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A New Method of Lung Nodule Detection in CT Scans using 3D U-Net Convolutional Neural Network

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ABSTRACT

Automatic detection of lung nodules in CT scans has attracted significant research interest in computer-aided diagnosis (CAD) system because it can help improve the early and accurate diagnosis, therefore reducing lung cancer mortality. The aim of this paper is to propose a new method of lung nodule detection in CT scans by using 3D U-Net convolutional neural networks (CNNs) which can successfully reflect the 3D characteristics of CT scans. We use 3D U-Net architecture for CNNs in order to accurately and automatically detect the lung nodules in CT scans. We employ the masked Lung Image Database Consortium (LIDC) dataset containing 400000 CT images of over 1000 patients for training the 3D U-Net model. We introduce an integrated loss function in order to detect lung nodules with different sizes and prepare 3D input data by the use of 2D CT images fixing the hyper parameters of CNNs. Our method successfully detects the lung nodules with different sizes ranging from 3mm to 30 mm exhibiting higher sensitivity of 93.2, 94.5 and 94.8% at 1.0, 2.0 and 3.0 FPs per patient, respectively than the state-of-the-art methods. The proposed method of using 3D U-Net CNNs and integrated loss function is effective for early diagnosis of lung nodules in different sizes with improved sensitivity.

Keywords - **3D U-Net CNNs, CT scans, LIDC dataset, lung nodule detection.**

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1. INTRODUCTION

Lung cancer still remains a major public health problem and is one of the commonest malignant causes of death, accounting for more than a quarter of cancer deaths. In order to minimize the lung cancer mortality, it is necessary to early diagnose and timely cure the lung nodules. According to the previous studies [1], [2], early diagnosis and treatment could significantly increase the 5-year survival rate of patients from 4~16 % to 54 %. In fact, the lung nodules have different sizes and shapes, and moreover are easily confused with other lung tissues. Therefore, it is a time-consuming and challenging task even for an experienced radiologist to manually detect small different-shaped nodules in computed tomography (CT) images. In recent years, computer aided detection (CAD) and diagnosis systems using convolution neural networks (CNNs) are widely utilized to help the radiologists in early, accurately and easily detecting the lung nodules with different shapes and sizes [3].

At early stage on CAD system, using hand-crafted features of lung nodules was a dominant method and thus many studies focused on designing the representative hand-crafted features including density, shape, and texture of lung nodule regions from the CT scans [4]-[6]. However, the wide variation of lung nodules in CT scans is a great obstacle to improvement of the performance in the conventional machine learning methods using the hand-crafted features. To overcome the drawback of the conventional methods using hand-crafted features, deep

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learning methods were employed for automatic recognition, classification and segmentation of lung nodules in CT scans, significantly outperforming the conventional methods [7]-[9].

For the last decade, two methods using CNNs are mainly applied to the lung nodule detection. One employs pre-trained model for object recognition via transfer learning and the other employs special model carefully designed and trained for lung nodule detection. In order to train the CNNs, a large amount of training data is required. Compared to the object recognition, labeled data of medical images can be obtained by the labors of professional experts. Therefore, the transfer learning method was introduced for lung nodule detection in CT scans [10]. For instance, Sun et al. [11] efficiently detected the pulmonary nodule by the use of the transfer learning method based on pre-trained AlexNet model. On the other hand, Ramachandran et al. [12] successfully applied the YOLO model-based transfer learning method to lung nodule detection, which has been widely used in object recognition. As the transfer learning methods adopt the feature extraction network retraining the classification only, the pulmonary nodule detection cannot be carried out as end-to-end framework thereby reducing its detection accuracy. In addition, many hybrid technologies of CNN, such as CNN+BilSTM [13], have been developed and applied in various fields.

In the meantime, training the special models for the purpose of detection, classification and segmentation of pulmonary nodules needs a large amount of CT images. Fortunately, the Lung Image Database Consortium (LIDC) dataset [7] contains four hundred thousand CT images of over thousand lung cancer patients which were labelled by professional radiologists. The LIDC dataset is used to benchmark the performance of state-of-the-art nodule CAD systems and to train the special models for detection, classification and segmentation of pulmonary nodules. The U-Net [14], [15] and V-Net [16] CNNs have been widely used for medical image processing such as lung nodule segmentation.

