the mission to lung cancer till now. The major challenge that needs to be overcome for successful implementation of such programs is the analysis of huge number of CT images recorded. For the best set of radiologists too, there is every chance of human error which may be due to fatigue or any kind of distraction while dealing with such a large number of images [3]. Development of an effective CADe system enabling analyses of CT images to detect lung nodules has been seen as the best possible solution in this scenario and so, researchers throughout the globe have been found actively involved to contribute their part to the cause during the last two decades. Meanwhile, many CADe systems have been evolved and a few of them have been tested within lung cancer screening trial which have enjoyed mixed results [9,10]. However, the answer to the quest of efficient CADe systems for accurate detection of pulmonary nodules till date has been felt to be fairly behind the actual target. CADe systems have not commonly been used in current clinical daily practice due to the drawback of finding high false positive values demanding a radiologist's attention [11].

Realizing the urgency of developing potential CADe systems to detect pulmonary nodules and believing that CADe will progressively be integrated in clinical practice, we have got attracted to this interesting and important field of research. This report describes our developed CADe system capable of detecting solid nodules (size > 2 mm) at different locations.

2. Literature survey

Literature reports suggest that a large number of research groups across the world are engaged in this field of research in the mission of developing efficient CADe systems for pulmonary nodule detection. Although pulmonary nodules are roughly categorized into three wide categories viz. solitary pulmonary nodules (SPNs), juxta-vascular nodules (JVN) and juxta-pleural nodules (JPN) based on their spatial locations [1], however large variations in their shapes, scales and densities make it difficult to generalize the nodules into specific groups which in turn increases the difficulties of lung nodule detection [12]. Among the nodules, detection of SPNs is observed to be somewhat easy, while that of other types of nodules demand extra effort due to their complex surroundings. Two different approaches namely feature engineering-based approach and deep learning-based approaches are found to be mostly adopted for the purpose locations [1].

B. Golosio et al. reported a multistage CADe system in 2007 which was found effective for detection of various nodules including juxta-pleural and juxta-vascular nodules [13]. A multi-threshold surface-triangulation approach was adopted in their system for identification of regions of interest (ROIs). They computed five parameters viz. moments of inertia, density, surface area, volume and roundness as functions for thresholding for each ROI using an artificial neural network (ANN) based classifier system. For nodules with diameter ≥3 mm, the system delivered 84% and 71% sensitivity at false positive/scan values of 10 and 4 respectively. Sensitivity increased for nodules with diameter ≥4 mm.

W.-J. Choi et al. developed a CADe system which was evaluated using 58 CT scans from LIDC with nodule range from 3-30 mm [14]. Their system was consisted of three steps: a) splitting of CT images into three dimensional block images, b) segmentation of block images and adjustment for nodule candidates’ detection and c) classification of candidates into nodule and non-nodule candidates. They carried out entropy analysis of the block images for identification of the informative blocks. Support vector machine (SVM) classifier was used in the final step for classification of the nodule candidates. The developed CADe system was capable of delivering 95.28% sensitivity at 2.27 false positives/scan.
In their report, G. Aresta et. al. displayed their CADe system which was specially designed for detection of juxta-pleural lung nodules only [15]. Lung segmentation was done using region-growing followed by refinement with morphological operations and active contours to include juxta-pleural nodules. Enhancement of sub-solid and non-solid nodules were done with a multiscale Laplacian-of-Gaussian filter. A support vector machine (SVM) with radial basis function was trained and used to reduce the number of false positives. They achieved 57.4% sensitivity with 4 false positives/scan.

M. Javaid et al. reported a CADe method for segmentation and detection of juxtavascular and juxtpleural nodules [16]. They used intensity thresholding for lung segmentation from CT images. They achieved 91.65% sensitivity at 3.19 false positives/scan using their CADe system. Subsolid nodules were found to be less frequent than the solid nodules, although the former show a significantly higher malignancy rate (Silva, Milanese, Seletti, Ariani & Sverzellati, 2018). C. Jacob et al. developed a CADe system for auto-detection of subsolid lung nodules in the year 2014 which was trained, optimized and evaluated using 318 scans collected from two different sites under NELSON trial [17]. In their work, they introduced a novel set of context features along with previously used features viz. intensity, shape and texture features and made special remark that the introduction of the new set features significantly improves the classification performance. Their CADe system reached a sensitivity of 80% for subsolid nodules with diameter varied between 5-34 mm at an average of 1.0 false positive/scan. In recent years, deep learning technique has become very popular as it enjoys certain distinct advantages over traditional method [18]. It provides an alternative way to bypass the troublesome manual feature extraction and thus minimizes both time and effort requirement [13]. In their report, A. A. A. Setio et al. described development of a CADe system in which multi-view convolutional network (ConvNets) was used for false reduction of the CADe system [19]. They trained their CADe system using LIDC-IDRI (Lung Image Database Consortium and Image Database Resource Initiative) data set, while they validate it using both LIDC-IDRI and ANODE09 datasets independently and showed that their proposed multi-view ConvNets is very effective for false positive reduction. Similar to A. A. A. Setio et al., Q. Dou et al. too emphasized on false positive reduction and proposed a CADe system for automated detection of pulmonary nodules from volumetric CT scans [20]. They used 3D convolutional neural networks (CNNs) for false positive reduction. Their proposed scheme was validated in the LUNA 16 challenge [7], where they achieved best competition performance matric (CPM) score for false reduction which showcased the efficiency of their developed methodology.

