CAHIERS MAGELLANES-NS
Volume 06 Issue 2
2024

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

"A COMPREHENSIVE REVIEW OF DEEP LEARNING TECHNIQUES FOR LUNG CANCER DETECTION AND CLASSIFICATION"

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Abstract
A crucial problem in medical imaging, the identification and categorization of lung cancer using computed tomography (CT) scans has significant consequences for early diagnosis and therapy. With an emphasis on different models and their performance evaluation, this study reviews and synthesizes recent advancements, spanning from traditional machine learning to advanced deep learning methods, for diagnosing lung cancer. The approaches cover a broad spectrum of methods, from conventional machine learning to advanced deep learning models and each brings a special strength to the field of lung cancer diagnosis. The combined results show that hybrid models, multi-scale learning, and 3D methods greatly improve detection robustness and accuracy. In order to increase model transparency and clinical acceptance, future research directions include integrating multi-modal data, improving data augmentation methods, and utilizing explainable AI.

Keywords: *Lung Cancer, Computed Tomography, Deep Learning methods, Data Augmentation, Performance Evaluation.*

1. Introduction
Radiologists use low-dose helical computed tomography (LDCT) to detect lung nodules but whether the nodules are benign or malign cannot be confirmed. Depending on the size and traits of nodules present in an LDCT scan, a follow-up LDCT or a chest CT scan with contrast and/or a Positron Emission Tomography (PET) –CT scan may be taken for diagnosing lung cancer. Such screening measures would require radiologists to examine a vast number of computed tomography (CT) scans, making the process time-consuming and labor-intensive. Deep learning techniques are increasingly utilized in medical imaging and this has led to the development of modern Computer-aided Diagnosis (CAD) systems which assists radiologists in reading CT scans [29]. Deep Learning in CAD systems is used because they enable us to develop an end-to-end system which learns both the salient features and classification stages on its own during training. Though neural networks produce results with acceptable accuracy, they lack transparency. Hence they are called "Black-Box models". To overcome this gap, researchers are using Explainable Artificial Intelligence (XAI) to explain the outcomes of their algorithms.

2. Objectives of the review
- To provide a comprehensive overview of deep learning techniques.
- To provide an overview of commonly used datasets and preprocessing techniques.

CAHIERS MAGELLANES-NS
Volume 06 Issue 2
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ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

- To evaluate the performance of different models.
- To identify current challenges and future directions.

3. Methodology

The literature search includes databases such as PubMed, IEEE Xplore, Scopus, arXiv, and Google Scholar. The keywords used for search are ‘lung cancer detection’, ‘Deep learning for lung cancer diagnosis’, ‘Convolutional Neural Networks’, and ‘AI in health care’. Papers published within the last 8 years that focus on non-invasive techniques for lung cancer detection and classification are considered.

4. Lung Cancer

Common symptoms of lung cancer are shortness of breath, chest pain, and persistent cough. The most common lung cancers are small cell carcinoma (SCLC) and non-small cell carcinoma (NSCLC). The distinction between the two is that SCLC (Small Cell Lung Cancer) is less common but grows rapidly, whereas NSCLC (Non-Small Cell Lung Cancer) is more prevalent and tends to grow more slowly.

Diagnosis:

Diagnosing lung cancer involves a variety of methods, including physical examinations, imaging techniques such as CT scans, MRIs, and chest X-rays, bronchoscopy to examine the inside of the lung, biopsies to collect tissue samples for histopathology analysis and subtype identification (such as distinguishing NSCLC from SCLC), and molecular testing to detect specific genetic mutations or biomarkers. These approaches collectively contribute to an accurate diagnosis and inform treatment decisions tailored to the individual patient's condition.

Survival:

In males, the one-year survival rate for lung cancer is 30%, while in females, it is slightly higher at 35% and the overall five-year survival rate is a dismal 9.5%. These statistics underscore the serious and often fatal nature of the disease, highlighting the urgent need for improved diagnostic and treatment strategies.