Table1. Summary of previous methods for lung nodule detection

Year	Author	2D/3D	Main Method	Sensitivity (%)	FPs/scan
2016	Golan et al. [2]	3D	3D CNN, volume features, patch size is 3×20×20	78.9 71.2	20 10
2016	Rushil et al. [16]	3D	3D CNN, 2 way softmax classifier, point labels	80	10
2016	Javaid et al. [4]	2D, 3D	Handcrafted features, SVM, K-means	91.65	3.19
2016	Setio et al. [22]	2D + 3D	multi-view CNN, false positive reduction	85.40 90.10	1.0 4.0
2017	Fu et al. [21]	2D	CNN features + handcrafted features + SVM classifier, false positive reduction	90.9	4
2017	Nibali et al. [1]	2D	ResNet	91.1	-
2017	Dou et al. [20]	3D	Multilevel Contextual 3D CNN, false positive reduction	84.80 90.70	1.0 4.0
2018	Xie et al. [27]	2D	Deep Believe Network, texture, shape and deep features	84.2	-
2018	Xie et al. [10]	2D	Improved Faster R-CNN + three slices results fusion, false positive reduction	86.42	4.67
2018	Da Silva et al. [23]	2D	CNN+ PSO, false positive reduction	92.2	
2018	Gruetzemacher et al. [19]	3D	DCNN	94.2	-
2018	Zhang et al. [25]	2D + 3D	Multi-scale LoG filters & shape/size constraints + 3D CNN	94.9	1.0
2020	Zheng et al. [24]	2D, 3D	MIP images, 2D U-Net, candidate nodule classification using 3D CNN	92.67 94.19	1.0 2.0
2022	Khan et al. [28]	2D	adaptive boosting self-normalized multiview CNN,	93	-
2023	Yang et al. [29]	2D	improved GhostNet, Yolov4-GNet network	86.69	52
2023	Wang et al. [30]	3D	PSV-AM, UPSV-Net of 9 modules, false positive reduction	97.6	12
2023	Lydia and Prakash [31]	2D, 3D	modified regularized K-means clustering, improved CNN	96.5	-
2024	Liu et al. [32]	3D	3D ARCNN framework, internally cascaded multi-level residual model	91.6 92.7 93.2 95.8	1 2 4 8

The original CNN models are based on the 2D CT images by which it is actually difficult task to discriminate between some micro-nodules and non-nodules by the 2D visual characteristics [10]. Based on the fact that a series of CT images of the pulmonary region can be obtained by CT scan, 3D CNN models using 3D CT images as input data were proposed [16]-[20]. The 3D CNN models exhibited higher accuracy than the 2D CNN models because they can effectively reflect the three-dimensional characteristics of the lung nodules.

Meanwhile, many investigations have been carried out for improving the detection performance of lung nodule. According to the previous works [21]-[23], sensitivity is defined with TP (true positive) rate and FP (false positive) per scan, so these two factors play important role for lung nodule detection. Zheng et al. [24] adopted the maximum density projection image to distinguish between isolated lung nodules and vessels in order to detect the candidate nodules using the 2D U-Net CNN. They added three-dimensional structural information to two-dimensional images by using the series of tomographic images and the maximum density projection image. To classify the candidate nodules, they then employed 3D CNN consequently reducing the FP rate of lung nodule detection. To increase the accuracy of lung nodule detection, Meanwhile, some investigations [21], [25] have used both the deep features extracted by CNN and hand-crafted features. We summarize the previous methods using CNNs for lung nodule detection in CT scans in Table 1.

It is worth noting that the U-Net CNNs employed for lung nodule segmentation [14] are considered as a powerful tool for the medical image segmentation and localization. Moreover, lung nodule detection can be essentially treated as localization, which is the first motivation for the approach of lung nodule detection proposed in this work. The second motivation is that 3D CNNs can improve the accuracy of lung nodule detection compared to the one of 2D CNNs. In the previous work [14], the authors focused on the segmentation of lung nodules training the 2D CNNs using 2D CT images. However, we construct 3D U-Net CNNs and determine the hyper parameters of network to detect the lung nodules from the series of CT images. In this paper, we propose a new method of lung nodule detection in CT scans using 3D U-Net CNN. We design 3D U-Net CNN architecture to detect the lung nodules in CT scans taking the advantages of U-Net architecture and 3D CNNs to improve the accuracy of lung nodule detection. We define a new integrated loss function to train 3D U-Net CNN using the masked training data from the LIDC dataset making it possible to detect the nodules with different sizes. By providing the 3D U-Net CNN with 3D input data, we improve the detection sensitivity of lung nodules with different sizes in LIDC dataset.

