

REVIEW ARTICLE

Artificial intelligence for surgically resectable lung cancer: Toward a multimodal and clinically actionable framework

Zhuowei Li^{1,2,3,4†} , **Xiaoqiu Yuan**^{1,2,3,4†} , **Yukun Chen**^{1,2,3,4} , **Ruoyi Jin**^{1,2,3,4} , **Yunchu Wei**^{1,2,3,4} , **Xu Liu**^{1,2,3,4} , **Lin Weng**^{1,2,3,4} , **Huiting Su**^{1,2,3,4} , and **Kezhong Chen**^{1,2,3,4*} 

¹Department of Thoracic Surgery, Thoracic Oncology Institute, Peking University People's Hospital, Beijing, China

²Research Unit of Intelligence Diagnosis and Treatment in Early Non-small Cell Lung Cancer, Chinese Academy of Medical Sciences, Beijing, China

³Institute of Advanced Clinical Medicine, Peking University, Beijing, China

⁴Frontiers Science Center for Cancer Integrative Omics, Peking University People's Hospital, Beijing, China

Abstract

Lung cancer remains the leading cause of cancer incidence and mortality worldwide, and surgically resectable disease represents a critical window for cure. However, the current care continuum for resectable lung cancer remains limited by heterogeneous risk profiles, empirical decisions, fragmented integration of multi-dimensional information, and insufficient prediction of clinical outcomes. Under these circumstances, artificial intelligence (AI) has emerged as a promising approach for extracting clinically relevant information from complex data. Nevertheless, a synthesis of AI evidence across the full pathway of resectable lung cancer remains lacking, leaving clinicians uncertain about its clinical implementation. To address this gap, we narratively synthesize representative evidence regarding the evolution, technical platforms, and clinical applications of AI in resectable lung cancer, integrating how AI could support preoperative screening and diagnosis, intraoperative decision-making and procedures, as well as postoperative treatment and surveillance. We further discuss the major barriers to clinical translation, including limited external and prospective validation, patient safety, and accountability, followed by future directions. At present, many AI applications remain at an early exploratory stage, and further prospective evaluation is required to establish their clinical utility.

Keywords: Resectable lung cancer; Artificial intelligence; Precision surgery; Perioperative management; Multimodal data integration; Diagnosis and treatment

†These authors contributed equally to this work.

***Corresponding author:**
Kezhong Chen
(chenkezhong@pku.edu.cn)

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1. Introduction

Lung cancer remains the leading malignancy worldwide in terms of both incidence and mortality. Surgically resectable lung cancer generally refers to lung cancer considered amenable to complete surgical resection after multidisciplinary evaluation^{1,2}, accounting for approximately 30% of cases.^{3,4} For patients with resectable lung cancer, curative

surgery represents the cornerstone treatment for long-term survival.⁵ However, conventional diagnostic and therapeutic pathways still face limitations in early detection, risk prediction, and individualized decision-making.^{6,7} For example, although the tumor–node–metastasis (TNM) staging serves as the foundation of clinical management, it has limited discriminatory ability for individualized prognostic stratification when compared with tools incorporating imaging, pathological, or molecular information.⁸ Against this background, artificial intelligence (AI) has been developed to standardize and integrate large-scale multi-dimensional data.⁶ Technologies such as machine learning and natural language processing (NLP) have shown potential advantages over conventional approaches for surgically resectable lung cancer, particularly in providing data-driven and reproducible assessments, supporting individualized risk stratification and treatment planning, and facilitating more integrated clinical workflows (Table 1).^{9–11} For instance, in medical imaging, AI helps reduce false-positive findings of low-dose computed tomography (LDCT) and exceeds conventional statistical models in recurrence prediction.^{12,13}

Despite these advances, guidance on using AI tools in the routine care of patients with resectable lung cancer is currently lacking. Existing reviews largely focused on the

diagnostic or prognostic performance of AI in individual scenarios^{14–16}, while few have compiled the usage of AI across the entire care pathway, leaving clinicians in a dilemma where they intend to adopt AI yet remain uncertain about the specific implementation.

This article is a narrative review focusing on the applications of AI in the diagnosis and management of surgically resectable lung cancer. We searched PubMed, Embase, and Web of Science for English-language studies published from database inception to May 17, 2026, using combinations of terms related to “resectable lung cancer,” “thoracic surgery,” “artificial intelligence,” “machine learning,” “deep learning,” “radiomics,” “computer vision,” and “large language models.” The reference lists of relevant original studies and review articles were also examined to identify additional publications. We included representative studies addressing AI applications across the care pathway of surgically resectable lung cancer and provide a clinically oriented synthesis of recent advances in preoperative risk assessment and staging, intraoperative decision support, postoperative follow-up, and prognostic prediction, while also analyzing the potential advantages and practical challenges of AI. This review aims to provide a clinically oriented framework for evaluating the potential integration of AI into precision thoracic oncology.

Table 1. Comparison between conventional and artificial intelligence-assisted clinical practice for surgically resectable lung cancer

Comparison criteria	Conventional practice	Artificial intelligence-assisted practice
Decision-making basis	Subjective and experience-dependent	Data-driven and quantitatively supported ⁶
Observer variability	Relies on individual expertise and is prone to interobserver differences	Provides more standardized and reproducible assessments ^{17,18}
Use of nontraditional risk factors	Limited ability to incorporate risk factors beyond conventional criteria	Integrates diverse clinical, environmental, imaging, and molecular variables ¹⁹
Nonlinear relationships	Difficult to capture complex nonlinear associations among variables	Learns nonlinear patterns from high-dimensional data ²⁰
Multimodal information integration	Fragmented integration of imaging, pathology, molecular, and clinical data	Enables unified analysis of multimodal information ²¹
Individualization	Limited ability to tailor diagnosis, treatment, and follow-up to each patient	Supports individualized risk stratification and treatment planning ^{22,23}
Preoperative molecular subtyping	Often depends on invasive biopsy or surgical specimens	Enables noninvasive prediction of molecular and immune phenotypes from imaging and multimodal data ²⁴
Dependence on data or specimen quality	Diagnostic accuracy is easily affected by image quality, sampling adequacy, artifacts, and tissue heterogeneity	Can enhance feature extraction, identify subtle patterns, and assist interpretation in suboptimal or heterogeneous samples ²⁵
Prediction of long-term outcomes	Limited capacity to predict long-term recurrence and survival	Improves prediction of recurrence risk and survival ²⁶
Clinical workflow	Often relies on separate, sequential diagnostic steps	Facilitates integrated, continuous, and decision-oriented clinical workflows ¹⁹

2. Histories and platforms of artificial intelligence in resectable lung cancer

2.1. Brief history of artificial intelligence application in surgical thoracic oncology

The application of AI in surgically resectable lung cancer has evolved over three decades. Early efforts mainly relied on Bayesian algorithms and shallow artificial neural networks for diagnostic and prognostic prediction. As early as 1989, a Bayesian computer-assisted model was used to distinguish benign from malignant pulmonary lesions in patients undergoing thoracotomy for suspected cancer, achieving high diagnostic accuracy (95/100 concordance with pathological diagnosis) and representing one of the earliest attempts to integrate AI into thoracic evaluation.²⁷ In the mid-1990s, neural network analysis was increasingly applied to estimate the probability of malignancy and stage in pulmonary nodules using clinical and radiographic features.^{28,29} Subsequently, AI models were extended from preoperative diagnosis to postoperative outcome and surgical risk prediction. Genetic algorithm neural networks were used to predict survival after surgery for patients with non-small cell lung cancer (NSCLC) and outperformed logistic regression in individual outcome classification.^{30,31} Later neural network models further integrated multiple clinical, laboratory, and physiologic variables to estimate postoperative mortality and major complications after lung resection.³² These early studies established the initial concept that computational models could assist in diagnosis and risk stratification.

In the 2000s, AI-related technologies gradually moved beyond static diagnostic prediction toward computer-assisted procedural guidance. In virtual reconstruction and planning, Kiraly *et al.*³³ developed a computational image-analysis method for three-dimensional (3D) path designing in virtual bronchoscopy, in which airway structures in multidetector computed tomography (CT) images were skeletonized and refined into smooth central airway paths suitable for quantitative airway analysis and subsequent image-guided bronchoscopy. In intraoperative navigation, Nakamoto *et al.*³⁴ introduced a computer-assisted thoracoscopic surgical navigation system for localizing small lung cancers in the collapsed lung, combining preoperative CT surface models, intraoperative surface digitization, rigid registration of the thoracic cage and mediastinum, and nonrigid estimation of lung deformation to predict and superimpose tumor locations during thoracoscopy. These developments indicated a shift from image interpretation alone to spatial modeling and navigation.

Since the late 2010s, rapid advances in medical imaging

and digital pathology have substantially expanded the scope of AI applications in resectable lung cancer. CT-based deep learning models have been applied to scenarios such as predicting the invasiveness of lung adenocarcinomas³⁵ and disease-free survival after resection.³⁶ Meanwhile, the integration of AI with evolving medical technologies has further extended its role, as exemplified by shape-sensing robotic-assisted bronchoscopy (RAB) for sampling challenging pulmonary lesions³⁷ and digital rapid on-site evaluation (ROSE) during endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA).³⁸ Together, these advances have shifted AI development toward multimodal integration to support more comprehensive decision-making.³⁹

In the past two years, the burst of large language models (LLMs) and NLP systems has begun to support text-based clinical tasks, including treatment recommendations in thoracic multidisciplinary boards⁴⁰ and automated staging with rationale generation from surgical pathology reports.⁴¹ Meanwhile, AI is increasingly moving beyond clinician-facing applications toward public and patient-oriented use. For example, AI-integrated screening programs can facilitate high-risk population recruitment and lung nodule management¹⁹, while AI chatbots may provide accessible, understandable, and evidence-based answers to common patient questions.⁴² Thus, AI in surgically resectable lung cancer has progressed from early diagnostic classifiers to multimodal, workflow-integrated systems that support the entire perioperative care pathway.

2.2. Artificial intelligence platforms and algorithms applied in resectable lung cancer

At present, AI applications in surgically resectable lung cancer can be broadly categorized into three major technical platforms: machine learning, deep learning, and LLMs. Machine learning refers to algorithms that learn mappings between input features and clinical labels from structured tabular data, and is particularly useful for risk stratification, staging, complication prediction, and length-of-stay estimation.⁴³ Tree-based ensemble methods, such as random forest⁴⁴, extreme gradient boosting⁴⁵, and light gradient boosting machine⁴⁶, are widely used for their ability to capture nonlinear feature interactions with relatively high efficiency and interpretability; support vector machines (SVMs) and regularized regression models remain useful alternatives for small-sample or high-dimensional structured data.^{47–49} To improve clinical interpretability, the Shapley additive explanations (SHAP) method is typically incorporated to visualize the contribution of each feature to model predictions.⁵⁰ Deep learning, especially convolutional neural networks (CNNs) and related architectures, can automatically extract high-

dimensional representations from various kinds of medical images (CT, positron emission tomography[PET]/CT, histopathological images, EBUS images, and thoracoscopic videos), reducing reliance on handcrafted features.⁵¹ In resectable lung cancer, deep learning has been applied not only to diagnostic or prognostic prediction models⁵², but also to AI-assisted 3D reconstruction of anatomical structures⁵³, computer-vision-based surgical video analysis⁵⁴, and rapid pathological assessment.⁵⁵ Commonly used architectures include residual networks (ResNet) for image classification⁵⁶, U-Net and its variants for segmentation⁵⁷, recurrent neural networks or temporal convolutional models for sequential video analysis⁵⁸, and more recently vision transformers for image classification based on sequences of image patches.^{59,60} LLMs, as an advanced branch of NLP, excel at processing free-text clinical information^{61,62}, supporting their applications in multidisciplinary decision-making⁴⁰, pathology report structuring⁴¹, and patient education.⁶³ Technically, most recent LLMs are built on transformer architectures⁶⁴, with current hotspots including instruction tuning⁶⁵, retrieval-augmented generation⁶⁶, multimodal LLMs⁶⁷, and reasoning-oriented models⁶⁷, which may improve their usefulness in evidence synthesis and clinical text-based decision support.

Since these technical platforms are frequently combined according to the type of input data and the intended clinical task, AI applications in surgically resectable lung cancer can be further organized into six methodological categories: imaging-based AI, pathology-based AI, multi-omics AI, clinical-data-driven AI, image- and video-based procedural AI, and text-based AI and LLMs. Imaging-based AI mainly processes radiological and ultrasound images for screening, diagnosis, staging, or surveillance. Representative algorithms include radiomics-based machine learning, CNNs, ResNet, U-Net, 3D CNNs, and vision transformers, among which ResNet⁵⁶ and vision transformers⁵⁹ are widely used for image classification, the U-Net for segmentation⁵⁷, and 3D CNNs for volumetric imaging.⁶⁸

Pathology-based AI analyzes cytology, biopsy, frozen-section, and histology specimens, as well as advanced optical imaging data, for rapid diagnosis and margin and risk assessment. Multiple instance learning and attention-based weakly supervised models are particularly important for whole-slide image analysis because they can aggregate patch-level information into slide-level predictions without dense pixel-level annotations.^{69,70}

Multi-omics AI integrates tissue-derived and liquid-biopsy signals for early detection, molecular subtyping, and recurrence monitoring. Commonly used strategies

include regularized regression, random forest, SVMs, and latent factor models, such as multi-omics factor analysis⁷¹, and deep learning-based fusion models that project heterogeneous omics layers into shared latent spaces.⁷²

Clinical-data-driven AI uses structured clinical, laboratory, and physical data for risk prediction and follow-up management. It mainly relies on the machine learning algorithms described above, especially tree-based ensemble models⁷³ and regularized models⁷⁴, to transform heterogeneous tabular variables into individualized risk estimates and clinically interpretable predictions.

Image- and video-based procedural AI focuses on bronchoscopy, intraoperative navigation, and surgical video analysis. Object detection and instance segmentation models, such as You Only Look Once (YOLO)⁷⁵ and Mask R-CNN⁷⁶, support real-time localization of instruments or anatomical structures, whereas temporal CNNs⁷⁷, recurrent networks⁷⁸, and registration-based methods⁷⁹ are commonly used for surgical phase recognition, navigation, and image-to-patient alignment.

Text-based AI and LLMs process clinical narratives, guidelines, pathology reports, and patient questions to support decision-making and patient communication. Representative methods include bidirectional encoder representations from transformer-like encoder models for information extraction and classification⁸⁰, transformer-based generative models for dialogue and summarization⁶⁴, and retrieval-augmented generation⁶⁶ or instruction-tuned LLMs⁶⁵ for more controllable evidence-based responses. The methodological categories, corresponding technical platforms, representative algorithms, and main clinical tasks are summarized in [Table 2](#).

3. Applications of artificial intelligence in preoperative evaluation of lung cancer

Artificial intelligence has shown substantial potential across the entire preoperative pathway of surgically resectable lung cancer, from early screening and radiological diagnosis to biopsy-based staging, molecular subtyping, and treatment decision-making ([Figure 1](#)).

3.1. Applications of artificial intelligence in early screening and diagnosis of resectable lung cancer

3.1.1. Artificial intelligence-enhanced early screening and risk stratification

Artificial intelligence-assisted screening for surgically resectable lung cancer has the potential to support early detection by identifying non-classical high-risk individuals, streamlining screening entry, and integrating multimodal information.

