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Detection and diagnosis of lung cancer using region based convolutional neural network model on computed tomography images

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***Abstract*---**Computed tomography is one of the most sensitive imaging techniques for the segmentation of lung cancer. Since lung cancer has the high mortality rate among all the cancers so it becomes so important to detect and diagnose the cancer at beginning stage itself. Segmentation is an important step in medical image analysis and classification for radiological evaluation or computer aided diagnosis. The CAD (Computer Aided Diagnosis) of lung CT generally first segment the area of interest (lung) and then analyse the separately obtained area for nodule detection in order to diagnosis the disease. In this work, implemented a semantic segmentation method using region based convolutional neural network in order to segment the lung nodule part separately from the lung which will enhance the chances of detection of lung cancer and will optimize the extraction of candidate nodules. R-CNN is developed to be used to segment lung regions. The network consists of total 4 convolution layers and 2 max pooling layers. This network has provided an accuracy of 98.28%.

***Keywords*---**lung cancer, deep learning, semantic segmentation, convolution neural network, computer tomography (CT), lung nodule detection.

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Introduction

Lung cancer is one of the most frequent malignancies and the leading cause of cancer death in the United States, accounting for roughly a quarter of all cancer-related deaths. The high death rate linked with lung cancer is due in part to the fact that symptoms do not appear until the illness has progressed to an advanced stage [1]. The computed tomography (CT) imaging technique can create high resolution, minimal distortions, and great contrast of anatomical structures in the chest, which is sensitive to lung cancer diagnosis after decades of research and verification [2].

Lung anatomy

The lungs are a pair of spongy, air-filled organs located on either side of the chest. The trachea (windpipe) conducts inhaled air into the lungs through its tubular branches, called bronchi. The bronchi then divide into smaller and smaller branches (bronchioles), finally becoming microscopic. Figure 1 shows the parts of human Lung.

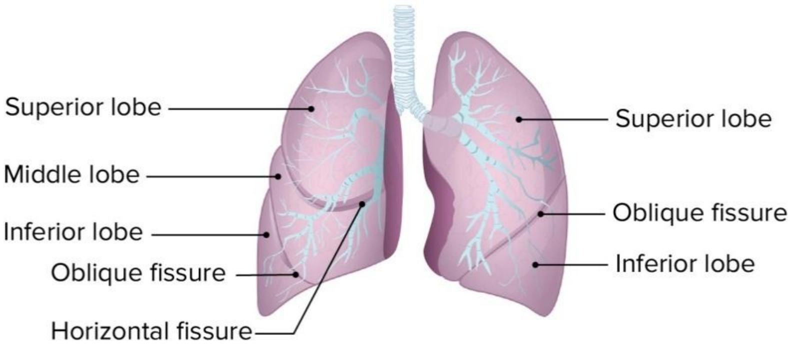

Figure 1. Anatomy of Lung

Lung cancer

Lung cancer is a type of cancer that occurs in lung and can be spread over different parts based on the tumour. The most common type is non-small cell lung cancer (NSCLC). NSCLC makes up about 80 to 85 percent of all cases. Thirty percent of these cases start in the cells that form the lining of the body’s cavities and surfaces. This type usually forms in the outer part of the lungs (adenocarcinomas). Another 30 percent of cases begin in cells that line the passages of the respiratory tract (squamous cell carcinoma). A rare subset of adenocarcinoma begins in the tiny air sacs in the lungs (alveoli). It’s called adenocarcinoma in situ (AIS). This type isn’t aggressive and may not invade surrounding tissue or need immediate treatment. Faster-growing types of NSCLC include large-cell carcinoma and large-cell neuroendocrine tumors. Small-cell lung cancer (SCLC) represents about 15 to 20 percent of lung cancers. SCLC grows and spreads faster than NSCLC. This also makes it more likely to respond to chemotherapy. However, it’s also less likely to be cured with treatment.

In some cases, lung cancer tumors contain both NSCLC and SCLC cells. Mesothelioma is another type of lung cancer. It's usually associated with asbestos exposure. Carcinoid tumors start in hormone producing (neuroendocrine) cells. Tumors in the lungs can grow quite large before you notice symptoms. Early symptoms mimic a cold or other common condition, so most people don't seek medical attention right away. That's one reason why lung cancer isn't usually diagnosed in an early stage.

Causes: Anyone can get lung cancer, but 90 percent of lung cancer cases are the result of smoking. From the moment you inhale smoke into your lungs, it starts damaging your lung tissue. The lungs can repair the damage, but continued exposure to smoke makes it increasingly difficult for the lungs to keep up the repair. Once cells are damaged, they begin to behave abnormally, increasing the likelihood of developing lung cancer. Small-cell lung cancer is almost always associated with heavy smoking. When you stop smoking, you lower your risk of lung cancer over time. Exposure to radon, a naturally existing radioactive gas, is the second leading cause, according to the American Lung Association. Radon enters buildings through small cracks in the foundation. Smokers who are also exposed to radon have a very high risk of lung cancer.

