Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2017, 6(8): 111-118

Nodular-Deep: Classification of Pulmonary Nodules using Deep Neural Network

Qaisar Abbas*

College of Computer and Information Sciences, Al-Imam Mohammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia

**Corresponding e-mail: qaisarabbasphd@gmail.com*

ABSTRACT

Pulmonary nodules represent higher malignancy rate and an accurate detection is very crucial when clinically diagnosis by radiologists from high-resolution computed tomography (HRCT) images. At an early stage, if lung cancer is not diagnosis then it leads toward death. In the past studies, it noticed that many computer-aided diagnostic (CADe) system for classification of lung nodules are developed but tested on the limited dataset and focused on domain expert knowledge. Therefore, those CADx systems were not suitable for large-scale environments. To address these issues, an efficient and effective CADe system is developed to classify the pulmonary lung nodules into benign and malignant classes. In this paper, a new CADe system is implemented through the integration of variants of advanced deep learning algorithms known as Nodular-Deep. Convolutional neural network (CNN) and recurrent neural network (RNN) algorithms are combined with softmax linear classifier without using hand-crafted features and any pre- or post-processing steps. The Nodular-Deep system is tested on the 1200 scans obtained from LIDC-IDRI database covers a set of 2600 pulmonary nodules. This dataset contains an equal number of benign (non-cancerous) and malignant (cancerous) nodules. The performance of nodular-deep system is evaluated through 10-fold cross validation test through the statistical metrics such as sensitivity (SE), Specificity (SP) and area under the receiver operating curve (AUC). On this 2600 pulmonary nodules, the Nodular-Deep system is achieved on average result such as 94% of SE, 96% of SP and 0.95 of AUC. This obtained results demonstrate that this nodular-Deep system outperforms compared to manual segmentation by a radiologist.

Keywords: Lung nodule, Pulmonary nodules, Computer-aided diagnostics, Deep learning, Convolutional neural network, Recurrent neural network, Hand-crafted features

INTRODUCTION

Lung cancer is the most common form of deaths among patients [1] if it is not detected at early stages. Over the past few decades, the early detection of lung cancer remains the challenging task and accounts of 27% deaths. It is also common in the USA. In the past studies, the high-resolution computed tomography (HRCT) is considered to be the most cost-effective and accurate imaging modality [2] available for early detection of pulmonary nodules. In fact, the recognition of malignant and benign pulmonary nodules is a vital task for further diagnosis plan of lung cancer. There are many automatic computer aided diagnostic (CADe) systems developed to assist radiologists for identification of lung nodules from HRCT scan images. In general, the primary aim of CADe system is to identify and classify pulmonary nodules into two categories such as malignant (cancerous) and benign (non-cancerous).

The detection and classification of lung nodules for the clinical experts is a tedious and difficult task, leading to a high false-negative rate and low sensitivity. Since the interpretation of radiologists of CT scan images is very clear but the assessment of the likelihood of malignancy of nodules is difficult and only 50% of nodules resected [3] at surgery are benign. According, the radiologists need some automatic CADe methods to improve this accuracy. To differentiate between benign and malignant lung nodules, there are many CADe [4-9] systems developed. There were two different main categories of CADe systems such as hand-crafted features and deep-learning [10-18] based methods.

The CADe systems [4-9] were predicted lung nodules based on the hand-crafted features set that derived from CT scan images. In practice, those CADe systems first extracted the features and then used an automatic classifier to recognize nodules based on the hand-crafted features. All those CADe systems used different image processing techniques to extract the hand-crafted features and those features were classified through machine learning classifiers. According to literature, those studies utilized LIDC-IDRI dataset to evaluate their performance. Those CADe systems are briefly explained in the subsequent paragraphs.

