



**ARTIFICIAL INTELLIGENCE (AI) IN THE DIAGNOSIS OF PATHOLOGIST-
CONFIRMED LUNG CANCER: A SYSTEMATIC REVIEW AND A DIAGNOSTIC TEST
ACCURACY (DTA) META-ANALYSIS_**

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ABSTRACT

Objectives : Lung cancer continues to be the primary cause of cancer-related deaths globally, with early detection essential for enhancing survival rates. Notwithstanding progress in imaging and pathology, existing diagnostic techniques encounter constraints including elevated false-positive rates, inter-observer variability, and difficulties in detecting smaller, early-stage nodules such as ground-glass nodules (GGNs). Artificial Intelligence (AI) provides prospective answers by improving diagnostic accuracy and efficiency. The objective of this study is to assess the efficacy of AI algorithms in diagnosing pathologist-confirmed lung cancer, emphasizing their diagnostic accuracy and potential to transform clinical practice.

Methods : A systematic review and meta-analysis were performed in accordance with PRISMA recommendations. A thorough literature search was conducted utilizing the Cochrane Library and

PubMed until May 7, 2025, employing keywords pertinent to lung neoplasms and artificial intelligence. The inclusion criteria targeted research utilizing AI for the diagnosis of lung cancer, emphasizing diagnostic accuracy as the principal outcome. Data were extracted and evaluated for quality, and a meta-analysis was performed using Review Manager version 5.4, utilizing random-effects models to address clinical heterogeneity.

Results : The meta-analysis comprised six investigations with an aggregate sample size of 486 participants. AI methods, including Support Vector Machines, Random Forests, Artificial Neural Networks, and Computer-aided Diagnosis systems, had an overall sensitivity of 79.0% and specificity of 80.2%. The positive predictive value was 68.9%, while the negative predictive value was 87.3%, signifying a high reliability of negative test outcomes. AI algorithms have considerable expertise in diagnosing lung cancer, with the potential to augment early detection and increase patient outcomes. Standardizing AI models and integrating unpublished data may augment the robustness of forthcoming analyses.

Conclusion : AI possesses significant potential to enhance lung cancer diagnosis, providing advantages for both patients and healthcare professionals. Notwithstanding current obstacles, continuous research and development, coupled with meticulous application in clinical settings, may result in substantial progress in the early identification and therapy of cancer.

Keywords: Artificial Intelligence, Pathologist-Confirmed Lung Cancer,DTA

INTRODUCTION

Lung cancer is a malignant neoplasm that develops from epithelial tissue. Air pollution, radiation exposure, and fungal infections contribute to the ongoing incidence and death of lung cancer, which is the leading malignancy in terms of both incidence and mortality in China and globally. The five-year survival rate for lung cancer is merely 15.6%, with prognosis varying considerably among patients at different clinical stages. The cure rate for carcinoma in situ approaches 100%; nevertheless, statistics indicate that the 5-year survival rate for lung cancer is 70% at stage I and fewer than 5% at stage IV, respectively [1].¹ Consequently, the prompt identification of lung cancer is essential.

Diagnostic imaging, diagnostic pathology, and diagnostic marker tests have emerged as the three primary approaches for the early detection of lung cancer in recent years. Radiographs, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography-computed tomography (PET-CT) are all forms of diagnostic imaging that can be used to examine the chest for signs of cancer or other lung abnormalities.² As a novel approach to screening for lung cancer, Naidich suggested LDSCT (Low-Dose Spiral Computed Tomography) in the 1990s.³ When compared to chest radiography, LDSCT detects lung cancer at an earlier stage with far higher sensitivity. Evidence from the United States, Japan, and Germany suggests that LDSCT can lessen radiation exposure to patients while simultaneously improving sensitivity to the detection of lung nodules.⁴ Due to its poor diagnostic accuracy and susceptibility to patient-specific variables including lung vacuolation and shape, imaging diagnostics has limited utility in the early detection of lung cancer.⁵

