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Review

The advancements in artificial intelligence towards the diagnosis of lung cancer

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Abstract

Lung cancer remains the leading cause of cancer-related mortality worldwide, with delayed diagnosis being a major contributor to poor outcomes. Artificial intelligence (AI) has emerged as a transformative tool for enhancing diagnostic accuracy, improving early detection, and enabling personalized treatment strategies. This non-systematic review evaluates current advancements in AI for lung cancer diagnosis across imaging, pathology, and integrative risk stratification. AI-assisted radiological tools, including deep learning models applied to chest X-rays, CT scans, PET/CT, and thoracoscopic images, have demonstrated superior sensitivity and specificity in detecting pulmonary nodules and staging disease compared to conventional radiology. In pathology, AI applications in histological classification, biomarker detection, and prediction of tumor invasiveness have significantly improved diagnostic precision and reproducibility, supporting tailored therapeutic decision-making. Integrative multimodal AI models that combine imaging, clinical, and genomic data have further enhanced prognostic assessment and risk stratification. Despite these advancements, challenges remain regarding data availability, interpretability, ethical concerns, and legal implications of AI autonomy in clinical practice. Future progress will require explainable, transparent, and prospectively validated AI systems developed in close collaboration between clinicians and technology experts. Overall, AI holds the potential to revolutionize lung cancer diagnostics by enabling earlier detection, personalized care, and improved patient outcomes.

Keywords

artificial intelligence, early diagnosis, lung cancer, personalized medicine, radiomics and pathomics

Introduction

Lung cancer is one of the most prevalent cancers globally, and despite considerable knowledge and information gained regarding it over the years, it remains the leading cause of cancer death. The leading cause of lung cancer is tobacco smoking, although various environmental, occupational, and lifestyle factors and chronic lung diseases can also promote the onset of non-tobacco-related lung cancer.[1] Lung cancer is at the top of the list of cancers that require new interventions for early diagnosis, since it is often not diagnosed until the cancer is at an advanced stage.[2] Lung cancer can be classified as small cell carcinoma or non-small cell carcinoma (adenocarcinoma, squamous cell

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carcinoma, or large cell carcinoma). These different subtypes play a role in determining the treatment decisions for patients and their expected prognosis.[3] Early detection and accurate diagnosis of lung cancer are essential for optimal therapeutic outcomes. Advancements in the field of AI have enhanced possibilities for early detection and more tailored medical treatments according to the pathomics and genomics of tumors as inferred by AI. AI has shown the ability to effectively enhance the diagnostic process by making it more efficient.[4] Some lung cancer tumors may have specific receptors within their biological pathways that play a considerable role in their growth and survival; one such example is EGFR. Detection of these is crucial for treatment, but despite this, not all patients who have EGFR mutations will have a good prognosis.[5] Early detection of lung cancer has also been revolutionized by advancements in AI, including the ability for computer-aided detection to identify lung nodules as well as AI models that have the ability to combine clinical and imaging data to provide predictions about patient outcomes. Despite advancements in imaging, pathology, and genomic profiling, challenges persist in timely and accurate lung cancer diagnosis. The integration of AI into these domains not only promises to accelerate diagnostic processes but also provides the opportunity to unify multimodal data, thus enhancing precision medicine approaches.

This paper aims to delve into the numerous ways in which artificial intelligence can be applied to lung cancer diagnosis and the impact such advancements have had on clinical efficiency and patient outcomes.

Materials and methods

This paper has been structured as a non-systematic review and obtained data from PubMed and Google Scholar databases in order to analyze research data focusing on the use of artificial intelligence in the diagnosis of lung cancer. A scope of keywords and phrases was used as the framework to search these databases for articles related to the topic, including convolutional neural network, artificial intelligence, deep learning, computer-aided detection, imaging, genomics, pathomics, radiomics, EGFR, X-rays, CT, pathology, lung cancer, non-small cell lung cancer, and adenocarcinoma. The articles used were published up to July 2025. Articles not published in English were excluded. We acknowledge that our search strategy was limited to PubMed and Google Scholar. Important databases such as Scopus, Web of Science, and IEEE Xplore were not included, which may have resulted in the omission of relevant, high-quality AI and computer science studies. Future reviews should consider a broader database inclusion to ensure comprehensive coverage.

Inclusion criteria

- Articles that are related to the use of artificial intelligence for the diagnosis of lung cancer
- Abstracts and review articles
- Original articles assessing the use of AI for diagnosing, treating, and predicting prognosis of lung cancer
- Why did we choose to conduct a non-systematic review?
- Because of the broad scope of the clinical fields, non-systematic reviews are less constrained than systematic reviews and enable a more thorough analysis of both older and more recent advancements using a variety of criteria and techniques.
- Non-systematic reviews utilize various sources of information allowing for a comprehensive overview.

Results

AI-enhanced imaging: X-ray, CT, thoracoscopic imaging

The use of imaging in lung cancer is pivotal. Lung cancer (LC) is one of the leading causes of cancer-related deaths and an exceptionally high incidence. Early detection of lung cancer offers an increased chance of survival. Chiu et al. studied a machine learning method processing chest X-rays (CXRs) to detect LC early.[6] They initially preprocessed their data sets using monochrome and brightness correction, followed by enhancing contrast, and finally used U-Net for lung segmentation. They trained the deep learning software YOLOv4 to detect lung nodules using 559 CXRs with a single lung nodule. They then assessed 100 CXRs from patients at Taipei Veterans General Hospital and 154 CXRs from datasets from the Japanese Society of Radiological Technology. AI systems that utilized different types of preprocessing methods were superior at 79% with 3.04 false positives per image. They observed the AI software using 383 CXRs obtained within 5 years prior to LC diagnosis. The median time from detection to diagnosis for AI-assisted radiologists was 46 (3-523) days, and for radiologists alone, 80 (0-263) days. The overall inference here is that AI models have the capability to enhance the early detection of lung nodules, offering an essential aid in LC diagnosis.[6] The summarized performance of AI-assisted imaging studies is presented in **Fig. 1** and **Table 1**.

