AI-Based Diagnosis of Small Pulmonary Nodules on CT Imaging: Current Status and Future Prospects

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Abstract. The early and accurate diagnosis of small pulmonary nodules (typically defined as nodules with a diameter ≤10 mm) is crucial for improving the survival rate of lung cancer patients. However, their detection and differentiation pose numerous clinical challenges. Artificial intelligence (AI), particularly deep learning technology, offers promising solutions to these problems. This paper focuses on recent significant international and domestic research achievements supported by clinical validation data, systematically reviewing and analyzing the research progress, core technical methods, clinical application status, and key challenges of AI-based diagnosis of small pulmonary nodules using computed tomography (CT) images over the past decade. It also explores future development trends. Research findings indicate that AI has made remarkable progress in the detection, segmentation, and differentiation of benign from malignant small pulmonary nodules. Deep learning models such as convolutional neural networks (CNNs) and Transformers have continuously evolved, significantly enhancing diagnostic efficiency and accuracy, and to some extent assisting clinical decision-making. Nevertheless, AI still faces substantial challenges in the diagnosis of small pulmonary nodules. At the technical level, these include difficulties in accurately identifying tiny lesions, scarcity of high-quality annotated data, and limitations in model interpretability and robustness. At the application level, challenges involve effectively integrating AI into clinical workflows, gaining physician acceptance, addressing regulatory and ethical lag, and considering cost-effectiveness. Future directions for AI-empowered small pulmonary nodule diagnosis include developing data-efficient and trustworthy AI algorithms, advancing multimodal information fusion, building intelligent diagnostic and treatment systems based on human-machine collaboration, and promoting widespread AI applications in large-scale lung cancer screening, personalized therapy, and comprehensive disease management. These efforts aim to contribute to the precise prevention and treatment of lung cancer.

Keywords: Small pulmonary nodule; CT imaging; Artificial intelligence; Deep learning; Future prospects.

1. Introduction

Pulmonary nodules, particularly small pulmonary nodules (SPNs, ≤ 10 mm in diameter), manifest on imaging as focal areas of increased attenuation surrounded by lung parenchyma, without complications such as atelectasis or pleural effusion. The widespread adoption of high-resolution CT (HRCT) and lung cancer screening programs has led to a significant increase in the detection rate of SPNs[1]. These nodules may harbor early-stage lung cancer or precancerous lesions, and their accurate diagnosis is directly linked to patient prognosis—for instance, stage I non-small cell lung cancer patients exhibit a 5-year survival rate of 70%-90%, which declines drastically in advanced stages [2].However, traditional manual interpretation faces a triple challenge: heavy workloads increase the risk of missing subtle or atypical nodules; diagnostic outcomes are highly dependent on physician experience, leading to significant inter-observer variability; and distinguishing benign from malignant nodules, especially complex types like ground-glass nodules (GGNs), remains difficult, potentially resulting in misdiagnosis or delayed treatment.

Artificial intelligence (AI) technology offers novel pathways to overcome these bottlenecks. Deep learning techniques, particularly convolutional neural networks (CNNs) and Transformers, demonstrate robust capabilities in autonomously learning features from vast imaging datasets. These techniques excel in pulmonary nodule detection, precise segmentation, benign-malignant differentiation, and dynamic follow-up assessment. Recent studies have confirmed diagnostic performance comparable to expert levels, highlighting transformative potential for early lung cancer detection. Given the significant clinical value and rapid advancements in this field over the past decade (2014-2024), this review conducts a systematic analysis of domestic and international research progress, focuses on core technological breakthroughs, evaluates clinical application outcomes and existing limitations, provides an in-depth assessment of implementation challenges, and outlines future development directions.

