Article published online: 2024-11-04

Deep Learning-Based Pulmonary Nodule Screening: A Narrative Review

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Ind J Med Paediatr Oncol

Abstract

Given its capacity to generate three-dimensional pictures, computed tomography is the most effective means of detecting lung nodules with more excellent resolution of detected nodules. Small lung nodules can easily be overlooked on chest X-rays, making interpretation difficult. Artificial intelligence algorithms have recently demonstrated remarkable progress in medical imaging, especially with deep learning techniques such as convolutional neural networks (CNNs). CNN produces excellent results in natural image recognition and classification using abundant available data and the computational abilities of modern computers. It further reduces false-positive pulmonary nodules in medical image processing. This review article provides a detailed and inclusive review of recent advances, challenges, performance comparisons, and possible future directions for the problem of pulmonary nodule screening using deep learning methods.

Keywords
- deep learning
- lung neoplasms
- screening
- AI
- diagnosis
- treatment outcome
- prognosis

Introduction

Lung cancer is one of the most prevalent cancers and a major reason for cancer-related deaths across the world. Patients' survival and prognosis largely depend on age, morphology, and stage at detection time.[1] The number of fatal cases can be significantly decreased by early diagnosis as early detection of lung cancer improves the survival rate. Different diagnostic procedures available for the early diagnosis of lung cancer include chest radiographs, computed tomography (CT) scans, positron emission tomography (PET), and biopsy.

The best method for investigating lung pathologies is CT imaging.[2] Due to its capacity to provide three-dimensional (3D) pictures with the superior resolution of identified nodules, CT is the most efficient tool for locating lung nodules. However, CT scans have a high rate of false-positive (FP) findings with an additional burden of potential adverse effects of radiation. For screening purposes, low-dose CT has shown promising results in decreasing mortality. While a regular chest CT has an effective dose of 4 to 18 mSv, low-dose CT has an effective dose of only ∼1.5 mSv. Low-dose CT can depict the structure of the lung without superimposition while causing less radiation exposure than conventional CT.[3] Hence, it has been used widely given its efficiency and ease of performance.

Besides CT, a chest X-ray is a potential option for screening nodules. Interpretation of chest X-rays is usually difficult, as small lung nodules can be missed. For effective lung cancer

DOI https://doi.org/10.1055/s-0044-1791954.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

screening, it is highly necessary to maintain a low false-negative rate. Cancer-related mortality in the study population was dramatically decreased in those who underwent low-dose CT scans compared with chest radiographs, as seen in the National Lung Screening Trial database.[4,5]

Artificial intelligence (AI) algorithms have recently demonstrated remarkable progress in medical imaging, especially with deep learning techniques such as convolutional neural networks (CNNs). CNN produces excellent results in natural image recognition and classification using abundant available data and the computational power of modern computers. Efforts in AI are advancing to reduce FP pulmonary nodules in automated methods of medical image processing.[6–8]

This review article will provide a comprehensive review of recent advances, challenges, performance comparisons, and possible future directions for the problem of pulmonary nodule screening using deep learning methods. We will also discuss the following:

- Available public datasets with a brief overview of deep learning.
- Recent advances in deep learning for pulmonary nodule screening.
- The clinical application of deep learning models.

Finally, this study summarizes the current state of AI for pulmonary nodule screening and shares future research directions in pulmonary nodule detection.

Current Scenario

The sensitivity for detection of pulmonary nodules relies on the number of CT slices, more for thinner slices and with better image registration techniques. One scan can generate up to 500 sections or slices, depending on the slice thickness.[9] It takes ~2 to 3.5 minutes for an experienced radiologist to observe a single slice.[10] There is a significant increase in the radiologist's workload to screen a CT scan for the presence of a lung nodule. In addition to the section thickness of the CT slices, detection sensitivity also depends on multiple different features of the nodule, such as size, location, shape, adjacent structures, edges, and density. The following important task is to assess whether the nodules detected are benign or malignant. Benign and malignant nodules have considerable feature overlaps. Estimating the probability of malignancy is challenging but essential for follow-up and further management. Morphological examination using thin-section CT is crucial in addition to the clinical context and metabolic assessment. The most critical elements in determining a nodule's malignant potential are its size and growth. The chance of malignancy is directly proportional to nodule diameter: as the diameter grows, the risk of malignancy increases proportionately. Even though benign and malignant nodules share many characteristics, morphology is still essential and should not be undervalued.[8–10]