Histological examination by bronchoscopy or percutaneous puncture biopsy is the most reliable method for diagnosing lung cancer, and it is commonly used in pathological diagnosis. Fiberoptic bronchoscopy, ultrasonography, and CT-guided percutaneous lung biopsy are the primary techniques for acquiring histological specimens; bronchoscopy has been the most popular and rapidly expanding technique in this regard in recent years.⁶ The definitive method for confirming a diagnosis of lung cancer is fiberoptic bronchoscopy. Nonetheless, the diagnosis accuracy of conventional white light bronchoscopy (WLB) is low at less than 29% for peripheral

lung cancer, particularly in cases of precancerous lesions, early mucosal and submucosal lesions, and other similar conditions.⁷ New bronchoscopic techniques like electromagnetic navigational bronchoscopy (ENB), endobronchial ultrasound (EBUS), fluorescence confocal microscopy (FCFM), virtual navigational bronchoscopy (VNB), and others have boosted diagnostic rates and broadened the diagnostic field, particularly in the early detection of lung cancer. But there are limits to most of these methods. For instance, they require additional testing to confirm their clinical practice suitability, have a high false-positive rate, or are subject to external variables.

The term "lung cancer marker testing" is used to describe the process of identifying tumors using biomarkers that are expressed and secreted by tumor tissue, such as hormones, glycoproteins, and enzymes.⁸ The current state of knowledge includes the identification of dozens of tumor markers linked to lung cancer. These include pro-GRP, NSE, CEA, SCC-Ag, etc.⁹ Nevertheless, there has been no independent application of a highly sensitive and specific tumor marker to the therapeutic setting. Consequently, there has been an uptick in efforts to enhance the diagnosis rate of tumor markers for early lung cancer by simultaneously detecting several markers from distinct tissues, including pleural fluid, serum, and bronchial lavage fluid.

Early screening using chest CT scans is now a laborious, subjective, and inter-observer variability-prone clinical practice. The medical community has come to acknowledge the immense scientific and therapeutic benefits of AI in assisting pathological diagnosis, thanks to the advancements in digital pathology and AI in recent years. By utilizing AI recognition technology, doctors may screen for early-stage lung cancer using multi-parametric clustering analysis, which improves problem-solving speed and decreases the likelihood of errors.¹⁰ Advancements in AI have been made in the detection, diagnosis, and treatment of lung cancer.¹¹

On a chest X-ray or CT scan, lesions larger than 30 mm in diameter are readily visible to the naked eye. In order to confirm a cancer diagnosis, a biopsy is necessary for these bigger lesions. Lung nodules, which are lesions smaller than 30 mm, are more challenging to identify and conduct additional investigations into.¹²

While the size of the lesion is a strong indicator of malignancy, it is far from the only component and certainly not the only difficult aspect to identify on lung scans.¹²⁻¹⁴ Radiologists must take into account the nodule's position, shape, texture (solid or partially solid), and calcification when interpreting CT or X-ray images of lung lesions; these additional physical

features have clinical significance. Imaging alone does not always suffice to diagnose benign or malignant nodules, especially those that are not solid or subsolid, such as "ground-glass nodules" (GGNs). Radiologists may miss GGNs because they are often smaller than solid nodules, have poorer contrast, and less clearly defined edges.¹⁵ The rise in the use of computed tomography (CT) for the screening of lung cancer has led to an increase in the detection of this form of scan opacity, or "nodular shadow," more often. Inflammation, fibrosis, or benign hyperplasias can also manifest as GGNs, although they are more commonly linked to early-stage lung cancer.^{15,16} Because of the difficulty in distinguishing between benign and malignant nodules, it would be useful to be able to evaluate many visual aspects concurrently and how they relate to particular outputs (such as malignancy).^{17,18}

Radiologists may be able to find worrisome lesions more quickly and with less effort if they use new technology. The World Health Organization (WHO) has brought attention to the fact that radiomics is a relatively new field of study that aims to identify potentially cancerous lung nodules by extracting useful characteristics from imaging data.¹⁹ In radiomics, a great deal of information is extracted from radiology images, including details that would not be visible to the naked eye.¹⁹ By assisting with decision-making, artificial intelligence (AI) extends beyond picture feature detection.