Computerized tomography (CT) is the gold standard in diagnosing lung cancer (LC). Zhang et al.[7] assessed the detection rate of lung nodules between radiologists and AI-assisted reading in LC CT screening. They studied 860 chest CT screenings between November and December 2019. The real-world observation involved 14 residents and 15 radiologists. The AI-assisted group involved one resident and one radiologist. A separate panel determined the type of detected lung nodules and the total number of detected lung nodules between the two groups. Of the 860 participants (aged 57±7 years), the reading panel determined 250 patients had more than 1 solid lung nodule. The radiologists observed 131, whilst the AI-assisted radiolo-

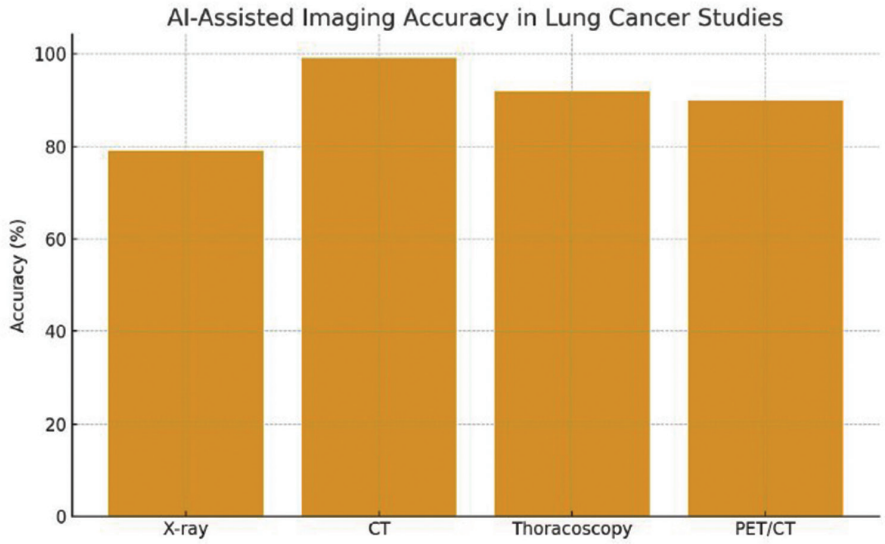

Figure 1. Accuracy of AI-assisted imaging methods (Values represent findings from individual studies rather than pooled averages.

Table 1. AI-assisted imaging studies in lung cancer

Accuracy/Sensitivity	Key Findings	Modality	Study
N/A / 79%	YOLOv4 detected nodules, faster diagnosis	Chest X-ray	Chiu et al. (2022) [6]
98.8% / 99.1%	AI radiologists detected more nodules	CT	Zhang et al. (2022) [7]
Precision 91.9%	Surface tumors detection >90%	Thoracoscopy	Ishikawa et al. (2023) [8]
High specificity	AI staging TNM improved classification	PET/CT	Trabelsi et al. (2024) [9]
Confidence ≥0.87	AI classified solid vs. non-solid nodules	PET/CT	Kudo et al. (2024) [10]

gists observed 247 (p<0.001). For solid nodules, the accuracy/sensitivity of the radiologists was 86.2% and 52.4%, respectively, whilst for the AI-assisted radiologists, it was 99.1% and 98.8%. The reading panel also found 111 of the 860 participants had more than 1 non-solid lung nodule. The radiologists' group identified 28, whilst the AI-assisted radiologists identified 110 (p<0.001). The accuracy/sensitivity of the radiologist group was 90.4% and 52.4%, respectively; for the AI-assisted reading group, it was 98.8% and 99.1%. The results emphasize that AI can considerably improve the accuracy of lung cancer detection for solid/non-solid nodules on CT.[7]

An integral part of the diagnosis and early interventions in lung cancer is minimally invasive thoracoscopic surgeries. Ishikawa et al.[8] aimed to demonstrate how intraoperative thoracoscopic images analyzed using a deep convolutional neural network (DCNN) can help detect tumors on pulmonary surfaces. Their study utilized 644 thoracoscopic images, which involved pulmonary surface changes in 427 lung cancer patients between 2012 and 2021. The lesion areas were isolated on these thoracoscopic images by bounding boxes formed through the use of YOLO, a DCNN used for this purpose. Using a 15-fold cross-validation scheme, the DCNN model was trained and evaluated. They found precision, recall, and F1-measured values of 91.9%, 90.5%, and 91.1%, respectively. The DCNN was successful at detecting lymphatic invasion (p=0.045) and pathological pleural invasion (p=0.081). The DCNN had an overall tumor detection accuracy of over 90%. This highlights that the use of AI in imaging diagnostics of lung cancer is not limited to radiological use, as it can provide considerable assistance to surgeons through automatic detection of lung cancer during thoracoscopic surgeries.[8]