2. Current Status of AI in CT Diagnosis of Small Pulmonary Nodules

In recent years, deep learning has significantly propelled the development of AI for SPN diagnosis on CT. AI technology has evolved from early computer-aided detection/diagnosis (CADe/CADx) systems into neural network-based intelligent analysis platforms, with its potential to enhance diagnostic efficiency, accuracy, and consistency gaining widespread recognition. Current applications span the entire workflow—screening, detection, segmentation, qualitative assessment, and follow-up management—aiming to overcome the diagnostic limitations of traditional methods for occult SPNs. As the technology matures, AI products are progressively entering clinical trials and real-world practice, where their clinical value and practical challenges are increasingly evident.

2.1 Technological Methods and Advancements

AI advancements are primarily reflected in three interconnected areas: algorithmic innovation, construction of high-quality datasets, and refinement of clinical validation systems, collectively driving improvements in nodule detection, segmentation, and classification performance

2.1.1 Mainstream Algorithms and Applications

Convolutional Neural Networks (CNNs) and their variants form the current technological core. U-Net series architectures enhance boundary segmentation accuracy, laying the foundation for quantitative nodule analysis and malignancy prediction. Object detection algorithms (e.g., Faster R-CNN, YOLO) enable rapid localization of suspicious nodules within CT images. Deep models like ResNet and DenseNet leverage large-scale annotated data for training to predict malignancy risk. Emerging technologies further expand capabilities: attention mechanisms enhance the model's ability to capture critical features of SPNs; Transformer architectures (e.g., ViT, Swin) utilize self-attention to integrate global contextual information, showing promise for multimodal data processing; semi-supervised and self-supervised learning paradigms significantly reduce reliance on expensive annotated data, boosting model performance in resource-constrained scenarios. Chinese scholars actively contribute localized innovations: optimizing algorithm models for the imaging characteristics of the Chinese population and promoting standardized technology implementation through participation in the *Chinese Expert Consensus on AI for Pulmonary Nodule Diagnosis and Management (2022/2024)* [6, 7].

2.1.2 Datasets and Preprocessing

High-quality datasets are fundamental to model robustness. International public repositories (e.g., LIDC-IDRI, LUNA16, NLST) provide diverse annotated data; domestic institutions are concurrently building local databases tailored to the characteristics of the Chinese population. Preprocessing directly impacts model performance: image standardization (window width/level adjustment) and denoising (Gaussian/median filtering) optimize visual information; precise lung parenchyma segmentation defines the region of interest; data augmentation techniques (rotation/scaling/noise addition) enhance sample diversity and model generalization. Radiomics serves as a vital complement, extracting high-throughput quantitative features (morphology, texture, etc.) and combining them with machine learning to uncover deeper information for aiding benign-malignant differentiation and prognosis assessment [10].

2.1.3 Performance Evaluation and Clinical Validation

Objective evaluation requires metrics aligned with the task: Free-Response Receiver Operating Characteristic (FROC) curves and false positives per scan (FPs/scan) for detection; Dice coefficient, Intersection over Union (IoU) for segmentation; sensitivity, specificity, and Area Under the Curve (AUC) for classification [11]. Clinical validation is paramount for assessing real-world utility: combining retrospective and prospective studies using pathology or multidisciplinary team (MDT) consensus as the gold standard; multicenter validation specifically examines model generalization across institutions and robustness against interference (e.g., image noise). Studies confirm AI significantly boosts nodule detection rates for junior radiologists (Figure 1) [1], though its impact is more limited for senior experts, highlighting its differential clinical value

2.2 Application Status and Challenges

AI technology is gradually transitioning from theoretical research to clinical deployment, revealing key bottlenecks alongside its demonstrated value.