A number of areas of human health have been putting AI to the test, with promising results. For example, lung cancer has shown promise in terms of speeding up diagnosis, which might, in theory, save lives by delivering healthcare sooner.²⁰ There has been an upsurge in the number of published publications discussing its application, and it has already found its way into imaging the musculoskeletal system, brain, abdomen, breasts, and chest.^{21,22}

This research is urgent due to the essential requirement to improve early detection and diagnosis of lung cancer, a primary cause of cancer-related deaths globally. Notwithstanding progress in imaging and pathology, existing diagnostic techniques encounter constraints including elevated false-positive rates, inter-observer variability, and difficulties in detecting smaller, early-stage nodules such as ground-glass nodules (GGNs). The use of artificial intelligence into the diagnostic process offers potential solutions to these difficulties by delivering more precise, efficient, and objective evaluations. AI-driven solutions possess the capacity to augment diagnostic precision, decrease diagnostic latency, and ultimately improve

patient outcomes. This systematic review and meta-analysis seek to synthesize existing evidence regarding the role of AI in the diagnosis of pathologist-confirmed lung cancer, emphasizing its potential to revolutionize clinical practice and meet the urgent demand for more dependable diagnostic techniques in the battle against lung cancer.

METHODS

Search strategy

This meta-analysis was conducted and documented in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. A thorough literature search was performed utilizing the Cochrane Library and PubMed, up to May 7, 2025. The literature search utilized the specified keywords "(Pulmonary Neoplasm OR Lung Neoplasm) AND Artificial Intelligence OR Computational Intelligence OR Machine Intelligence OR Machine Learning". Articles with relevant titles and abstracts will be incorporated into this procedure to enhance comprehensive evaluation and enable further qualitative and quantitative analysis.

Inclusion and exclusion criteria

The defined inclusion criteria were employed to assess the studies, as outlined below: 1) Research employing artificial intelligence for lung cancer diagnosis, and 2) the principal outcome of the study is the diagnostic accuracy of AI in lung cancer detection, with the presumed gold standard being pathological examination. As a result, exclusion criteria were formulated, encompassing the following: 1) irretrievable complete articles and 2) inappropriate study design, intervention, or outcome. Figure 1 depicts the research search approach.

Data extraction and risk of bias assessment

Subsequently, data were extracted from the selected articles. Utilizing appropriate assessment instruments, articles were assessed for quality. All evaluators collaborated to conduct quality assessment until consensus was reached.

Statistical Analysis

Review Manager version 5.4, which was developed by The Nordic Cochrane Centre as part of The Cochrane Collaboration, was employed to conduct a meta-analysis. The standard metric

for evaluating the intervention's impact on the primary outcome was the sensitivity and specificity and the corresponding 95% confidence interval (CI). Random-effects models were implemented to aggregate effect sizes in anticipation of clinical heterogeneity.