Normally, the division and growth of cells is orderly and controlled but if this process gets out of control for some reason, the cells will continue to divide and develop into a lump which is called a tumour. Tumours can either be benign or malignant. Cancer is the name given to a malignant tumour. A cancerous (malignant) tumour consists of cancer cells which have the ability to spread beyond the original site. If left untreated, they may invade and destroy surrounding tissues. Sometimes cells break away from the original (primary) cancer and spread to other organs in the body by traveling in the bloodstream or lymphatic system. When these cells reach a new area of the body they may go on dividing and form a new tumour, often referred to as a "secondary" or a "metastasis". It is important to realize that cancer is not a single disease with a single type of treatment. There are more than 200 different kinds of cancer, each with its own name and treatment. The automatic lung cancer detection process is divided into two steps:

- extracting all suspected candidate nodules
- Classifying the extracted nodules into two categories (positive and false-positive nodules).

Since the classification object in the second step comes from the recognition results in the first step, all positive nodules should be identified in the first step; otherwise, the diagnosis will be missed. Traditional CAD is an image-detection technology based on threshold adjustment and morphological detection. In practice, some low-density ground-glass opacity is often neglected, while some nodules close to the external tissues are sometimes neglected. In addition, the lung cancer nodules' sizes are highly variable, and CAD technology based on manual feature classification cannot maintain a good detection rate in the face of a variety of nodules, resulting in the low accuracy of shape-based CAD diagnosis that leads to many missed diagnoses and misdiagnoses.

Deep learning is a particular kind of machine learning that is composed of multiple processing layers to achieve high levels of abstraction when it comes to learning representations of data. In different domains such as speech recognition and visual object recognition. Convolutional Neural Network (CNN), which is commonly known as a branch of machine learning approach and a class of deep learning, nowadays supersedes many image segmentation approaches. It is based on multiple layer processing to model high level and complex abstractions in data. Nowadays, the application of deep learning techniques for medical image segmentation received a great interest due to their ability to learn and process large amounts of data in a fast and accurate manners. In this paper we are introducing a lung cancer segmentation using one of the common architectures used for image segmentation with deep learning called Semantic segmentation.

Computer tomography

A computed tomography (CT) scan allows doctors to see inside your body. It uses a combination of X-rays and a computer to create pictures of your organs, bones, and other tissues. It shows more detail than a regular X-ray. You can get a computed tomography scan on any part of your body

Figure 2. Computer Tomography

A CT scan can be used for detecting both acute and chronic changes in the lung parenchyma, the tissue of the lungs. It is particularly relevant here because normal two-dimensional X-rays do not show such defects. A variety of techniques are used, depending on the suspected abnormality. For evaluation of chronic interstitial processes such as emphysema, and fibrosis, thin sections with high spatial frequency reconstructions are used; often scans are performed both on inspiration and expiration. This special technique is called high resolution CT that produces a sampling of the lung, and not continuous images. Bronchial wall thickening can be seen on lung CTs and generally (but not always) implies inflammation of the bronchi. Normally, the ratio of the bronchial wall thickness and the bronchial diameter is between 0.17 and 0.23.

An incidentally found nodule in the absence of symptoms may raise concerns that it might represent a tumor, either benign or malignant. Perhaps persuaded by fear, patients and doctors sometimes agree to an intensive schedule of CT scans, sometimes up to every three months and beyond the recommended guidelines, in an attempt to do surveillance on the nodules. However, established guidelines advise that patients without a prior history of cancer and whose solid nodules have not grown over a two-year period are unlikely to have any malignant cancer. For this reason, and because no research provides supporting evidence that intensive surveillance gives better outcomes, and because of risks associated with having CT scans, patients should not receive CT screening in excess of those recommended by established guidelines.

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Related work

Traditional CAD approaches relied on hand-engineered features and outdated image processing techniques [3]. Recent improvements in deep learning for computer vision have led to a significant shift toward deep learning-based solutions [4]. Ozdemir, Onur et.al. introduced a new computer-aided detection and diagnostic method that generates meaningful probability evaluations for lung cancer screening using low-dose CT images [5]. Li, Xiadong, et al. a new deep learning framework for delineating the internal gross target volume (IGTV) from 4-D computed tomography (4DCT) in patients with lung cancer who are receiving stereotactic body radiation treatment (SBRT) [6]. The diagnosis is carried out using the parameter Optimized-Faster Region Convolutional Neural Network (PO-FRCNN). The Improved Red Deer Algorithm (IRDA), which helps to tune the significant parameters that have a favourable influence on the accuracy, improves pattern generation and deep classification [7]. Jiang, Hongyang, et al. provides a method for detecting lung nodules that uses multigroup patches clipped from lung images and strengthened by the Frangi filter. A fourchannel convolution neural networks model is developed to learn the knowledge of radiologists for recognising nodules of four levels by integrating two groups of images [8].