In Ashish Kumar et al. study [4], the support vector machine (SVM) algorithm was used to differentiate between benign and malignant lung nodules through a semi-automated technique. In that paper, the authors used many shape-based, margin-based and texture-based hand-crafted features to characterize the pulmonary nodules from HRCT scan images. The 891 nodules were tested from LIDC-IDRI and private data sources. The performance is compared to an area under the receiver operating characteristic curve (AUC) and indicated AUC of 0.95. A hybrid feature set technique is implemented in Ahmet et al. study [5] to early detection of pulmonary nodules. A classification accuracy was obtained 90.7%. Whereas in Jacobs et al. study [6], the authors extracted 128 hand-crafted features to describe the nodules through developing optimization and training steps. The authors reported sensitivity (SE) of 80%. Moreover, in Ciompi et al. study [7], the authors used nodule morphology and pattern recognition techniques to encode hand-crafted features. The authors used bag-of-frequencies to describe the lung nodules.

The different statistical parameters like mean, standard deviation, skewness, kurtosis, fifth central moment and sixth central moment [8] were utilized to recognize pulmonary nodules from HRCT scan images. On this hand-crafted feature set, the authors used neural network (NN) model to do classification. They achieved 93.3% classification accuracy. In Zhang et al. study [9], the authors combined the lung nodule and surrounding anatomical structures to detect four different types of lung nodules such as well-circumscribed, vascularized, juxta-pleural, and pleural-tail.

Instead of using old these image processing techniques to define hand-crafted features for lung nodules, there are also latest deep-learning-based CADx systems. Those systems are not performing any pre- and or post- processing steps to extract and select the most discriminative features for classification tasks. In this paper, the advance deep-learning algorithms are utilized to classify benign and malignant lung nodules from CT scan images. This proposed system is known as the nodular-deep and the description can be found in the methodology section. However, the background about the state-of-the-art deep CADx systems was presented in the subsequent section.

Background

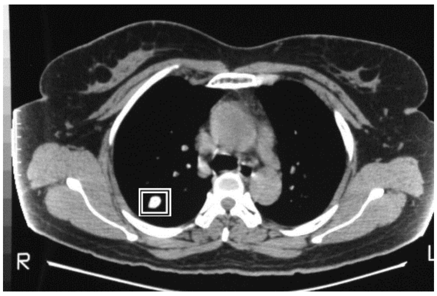
Computer-aided diagnostics (CADx) [10-18] systems are developed to detect and classify benign and malignant lung nodules from CT scan using advanced deep learning algorithms. However, the detection of pulmonary small nodules from volumetric CT scans is also a difficult task, and therefore lots of CADx tools are developed to compensate this problem. Those CADx systems are explained below.

In Cheng et al. study [10], the authors suggested that the tuning of previous CAD systems is very complicated and time-consuming task. Therefore, in that study, they used two models of deep learning algorithm such as a deep belief network (DBN) and a convolutional neural network (CNN) to recognize the lung nodules. They utilized two deep learning architectures for classification of the malignant or benign nature of lung nodules without computing handcrafted features whereas in Shen et al. study [11], the authors developed a computer-aided diagnosis (CADx) system by using the deep-learning algorithm to avoid potential errors caused by hand-crafted features and segmentation tasks. In that paper, the authors used stacked-based auto-encoder (SDAE) to differentiate lung nodules. They selected 700 malignant and 700 benign nodules to test the performance of SDAE algorithm and the authors reported significant results were obtained.

In Setio et al. study [12], lung nodules are classified through the development of Multi-Scale Convolutional Neural Networks (MCNN) approach. To capture nodule, the authors extracted discriminative features by using MCNN deep-learning classifier. They tested MCNN system on CT images from Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI). The authors achieved effective results by MCNN approach to recognizing malignant and benign lung nodules from CT scan images without nodule segmentation approach. A convolutional neural network (ConvNets) is used in Sun et al. study [13] to detect and classify pulmonary nodules without using hand-crafted features. On 888 scans of LIDC-IDRI dataset, the authors achieved the sensitivities of 85.4% and 90.1% at 1 and 4 false positives per scan, respectively. Jia et al. [14] implemented three deep learning algorithms such as convolutional neural network (CNN), deep belief networks (DBNs) and stacked autoencoder (SDAE) to recognize lung nodules on 174412 samples. The authors obtained the accuracies of CNN, DBNs, and SDAE is 0.7976, 0.8119, and 0.7929, respectively. To diagnose lung cancer, Nibali et al. [15] classified benign and malignant lung nodules through sparse autoencoder deep-learning technique. In that paper, the authors used sparse autoencoder to extract the features from each region-of-interests (ROIs) to identify it for best suitable for classification.