Accurate diagnosis and staging are integral for treatment/prognosis. Trabelsi et al.[9] aim to develop an AI system capable of identifying tumors on PET/CT imaging and staging them according to the TNM classification. Their databases were DICOM CT and 18FDG-PET/CT images. Segmentation of the lung tumors was made with RedNet-50 with high specificity and precision. These segments were reconstructed into 3D models to aid border visualization. Lobe segmentation was enhanced using the Pulmonary Toolkit. Using the CNN ResNet-50, the data from the segmented images helped to determine the T category of the tumors. Their model was superior for T1a, T2a, T2b, T3, and T4 tumors. This highlights that considerable benefits in patient outcomes can be achieved through the use of automated AI software to diagnose and stage lung cancer.[9]

Distinguishing between solid pulmonary nodules and ground-glass opacities is challenging. Current approaches to distinguish them are rather subjective, such that Kudo et al.[10] aim to develop an AI to fully automate this differ-

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entiation and detect highly malignant nodules. They retrospectively analyzed 246 patients who underwent PET/CT and who had clinically negative lymph node metastases and underwent lung resection for adenocarcinoma. In these patients, AI detected tumor sizes of less than or equal to 2 cm in size and also classified them as solid or non-solid. The confidence scores from these AI assessments were correlated with pathological findings. The confidence score of solid nodule detection with AI was greater than or equal to 0.87, especially for those with a purely solid component compared to those with non-solid characteristics. Of the nodules identified as solid with AI, 16% were with lymph node metastases, 94% were invasive, and 44% were upstaged preoperatively. Most of the solid nodules identified by AI were high-grade malignancies. This highlights that AI can detect and classify nodules less than or equal to 2 cm and is effective to predict aggressive tumor behavior and lymph node metastasis. AI, therefore, has potential use for preoperative risk assessment and surgical planning.[10]

Utilizing CT is an effective way to diagnose lung cancer; however, it can be tiring and often can result in missed nodules. Katase et al.[11] developed a computer-aided detection (CAD) that automatically detects lung nodules on CT images. Their algorithm was developed using deep learning and data from 1997 chest CT scans. The clinical efficacy of the CAD was assessed by 10 doctors. This investigated if CAD could be used as a second reader to prevent overlooking nodules that would typically just be followed up. Their analysis used the Jackknife Free-Response Receiver-Operating Characteristic (JAFROC). The performance of the CAD was compared with a phantom study. The CAD demonstrated a sensitivity of 0.98/0.96 at 3.1/7.25 false positives per case. There was no real difference in sensitivity within the same range of practical doses in the phantom study. A further reader study demonstrated enhancement in the ability to detect nodules that were identified clinically with p=0.026. Deep learning-based CAD is therefore considered to be beneficial in increasing the ability to detect nodules.[11]

Establishing an accurate interpretation of a chest X-ray (CXR) is crucial to alleviate the risks of failing to detect smaller/ambiguous lesions. Tam et al.[12] studied how using AI could enhance a radiologist's accuracy and efficiency when interpreting a new CXR. Their data included 400 CXRs, with 200 difficult-to-detect lung cancer cases. These were reviewed by three radiologists as well as an AI algorithm in order to compare tumor detection ability. They found that there was no difference in performance between AI and radiologists when AI was used as a standalone algorithm. The most optimal outcome was seen when the AI algorithm was utilized by radiologists in a combined approach. The most optimal outcome was seen when the AI algorithm was utilized by radiologists in a combined approach. This led to a 60% reduction in missed cancers on CXR. Such a combination helped to eliminate the impact of common pitfalls such as distraction. This emphasizes that a clinical approach from radiologists towards the implementation of AI can be considered promising in the ability to detect frequently missed lung cancers and therefore enhance patient care.[12]

Early detection of lung cancer (LC) through chest X-rays (CXR) can be challenging. A retrospective study by Tugwell-Allsup et al.[13] aimed to clinically validate the role of deep learning-based automatic detection (DLAD) in CXR detection of LC. Their data utilized CXRs and associated CT scans between January 2019 and 2020. The AI software they used evaluated 320 CXRs (<6 years prior to diagnosis). Of these 320, 105 were positive LC patients and 103 were negative LC patients. They compared clinical findings to those of the AI. 55% of the 105 LC patients were men aged between 68 and 83, for whom clinical reports detected LC in 61% of them, whilst the AI software detected it in 90%. The diagnostic and prognostic sensitivities of the AI software yielded 57.6 and 90%, respectively. The AI also detected LC nodules in 24% of chest X-rays more than 12 months before diagnosis, which were initially negative. The AI reduced the mean time-to-diagnosis by 193 days (IQR: 42-598) where it detected nodules on chest X-rays that were originally missed. Of the 103 negative LC patients, 20 were flagged as having some abnormality, yielding 19% false positive results. This highlights that AI can increase diagnostic accuracy and reduce the time to diagnosis, proving crucial for patient outcomes.[13]

Classifying chest nodules accurately is essential for accurate lung cancer diagnosis, although the process is considerably dependent on doctor interpretation, which may bring about challenges, particularly for the detection of smaller nodules. A deep convolutional neural network (TransUnet) proposed by Wang et al.[14] may allow for the automatic classification of lung nodules. TransUnet is comprised of a transformer, which encodes specific features on a CT image; the U-Net, which allows the detection of the exact location of the lung nodule; and the global average pooling, which categorizes the CT images. They found that the accuracy of TransUnet in training and testing was 87.9% and 84.62%, respectively. The sensitivity, specificity, and AUC of the TransUnet on the testing dataset were 70.92, 93.17, and 0.862%, respectively. This demonstrates that the TransUnet software is considerably accurate in classifying lung nodules and has potential for further use in LC diagnosis.[14]