Risk factors of lung cancer:

- Smoking cigarettes, both actively and passively.
- Come into contact with toxins such diesel fumes, radon, asbestos, and coal smoke.
- Genetic predisposition (family history): differences in the way that certain substances are metabolized.
- Scar carcinoma: tumours can develop from regions of persistent fibrosis.
- Idiopathic pulmonary fibrosis.
- Smoking has been linked to lung cancer in about 90% of cases. Lung cancer risk is increased 1.5 times by passive smoking.

Risk assessment:

Based on age and pack years of smoking, the National Comprehensive Cancer Network (NCCN) has separated the risk groups into two groups namely high-risk and low-risk. According to NCCN, “A pack-year is defined as the average number of packs of cigarettes smoked per day multiplied by the total number of years the individual has smoked.

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

High risk: anyone 50 years of age or older who has smoked cigarettes for at least 20 pack years. For individuals at high risk, it is recommended to undergo low-dose computed tomography (LDCT) screening.

Low risk: individuals who have smoked fewer than 20 pack years of cigarettes or are under 50 years of age. Screening of the lungs is not advised for low risk group.

4. Deep learning architectures used for lung cancer diagnosis

The deep learning techniques used for lung cancer diagnosis are described below.

4.1 Convolutional Neural Networks (CNNs)

CNNs (Convolutional Neural Networks) are key in computer vision tasks like image recognition, object detection, and image classification. They consist of several layers:
Convolutional Layers: Utilize learnable filters to perform convolution operations, extracting local patterns and generating feature maps that capture hierarchical features.
Activation Layers: Apply non-linear functions (e.g., ReLU) element-wise to enhance training convergence and introduce sparsity by replacing negative values with zeros.
Pooling Layers: Reduce spatial dimensions and provide translation invariance through functions like max pooling and average pooling.
Fully Connected Layers: Connect each neuron to every neuron in the previous layer, enabling high-level reasoning and complex relationship learning.
Output Layer: Uses a softmax activation function in classification tasks to produce class probabilities based on learned features.
Training Process: Involves backpropagation and gradient descent to iteratively adjust parameters, minimizing a loss function like cross-entropy.
Regularization Techniques: Include dropout (randomly ignoring neurons during training), batch normalization (normalizing layer inputs), and weight decay (penalizing large weights) to prevent overfitting and enhance generalization.

4.2 Ensemble

Ensembles are methods that combine several baseline models to create more powerful models [30]. Due to the variety of baseline models, ensemble learning has the advantage of lowering the danger of overfitting. Ensemble methods vary in how they integrate and train distinct baseline models. The different ensemble techniques include stacking, boosting, random forest, bagging, and averaging.

4.3 Transfer learning

Transfer learning involves training a model on a large, general dataset and then fine-tuning it on a smaller, application-specific dataset. The process transfers the learned weights from the initial task (task A) to a new task (task B), compensating for limited data in the target domain. In practice, this involves using a pre-trained model and fine-tuning it on the target task, such as detecting lung cancer in medical images. This approach allows the model to retain and adapt the knowledge (features, patterns) learned from the original dataset to the specifics of the new dataset.

4.4 Explainable Artificial Intelligence (XAI)

Neural Networks, despite their satisfactory outcomes, function as "black-boxes" with minimal transparency, making it difficult even for developers to understand their decision-making process. Explainability is crucial in complex situations, though developing explainable models requires

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

additional time and effort and may affect prediction accuracy. Combining deep neural networks with explainable AI enhances disease detection and diagnosis by providing medical professionals with insights, fostering trust in the model's decisions. An explainable model offers human-level explanations for its predictions, while an interpretable model allows for insights into its internal workings or predictions.

5. Imaging Data

Common imaging modalities employed in diagnosis of lung cancer include chest X-rays, computed tomography (CT), and positron emission tomography (PET) scans. Each modality offers distinct advantages and drawbacks in the detection and evaluation of lung cancer. Most of the papers we have gone through have used CT scans.

Chest X-rays (CXRs):

CXRs are frequently utilized as the first screening method for lung cancer. CXRs give a two-dimensional picture of the chest enabling radiologists to detect anomalies like masses, nodules, or infiltrates. The drawback of CXR is that they are less useful for identifying tiny or subtle lesions.