Yu, Heng, Zhiqing Zhou, and Qiming Wang suggested method includes multiple processes, including picture acquisition, preprocessing, binarization, thresholding, and segmentation, feature extraction, and deep neural network detection (DNN). The lung CT picture is segmented in order to extract any significant features from the segmented image, and a specific feature extraction approach is used [10]. Two multiple resolutions residually connected network (MRRN) formulations called incremental-MRRN and dense-MRRN has been deployed, this networks simultaneously combine features across multiple image resolution and feature levels through residual connections to detect and segment the lung tumors. They have evaluated this method on a total of 1210 non-small cell (NSCLC) lung tumors and nodules from three data sets consisting of 377 tumors from the open-source Cancer Imaging Archive (TCIA), 304 advanced stage NSCLC and 529 lung nodules from the Lung Image Database Consortium (LIDC). The algorithm was trained using 377 tumors from the TCIA data set and validated on the MSKCC and tested on LIDC data sets. The segmentation accuracy compared to expert delineations was evaluated by computing the dice similarity coefficient, sensitivity, and precision metrics [11]. In an average Dice coefficient of 0.975±0.006 and a mean absolute surface distance error of 0.84±0.23 mm [12].

Hybrid segmentation network (referred to as HSN) based on convolutional neural network (CNN) has been deployed to automatically segment SCLC from computed tomography (CT) images. The design philosophy of this model is to combine a lightweight 3D CNN to learn long-range 3D contextual information and a 2D CNN to learn fine-grained semantic information, which is essential for accurate cancer segmentation. They have proposed a hybrid features fusion module to effectively fuse the 2D and 3D features and to jointly train these two CNNs. They have utilized a generalized Dice loss function to tackle the severe class imbalance problem in data. A dataset consists of 134 CT scans was constructed to evaluate this model. This model achieved high performances with a mean Dice score of 0.888, a mean sensitivity score of 0.872 and a mean precision of 0.909 [13].

A lobe segmentation algorithm is used which consist two-stage approach: (1) adaptive fissure sweeping to find fissure regions and (2) wavelet transform to identify the fissure locations and curvatures within these regions. Tested on isotropic CT image stacks from nine anonymous patients with pathological lungs, the algorithm yielded an accuracy of 76.7%-94.8% with strict evaluation criteria. In comparison, surgeons obtain an accuracy of 80% for localizing the fissure regions in clinical CT images with a thickness of 2.5-7.0 mm. As well, this paper describes a procedure for visualizing lung lobes in three dimensions using Software-Amira-and the segmentation algorithm [14].

An architecture called U-Net convolutional network has been proposed and implemented exclusively for the segmentation of biomedical images. In this paper U-Net Convolution Net has been implemented on lungs dataset to perform lungs segmentation. The lungs dataset consists of 267 CT images of lungs and their corresponding segmentation maps. The accuracy and loss achieved is 0.9678 and 0.0871 respectively. Hence U-Net Convolution Net can be used for the segmentation of lungs in CT scans [15]. The detection of pulmonary cancer in the early stages can highly increase survival rate. Manual delineation of lung nodules by radiologists is a tedious task. We developed a novel computer-aided decision support system for lung nodule detection based on a 3D Deep Convolutional Neural Network (3DDCNN) for assisting the radiologists. Our decision support system provides a second opinion to the radiologists in lung cancer diagnostic decision making. In order to leverage 3-dimensional information from Computed Tomography (CT) scans, we applied median intensity projection and multi-Region Proposal Network for automatic selection of potential region-of-interests. Our Computer Aided Diagnosis (CAD) system has been trained and validated using LUNA16, ANODE09, and LIDC-IDR datasets; the experiments demonstrate the superior performance of our system, attaining sensitivity, specificity, AUROC, accuracy, of 94.4%, 92%, 94% and 94.51% with 2.1 FPs per scan. We integrated cloud computing, trained and validated our Cloud-Based 3DDCNN on the datasets provided by Shanghai Sixth People's Hospital, as well as LUNA16, ANODE09, and LIDC-IDR. Our system outperformed the state-of-the-art systems and obtained an impressive 94.7% sensitivity at 1.97 FPs per scan.