AI in biomarker detection, determination of invasiveness, enhancing pathological diagnostic accuracy

Histopathology is crucial for definitive lung cancer diagnosis and prognosis. Detecting genetic mutations/receptor expressions is also vital, i.e., programmed death-ligand 1 (PD-L1). Wu et al.[15] developed an artificial intelligence (AI) system capable of detecting PD-L1 expression on whole-slide images of the 22c3 assay, allowing for automatic tumor proportion score (TPS) determination. They investigated how the AI system could assist pathologists in the diagnosis of PD-L1 expression and its reliability in the AP263

assay. They found that the deep learning model used for the automated tumor detection had an accuracy of 0.9326 and a specificity of 0.9641. Further to this, after segmentation of the tumor cells, they were able to determine the TPS value. The comparison test with the 22c3 assay yielded strong consistency between the TPS calculated by the AI system and that of the trained pathologists with R=0.9429–0.9458. Further testing of AI assisted diagnostics, found enhanced repeatability and efficiency in untrained pathologists. They also found that the Ventana PD-L1 (SP263) assay provided accurate TPS values between AI systems and trained pathologists where R=0.9787. Overall, there are incentives for AI use due to the ability to enhance the repeatability/efficiency and to accurately detect PD-L1 expression status in non-small cell lung cancer (NSCLC).[15] The key findings from AI applications in pathology and biomarker detection are shown in **Fig. 2** and **Table 2**.

Determining and predicting the invasiveness of lung adenocarcinoma (LA) is considerably difficult since many classification efforts have not been integrated into practice. A study conducted by Du et al.[16] explored how combining deep learning and pathomics could help determine LA invasiveness. Their retrospective analysis used whole slide image data from 289 patients who had surgically resected ground-glass nodules. Initially, they used three ResNet deep-learning models to identify areas with tumors. Based on these findings, they extracted features from the best-performing models to develop pathomics using machine learning classifiers. Finally, they compared the effectiveness and accuracy of the pathomics in predicting the invasiveness of LA to that of junior and intermediate pathologists. Performance was evaluated with data from the area under the curve (AUC). They found that the deep learning model most optimal in identifying tumor areas was ResNet18 with AUC (0.956), sensitivity (0.832), and accuracy (0.904). Random forest was considerably reliable and accurate in assessing tumor invasiveness with AUC values of 0.814 and 0.807. Deep learning models are able to aid pathologists to accurately diagnose and determine invasiveness of LA with AUC increasing from 0.547 to 0.759 and 0.656 to 0.769, respectively, for junior and intermediate pathologists.[16]

Early and accurate diagnosis is essential to improve outcomes for patients. Deep learning may have a role to play in aiding the analysis of histopathological specimens of lung cancer, proving pivotal for treatment decision-making. Muniasamy et al.[17] conducted a study to apply a convolutional neural network called EfficientNetB7 to help with the classification of primary lung cancer histopathological images as either adeno, squamous cell, or large cell carcinomas, which is essential for early treatment and interven-

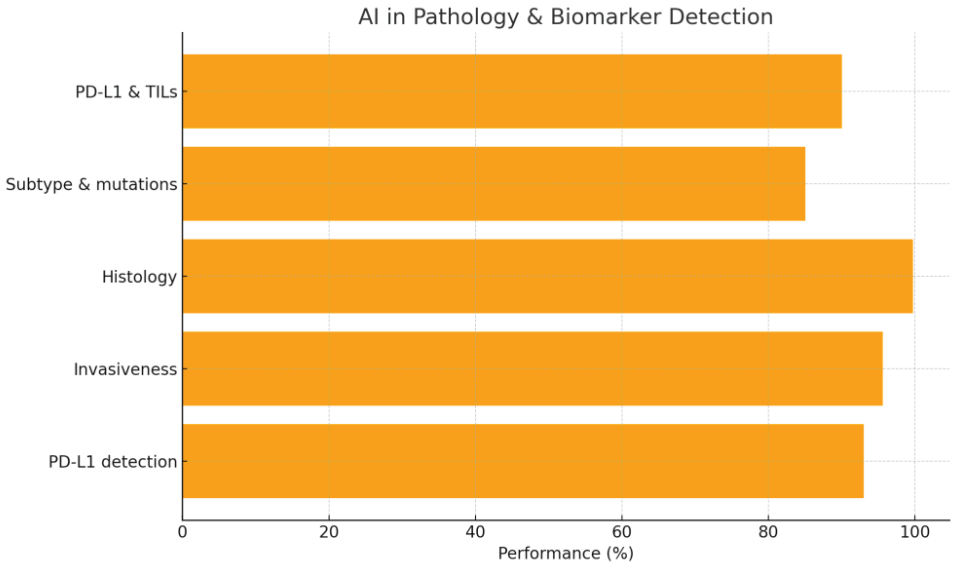

Figure 2. Performance of AI in pathology and biomarker detection.