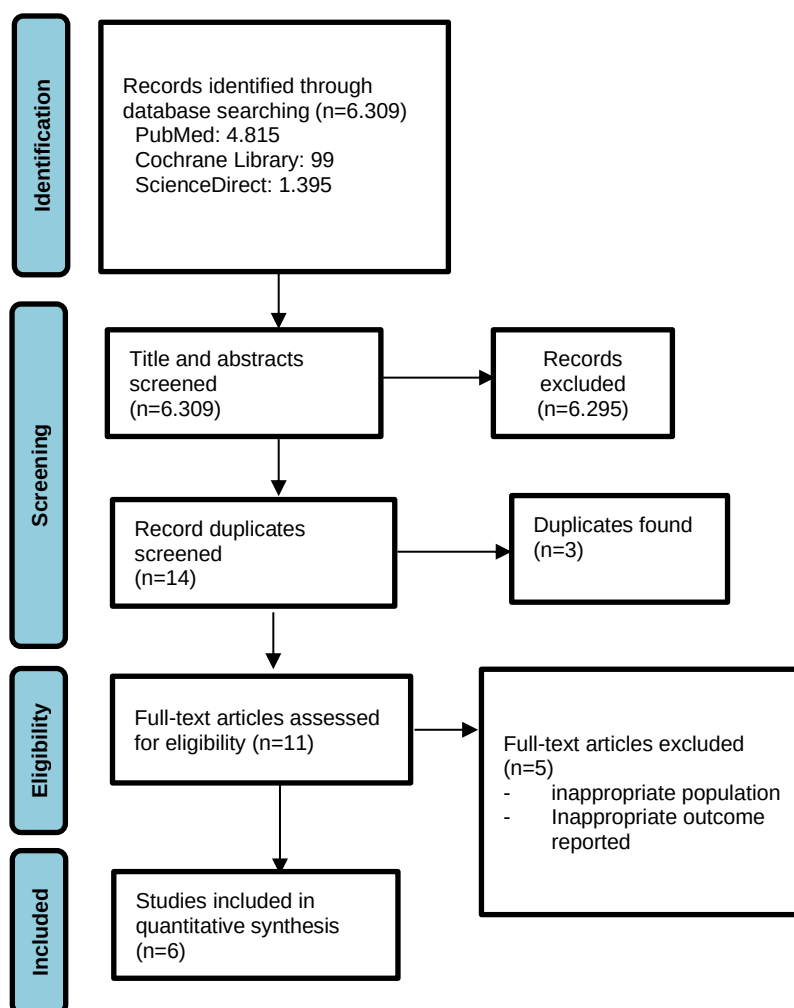


Figure 1. Diagram flow of literature search strategy for this meta-analysis

RESULTS

Author, year	AI Algorithm	Risk of Bias (QUADAS - C)			
		P	I	R	FT
Sun, 2013	Support vector machine	✓	✓	✓	?
Teramoto, 2019	Random Forrest	✓	?	✓	✓
Hsu, 2020	Artificial Neural Network	✓	✓	✓	✓
Dilger, 2015	Artificial neural network	✓	✓	✓	✓
Tian, 2020	Computer-aided diagnosis	✓	?	✓	?
Dilger, 2013	Artificial Neural Network	✓	✓	✓	✓

P = patient selection; I = index test; R = reference standard; FT = flow and timing.

✓ indicates low risk; ✗ indicates high risk; ? indicates unclear risk.

Table 1. Risk of bias of the included studies

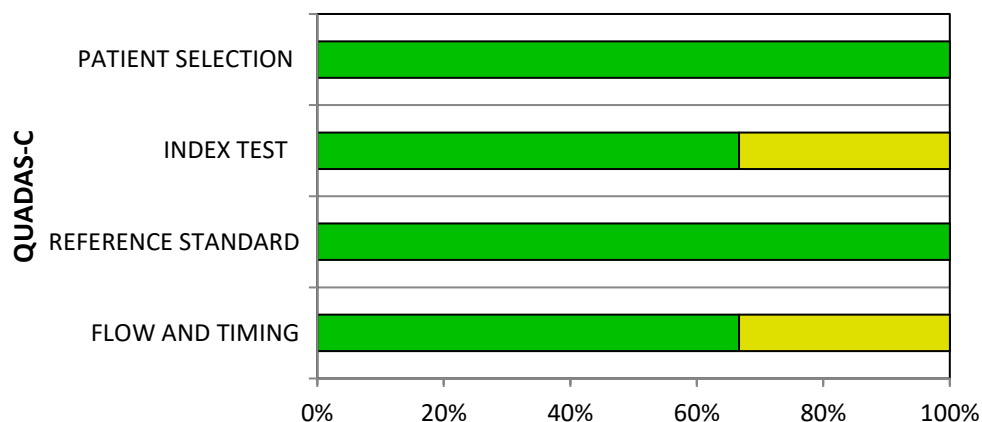


Figure 2. Risk of bias of the included studies

Author, year	AI Algorithm	Total sample	TP	FP	FN	TN
Sun, 2013	Support vector machine	33	15	2	2	14
Teramoto, 2019	Random Forrest	43	24	13	1	5
Hsu, 2020	Artificial Neural Network	234	6	34	2	192
Dilger, 2015	Artificial neural network	50	20	2	2	26
Tian, 2020	Computer-aided diagnosis	109	65	10	30	4
Dilger, 2013	Artificial Neural Network	27	10	2	0	15

Table 2. Characteristics and results of the included studies

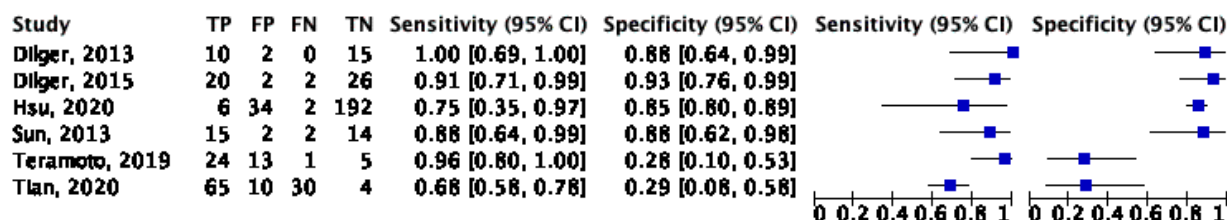


Figure 3. Pooled results of sensitivity and specificity for our meta-analysis

This meta-analysis comprised six diagnostic investigations, totaling 486 samples, to assess the efficacy of artificial intelligence (AI) algorithms in diagnosing pathologist-confirmed lung cancer. The AI algorithms evaluated encompassed a diverse range, including Support Vector Machines (SVM), Random Forests, Artificial Neural Networks (ANN), and Computer-aided Diagnosis (CAD) systems. These models were chosen for their proven efficacy in pattern recognition and classification tasks, which are essential in medical diagnostics.