2.2.1 Clinical Application Cases

In lung cancer screening scenarios, AI systems can automatically identify suspicious nodules in low-dose CT images, perform initial measurements and feature analysis, significantly improving reading efficiency(Table 1). Acting as a "second reader," AI can flag easily overlooked SPNs, effectively reducing missed diagnosis rates [12]. In the diagnostic phase, AI outputs malignancy probability scores by comprehensively analyzing nodule morphology, density, and surrounding tissue relationships, providing valuable references for clinical decisions. During follow-up management, AI automatically tracks dynamic changes like volume doubling time, aiding in formulating subsequent treatment plans [13]. Multiple AI products globally have received regulatory approvals (e.g., NMPA/FDA/CE). Chinese systems have demonstrated value in large-scale health screenings and deployments in primary hospitals. The Chinese Expert Consensus on Diagnosis and Treatment of Pulmonary Nodules (2024) [7] emphasizes the need for scientific evaluation of AI systems and advocates for human-AI collaborative MDT models to optimize diagnostic and therapeutic pathways.

Table 1. Performance Metrics for AI Diagnosis Systems

Metric	Detection	Segmentation	Classification
Primary Measure	FROC curve	Dice coefficient	AUC
Secondary Measure	FPs/scan	IoU	Sensitivity/Specificity
Typical Range	0.85-0.95	0.75-0.90	0.80-0.93

2.2.2 Existing Problems and Limitations

Performance Bottlenecks: Insufficient model generalization remains the core challenge—performance degrades significantly across institutions, populations, or varying scan parameters, particularly for identifying atypical SPNs (e.g., very low density). Some studies indicate certain AI systems offer no clear advantage over traditional models (e.g., Mayo model) [14]. Technical Obstacles: Model dependence on specific device parameters, lack of interpretability in decision-making processes reducing clinical trust, technical barriers to integration with hospital PACS/RIS systems, and suboptimal human-computer interfaces needing optimization for operational efficiency. Ethics and Regulation: Patient data privacy protection must comply with regulations. The Chinese Expert Consensus on AI for Pulmonary Nodules (2022) [6] explicitly proposes mitigating risks through human-AI MDT models, providing a framework for healthy technology development.

3. Analysis of Challenges in AI Diagnosis of Small Pulmonary Nodules

The inherent "smallness" of SPNs poses unique challenges for AI diagnosis. Compared to larger nodules, their imaging features are more subtle and variable, demanding higher perception and generalization capabilities from AI. These challenges permeate the entire process from technology development to clinical implementation.

3.1 Technical-Level Challenges

Identifying SPNs faces multiple obstacles: minute size (occupying only a few pixels), low density (especially pure ground-glass nodules - pGGNs), blurred margins, and variable morphology, making them easily confused with vascular cross-sections or inflammatory foci, leading to high false positive/negative rates in AI detection. Systematic reviews indicate persistent methodological flaws in existing deep learning approaches [8]. More challenging is the identification of early malignant signs (e.g., micro-solid components)—AI must extract discriminatory features from limited pixels, where traditional radiomics efficacy plummets. Quantifying subtle changes in nodule volume/density during follow-up also represents a major technical difficulty.

The scarcity of high-quality data exacerbates these challenges. Pixel-level annotation of SPNs relies on highly skilled physicians, is time-consuming, costly, and suffers from low inter-observer consistency, introducing annotation noise. Ethical approvals and data-sharing barriers further restrict the construction of multi-center databases. Data heterogeneity is particularly problematic: variations in CT equipment, scan parameters (slice thickness/dose), and reconstruction algorithms cause image feature discrepancies. This significantly impacts signal-weak SPNs, potentially causing precipitous performance drops when models are applied across centers. While domain adaptation techniques like transfer learning have been attempted, their upper limits in complex scenarios require further exploration.

The lack of model interpretability is a critical barrier to clinical adoption. The decision-making processes of "black box" models like CNNs and Transformers are opaque, making physicians hesitant to trust high-stakes diagnoses (e.g., labeling a small GGN as malignant). Explanation techniques like heatmaps (Grad-CAM) still lack sufficient explanatory power for complex decisions [10]. Robustness issues are equally severe: image noise, artifacts, or adversarial attacks can cause misdiagnosis, and SPNs are more vulnerable due to their weak signals. Robust model safety protection systems are urgently needed.