Table 2. AI in pathology and biomarker detection

Performance	Key Findings	Application	Study
Accuracy 0.93	Automated TPS determination	PD-L1 detection	Wu et al. (2022) [15]
AUC 0.956	Deep learning + pathomics	Invasiveness	Du et al. (2025) [16]
Accuracy 99.7%	CNN classified carcinoma types	Histology classification	Muniasamy et al. (2024) [17]
AUC 0.73–0.97	Detected LAC, LSCC, mutations	Subtype & mutations	Coudray et al. (2018) [18]
Correlation p<0.0001	AI improved detection & agreement	PD-L1 & TILs	Molero et al. (2025) [19]

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tions for lung cancer patients. One thousand five hundred histopathological images of lung cancer were examined using the EfficientNetB7, which was pretrained. They found that the model had a 99.77% accuracy, and previous studies had accuracy varying between 90% and 99%. The use of convolutional neural networks such as EfficientNetB7 is therefore considered to be beneficial towards the pathomics of lung cancer histological images, reducing burden upon and aiding pathologists to obtain a more accurate diagnosis.[17]

It is challenging to differentiate between lung adenocarcinoma (LAC) and squamous cell carcinoma (LSCC), one requiring inspection and examination by more experienced pathologists. Coudray et al.[18] trained a deep convolutional neural network (Inception v.3) to automatically classify whole-slide images from The Cancer Genome Atlas as either LAC, LSCC, or normal. The area under the curve (AUC) of their findings was 0.97, comparable to pathologists'. Independent validation of their software was conducted on frozen sections, formalin-fixed-paraffin tissues, and biopsies. They further developed the software to detect mutations in LAD, including STK11, EGFR, FAT1, SETBP1, KRAS, and TP53, from pathology images. In regard to this, their AUC ranged from 0.733 to 0.856. This further contributes to the abilities of AI to enhance pathological cancer subtype discrimination and genetic mutation determination.[18]

Targeted therapy and improved clinical outcomes for patients are reliant on accurate biomarker and mutation status determination of lung cancer specimens. Molero et al.[19] used an AI algorithm to assess the PD-L1 and tumor-infiltrating lymphocytes (TIL) status. They assessed 50 NSCLC samples. Three pathologists examined PD-L1-stained slides both manually and with two pieces of AI software (PathAI and Navify Digital Pathology). They assessed the TIL status digitally in hematoxylin eosin and CD8 immunohistochemically stained specimens using these two different AI software programs. They analyzed the agreement between observers and methods for each biomarker. The turnaround time for PDL-1 assessment between manual and AI detection was also determined. They found higher agreement in tumors that expressed low PD-L1 both manually and with AI. AI demonstrated, for both software programs, a considerably higher number of cases equal to or above 1% for PD-L1 expression with p=0.00015 when compared to the manual approach. The turn-around time with AI was also better with p<0.0001. They also found a significant positive correlation between TIL density evaluated with PathAI and CD8+ cell density with Navify Digital Pathology (τ=0.49, 95% CI 0.37 to 0.61, p<0.0001). These results highlight that AI algorithms can enhance PD-L1 detection as well as TIL in NSCLC. [19]

The degree of malignancy and invasiveness of lung nodules is essential to determine in order to conclude an accurate diagnosis critical for patient care. Zhao et al. [20] studied how AI could be used to assess this very thing. They studied 466 resected pulmonary nodules and found the AUC of deep learning in predicting malignancy compared to pathological reports to be 0.8 and 0.75, respectively, for subcentimeter and solid nodules. The AUC for a prediction of invasiveness of subsolid lesions with AI was 0.88. The AI misdiagnosed some lesions as benign, despite the fact that they had a diameter of more than 1 cm and appeared solid on CT. The AI models showed a 69% agreement with intraoperative invasive adenocarcinoma detection, with a sensitivity of 0.50 and specificity of 0.97. The AI model is, therefore, quite accurate in predicting adenocarcinoma invasiveness during intraoperative frozen section assessment, which can have significant implications for the continuation of surgical management.[20]

When it comes to determining the histological type of lung adenocarcinoma (LAC), there is a lot of subjectivity and disagreement, which can have a negative impact on patient care. As a result, Lami et al.[21] created a convolutional neural network capable of distinguishing between the various subtypes of LAC and predicting disease survival using the LAC tumor grading scale. The LAC histopathological images were collected by 17 pulmonary pathologists and one trainee pathologist. They trained two AI models (AI-1 and AI-2) to detect 8 different subtypes of lung adenocarcinoma. They further tested the trained models on a cohort of 133 patients. Both models achieved high precision, recall, and F1 scores above 90% for most of the subtypes of LAC. A Kaplan-Meier curve revealed significance in both AI models' ability to predict disease-specific survival, with p-values of 0.0017 and 0.0003, respectively. The study's findings demonstrated AI's ability to improve pathological diagnosis accuracy as well as LADC grading assessments.[21]

The diagnostic challenges in lung cancer are multifactorial, ranging from complex morphological patterns to significant intratumoral variation. This prompted Pan et al.[22] to create an artificial intelligence model to help with this. They developed a software program called ANORAK (pyrAmid pooliNg crOss stReam Attention networK) capable of encoding multiresolution inputs and describing the tumor growth pattern on hematoxylin eosin-stained slides. The AI was tested on 1372 lung adenocarcinomas from four independent cohorts. The AI's grading had prognostic significance and allowed for a more accurate prognosis for stage 1 tumors. The ANORAK model was also useful in assessing tumor morphology and acinar patterns. This demonstrates that Artificial Intelligence has the potential to help pathologists diagnose and stage lung cancer more accurately.[22]

Integrative AI models and risk stratification: combining clinical, genomic, and imaging data for a comprehensive diagnosis. Risk stratification

Early detection and effective treatment outcomes for lung cancer patients remain difficult to achieve. Oncu and Ciftci[23] created a multimodal artificial intelligence system that

uses both convolutional neural networks (CNNs) and artificial neural networks (ANNs) to improve LC classification and severity assessment capabilities. The CNN model was pretrained on 1,019 CT images and then classified them as adeno, large cell, or squamous cell carcinoma or totally normal with 92% accuracy. The ability of convolutional neural networks to accurately interpret these images was improved by using Gradient-weighted Class Activation Mapping (Grad-CAM), which highlights important regions on images. In line with this, the artificial neural network used was trained with clinical information from 999 patients, taking into account demography, symptoms, and genomics, resulting in 99% accuracy in predicting the severity of lung cancer as low, medium, or high. The artificial neural network's decision-making and the ability to incorporate these additional patient-specific factors were aided through the use of SHapley Additive exPlanations (SHAP). This model emphasizes the important role of the combined method of imaging data and clinical information interpreted by AI in the accurate prediction of the risk for and diagnosis of lung cancer.[23] The performance of integrative AI models for risk stratification is illustrated in **Fig. 3** and **Table 3**.

