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A Deep Learning Framework Using Enhanced Convolutional Neural Network for Detection of Lung Cancer from CT Images

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Abstract: Lung cancer is one kind of cancer which is causing deaths at an alarming rate across the globe. For patients to recover, early identification and treatment are essential. Histopathological images of tissue biopsies from possibly infected lung regions are used by medical practitioners to make diagnoses. The majority of the time, lung cancer cases are difficult to diagnose and take a long time. Convolutional neural networks are essential for figuring out the best course of therapy for patients and their chance of survival since they can quickly and accurately recognize and categorize different forms of lung cancer. In this paper, A deep learning framework is proposed for automatic detection of lung cancer. The convolutional Neural Network (CNN) model is enhanced for better diagnosis of lung cancer. An algorithm known as a learning-based Method for Lung Cancer Detection (LbM-LCD) is proposed to realize our framework. The empirical study is made with the LUNA-16 dataset. Our experimental results showed that the enhanced CNN outperforms the baseline CNN model with 98.34% accuracy.

Keywords: Lung Cancer Detection, Artificial Intelligence, Deep Learning, Machine Learning

1. Introduction

Lung cancer is one of the most common cancers that claim lives globally. For patients to recover, early identification and treatment are essential. Histopathological images of tissue biopsies from possibly infected lung regions are used by medical practitioners to make diagnoses. Nearly 25% of all cancer fatalities are caused by lung cancer, which is a common malignancy in both men and women [1]. Smoking is approximately 80% of the leading cause of mortality from lung cancer. Non-smokers can get lung cancer via exposure to radon, second-hand smoking, air pollution, or other causes such as asbestos exposure at work, diesel exhaust, or certain other substances [2]. Numerous diagnostic procedures, such as x-rays and CT scans, sputum cytology, and biopsies, are performed in order to detect malignant cells and rule out other potential illnesses. To establish the diagnosis and describe the kinds and subtypes of lung malignancies, skilled pathologists must evaluate the microscopic histopathology slides after performing the biopsy [3]. It takes a lot of time for pathologists and other medical personnel to diagnose different forms of lung cancer. There is a notable increase in the number of cancer types that are misdiagnosed, leading to inappropriate therapy that may result in patient death.

Through the exposure of computers to data sets, machine learning (ML), a branch of artificial intelligence (AI), enables machines to learn without explicit programming, enabling them to acquire expertise in doing certain tasks [4]. Prior research studies have mostly explored the use of machine learning approaches such as Convolutional Neural Networks (CNN) for the detection and identification of lung cancer in X-ray and CT scan images. While other studies also took into account the use of histological images, their accuracy in differentiating between images of carcinomas and non-carcinomas is lower. This study examined the use of Convolutional Neural Network (CNN) architecture for efficient detection of lung cancer. Our contributions are as follows.

1. A deep learning framework for automatic detection of lung cancer is proposed besides enhancing the Convolutional Neural Network (CNN) model for better diagnosis of lung cancer.
2. An algorithm known as a learning-based Method for Lung Cancer Detection (LbM-LCD) is proposed to realize our framework.
3. The empirical study is made with the LUNA-16 dataset. Our experimental results showed that the enhanced CNN outperforms the baseline CNN model with 98.34% accuracy.

An overview of some earlier relevant studies is provided in Section 2. Section 2 provides a brief description of the settings and techniques pertaining to the proposed methodology. Experimental results are presented in Section 4 to clarify and illustrate the research's findings. Discussion on the proposed work and also its limitations are in Section 5. The paper's conclusion is further upon in Section 6.

2. Related Work

This section reviews the literature on existing methods used for lung cancer detection. Sait [1] focused on real-time detection and benefited from the huge accuracy of a unique deep-learning model. Image quality and dataset imbalance are among the difficulties. Liquid neural networks and ensemble learning are the next big advances. Wang *et al.* [2] observed that although essential for early lung cancer detection, medical imaging technologies have drawbacks. While deep learning improves detection, classification, and segmentation speed and accuracy, problems still exist. Wankhade and Vigneshwari [3] opined that since lung cancer is lethal, an early and precise diagnosis is essential. The accuracy of cancer cell identification is increased using hybrid neural networks and 3D-CNNs, which successfully differentiate benign and malignant tumours.

Wenfa *et al.* [4] explored and opined that due to the aggravating effects of pollution and urbanization, lung cancer requires accurate detection. Using deep learning on CT scans improves the prediction of lung illness.

Mohammad *et al.* [5] draw attention to the seriousness of lung cancer and promote early detection. With CT images, deep learning facilitates accurate diagnosis. Diverse data, enhanced segmentation, and cloud-based diagnostics are among the recommendations.

Shakeel *et al.* [6] said that for clinical decision-making, a computer-aided detection system is essential. Machine learning and new image processing methods improve the prognosis of lung cancer. Shaif *et al.* [7] found that deep learning capabilities improve upon current techniques in providing accurate early-stage lung cancer identification. The hybrid SVM + CNN model guarantees accuracy and efficiency. Asuntha and Andy [8] focused on the identification and categorization of lung cancer nodules. FPSOCNN and other novel deep learning approaches perform better than others. The goal of future research is to enhance malignancy grading and categorization. Tekade and Rajeswari [9] investigated U-Net segmentation and a 3D multipath VGG-like network and effective lung cancer diagnosis is achieved with 95.60% accuracy and 0.387732 log loss. Shakeel *et al.* [10] observed that noise in image capture complicates the identification of lung illness and can even impair cancer diagnosis. The technique presented in this study minimizes classification error to 0.038 while obtaining huge accuracy. Rehman *et al.* [11] focused on a new machine-learning algorithm that achieves high accuracy, outperforming existing approaches. With a huge percentage of specificity, sensitivity, and accuracy for SVM, the suggested approach shows greater efficiency. Subsequent endeavours aim to enhance the identification of an expanded set of images.