Table 2. Methodological and technical classification of AI applications in surgically resectable lung cancer

Methodological category	Technical category	Representative algorithms/platforms	Main clinical tasks
Imaging-based AI	Machine learning and deep learning	Radiomics Machine learning: Logistic regression, LASSO, support vector machine, random forest ⁴⁴ , Naïve Bayes, XGBoost ⁴⁵ , LightGBM ⁴⁶ , SHAP ⁵⁰ Deep learning: CNN, 3D CNN ⁶⁸ , ResNet ⁵⁶ , U-Net ⁵⁷ , Transformer ⁵⁹ , attention-based models, Grad-CAM	Screening, preoperative diagnosis, staging, molecular feature prediction, surgical planning, and postoperative surveillance
Pathology-based AI	Deep learning and NLP/LLMs	Multiple-instance learning, hybrid attention networks, digital pathology classifiers, AI-ROSE, FSG-TL NLP/LLM-based report extraction ^{69,70}	Biopsy adequacy assessment, rapid pathology, subtype classification, margin/risk assessment, postoperative staging
Multi-omics AI	Machine learning and deep learning	Multimodal fusion machine learning or deep learning models ^{71,72}	Screening, nodule risk stratification, molecular subtyping, recurrence monitoring, perioperative treatment planning
Clinical-data-driven AI	Machine learning	Logistic regression, LASSO, support vector machine, random forest ⁴⁴ , Naïve Bayes, XGBoost ⁴⁵ , LightGBM ⁴⁶ , SHAP ⁵⁰	Risk stratification, treatment decision-making, complication prediction, recovery prediction, follow-up
Image- and video-based procedural AI	Deep learning	CNN, ResNet ⁵⁶ , U-Net ⁵⁷ , Faster R-CNN, Mask R-CNN ⁷⁶ , YOLO ⁷⁵ , Vision video-based CNNs ⁷⁷ , transformer ⁵⁹ , attention mechanisms, Grad-CAM	Bronchoscopy navigation, biopsy guidance, intraoperative navigation, surgical video analysis, precision surgery
Text-based AI and LLMs	NLP/LLMs	NLP, BERT/CancerBERT, ChatGPT, GPT, DeepSeek, Grok, generative language models, chain-of-thought fine-tuned LLMs ⁶⁵	MDT decision support, pathology report structuring, evidence synthesis, postoperative counseling, patient education

Abbreviations: 3D: Three-dimensional; AI: Artificial intelligence; AI-ROSE: Artificial intelligence-assisted rapid on-site evaluation; BERT: Bidirectional encoder representations from transformers; CancerBERT: Cancer-domain bidirectional encoder representations from transformers; CNN: Convolutional neural network; Faster R-CNN: Faster region-based convolutional neural network; FSG-TL: Feature selection and grouping-transfer learning; GPT: Generative pre-trained transformer; Grad-CAM: Gradient-weighted class activation mapping; LASSO: Least absolute shrinkage and selection operator; LightGBM: Light gradient boosting machine; LLMs: Large language models; Mask R-CNN: Mask region-based convolutional neural network; MDT: Multidisciplinary team; NLP: Natural language processing; ResNet: Residual network; SHAP: Shapley additive explanations; XGBoost: Extreme gradient boosting; YOLO: You Only Look Once.

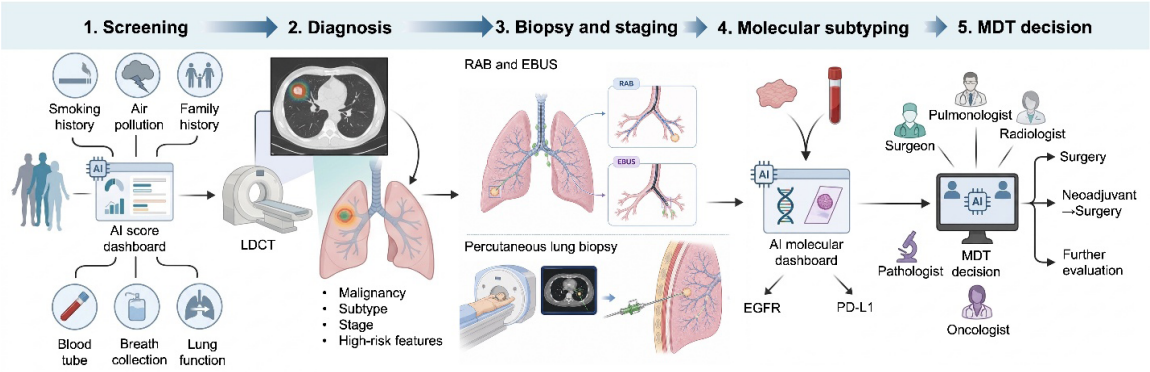


Figure 1. AI-assisted preoperative management workflow for surgically resectable lung cancer. Within the continuous preoperative diagnostic and decision-making workflow, AI can support the entire preoperative pathway, including early screening and risk stratification based on smoking history, environmental exposure, family history, liquid biopsy, exhaled breath analysis, and lung function; radiological diagnosis using LDCT/CT to assess nodule malignancy, subtype, stage, and high-risk features; biopsy and staging through robotic-assisted bronchoscopy, EBUS, and CT-guided percutaneous lung biopsy; molecular subtyping for EGFR mutation and PD-L1 expression status; and MDT-based treatment decision-making, including direct surgery, neoadjuvant therapy followed by surgery, or further evaluation.

Abbreviations: AI: Artificial intelligence; CT: Computed tomography; EBUS: Endobronchial ultrasound; EGFR: Epidermal growth factor receptor; LDCT: Low-dose computed tomography; MDT: Multidisciplinary team; PD-L1: Programmed death-ligand 1; RAB: Robotic-assisted bronchoscopy.

For screening candidates, traditional criteria primarily rely on age and smoking history⁸¹, which becomes largely insufficient for high-risk capture⁸² considering the increasing burden of lung cancer in never smokers (LCINS).⁸³ This issue is particularly relevant in East Asia, where LCINS accounts for a relatively high proportion of cases.⁸⁴ Its occurrence is associated with heterogeneous factors, including air pollution^{85–87}, radon exposure^{88,89}, family history^{90–93}, and genetic susceptibility^{87,94,95}, the risk state of which cannot be adequately characterized by a few simple clinical indicators. Existing studies have shown that multifactorial risk models exhibit moderate to strong stratification performance, with the area under the receiver operating characteristic curve (AUC) ranging from 0.673 to 0.774.^{96,97} However, among non-smoking individuals, combinations of risk factors unrelated to smoking (e.g., family history, fine particulate matter exposure, and radon exposure) often fail to reach an absolute risk level comparable to that associated with smoking (e.g., cumulative smoking exposure/pack-years and years since quitting smoking).²⁰ For instance, the PLCOall2014 model developed by Tammemägi *et al.*⁹⁸ did not identify any individuals exceeding the 6-year risk threshold of 1.5% commonly used for LDCT screening eligibility among 65,711 participants without a history of smoking. In addition, environmental and lifestyle factors usually generate nonlinear exposure-response patterns according to epidemiological studies⁹⁹, and are subject to measurement errors and lack standardized quantification^{96,97,100–103}, which further limits the implementation of traditional risk models. In contrast, AI has unique advantages in handling such interrelated information and may be better suited for identifying high-risk populations based on multiple risk factors beyond smoking.²⁰ However, evidence regarding the application of AI before LDCT screening remains limited, and further studies are needed to evaluate its performance in pre-screening risk stratification and candidate selection.

Artificial intelligence may also help simplify the entry into screening programs. To address practical barriers like insufficient recruitment, complex workflows, and suboptimal adherence, one study incorporated predefined AI software into a community-based screening program in China.¹⁹ By structurally collecting and automatically evaluating information on age, smoking status, passive smoking, occupational exposure, cooking oil fume exposure, personal history of cancer, and family history, this software provides risk-stratification results immediately after participants complete the questionnaire, allowing them to proceed directly to subsequent LDCT scheduling.¹⁹ This strategy leverages deep learning to integrate diverse factors into a low-burden, standardized, and scalable front-end screening pathway. It may help

streamline the identification of individuals who fall outside traditional screening criteria but have composite high-risk profiles and support their referral for LDCT screening.

In recent years, an increasing number of noninvasive technologies have emerged as promising tools for lung cancer screening. For example, liquid-biopsy-based multi-omics can comprehensively capture early molecular abnormalities in tumors, thereby improving the identification of high-risk individuals during the screening stage.^{104,105} A prospective study showed that a blood-based multi-omics screening model integrating cell-free DNA (cfDNA) methylation and protein features achieved an AUC of 0.966 in an independent validation cohort, with a reported sensitivity of 100% for stage I lung cancer, suggesting strong potential for early identification before LDCT.²¹ This strategy may facilitate preliminary population screening through a simple and radiation-free blood test, followed by referral of high-risk individuals to LDCT, potentially reducing unnecessary imaging while minimizing missed diagnoses. Meanwhile, this study also found that multi-omics integration outperformed single circulating tumor DNA (ctDNA) mutation or single protein indicators, suggesting the advantages of combining multidimensional information.²¹

Regarding another type of non-invasive omics, profiling of volatile organic compounds (VOCs) in exhaled breath with AI algorithms provides new possibilities for early screening. Unlike traditional VOC studies focusing on identifying specific compounds, AI approaches emphasize pattern recognition of the overall exhaled breath, thereby avoiding limitations caused by the instability of individual biomarkers, complex sources, and inconsistency across studies.^{106–108} A multicenter study showed that exhaled breath testing based on gas chromatography–ion mobility spectrometry combined with machine learning could effectively distinguish healthy individuals from patients with lung cancer¹⁰⁹, achieving an accuracy of 90%, sensitivity of 87%, and specificity of 92% for all cases. When only stage IA lung cancer was included, the accuracy remained at 90%, with sensitivity and specificity reaching 90% and 93%, respectively, indicating robust potential for detecting early-stage disease.¹⁰⁹ More importantly, this method does not require predefined VOC components but directly uses general spectral information for classification, greatly improving model transferability and practical deployability.¹⁰⁹ AI-assisted exhaled breath spectral analysis may serve as an auxiliary tool within screening systems, with higher-risk results prompting LDCT or further clinical evaluation, while still requiring broader external and prospective validation with further standardization of workflows.¹¹⁰

3.1.2. Artificial intelligence-enhanced early diagnosis and pulmonary nodule characterization

Radiomics-based AI has been widely applied to differentiate malignant from benign nodules and has demonstrated stable diagnostic performance. Although conventional imaging models offer some interpretability, they are inherently constrained by the subjectivity of semantic features and the limited dimensionality of manually defined variables, making it difficult to fully characterize invasive transitions.¹¹¹ Instead, radiomics and deep learning can automatically extract high-dimensional features from routine imaging and capture textural information difficult for the human eye to recognize, thereby optimizing the assessment of nodule characteristics.²⁵ Accordingly, CT-based deep learning models have achieved high discriminatory performance comparable to or higher than that of radiologists in selected datasets, including higher sensitivity in some studies^{112–117}, alleviating workforce demands and resource pressures associated with large-scale screening. At the same time, AI-based models maintain relatively stable predictive performance across different LDCT reconstruction parameters and equipment conditions, implying technical robustness and clinical generalizability.¹¹⁸ Recently, an attention-enhanced interpretable deep learning framework was developed to distinguish lung adenocarcinoma from normal lung tissue on CT images, achieving high classification accuracy and favorable discriminatory performance in a large dataset. Notably, the attention heatmaps generated by the model substantially overlapped with tumor regions manually annotated by radiologists, supporting the visual interpretability of the model.¹¹⁹ AI-derived nodule risk estimates may help support decisions among interval LDCT surveillance, additional PET/CT evaluation, bronchoscopic or percutaneous biopsy, and referral for surgical assessment. Cross-scenario comparisons of multiple prediction models indicate that the advantages of AI in differentiating malignant from benign pulmonary nodules depend on the specific application context. Single-time-point CT-driven AI models may be more suitable for screen-detected nodules, whereas models incorporating longitudinal follow-up imaging or clinical and biomarker information often perform more robustly in incidentally detected nodules. For nodules that have already entered the bronchoscopy biopsy pathway and are clinically highly suspicious, the performance of current models remains limited.¹²⁰ These findings suggest that applying AI to lung cancer diagnosis requires selecting appropriate modeling strategies based on the source and clinical context of the nodules, while integrating longitudinal information and multimodal fusion are needed to improve risk stratification

for complex and uncertain nodules. Current models still lack sufficient generalizability across centers; therefore, calibration, fine-tuning, and validation based on local cohorts are required during clinical translation. Beyond CT-based applications, deep learning models trained on chest radiographs can also accurately discriminate pulmonary nodules¹²¹, enabling lower-cost screening.

After accurate diagnosis, further clarification of pathological subtypes, degree of invasiveness, and staging is critical for formulating individualized surgical strategies. Studies have shown that the mean CT value and radiological nodule type are independent predictors of high-risk invasive lesions. For early-stage solitary NSCLC, AI software can automatically segment nodule boundaries and extract quantitative density parameters, enabling assessment of solid components and identification of nodules with higher invasive potential before surgery.¹²² For the classification of pulmonary ground-glass nodules into adenocarcinoma *in situ* (AIS), minimally invasive adenocarcinoma (MIA), and invasive adenocarcinoma (IAC), a multicenter study showed that deep learning models outperformed conventional methods based on handcrafted features, with a macro-AUC exceeding 0.80.¹²³ In terms of precise tumor staging, AI-based radiomics models constructed from quantitative preoperative CT features exhibit good discriminatory ability in predicting the T component, highly correlated with postoperative pathology.¹²⁴ Another multicenter study introduced AI prediction into the International Association for the Study of Lung Cancer (IASLC) pathological grading system. By integrating tumor heterogeneity indicators with imaging features, the composite model achieved favorable performance in distinguishing IASLC Grade 1 from Grade 2–3 lung adenocarcinoma before surgery and demonstrated stable discriminatory ability across datasets from different centers.¹²⁵ Together, these AI prediction models may provide supplementary information for assessing nodule invasiveness before surgery, which could support discussion of the suitability of surveillance, biopsy, sublobar resection, or lobectomy and the need for more detailed intraoperative pathological assessment.^{126,127}

Artificial intelligence has also been applied to predict pathological features associated with postoperative recurrence, such as lymph node metastasis and spread through air spaces (STAS). Regarding lymph node status, comparisons of multiple machine learning algorithms have shown that linear SVM can achieve an accuracy of more than 95% in predicting mediastinal lymph node metastasis (N2), with an AUC significantly higher than that of logistic regression.¹²⁸ While deep learning models that rely solely on CT images may be less effective¹²⁸, models that

integrate PET/CT features of both the primary tumor and lymph nodes with clinicopathological data can accurately identify mediastinal lymph node metastasis, highlighting the value of multimodal data fusion.¹²⁹ External validation further confirmed their generalizability across different populations, demonstrating specificity comparable to or superior to standard PET/CT interpretation and offering the possibility of reducing unnecessary invasive preoperative staging procedures.¹³⁰ Clinically, a higher model-predicted probability of N2 involvement may help identify patients who are more likely to benefit from invasive mediastinal staging, such as EBUS-TBNA or, where appropriate, mediastinoscopy, before proceeding directly to surgery.¹³¹ In addition, deep learning models have been retrospectively evaluated for STAS prediction, achieving an AUC of 0.918 by combining preoperative CT radiomics features with clinical data.¹³² A high predicted probability of STAS may provide supplementary information when evaluating the suitability of wedge resection, segmentectomy, or lobectomy and could prompt closer attention to margin adequacy and intraoperative pathological assessment.¹³³ Predicting occult pleural dissemination is crucial to avoid unnecessary surgery in patients with NSCLC. One retrospective study compared the performance of radiomics machine learning, deep learning, and a fusion model and found that the late-fusion model, which integrated the output probabilities of the two models, achieved the best predictive performance and the highest sensitivity across validation cohorts.¹³⁴ If AI indicates a high risk of occult pleural dissemination, additional imaging or invasive evaluation may be considered, together with contingency planning for intraoperative findings that could preclude curative resection.¹³⁵ Additionally, Cao *et al.*¹³⁶ constructed a hybrid model capable of predicting composite pathological features, involving high-grade histological subtype, lymph node metastasis, pleural/vascular/perineural invasion, and STAS, with AUC values exceeding 0.8 in external validation. Such predictions may help identify patients who warrant more extensive preoperative assessment, closer evaluation of resection margins and lymph-node management, or multidisciplinary team (MDT) discussion before surgery. Nevertheless, the outputs of these predictive models should not be used as the sole basis for decisions regarding invasive staging, resection extent, lymph-node management, or multimodal treatment, but should instead be interpreted alongside conventional imaging, pathological findings, guideline-based recommendations, patient characteristics, and multidisciplinary clinical judgment.