To segment lung nodule, they have proposed a method consists of two main processing steps. First, a novel robust active shape model (RASM) matching method is utilized to roughly segment the outline of the lungs. The initial position of the RASM is found by means of a rib cage detection method. Second, an optimal surface finding approach is utilized to further adapt the initial segmentation result to the lung. Left and right lungs are segmented individually. An evaluation on 30 data sets with 40 abnormal (lung cancer) and 20 normal left/right lungs resulted

Proposed architecture

There are different steps involved for the segmentation of the lung cancer, as shown in the fig 3.1 the input image has to go through several convolutions, activation and max pooling layers. Convolutional layers are the major building blocks used in convolutional neural networks. A convolution is the simple application of a filter to an input that results in an activation. Repeated application of the same filter to an input results in a map of activations called a feature map, indicating the locations and strength of a detected feature in an input, such as an image. The innovation of convolutional neural networks is the ability to automatically learn a large number of filters in parallel specific to a training dataset under the constraints of a specific predictive modelling problem, such as image classification. The result is highly specific features that can be detected anywhere on input images. A convolution is a linear operation that involves the multiplication of a set of weights with the input, much like a traditional neural network. Given that the technique was designed for two-dimensional input, the multiplication is performed between an array of input data and a two-dimensional array of weights, called a filter or a kernel.

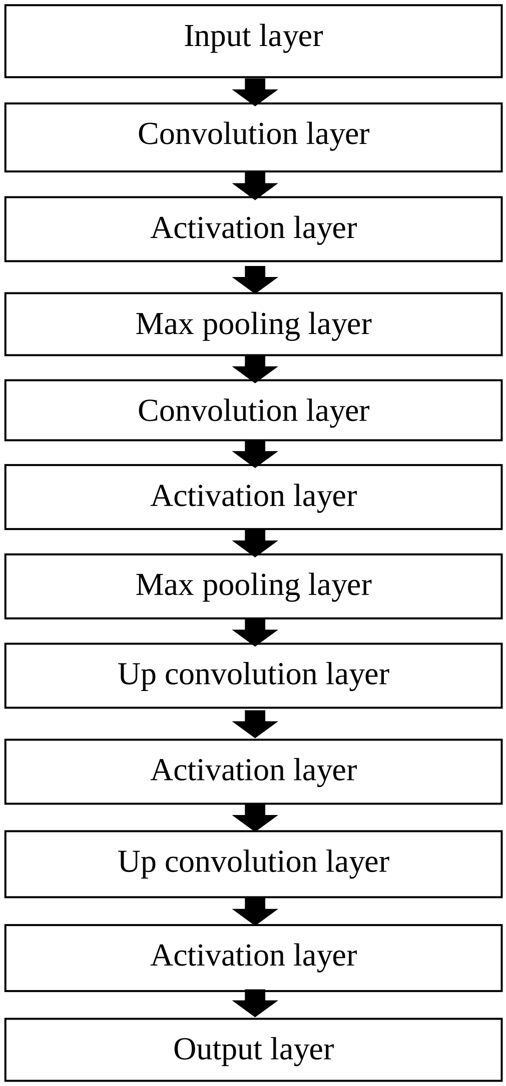


Figure 3. Architecture of lung cancer segmentation through CT

The filter is smaller than the input data and the type of multiplication applied between a filter-sized patch of the input and the filter is a dot product. A dot product is the element-wise multiplication between the filter-sized patch of the input and filter, which is then summed, always resulting in a single value. Using a filter smaller than the input is intentional as it allows the same filter (set of weights) to be multiplied by the input array multiple times at different points on the input. Specifically, the filter is applied systematically to each overlapping part or filter-sized patch of the input data, left to right, top to bottom. This systematic application of the same filter across an image is a powerful idea. If the filter is designed to detect a specific type of feature in the input, then the application of that filter systematically across the entire input image allows the filter an opportunity to discover that feature anywhere in the image. This capability is commonly referred to as translation invariance, e.g. the general interest in whether the feature is present rather than where it was present.

A pooling layer is another building block of a CNN. Its function is to progressively reduce the spatial size of the representation to reduce the amount of parameters and computation in the network. Pooling layer operates on each feature map independently. The most common approach used in pooling is max pooling. Max pooling is a sample-based discretization process. The objective is to down-sample an input representation (image, hidden-layer output matrix, etc.), reducing its dimensionality and allowing for assumptions to be made about features contained in the sub-regions binned. This is done to in part to help over-fitting by providing an abstracted form of the representation. As well, it reduces the computational cost by reducing the number of parameters to learn and provides basic translation invariance to the internal representation. Max pooling is done by applying a max filter to (usually) non-overlapping sub regions of the initial representation. Let's say, as well, that we have a 2x2 filter that we'll run over our input. We'll have a stride of 2 (meaning the (dx, dy) for stepping over our input will be (2, 2)) and won't overlap regions. For each of the regions represented by the filter, we will take the max of that region and create a new, output matrix where each element is the max of a region in the original input.