Das and Majumder [12] contrasted several techniques for detecting lung cancer, with Convolutional Neural Networks proving to be the most effective. The review advances the field of automated lung cancer identification research and paves the way for future work with deep learning algorithms. Huang *et al.* [13] explained how to improve PEC water oxidation by creating n-type ferroelectric BFCO photoelectrodes with p-type TCOs. Improves performance with p-NiO/n-BFCO heterojunctions and shows hours of stability. Kalaivani *et al.* [14] found that diseases of the lungs, such as cancer, affect breathing. Survival chances are increased by early diagnosis. A Deep CNN classifies lung images for cancer diagnosis with an accuracy of 90.85%. Shin *et al.* [15] found that it's critical to diagnose lung cancer early. Exosomes and deep learning are used in a liquid biopsy that achieves 95% accuracy, suggesting promise for early-stage diagnosis. Jenipher and Radhika [16] increased the accuracy of early lung cancer diagnosis, increasing the chances of survival with Machine learning algorithms. The research includes performance indicators, workflow methods, algorithms, and model parameters for efficient operations. Riquelme *et al.* [17] examined deep learning methods for detecting nodules and false-positive reduction systems in CT images to diagnose lung cancer. Future developments and difficulties are spoken about. Lakshmanaprabu *et al.* [18] observed that it is critical to discover lung cancer early. In CT image classification, an ODNN with feature reduction that has been suggested achieves high.

Elnakib and Amer *et al.* [19] suggested by utilizing LDCT images to detect lung nodules early with the CADe system. Uses an SVM classifier with huge accuracy with the VGG19 architecture. Wang et al. [20] presented a quick and efficient method for classifying full-slide lung cancer images using a weakly supervised approach. Overachieves high accuracy, outperforming the most advanced techniques. Sajja *et al.* [21] proposed the classify lung cancer from CT scan images, a deep neural network built on GoogleNet is suggested. More accurate than CNNs that have already been taught. Avanzo *et al.* [22] combined radiology and informatics, radiomics provides features of lung tumors, facilitating treatment planning, diagnosis, and prognosis. Future implementation and clinical effect expectations are highlighted. Hashemzadeh *et al.* [23] opined that using deep learning, namely ResNet18, to classify lung cancer cell lines accurately and efficiently, removes the need for a lot of human interaction and allows for the processing of vast amounts of image data.

Kancherla and Mukkamala [24] presented a novel, approach for detecting lung cancer utilizing sputum samples tagged with TCPP and nucleus-based characteristics. This method has the potential to be used for treatment monitoring and screening. Xu *et al.* [25] used time series CT images and deep learning networks to follow changes in tumour phenotype in patients with non-small cell lung cancer (NSCLC), improving prognosis and survival without the need for volumetric segmentation. Thallam *et al.* [26] discussed the effects of lung cancer worldwide, emphasizing the use of machine learning to provide precise, affordable forecasts. The study explores issues, model applicability, and enhancements, inspiring more research. Kadir and Gleeson [27] made an overview of the machine learning-based pulmonary nodule lung cancer prediction models that are intended to lower variability and enhance clinical decision-making. Discussions are held on difficulties with development, validation, and clinical adoption. Mhaske *et al.* [28] created a hybrid CNN-LSTM computer-aided diagnosis system that detects lung cancer at an astounding accurate rate.

Subramanian *et al.* [29] observed that with AlexNet and the softmax layer, a lung cancer detection model reaches a remarkable performance. Physiological parameters for prediction and IoMT application are future advancements. Kumar and Bakariya [30] presented a method for lung nodule detection on LIDC-IDRI datasets using AlexNet and Google. Analysis of performance, sensitivity, and specificity demonstrates their effectiveness. Yang *et al.* [31] investigated the identification of disease mimics and subtypes of lung cancer from entire slide photos using deep learning algorithms. Hosny *et al.* [32] used deep learning in medical imaging for patients with non-small cell lung cancer (NSCLC), presenting potential clinical applications by providing prognostic signals and mortality risk assessment. Jena *et al.* [33] intended to increase the accuracy of early lung cancer detection. Pre-processing uses the LIDC dataset and noise reduction. ROI extraction is aided by region-expanding segmentation. The DGMM-RBCNN reduction of significant features shows an accuracy, highlighting room for improvement.

Pham *et al.* [34] improved the precision of identifying lung cancer metastases in lymph node images, a two-step deep learning system was created. Ponnada and Srinivas [35] demonstrated excellent findings and the possibility for comprehensive lung organ disease identification with the introduction of EFFI-CNN, a seven-layer CNN for the detection of lung cancer. Cha *et al.* [36] surpassed the performance of human radiologists in focusing on a deep convolutional neural network (DCNN) for operable lung cancer identification in chest radiography. Katiyar and Singh [37] highlighted the importance of early lung cancer identification in India and presented solutions for computer-aided diagnosis that employ a variety of methods. Hatuwal and Thapa [38] found that it is critical to diagnose lung cancer early. The examination of histopathological images, particularly using CNN, enhances precision and helps with prompt and efficient treatment choices. Salaken *et al.* [39] achieved statistically significant improvements in lung cancer classification accuracy using deep learning, namely autoencoder-based, for high-dimensional, low-population datasets without the need for human feature engineering. Other important contributions found in the literature include image haze removal [40], blockchain for image evaluation [41] and lung image enhancement [42]. From the literature, it is observed that there is a need for enhancement of CNN for better diagnosis of lung cancer.

3. Proposed Methodology

A deep learning framework and methodology is proposed for the automatic detection of lung cancer. Our method is based on an enhanced CNN model. The following sub-sections provide more details of our methodology and algorithm.

3.1 Problem Definition

Provided lung CT image of a patient, developing a learning-based approach to detect the probability of lung cancer is the problem considered in this paper.

3.2 Our Framework and the Need

One of the deadliest malignancies in the world is lung cancer. Nonetheless, the survival rate of lung cancer is greatly increased by early identification. Small cell growths inside the lung called pulmonary nodules can be either benign or malignant. Early detection of malignant lung nodules is essential for determining the critical prognosis. Due to their similarity to noncancerous nodules in terms of morphology, location, and clinical indicators, early-stage cancerous lung nodules require a differential diagnosis. Determining the likelihood of malignancy for early-stage malignant lung nodules is a difficult assignment. Physicians employ a variety of diagnostic techniques to identify malignant lung nodules early on. Physicians utilize a range of diagnostic techniques to identify malignant lung nodules early on. These techniques include clinical settings, needle prick biopsy analysis, positron emission tomography (PET) metabolic assessments, and computed tomography (CT) scan analysis (morphological assessment). However, to distinguish between benign and malignant lung nodules, medical professionals mostly employ invasive techniques like biopsies and procedures.