3.2 Application-Level Challenges

Clinical integration requires solving workflow compatibility issues. The ideal scenario involves AI seamlessly embedded within PACS systems, providing real-time nodule detection and assessment without adding operational steps. The "Human-AI MDT" model proposed by Chinese scholars attempts to balance AI assistance with physician decision-making authority through multidisciplinary collaboration [7]. Physician acceptance is influenced by multiple factors: genuine trust in performance for subtle/difficult nodules, system usability, value of decision support, and clarity on misdiagnosis liability. Senior experts tend to prefer autonomous judgment, while junior physicians show higher demand for AI assistance [1].

Regulatory approval constitutes a market access barrier. Regulatory agencies in China, the US, and Europe (NMPA/FDA/CE) all require AI diagnostic software to undergo rigorous clinical trials, and lengthy approval cycles constrain technological iteration. Ethical dilemmas are also prominent: patient privacy protection must be balanced with data utilization needs; training data biases may lead to diagnostic discrimination; liability for AI misdiagnosis remains undefined; and patient informed consent frameworks are lacking. These require multi-stakeholder collaboration to establish ethical norms [15].

Lack of standardization hinders industry development. The absence of standardized performance evaluation metrics, benchmark datasets, and technical interface specifications makes fair comparison between different AI products difficult. Business model sustainability is also tested: high R&D and deployment costs (algorithm optimization, hardware maintenance, system integration) need to be offset by demonstrated clinical value. Current healthcare reimbursement systems provide insufficient coverage for AI technologies. Demonstrating their economic value in improving diagnostic efficiency and reducing late-stage treatment costs is essential to establish reasonable pricing and payment pathways.

4. Future Prospects and Research Directions

Despite the numerous challenges, the immense clinical potential and broad application prospects of AI-based CT diagnosis for SPNs remain highly anticipated. With continuous algorithmic innovation, deeper fusion of multimodal data, and the gradual establishment of trustworthy AI systems, AI technology is expected to play an increasingly vital role throughout the entire lung cancer care continuum—prevention, screening, diagnosis, treatment, and management—for SPNs and beyond.

4.1 Emerging Technological Trends and Breakthroughs

Future efforts will focus on enhancing AI efficiency, robustness, and clinical utility. To reduce dependence on finely annotated data, self-supervised learning and few-shot learning are key directions, while federated learning enables multi-center collaboration while preserving data privacy. In network architecture, Graph Neural Networks (GNNs) can analyze internal nodule structures and spatial relationships with surrounding tissues, while multimodal Transformers aim to fuse CT/PET images, clinical text, and genomic data. Model lightweighting designs (e.g., knowledge distillation) will also facilitate AI deployment in primary care settings.

Multimodal fusion is breaking the limitations of single-modality image analysis. Integrating CT anatomical information, PET metabolic activity, clinical data (age/smoking history), and molecular biomarkers (e.g., ctDNA methylation profiles [16]) can build more precise diagnostic models. PulmoSeek Plus, developed by Chinese scholars, significantly improved benign-malignant classification accuracy by combining CT imaging with cfDNA methylation [17]. Such systems will enable intelligent full-cycle management: from high-risk population screening and nodule classification to personalized treatment decisions (surgical indication assessment/ablation strategy recommendation) and prognosis monitoring, forming a prevention-diagnosis-treatment closed loop.

Building trustworthy AI is central to clinical adoption. This requires transparent decision processes (e.g., causal inference techniques surpassing basic heatmaps), strong robustness against data perturbations, and fairness to avoid diagnostic bias. Human-AI collaboration will then unlock maximum value: AI handles initial screening and quantitative analysis, while physicians integrate comprehensive clinical information for final decision-making, creating a synergistic "1+1>2" model.