Integration of imaging and multimodal data shows further potential for improving the performance of benign-malignant pulmonary nodule discrimination. Compared to

models relying solely on nodule morphological features or a single AI imaging score, a unified prediction framework incorporating clinical information, imaging features, AI-assisted LDCT analysis results, and liquid biopsy signals more comprehensively characterizes the malignant risk of nodules.²¹ Among individuals with intermediate- to high-risk pulmonary nodules, liquid biopsy and AI-based imaging analysis showed strong complementarity with clinical factors. The integrated model achieved diagnostic performance superior to that of traditional models¹³⁷ and maintained high sensitivity in early-stage lung cancer.¹³⁸ To reduce the reliance on predefined clinical factors or semantic imaging variables, Jin *et al.*²¹ developed an AI-assisted pulmonary nodule diagnostic model that integrated CT radiomics/deep learning features with cfDNA methylation information. In the independent validation cohort, the model achieved a sensitivity of 81.1% and a specificity of 76.0%, superior to that of conventional prediction models based on clinical information and imaging semantic features, as well as the judgments of some clinical experts. Although still demanding prospective validation and standardization, liquid biopsy is promising for providing biological information beyond AI-assisted image interpretation, thereby improving specificity while maintaining high sensitivity.^{21,137,139}

3.2. Artificial intelligence-assisted preoperative staging of resectable lung cancer

3.2.1. Artificial intelligence-assisted robotic-assisted bronchoscopy systems and endobronchial ultrasound

In preoperative bronchoscopic evaluation, RAB relies on 3D reconstruction of the bronchial tree and target lesion using preoperative CT images, and combines electromagnetic navigation or catheter shape-sensing technology to enable automated path planning for peripheral pulmonary nodules¹⁴⁰, where AI can assist throughout the entire process. For shape-sensing catheters in RAB systems, such as those based on fiber Bragg grating technology, AI algorithms continuously track catheter location and orientation, reducing navigation errors specific to tip localization.¹⁴¹ At the same time, RAB can integrate multimodal intraoperative imaging, such as augmented fluoroscopy, for real-time registration and target position correction.^{142–145} During this process, AI algorithms project and overlay the target lesion onto real-time fluoroscopic images, creating an augmented reality display. This allows physicians to more accurately localize lesions and clarify their spatial relationship with the biopsy instrument, even when the target is not directly visible¹⁴⁵, thereby increasing the confirmation rate of “tool-in-lesion” positioning.¹⁴⁶ Several meta-analyses have reported a significantly higher diagnostic yield for RAB than for some

conventional bronchoscopic techniques for peripheral pulmonary nodules smaller than 20 mm.^{147–149}

Artificial intelligence has also been explored for real-time anatomical recognition and segmental localization by applying deep learning to bronchoscopic video streams, with early studies suggesting improved automatic annotation and navigation accuracy within the bronchial tree, particularly through complex branches and distal airways^{150,151}, although these systems remain investigational and require prospective evaluation within real bronchoscopic workflows. For medical training, AI-driven virtual or model-based airway navigation systems can provide real-time feedback on deviations from the planned route and have shown learning curves superior to those of traditional manual instruction, potentially lowering the technical barrier for complex navigational bronchoscopy.^{152–155}

For mediastinal staging, the refinement of N staging in the ninth edition of the IASLC TNM staging has further increased reliance on accurate lymph node assessment under EBUS guidance.¹⁵⁶ Deep learning-based image analysis has been introduced into real-time ultrasound image analysis during EBUS-TBNA, enabling imaging-based identification of involved lymph nodes and optimizing the selection of puncture targets. Deep learning-based EBUS analysis automatically extracts features from B-mode ultrasound images and elastography, showing high accuracy, specificity, and positive predictive value in predicting mediastinal lymph node metastasis in mainly retrospective studies^{157–160}, which exceeded that of manual interpretation of ultrasound features in some reports.^{158,161} Prospective workflow studies are still required to determine whether such models improve target selection, sampling adequacy, or staging accuracy in routine practice.

During sampling, AI-assisted image integration and rapid pathological assessment—including ROSE and frozen section examination—allow the sequential completion of lesion biopsy, mediastinal lymph node sampling and staging under a single anesthesia session, thereby providing immediate decision support for subsequent curative therapy.^{146,162,163} For immediate cytological assessment, ROSE is commonly used in EBUS-TBNA and transthoracic needle sampling to immediately determine whether the collected material is adequate.¹⁶⁴ However, not all centers have access to experienced cytopathologists to perform ROSE, limiting its clinical application.¹⁶⁵ In recent years, AI-driven ROSE systems have used deep learning to automatically interpret cytological images in the absence of pathologist support, with retrospective studies suggesting that they may shorten procedure time^{166,167}, reduce interoperator variability^{17,18}, and achieve

performance in specimen-adequacy assessment and cell classification approaching that of conventional ROSE.^{168–170} Combining remote image sharing (E-ROSE) with AI-based interpretation (AI-ROSE) can establish a parallel interpretation by remote cytopathology experts and machine learning models. This transforms intraoperative rapid pathology from a single-operator, on-site process into a composite decision that integrates expertise and algorithmic output.¹⁷¹ Even without an on-site cytopathologist, this model maintains high consistency and stability. Standardizing image input and algorithmic output reduces interpretive differences among centers and operators, potentially improving the consistency of ROSE interpretation.¹⁷¹ Beyond ROSE, some tissue-type-agnostic assessment platforms based on metabolic imaging can also be integrated with machine learning algorithms to provide rapid and reproducible intra-procedural feedback on biopsy specimen quality and adequacy.¹⁷² However, the safety and reliability of these models across institutions and specimen types still require prospective validation.

Meanwhile, novel EBUS-guided biopsy techniques, such as intranodal forceps biopsy and cryobiopsy, can yield larger tissue specimens for molecular profiling, which is especially useful in neoadjuvant settings.^{173,174} Beyond cryobiopsy, rapid on-site histological assessment that does not require freezing or section preparation has also emerged in recent years, and its integration with AI-based image analysis may further support intra-procedural biopsy evaluation. Higher harmonic generation microscopy (HHG) can simultaneously acquire third-harmonic generation (THG), second-harmonic generation (SHG), and two-photon excited autofluorescence signals, enabling simultaneous visualization of cellular structures, collagen, and elastic fibers in fresh biopsy specimens without fixation, embedding, or staining.¹⁷⁵ Compared to ROSE, HHG can provide an on-site assessment of biopsy tissue that more closely resembles conventional histology. Compared to frozen-section examination, HHG does not require slide preparation and can generate a specimen image within minutes, while avoiding interpretation interference from freezing artifacts.¹⁷⁵ Importantly, this study further developed a deep learning-based diagnostic pipeline for HHG images, using a fully convolutional ensemble model with multi-instance learning to classify tissue as malignant or non-malignant and to highlight anomalous or suspicious regions. Although its performance remained preliminary, with an accuracy of 71.1% and an AUC of 0.71 in the independent test set, these results suggest the potential of the AI-assisted HHG framework for real-time tumor indication, biopsy representativeness assessment, and region-of-interest marking during bronchoscopic or thoracoscopic procedures.¹⁷⁵ As this evidence is derived

from an exploratory *ex vivo* study, the system should be regarded as a proof-of-concept platform rather than a clinically validated alternative to ROSE or conventional pathology. When navigational bronchoscopy yields negative or indeterminate sampling results, multimodal models combining digital pathology and clinical as well as imaging features can mine occult malignant morphological features from routine biopsy sections, potentially reducing false negatives and optimizing subsequent surgical, percutaneous biopsy, or follow-up strategies.¹⁷⁶

Although AI applications in interventional pulmonology remain investigational, their potential in CT image analysis, navigation optimization, and automated cytological interpretation is gradually forming a full-process support system for precise preoperative staging and individualized treatment planning in lung cancer.^{151,167,177}

3.2.2. Artificial intelligence-assisted computed tomography-guided percutaneous lung biopsy

When a transbronchial lung biopsy fails, CT-guided percutaneous needle lung biopsy (PNLB) can be further applied. To support this procedure, machine learning models can integrate patient characteristics, lesion imaging features, puncture-related parameters, and post-bronchoscopy pathological information to predict both the risk of PNLB-related serious adverse events and the probability of diagnostic success with salvage PNLB, which helps clinicians choose among repeat bronchoscopy, percutaneous biopsy, surgery, or continued imaging follow-up, and reduces unnecessary transitions to invasive procedures.¹⁷⁸ In addition, automated CT image analysis algorithms can directly extract quantitative features from preoperative CT to refine individualized assessment of biopsy-related risks. By automatically calculating the percentage of intrapulmonary voxels with CT attenuation values ≤ -950 Hounsfield units within the punctured lobe, AI can quantify the degree of local emphysema, indicating the risk of severe pneumothorax requiring chest tube placement.¹⁷⁹

In CT-guided percutaneous lung biopsy, AI-driven robot-assisted navigation systems have the potential to optimize the puncture workflow and procedural accuracy by integrating preoperative image reconstruction, path planning, and intraoperative real-time localization. In the reported clinical study, these systems were associated with shorter puncture times, fewer needle adjustments and CT scans, and a lower incidence of bleeding complications, particularly for lower-lobe lesions and lesions larger than 30 mm¹⁸⁰; however, broader prospective validation is still required. Regarding AI-assisted real-time target localization, a recent study has developed automated biopsy

systems integrating image-processing algorithms with multi-degree-of-freedom robotic arms to continuously track tumor positions under respiratory motion. In such systems, AI extracts the centroid coordinates of the lesion in real time via image segmentation, then combines trajectory generation with finite-time convergence control algorithms to guide the puncture needle steadily toward the target in a dynamic environment, controlling localization error within the millimeter range. When coupled with digital twin technology, respiratory-driven tumor motion trajectories and puncture paths may be simulated in advance in a virtual environment, enabling integrated verification of preoperative planning and intraoperative execution. By unifying image recognition, path planning, and motion control, this engineering prototype is intended to address limitations of conventional CT guidance related to static imaging and respiratory motion. It provides a proof-of-concept for continuous dynamic navigation, but its accuracy, safety, and clinical benefit have not yet been established in routine patient care.¹⁸¹

In addition to robotic arm-assisted dynamic navigation, AI can be further applied to real-time recognition of microscopic structures. The AI-enabled integrated light-field microscopic endoscopic puncture needle incorporates cellular-level microscopic imaging capabilities into a clinically compatible 25-gauge puncture needle, obtaining real-time microscopic structural information from tissue in front of the needle tip and along the puncture route.¹⁸² Employing closed-loop adaptive optical correction to maintain diffraction-limited resolution during puncture, this system leverages algorithms such as K-means clustering and CNNs to perform *in situ* pathology-like tissue discrimination on images acquired along the needle tract. In animal experiments, it identified both regular alveolar structures as well as the gradual microstructural disruption from the tumor margin to its core, suggesting a potential approach to reducing false-negative risk in biopsies of millimeter-scale or smaller lesions.¹⁸² Compared to the traditional approach, this technology can provide near-histological instant feedback during puncture without interrupting the procedural workflow. It not only compensates for the inability of macroscopic imaging to reveal cellular-level heterogeneity but also offers a new technical pathway for biopsy navigation, lesion boundary identification, and early diagnosis of small lesions. That said, this method remains largely confined to animal models. Moreover, distinguishing tumor from normal tissue using this system alone may be insufficient; integration with multimodal microscopic imaging or other auxiliary strategies will be needed to improve discriminatory robustness in complex clinical scenarios.¹⁸²

3.3. Artificial intelligence-assisted decision-making before initial treatment for resectable lung cancer

In the context of neoadjuvant therapy, deep learning models constructed from preoperative CT images can predict major pathological response (MPR) or pathological complete response (pCR) in NSCLC patients and maintain stable discriminatory performance in multicenter external validation¹⁸³, supporting risk-adapted MDT discussions, the identification of patients who may benefit from closer response assessment, and consideration of whether additional imaging, biopsy, or evaluation for treatment modification is warranted. Multimodal prediction models that integrate clinical information, longitudinal CT data, and radiomics further improve predictive accuracy.^{183,184} Meanwhile, the model-derived phenotype of good response is associated with downregulation of tumor proliferation-related pathways and enhanced infiltration of antitumor immune cells, providing a potential explanation.¹⁸⁵

Artificial intelligence also shows strong potential in individualized treatment recommendations. Retrospective interpretable machine learning models constructed from large-scale clinical databases can estimate outcomes under different treatment strategies and compare the expected survival benefits, thereby providing exploratory decision support.²³ A recent study developed an interpretable model to evaluate potential benefits from surgery or radiotherapy among different patient subgroups.²² These models also achieve interpretability by clarifying feature weights and decision mechanisms. Importantly, treatment decisions should not rely on these models alone, and their clinical applicability remains to be established through prospective external validation and evaluation in real-world workflows.

The role of LLMs in MDT decision-making is becoming increasingly prominent. By integrating patient clinical summaries and evidence-based treatment guidelines, LLMs can generate structured treatment recommendations for multidisciplinary tumor boards.⁴⁰ Their recommendations have shown moderate agreement with decisions made by human committees and exhibit relatively high stability and reproducibility when surgical indications are involved⁴⁰, while also reducing the time and labor costs required for conventional expert assessment.¹⁸⁶ These findings suggest that LLMs could reproduce clinical decision logic under standardized information input and may serve as an auxiliary reference tool during MDT discussions. Further analysis revealed that the concordance between AI and MDT decisions improved markedly when clinical staging was complete. However, when decisions required careful consideration of unstructured factors such as patient functional status, comorbidities, and individual preferences, final judgment still depended on human clinical experience.⁴⁰ This reflects the advantages

of AI in standardized pathway formulation, as well as its limitations in complex contextual judgment. Overall, by rapidly summarizing patient information and generating preliminary recommendations, LLMs may provide support in medical institutions with limited MDT resources.^{62,186}

The performance of LLMs in specific evidence-based surgical planning scenarios has been quantitatively assessed. Using the choice between robot-assisted surgery and video-assisted thoracoscopic surgery in early-stage NSCLC as an example, one study compared LLM-generated responses with evidence-based topic reports constructed through systematic searches. The study found that although LLMs could generate structured answers within a short time, they still had limitations in the relevance and accuracy of evidence matching, including citation of literature that did not fully correspond to the target population and the occurrence of fabricated or incorrect data. In contrast, human-led evidence synthesis showed advantages in the reliability of conclusions and contextual adaptability.¹⁸⁷ Comparative studies have also evaluated the performance of LLMs such as ChatGPT, DeepSeek, and Grok in lung cancer clinical decision-making. The results showed that reasoning-based models exhibited uneven but quantifiable differences across multiple dimensions, including diagnostic staging, treatment choice, complication management, prognostic assessment, and patient education. The performance of different LLMs in lung cancer decision support is scenario-dependent. Their main strengths lie in the rapid generation of evidence-oriented options and information synthesis, whereas complex trade-offs, such as unusual imaging findings or rare lesions, still require correction by human experts.¹⁸⁸ These findings suggest that current LLMs are better suited as auxiliary tools that provide preliminary information and frame clinical questions.¹⁸⁷

3.4. Applications of artificial intelligence in molecular subtyping of resectable lung cancer

For resectable lung cancer, the mutational status of driver genes and the expression of immune-related biomarkers are closely associated with recurrence risk management and selection of neoadjuvant or adjuvant therapy. Over the past two decades, targeted therapy has significantly prolonged survival in patients with NSCLC¹⁸⁹, especially epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors in the adjuvant settings.^{190–192} Meanwhile, the role of immunotherapy in localized or locally advanced lung cancer is increasing. Tumor-cell programmed death-ligand 1 (PD-L1) expression remains the only approved diagnostic biomarker for immunotherapy in NSCLC and has been shown to be associated with the efficacy of immune checkpoint inhibitors.^{193,194}

For patients with surgically resectable NSCLC, conventional molecular testing and immune biomarker assessment mainly rely on tumor tissue obtained through surgery or needle biopsy.¹⁹⁵ In addition, tissue sampling typically captures only a portion of the tumor and may not fully characterize intratumoral heterogeneity, thereby limiting the representativeness and stability of molecular assessment.¹⁹⁶ For EGFR mutations, ctDNA analysis provides a more convenient alternative. However, in most stage I patients, ctDNA levels are low, resulting in limited sensitivity and variable concordance with tissue testing.^{104,196,197} For PD-L1 expression, in addition to sampling limitations, immunohistochemical testing itself is time-consuming, highly dependent on pathologist expertise, and affected by differences in antibodies, testing platforms, and scoring criteria, which complicates result interpretation.^{136,137} Moreover, PD-L1 expression may change dynamically during treatment, further increasing the uncertainty of single-time-point tissue testing.¹⁹⁸ Therefore, identifying molecular subtypes and immune phenotypes noninvasively has become a clinically meaningful direction for AI applications.