In Li et al. study [16], the lung nodules are classified into benign and malignant categories by developing deep residuals network. The authors also compared the developed system with other two state-of-the-art deep learning systems on LIDC-IDRI dataset and achieved higher performance value of sensitivity, specificity, precision, AUROC, and accuracy. Similarly, in Liu et al. study [17], a deep convolutional neural networks (CNN) method was designed for the classification of nodules. Experimental results demonstrate the effectiveness of the proposed method in terms of sensitivity and overall accuracy and that it consistently outperforms the competing methods. To detect and classify lung nodules, Kalchbrenner et al. [18] utilized multi-view convolutional neural networks (MV-CNN. Unlike the traditional CNNs, an MV-CNN takes multiple views of each entered nodule. Afterward, the authors did a differentiation between benign and malignant lung nodules on an LIDC-IDRI database. They achieved an error rate of 5.41% and 13.91% for binary and ternary classifications of lung nodules.

In this paper, automatic features are learned through deep learning algorithm to test the classification of lung nodules on CT scan images. To develop deep learning algorithm, the region-of-interests (ROIs) were obtained from LIDC-IDRI dataset through an expert radiologist. In the domain of deep learning algorithms, there is the convolutional neural network (CNN), deep belief networks (DBNs), stacked denoising autoencoder (SDAE), recurrent neural network (RNN) and Restricted Boltzmann Machine (RBM). According to limited knowledge, the integration of CNN [19,20] and RNN [21,22] deep learning algorithms are considered in the past techniques to classify benign and malignant lung nodules. Therefore, the integration feasibility of CNN and RNN is considered in this paper to classify pulmonary nodules.



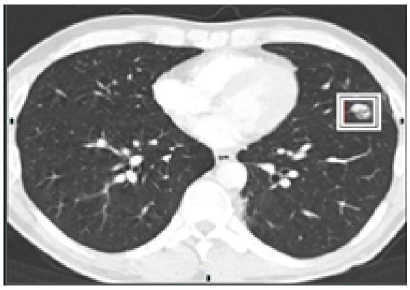


Figure 1 (a) **Figure 1 (b)**

Figure 1 An example of lung nodules region-of-interest (ROI) taken from LIDC-IDRI database where figures (a) represent benign and (b) shows malignant lung nodules

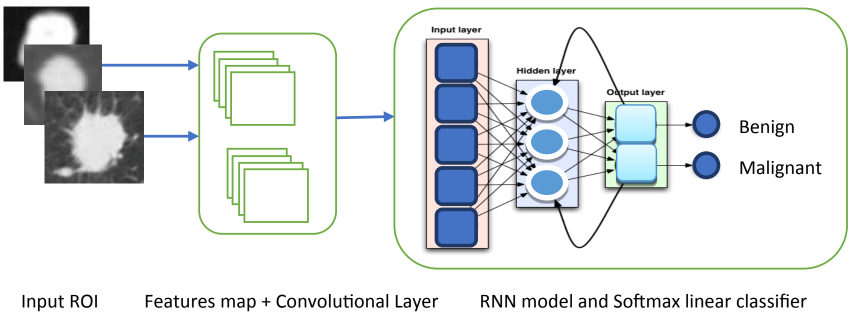


Figure 2 A systematic flow diagram of proposed Nodular-Deep system to recognize benign and malignant lung nodules from HRCT scan images

METHODOLOGY

Nodular-Deep system is used to do classification of lung nodules. The systematic flow diagram of Nodular-Deep system is presented in Figure 2. The proposed system contains three main steps such as features extraction using CNN and then select most discriminate features through RNN on the manual segmented ROI image of lung nodules. Afterward, the softmax linear classifier is used to recognize benign and malignant lung nodules.