Computed Tomography (CT) scans:

CT scans are radiographic scans that produces internal images of the chest using x-ray technology. The scan involves a specialized machine that captures multiple images of your lungs, referred to as slices. These slices are subsequently compiled to generate a comprehensive picture of your lungs, enabling radiologists to assess and evaluate them thoroughly. CT scans are generally considered as the gold standard for lung cancer imaging because of their superior spatial resolution and ability to show small lesions.

Positron Emission Tomography (PET) scans:

PET (Positron Emission Tomography) is a nuclear imaging technique that visualizes metabolic activity within the body. It involves injecting a radiotracer, fluorodeoxyglucose (FDG), which accumulates in cancer cells due to their high sugar consumption. Increased FDG uptake on the scan indicates higher metabolic activity, suggesting cancerous growths. PET scans assess cancer spread and treatment response, often combined with CT scans to create PET-CT scans. This dual-modality approach integrates metabolic information from PET with anatomical details from CT, offering detailed insights for accurate staging and effective treatment planning in lung cancer.

6. Commonly used datasets

Trajanovski et al. [9], Ardila et al. [12], and Afshar et al. [15] have used The National Lung Screening Trial (NLST) dataset. This dataset has details of 53,000 people who participated in the trail. NLST dataset includes **demographic data such as a**ge, gender, smoking history, Low Dose Computed Tomography (LDCT) and chest X-ray screenings, information on diagnostic procedures, follow-up screenings, and biopsy results, data on lung cancer diagnoses, cancer staging, treatments, and mortality. Trajanovski et al. [9] have also used Lahey Hospital and Medical Center (LHMC), Kaggle competition data (from both stages 0f 2017), and the University of Chicago data (UCM) a subset of NLST, annotated by radiologists.

Yan et al. [10] and Ling Fu et al. [18] have used Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI) [11] data set. The LIDC/IDRI Database comprises 1,018 cases, each containing clinical thoracic CT scan images and an XML file detailing a two-phase annotation process

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

by four thoracic radiologists. In the initial blinded-read phase, each radiologist independently marked lesions as "nodule ≥3 mm," "nodule <3 mm," or "non-nodule ≥3 mm." In the subsequent unblinded-read phase, radiologists reviewed their marks alongside anonymized marks from their peers to render final opinions. This comprehensive dataset supports the development and evaluation of computer-aided detection and diagnostic algorithms for lung cancer.

Rehan Raza et al. [23] used the lung cancer dataset from the Iraq-Oncology Teaching Hospital/National Center for Cancer Diseases (IQ-OTH/NCCD), which contains three classes: benign, malignant, and normal.

7. Preprocessing

Preprocessing steps for lung CT scan images typically involve several essential procedures to ensure optimal quality and compatibility for training deep learning models:

a) **Acquiring and Format Conversion**: Obtain high-resolution CT scan images of the lungs in DICOM format, a standard for medical imaging.
b) **Annotation and Quality Control**: Radiologists manually annotate images to identify regions of interest (e.g., tumors). Images with significant artifacts or low quality are excluded to prevent interference during training.
c) **Standardization of Image Size**: Resize all images to a uniform size because CNNs (Convolutional Neural Networks) require fixed-size inputs for processing.
d) **Intensity Normalization**: Normalize pixel values across images to ensure consistency in image contrast and brightness. This step helps in standardizing the input data range, which aids in model convergence during training.
e) **Denoising Techniques**: Apply denoising algorithms to enhance image quality by reducing noise and artifacts. This step improves the clarity of features crucial for accurate analysis.
f) **Data Augmentation**: Image transformation techniques are applied to increase the number of images in the input dataset. Common techniques applied are rotation, flipping, scaling, and adding noise. Data augmentation is also done to avoid overfitting and improve model generalization by exposing it to variations in input data.

8. Performance Evaluation

The statistical measures used by the authors of the reviewed papers to evaluate the performance of their models are Recall or Sensitivity or True Positive Rate (TPR), Precision or Confidence or True Positive Accuracy (TPA), Specificity or Inverse Recall or True Negative Rate (TNR), Precision or Confidence or True Positive Accuracy (TPA), Specificity or Inverse Recall or True negative rate (TNR), Accuracy (Total true results), Fallout or False Positive Rate (FPR), F1-Score, Receiver Operating Characteristic (ROC) curve.