In India too, a few research groups have been involved in this field of interesting research. G. S. Nair et al. worked on development of segmentation system for lung nodule detection [21]. In their system, the lung lobes and nodules in CT images were segmented using adaptive fissure sweep and adaptive thresholding. In their report, S. Sivkumar et al. demonstrated a CADe system in which nodule segmentation was performed using fuzzy based clustering models while classification of nodule were done using Support Vector Machine (SVM) technique [22]. S. Aswin et al. developed a two stage CADe system in which first stage involved pre-processing while the second step involved ANN architecture [23].

3. Methodology
The steps adopted for successful development of our CADe system has been summarized Figure 1. MATLAB and Weka software were used to carry out the study. Brief description of our approach has been presented here.

![Figure 1. Flowchart of the adopted methodology.](image-url)
3.1. Data acquisition:
16 lung CT-images were used in our work, 15 of which were collected from LIDC (Lung Image Database Consortium) open source database while one from open web source which was retrieved on 12th June, 2020 using the link https://www.nytimes.com/2007/03/07/health/07lung.html. All the images were in DICOM (Digital Imaging and Communications in Medicine) format.

3.2. Pre-processing:
Collected images were pre-processed using Otsu's global image threshold method (graythreshold) and morphological open operation to improve the quality and interpretability of the input images for better results in pulmonary nodule detection. Otsu’s thresholding method was used to achieve spontaneous image thresholding as it can simply separate the image pixels into two main classes (background and foreground) by the help of single intensity threshold. This stage is crucial because lots of fats, vessels and tissues might present in lung parenchyma causing confusion in detecting nodules.

3.3. Lung image segmentation:
Lung parenchyma was extracted from the pre-processed lung images by using morphological operations such as erosion and dilation operators and then digital logical gate operations techniques. Digital gate operations are novel techniques to extract the parenchyma from lung CT images with high accuracy.

3.4. Nodule detection:
As lots of residual parts are generally present around the tumor region and some tumours are not homogenous (there may be some fats, non-solid substances, vessels present in the tumor mass) also, morphological procedure was therefore used on these binary images to refine the margin and content of the tumor images. In this step, the lung CT images were converted into RGB plan during the process of which the region of interests (ROIs), i.e. the nodule parts became red in colour as depicted in Fig. 2. This happens as the nodules’ texture and intensities are different from other parts of lungs. In this way, the pulmonary nodules were extracted from the lung parenchyma by removing other lung tissues.

We created a MLP (multilayer perceptron) network using an MLP algorithm with one input layer, one hidden layers and one output layer with learning rate 0.3 and 10- fold cross validation with 66% for training and 34% for testing and validation purpose using WEKA.

WEKA (Waikato Environment for Knowledge Analysis) is a machine learning software based on Java. It was developed at the University of Waikato, New Zealand [24]. It contains a group of algorithms for data analysis and predictive modeling and visualization tools, organized with GUI (graphical user interfaces) for easy access to this functionality.

In MLP, cross-validation was done to evaluate the predictive model by splitting the experimental samples into a training set to train the model, and a test set to evaluate it. MLP is a class of feedforward ANN (Artificial Neural Network) which utilizes a supervised learning method called backpropagation for training. Every nodes in MLP is a neuron except the input nodes and each node uses a nonlinear activation function. The main differences between linear perceptron and MLP are: multiple layers and non-linear activation of MLP. It can differentiate data that is not linearly distinguishable.

4. Result and discussion
All the downloaded images were processed as described in methodology section, the result for one image has been depicted in Figure 2. The lung nodule was segmented properly from lung CT image and its properties were found out using MATLAB.
The region property features were extracted from the ROIs (region of interest) of all the CT images. We extracted seven numbers of features namely area, major-axis, minor-axis, eccentricity, solidity, entropy and perimeter for each CT images and the results are summarized in Table 1. The features under study have been defined briefly.