Acquisition of dataset

To evaluate the performance of proposed nodular-deep system, the dataset was acquired as a free resource from Lung Image Database Consortium and Image Database Resource Initiative (LIDC/IDRI) that consisted of CT scans of annotated lesions. This database is publicly available and used in many studies. An experienced radiologist was requested to label the lung nodules into two categories such as benign and malignant nodules. The Figure 1 represents an example of benign and malignant lung nodules in HRCT scan images obtained from LIDC-IDRI dataset and its boundaries marked by an experienced radiologist. From the LIDC-IDRI dataset, the 1200 slices were selected that contained 2600 equal number of benign and malignant lung nodules in this paper.

Extraction of deep features

Features extraction is very important and crucial step for automatic classification of benign and malignant lung nodules when diagnosis through HRCT scan images. In the previous studies, there are some studies that utilized the deep learning algorithms [10-18] to select features from region-of-interest (ROI) of lung nodules without using hand-crafted features. Therefore, in this paper, a convolutional neural network (CNN) [19,20] is a type of classifier is selected to automatically extract features from images without focused on hand-crafted features. In the past studies, the CNN architecture has been utilized for features selected in many different computer vision tasks. However, the CNN model facing the challenges of features optimization and texture recognition. To solve these problems, the recurrent neural network (RNN) with softmax linear classifier are integrated to select an optimal set of features and recognition tasks, respectively.

In general, the CNN model is a top variant of deep-learning algorithms to automatic isolate the edges and distinguish them from appearance edges. It has many applications in practice such as it is also used in real-time robotics applications to segment the different objects from the scene. Similarly, the CNN model is also utilized in many computer vision applications to perform automatic scene recognition. Inspire by the past studies, the CNN model is used to effectively and efficiently segment the features from each ROI lung nodule images. However, the CNN used in this study in the form of an unsupervised classifier.

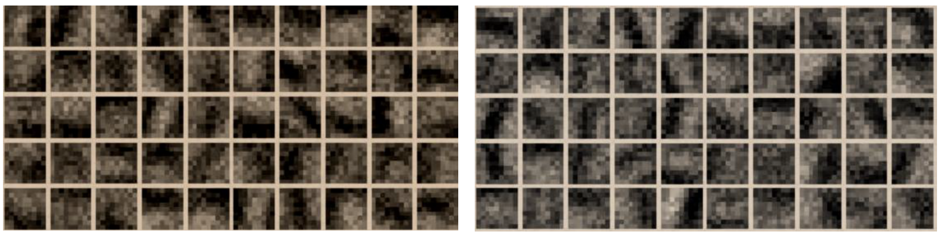


Figure 3 (a) Figure 3 (b)

Figure 3 Sample feature maps extracted by a first layer of convolution neural network (CNN) model of five different lung nodules where figures (a) represents malignant and (b) shows the benign lung nodules

The convolutional layers (CC-layer) contains neurons connected to previous layer and extracted a small region from images such as 5 × 5 or 8 × 8 pixels. The mathematical description of 2D CC-layer is defined in Equation 1. From Equation 1, the discrete convolution of the input ($I_p^{(l-1)}$) with a filter (f^l) and adding the bias (b^l), followed by the non-linear function (α) as:

$$O_{mn}^{l} = \alpha(\Sigma_{i=1}^{m}\Sigma_{j=1}^{n} I_p^{l-1}(m+i-1)(n+j-1)(f_m n^l + b^l) \qquad (1)$$

Where, O_{mn}^{l} is the output unit at row (m) and column (n) from the 2-D image. The equation (1) is clearly indicated that the convolutional layer is used to apply the filters for all inputs taken from 2-D image. The CNN variant of deep-learning algorithm contains small neurons to best describe the features. These small neurons have the capability to process the input image and provide an output in the form of overlapping of the input regions that provided a vibrant demonstration of the original image. This process is repeated for all multi-layers of CNN model. There are many advantages of using the CNN model deep-learning algorithm for features extraction from lung nodules ROI images. Firstly, the use of shared weights in convolutional layers paves the way to use the same filter for each pixel in the layer. Afterward, the CNNs use relatively little pre-processing which means that the CNN network is responsible for learning the filters where the traditional algorithms are hand-engineered. For an example, the Figure 3 represents the feature maps extracted by the first layer of convolution neural network (CNN) model of five different lung nodules from HRCT scan images.