Computed tomography-based AI models have shown potential for predicting mutation status preoperatively. Certain CT imaging features extracted by radiomics and deep learning analysis, such as nodule morphology, spiculation, and pleural indentation, are significantly associated with EGFR mutation status.¹⁹⁹ The term “habitat” is used to describe distinct, regional, and heterogeneous volumes within a tumor, and habitat imaging involves obtaining these volumes.²⁰⁰ Unlike traditional approaches that focus only on intratumoral morphological features, AI can further integrate heterogeneity information from intratumoral, peritumoral, and different “habitat” subregions, extracting deeper spatial and textural features from routine imaging to characterize tumor molecular features. Relevant studies have shown that, in stage I NSCLC, models constructed using habitat radiomics have better discriminatory ability for EGFR mutations than models based solely on intratumoral or peritumoral features. After further integration of deep learning features and clinical variables, the resulting nomogram model maintained favorable AUC performance in the validation and external test sets.²⁴

Beyond driver mutation status, the value of AI in the noninvasive assessment of immune-related biomarkers such as PD-L1 is also receiving increasing attention. Compared to approaches relying solely on CT morphological information, multimodal PET/CT image

fusion can simultaneously integrate CT anatomical information and PET metabolic activity information, thereby more comprehensively capturing imaging phenotypes associated with PD-L1 expression in both the tumor body and peritumoral regions. Existing studies have shown that deep learning-based PET/CT fusion models can stably distinguish PD-L1-positive from PD-L1-negative status²⁰¹, and significantly outperform models using CT or PET input alone.²⁰² Meanwhile, their ability to predict immunotherapy benefit, progression-free survival, and overall survival can approach that of PD-L1 status assessed by immunohistochemistry.²⁰¹

Recently, AI-based molecular subtyping has evolved toward multitask, integrated frameworks that more closely reflect real-world scenarios. Existing multitask AI systems have attempted to simultaneously evaluate EGFR mutation status and subtypes, PD-L1 expression status and levels, as well as unified EGFR/PD-L1 status based on a single preoperative CT examination, demonstrating favorable discriminatory ability.²⁰³ Compared to traditional analytical paradigms, such multitask models exploit shared imaging information while simultaneously mining distinct yet potentially correlated phenotypic clues across different biomarkers, which may better align with the stratification needs of clinical decision-making around targeted therapy and immunotherapy²⁰³ and help streamline the workflow associated with multiple tests. In addition, these frameworks can be further extended to prognostic assessment. A preoperative CT-based multitask prognostic prediction model can jointly model EGFR genotype recognition and overall survival prediction for stage I–III resectable NSCLC.²⁶ The rationale is that EGFR genotype, tumor stage, and prognosis are correlated, allowing CT features related to tumor biology to be learned across different tasks, thereby improving the primary task performance. This model can further identify high- and low-risk subgroups among patients with the same TNM stage or EGFR genotype.²⁶

Clinically, AI-based prediction of EGFR mutation and PD-L1 expression may be most useful as a prescreening tool when biopsy is temporarily infeasible or tissue is insufficient. A high predicted probability of EGFR mutation or PD-L1 expression may prompt additional tissue acquisition or referral for further molecular and pathological evaluation. Importantly, these tools remain investigational and may support, but should not replace, standard molecular and immunohistochemical testing at present. They should not be used to prescribe EGFR-targeted therapy or select immunotherapy without confirmation by an approved biomarker assay.

4. Applications of artificial intelligence in intraoperative navigation and precision surgery of resectable lung cancer

4.1. Artificial intelligence-driven three-dimensional reconstruction and precision surgical planning

With the increasing detection of early-stage lesions, lung cancer surgery for these patients has gradually shifted from standard lobectomy toward selective lung parenchyma-preserving segmentectomy, placing intense demands on refined preoperative anatomical assessment, where 3D reconstruction serves as an important tool to depict complex anatomy.²⁰⁴ In recent years, AI has advanced 3D reconstruction from previously manual segmentation toward highly accurate automated workflows (Figure 2), accelerating its incorporation into routine preoperative assessment.²⁰⁵ This technology enables rapid construction of patient-specific anatomical models, easing the identification of anatomical variations and planning for segmentectomy.²⁰⁶ Compared to conventional reconstruction, AI-driven models can complete automated modeling in 5–10 min, with results highly consistent with manual annotations, which substantially reduces the labor costs and time requirement, making them more suitable for high-throughput clinical practice.^{207,208} At the same time, AI-based reconstruction has been reported to outperform two-dimensional (2D) CT in identifying pulmonary vessels and bronchi, with accuracy exceeding 95% in detecting anatomical variations^{53,204,209–211}, which may improve preoperative anatomical understanding. Algorithmic optimization may further expand the technical feasibility by reducing reliance on contrast agents while preserving the ability to identify fine anatomical structures comparable to manual reconstruction methods and contrast-enhanced CT. When performed using conventional CT images, AI-assisted 3D reconstruction may still improve the efficiency and consistency of anatomical interpretation.^{212–214}

The AI-based 3D reconstruction also helps accurately localize the involved pulmonary segment and optimize the extent of resection, especially in complex or multiple lesions.^{215–217} Compared to invasive localization, retrospective comparative studies have associated AI-based 3D planning and lesion localization with lower intraoperative blood loss and thoracic drainage volume, shorter operative time and hospital stay, fewer localization-related complications, maintenance of R0 resection, and greater surgeon satisfaction.^{204,210,218–222} Meanwhile, better control of the resection extent may help preserve the remaining lung tissue. In a retrospective propensity score-matched study, AI-assisted 3D planning was associated

with better pulmonary function and quality of life at six months after surgery.²²³ In the context of robot-assisted surgical platforms, higher-degree-of-freedom instruments and stable manipulation have refined the management of complex segmental anatomy²²⁴, but suffer from the lack of tactile feedback, which may be partly compensated for by additional visual and spatial information provided by 3D modeling and AI navigation.²²⁵ Nevertheless, these findings remain susceptible to selection bias, institutional experience, and procedural heterogeneity, and require confirmation in prospective comparative studies.

In addition, interactive and 3D-printed physical models have transformed complex anatomy from abstract information into visualized structures. These models provide young surgeons with an intuitive platform for anatomical understanding and may help shorten the learning curve for segmentectomy. They also offer unique advantages in doctor–patient communication.^{226–230} Currently, 3D lung models have evolved from static visualization toward dynamic modeling that integrates AI segmentation with virtual reality or augmented reality technologies. These approaches provide more intuitive spatial perception and real-time anatomical reference during preoperative planning and intraoperative navigation, and have shown educational value in complex segmentectomy. However, their broader implementation still requires higher-quality comparative studies.^{231,232} Overall, AI-driven 3D reconstruction is among the more clinically mature applications discussed in this review and may improve the consistency of anatomical visualization and segmentectomy planning; yet, evidence for patient-centered and long-term oncological benefits remains limited.

4.2. Artificial intelligence-assisted real-time non-contact intraoperative three-dimensional navigation

Non-contact AI-assisted intraoperative navigation offers a human–machine interaction paradigm that is closely aligned with the practical demands of precision lung cancer surgery (Figure 3). Based on preoperative 3D reconstruction, this technology enables real-time intraoperative visualization of the subtle pulmonary anatomy and, through computer vision and deep learning, allows surgeons to manipulate the reconstructed structures in the air (zooming, rotation, and localization), so that they can directly control the navigation interface. Compared to the traditional indirect navigation mode, in which an assistant operates the display, surgeon-led real-time interaction helps reduce workflow disruption caused by communication errors.²³³ Technically, this system integrates binocular infrared sensing, hand key-point tracking, and

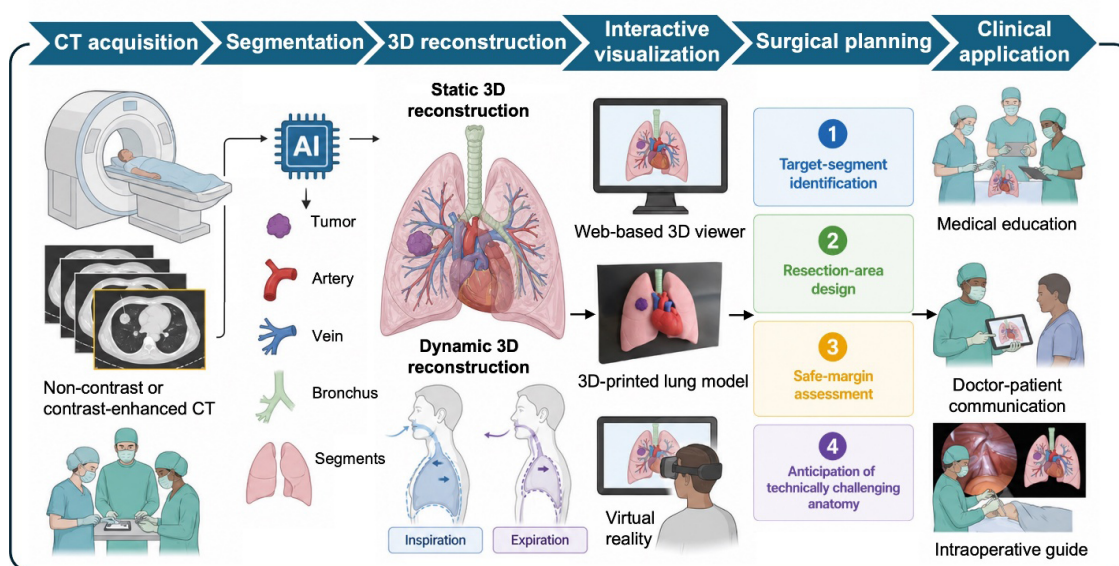


Figure 2. Clinical workflow of AI-assisted 3D lung reconstruction from preoperative CT acquisition to surgical planning and clinical application. Non-contrast or contrast-enhanced CT images are processed using AI-based segmentation to identify the tumor, pulmonary arteries, pulmonary veins, bronchi, and relevant pulmonary segments. These segmented structures are then used to generate patient-specific static and dynamic 3D reconstructions, including visualization of tumor–vessel–bronchus relationships and respiratory-phase changes. The reconstructed models can be presented through a web-based 3D viewer, a 3D-printed lung model, or virtual reality, enabling surgeons to interact with patient-specific anatomy before surgery. These interactive models may assist with target-segment identification, resection-area design, safe-margin assessment, and anticipation of technically challenging anatomy. The same 3D models may also be used for medical education, doctor–patient communication, and intraoperative anatomical reference.

Abbreviations: 3D: Three-dimensional; AI: Artificial intelligence; CT: Computed tomography.

CNNs to stably recognize complex gestures, which can be further optimized using error backpropagation and SVMs.²³⁴ This AI-driven gesture recognition mechanism enables the 3D model to dynamically adjust its viewing angle and anatomical layers as the operation progresses, thereby strengthening the spatial correspondence between deeply located lesions and key anatomical structures. Compared with static 3D-printed models or unidirectional virtual reconstruction displays, this approach emphasizes real-time operability, transforming imaging from a purely referential tool into an interactive decision-support interface.

The main advantages of non-contact navigation are reported to be improvements in efficiency and user experience. In small, single-center feasibility studies, non-contact navigation was associated with shorter navigation and operative times, while blood loss and surgical success rates remained comparable to those using conventional methods. Notably, surgeons report significantly higher satisfaction with the AI-assisted system.²³³ Returning image control to the surgeon creates a tighter connection among spatial understanding, operative planning, and surgical execution²³⁵, which is especially beneficial when dealing with cases involving unusual anatomical variations

or occult lesion locations.²³⁶ Nevertheless, challenges remain, including gesture recognition latency, insufficient fine-motion control, and environmental interference. Existing studies suggest that single-modality gesture input is susceptible to changes in lighting and body position, whereas multimodal interaction strategies incorporating gaze direction, trunk orientation, or voice commands could reduce misrecognition and improve system stability.²³⁷ Overall, real-time non-contact intraoperative 3D navigation remains an early-stage technology supported mainly by small feasibility studies, and its reliability, learning curve, and impact on surgical outcomes require prospective evaluation.

One obvious obstacle is the spatial mismatch between preoperative 3D models and collapsed lungs during surgery. Lung tissue can undergo more than 50% volume change during surgery²³⁸, and the thoroscopic field of view usually reveals only part of the lung surface. Previously, attempts at preoperative-to-intraoperative registration mainly relied on manual adjustment.²³⁹ Others have adopted iterative optimization-based registration, in which algorithms repeatedly adjust parameters such as thoroscopic camera viewpoint and organ deformation so that the projection of the preoperative 3D model

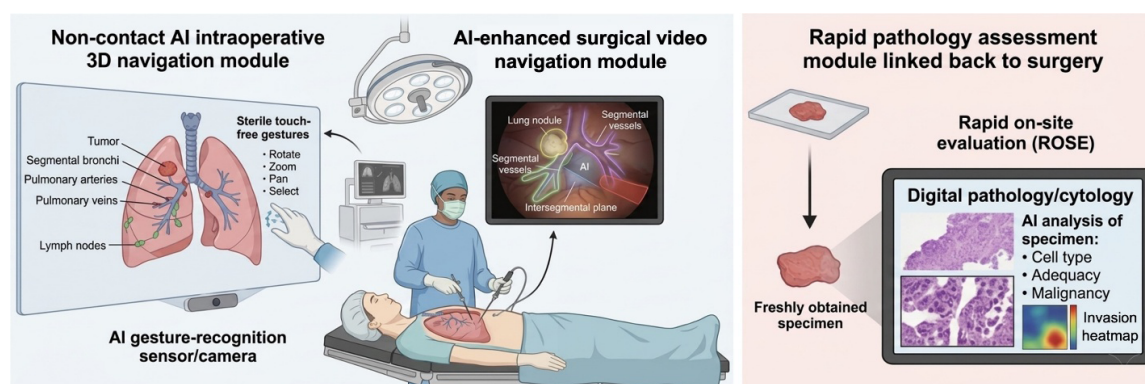


Figure 3. Visual representation of an AI-integrated lung cancer surgical setting within the context of precision surgery. AI can interact with thoracic surgeons during minimally invasive lung cancer surgery through multiple intraoperative modules. In the non-contact 3D navigation module, AI-based gesture-recognition sensors or cameras enable surgeons to manipulate patient-specific anatomical models using sterile touch-free gestures, such as rotation, zooming, panning, and structure selection. These models provide real-time visualization of tumors, segmental bronchi, pulmonary arteries, pulmonary veins, and lymph nodes, supporting anatomical localization and intraoperative decision-making. In the AI-enhanced surgical video navigation module, deep learning algorithms analyze thoracoscopic video streams to identify lung nodules, segmental vessels, intersegmental planes, and other key anatomical landmarks, thereby providing visual guidance during precision resection. In the rapid pathological assessment module, freshly obtained specimens can be processed through digital pathology platforms, with AI-assisted analysis used to evaluate cell type, specimen adequacy, malignancy, invasion risk, and heatmap-based suspicious regions. Together, these modules establish a conceptual intraoperative support system linking pre-resection anatomical localization, real-time guidance, and rapid pathological feedback.