A perifissural position, a triangular morphology, interior fat, and benign calcifications are characteristics of benignity. Nodules with spiculation, lobulation, pleural indentation, vascular convergence sign, related cystic airspace, bubble-like lucencies, irregular air bronchograms, and subsolid morphology are suspicious for malignancy. Nodules frequently display a variety of characteristics, and the combined information is more useful.[11] However, radiologists may still overlook pulmonary nodules for multiple reasons. Besides the individual performance of observers, nodule characteristics such as small size, inconspicuity, ill-defined margins, and location very close to adjacent vessels may result in missed lung cancers on CT.[12] Large sets of images, now available due to multidetector low-dose CT, can result in visual and mental fatigue for radiologists, leading to errors in interpretation during routine practice.[13] Also, radiologists who evaluate CT screening images face challenges such as the mechanical and tedious nature of work, small nodules being easy to miss, and the lack of consistent criteria. Missing a lung nodule/cancer in a radiological investigation is very concerning and is among the common causes of malpractice claims against radiologists.[14,15]

Computer-Aided Detection

As mentioned earlier, extensive research is ongoing with computer-aided diagnosis to overcome the challenge. Research in computer-aided detection (CAD) has been ongoing for more than 20 years to improve the accuracy and efficiency of detecting small lung nodules. Typical traditional CAD processes included image acquisition, lung field segmentation, candidate nodule detection, and FP mitigation (►**Fig. 1**).

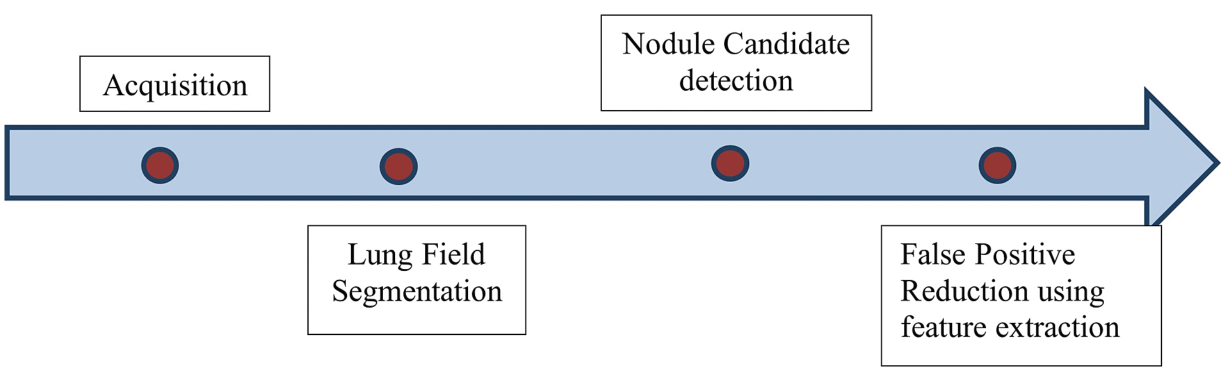

Fig. 1 Typical computer-aided detection processes: image acquisition, lung field segmentation, candidate nodule detection, and false-positive mitigation.

However, advanced detection algorithms and high-speed calculations have allowed the development of new CAD systems to be more effective and given them the ability to assist radiologists in detecting and characterizing lung nodules. Presently, using CAD alone is not generally acceptable in clinical practice.[16–18]

The CAD, as mentioned earlier, can be designed in multiple ways. (1) *Heuristic-based systems* use expert knowledge and traditional software. (2) *Data-driven systems* that learn the patterns in the data to meet specific objectives. Due to the complexity of the problem, the performance of heuristic-based systems is limited, and they are not robust to dynamic data. In recent years, data-oriented systems have surpassed the performance of heuristic-based systems. Earlier data-oriented systems were designed with manual handcrafted features such as histogram of oriented gradients), local binary patterns, and scale-invariant feature transform. These systems showed much promise; however, designing manual handcrafted features is challenging and domain-specific. Current state-of-the-art systems for AI are designed using deep learning methods that do not require feature engineering. These systems have surpassed heuristic-based systems and manual handcrafted features in terms of performance. Due to their adaptability and cutting-edge performance, these systems are rapidly being used to solve most computer vision challenges.[16–18]

Convolutional Neural Networks

CNNs, a particular type of deep learning model, are utilized for image interpretation. CNNs are effectively employed in various imaging detection and assessment procedures, including the identification of strokes, breast cancer lymph node metastases, skin cancer, diabetic retinopathy, colonic polyps, brain tumors, and lung cancers.[19–25]

AI detection of lung nodules has been awaited as a practical assistant in daily practice, especially for low-dose CT lung nodule screening. So far, multiple new deep neural network-based systems have shown potential for use in assisting radiologists to increase the accuracy and efficiency of nodule detection while being cost-effectiveness.