Example:

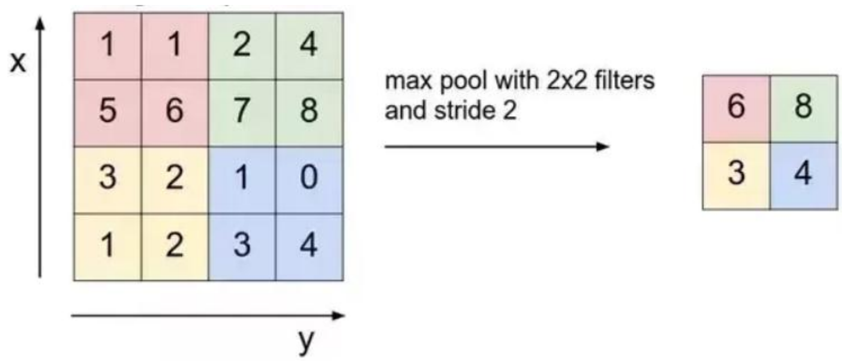


Figure 4. Example of max pooling

Methods of Semantic segmentation
Region based convolutional neural network

R-CNN (Regions with CNN feature) is one representative work for the region-based methods. It performs the semantic segmentation based on the object detection results. To be specific, R-CNN first utilizes selective search to extract a large quantity of object proposals and then computes CNN features for each of them. Finally, it classifies each region using the class-specific linear SVMs. Compared with traditional CNN structures which are mainly intended for image classification, R-CNN can address more complicated tasks, such as object detection and image segmentation, and it even becomes one important basis for both fields. Moreover, R-CNN can be built on top of any CNN benchmark structures, such as AlexNet, VGG, GoogLeNet, and ResNet.

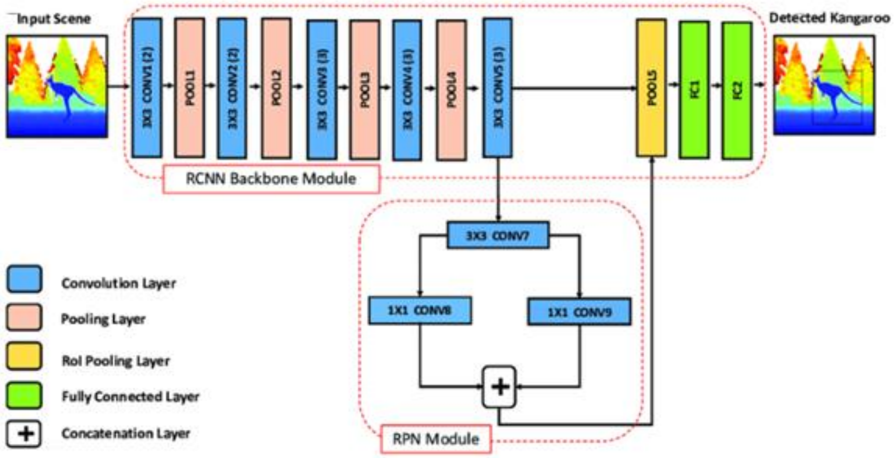


Figure 5. R-CNN

The region-based methods generally follow the "segmentation using recognition" pipeline, which first extracts free-form regions from an image and describes them, followed by region-based classification. At test time, the region-based predictions are transformed to pixel predictions, usually by labelling a pixel according to the highest scoring region that contains it. For the image segmentation task, R-CNN extracted 2 types of features for each region: full region feature and foreground feature, and found that it could lead to better performance when concatenating them together as the region feature. R-CNN achieved significant performance improvements due to using the highly discriminative CNN features. However, it also suffers from a couple of drawbacks for the segmentation task:

- The feature is not compatible with the segmentation task.
- The feature does not contain enough spatial information for precise boundary generation.
- Generating segment-based proposals takes time and would greatly affect the final performance.
- Due to these bottlenecks, recent research has been proposed to address the problems, including SDS, Hyper columns, Mask R-CNN.

Fully convolutional network-based semantic segmentation

The original Fully Convolutional Network (FCN) learns a mapping from pixels to pixels, without extracting the region proposals. The FCN network pipeline is an extension of the classical CNN. The main idea is to make the classical CNN take as input arbitrary-sized images. The restriction of CNNs to accept and produce labels only for specific sized inputs comes from the fully-connected layers which are fixed. Contrary to them, FCNs only have convolutional and pooling layers which give them the ability to make predictions on arbitrary-sized inputs.