Abbreviations: 3D: Three-dimensional; AI: Artificial intelligence; ROSE: Rapid on-site evaluation.

progressively approaches the actual intraoperative image.²⁴⁰ However, these methods often rely on experiential judgment or repeated computation, failing to simultaneously satisfy the requirements of real-time performance and stability in thoracoscopic scenarios characterized by substantial occlusion and marked deformation. To address this issue, a recent study proposed a 2D/3D deformable framework based on single-view thoracoscopic images. The core objective is to automatically register a patient-specific 3D lung model constructed from preoperative CT to the lung surface that undergoes marked deformation under intraoperative artificial pneumothorax, aiming to provide images that more closely reflect the actual intraoperative anatomical state.²⁴¹ Based on an established lung deformation model and the initial lung shape obtained from preoperative CT, researchers generated images under different degrees of lung collapse and different camera viewpoints, followed by developing a CNN through self-supervised offline learning to estimate the differences between assumed images and the actual scenario. During surgery, the trained model rapidly predicts the registration parameters from the current thoracoscopic image, achieving stable automatic registration without any additional intraoperative 3D measurement information.²⁴¹ In practice, this technology does not require surgeons to interpret complex parameters; it directly provides visual navigation results. Specifically, the registered lung surface mesh can be overlaid onto the thoracoscopic image, and

hidden anatomical structures can be highlighted using augmented visualization. The real-time performance and feasibility of this approach were evaluated using videos from 16 right-sided thoracoscopic surgeries, with the mean computation time of 65.4 ms, corresponding to 15.3 frames per second. For real thoracoscopic images, the registration accuracy reached an absolute error of <10 mm and an average distance of <5 mm, superior to that of conventional comparator methods.²⁴¹ Future studies could integrate such deformable registration technologies with non-contact intraoperative 3D navigation systems, preserving the advantages of surgeon-led interaction while enabling dynamic 3D navigation that better matches the real intraoperative anatomy. Given the small sample size and offline or technically controlled evaluation, this framework remains at the proof-of-concept stage.

4.3. Artificial intelligence-based surgical image recognition and video analysis

Computer-vision and deep learning models have been used to analyze intraoperative recordings, enabling automatic recognition of surgical phase and key anatomical structures, as well as real-time assessment of pathological status. The LungSurg system is a generative AI framework designed for interpreting videos of thoracoscopic lobectomy. By integrating image-inpainting-based generative learning with deep segmentation networks, it enables simultaneous recognition and dynamic

analysis of essential intrathoracic structures, surgical instruments, and operative phases. Externally validated on multicenter video datasets, this system demonstrated stable segmentation of bronchovascular structures and accurate identification of surgical workflow nodes even in complex anatomical cases, although its real-time clinical utility and impact on intraoperative outcomes have not yet been prospectively established. Its recognition ability was comparable to that of experienced surgeons, while showing higher sensitivity. In challenging scenarios such as smoke interference, instrument occlusion, and tissue traction-induced deformation, LungSurg remained able to identify key anatomical information.⁵⁴ In addition, the system can automatically decompose the highly experience-dependent process of thoracoscopic lobectomy into standardized units, allowing young surgeons to more rapidly learn the operative steps via postoperative review and significantly enhancing learning outcomes in structural recognition and surgical phase judgment.⁵⁴

On this basis, deep learning-based image segmentation has also been explored for recognizing fine nerves that require special protection during thoracic surgical procedures, as injury to any of the pivotal intrathoracic nerves significantly affects postoperative rehabilitation.²⁴² Relevant studies have developed AI support systems based on deep learning segmentation. By training with precise annotations of nerves in intraoperative images, this system can identify and highlight the vagus, recurrent laryngeal, and phrenic nerves in real time during thoracoscopic surgery. Expert evaluation showed high recall and precision, with almost no obvious time delay or degradation in image quality compared with the original surgical monitor.²⁴³ By recognizing these key structures, AI may reduce the risk of intraoperative accidental injury caused by fatigue, insufficient experience, or fluctuations in attention, providing supplementary visual support during technically demanding steps such as hilar dissection. However, whether it reduces intraoperative nerve injury or improves postoperative recovery remains unknown.

In addition to anatomical landmarks, computer vision models can be applied to lesion localization. In minimally invasive surgery, the smaller incisions used in thoracoscopic and robot-assisted procedures limit intraoperative palpation, making lesion localization largely dependent on the surgeon's experiential judgment of lung surface changes. Deep CNNs, such as the YOLO system, can automatically learn complex visual patterns associated with tumors from thoracoscopic images, including vascular proliferation, pleural indentation, local bulging, and atelectasis on the lung surface. They can then mark the lesion region immediately using bounding

boxes, achieving localization accuracy of more than 90% on intraoperative thoracoscopic images and providing visual guidance for lesion identification. This suggests that AI may serve as a complementary tool to surgeons' visual judgment when tactile feedback is limited²⁴⁴, although its effectiveness requires further prospective evaluation.

By extracting deep features from continuous video frames, AI can also provide intraoperative risk assessment of pathological status. In clinical stage I lung adenocarcinoma, visceral pleural invasion (VPI) affects T staging and is critical in determining whether sublobar resection is appropriate.^{245,246} However, neither preoperative CT nor intraoperative inspection provides stable and objective criteria for evaluating VPI.²⁴⁷ Compared to the traditional approach, which relies on surgeons' subjective inferences, deep learning, represented by VPI-Net, directly extracts latent features associated with VPI from thoracoscopic images²⁴⁸ and demonstrates superior discriminatory performance in intraoperative risk assessment compared to intraoperative experiential judgment and preoperative imaging assessment in retrospective internal and external datasets.²⁴⁹ It also showed potential advantages over less experienced surgeons in terms of specificity, positive predictive value, and negative predictive value.²⁴⁸ Beyond its immediate diagnostic value, the VPI risk score output by the model was significantly associated with recurrence-free survival and time to progression, and retained prognostic discriminatory ability among patients with small tumors.²⁴⁹ To improve usability, the study also introduced automatic region-of-interest cropping and gradient-weighted class activation mapping-based visual attention maps²⁵⁰, which enabled the model to be embedded into real-time video-stream analysis without requiring additional manual annotation.²⁴⁹ An elevated intraoperative VPI risk score may prompt more careful inspection of the pleural surface, targeted pathological confirmation, reassessment of clinical T staging, and closer consideration of resection extent and lymph-node evaluation. However, the current evidence does not support using AI-predicted VPI alone to determine whether sublobar resection should be converted to lobectomy or to alter lymph-node dissection.

4.4. Artificial intelligence-enabled rapid pathologic assessment

Deep learning on intraoperative frozen sections can be leveraged to rapidly diagnose lesion nature and lung cancer subtypes. By constructing task-specific deep neural networks, such approaches can automatically distinguish AIS from IAC on frozen sections. For example, the feature selection and grouping-transfer learning system was developed specifically for intraoperative diagnosis of lung adenocarcinoma, integrating multiple-instance

learning with a hybrid attention mechanism, which can localize cancerous regions on whole-slide frozen-section images within approximately 3 min and achieve subtype classification accuracy exceeding 90%. This system adopts a tree-structured classification framework that simulates clinical diagnostic reasoning, prioritizing the distinction between tumor and non-tumor regions and then further differentiating AIS from IAC. The generated attention heatmaps closely correspond to the regions of interest selected by pathologists, and effectively assist in identifying subtle differences in histology between early and invasive lesions. A unique strength of this technique is specific optimization for the poor image quality commonly encountered in intraoperative frozen sections, resulting from artifacts and uneven staining, while also providing intuitive visualization of prediction confidence in the form of heatmaps. In the retrospective validation setting, the system reduced the number of regions requiring manual review and may assist pathologists in identifying subtle histological differences.⁵⁵ Whether it reduces diagnostic errors in routine intraoperative practice requires prospective evaluation.

Independent of frozen sections, AI-assisted optical coherence tomography (OCT)-based intraoperative grading provides a new approach for surgical margin assessment in fresh lung cancer tissue. This strategy is based on high-resolution, real-time cross-sectional images of fresh *ex vivo* tissue acquired by OCT. Combined with deep learning algorithms and attention mechanisms, it can automatically annotate lesion regions and perform tumor grading, potentially addressing some limitations of conventional sections in sampling coverage and interpretive consistency. Unlike frozen sections, which rely on a single sampling plane, OCT provides continuous tomographic information within a millimeter-scale field of view. AI models then automatically extract microscopic structural features, enabling strong discriminatory performance in distinguishing normal tissue, MIA, and IAC, with diagnostic accuracy significantly superior to that of conventional intraoperative pathology in an *ex vivo* proof-of-concept study.²⁵¹ In addition, the interactive human-machine interface developed in this study allows clinicians to click on a region of interest and immediately retrieve the corresponding OCT image, attention heatmap, and AI-predicted probability. This provides a more intuitive and interpretable visualization of features potentially related to tumor invasion depth and potential margin risk.²⁵¹ On this basis, remote sharing and collaborative interpretation mechanisms can be further introduced by integrating mobile OCT imaging, AI analysis, and network platforms, thereby conceivably expanding the application to cross-

regional consultation²⁵¹, which is particularly meaningful for primary care facilities. Compared with frozen sections, which typically require 20–30 min for preparation and interpretation, the OCT-AI system completes data acquisition and analysis within tens of seconds to several minutes, suggesting potential compatibility with intraoperative decision-making needs.²⁵¹ This method also offers unique advantages, including non-contact, radiation-free imaging characteristics and preservation of tissue structural continuity. Because the system was evaluated on fresh *ex vivo* specimens rather than in a prospective intraoperative workflow, its diagnostic accuracy, margin-assessment utility, and effect on operative decisions require further clinical validation.

In addition to OCT-AI, AI-assisted rapid assessment based on multiphoton microscopy (MPM) also shows potential for intraoperative biopsy diagnosis. This approach uses label-free signals such as SHG and two-photon excited fluorescence to simultaneously obtain images of collagen and elastic fibers, focusing on the structural features of extracellular matrix (ECM) remodeling during tumorigenesis. By constructing a similarity coefficient for collagen-elastic fiber interactions and combining it with an AI-ECM analytical framework based on a fiber-voxel dictionary, this method quantifies 3D morphological features of ECM fibers, including orientation, arrangement, curvature, thickness, and local coverage, which enables further identification of tumor-risk regions and boundary indication.²⁵² Compared to traditional approaches that rely primarily on cytomorphology, this strategy shifts the diagnostic focus to tumor microenvironment remodeling, resulting in a high sensitivity of 99.37% in *ex vivo* human lung cancer samples. The generated risk-visualization heatmaps could serve as reference points for selecting intraoperative biopsy sites and assessing surgical margins.²⁵² This method may complement systems such as OCT-AI by adding information on microenvironmental structural features, although its ability to improve intraoperative diagnostic accuracy has not yet been clinically demonstrated.

Notably, the HHG technology described above may also theoretically be extended to rapid pathological assessment of intraoperative specimens. HHG may provide more cellular morphological and tissue-architectural information than OCT, while potentially offering greater workflow efficiency than MPM (Table 3). Therefore, it may achieve a favorable balance between speed and histological information richness, although its clinical value in this scenario still requires validation. Figure 3 illustrates how AI interacts with surgeons during lung cancer surgery, including non-contact 3D navigation, surgical video analysis, and rapid pathological feedback.

Table 3. Comparison of OCT, MPM, and HHG for AI-assisted rapid pathological assessment in lung cancer

Comparison criteria	OCT ²⁵¹	MPM ²⁵²	HHG ¹⁷⁵
Imaging principle	Tomographic imaging based on low-coherence interferometry, providing real-time, depth-resolved structural images of tissue	A nonlinear label-free optical microscopy technique that mainly uses SHG and 2PEF to simultaneously visualize collagen and elastic fibers	Label-free high-resolution imaging of unprocessed tissue based on nonlinear optical signals, with simultaneous acquisition of THG, SHG, and 2PEF signals
Main information displayed	Continuous tomographic structure, lesion extent, and invasion depth-related information; suitable for grading and margin assessment	3D morphology, arrangement, orientation, curvature, thickness, and local coverage of collagen and elastic fibers	Cellular structures, collagen, elastic fibers, and overall tissue architecture
Current main application scenario	Rapid intraoperative pathological assessment	Rapid intraoperative pathological assessment	Rapid preoperative biopsy assessment
Specimen status	Mainly used for fresh, unprocessed <i>ex vivo</i> surgical specimens	Main evidence comes from <i>ex vivo</i> human lung cancer samples, with further <i>in vivo</i> imaging validation in mouse models bearing human lung cancer	Mainly used for fresh, unprocessed <i>ex vivo</i> biopsy specimens
Speed	Tens of seconds to several minutes	10–30 min	Approximately 6 min
Relative advantages	Fast imaging with continuous tomographic structural information	Most sensitive to ECM microenvironmental remodeling, with strong interpretability for tumor boundary identification and risk mapping; validated by <i>in vivo</i> imaging in mouse lung cancer models	May provide a favorable balance between speed and histological information content
Main limitations	Provides less detailed histological information than HHG or MPM; currently mainly applied to <i>ex vivo</i> specimens	Has the weakest clinical time efficiency; in situ human <i>in vivo</i> application remains to be validated	Less capable of fine grading and boundary determination than MPM, and provides less depth-resolved structural information than OCT; currently mainly applied to <i>ex vivo</i> biopsy specimens, and its value in rapid pathological assessment of intraoperative resection specimens requires further validation

Abbreviations: 2PEF: Two-photon excited fluorescence; 3D: Three-dimensional; ECM: Extracellular matrix; HHG: Higher harmonic generation imaging; MPM: Multiphoton microscopy; OCT: Optical coherence tomography; SHG: Second-harmonic generation; THG: Third-harmonic generation.

5. Applications of artificial intelligence in postoperative management of resectable lung cancer

5.1. Artificial intelligence-based prediction of postoperative complication risk

In patients undergoing lung cancer surgery and related thoroscopic procedures, postoperative pulmonary complications (PPCs) remain major factors affecting recovery and short-term prognosis. While regression-based traditional models often fail to capture the complex nonlinear relationships among perioperative inflammatory

responses, metabolic status, and surgical trauma, machine learning and deep learning models have demonstrated better performance in predicting PPCs in mainly single-center retrospective studies. By integrating demographic characteristics and common clinical factors, AI models can provide individualized risk assessment for PPCs. For example, one prediction model incorporating preoperative white blood cell count, body mass index, surgical approach, age, intraoperative blood loss, and C-reactive protein achieved excellent discrimination and significant net clinical benefit.²⁵³ Another study compared multiple machine learning and deep learning algorithms and showed that light gradient boosting machine and pruning

Bayesian neural network achieved the highest AUCs for predicting PPCs after thoracoscopic surgery in the test group (0.873 and 0.869, respectively), identifying single-lung ventilation duration, smoking history, operative time, American Society of Anesthesiologists classification, and blood glucose level as variables closely associated with the occurrence of PPCs.²⁵⁴ Such models can also be combined with SHAP interpretability analysis to reveal the contribution of each factor, ensuring the biological plausibility of risk prediction.²⁵³ In addition to conventional clinical indicators, imaging-driven functional assessment can overcome the limitations of traditional testing in reflecting the regional heterogeneity of lung function. The AI-CT system was reported to estimate postoperative pulmonary function parameters at the segmental level, and its output (predicted forced expiratory volume in 1 s, FEV1_AI-CT) independently predicted PPCs, with performance superior to models relying on conventional function testing or anatomical segment counting.²⁵⁵ These tools may support the identification of high-risk patients and the planning of intensified perioperative respiratory management.