4.2 New Clinical Application Horizons and Societal Value

AI technology promises revolutionary changes in SPN diagnosis and treatment, with societal value concentrated in three key areas. In screening and prevention, leveraging its low cost and high efficiency, AI can empower large-scale opportunistic lung cancer screening: automatically analyzing routine health check-up or cardiovascular patient chest CTs to concurrently perform initial SPN screening, detecting early-stage lung cancer in broader populations (beyond traditional high-risk definitions), significantly boosting early diagnosis rates and patient quality of life. Furthermore, by integrating multi-source data (imaging features, genetic information, environmental exposure, etc.), AI can precisely quantify individual lung cancer risk, enabling tailored prevention strategies (e.g., personalized screening frequency, smoking cessation guidance), shifting the paradigm from passive reaction to active prevention.

In treatment decision-making, AI will not only differentiate benign from malignant nodules but also synthesize imaging characteristics (growth rate/surrounding structure relationships), molecular markers, and patient clinical status to assist in formulating personalized plans: assessing surgical necessity, indications for minimally invasive ablation, or active surveillance strategies, thereby avoiding overtreatment. For treatment efficacy assessment, analyzing dynamic radiomics changes pre- and post-treatment, combined with molecular pathology data, AI can predict short-term response and long-term survival outcomes for various therapies (including immunotherapy [18]), providing evidence-based support for regimen adjustment and advancing precision oncology in lung cancer.

Regarding healthcare resource optimization, AI is a core engine for smart healthcare. Cloud-based diagnostic platforms and primary care PACS systems integrated with AI can extend the expertise of tertiary hospital specialists to community settings, elevating the standardized diagnostic and therapeutic capabilities of primary care physicians for SPNs and narrowing urban-rural health disparities. Additionally, AI accelerates scientific innovation: mining novel imaging biomarkers from vast clinical data, optimizing clinical trial design; and providing standardized virtual case libraries in medical education, enhancing physician training efficiency.

5. Conclusion

AI-based diagnosis of small pulmonary nodules on CT imaging stands as one of the most dynamic and promising research directions in medical image analysis today, holding significant clinical importance and vast developmental potential for achieving early detection, precise diagnosis, and personalized treatment of lung cancer. Over the past decade, fueled by the rapid advancement of deep learning and other AI technologies, encouraging progress has been made in algorithmic model innovation, diagnostic performance enhancement, and preliminary clinical application. AI systems have demonstrated excellent auxiliary capabilities in the automatic detection, precise segmentation, benign-malignant differentiation, and dynamic follow-up of pulmonary nodules, providing powerful tools for radiologists.

However, translating AI technology into mature clinical applications that widely benefit patients still faces numerous formidable challenges. Particularly in the specific domain of SPNs, due to their inherent imaging characteristics and the complexity of clinical management, AI must overcome several technical bottlenecks to achieve high-precision, robust, and trustworthy diagnosis. These include the accurate identification of minute lesions, the acquisition and sharing of high-quality annotated data, improving model interpretability, and ensuring generalization in diverse, real-world clinical environments. Simultaneously, seamless integration into clinical workflows, fostering physician trust and acceptance, establishing rigorous regulatory approvals and ethical frameworks, and developing sustainable business models and reimbursement systems are essential hurdles that must be crossed for AI technology to mature into widespread clinical use.

Looking ahead, the key to overcoming these challenges lies in continuous technological innovation and close multidisciplinary collaboration. Core future research directions will focus on developing novel AI algorithms that are data-efficient, robust, and highly interpretable; achieving deep intelligent fusion of imaging, clinical, pathological, and molecular multimodal data; and building a trustworthy AI technology ecosystem that is technically reliable, ethically sound, and clinically practical. Concurrently, the application scenarios of AI across the entire lung nodule care cycle—screening, diagnosis, treatment decision-making, efficacy assessment, and follow-up management—should be continually expanded and deepened, with real-world effectiveness and value rigorously validated through clinical trials. We have reason to believe that with ongoing technological progress and deepening application, artificial intelligence will undoubtedly contribute significantly to greater victories in humanity's fight against lung cancer and make vital contributions to improving population health.

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