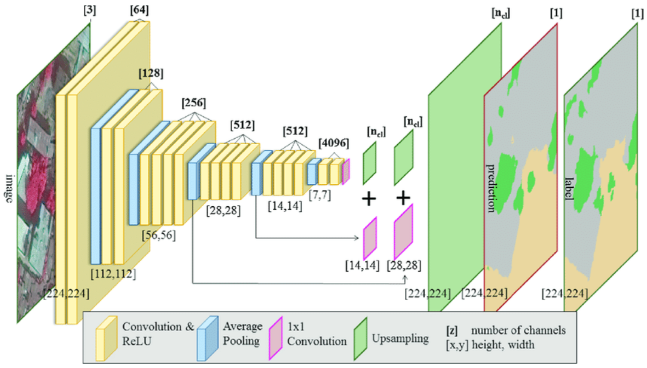


Figure 6. FCNN

One issue in this specific FCN is that by propagating through several alternated convolutional and pooling layers, the resolution of the output feature maps is down sampled. Therefore, the direct predictions of FCN are typically in low resolution, resulting in relatively fuzzy object boundaries. A variety of more advanced FCN-based approaches have been proposed to address this issue, including SegNet, DeepLab-CRF, and Dilated Convolutions.

U-NET (unity networking)

U-Net is a convolutional neural network that was developed for biomedical image segmentation at the Computer Science Department of the University of Freiburg, Germany. The network is based on the fully convolutional network and its architecture was modified and extended to work with fewer training images and to yield more precise segmentations. The main idea is to supplement a usual contracting network by successive layers, where pooling operations are replaced by up sampling operators. Hence these layers increase the resolution of the output. What's more, a successive convolutional layer can then learn to assemble a precise output based on this information.

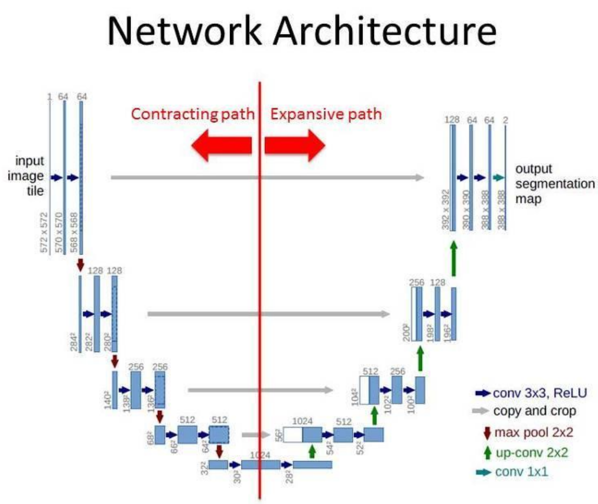


Figure 7. U-net

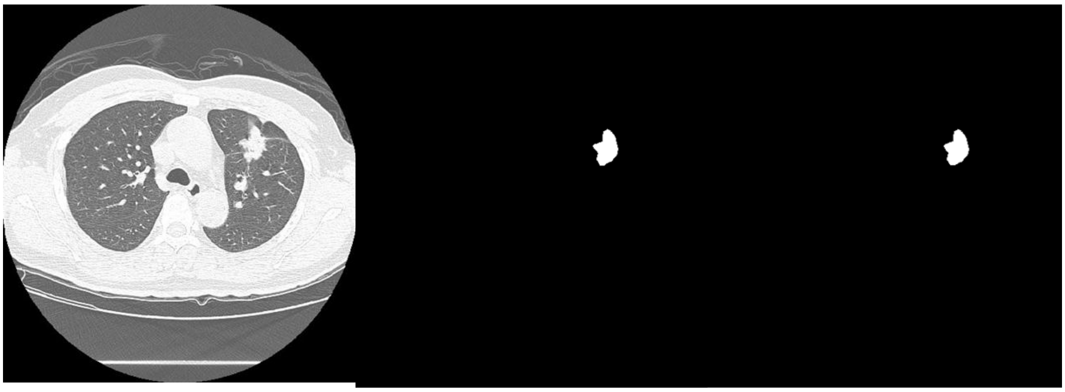
One important modification in U-Net is that there are many feature channels in the up-sampling part, which allow the network to propagate context information to higher resolution layers. Therefore, the expansive path is more or less symmetric to the contracting part and yields a u-shaped architecture. The network only uses the valid part of each convolution without any fully connected layers. To predict the pixels in the border region of the image, the missing context is extrapolated by mirroring the input image. The network consists of a contracting path and an expansive path, which gives it the u-shaped architecture. The contracting path is a typical convolutional network that consists of repeated application of convolutions, each followed by a rectified linear unit (ReLU) and a max pooling operation. During the contraction, the spatial information is reduced while feature information is increased. The expansive pathway combines the feature and spatial information through a sequence of up-convolutions and concatenations with high-resolution features from the contracting path.

Experimental Results and Discussions

The steps mentioned above are performed on an CT lung image obtained in LIDC DATASET and the results are declared in the following subsections.

Image Segmentation Results

Image segmentation is a process of partitioning an image into multiple segments. Several general-purpose algorithms and methods have been developed for image segmentation which are mentioned in chapter 5. In this project, implemented semantic segmentation using region based convolutional neural network and the resulted images are shown below.