2. METHOD

2.1 U-NET CONVOLUTIONAL NEURAL NETWORK

The U-Net CNN was designed from the structure of a fully convolutional network [26], while the input size of network was fixed in general. If the trained model receives an image that is larger than the input size trained already, it usually tests the whole image with sliding window to generate a feature map.

However, this method has an expensive computational cost. To deal with this problem, fully convolutional network (FCN) structure has been proposed. The FCN converts the fully connected layers of CNNs into convolutional layers. The feature maps of whole image are obtained through FCN, even if the sizes of input data are various.

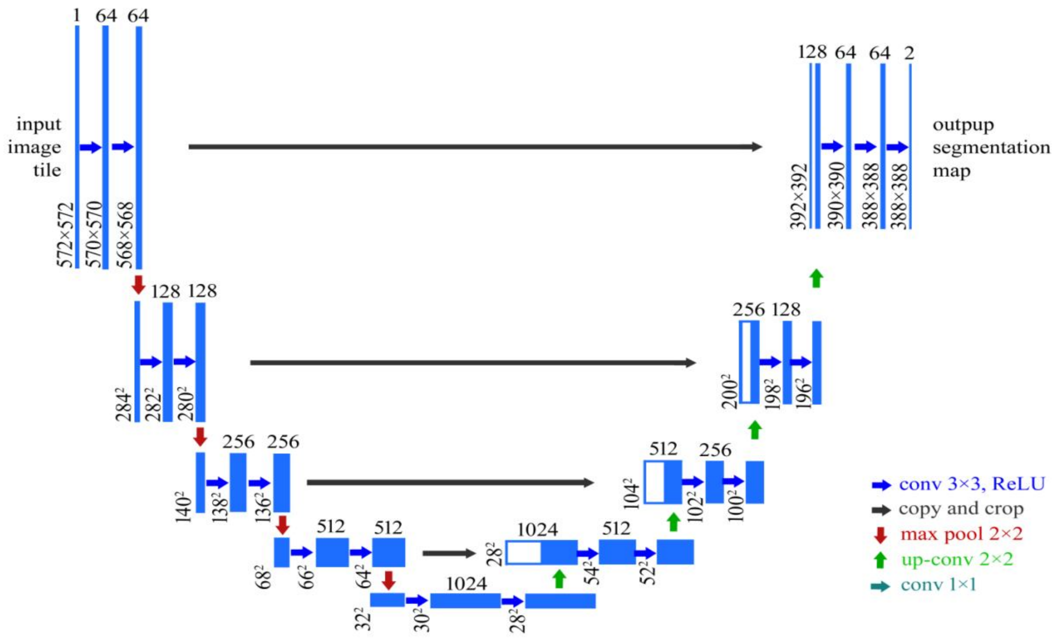

Fig. 1 2D U-Net CNN Structure

The U-Net CNNs [14], [15] are widely used in medical image segmentation producing masks of region of interests (ROIs) via the input image. The U-Net CNNs is performed in two stages. In the first stage, the feature maps are generated through convolution layers (conv) and in the second stage, the predicted masks of ROIs are produced through de-convolution layers (up-conv). Moreover, the convolution layers make down-sampling of input images (or feature maps) of each layers, since the de-convolution layers make up-sampling of input feature maps of each layers. Fig. 1 shows the structure of 2D U-Net CNN for lung nodule segmentation introduced by Tong and co-workers13. This network inputs 2D images and outputs 2D segmentation maps of lung nodules.

2.2 PROPOSED 3D U-NET CONVOLUTIONAL NEURAL NETWORK

In general, the boundary information of ROIs is lost by convolutional and max pooling operations of CNNs while it reduces the feature map size. However, the boundary information of lung nodules is important for distinguishing nodules from other tissues or organs in CT images. The U-Net CNNs consist of contraction and expansion processes. That is, in the contraction phase, the features are extracted contracting the feature map size, while in the extension phase, the number of features is halved extending the feature maps, i.e. the feature map size is twice. The U-Net CNNs concatenate output feature maps in the expansion phase with the corresponding feature map in the extension phase to supplement the lost boundary information so that this can help increase the training accuracy.