Optimization of features

The deep features are correctly extracted from the previous section through a convolutional neural network (CNN) deep-learning model. Since, these deep features are not optimized so the recurrent neural network (RNN) [21,22] model is integrated into this study to effectively optimized features that are the best candidate of classification phase. In this paper, the RNN model is as supervised manner. In the past studies, the RNN model is applied in many different fields such as biomedical image processing, computer vision and motion capture. In practice, the RNN have the capability to process real features in one step time and predict the features based on the training dataset. In fact, the RNN model uses fuzzy rules to generate new features based on hidden units so it is the best model for optimization tasks because it has not the capability to store past inputs for a very long time. Therefore, to select the optimized features that are generated by CNN model, the RNN model is used as a pre-trained machine learning algorithm.

The RNN model is very powerful for optimization task due to the training method that formulates the learning process of RNN model in the form of cross-entropy. The experimental results indicate that the RNN model has a fixed value to guarantee the superior performance in case of features optimization tasks. As a result, the 2-layers based RNN model is used to optimize the features that were generated by the convolutional layer. The visual representation of this step is shown in Figure 2. The final classification decision is performed by softmax linear classifier.

Classification of features

The optimize features generated by RNN model is finally classified using supervised softmax linear classifier. The softmax linear classifier is used in this paper to differentiate between two class problems such as benign and malignant lung nodules. The softmax classifier works just to predict the label of the input based on the maximum score of the class. It is a basically generalized form of binary logistic regression expression to map function f. In fact, the softmax linear classifier takes an input set of data (dx) and maps to output label (Y) via a simple linear dot operation and it is defined mathematically as:

$$Predict(Y = c \mid z_i) = softmax(z_i) = \Sigma_{i=0}^{m} w_i . dx_i \tag{2}$$

Where, w is the weight vector, dx is the feature vector of the training sample, and w is the bias unit. Based on the above formula, the softmax linear classifier computes the probability that this training sample dx belongs to class (c) given the weight (w) for each class label.

Experimental results

The Nodular-Deep system for differentiation between benign and malignant nodules is implemented on MATLAB 2016 and Windows 10 platform. To evaluate the performance of Nodular-Deep system, the statistical measures are used based on 10-fold cross validation test. In statistical analysis, the sensitivity (SE), specificity (SP), accuracy (ACC) and area-under-receiver-operative curve (AUC) were measured. The value of AUC is varied from 0.5 to 1.0. The higher the value of AUC indicates that the algorithm is performed significantly well. The mathematical descriptions of these statistical measures are shown below and discussed in the subsequent paragraphs.

To measure the performance, the sensitivity (SE) is also known as a true positive rate (TPR). The TPR rate is provided the corrected identified lung nodules as benign and malignant. Whereas the specificity (SP) is the measure known as a true negative rate (TNR). The TNR is calculated when the lung nodules are not correctly classified as benign or malignant classes. However, the sensitivity (SE) is quantified the avoiding false negative (FN). These statistical measures can be calculated as:

Sensitivity (SE) = TP / (TP + FN) (3)

Specificity (SP) = TN / (TN + FP) (4)

Accuracy (ACC) = (TP + TN) / (TP + FP + FN + TN) (5)

Table 1 Performance results of the proposed nodular-deep system on 2600 lung nodules for classification of lung nodules