Open Datasets

Most of these systems have been taught using CT scans from the Lung Image Database Consortium/Image Database Resource Initiative, the Lung Nodule Analysis 2016 database, and the Automatic Nodule Detection 2009 database.[6,26–34]

Deep Learning

This section introduces deep learning, primarily deep convolutional neural networks (DCNNs). In general, deep neural networks process the input data layer by layer, feeding and output of one layer into the following. The output of the first layer is passed through a nonlinear activation function before passing it to the next layer. This design allows deep neural networks to learn very complex functions of data. Deep neural networks are also hierarchical because of their layered structure. Initial layers of the networks learn simple patterns, and later layers learn higher-level features. DCNNs are a specific type of neural network where shared weights of the neurons are designed with inductive bias that allows them to be shift/space invariant. The shared weights are used to perform an operation known as convolution.[6,26–30]

DCNNs are compelling models to work with image understanding problems. They were successfully used in LeNet for handwritten digit recognition. In 2012, Krizhevsky et al[35] used a DCNN named AlexNet to win the image challenge. With minimal preprocessing and no handcrafted features, the AlexNet-based solution won ILSVRC 2012 challenge by a large margin. This led to the adoption of DCNNs in various computer vision tasks. In the following years, new and improved architectures named VGG, ResNet, and DenseNet[36] have been proposed to improve the performance, ease of training, and scaling issues. Due to their effectiveness in computer vision, DCNNs have been the default first choice for medical imaging applications.

Deep Learning for Pulmonary Nodule

Pulmonary nodule-related AI applications can be divided into three settings: detection, segmentation, and classification. In detection, the objective of AI is to predict the position of the nodules inside the lung. Segmentation tries to predict the pixels or voxels of the nodule. Classification setting tried to predict the type of nodule, that is, benign or malignant.[6,26–36]

We will present these three applications of deep learning methods in this section.[6,26–36]

Pulmonary Nodule Segmentation

In this setting, AI aims to predict pixels/voxels of the nodule. The predictions can be used to do quantitative analysis of various clinical parameters of nodules, such as shape, volume, and distribution of pixel values (►**Fig. 2**).

Pulmonary Nodule Detection

The nodule detection setting locates the nodules by predicting 3D cubes around the nodule (►**Fig. 3**). This setting makes nodule AI explainable, which can assist radiologists in scan interpretations. The predictions can be used to analyze the size and location of the nodule.

Pulmonary Nodule Classification

Nodule classification AI uses predictions from nodule segmentation, nodule detection, or both modules. After extracting features using outputs from previous steps, AI can be trained on the features to classify the nodule into benign or malignant.

Major Challenges

As highlighted in the section on Deep learning for Pulmonary Nodule, many advances in AI have been using deep learning in recent years. Performance shows that, when deployed, these technologies can assist radiologists or can even operate

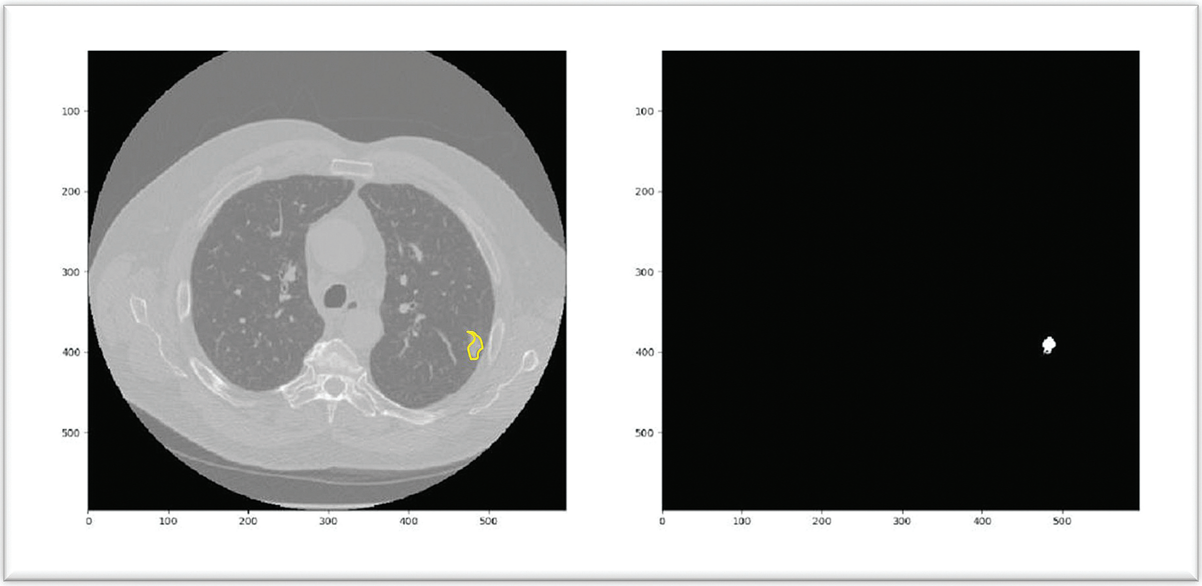

Fig. 2 Pulmonary nodule segmentation: an irregular solid nodule is segmented in the left lung highlighted in yellow.

independently. It will reduce the load on radiologists and also reduce diagnosis duration. However, there are challenges as we develop these systems for real-world deployments.[6,26–36] We highlight these challenges in this section.