Invasive procedures provide a great deal of risk and exacerbate patients' worries since the organ is so delicate and sensitive. When examining lung illnesses, computed tomography (CT) imaging is the most appropriate technology. However, due to the radiation's carcinogenic effects, there is a significant risk of false positive results from CT scan investigations.

Compared to standard-dose CT, low-dose CT utilizes significantly less radiation contact power. The findings indicate that there is no discernible difference in low-dose and standard-dose CT image detection sensitivity. On the other hand, the National Lung Screening Trial (NLST) database shows that among the chosen group subjected to low-dose CT scans, cancer-related mortality was considerably lower than those attributable to chest radiography. Better image registration techniques and more complex anatomical features (thinner slices) increase the sensitivity of lung nodule identification. That being said, this greatly expands the datasets. A single scan can provide up to 500 sections or slices, depending on the slice thickness. It takes a skilled radiologist around two to three minutes to view a single slice. When a radiologist screens a CT image for the potential presence of a nodule, their workload considerably rises. The sensitivity of the identification of nodules is dependent on several factors, including size, position, form, neighbouring structures, edges, and density, in addition to the thickness of the CT slices. The findings indicate that when a single radiologist reviews the scan, lung cancer nodules are only correctly diagnosed 68% of the time; when two radiologists evaluate the image, the accuracy rate rises to 82%. For radiologists, identifying malignant lung nodules early on is a challenging, laborious, and time-consuming process. It takes a lot of time for the radiologist to carefully screen several images, and in the meanwhile, finding tiny nodules is exceedingly error-prone. The proposed framework provides the modus operandi of our method for automatic detection of lung cancer. In fact, it shows different activities involved in the system based on a supervised learning approach. Our framework is presented in Figure 1 which is based on the enhanced CNN model described in Section 3.3.

The given dataset is subjected to pre-processing where images are resized and made suitable for supervised learning. The data is divided into training (T1) and test (T2) datasets at 80% and 20% respectively. Data augmentation techniques like rotation, flip, zoom, shear and centre shift towards training the model for better performance. The enhanced CNN model presented in Section 3.3 is used in the training phase. In other words, the enhanced CNN model is trained with 80% training data. The model learns from the training data and gains discriminatory knowledge. The model is persisted for future reuse with transfer learning. The trained model is tested with unlabelled data. The model performs its predictions and it results in predicted labels about the presence of absence of lung cancer. Section 3.5 describes how the model is evaluated and performance statistics are derived. Our initial strategy for dealing with error-prone diagnosis of lung cancer is to segment the CT scan images following pre-processing. To create segmentation, a watershed algorithm is used. In lung images, watershed algorithms provide a camouflage for cancer cells. Ultimately, the optimized and trained models will be integrated to create a comprehensive final model for lung cancer classification.

3.3 Enhanced CNN Model and Algorithm

In this research, CNN model is preferred as the literature revealed that CNN is the most suitable deep-learning technique for medical image processing. An empirical study is made with the baseline CNN model and then enhanced it with different layers and configurations as illustrated in Figure 2.