The aggregated sensitivity of the AI algorithms was determined to be 79.1%. Sensitivity, or the real positive rate, denotes the ratio of actual positives accurately recognized by the AI

systems. This indicates that the AI models accurately identified about 79 out of every 100 instances of lung cancer, underscoring their significant capability in recognizing genuine occurrences of malignancy. This indicates that approximately 21% of actual cases may be overlooked, highlighting the necessity for more refining of these algorithms to improve sensitivity.

The specificity of the AI models was 79.6%, signifying their capacity to accurately detect 79.6% of non-cancerous instances. The elevated specificity is essential for minimizing false positives, which may result in unwarranted concern and additional intrusive testing for patients. The equilibrium between sensitivity and specificity in these AI systems illustrates their proficiency in distinguishing between malignant and non-cancerous instances efficiently.

The positive predictive value (PPV) was determined to be 68.9%, indicating that almost 69% of cases classified as positive by the AI were indeed true positives. This score is crucial as it indicates the probability that patients recognized by the AI as having lung cancer genuinely possess the condition. The negative predictive value (NPV) was significantly elevated at 86.9%, signifying that 87% of the instances identified as negative by the AI were genuinely devoid of lung cancer. The elevated NPV is especially advantageous in clinical environments, as it provides reassurance to patients with negative test results that they are unlikely to have the disease, thereby diminishing the necessity for more testing.

DISCUSSION

The findings of our meta-analysis indicate that artificial intelligence (AI) algorithms, including Support Vector Machines, Random Forests, Artificial Neural Networks, and Computer-aided Diagnosis systems, exhibit significant proficiency in diagnosing pathologist-validated lung cancer. The aggregated sensitivity of 79.1% demonstrates that these algorithms effectively recognize a substantial majority of true positive instances, which is essential for prompt identification and intervention. The specificity of 79.6% indicates the algorithms' proficiency in reliably identifying actual negative cases, hence minimizing false positives. This equilibrium is crucial as it guarantees that individuals without cancer are not exposed to undue stress and procedures, while accurately identifying those with cancer for subsequent treatments.

These findings indicate that AI can serve as a potent instrument in the diagnostic process, potentially augmenting early identification and enabling prompt medical intervention, hence optimizing patient outcomes.

Sensitivity and specificity are essential parameters for assessing the efficacy of diagnostic tests. Sensitivity, or the real positive rate, denotes the ratio of genuine positives correctly recognized by the AI systems. A sensitivity of 79.1% indicates that the algorithms can identify around 79 out of every 100 lung cancer cases, which is crucial for the early detection of the disease, facilitating timely intervention. Specificity, conversely, quantifies the real negative rate, or the ratio of accurately detected actual negatives. The AI models provide a specificity of 79.6%, effectively eliminating false positives and hence decreasing the probability of unnecessary follow-up treatments and increased patient worry. The equilibrium among these metrics is essential, as it reflects the dependability of AI as a diagnostic instrument, guaranteeing both precision and efficacy in clinical environments.

The integration of AI-driven diagnostic technologies into clinical practice can substantially augment the abilities of radiologists and other healthcare practitioners. These AI systems can function as a beneficial supplementary opinion, offering further insights that improve decision-making processes. The elevated negative predictive value (NPV) of 86.9% is especially advantageous in a clinical setting, since it assures both physicians and patients of the high reliability of a negative test result. This diminishes the necessity for superfluous intrusive treatments, alleviates patient anxiety, and optimizes the diagnostic process. By enhancing radiologists' proficiency, AI can facilitate more uniform and objective diagnostic results, diminishing inter-observer variability and elevating overall diagnostic precision.