The immune status of lung cancer is critical to treatment and prognosis. Tong et al.[24] emphasized the importance of the tumor immune microenvironment (TIME) for immunotherapy. They used a machine learning model to predict the TIME profile of non-small cell lung cancer (NSCLC) patients based on 18F-FDG PET/CT radiomics and clinical data. They assessed RNA-seq data of 1145 NSCLC patients from the Cancer Genome Atlas. The researchers then investigated the CD8 expression of 221 NSCLC patients from Daping Hospital who had received 18F-FDG PET/CT scans prior to treatment. AI analyzed PET/CT images to develop a radiomic signature. The model incorporated radiomics, clinical features, and a radiomics-clinical combination. The performance of these models was assessed using receiver operating curves (ROCs). The DeLong statistical test was used to compare the data. Clinical features and radiomic scores were combined to generate a nomogram. The combined model was used to assess the TIME phenotype in 39 NSCLC patients from The Cancer Imaging Archive (TCIA). The data from The Cancer Genome Atlas showed that the CD8 expression represented the TIME profiles of NSCLC patients. In the Daping Hospital cohort, the PET/CT radiomics model predicted CD8 expression better than the CT model (AUC: 0.907 vs. 0.861, p=0.0314). The PET/CT radiomics-clinical combined model (AUC: 0.932) outperformed both the PET/CT radiomics-only model (AUC: 0.907, p=0.0326) and the clinical-only model (AUC: 0.868, p=0.0036). This demonstrates that AI models using combined data can provide a

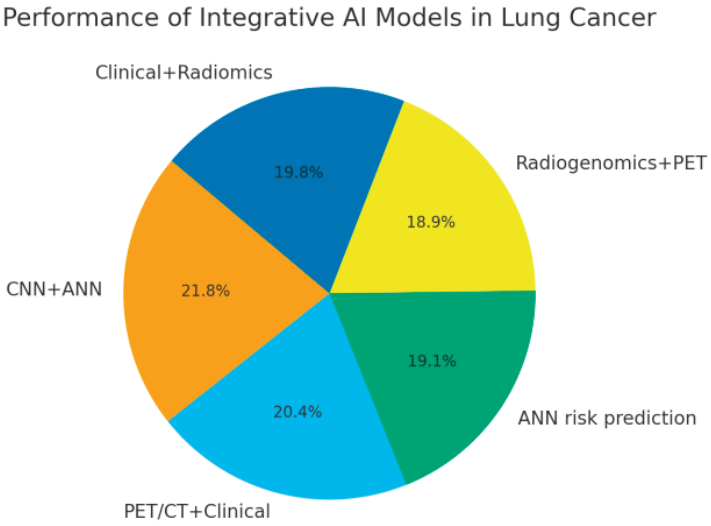

Figure 3. Performance distribution of integrative AI models. (The percentages represent the accuracy and AUC values reported in the studies mentioned. These are not averages, but rather values extracted from individual publications, as shown in **Table 3**).

Table 3. Integrative AI studies in lung cancer risk stratification

Performance	Key findings	Approach	Study
Accuracy 99%	Multimodal improved classification	CNN + ANN	Oncu & Ciftci (2025) [23]
AUC 0.93	Predicted TIME profiles	PET/CT + Clinical	Tong et al. (2022) [24]
AUC 0.85–0.88	Personal health info predicted risk	ANN risk prediction	Hart et al. (2018) [25]
AUC >0.85	Survival risk scoring	Radiogenomics + PET	Taheri & Golden (2025) [26]
Accuracy 79%-94%	Improved malignancy prediction	Clinical + Radiomics	Baeza et al. (2024) [27]

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non-invasive method for determining immune status in NSCLC.[24]

When it comes to the risk of developing lung cancer, several factors come into play. Hart et al.[25] aimed to train and use a multi-parameterized artificial neural network to predict people's risk of developing lung cancer based on their personal information. They trained and validated the ANN using data from the National Health Interview Survey conducted between 1997 and 2015, which included sex, age, BMI, diabetes, smoking status, emphysema, asthma, race, Hispanic ethnicity, hypertension, heart disease, vigorous exercise habits, and stroke history. This data set yielded 648 lung cancer patients and 488,418 non-cancer cases. This training set produced a sensitivity of 79.8% (95% CI 75.9-83.6%), a specificity of 79.8%-80.1%, and an area under the curve (AUC) of 0.85-0.88. On the other hand, the validation set of date provided a sensitivity of 75.3%, specificity between 80.3% and 80.8%, and AUC of 0.86. These findings all showed that using ANNs to assess personal health information can provide a high level of specificity and somewhat reliable sensitivity for lung cancer diagnosis. This enables a risk stratification procedure that is both non-invasive and cost effective.[25]