**Area:** It is a scalar quantity and refers the total no. of pixels which are present in the ROIs.

**MajorAxis Length:** It is a scalar quantity specifying the length of the major axis of the ROIs.

**MinorAxis Length:** It is a scalar quantity that identifies the length of the minor axis of the ROIs.

**Eccentricity:** It is a real number with non-negative value that can uniquely characterizes the shapes of a ROI. The eccentricity of a circle, ellipse, parabola, and hyperbola are 0, 0 to <1), 1 and >1 respectively.

**Solidity:** It is a dimensionless value and it measures the complete concavity of a nodule with the value ranges between 0-1. 1 represents very smooth nodule shape, 0 represents an irregular shape.

**Perimeter:** This scalar quantity measures the total distance around the boundary of the ROIs. It actually calculates the distance between each neighbouring pair of pixels nearby the border of the region.

**Entropy:** The average information or the entropy of an image is a statistical measurement which indicates the degree of randomness in the image. It is used to characterize the texture of the ROIs.

\[
\text{Entropy} = \sum \left( p \cdot \log_2(p) \right)
\]

In the entropy equation \( p \) indicates the normalized histogram counts.

**Figure 2.** Processed lung CT image.
The developed multilayer neural network for our CADe system has been depicted in Figure 3. Seven features viz. area, major-axis, minor-axis, eccentricity, solidity, entropy and perimeter were fed in the input layer to identify the benign and malignant nodules in the output layer.

![Figure 3. Multilayer neural network developed for the CADe system.](image)

Snapshot of the results of MNP has been depicted in Figure 4. The correctly and incorrectly classified instances display the percentage of test instances that were classified correctly and incorrectly. The total instances can be seen in the confusion matrix representing two class labels: malignant and benign. The percentage of correctly classified instances is called accuracy, thus the accuracy of our system is found to be 81.25%. A positive kappa statistic value (0.5385) was obtained which indicates that the classifier is working satisfactorily.

### Table 1. Quantitative CT features of the lung nodule under the study.

| Image no. | Area (mm$^2$) | Major axis length (mm) | Minor axis length (mm) | Eccentricity | Solidity | Perimeter (mm) | Entropy | Nodule (Yes/No) |
|-----------|---------------|------------------------|------------------------|--------------|----------|----------------|---------|----------------|
| 01        | 1338          | 58.85                  | 30.49                  | 0.85         | 0.87     | 167.96         | 0.05    | yes            |
| 02        | 8             | 3.65                   | 3.05                   | 0.54         | 1        | 7.22           | 0.0005  | yes            |
| 03        | 16            | 5.03                   | 4.16                   | 0.56         | 1        | 11.65          | 0.0009  | Yes            |
| 04        | 8             | 3.65                   | 3.05                   | 0.54         | 1        | 7.22           | 0.0005  | yes            |
| 05        | 8             | 3.65                   | 3.05                   | 0.54         | 1        | 7.22           | 0.0005  | yes            |
| 06        | 5             | 2.78                   | 2.78                   | 0            | 1        | 5.62           | 0.0003  | yes            |
| 07        | 11            | 5.10                   | 3.07                   | 0.79         | 1        | 10.03          | 0.0006  | yes            |
| 08        | 5             | 2.78                   | 2.78                   | 0            | 1        | 5.62           | 0.0003  | yes            |
| 09        | 474           | 38.19                  | 24.50                  | 0.76         | 0.52     | 159.22         | 0.0191  | no             |
| 10        | 291           | 46.35                  | 20.24                  | 0.89         | 0.44     | 127.42         | 0.0125  | no             |
| 11        | 5             | 2.78                   | 2.78                   | 0            | 1        | 5.62           | 0.0003  | yes            |
| 12        | 65            | 9.63                   | 8.82                   | 0.42         | 0.97     | 25.95          | 0.0033  | No             |
| 13        | 65            | 26.87                  | 3.56                   | 0.99         | 0.80     | 49.97          | 0.0033  | no             |
| 14        | 85            | 26.79                  | 4.26                   | 0.98         | 0.88     | 51.93          | 0.0042  | no             |
| 15        | 49            | 16.06                  | 4.16                   | 0.96         | 0.85     | 31.09          | 0.0026  | no             |
| 16        | 5             | 2.78                   | 2.78                   | 0            | 1        | 5.62           | 0.0003  | yes            |

The developed multilayer neural network for our CADe system has been depicted in Figure 3. Seven features viz. area, major-axis, minor-axis, eccentricity, solidity, entropy and perimeter were fed in the input layer to identify the benign and malignant nodules in the output layer.
5. Conclusion

In conclusion, we have developed a CADe for detection of lung nodules of size > 2 mm. Lung nodules of solid, juxtapleural and juxtavascular type could be detected successfully from 16 number of lung CT images collected from LIDC and open web source with an accuracy of 81.25%. While MATLAB was used to carry out pre-processing, segmentation and nodule detection, testing of datasets was done by a MLP network using WEKA software. The suitability of the classifier was indicated by the resulting positive kappa statistic value (0.5385).