9. Models for Lung Cancer classification

Conventional techniques for classifying images required two steps: First, features are extracted from images using hand-crafted feature extraction approaches such as Color Histograms, Local Binary Patterns (LBP), Histogram of Oriented Gradients (HOG), and Scale Invariant Feature Transform (SIFT). These methods analyze specific characteristics of the image, capturing information like color distribution (Color Histograms), texture patterns (LBP and HOG), and distinctive keypoints (SIFT). The second phase is a learning process called classification. Machine learning methods like Random Forests, k-Nearest Neighbours (k-NN), Support Vector Machines (SVM), and Naive Bayes Classifier are used for classification. After extracting key features from images, they are used as inputs to train a

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

classifier. The classifier learns from these extracted features to identify the category of lung cancer.

Convolutional Neural Networks (CNNs) are utilised for classification of image since the development of deep learning. CNNs are fully trainable end-to-end models that simultaneously learn the features and classification phases. Convolutional neural network (CNN) [4] models have demonstrated exceptional performance in picture classification and recognition tasks. Examples of these models are AlexNet, VGG, ResNet, and Inception. [5] [6] [7]. Transfer learning is employed to reduce training time and is also used in situations where sufficient training data is not available. Explainable AI (XAI) is utilized to enhance the interpretability of complex machine learning models and to ensure compliance with regulatory requirements. [8] covers popular medical imaging modalities, clinical applications of machine learning (ML) and deep learning (DL) models, and techniques to guarantee secure, confidential, and reliable ML for healthcare applications.

Trajanovski et al. [9] developed a two-stage Machine Learning framework for assessing cancer risk in CT scans. In the first stage, an SVM detects nodules using metadata like location, size, sphericity, and confidence. In the second stage, the top ten nodules are analyzed using a ResNet-like architecture to evaluate cancer risk. They tested the framework with two nodule detectors: Liao et al.'s deep neural network semantic segmentation and Bergtholdt et al.'s hierarchical SVMs. Localized cubes ($32 \times 32 \times 32$ mm^3) around detected nodules were used to extract random subimages ($28 \times 28 \times 28$ mm^3) for training, improving generalization and reducing overfitting. Three 2D projections (coronal, sagittal, transverse) from these subimages were used as input to the neural network. The framework was trained on subsets of the NLST dataset and validated on various datasets. They found that nodule location and patient outcomes were sufficient for training, while additional characteristics like spiculation were unnecessary.

The 3D CNN modeled proposed by Yan et al. [10] employs 3D filters for malignancy classification and have used Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI) [11] data set. 3D filters, due to their ability to capture the spatial relationships across different axial slices and also detect volumetric variations within nodules, are a preferred choice compared to 2 D filters. This capability allows them to analyze three-dimensional structures more comprehensively compared to their 2D counterparts, which operate solely within individual image planes. There are different number of filters in the convolutional layers (20, 40, 80, and 80 filters) and uses kernels of varying sizes (5x5x2, 5x5x2, 4x4x2, and 4x4x2). Max-pooling with a size of 2x2 is applied in both the x and y dimensions within the pooling layers. Stochastic gradient descent is used to train the 3D network, utilizing a 64x64x5 patch for training and comparison. They have also developed a 2D slice-level CNN and a 2D nodule-level CNN, achieving classification accuracies of 86.7% and 87.3%, respectively. Their 3D model with a classification accuracy of 87.4% was only slightly better than the 2D models.

Ardila et al. [12] developed a deep learning framework for lung cancer screening comprising three models. The Full-Volume 3D CNN analyzes entire CT volumes end-to-end, trained with low-dose CT data. The Cancer ROI Detection Model identifies potential malignancy regions using both current and prior CT volumes. The Risk Prediction Model combines outputs from the previous two models to predict cancer risk and assign a malignancy score. Tested on the NLST dataset (42,290 CT cases), the model achieved an AUC of 94.4%, outperforming six radiologists in sensitivity and specificity. It also performed well in a retrospective reader study, even without baseline CT scans.