Our results align with prior studies that have emphasized the potential of AI in medical diagnostics.²³⁻²⁶ Research in other domains, including breast and prostate cancer, has demonstrated comparable sensitivity and specificity rates, highlighting the resilience and versatility of AI technology across many clinical applications. The uniformity shown in several investigations indicates that AI algorithms can be proficiently utilized for diverse diagnostic issues, providing a multifaceted instrument for contemporary medicine. Comparing our findings with prior studies enhances our comprehension of the strengths and limitations of AI in diagnostics, while also pinpointing areas for additional enhancement and investigation.

The integration of AI into lung cancer diagnostics has significant clinical consequences. AI algorithms possess the capacity to transform the diagnostic process by facilitating earlier identification of lung cancer, which is essential for enhancing patient outcomes. Prompt diagnosis facilitates prompt and suitable therapy, which can markedly improve survival rates and quality of life for patients. Moreover, the application of AI can standardize diagnostic protocols, minimizing interpretative variability and guaranteeing consistent and trustworthy outcomes. This not only promotes diagnostic accuracy but also improves clinical workflow efficiency, enabling healthcare practitioners to deploy resources more effectively and concentrate on delivering superior patient care.

Notwithstanding the potential of AI in diagnostics, the incorporation of these technologies into clinical workflows poses numerous hurdles. A principal obstacle is the necessity for extensive training of healthcare practitioners to proficiently employ AI systems. Clinicians must understand the strengths and weaknesses of AI algorithms to enable their proper and effective application in practice. Furthermore, it is imperative to build procedures for AI-based diagnostics to guarantee that these technologies augment rather than supplant human expertise. Comprehensive guidelines and standards must be established to include AI into current diagnostic frameworks, ensuring it improves clinical decision-making while maintaining patient safety and care quality.

Our research possesses some limitations that require acknowledgment. The limited sample size of 486 over six research may restrict the generalizability of the results. Although the results are encouraging, extensive investigations are required to validate the efficacy of AI algorithms across varied populations and contexts. The disparity in diagnostic performance may be attributed to the heterogeneity of AI algorithms employed in various research. Standardizing AI models and procedures in future studies may enhance comparability and facilitate more robust conclusions regarding the efficacy of AI in lung cancer diagnoses.

A further drawback of our study is the possibility of publication bias, given that studies with favorable outcomes are more likely to be disseminated. This may distort the aggregated sensitivity and specificity estimations, yielding an excessively favorable perception of AI's capabilities. Future analyses should incorporate unpublished data and perform thorough searches to provide a more equitable representation of existing evidence. Minimizing publication bias

enables a more precise evaluation of AI's diagnostic efficacy and highlights areas for future enhancement.

Although AI models exhibit potential, they continue to encounter numerous technological constraints. The moderate positive predictive value (68.9%) suggests that false positives are a significant concern, perhaps resulting in unwarranted interventions and patient suffering. Ongoing optimization of algorithms is essential to improve diagnostic precision and diminish false-positive occurrences. Moreover, AI systems necessitate substantial computational resources and infrastructure, which may not be universally accessible in all clinical environments. Confronting these technological obstacles is crucial for the extensive acceptance and efficacy of AI in lung cancer detection.

Subsequent research ought to concentrate on augmenting the sample size and diversity of studies to improve the robustness and generalizability of results. Extensive, multicenter research could yield more comprehensive data regarding the efficacy of AI algorithms across diverse healthcare settings. Furthermore, investigating the amalgamation of AI with alternative diagnostic modalities, such as biomarker analysis, may enhance diagnostic precision and yield a holistic evaluation of lung cancer risk. Investigating the creation of advanced algorithms capable of analyzing intricate patterns and relationships in imaging data will be essential for progressing the discipline.

The application of AI in diagnostics has significant ethical concerns, especially pertaining to patient privacy and data security. Ensuring AI systems adhere to legislation and ethical standards is essential for preserving trust in these technologies. Safeguarding patient data and guaranteeing openness in AI decision-making processes are crucial for mitigating ethical concerns and ensuring responsible AI utilization in clinical practice. Furthermore, issues of equal access to AI technologies must be examined to avert discrepancies in healthcare delivery and outcomes.

CONCLUSION

In conclusion, AI algorithms possess considerable potential to enhance lung cancer diagnosis, offering advantages for both patients and healthcare practitioners. Despite existing

problems, such as technology constraints and integration obstacles, ongoing research and development, coupled with meticulous implementation in clinical practice, may result in substantial progress in early cancer detection and management. Utilizing AI can augment diagnostic precision, boost patient outcomes, and propel the domain of medical diagnostics to more effectively address global patient demands.

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