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References

[1] Zhang J, Xia Y, Cui H and Zhang Y 2018 *Biomed. Signal. Process. Control* **43** 138.
[2] Garfinkel L and Silverberg E 1991 *CA Cancer J. Clin.* **41** 137.
[3] Valente I R S, Cortez P C, Neto E C, Soares J M, de Albuquerque V H C and Tavares J M R S 2016 *Comput. Methods Programs Biomed.* **124** 91.
[4] Baldwin D R 2015 *Lung Cancer* **89**(1) 1.
[5] Camarlinghi N 2013 *Eur. Phys. J. Plus* **128** 110.
[6] Aberle D R, Adams A M, Berg C D, Black W C, Clapp J D, Fagerstrom R M, Gareen I F, Gatsonis C, Marcus P M and Sicks J D 2011 *N. Engl. J. Med.* **365**(5) 395.
[7] Setio A A A, Traverso A, de Bel T, Berens M S N, van den Bogaard C, Cerello P, Chen H, Dou Q, Fantacci M E, Geurts B, van den Guetten R, Heng P A, Jansen B, de Kaste M M J, Kotov V, Yu-Hung Lin J, Manders J T M C, Sőhöra-Mengana A, García-Naranjo J C, Papavasileiou E, Prokop M, Saletta M, Schaefer-Prokop C M, Scholten E T, Scholten L,
Snoeren M M, Torres E L, Vandemeulebroucke J, Walasek N, Zuidhof G C A, van Ginneken B and Jacobs C 2017 *Med. Image Anal.* **42** 1.

[8] Bagcchi S 2016 *BMJ* **355** i5574.

[9] van Klaveren R J, Oudkerk M, Prokop M, Scholten E T, Nackaerts K, Vernhout R, van Iersel C A, van den Bergh K A M, van’t Westeinde S, van der Aslst C, Thunnissen E, Xu D M, Wang Y, Xhao Y, Gietema H A, de Hoop B-J, Groen H J M, de Bock G H, van Ooijen P, Weenink C, Verschakelen J, Lammers J-W J, Timens W, Willebrand D, Vink A, Mali W and de Koning H J 2009 *N. Eng. J. Med.* **361**(23) 2221.

[10] Sverzellati N, Silva M, Calareso G, Galeone C, Marchiano A, Sestini S, Sozzi G and Pastorino U 2016 *Eur. Radiol.* **26**(11) 3821.

[11] Silva M, Milanese G, Seletti V, Ariani A and Sverzellati, N. 2018 *Br. J. Radiol.* **91**, 1083.

[12] Jiang H, Ma H, Qian W, Gao M and Li Y 2018 *IEEE J. Biomed. Health. Inf.* **22**(4) 1227.

[13] Golosio B, Masala G L, Piccioli A, Oliva P and Carpinelli M 2009 *Med. Phys.* **36**(8) 3607.

[14] Choi W-J and Choi T-S 2013 *Entropy* **15** 507.

[15] Aresta G, Cunha A and Campilho A 2017 *SPIE Med. Imag.* 101343N.

[16] Javaid M, Javid M, Rehman M Z U and Shah S I A 2016 *Comput. Methods Programs Biomed.* **135** 125.

[17] Jacobs C, van Rkxoort E M, Twellmann T, Scholten E T, de Jong P A, Kuhnigk J-M, Pudkerk M, de Koning H J, Prokop M, Schaefer-Prokop C and van Ginneken B 2014 *Med. Image Anal.* **18** 3745.

[18] Litjens G, Kooi T, Bejnordi B E, Aaa S, Ciompi F, Ghafoorian M, Jawm V D L, Van G B, and Sanchez C I 2017 *Med. Image Anal.* **42**(9) 60.

[19] Setio A A A, Ciompi F, Litjens G, Gerke P, Jacobs C, van Riel S J, Wille M M W, Naqibullah M, Sanchez C I and van Ginneken B 2016 *IEEE Trans. Med. Imag.* **35**(5) 1160.

[20] Dou Q, Chen H, Yu L, Qin J and Heng P A 2017 *IEEE Trans. Med. Imag.* **64**(7) 1558.

[21] Nair G S and Ajij S D 2012 *Int. J. Comp. Appl.* **54** 13.