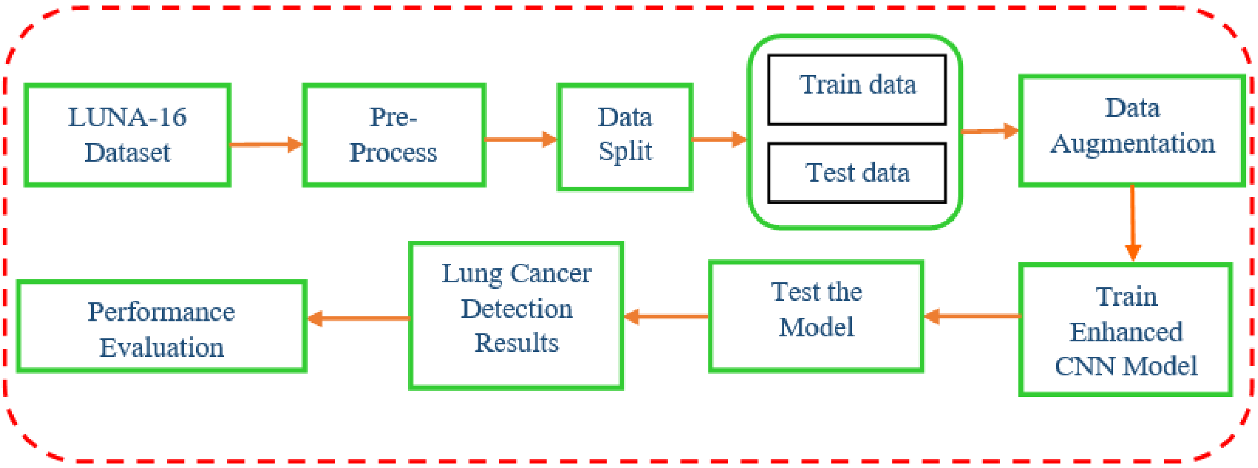


Figure 1. Proposed deep learning framework for lung cancer detection

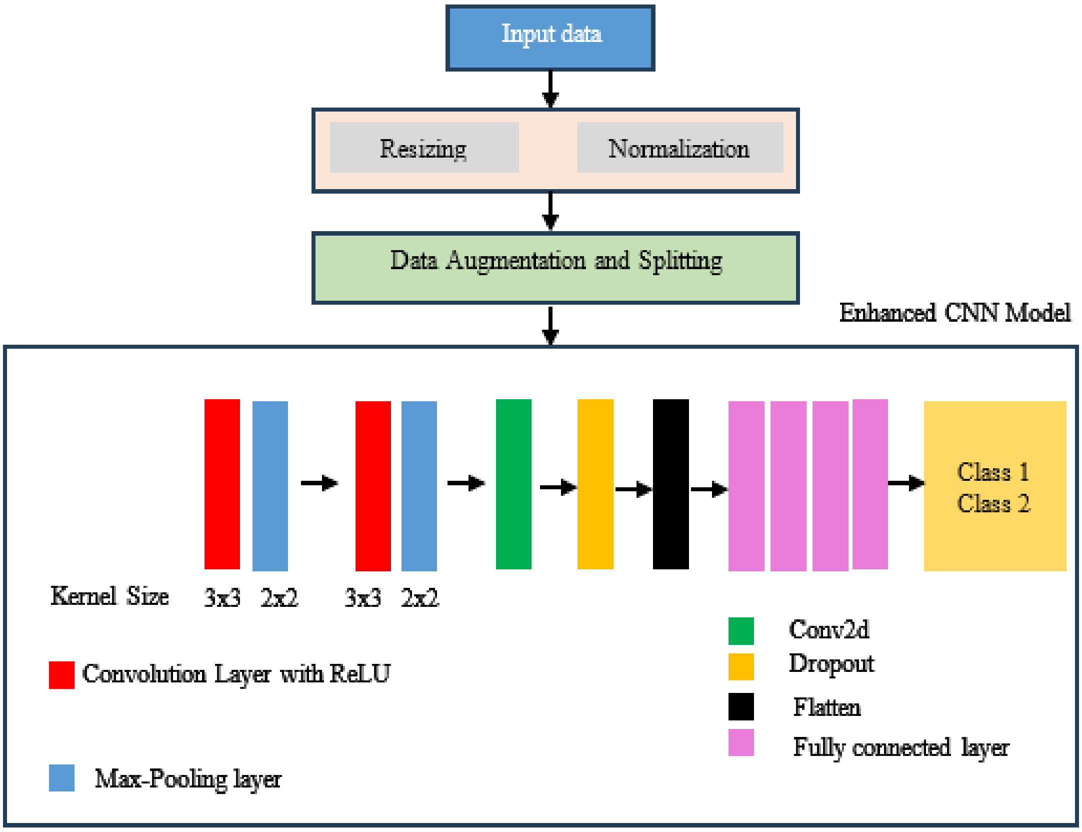


Figure 2. Proposed enhanced CNN model

Two pairs of convolutional and max pooling layers are configured first. In both convolutional layers, 32 filters are used and ReLU is the activation function used along with kernel size 3x3. In the two max pooling layers 2x2 is the kernel size, pool size 2 and stride is set to 2. Afterwards, a convolution is added with 32 filters and, 3x3 kernel with ReLU activation. This layer is followed by the dropout and flattening layer. Afterwards, a fully connected layer is configured with a dense layer with 128 units and ReLU, a dropout with 0.5, another dense layer with 128 units and ReLU and another dense layer with sigmoid activation function for binary classification of lung cancer with 2 labels.

Experiments are made with the baseline CNN model and also enhanced CNN model to detect lung cancer. An algorithm known as a learning-based Method for Lung Cancer Detection (LbM-LCD) is proposed to realize our framework. Empirical study is made with the LUNA-16 dataset.

Algorithm 1. Learning-based Method for Lung Cancer Detection (LbM-LCD)

Algorithm: Learning-based Method for Lung Cancer Detection (LbM-LCD)
Input: LUNA-16 dataset D
Output: Lung cancer detection results R, performance statistics P

1. Begin
2. D'←Preprocess(D)
3. (T1, T2)←DataSplit(D')
4. Configure enhanced CNN model m (as in Figure 2)
5. Compile m
6. Train m using T1
7. Save m for future reuse
8. Load m
9. R←Test(m, T2)
10. P←Evaluate(R, ground truth)
11. Display R
12. Display P
13. End

As presented in Algorithm 1, it takes the LUNA-16 dataset as input. The given dataset is subjected to pre-processing where images are resized and made suitable for supervised learning. The data is divided into training (T1) and test (T2) datasets in 80% and 20% respectively. Data augmentation techniques like rotation, flip, zoom, shear and centre shift towards training the model for better performance. The enhanced CNN model presented in Section 3.3 is used in the training phase. In other words, the enhanced CNN model is trained with 80% training data. The model learns from the training data and gains discriminatory knowledge. The model is persisted for future reuse with transfer learning. The trained model is tested with unlabelled data. The model performs its predictions and it results in predicted labels about the presence of absence of lung cancer.

3.4 Dataset Details

LUNA-16 is the dataset used for our empirical study. This dataset was made available in 2016 and since then it has been widely used in lung cancer research, particularly for lung segmentation. It has 888 CT images with 1186 annotated lung nodules. The dataset was collected from [43]. The LUNA16 dataset serves as the dataset's source. A subset of the LIDC-IDRI dataset, the LUNA16 dataset contains heterogeneous scans that have been filtered using several criteria. Because pulmonary nodules can be quite tiny, it is best to select a thin slice. Scan results that had a slice thickness more than 2.5 mm were thus rejected. Moreover, images that had missing slices or uneven slice spacing were not included. This resulted in 888 CT scans and 36,378 radiologists' annotations overall. Only the annotations classified as nodules > 3 mm are deemed significant in this dataset; non-nodules and nodules < 3 mm are not deemed useful for lung cancer screening techniques. When nodules discovered by several readers were closer together than the total of their radii, they were combined. Positions and sizes of these combined annotations were averaged in this instance.

3.5 Evaluation Methodology

Since the learning-based approach (supervised learning) is employed, metrics derived from the confusion matrix, shown in Figure 3, are used for the evaluation our methodology.

Based on the confusion matrix, the predicted labels of our method are compared with ground truth to arrive at performance statistics. Eq. 1 to Eq. 4 express different metrics used in the performance evaluation.

$$\text{Precision (p)} = \frac{TP}{TP+FP} \tag{1}$$

$$\text{Recall (r)} = \frac{TP}{TP+FN} \tag{2}$$

$$\text{F1-score} = 2 * \frac{(p * r)}{(p+r)} \tag{3}$$

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \tag{4}$$

The measures used for performance evaluation result in a value that lies between 0 and 1. These metrics are widely used in machine learning research.