On the other hand, the U-Net structure can reduce the number of parameters and training time of network, and efficiently train with less training data compared with other networks. In addition, the U-Net has a potential of ROI segmentation and localization. Moreover, the detection of ROI can be essentially treated as the localization. In this work, we hence design the network for lung nodule detection based on U-Net structure. The U-Net CNN proposed in this work trains the model to reduce the error compared with the ground truth and predicts the nodule masks.

Our proposed 3D U-Net CNN structure is shown in Fig. 2. Input data of this network has a size of 5×512×512, i.e. 5 serial images of CT scans with 512×512 pixels of size. The reason why we set 5 images as input will be explained later. The 3D U-Net CNN has 120 layers and consists of contraction (down-sampling) and expansion (up-sampling) blocks. As shown in Fig. 3, the down-sampling block consists of two convolutional layers with 1×3×3 filter size, one convolutional layer with 3×1×1 filter size and one max-pooling layer with 1×2×2 filter size. Meanwhile, the up-sampling block consists of one de-convolutional layer with 1×2×2 filter size, one concatenation layer joining the up-sampling feature map with the corresponding down-sampling feature map, and one convolutional layer with 1×1×1 filter size (Fig. 4). In this block we use dropout with rate of 0.6. Both the down-sampling and up-sampling blocks have the batch normalization layers to reduce the over-fitting.

To detect the lung nodules with different sizes, the proposed 3D U-Net CNN outputs from each up-sampling block and integrate them at the end. Each up-sampling block produces the various scale feature maps. The proposed 3D U-Net CNN can sufficiently capture the 3D spatial information of the nodules with different sizes in CT serial images increasing the accuracy of lung nodule detection.

2.3 Calculation of the Integrated Loss Function

To deal with the gradient vanishing problem in deep CNNs, several techniques have been proposed such as batch normalization, residual module, depth-wise convolution and so on. However, they are not enough to train deep CNNs and so it is necessary to define a suitable loss function for CNN training.

In general, CNNs calculate the loss only in the output of the last fully connected layer. In contrast to the traditional loss, we calculate the loss function for the output of each up-sampling block and then integrate them as a final loss. In each up-sampling block, the loss function is defined by calculating the error between the mask of predicted nodule and the ground truth mask.

When m lung nodules were detected in the output feature map of i th up-sampling block, the loss function for the j th lung nodule is calculated as follows:

$$L_i = \frac{1}{m}\sum_{j=1}^{m} S(X_{ij}, Y_{ij}), \qquad (1)$$

where X_{ij} is the output (predicted) mask for the j th nodule detected in the i th block, Y_{ij} is the ground truth mask of corresponding nodule and k is the constant for avoiding the division by zero. Such loss function reflects the overlapping ratio between two regions of the predicted and ground truth masks. Then the loss for i th up-sampling block is estimated as follows:

$$L_i = \frac{1}{m}\sum_{j=1}^{m} S(X_{ij}, Y_{ij}) \ . \qquad (2)$$

Hence, the final loss function for the whole image to detect lung nodules was calculated as arithmetic average of loss function over each block:

$$Loss = \frac{1}{n}\sum_{i=1}^{n} L_i \ , \qquad (3)$$

where n is the number of up-sampling blocks.

2.4 Model Training

For the 3D U-Net CNN, it is important how many number of serial images are used as an input of network. If the number of serial images is too small, the superiority of the 3D CNN will not be well demonstrated, while if too large, the number of parameters will be more than the necessity. We examined the training results increasing the number of input images from 1 with an interval of 2. and we obtained the best performance when the number of input images was 5. Thereby, we fixed the input layer size of the 3D U-Net CNN as 5×512×512.