No.	Classification of benign and malignant lung nodules			
	SE [a]	SP [b]	ACC [c]	AUC [d]
Benign	93.00%	97.00%	95.00%	0.95
Malignant	94.00%	96.00%	95.00%	0.94
Total	94%	96%	95%	0.95
[a] Sensitivity, [b] Specificity, [c] Accuracy and [d] Area-under receiver operating curve				

To compare the performance of Nodular-Deep with other state-of-the-art techniques such as basic models of CNN and RNN were utilized. The Table 1 shows the performance compressions results in terms of SE, SP, ACC, and AUC statistical measures. As shown in this table, the Nodular-Deep is achieved higher performance rate compared to other two systems based on individual deep learning algorithms such as CNN and RNN. On average, the nodular-deep system is obtained 94% of SE, 96% of SP, ACC of 95% and 0.95 of AUC values higher than other two systems when compared with benign and malignant lung nodules on this dataset. The AUC curve is shown in Fig.4 and the proposed Nodular-Deep system is achieved higher accuracy trend compared to two other systems.

Tables 2 and 3 are displayed the comparisons results of the convolutional neural network (CNN) and recurrent neural network (RNN) with softmax classifier, respectively. In particular, the Table 2 represents the results in case of benign (SE of 89.0%, SP of 92.0%, ACC of 90.0% and AUC of 0.90) and whereas in case of malignant (SE of 86.0%, SP of 88.0%, ACC of 87.0% and AUC of 0.88) lung nodules when utilized CNN model. Moreover, the Table 3 shows the result in case of benign (SE of 82.0%, SP of 88.0%, ACC of 85.0% and AUC of 0.85) and malignant (SE of 84.0%, SP of 88.0%, ACC of 86.0% and AUC of 0.85) lung nodules when utilized RNN model. It noticed that the RNN model is not directly applied to image pixels. The man and variance intensities values are measured from each ROI lung nodule image and submit as a feature-set to RNN model. From these two tables, the CNN model is achieved higher classification accuracy when compared with RNN model but less than the proposed nodular-deep system. Hence, the proposed nodular-deep, when combined with CNN and RNN, achieved higher classification results compared to use them on an individual basis for classification tasks.

Table 2 Comparison of deep learning algorithms based on convolutional neural network (CNN) with softmax linear classifier on 2600 lung nodules for classification of lung nodules

No.	Classification of benign and malignant lung nodules			
	SE [a]	SP [b]	ACC [c]	AUC [d]
Benign	89.00%	92.00%	90.00%	0.9
Malignant	86.00%	88.00%	87.00%	0.88
[a] Sensitivity, [b] Specificity, [c] Accuracy and [d] Area-under receiver operating curve				

This study used the advanced concepts of deep learning algorithms to automatically extract the features through the convolutional neural network on the manual segmented ROI for lung nodules. These features are then optimized using the unsupervised RNN model to select most discriminative features. Afterward, these optimize deep features are classified the lung nodules into two categories such as benign and malignant lung nodules through softmax linear classifier. Moreover, the features generated by CNN deep learning model is comparable with hand-crafted features, which made the CADe system very complicated. However, instead of using hand-crafted features, the well-tuned deep learning algorithms have better performance than traditional CADx in terms of AUC and accuracy as represented in Table 1. It was also noticed that the proposed Nodular-Deep learning algorithm is able to easily differentiate the malignant and benign lung nodules on 1300 benign and 1300 malignant lung nodules ROI images. The significance of this result is also visually represented in Figure 4 as a ROC curve. Furthermore, the differentiation between benign and malignant lung nodules is visually represented in Figure 5.