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
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The classification algorithm, termed "Kernel Attribute Selected Classifier (KASC)", proposed by Pankaj Nanglia et al. [13], is a hybrid approach that integrates Support Vector Machine (SVM) and Neural Network (NN) techniques. KASC leverages the ELCAP lung image dataset initially developed by Cornell University in 2003, which includes fifty low-dose CT scan images having a slice thickness of 1.25 mm. In KASC, the Neural Network component consists of a combination of Feed Forward (FF) and Back Propagation (BP) networks, referred to as Feed Forward Back Propagation Neural Network (FFBPNN). The algorithm is structured into three main blocks:

1. **Data Preprocessing (BLOCK-PP)**: In this block, the dataset undergoes preprocessing steps to improve the quality of images that are used for subsequent analysis.
2. **Feature Extraction and Optimization (BLOCK-FEO)**: Here, Key features are extracted from the preprocessed data and optimized to enhance classification performance.
3. **Hybridization of SVM and NN for Prediction (BLOCK-HB)**: This block integrates SVM and the FFBPNN to make predictions. SVM is known for effective classification based on kernel functions, while the FFBPNN provides additional learning capabilities through its neural network architecture.

By combining these methods, KASC aims to leverage the strengths of both SVM and NN to enhance classification accuracy and robustness in the context of lung image analysis. This hybrid approach facilitates more effective detection and characterization of lung abnormalities, contributing to advancements in medical imaging diagnostics. Though KASC algorithm for lung cancer classification uses just 500 CT image data samples, it achieves impressive performance metrics. Precision is 98.17%, Accuracy is 98.08%, Recall is 96.5% and F-measure is 97%.

Afshar et al. [15] developed two models for predicting lung nodule malignancy: the 3D Multi-Scale Capsule Network (3D-MCN) and a 3D-CNN, which lacks the Capsule design. The 3D-MCN uses three Capsule Networks to process nodule patches at multiple scales, learning from regions around the nodule. The 3D-CNN model, similar but without Capsules, relies solely on convolutional operations. Nodule patches were extracted at three scales and resized to 80 × 80 pixels. After normalization and augmentation, the models were trained and evaluated. The 3D-MCN achieved an AUC of 0.9641, accuracy of 93.12%, sensitivity of 94.94%, and specificity of 90%, showcasing its high performance in distinguishing between benign and malignant nodules.

Causey et al. [16] developed two deep learning models, CNN47 and CNN21, for predicting lung nodule malignancy using CT scans. The models used small 3D volumes extracted from full CT scans: CNN21 utilized 21x21x5 pixel volumes, and CNN47 used 47x47x5 pixel volumes. Radiologists segmented nodules, determined their centroids, and extracted 3D volumes centered on the average centroid. The dataset was split into 80% for training and 20% for testing, with a batch size of 64 and 200-400 epochs for training. The study compared two approaches: one using CNN features alone and another combining CNN features with 50 quantitative image features (QIFs). While a softmax classifier was used for CNN features alone, a Random Forest classifier was employed for the combined feature vector of 200 CNN features and 50 QIFs. The CNN47+RF model achieved an AUC of 0.993, accuracy of 0.952, sensitivity of 0.942, and specificity of 0.962, highlighting the benefit of integrating QIFs with CNN features for enhanced prediction performance.

Hongtao Xie et al. [17] proposed a two-stage deep learning framework to automate the process of pulmonary nodule detection in CT images. The key aspects of their approach are nodule candidate detection in stage 1, and false positive reduction in stage 2. The nodule candidate detection stage uses a 2D convolutional neural network (CNN) comprising of three sub-networks namely, Region-of-

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
http://magellanes.com/

Interest (ROI) classifier, Feature extraction network (using VGG16), and Region proposal network. To capture nodules of different sizes, the researchers used three separate models trained on the middle slice, top neighboring slice, and bottom neighboring slice, along with their two adjacent slices. The output of this stage is a set of nodule candidates with high objectness scores. A boosting-based classifier is used in the false positive reduction stage. This classifier is trained to reduce the number of false positive detections from the first stage. This classifier leverages the features extracted by the CNN to distinguish true nodules from false positives.