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The training data consists of positive and negative samples. The positive samples are 3D CT serial images including nodules while the negative samples are those not including nodules. To improve the performance of the network training, false positive samples obtained by our model are added to the training data. These false positive samples are negative data which is difficult to distinguish from true positive samples. So it is helpful to accurately

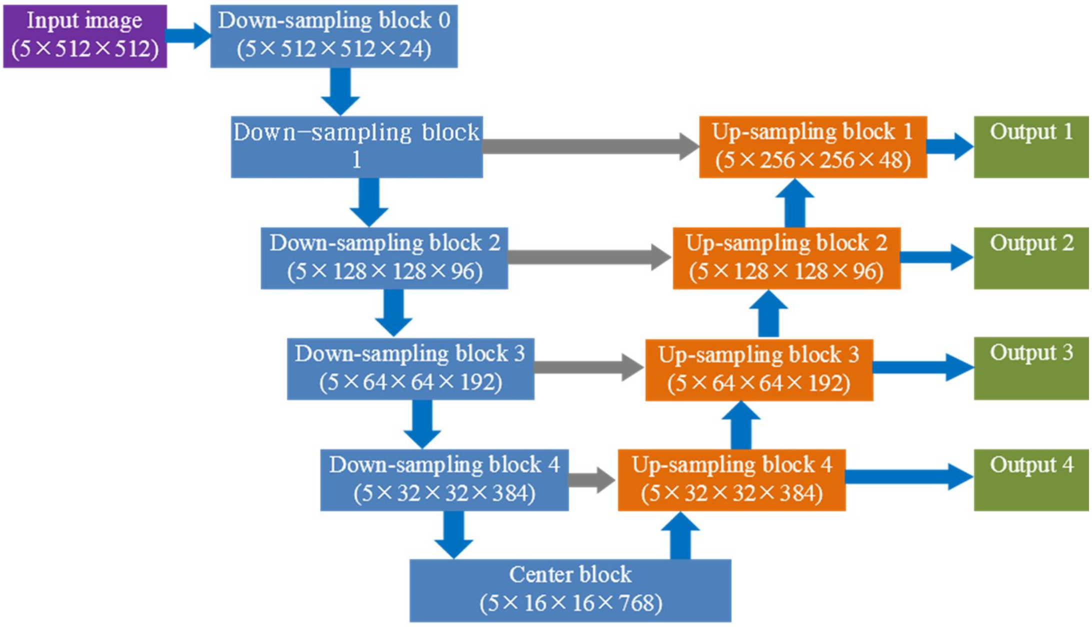

Fig. 2 3D U-Net CNN structure for lung nodule detection

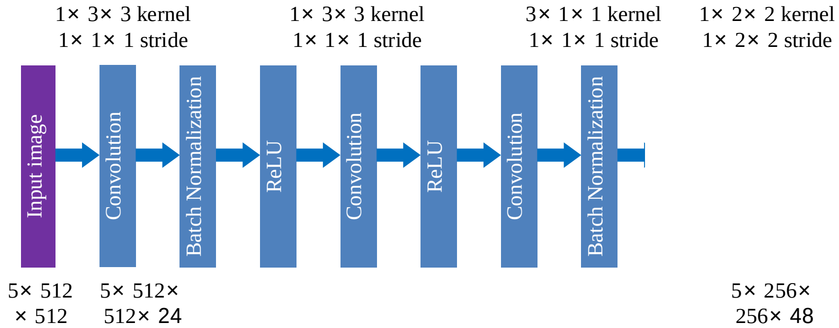

Fig. 3 Down-sampling block 0 of 3D U-Net CNN

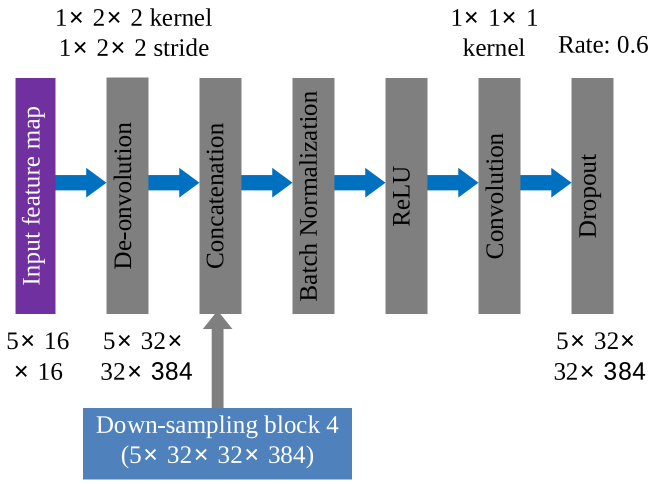

Fig. 4 Up-sampling block 4 of 3D U-Net CNN

distinguish between the nodules and non-nodules that can be easily confused with the nodules. We retrain the network based on the new training data obtained in this way.