Table 3 Comparison of deep learning algorithms based on recurrent neural network (RNN) with softmax linear classifier on 2600 lung nodules for classification of lung nodules

No.	Classification of benign and malignant lung nodules			
	SE [a]	SP [b]	ACC [c]	AUC [d]
Bengin	82.00%	88.00%	85.00%	0.85
Malignant	84.00%	88.00%	86.00%	0.85
[a] Sensitivity, [b] Specificity, [c] Accuracy and [d] Area-under receiver operating curve				

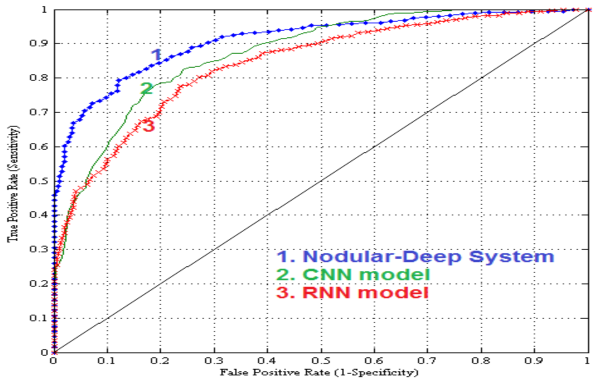


Figure 4 Comparison of ROC curve for different deep learing methods on 2600 lung nodules

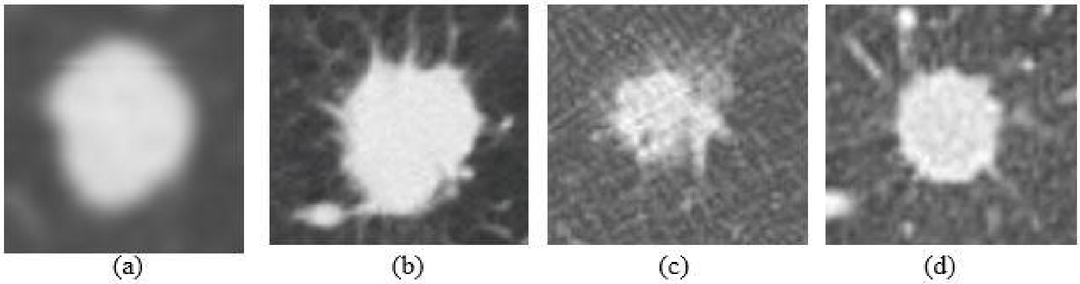


Figure 5 Results produced by Nodular-Deep system on 2600 selected ROI lung nodules where (a) represents benign and (b) (c) and (d) shows malignant lung nodules

CONCLUSION

In this paper, the convolutional neural network (CNN) and recurrent neural network (RNN) with softmax linear deep learning classifiers are integrated to design a new computer-aided diagnostic (CADe) system for recognition of pulmonary lung nodules on a high-resolution computed tomography (HRCT) images. The proposed Nodular-Deep system is tested on the 1200 scans obtained from LIDC-IDRI database covers a set of 2600 pulmonary nodules. By using 10-fold cross-validation test, the nodular-deep system is obtained 94% of SE, 96% of SP and 0.95 of AUC. This obtained results indicate that the nodular-deep system is having higher performance compare to other state-of-the-art systems for differentiation between benign and malignant lung nodules. As a result, it can be used to automatically diagnosis lung-related diseases compared to manual annotation by health-care professionals.

It demonstrated that the learned deep features were able to capture the differentiation between these two classes while maintaining the high accuracy. As a result, the Nodular-Deep system does not require any pre- and or post-processing steps to classify lung nodules because of using deep learning architectures. In the future work, the training of deep-learning system may be improved by the addition of hand-crafted features with deep features to enhance the precision performance of lung cancer patients.

ACKNOWLEDGEMENT

The author would like to thank radiologists to manually annotate the region-of-interest (ROI) from each CT scan images of lung nodules.

REFERENCES

[1] Mitrou, Sotirios, et al. “Lung cancer during pregnancy: A narrative review.” *Journal of advanced research* 7.4 (2016): 571-574.

[2] Abbas, Qaisar. “Segmentation of differential structures on computed tomography images for diagnosis lung-related diseases.” *Biomedical Signal Processing and Control* 33 (2017): 325-334.

[3] Prakashini, K., et al. “Role of Computer Aided Diagnosis (CAD) in the detection of pulmonary nodules on 64 row multi detector computed tomography.” *Lung India: Official organ of Indian Chest Society* 33.4 (2016): 391-397.