Deep Learning Requires Large Datasets

Deep learning systems require large amounts of data to learn patterns in the data that are generalized well. Otherwise, they tend to overfit the data, and predictions on new patients will not be good. There have been significant strides in this direction with the release of many datasets in recent years, as described in the section on deep learning. However, more data will further help improve these systems, especially for different demographics of patients. Collaboration between AI research laboratories and hospitals might lead to more such datasets. It will also lead to a detailed analysis of the weaknesses of these systems.[6,26–36]

Need for Transfer Learning

Even though these systems perform well on large-scale open-source datasets, making them work on datasets specific to a demographic based on country or gender requires retraining for a particular dataset. Transfer learning resolves this by taking a pretrained network on a sizeable open-source dataset and retraining the last few layers of the network for a specific dataset. This is required because there are variations in scans such as size, resolution, and quality. Most of the time, this dataset also needs to be large enough for the AI to get the

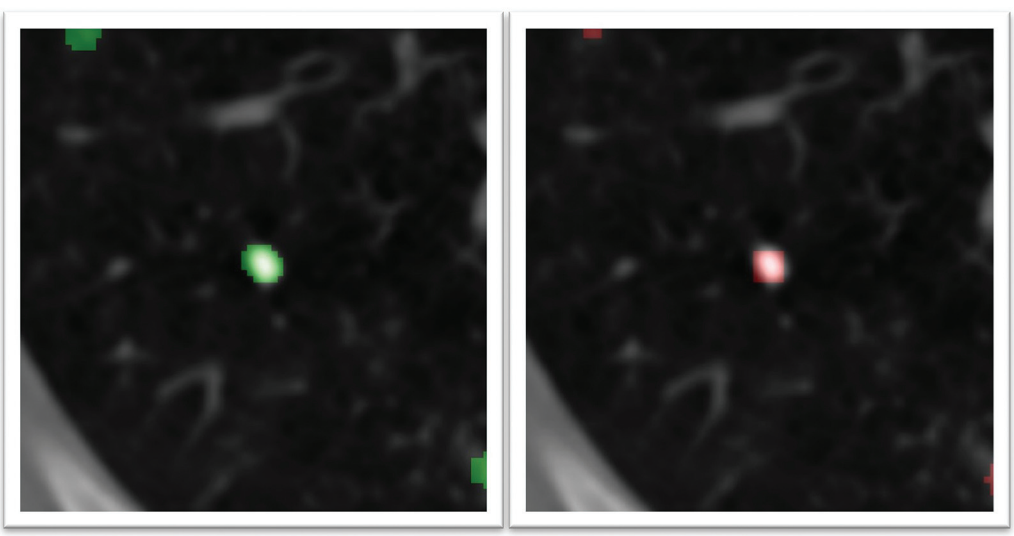

Fig. 3 Pulmonary Nodule deep learning model detected a nodule in the right lower lobe (highlighted in green) which corresponds to the nodule marked by the radiologist (highlighted in red).

expected performance. Further reducing this data requirement will improve the deployment of these systems.[6,26–36]

Interpretability, Explainability, and Bias

For health care systems such as pulmonary nodule AI, the system must be interpretable, explainable, and unbiased. Due to the complex nature of deep neural networks, making them interpretable and explainable is challenging. However, improving interoperability and explainability will give radiologists more confidence, and AI. as assistive technology will benefit tremendously.[6,26–36]

There is also inherent bias in deep learning systems if the systems are not trained on carefully curated datasets and evaluated before deployment. This also makes it necessary to test these systems against bias on carefully curated data before deployment.[6,26–36]

Conclusion

The conclusion infers that AI detection modules with/without CAD can be an effective tool to help future radiologists with adequate global and local standards for early diagnosis of lung malignancies and lowering mortality.

Ethical Approval
Not applicable.

Consent to Participate
Not applicable.

Note
The article is not under consideration for publication elsewhere. Each author participated sufficiently for the work to be submitted. The publication is approved by all authors.

Authors' Contribution
A.M. and K.S.S.B. contributed to the conceptualization, and design of the work. A.M., U.A., R.A., A.V., S.S., K.S.S.B., M.L.V.A., V.P., and V.P. contributed to writing—original draft, and writing—review and editing.

Patient Consent
N/A

Funding
None.

Conflict of Interest
None declared.

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