We utilized a device of Intel Core i5-3570 CPU@3.4 GHz×4, TITAN XP GPU@16G RAM. Considering the RAM of GPU, we set the training batch size as 3. We initially set the learning rate as 5×10^{-4} and then decrease it as 10^{-1} per each 10 epoch. Through training the 3D U-Net CNN, we obtained the model for detecting the lung nodules in CT images and by using it, the lung nodules in unknown CT scans were detected.

3. RESULTS AND DISCUSSIONS

We employed the Lung Image Database Consortium (LIDC) dataset which were labeled by four professional radiologists. This dataset contains hundreds images of CT scans per a patient with the image size of 512×512 pixels and the file format of DICOM. We divide this dataset into training, validation and test set with a ratio of 8:1:1. That is, 975 nodules are used as training data, 130 nodules as validation, and 140 nodules as test.

To evaluate the performance of the proposed method compared with the previous ones, we use the detection sensitivity defined as follow.

$$Sensitivity = \frac{TP}{(TP + FN)}, \tag{4}$$

where *TP* is the number of true positive and *FN* is the number of false negative.

We first examined the sensitivity of lung nodule detection according to the number of convolutional blocks and the number of input images for 3D U-Net CNN. Table 2 and 3 show the sensitivity comparison associated with the number of convolutional blocks and the number of input images. The highest sensitivity was achieved when the number of convolutional blocks was 9 and the number of input images was 5. Therefore, we adopt these values and carry out experiment.

We estimated the sensitivity of lung nodule detection using our proposed loss function and compared it with the sensitivity using the conventional loss function where the loss is calculated only in the final layer. The result showed that the sensitivity using the previous loss is 89.4% while the sensitivity using our integrated loss is 93.2% confirming the efficiency of our proposed loss function.

We then compared the sensitivity of lung nodule detection with previous benchmark methods (see Table 4). Our proposed method achieved a sensitivity of 94.8% at FPS 4.0 and 93.2% at FPS 1.0, providing a higher sensitivity than the previous methods. In particular, the sensitivity of our proposed method does not decrease even if the FP rate is greater than 4.0 demonstrating that FP rate can be effectively reduced in the proposed method.

Finally, we evaluated the training time of the CNN models. Table 5 shows the number of training parameters and time of the proposed 3D U-Net CNN compared with previous 2D and 3D CNN models. In 3D CNNs, the number of training parameters is larger and the training time is longer than those in 2D CNNs. However, we find that in the proposed 3D U-Net CNN, the number of training parameters is smaller and the training time is shorter than those in the previous 3D CNNs.

Table 2. Sensitivity comparison associated with the number of convolutional blocks

Number of conv blocks	Sensitivity (%)
5	89.2
7	92.7
9	93.2
11	91.9
13	90.3

Table 3. Sensitivity comparison associated with the number of input images

Number of input images	Sensitivity (%)
1	78.4
3	87.6
5	93.2
7	92.8

Table 4. Sensitivity comparison with previous methods

Method	2D/3D	Sensitivity (%)	FPS
Fu et al. [21]	2D	90.9	4.0
Dou et al. [20]	3D	84.8 90.7	1.0 4.0
Zheng et al. [24]	2D, 3D	92.67 94.19	1.0 2.0
Zhang et al. [25]	2D + 3D	94.9	1.0
Proposed method	3D	93.2 94.5 94.8	1.0 2.0 4.0

Table 5. Comparison of the number of training parameters and time

Method	2D/3D	Parameter ($\times10^6$)	epoch	training time (hour)
Fu et al. [21]	2D	0.94	20	8
Dou et al. [20]	3D	2.68	20	21
Zheng et al. [24]	2D, 3D	2.14	20	18
Zhang et al. [25]	2D + 3D	3.76	20	36
Proposed method	3D	2.28	20	19

4. CONCLUSION

In this work, we have established a lung nodule detection method analyzing 3D CT images with deep 3D CNNs. We designed the 3D U-Net CNN and proposed an efficient loss function to efficiently detect lung nodules in CT scans. We evaluated the efficiency of the proposed method through the experiments using the LIDC dataset. Compared with the previous 2D and 3D CNNs, our proposed method achieved high performance for detecting the lung nodules with different sizes. This work paves an effective way to make early and exact diagnosis of pulmonary cancer by using auto-detection of the lung nodules in CT scans.

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