When diagnosing malignancies such as lung cancer, detecting and diagnosis is not the only essential criteria. The diagnostic process incorporates additional data to provide more comprehensive information, such as tumor genomic characteristics and survival risk scoring. Taheri and Golden[26] planned to create an 18F-FDG PET system that would use radiomic features of non-small cell lung cancer to calculate survival risk. They performed radiomic analysis on multiple NSCLC data from the cancer imaging archive, identifying 945 radiomic features. The radiomic model they developed was used to calculate a risk score. Following this, radio-genomic analysis was conducted to assess the correlation between the risk score and the tumor characteristics. They found the PET-radiomic model was considerably accurate at predicting the 5-year survival rate with an area under the curve of 0.78, 0.71, and 0.73 for training, validation, and testing, respectively. Furthermore, after accounting for clinical features and radiomic risk, the AUC was greater than 0.85. The PET-radiomic model successfully distinguished between high- and low-risk NSCLC, resulting in an accurate prognosis for patients based on a variety of factors including clinical features, radio-genomics, radiomic risk, and individual tumor-specific characteristics such as cell types and gene mutations.[26]

It is well known that diagnosing LC early is critical, so multiple factors must be considered to improve diagnosis. Baeza et al.[27] investigated whether integrative clinical and radiomic deep learning models can predict the malignancy of pulmonary nodules (PN). They conducted a cross-sectional study with 97 PNs from 93 patients. The clinical data included epidemiological risk assessments and pulmonary function tests. The radiomic model analyzed CT images with a pre-trained convolutional network. Using the clinical data, they created a logistic regression model to estimate the clinical model. The clinical model's information on malignancy probability allowed the radiomic model's malignancy probability to be updated using the Bayes' theorem nomogram. The radiomic model had a positive predictive value of 86%, accuracy of 79%, and an AUC of 0.67. The clinical model found that the lung's diffusion capacity for carbon monoxide (DLCO), obstruction index, and smoking status were all significant clinical predictors of patient outcome. Combining clinical features with the deep learning radiomic model resulted in a positive predictive value of 94%, accuracy of 76%, and an AUC of 0.80. This demonstrates how incorporating such data can improve LC diagnosis and pulmonary nodule malignancy prediction.[27]

The ability of integrative AI models to integrate imaging, clinical, and genomic data is their main advantage. This allows for more thorough risk stratification and individualized treatment plans. This multimodal strategy improves prediction accuracy and lessens the drawbacks of single-data-source models.

Issues with implementation of AI in lung cancer diagnosis

Whilst there have been considerable advancements in the development of AI towards lung cancer diagnosis, it is crucial to avoid overdependence on such new technologies, particularly due to risks regarding inaccuracies such as diagnostic misclassification, biased training data, or lack of generalizability across diverse patient populations. In their review, Zhang and Chen[28] emphasize the need for more work to address issues of AI model interpretability as well as concerns about patient data privacy. They also emphasize the challenges of limited access to annotated data sets. All of this highlights the need for an AI system that performs comprehensive analysis on high-yield data.[28] The main challenges of AI implementation in lung cancer diagnosis are summarized in **Fig. 4** and **Table 4**.

Artificial intelligence is growing in its use across the world for cancer diagnosis amongst other things, with the potential to replace human radiologists. Jonathan Mezrich[29] explains that this is a potential legal issue. While AI has been incorporated into some aspects of the healthcare system, it remains a concern to what extent AI can have legal autonomy within a healthcare team as well as implications for any imaging-based inference errors it may make. As such, liability risks and legal implications of AI need to be considered when increasing its use within various healthcare settings.[29]

Reyes et al.[30] emphasize the need for assurance of accuracy and correct functioning of AI algorithms as they gradually integrate within clinical radiology. They further highlight the necessity for AI to provide data that is easily interpretable for enhanced accuracy in clinical practice.

A lot of effort has been put into developing cost-effective and accurate artificial intelligence software capable of detecting lung cancers on routine CT scans; however, according to Mulshine et al.[31], this has been a time-con-

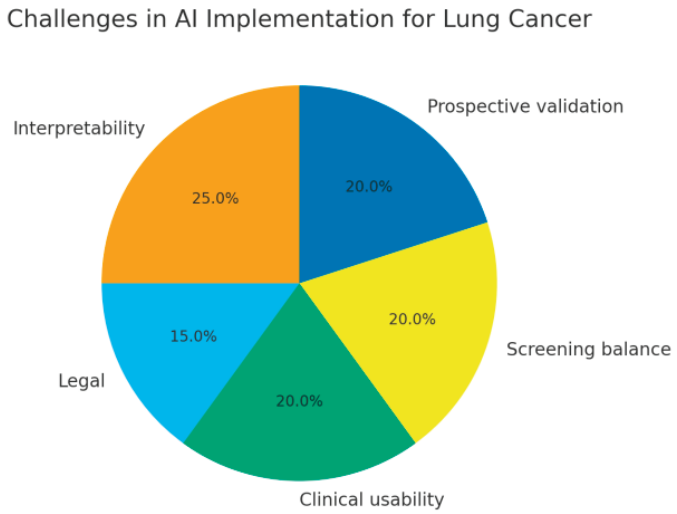

Figure 4. Distribution of key challenges in AI implementation for lung cancer.