Similarly, AI methods are increasingly used to predict systemic complications. A single-center retrospective study suggested that machine learning models could identify patients at high risk of moderate-to-severe pain after thoracoscopic surgery for NSCLC by integrating indicators of tumor burden, laboratory parameters, and anesthesia factors, while interpretability algorithms help enhance their clinical plausibility.²⁵⁶ Such models maintain stable performance after simplification to a small number of core variables, suggesting the potential for broader clinical use.²⁵⁶ Analogous strategies have also been applied to risk prediction in retrospective studies for intraoperative hypothermia (IOH), postoperative delirium (POD), and postoperative cardiovascular and neurological complications (PCNCs) in lung cancer patients. IOH occurrence is closely associated with patient age, body mass index, hemoglobin level, and intraoperative factors, including operative duration, anesthesia time, and infusion volume. Existing studies have used these factors to predict IOH through machine learning, enabling accurate identification of high-risk patients and individualized interventions in advance, such as active warming of infused fluids and optimization of anesthesia management.²⁵⁷ POD is a neuropsychiatric complication associated with prolonged hospitalization and adverse prognosis.²⁵⁸ By integrating preoperative indicators such as blood glucose level, pulmonary function, mean corpuscular volume, and serum albumin, machine learning models can effectively predict patients at high risk of delirium after lung cancer resection.²⁵⁹ PCNCs represent major adverse events

affecting postoperative prognosis in thoracic surgical patients.²⁶⁰ Machine learning that integrates demographics, surgical procedures, and anesthesia-related factors has shown good discrimination in risk prediction of PCNCs, and may assist in optimizing anesthesia and analgesia strategies.²⁶¹ Beyond individual complications, AI models also facilitate the assessment of short-term mortality and overall complication burden after lung cancer surgery, showing good discriminatory ability in external validation, and may help optimize surgical decision-making.²⁶²

5.2. Artificial intelligence-based prediction of treatment outcomes and functional recovery

In recent years, AI has been widely applied to identify patients at high risk of prolonged length of stay (PLOS). By integrating multidimensional data, including demographic characteristics, comorbidities, pulmonary function parameters, laboratory test results, tumor pathological features, and surgical approaches, deep learning models can effectively predict whether postoperative hospitalization in patients with NSCLC will exceed nine days in a retrospective institutional cohort.²⁶³ In addition, machine learning models based on electronic clinical pathway systems can incorporate dynamic variables from the preoperative period to postoperative day 4, enabling continuous assessment of PLOS risk. Counterfactual analysis of these models helps identify clinical factors that are closely associated with prolonged hospitalization, including abnormal breath sounds, postoperative fever, arrhythmia, limited mobility, drainage-related abnormalities, and persistent air leakage.²⁶⁴ In the setting of day surgery for lung cancer, which relies more heavily on enhanced recovery pathways, PLOS is defined earlier as a postoperative hospital stay longer than 48 h.²⁶⁵ A study including 1,009 patients constructed a machine learning model tailored to this specific scenario and achieved high accuracy. By incorporating SHAP-based interpretation, the model identified fatigue, subcutaneous emphysema, pain, and cough as the main factors influencing PLOS risk.²⁶⁶ Overall, AI may help identify patients with insufficient recovery before discharge decisions are made and optimize perioperative care pathways, but its ability to improve discharge safety or shorten hospitalization requires prospective workflow evaluation.

Besides short-term hospitalization indicators, medium- and long-term functional recovery and quality of life after discharge further reflect the physical influence of surgical intervention. Multidimensional information, including demographic characteristics, baseline health status, tumor biological features, treatment-related factors, preoperative pulmonary function, and perioperative laboratory parameters, can be used to construct prediction

models for frailty risk at three months after surgery.²⁶⁷ In addition, the quality of early recovery at one month after surgery is negatively correlated with predicted frailty status, suggesting the potential to evaluate early recovery indicators synchronously.²⁶⁷ Through visual nomograms or online risk calculators, these AI tools may help identify populations with poor rehabilitation early after discharge, thereby guiding individualized rehabilitation interventions and optimizing follow-up strategies.

5.3. Artificial intelligence-based prediction of recurrence and survival outcomes

5.3.1. Artificial intelligence-based data integration improves survival prediction

In resectable early-stage NSCLC, postoperative recurrence and survival outcomes remain highly heterogeneous. Traditional risk stratification centered on TNM staging and routine pathological indicators is now insufficient. Conversely, radiomics and deep learning models can automatically extract high-dimensional features, process nonlinear relationships, and enable information fusion, with evident advantages in identifying microenvironmental and peritumoral imaging features. A systematic review evaluated AI models used in predicting postoperative recurrence in early-stage NSCLC and found that various AI models generally achieved favorable predictive performance, demonstrating higher discriminatory ability than TNM staging and conventional clinical scoring.²⁶⁸ In addition, multimodal integration of clinical features, radiomics parameters, and pathological image information showed significantly better predictive performance than single-modality models.²⁶⁹ AI has also been used to model the risk of postoperative distant metastasis, for which machine learning models based on large-sample multivariable data showed significantly better discriminatory ability than traditional regression.²⁷⁰

For resectable NSCLC after neoadjuvant therapy, the value of AI in assessing postoperative prognosis is also reflected in the quantitative assessment of residual disease in the tumor bed and the stromal microenvironment. Compared to conventional evaluation that uses MPR or pCR alone as endpoints, whole-slide quantitative analysis of resected specimens combining morphometry and AI algorithms can more objectively characterize the composition of the tumor bed, uncovering additional prognostic information.²⁷¹ Studies have shown that tumor-bed stromal components, which are highly subjective and less reproducible when assessed by traditional gross or semiquantitative pathology, exhibit independent prognostic value after computer-assisted morphometry.²⁷¹ Furthermore, AI-based quantitative analysis of

immunohistochemistry whole-slide images can refine the identification of immune features, including CD4⁺, CD8⁺, CD68⁺, and FOXP3⁺ cells.²⁷¹ Notably, a ClinPATH composite score integrating MPR, baseline lymphocyte count, perineural/vascular invasion, Ki-67, fibrosis extent, and the AI-quantified proportion of CD4⁺ cells showed better predictive ability for disease-free survival and overall survival than any single indicator. This indicates that AI-supported integrated modeling of clinical, pathological, and immune microenvironmental features may enable more refined prognostic stratification than single pathological response indicators, providing a more nuanced basis for subsequent adjuvant treatment decision-making and adjustment of follow-up intensity.²⁷¹

Although AI models have shown high prognostic value in lung cancer, existing studies still have several limitations in methodology and clinical translation. Most current studies suffer from insufficient sample sizes, small test sets involving fewer than 100 cases, a lack of external validation, and a risk of overfitting. A systematic review showed that more than half of the studies were assessed as having a high risk of bias during the validation phase.²⁶⁹ Therefore, future studies should include multicenter, large-sample prospective validation, standardize data preprocessing workflows, and improve model interpretability. Together, the multimodal data inputs that can be integrated by postoperative AI models and the major risk outcomes that can be predicted are summarized in [Figure 4](#).

5.3.2. Data advances in artificial intelligence-assisted evaluation of postoperative prognosis

In recent years, research on AI-based prediction of postoperative recurrence and survival outcomes in lung cancer has expanded, especially in terms of data forms. Its innovations are mainly reflected at several levels. At the pathology-data level, traditional models usually require manual region annotation or predefined feature extraction. In contrast, the patient-level weakly supervised multimodal learning framework proposed by Li *et al.*²⁷², AIM-LCpro, does not require this process. Through a weakly supervised mechanism, this framework can automatically select prognosis-related regions across entire whole-slide images, avoiding biases introduced by human feature selection and allowing discovery of digital pathology biomarkers. This model not only showed high discrimination and calibration, but also generated predicted survival curves that closely resembled the actual Kaplan–Meier curves, suggesting accurate agreement with real-world trajectories.²⁷² At the imaging-data level, the “entire thoracic cavity” has been used as the analytical target, integrating global information from lung parenchyma, mediastinum, pleural interfaces, and thoracic vertebral regions on fluorodeoxyglucose PET

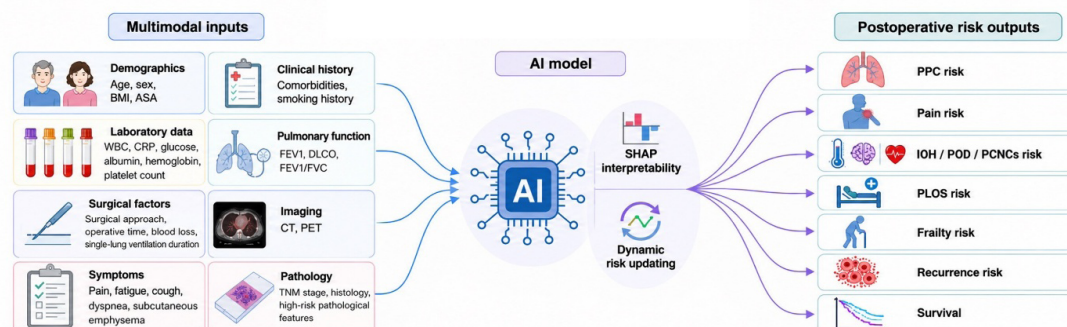


Figure 4. AI-based postoperative risk prediction using multimodal perioperative data. This framework comprehensively integrates clinical multimodal data, including demographic characteristics, clinical history, laboratory indicators, pulmonary function, surgical factors, imaging data, symptoms, and pathological information, into machine learning or deep learning models. Combined with SHAP-based interpretability and dynamic risk updating, these models can generate individualized predictions for PPCs, pain, systemic complications including IOH, POD, and PCNCs, PLOS, frailty, recurrence, and survival.

Abbreviations: AI: Artificial intelligence; ASA: American Society of Anesthesiologists; BMI: Body mass index; CRP: C-reactive protein; CT: Computed tomography; DLCO: Diffusing capacity of the lung for carbon monoxide; FEV1: Forced expiratory volume in 1 s; FVC: Forced vital capacity; IOH: Intraoperative hypothermia; PCNCs: Postoperative cardiovascular and neurological complications; PET: Positron emission tomography; PLOS: Prolonged length of stay; POD: Postoperative delirium; PPC: Postoperative pulmonary complication; SHAP: Shapley additive explanations; TNM: Tumor–node–metastasis; WBC: White blood cell.

and CT images with clinical, surgical, and pathological variables to uncover potential prognostic signals.^{273,274} At the clinical-data level, nutritional and immune-inflammatory indicators have been introduced into the prediction framework, representing the incorporation of accessible and low-cost physiological status indicators into AI models.²⁷⁵ At the temporal level, baseline information has been combined with continuously collected laboratory indicators and CT imaging during follow-up to construct a time-updated risk score (e.g., the Radiologic Assessment in Lung Cancer to Derive Artificial Intelligence Risk score)²⁷⁶.

Intriguingly, although many studies emphasize multimodal data fusion, some studies have shown that ensemble learning models relying only on routine indicators can still achieve stable predictive performance and good calibration without incorporating radiomics or genomic data.²⁷⁷ This suggests that AI can be directly deployed into existing follow-up workflows with high scalability and feasibility. AI models now cover a range of treatment scenarios beyond surgery, evolving into a general prognostic assessment tool across stages.

5.3.3. Unique advantages of liquid biopsy in artificial intelligence-assisted recurrence surveillance

Liquid biopsy has been introduced into AI prediction frameworks, involving baseline ctDNA status, post-treatment minimal residual disease (MRD), mutations detected in blood, and whole-genome sequencing

(WGS)-derived features.^{278,279} This data modality has attracted considerable attention in postoperative lung cancer settings, given its advantages of noninvasiveness, repeatability, and dynamic monitoring. Blood-based biomarkers such as ctDNA, cfDNA, circulating tumor cells, exosomes, noncoding RNAs, proteins, and metabolites can be integrated by AI models into continuously updated molecular risk trajectories to help evaluate tumor burden, molecular residual disease, and clonal evolution in the postoperative management of lung cancer.²⁸⁰ Currently, imaging-based follow-up remains the main approach for recurrence surveillance; however, more intensive chest CT follow-up has not demonstrated a survival benefit²⁸¹, and traditional staging cannot fully explain recurrence-risk heterogeneity at the individual level.²⁸² Chen *et al.*²⁸⁰ proposed that incorporating blood-based MRD status into the traditional TNM staging system to construct a TNM–blood staging system could more individually define postoperative disease status in patients with lung cancer.

Liquid biopsy also faces several challenges. In resectable early-stage lung cancer and postoperative settings, ctDNA abundance is usually low and can be confounded by factors such as clonal hematopoiesis. Reliance on mutation detection alone may therefore carry a risk of missed detection.^{104,283,284} To address this issue, the low-depth WGS-based platform combines multi-omics features, including cfDNA fragment length, end motifs, genome-wide copy number distribution, and co-methylation

patterns, with machine learning methods to improve the capture of residual disease signals under low tumor burden. Compared to ctDNA mutation detection alone, the combined ctDNA and WGS strategy improves MRD detection sensitivity and increases recurrence prediction accuracy while maintaining high specificity.²⁷⁹ The combination of AI and liquid biopsy enables prognostic prediction beyond anatomical staging and toward individualized molecular stratification, allowing more precise decisions regarding adjuvant treatment and early intervention for recurrence.

5.4. Artificial intelligence-enabled patient rehabilitation and full-course management

5.4.1. Artificial intelligence-integrated wearable devices and continuous monitoring

In perioperative management, the conventional monitoring based on ward rounds and scheduled measurements is often unable to continuously characterize patients' physiological status and subjective symptoms. Some transient or fluctuating abnormal signals may be missed between two measurements, thereby delaying the intervention.²⁸⁵ With the development of wearable devices and electronic patient-reported outcomes (ePROs), it has become possible to construct a continuous perioperative monitoring system based on multimodal digital devices.^{286,287} A recent prospective study integrated smartwatches with ePRO in patients with NSCLC undergoing thoracic surgery, enabling synchronous collection of physiological parameters, such as body temperature, heart rate, oxygen saturation, and activity level, together with subjective symptoms, including pain, dyspnea, fatigue, and sleep quality. These data were then validated against electronic health record (EHR) data, revealing high concordance between wearable-device measurements and EHR data.²⁸⁵

Within this monitoring framework, AI is embedded in both device-side and backend algorithms to perform automated quality control, time-series analysis, and anomaly detection on high-frequency vital-sign signals collected by wearable devices, transforming raw continuous data into clinically meaningful dynamic indicators. Machine learning algorithms can identify abnormal patterns that deviate from an individual's baseline, thereby enabling prospective warning of adverse events. In one study, a prediction model constructed using nocturnal resting heart rate data collected by smartwatches provided warnings before clinical symptoms appeared for most postoperative complications after lung cancer surgery.²⁸⁸ In addition, multimodal data fusion can be used to model the relationship between objective physiological parameters and the subjective symptom burden reflected by ePROs,

thereby constructing individualized digital phenotypes of postoperative recovery.²⁸⁵ Under the concept of enhanced recovery after surgery, this approach may facilitate timely intervention for symptom management and rational allocation of nursing and medical resources.²⁸⁹

Beyond identifying postoperative risk, AI can also support supervision and feedback during the rehabilitation process. A recent study introduced a mobile application, RehabLung, designed to enable remote supervision and individualized management of breathing exercises and thoracic mobility training for postoperative lung cancer patients based on AI-powered visual recognition.²⁹⁰ The system uses a smartphone camera to analyze trunk and upper-limb posture, mouth shape, breathing duration, and the number of completed movements. Combined with gamified feedback, individualized exercise prescriptions, and a web-based healthcare management platform, it enables remote supervision of patients' breathing and thoracic mobility training.²⁹⁰ Its rehabilitation prescriptions can be adjusted weekly according to surgical type, pulmonary function, symptom burden, real-time movement performance, and therapist assessment, and the system can alert the clinical team when adherence is insufficient or when there is a potential risk of complications.²⁹⁰ Although this study remains a trial protocol and cannot yet directly demonstrate clinical efficacy, it suggests that AI may transform postoperative pulmonary rehabilitation into a clinician-patient collaborative management model, improving the accessibility, adherence, and individualization of pulmonary rehabilitation.