(a) (b) (c)

Figure 8. Segmented Image along with Input and Ground Truth Image

In Fig 8. (a) shows the input lung image which is passed through several convolution and max-pooling layers in order to get the (b) segmented image which is then compared with the (c) ground truth image to obtain the testing results.

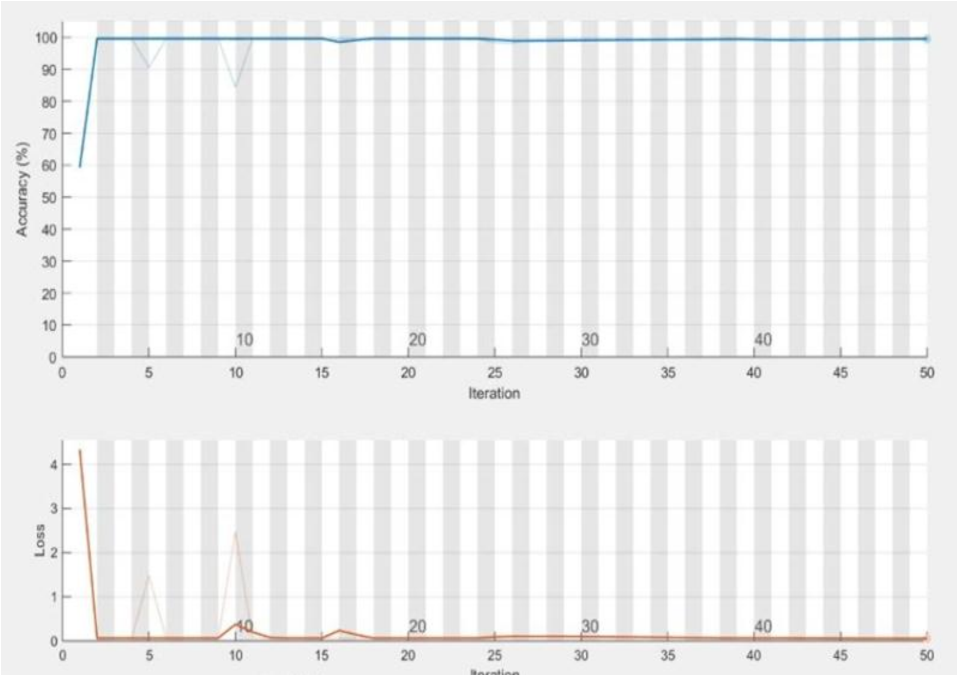


Figure 9. Training data simulation progress

After the segmentation of each image the images and corresponding labels are pass through training in order to get the training results, Fig 9 shows the simulation progress of the training data.

```
Command Window
Training on single GPU.
Initializing input data normalization.
|======================================================================================|
|  Epoch  |  Iteration  |  Time Elapsed  |  Mini-batch  |  Mini-batch  |  Base Learning  |
|         |             |   (hh:mm:ss)   |   Accuracy   |     Loss     |      Rate       |
|======================================================================================|
Warning: GPU is low on memory, which can slow performance due to additional data transfers with
main memory. Try reducing the 'MiniBatchSize' training option. This warning will not appear again
unless you run the command: warning('on','nnet_cnn:warning:GPULowOnMemory').
|       1 |           1 |       00:00:37 |       59.29% |       4.3285 |          0.0010 |
|      10 |          10 |       00:01:49 |       84.41% |       2.4692 |          0.0010 |
|      20 |          20 |       00:02:37 |       99.61% |       0.0642 |          0.0010 |
|      30 |          30 |       00:03:27 |       99.46% |       0.0791 |          0.0010 |
|      40 |          40 |       00:04:16 |       99.23% |       0.0653 |          0.0010 |
|      50 |          50 |       00:05:05 |       99.47% |       0.0536 |          0.0010 |
|======================================================================================|
```

Figure 10. Segmentation results of the Trained Network

The above Fig shows the evaluation of the train network by segmenting a test image its shows accuracy, loss, and basic learning rate which has deployed for training the network.

Performance Evaluation

The segmented images are evaluated using performance matrix discussed in chapter 6. The results are mentioned as shown in the table 1.