Table 4. Challenges in AI implementation for lung cancer diagnosis

Implications	Key Issues	Focus	Study
Need comprehensive AI systems	Limited datasets, privacy	Interpretability	Zhang & Chen (2022) [28]
Potential legal hurdles	AI autonomy and liability	Legal	Mezrich (2022) [29]
Clinically usable AI	AI must provide clear outputs	Interpretability	Reyes et al. (2020) [30]
Broadened access required	AI vs. public health screening	Screening balance	Mulshine et al. (2025) [31]
Need prospective validation	AI lacks real-time use	Prospective data	Yu & Kohane (2019) [32]

suming process that may be neglecting and disrupting imaging, such as chest CT screening for lung cancer in older tobacco-exposed people. Therefore, they highlight a need for balance between developing precise AI tools while also addressing the need for public health screening for early disease detection. There is a need for wider access to advanced and cost-effective AI-incorporated CT screening tools to broaden the scope for screening.

A lot of data utilized for the training and development of computational neural networks, artificial intelligence software, and deep learning models incorporates predominantly retrospective data for a variety of uses in medical practice, including chest radiography interpretation. Kun-Hsing Yu from Harvard Medical University highlighted this challenge, explaining that AI systems 'have not entered into routine prospective use in the clinic where the Frame Problem will manifest itself most pathologically.' This targets the need for comprehensive prospective studies for the purpose of real-time ability of AI-aided diagnostics.[32]

The use of digital databases through AI software raises concerns for ethical issues for its incorporation into the medical field. In the European Union, General Data Protection Regulation was developed for the purpose of increasing privacy and confidentiality of personal data and ensuring that data processed by foreign communities and companies must pass through the union-based data processor or controller to protect personal information. Growing concerns have arisen with regard to insufficient laws in healthcare to protect individual health data as well as the risk of use of data for malicious/commercial purposes, such as sharing of consumer data with pharmaceutical and biotechnology firms.[33]

The utilization of AI in various aspects of medicine often comes with limited scrutiny and comprehensibility. In light of that, it is crucial to consider the need for explainable AI software, which has the capability to increase transparency and confidence in the abilities of AI technology. Such explainable AI software may have the potential to align the performance of the AI model to that of the clinical guideline objective of different institutions. Such models can also enhance interpretability and comprehension for clinicians due to increased evidence-based practice of the AI software.[34]

Lung cancer diagnosis and testing require a thorough investigation of not only the presence of the tumor but also its biological and genetic characteristics essential for treatment. As highlighted in a study by Wang et al., there are some limitations to this with deep learning models since they are mainly trained from input data and outcomes. It is therefore necessary to integrate current knowledge of biological and genetic mechanisms into deep-learning models to enhance their histopathological assessment and further the possibilities of such systems.[35]

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Further developments are required in order to be able to have an AI system that is capable of drawing conclusions from and detecting a scope of different diseases. The insufficient level of data predominantly due to pathological changes over time is a hurdle that needs to be overcome. Finding such varied data is expensive, time-consuming, and significantly challenging. There is a growing need for the integration of imaging, molecular, histopathological, genetic, and clinical manifestation-related data to have a comprehensive AI system capable of classifying patients into different subgroups to drive more tailored and beneficial care to patients.[36]

Beyond technical challenges, ethical concerns arise regarding patient data confidentiality, potential misuse of sensitive medical information, and algorithmic bias. Ensuring transparent, fair, and accountable AI systems is essential before widespread clinical adoption.

Conclusions

In conclusion, the sophisticated and targeted approach towards the incorporation of artificial intelligence into lung cancer diagnostics has been revolutionary. Across imaging studies, AI-assisted systems achieved sensitivities ranging from 79% to 99%, demonstrating improved detection of both solid and non-solid nodules. In pathology, deep learning approaches achieved accuracies above 90% for histological subtyping and biomarker detection. Integrative AI models that combined clinical, radiological, and genomic data showed accuracies up to 99%, highlighting their potential in comprehensive risk stratification. Despite these advances, limitations such as dataset availability, ethical concerns, and interpretability issues remain. Artificial intelligence has demonstrated the capability of being able to process large data sets for enhanced imaging and pathological diagnostics, leading to earlier diagnostic capabilities. AI has shown its potential in the detection of genetic and receptor biomarkers in lung cancer tumor structures, which is crucial for tailored and personalized treatment plans, allowing for improved prognostic outcomes. Sophisticated tumor segmentation ability and localization on imaging have allowed for more discrete nodules to be detected that may have otherwise been missed by the naked eye. As AI software in this field continues to grow, it is important to ensure more comprehensive abilities in allowing for the integration of multiple data sets, the ability for explainable decision-making to allow for scrutiny, and prospective data analysis to solidify its capabilities in diagnostics. It must also be emphasized that the success of AI in lung cancer diagnosis depends on carefully curated training datasets. Building such datasets requires the expertise of experienced pathologists and may benefit from the creation of standardized worldwide databases to ensure reproducibility and equity in AI applications. Future prospects for AI in lung cancer diagnosis include the development of explainable models to improve interpretability, the creation of international standardized datasets for training, and the integration of prospective real-world data to enhance generalizability. With these advancements, AI may become an indispensable tool in routine clinical practice, supporting earlier detection and more precise, individualized patient care. The need for increased collaboration between AI technology developers and medical workers in fields related to lung cancer is crucial for addressing and overcoming hurdles and limitations and increasing opportunity for the development of a state-of-the-art system capable of transforming care for lung cancer patients.

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The authors have declared that no competing interests exist.

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- The authors declared that no clinical trials were used in the present study.

- The authors declared that no experiments on humans or human tissues were performed for the present study.
- The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.
- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalized human and animal cell lines were used in the present study.

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Data availability

Dataset available on request from the authors.