Ling Fu et al. [18] developed a two-stage system for detecting lung nodules in CT scans using CNNs and hand-crafted features to reduce false positives. Utilizing the LIDC-IDRI database, they extracted 27 patches per candidate nodule from 9 specific planes and incorporated blood vessel-enhanced and nodule-enhanced images. They trained 27 CNNs, extracting 32 features from each, totaling 864 CNN features, and compared them with 288 features extracted from lung CT scans. Hand-crafted features included 14 intensity-related, 8 shape-related, and 66 texture-related features, totaling 88. Classification was done using SVM, evaluated with FROC curves. The CNN with 864 features outperformed the one with 288 features when false positives per scan exceeded 1.5. Integrating hand-crafted features with CNN features enhanced performance, achieving sensitivities of 90.9% at 4 false positives per scan and 78.2% at 1 false positive per scan.

Rehan Raza et al. [23] proposed "Lung-EffNet" for classifying lung cancer from CT scans using transfer learning with EfficientNet variants (B0 to B4) pre-trained on ImageNet. The dataset from IQ-OTH/NCCD includes benign, malignant, and normal classes. Images were preprocessed and augmented to address class imbalance. The model features a Global Average Pooling layer, dropout layer (0.5), and a 3-unit output layer with softmax activation for multi-class classification. The EfficientNet kernels remained unchanged to prevent overfitting. Lung-EffNet achieved a test accuracy of 99.10%, precision of 100%, and ROC scores ranging from 0.97 to 0.99.

10. Research findings

The studies reviewed demonstrate significant progress in the detection and classification of lung cancer by making use of deep learning models. These models leverage advanced techniques like CNNs, 3D CNNs, SVMs, Capsule Networks, and hybrid models to enhance accuracy, sensitivity, and specificity in identifying malignant lung nodules. Common datasets such as NLST, LIDC-IDRI, and others serve as benchmarks, allowing for performance comparison across different methods. Our research underscores the versatility and efficacy of deep learning techniques in lung cancer detection. Several key insights emerge:

- **3D Data Utilization:** Models that incorporate 3D data (e.g., Yan et al., Ardila et al., Afshar et al.) consistently outperform their 2D counterparts, leveraging volumetric information for better spatial context.
- **Hybrid and Ensemble Models:** Combining different models or techniques, as seen in Trajanovski et al. and Causey et al., often results in superior performance, highlighting the value of integrating multiple methodologies.
- **Data Augmentation and Preprocessing**: Effective preprocessing steps and data augmentation (e.g., Raza et al.) are crucial for improving model robustness and generalizability.
- **Transfer Learning:** The power of transfer learning is demonstrated by the ability to achieve high performance even with limited data wherein models that are pre-trained are used and fine-tuned for particular task. (e.g., Raza et al.).

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632574
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11. Future Directions

Future research can prioritize the following areas to improve the effectiveness of lung cancer detection.

Enhancing Model Generalizability: Utilize multi-institutional datasets to improve model performance across diverse populations and scanning protocols. Explore advanced transfer learning techniques, such as EfficientNet, to boost performance on limited datasets.

Model Interpretability: Develop explainable AI models that provide clear reasoning for predictions, crucial for clinical trust and decision-making.

Integration with Clinical Workflows: Conduct clinical trials to evaluate real-world utility and impact. Design user-friendly interfaces that integrate smoothly with existing clinical practices.

Robustness and Reliability: Implement adversarial training to make models robust against data perturbations and establish continuous learning systems to keep models updated with new data.

Combining Imaging with Non-imaging Data: Integrate imaging data with other clinical information, such as genetic or pathological data, to enhance diagnostic accuracy and provide a comprehensive assessment.

12. Conclusion

The reviewed literature demonstrates the noteworthy progress made in the detection and classification of lung cancer through the use of deep learning. Models leveraging 3D data, hybrid approaches, and transfer learning show the most promise, achieving high accuracy, sensitivity, and specificity. Future research should focus on enhancing generalizability, interpretability, and integration with clinical workflows to maximize the impact of these technologies in healthcare. By tackling these issues, we can get closer to utilizing AI to its fullest potential in detecting lung cancer early and enhancing patient outcomes.

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