[4] Dhara, Ashis Kumar, et al. "A combination of shape and texture features for classification of pulmonary nodules in lung CT images." *Journal of Digital Imaging* 29.4 (2016): 466-475.

[5] Tartar, Ahmet, Niyazi Kilic, and Aydin Akan. "Classification of pulmonary nodules by using hybrid features." *Computational and Mathematical Methods in Medicine* 2013 (2013).

[6] Jacobs, Colin, et al. "Automatic detection of subsolid pulmonary nodules in thoracic computed tomography images." *Medical Image Analysis* 18.2 (2014): 374-384.

[7] Ciompi, Francesco, et al. "Bag-of-frequencies: A descriptor of pulmonary nodules in computed tomography images." *IEEE Transactions on Medical Imaging* 34.4 (2015): 962-973.

[8] Hua, Kai-Lung, et al. "Computer-aided classification of lung nodules on computed tomography images via deep learning technique." *Onco-Targets and therapy* 8 (2015): 2015-2022.

[9] Zhang, Fan, et al. "Lung nodule classification with multilevel patch-based context analysis." *IEEE Transactions on Biomedical Engineering* 61.4 (2014): 1155-1166.

[10] Cheng, Jie-Zhi, et al. "Computer-aided diagnosis with deep learning architecture: Applications to breast lesions in US images and pulmonary nodules in CT scans." *Scientific Reports* 6 (2016): 24454.

[11] Shen W., Zhou M., Yang F., Yang C., Tian J. Multi-scale Convolutional Neural Networks for Lung Nodule Classification. In: Ourselin S., Alexander D., Westin CF., Cardoso M. (eds) Information Processing in Medical Imaging. IPMI 2015. Lecture Notes in Computer Science, vol 9123. Springer, Cham.

[12] Setio, Arnaud Arindra Adiyoso, et al. "Pulmonary nodule detection in CT images: false positive reduction using multi-view convolutional networks." *IEEE Transactions on Medical Imaging* 35.5 (2016): 1160-1169.

[13] Sun, Wenqing, Bin Zheng, and Wei Qian. "Computer aided lung cancer diagnosis with deep learning algorithms." *SPIE Medical Imaging*. Vol. 9785. *International Society for Optics and Photonics*, 2016.

[14] Jia, T., H. Zhang, and Y. K. Bai. "Benign and malignant lung nodule classification based on deep learning feature." *Journal of Medical Imaging and Health Informatics* 5.8 (2015): 1936-1940.

[15] Nibali, Aiden, Zhen He, and Dennis Wollersheim. "Pulmonary nodule classification with deep residual networks." *International Journal of Computer Assisted Radiology and Surgery* (2017): 1-10.

[16] Li, Wei, et al. "Pulmonary nodule classification with deep convolutional neural networks on computed tomography images." *Computational and Mathematical Methods in Medicine* 2016 (2016).

[17] Liu, Kui, and Guixia Kang. "Multiview convolutional neural networks for lung nodule classification." *International Journal of Imaging Systems and Technology* 27.1 (2017): 12-22.

[18] Kalchbrenner, Nal, Edward Grefenstette, and Phil Blunsom. "A convolutional neural network for modelling sentences." *arXiv preprint arXiv:1404.2188*(2014).

[19] Kim, Yoon. "Convolutional neural networks for sentence classification." *arXiv preprint arXiv:1408.5882* (2014).

[20] Zbontar, Jure, and Yann Le-Cun. "Computing the stereo matching cost with a convolutional neural network." *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*. 2015.

[21] Zaremba, Wojciech, Ilya Sutskever, and Oriol Vinyals. "Recurrent neural network regularization." *arXiv preprint arXiv:1409.2329* (2014).

[22] Graves, Alex, Abdel-Rahman Mohamed, and Geoffrey Hinton. "Speech recognition with deep recurrent neural networks." *Acoustics, speech and signal processing (ICASSP), 2013 IEEE International Conference on*. IEEE, 2013.