4. Experimental Results

This section presents results of our experiments. Enhanced CNN model is used with Adam optimizer, binary cross entropy as loss function and number of epochs is 50. LUNA-16 dataset is used for experiments. Porotype is implemented using Python 3, Keras and Tensorflow libraries.

As presented in Figure 4, the LUN-16 dataset contains lung CT scan imagery from which an excerpt is provided.

4.1 Lung Analysis and Visualization

This section presents the results of lung analysis in terms of segmentation, marker-based analysis and nodule-based analysis. As presented in Figure 5, given patient's lung image is analysed and visualized for understanding its different views.

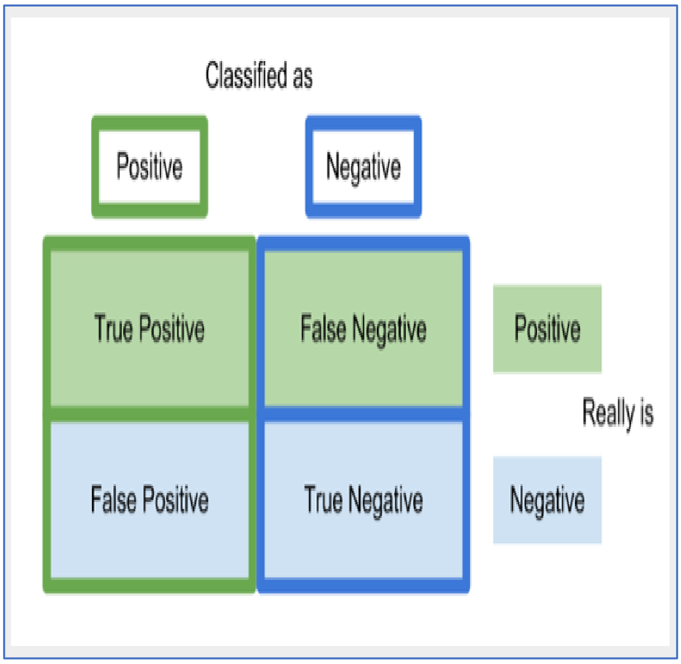


Figure 3. Confusion matrix

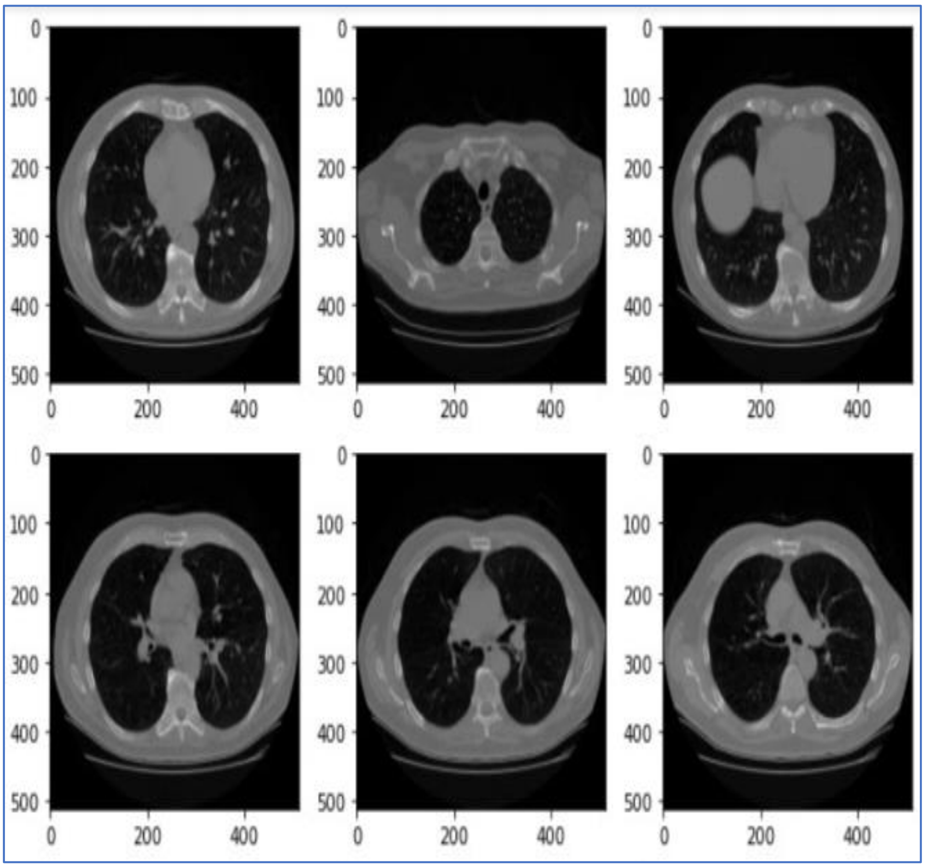


Figure 4. An excerpt taken from LUNA-16 dataset

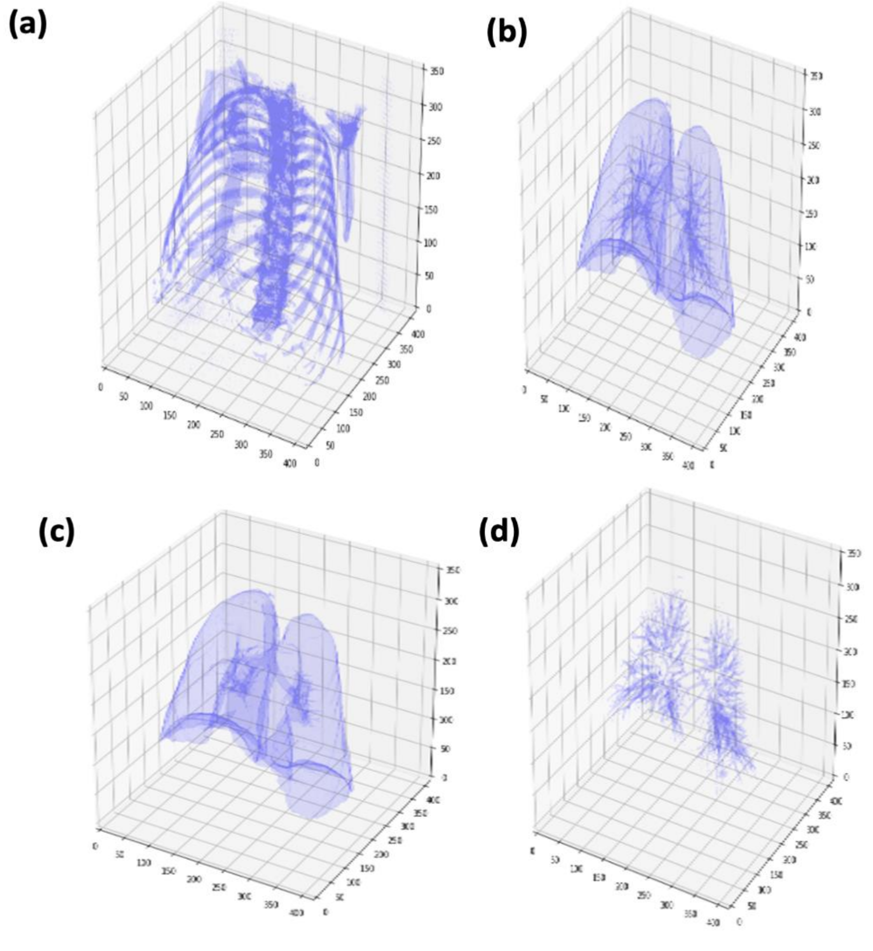
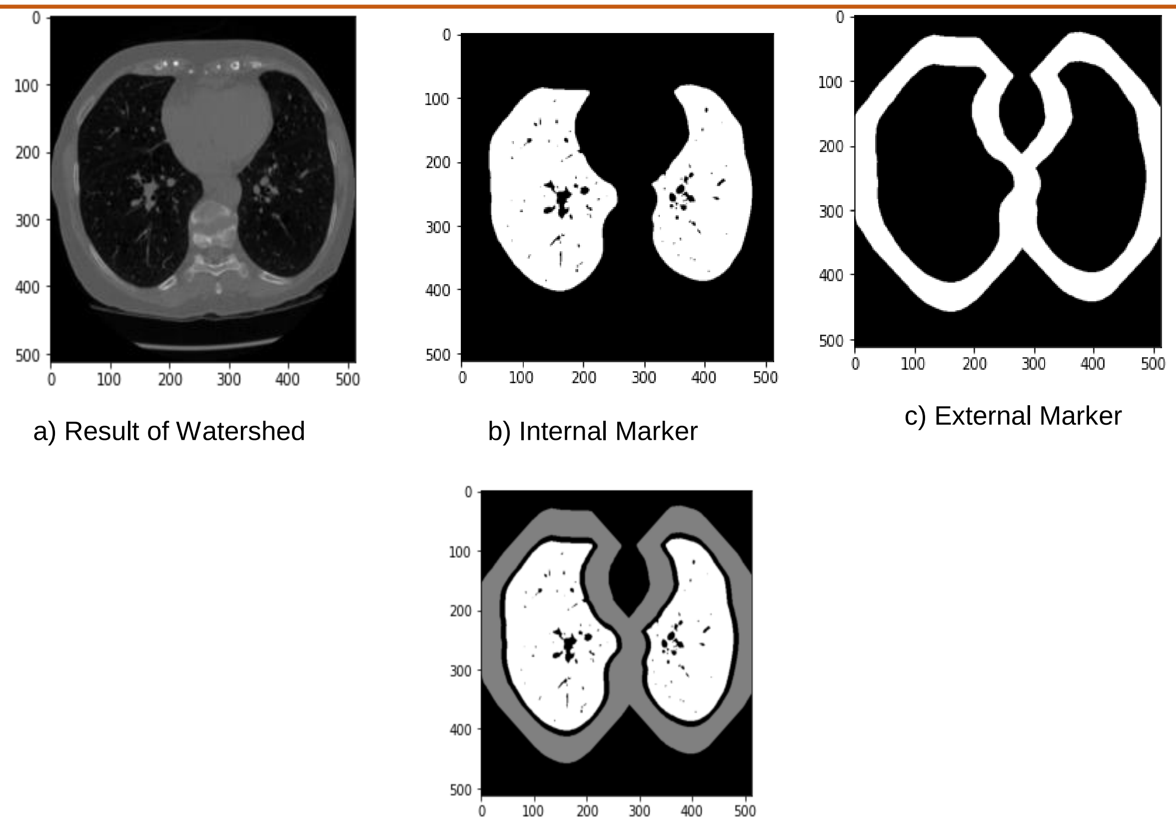