5.4.2. Artificial intelligence-assisted postoperative health education and psychological intervention

For lung cancer patients who require systematic education on disease management and symptom control during postoperative recovery, AI-enabled disease-specific management platforms provide an important carrier for health-management-oriented education. Supported by AI algorithms, such platforms incorporate health education content, symptom self-assessment scales, and feedback from healthcare teams into a unified data framework. They automatically classify and quantitatively analyze daily patient-reported information, such as cough, pain, sleep, and fatigue, and dynamically assess recovery status according to the typical evolution of symptoms at different postoperative stages. On this basis, the system can match educational content and intervention recommendations to the corresponding recovery stage, enabling a shift from passive follow-up to proactive management.²⁹¹ Compared with traditional follow-up models mainly based on telephone calls or outpatient visits, AI platforms can identify key time windows in the early post-discharge

period when patient needs are concentrated and can provide timely intervention for symptom burden through staged management strategies. This may help reduce patients' uncertainty about the recovery process and enhance their self-management ability. It may also allow healthcare professionals to identify common problems at the population level while providing differentiated guidance to individuals, improving follow-up efficiency while maintaining refinement and continuity of management.²⁹¹

At present, the scope of perioperative health education is gradually extending from the delivery of disease and rehabilitation knowledge to intervention in patients' psychological states and behavioral patterns. Accordingly, the role of AI is expanding from an information and data-processing tool to an intelligent intervention method for psychological support and behavioral guidance. A small clinical study of patients undergoing radical surgery for NSCLC showed that, based on conventional perioperative health education, introducing an AI-assisted system to generate individualized educational and psychological counseling content, followed by nurse review and implementation, was associated with improvements in psychological adaptation and emotional status.⁶³ At the cognitive level, this model provides more targeted explanations and interactive question-and-answer support by incorporating patients' disease characteristics, educational background, and cognitive ability. At the emotional level, compared to traditional education, this approach can markedly reduce postoperative depression and anxiety and improve psychological and social functioning dimensions in quality-of-life assessments. At the volitional level, AI-assisted health education encourages patients to adopt more confrontive coping strategies rather than avoidance or passive compliance, thereby psychologically strengthening their willingness to actively participate in treatment and rehabilitation.⁶³ The unique value of AI in this process lies in two aspects. On the one hand, AI can combine standardized medical information with individualized modes of expression, compensating for the limitations of traditional education, which often has fixed content and insufficient interactivity. On the other hand, through continuous and repeatable explanations and emotional support, AI can, to some extent, serve as a patient and responsive digital psychological companion, alleviating patients' concerns about surgical trauma, pain, and prognosis. This not only improves the accuracy and accessibility of information delivery but also provides a low-cost and scalable new pathway for postoperative psychological intervention. Its effectiveness, safety, scalability, and cost-effectiveness require confirmation in larger prospective studies.

6. Applications of artificial intelligence in scientific research and patient education of resectable lung cancer

6.1. Large language model-assisted clinical information extraction

In clinical information extraction, NLP models can transform free-text information in electronic medical records and reports into computable structured data, promoting the efficient use of real-world data.

At the level of medical reports, LLMs have been explored for automatically inferring pathological T and N stages directly from lung cancer surgical pathology reports while generating corresponding staging rationales. In one study, multiple lightweight open-source LLMs were fine-tuned according to the eighth edition of the American Joint Committee on Cancer staging criteria, enabling the models to infer the corresponding T and N classification from pathological text containing tumor size, extent of invasion, and lymph node involvement, and to provide staging rationale in the form of a "chain of thought".⁴¹ The results showed that the best-performing model achieved an exact-match rate of more than 0.90 in TN-stage prediction and maintained high semantic consistency in staging explanations.⁴¹ Compared to traditional NLP methods based on rules and entity recognition, this generative model-based strategy is no longer limited to explicit keyword matching. Instead, it can integrate pathological clues scattered across different sentences for holistic inference, thereby reducing the workload and variability of manual staging entry and facilitating rapid reclassification when staging criteria are updated.⁴¹ This approach provides a new pathway for automatically structuring key information, such as tumor stage, from pathology reports, and may improve the consistency and traceability of staging data, laying the foundation for large-scale retrospective studies.

At the level of clinical narrative texts such as medical records and operative notes, generative LLMs have also been used to automatically convert complex free-text operative records into standardized structured data. A multicenter study based on lobectomy operative notes constructed an automated workflow consisting of optical character recognition preprocessing, text normalization, and model fine-tuning. This enabled the model to map surgical narrative texts from different language environments into structured templates containing items such as patient information, surgical approach, and key intraoperative steps.²⁹² The results showed that this method maintained high accuracy and consistency in both Chinese and English contexts, significantly outperforming traditional

rule-driven or few-shot learning strategies, while reducing the time required for operative-note structuring to a small fraction of that required for manual processing. Compared to previous NLP methods relying on fixed-field matching, such generative models can understand implicit semantic information, including intraoperative decision-making, operative sequence, and surgical variations, thereby better handling the highly individualized and dynamic expressions characteristic of thoracic surgical records.²⁹² Although errors may still occur when interpreting complex intraoperative details and specialized terminology, this approach offers unique advantages in improving record standardization, promoting comparability of multicenter data, and supporting real-world studies. Another recent study of NSCLC clinical notes constructed an end-to-end NLP pipeline that combined rule-based entity recognition for extracting specific treatment modalities and response descriptions with relationship classification based on a biomedical pretrained language model, achieving automatic association of treatment–response information.²⁹³ In the test set, the system maintained strong discriminatory performance in pairing treatments with Response Evaluation Criteria in Solid Tumors response categories, including complete response, partial response, stable disease, and progressive disease, demonstrating stable recognition of key information in clinical narrative texts. Its entity extraction module also maintained high precision across multiple treatment types and response descriptions, suggesting that AI can reduce manual annotation burden and improve data consistency.²⁹³ Although performance declined during external validation across different institutions, this finding reflects the effect of cross-center differences in text style on model generalizability and highlights the importance of continuous optimization and multicenter training.²⁹³

Despite these promising results, LLMs used for information extraction or report structuring should not be regarded as autonomous staging or clinical decision-making systems. Their outputs are more appropriately used to summarize source documents, populate structured fields, identify missing information, or check consistency with predefined staging criteria, with final interpretation retained by qualified clinicians and pathologists.^{294–296} Because LLMs may omit relevant details, generate plausible but unsupported statements, or misinterpret institution-specific terminology, every clinically relevant output should be verified against the original medical record, pathology report, and current guideline criteria before use.^{295–297} Models should also undergo institution-specific validation using local documentation styles, languages, information systems, and patient populations before clinical deployment, rather than relying solely

on performance reported in external benchmark datasets.^{296,298} When external or cloud-based LLMs are used to process operative notes, pathology reports, or other protected health information, data minimization, de-identification, secure deployment, access control, and clear institutional governance are required to reduce privacy and confidentiality risks.^{294–296}

Overall, LLM-driven automated clinical information extraction may help overcome the scale and efficiency bottlenecks of traditional manual data curation and standardize the expression of core variables such as treatment regimens and responses. It provides a key data foundation for real-world multimodal data analysis and prognostic modeling in surgically resectable lung cancer, but extracted or generated information should remain subject to professional verification before being incorporated into clinical records, research databases, or treatment-related workflows.

6.2. Large language model-enabled patient information access and education

With the rapid development of LLMs, AI chatbots are increasingly entering the field of lung cancer patient education and information access, demonstrating potential value in answering common questions related to surgically resectable lung cancer. Multiple clinical studies have evaluated the accuracy and relevance of responses generated by AI models such as ChatGPT to frequently asked patient questions about lung cancer surgery. For high-frequency patient questions regarding lung cancer surgery, the answers generated by AI models were generally rated by thoracic surgery experts as evidence-based, largely accurate, and minimally biased. Their language was easy to understand, and in most cases, only minor supplementary explanations were needed to meet clinical communication needs.⁴² Particularly, when responding to specific decision-making scenarios raised by patients, such as the choice of surgical approach and perioperative risks, AI models can rapidly generate clearly structured and readable explanatory text, offering substantially greater time efficiency than traditional manual literature-search workflows.¹⁸⁷ Another study used the same evaluation framework to separately assess “general lung cancer questions” and “lung cancer surgery questions,” and found that the model maintained high consistency and stability across different topical contexts.²⁹⁹ These findings suggest that LLMs have strong capabilities in the standardized and structured integration of medical knowledge. They can transform information scattered across guidelines and evidence-based literature into patient-understandable language, thereby partially addressing the limitations of traditional outpatient education, including limited consultation

time, information asymmetry, and comprehension gaps. At the same time, AI-generated responses often proactively remind patients to communicate further with their treating clinical team, which may help reinforce the concept of shared decision-making.⁴² Some models can also actively generate lists of questions for patients to ask their physicians or provide visual information, which may improve patient engagement during consultations.¹⁸⁷ It should be noted, however, that model output length can fluctuate, potentially leading to information overload. This suggests that future integration of AI tools into the management of resectable lung cancer should include adaptive functions that allow responses to be adjusted in length and complexity according to each patient's needs and level of understanding.⁴² Conversely, excessive simplification may weaken key information, and attention should still be paid to the timeliness of training data and the risk of hallucination.²⁹⁹ In addition, model access to paid databases and copyrighted literature remains uncertain, which may affect the ability to integrate the latest high-quality evidence. If the training data are not sufficiently representative, information bias for certain populations may also be amplified.¹⁸⁷ Therefore, although AI has clear advantages in the speed of information generation and the organization of explanations, professional oversight remains necessary to ensure evidence-based rigor and contextual sensitivity.

Despite these potential benefits, LLM-generated responses may contain fabricated references, unsupported recommendations, internally inconsistent statements, or confidently expressed factual errors. Because model knowledge depends on the content and update date of its training and retrieval sources, responses may also fail to reflect newly revised guidelines, recently approved therapies, or institution-specific clinical pathways.^{294–297} Accordingly, LLMs should not independently recommend surgical approaches, determine operability, interpret pathological or molecular findings, or select perioperative systemic treatment. Their more realistic role is to summarize clinical information, translate professional terminology into understandable language, structure questions for consultation, check the apparent consistency of information with current guidelines, and support patient communication under physician supervision.^{295–297} Accountability must also remain clearly assigned. The treating clinical team and healthcare institution, rather than the LLM itself, should retain responsibility for reviewing the accuracy, relevance, and appropriateness of information provided to patients. Institutions should establish procedures for human review, documentation of model use, correction of harmful or misleading outputs, and escalation of high-risk questions to qualified

professionals.^{294–296} Patient-facing systems may process sensitive information regarding diagnosis, pathology, genetic testing, treatment, and prognosis; therefore, identifiable patient data should not be entered into publicly accessible models without appropriate consent, privacy protection, and institutional authorization. Secure local deployment or governed interfaces may be preferable when protected health information is involved.^{294–296} Before routine use, each institution should validate the selected LLM for its intended population, language, clinical context, and task, including evaluation of factual accuracy, completeness, readability, bias, hallucination frequency, and potential patient harm. Ongoing monitoring is also necessary because model versions, retrieval sources, and outputs may change over time.^{294,296,298}

In summary, LLM-based chatbots can serve as physician-supervised auxiliary education tools and have practical feasibility in improving patient understanding, optimizing perioperative communication workflows, and supporting health management. However, their application must still be grounded in professional supervision and contextual interpretation to ensure both medical accuracy and emotional support for patients.

7. Challenges and solutions of artificial intelligence application in resectable lung cancer

7.1. Technical barriers to reliable and generalizable artificial intelligence implementation

Although AI prediction models have demonstrated favorable discriminatory ability in perioperative risk assessment, current technical bottlenecks still limit their transferability in surgically resectable lung cancer.

At the algorithmic level, existing AI prediction models still have clear limitations in interpretability and reliability. Most deep learning algorithms generate outputs in a “black-box” manner, making it difficult to explain how imaging features or clinical variables contribute to the decision-making process. This weakens clinicians' trust in model conclusions and limits their use in high-risk surgical decision-making scenarios.^{300,301} In addition, model training depends heavily on large-scale, high-quality data. In real-world settings, however, electronic medical record systems and imaging protocols lack unified standards, while data preprocessing methods and model architectures vary across studies. As a result, data from multiple sources are difficult to integrate, and model generalizability and reproducibility are affected.^{15,302,303} For example, one study compared random forest models based on CT semantic features interpreted by radiologists with those based on

radiomics features for NSCLC subtype classification. The model based on semantic features performed robustly in an independent external validation dataset, whereas the radiomics-based model, despite achieving perfect performance in the training set, dropped to random-level performance during external validation. This suggests that radiomics models may be prone to overfitting and that their generalizability must be evaluated through rigorous external validation.³⁰⁴ To address these issues, future studies should adopt standardized reporting and validation frameworks, with routine external validation, calibration assessment, and transparent reporting of preprocessing, model development, and evaluation procedures.³⁰⁵

At the data level, selection bias in the training samples and insufficient population representativeness also constitute important risks. If models are primarily derived from specific institutions or specific populations, they may produce systematic errors in different regions or clinical contexts, thereby affecting the stability and safety of risk prediction.^{302,303} At the same time, AI systems must process large amounts of sensitive medical information, but data security and privacy-preserving mechanisms remain incomplete. Potential risks of data leakage create additional technical burdens for clinical deployment.³⁰² These problems may be mitigated by establishing standardized and interoperable multicenter data systems and by using privacy-preserving approaches such as federated learning, which enables collaborative model training across institutions without directly sharing sensitive patient-level data.³⁰⁶

Moreover, most current studies have only shown that AI models are “non-inferior” to traditional methods in predictive performance. There remains a lack of multicenter, large-sample prospective validation demonstrating their incremental value in improving real-world clinical outcomes. This limits the translation of prediction models from research tools into routine clinical decision-support systems.³⁰³ Therefore, AI tools should be tested in real clinical workflows through prospective pilot studies and randomized trials. These studies should follow established AI-specific reporting guidelines, including the Developmental and Exploratory Clinical Investigations of Decision Support Systems Driven by AI (DECIDE-AI) guideline for early clinical evaluation, the Standard Protocol Items: Recommendations for Interventional Trials–AI (SPIRIT-AI) extension for trial protocol design, and the Consolidated Standards of Reporting Trials–AI (CONSORT-AI) extension for randomized trial reporting.³⁰⁷ The detailed clinical implementation roadmap is provided in Section 8.