Table 1
Performance evaluation of R-CNN on LIDC dataset

Dataset	Method	Sensitivity	Specificity	Accuracy
LIDC	R-CNN	96.96	98.72	98.28

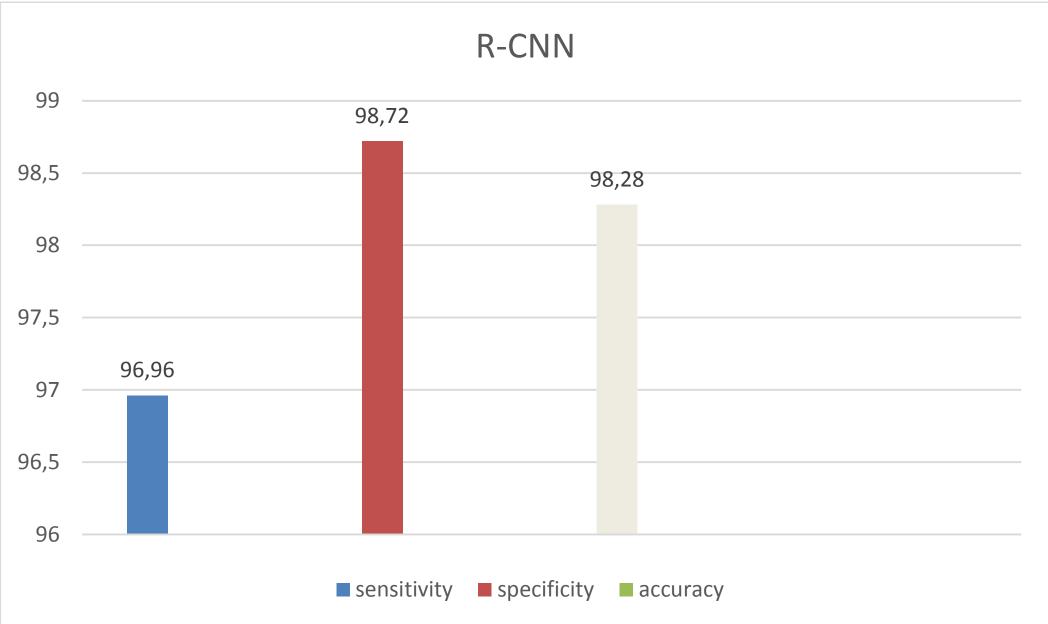


Figure 11. Performance evaluation chart for R-CNN

Performance evaluation of LIDC dataset using different methods is shown in Table 2.

Table 2
Performance evaluation of different methods on LIDC dataset

Method	Sensitivity	Specificity	Accuracy
U-Net	83.67	96.17	96.33
FCN	94.77	98.04	98.02
R-CNN	96.96	98.72	98.28

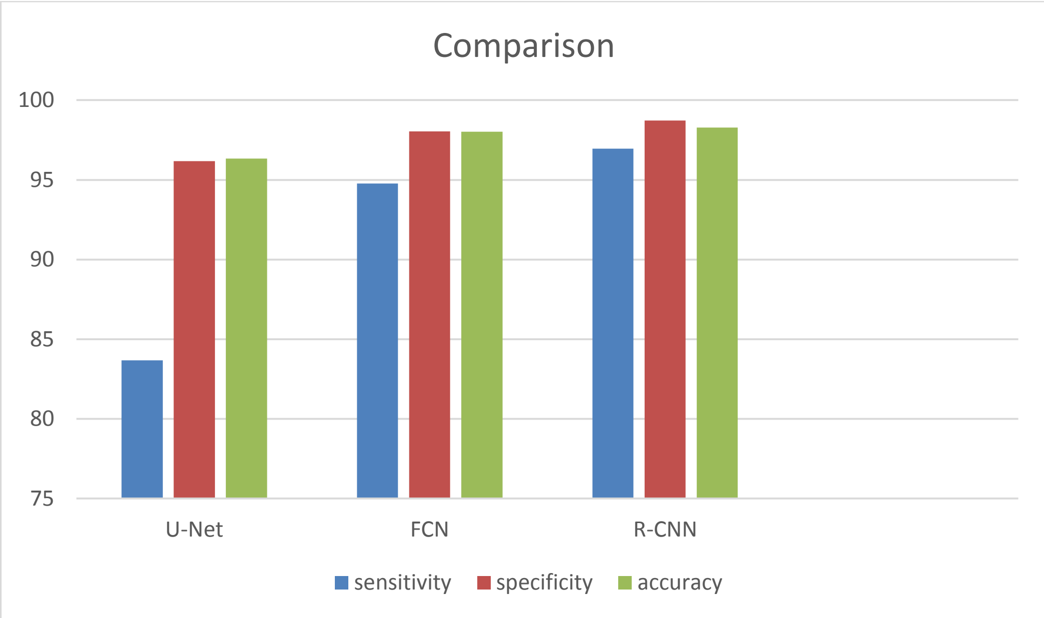


Figure 12. Comparison of performance evaluation for different segmentation methods

Conclusion

The lung segmentation step is a prerequisite for any automated analysis of lung CT image to detect and diagnose lung disease. Basic methods of deep learning have been applied for lung segmentation task. R-CNN has performed exceptionally good on the segmentation of cell and neurons in electron microscopic images. In this work, R-CNN is developed to be used to segment lung regions. R-CNN originally developed for segmenting microscopic images have been successfully applied to lung segmentation on CT images. The network consists of total 4 convolution layers and 2 max pooling layers. This network has provided an accuracy of 98.28%. The number of convolution layers and the size of filter can be increased for improve accuracy.

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