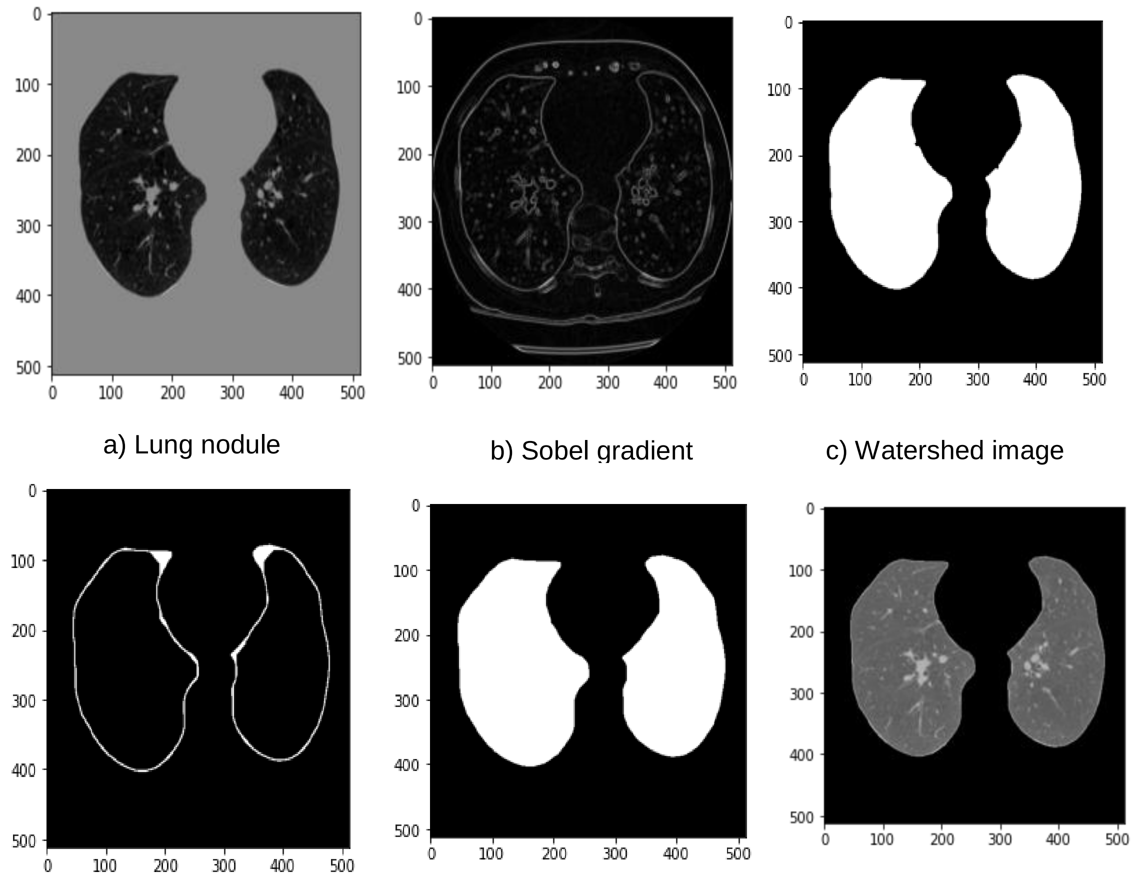
Figure 5. Results of lung analysis with visualization



a) Result of Watershed b) Internal Marker c) External Marker

d) Watershed Marker

Figure 6. Results of marker analysis on given patient's lung image



a) Lung nodule b) Sobel gradient c) Watershed image

d) Outline after e) Lung filter after f) Segmented lung

Figure 7. Results of nodule analysis on given patient's lung image

As presented in Figure 6, given patient's lung image is analysed and visualized for understanding its different views with marker analysis.As presented in Figure 7, given patient's lung image is analysed and visualized for understanding its different views with nodule analysis.

4.2 Results of Baseline CNN Model

Empirical observations of CNN baseline model are provided in this section in terms of loss and accuracy in the detection of lung cancer. As presented in Figure 8a, baseline CNN model's performance is provided in terms of accuracy against a number of epochs. As presented in Figure 8b, the baseline CNN model's performance is provided in terms of loss against number of epochs.

4.3 Results of Enhanced CNN Model

Empirical observations of the enhanced CNN model are provided in this section in terms of loss and accuracy in the detection of lung cancer.As presented in Figure 8c, the enhanced CNN model's performance is provided in terms of accuracy against a number of epochs.

As presented in Figure 8d, the enhanced CNN model's performance is provided in terms of loss against number of epochs.

4.4 Performance Comparison

This section compares the performance of baseline and enhanced CNN models for the automatic detection of lung cancer. As presented in Figure 12, the performance of the proposed enhanced CNN model is compared with the baseline CNN model. Different metrics are used for the evaluation of performance. A higher in value of any metric indicates better performance. The baseline CNN model achieved a precision of 94.56%, recall of 82.56%, F1-score 88.56% and accuracy 94.70%. The enhanced CNN model achieved a precision of 97.98%, recall of 93.86%, F1-score 95.92% and accuracy 98.34%.