7.2. Clinical, ethical, and governance challenges in artificial intelligence translation

At the level of clinical translation, integrating AI prediction models into real-world workflows remains constrained by multiple structural factors.³⁰⁸ For example, model deployment often requires additional computational resources and support from information system interfaces, while insufficient interoperability among existing clinical information systems makes it difficult to embed AI tools seamlessly into perioperative decision-making processes. In resource-limited regions, these technical and economic barriers may further widen the application gap among medical institutions, leading to potential AI accessibility inequality.³⁰⁹ In addition, most existing studies are conducted in idealized research settings, whereas fragmented data flows and disconnected workflows in the real world still hinder AI implementation.¹⁵ To improve clinical deployability, future AI systems should be embedded into existing clinical workflows and connected with hospital information systems.^{306,308}

At the ethical level, data privacy and information security risks are particularly prominent. AI systems need to process large volumes of highly sensitive individual medical data. Once data leakage occurs, it may not only lead to legal consequences but also undermine patients’ trust in intelligent healthcare systems. In addition, if training data are biased in population composition, the model may show inconsistent predictive accuracy across different sexes, ages, or ethnic groups, thereby amplifying health inequalities and affecting the fairness of clinical decision-making.³⁰³ For example, NSCLC survival and surgical recommendation models constructed using Surveillance, Epidemiology, and End Results registry data showed that, even when race was not included as an input variable, machine learning models could still generate unfavorable predictive bias against Black patients. This disparity was further amplified after race was included as a variable, suggesting that structural inequalities in data can be inherited and reinforced by algorithms.³¹⁰ This may be related to the persistent racial and ethnic disparities in NSCLC mortality over the past two decades, which are closely associated with disease stage, access to surgery, and socioeconomic factors, leading to potential structural bias in algorithm training data.³¹¹ More complex still, once AI is incorporated into clinical decision-making, responsibility attribution and legal boundaries remain unclear. In scenarios where predictive results affect treatment pathways or even surgical strategies, it remains difficult to determine whether responsibility for misjudgment should lie with clinicians, medical institutions, or algorithm developers. This reflects the lagging state of relevant regulatory

frameworks.^{303,312} Meanwhile, patients' understanding of AI involvement in diagnosis and treatment remains limited. Without sufficient communication, this may affect their informed consent and perception of autonomy in treatment decision-making.³⁰² These ethical risks require clear governance mechanisms before clinical deployment, including privacy-preserving data management,

subgroup-specific performance evaluation, transparent reporting of model limitations, clear assignment of clinical responsibility, and explicit patient communication regarding the supportive rather than autonomous role of AI.³⁰⁵ The key challenges and corresponding potential solutions across the algorithmic, data, clinical research, clinical integration, and ethical levels are summarized in Table 4.

Table 4. Challenges and potential solutions for clinical translation of AI in surgically resectable lung cancer

Challenge domain	Major challenges	Potential solutions
Algorithmic level	Black-box outputs ³⁰⁰ ; limited interpretability ³⁰⁰ ; overfitting ³⁰⁴ ; unstable external performance ³⁰⁴	Use SHAP/Grad-CAM; report preprocessing and model architecture; perform calibration and external validation ³⁰⁵
Data level	Heterogeneous EMR systems; inconsistent imaging protocols; variable preprocessing workflows; difficult data integration ^{302,303}	Standardize data collection, annotation, preprocessing, and reporting pipelines across centers ³⁰⁶
Clinical research level	Limited prospective evidence; non-inferiority-focused studies; insufficient proof of real-world clinical benefit ³⁰³	Conduct prospective pilot studies and randomized trials; follow DECIDE-AI, SPIRIT-AI, and CONSORT-AI guidance ³⁰⁷
Clinical integration level	Poor interoperability with EHR/PACS/pathology systems ³⁰⁹ ; fragmented workflows ¹⁵ ; additional workload ³⁰⁹ ; unequal access across institutions ³⁰⁹	Embed AI into existing hospital systems; design workflow-integrated decision-support tools with clinician review ³⁰⁶
Ethical level	Population bias ³⁰³ ; subgroup performance variation; privacy risks ³¹⁰ ; unclear responsibility ^{303,312} ; insufficient informed consent ³⁰²	Use diverse multicenter cohorts; perform subgroup fairness auditing; apply privacy-preserving methods; clarify responsibility and AI's supportive role ³⁰⁵

Abbreviations: AI: Artificial intelligence; CONSORT-AI: Consolidated Standards of Reporting Trials–Artificial Intelligence; DECIDE-AI: Developmental and Exploratory Clinical Investigation of Decision Support Systems Driven by Artificial Intelligence; EHR: Electronic health record; EMR: Electronic medical record; Grad-CAM: Gradient-weighted class activation mapping; PACS: Picture archiving and communication system; SHAP: Shapley additive explanations; SPIRIT-AI: Standard Protocol Items: Recommendations for Interventional Trials–Artificial Intelligence.

8. Future perspectives

As AI continues to permeate the entire continuum of oncology care, its validation in surgically resectable lung cancer will gradually shift from performance to clinical value. Future research should systematically evaluate the safety and stability of AI prediction models through multicenter, large-sample prospective clinical trials, as well as their incremental benefits for patient outcomes in real-world clinical settings. This will help promote their transition from experimental tools to standardized decision-support systems.^{15,16} A stepwise roadmap for the clinical implementation of AI can be outlined. First, each AI system should have a clearly defined intended use, target population, position within the care pathway, and prespecified clinical action triggered by its output, with model development and reporting conducted transparently in accordance with frameworks such as Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis Plus AI.³⁰⁵ Second, technical performance should be

confirmed through independent multicenter external validation, including assessment of calibration, subgroup performance, robustness to variations in data acquisition, and comparison with the existing standard of care.³⁰⁵ Third, models that retain adequate performance should undergo prospective evaluation in live clinical workflows, initially through silent deployment or small-scale feasibility studies to assess usability, human–AI interaction, workflow disruption, and potential safety risks in accordance with DECIDE-AI.³⁰⁷ Fourth, prospective comparative studies or randomized trials should determine whether AI-assisted care improves clinical decision-making, efficiency, safety, patient-reported outcomes, or other clinically meaningful endpoints, with protocols and reports following SPIRIT-AI and CONSORT-AI guidance.^{313,314} Finally, systems that demonstrate clinical utility should be integrated into existing EHR, imaging, and pathology infrastructures under defined governance and clinician-oversight mechanisms, followed by continuous post-deployment monitoring for data drift, performance degradation,

subgroup inequity, unintended consequences, and the need for model updating.³¹⁵

Beyond the trend toward multimodal integration, traditional risk assessment based on static baseline information is evolving toward dynamic prediction systems. By incorporating continuously updated imaging data, perioperative monitoring parameters, and potential wearable-device data, AI models can enable real-time refinement of predictions for complications, recurrence risk, and functional recovery trajectories. In this way, AI will shift from one-time prediction to continuous risk warning, providing prospective intervention windows for perioperative management.^{276,285}

With the goal of individualized precision surgery, the construction of a “digital twin lung” model based on patient-specific imaging, pathological, and functional data represents a promising direction. Such models could simulate, in a virtual environment, the effects of different resection extents, surgical pathways, and perioperative management strategies on function and prognosis. This would allow multiple surgical scenarios to be tested before surgery and provide quantitative estimates for future studies of surgical approach selection and risk control.^{316,317}

The future application of AI prediction models in surgically resectable lung cancer will move toward multimodal integration, dynamic updating, and individualization. However, this transition still depends on rigorous external validation, standardized data governance, and frameworks aligned with clinical workflows to ensure that AI truly supports safe, interpretable, and equitable clinical decision-making.³⁰⁰

9. Conclusion

Artificial intelligence has demonstrated substantial potential to improve the entire care pathway of surgically resectable lung cancer, from early screening, preoperative diagnosis, and treatment decision-making to intraoperative navigation and postoperative management, as summarized in Table 5. To provide a transparent overview of translational maturity, we classified the available evidence into four levels according to the most advanced stage of evaluation, ranging from exploratory or preclinical evidence to prospective real-world implementation with demonstrated clinical utility. Given the current evidence, mainly derived from retrospective studies and small-sample validations, future investigations require interdisciplinary collaboration, rigorous clinical validation, interpretable model development, and system designs that are deeply integrated with clinical workflows. These efforts will be essential to truly translate AI technologies into clinical practice of resectable lung cancer and to advance toward greater precision, intelligence, and personalization.

Table 5. Overview of AI-enabled tasks, input data, output formats, implementation status, and levels of evidence across the care continuum of surgically resectable lung cancer

Clinical phase/ scenario	AI-enabled tasks	Methodological category	Input data	Output format	Implementation status	Level of evidence
Preoperative stage	High-risk population identification and screening triage	Clinical-data-driven AI; Multi-omics AI; Imaging- based AI	Demographic data, smoking and exposure history, family history, environmental factors, serum biomarkers, pulmonary function, liquid biopsy, exhaled VOCs, LDCT	Patient risk stratification ^{19,21}	Prospective validation	Level 3
	Pulmonary nodule detection and benign- malignant discrimination	Imaging-based AI; Multi- omics AI; Clinical-data- driven AI	LDCT/CT, chest radiography, radiomics features, clinical variables, longitudinal imaging, liquid biopsy signals	Nodule malignancy score/risk category ^{112–117}	Independent external validation	Level 3
	Prediction of pathological subtype, invasiveness, and high-risk pathological features	Imaging-based AI; Clinical-data-driven AI	CT, PET/CT, radiomics, deep learning features, clinical data	Pathological subtype, stage, and high-risk feature probabilities ^{122–125}	Independent external validation	Level 3

(Cont'd...)

Table 5. (Continued)

Clinical phase/ scenario	AI-enabled tasks	Methodological category	Input data	Output format	Implementation status	Level of evidence
Preoperative stage	Bronchoscopy, EBUS, and percutaneous biopsy support	Image- and video-based procedural AI; Imaging- based AI; Pathology- based AI	Preoperative CT, bronchoscopic video, EBUS B-mode ultrasound, elastography, CBCT/DT/fluoroscopy, cytology, biopsy pathology	Navigation path, target selection, and sampling adequacy assessment ¹⁴⁰	Clinical implementation for selected navigation systems; multicenter retrospective study for AI-assisted image and sampling assessment	Level 4 for commercially implemented navigation systems; Level 2 for image assessment
	Molecular subtyping	Imaging-based AI; Pathology-based AI; Multi-omics AI	CT, PET/CT, radiomics, habitat imaging, pathology, liquid biopsy, molecular testing data	EGFR/PD-L1 prediction report ^{40,187}	Independent external validation	Level 3
	MDT and treatment decision support	Text-based AI and LLMs; Clinical-data-driven AI	Clinical summaries, imaging, staging information, pathology, molecular data, treatment guidelines, evidence-based reports	Structured treatment recommendation ^{40,187}	Multicenter retrospective study	Level 2
	Surgical planning and AI-assisted 3D reconstruction	Imaging-based AI	Preoperative CT, non-contrast/contrast- enhanced CT, pulmonary artery/vein/ bronchus segmentation, tumor location data	Patient-specific 3D lung model ^{204,207,208}	Clinical implementation	Level 4
Intraoperative stage	Real-time non-contact intraoperative 3D navigation	Image- and video-based procedural AI	Patient-specific 3D models, gesture- recognition signals, binocular infrared sensing, hand keypoint tracking, thoracoscopic images	Interactive 3D navigation interface ^{233,234}	Small-sample study	Level 3
	Deformable registration and dynamic navigation	Image- and video-based procedural AI	Preoperative 3D-CT, intraoperative single- view thoracoscopic images, pneumothorax deformation models, and synthetic images	Registered intraoperative anatomy overlay ^{79,238}	Proof-of-concept	Level 1
	AI-based surgical image recognition and video analysis	Image- and video-based procedural AI	Thoracoscopic videos, surgical images, annotated anatomical structures, surgical instrument images, and continuous video frames	Real-time visual annotations and phase labels ²⁴³	Independent external cohort validation	Level 3
	Rapid pathological assessment	Pathology-based AI	Frozen-section WSIs, OCT images, MPM images, HHG images, fresh tissue specimens, digital pathology data	Subtype classification, heatmaps, and margin/risk maps ¹⁷⁶	Single-center retrospective study for frozen-section models; proof-of-concept for OCT, MPM, and HHG	Level 2 for frozen- section models; Level 1 for OCT, MPM, and HHG systems

(Contd...)

Table 5. (Continued)

Clinical phase/ scenario	AI-enabled tasks	Methodological category	Input data	Output format	Implementation status	Level of evidence
Postoperative stage	Pulmonary complication risk prediction	Clinical-data-driven AI; Imaging-based AI	Demographics, comorbidities, WBC, CRP, BMI, pulmonary function, blood glucose, operative time, single-lung ventilation duration, AI-CT	ppC risk score ^{253,255}	Single-center retrospective study	Level 2
	Systemic complication prediction	Clinical-data-driven AI	Perioperative clinical data, laboratory indicators, anesthesia variables, operative duration, analgesia information, and comorbidity data	Systemic complication risk scores ^{256,262}	Independent external cohort validation	Level 3
	Length of stay and recovery prediction	Clinical-data-driven AI	Clinical pathway data, symptoms, laboratory tests, pulmonary function, surgical approach, postoperative day variables, ePath data	PLOS probability and modifiable-factor alerts ^{263,266}	Single-center retrospective study	Level 2
	Functional recovery and frailty prediction	Clinical-data-driven AI	Demographics, ASA, comorbidities, TNM stage, treatment history, pulmonary function, postoperative laboratory indicators, and early recovery status	Recovery trajectory and frailty-risk estimate ²⁶⁷	Single-center retrospective study	Level 2
	Recurrence and survival prediction	Clinical-data-driven AI; Imaging-based AI; Pathology-based AI; Multi-omics AI	Clinical data, CT, PET/CT, radiomics, pathology WSIs, tumor microenvironment features, laboratory data, ctDNA/MRD, WGS-derived features	Recurrence-risk group and survival estimate ²⁷⁰	Independent external validation	Level 3
	Patient education and postoperative psychological support	Text-based AI and LLMs	Patient questions, educational materials, symptom self-assessments, recovery-stage data, clinician-reviewed AI-generated content	Personalized educational and counseling content ²⁹¹	Small-sample study	Level 1
	Wearable device and ePRO-based continuous monitoring	Clinical-data-driven AI	Smartwatch data, heart rate, oxygen saturation, body temperature, activity, ePRO symptoms, EHR data	Real-time alerts and recovery-status dashboard ^{285,289}	Prospective validation	Level 3
	AI-assisted rehabilitation management	Imaging-based AI	Smartphone camera images, breathing exercise performance, posture, mouth shape, movement completion, therapist feedback	Exercise feedback and individualized rehabilitation plan ^{290,291}	Small-sample study	Level 1

Notes: Levels of evidence were categorized as follows: Level 1: preclinical or exploratory evidence derived from proof-of-concept studies, animal experiments, engineering prototypes, or small-sample studies; Level 2: retrospective clinical validation based on single-center or multicenter retrospective studies without independent external or prospective validation; Level 3: external or prospective validation supported by an independent external cohort or prospective study; and Level 4: clinical implementation within a real-world workflow with evidence of clinical utility or patient-centered outcomes. Abbreviations: 3D: Three-dimensional; AI: Artificial intelligence; AI-CT: Artificial intelligence-assisted computed tomography; ASA: American Society of Anesthesiologists; BMI: Body mass index; CBCT: Cone-beam computed tomography; CRP: C-reactive protein; CT: Computed tomography; ctDNA: Circulating tumor DNA; DT: Digital tomosynthesis; EBUS: Endobronchial ultrasound; EGFR: Epidermal growth factor receptor; EHR: Electronic health record; ePath: Electronic clinical pathway; ePRO: Electronic patient-reported outcome; HHG: Higher harmonic generation imaging; LDCT: Low-dose computed tomography; MDT: Multidisciplinary team; MPM: Multiphoton microscopy; MRD: Minimal residual disease; OCT: Optical coherence tomography; PD-L1: Programmed death-ligand 1; PET/CT: Positron emission tomography/computed tomography; PLOS: Prolonged length of stay; PPC: Postoperative pulmonary complication; TNM: Tumor-node-metastasis; VOC: Volatile organic compound; WBC: White blood cell; WGS: Whole-genome sequencing; WSIs: Whole-slide images.

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Author contributions

Conceptualization: Kezhong Chen

Writing—original draft: Zhuowei Li, Xiaoqiu Yuan

Writing—review & editing: All authors

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