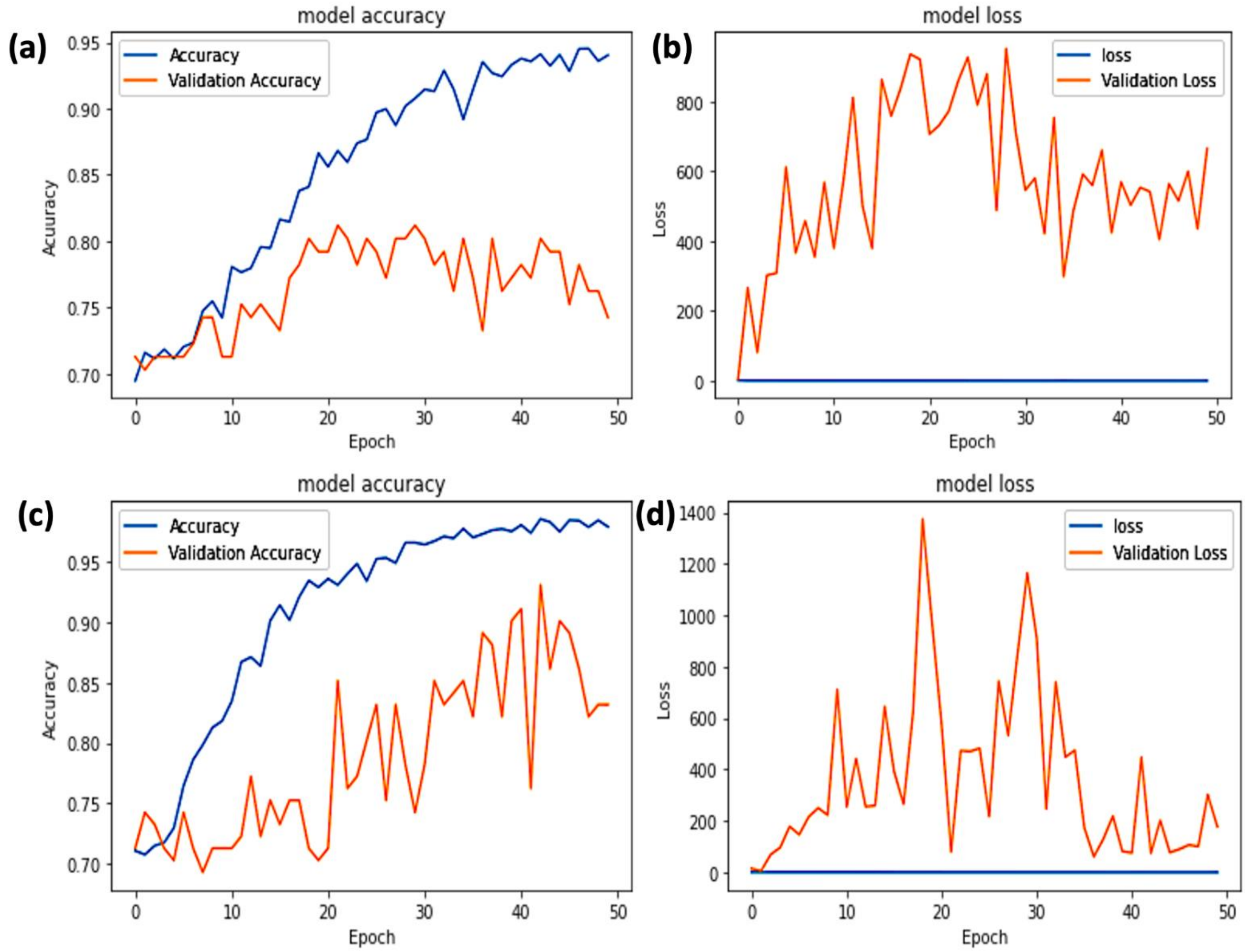


Figure 8(a). Accuracy dynamics of baseline CNN model **(b)** Loss dynamics of baseline CNN model, **(c)** Accuracy dynamics of enhanced CNN model, **(d)** Loss dynamics of enhanced CNN model

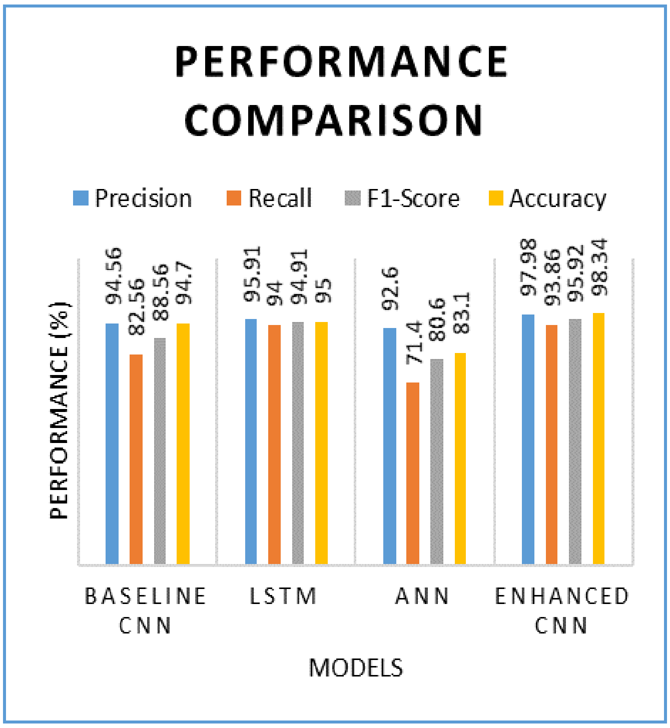


Figure 12. Performance comparison

LSTM showed 95.91 precision, 94% recall, 94.91% F1-score and 95% accuracy. ANN model achieved 92.60% precision, 71.40% recall, 80.60% F1-score and 83.10% accuracy. From the results, it is observed that the enhanced CNN model outperforms the baseline model in the detection of lung cancer with 98.34% accuracy.

5. Discussion

A deep learning framework and methodology is proposed for the automatic detection of lung cancer. Our method is based on an enhanced CNN model. The given dataset is subjected to pre-processing where images are resized and made suitable for supervised learning. Data augmentation techniques like rotation, flip, zoom, shear and centre shift towards training the model for better performance.

The model learns from the training data and gains discriminatory knowledge. The model is persisted for future reuse with transfer learning. The trained model is tested with unlabelled data. The model performs its predictions and it results in predicted labels pertaining to the presence of absence of lung cancer. CNN model was preferred as the literature revealed that CNN is the most suitable deep learning technique for medical image processing. An empirical study was made with the baseline CNN model and then enhanced it with different layers and configurations. Our framework is found to be useful in lung cancer detection. However, it has certain limitations.

5.1 Limitations

The first limitation of the proposed work is that it considers the detection of lung cancer but has no provision for the identification of different lung cancer types. In the empirical study, it was observed that the proposed model suffers from mediocre performance when low-quality lung CT images are used for detection. The enhanced CNN model was evaluated with a laboratory study. There is need for testing it with live samples in a healthcare unit.

6. Conclusion and Future Work

A deep learning framework for automatic detection of lung cancer is proposed besides enhancing the Convolutional Neural Network (CNN) model for better diagnosis of lung cancer. An algorithm known as a learning-based Method for Lung Cancer Detection (LbM-LCD) is proposed to realize our framework. Our algorithm takes given dataset, performs pre-processing, and splits it into training and test datasets for enabling supervised learning. The enhanced CNN model is configured in such a way that its performance is improved with the given dataset. Data augmentation also helped the proposed framework to improve the quality of training samples leading to better performance. The empirical study is made with the LUNA-16 dataset. Our experimental results showed that the enhanced CNN outperforms the baseline CNN model with 98.34% accuracy. Our research in this paper has certain limitations as mentioned in Section 5.1. In future, there is a chance to improve our framework for overcoming the aforementioned limitations and improving lung cancer detection and classification performance further.

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Authors Contribution Statement

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed By Sreedar Bhukya, Vishnu Ganagoni, Sujith Sriram Nangunoori, Sai Tharun Enapothula. The first draft of the manuscript was written by Sreedar Bhukya all authors reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Competing Interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject or materials discussed in this manuscript

Data Availability

The data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

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