Journal of Cancer Research and Clinical Oncology (2026) 152:92
https://doi.org/10.1007/s00432-026-06465-1

REVIEW

Artificial intelligence construction: a review of the bridge between CT imaging features of lung ground-glass nodules adenocarcinoma and carcinogenic driver genes

Weikuan Xue[1] · **Jinchun Chen**[1]

Received: 10 January 2026 / Accepted: 16 March 2026

Abstract

Lung ground-glass nodules (GGNs) represent a critical early imaging manifestation of lung adenocarcinoma, and exploring the relationship between their CT imaging features and oncogenic driver genes holds significant promise for precision diagnosis and personalized treatment. In recent years, artificial intelligence (AI) technologies, particularly deep learning and machine learning methods, have demonstrated remarkable potential in the integrative analysis of radiomic and genomic data. This review summarizes the current advances in AI applications for extracting CT imaging features of lung GGNs, identifying oncogenic driver genes, and analyzing their correlations. Key AI-driven techniques enabling the construction of a bridge between imaging phenotypes and genetic alterations are discussed, alongside challenges such as data heterogeneity, limited annotated datasets, and interpretability. Future research directions emphasize the development of robust, explainable AI models and multi-omics integration to enhance early lung cancer diagnosis and therapeutic strategies. By providing a comprehensive overview of the intersection between AI, radiomics, and genomics in lung GGN adenocarcinoma, this article aims to offer theoretical insights and technical references to advance early detection and precision oncology.

Keywords Artificial intelligence · Lung ground-glass nodule · Adenocarcinoma · CT imaging features · Oncogenic driver genes · Radiomics · Genomics · Deep learning

Introduction

Lung adenocarcinoma presenting as ground-glass nodules (GGNs) on computed tomography (CT) imaging represents a critical early manifestation of lung cancer, with significant implications for diagnosis, treatment, and prognosis. GGNs, especially pure ground-glass nodules (pGGNs), are increasingly detected due to widespread use of low-dose CT screening and advances in imaging technology (Yu et al. 2021), Compared to solid nodules or part-solid nodules, pure ground-glass nodules (pGGNs) are more commonly associated with early lung adenocarcinoma or its precursor lesions, such as adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA) (Lu et al. 2020). The indolent growth pattern of GGNs provides a unique window for studying early events in lung cancer.

The CT imaging features of lung GGNs are diverse and complex, encompassing variations in size, density, morphology, and the presence or absence of solid components. These features are crucial for differentiating benign from malignant lesions and for assessing the invasiveness of lung adenocarcinoma, which directly influences surgical planning and patient management (Wang et al. 2024a; Feng et al. 2023). However, traditional imaging diagnosis is often limited by subjectivity and inter-observer variability, as well as by the subtlety of some imaging signs, especially in small or pure GGNs (Digumarthy et al. 2020). Quantitative imaging techniques such as spectral CT and multi-detector CT have shown promise in providing objective parameters like water concentration and iodine concentration that may

✉ Jinchun Chen
992327395@qq.com

Weikuan Xue
584112594@qq.com

[1] Rui'an People's Hospital, Rui'an, Wenzhou 325200, Zhejiang, China

Published online: 22 April 2026

aid in distinguishing invasive adenocarcinoma from non-invasive lesions (Yu et al. 2021; Du et al. 2022a). Moreover, radiomics approaches that extract high-dimensional quantitative features from CT images have demonstrated improved performance in predicting tumor invasiveness and distinguishing pathological subtypes of lung adenocarcinoma manifesting as GGNs (Feng et al. 2023; Xiong et al. 2022; Wu et al. 2020). These advances underscore the need for more precise, reproducible, and automated image analysis methods to better characterize GGNs.

At the molecular level, oncogenic driver gene alterations play a pivotal role in the pathogenesis, progression, and therapeutic targeting of lung adenocarcinoma. Key driver genes such as epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and Kirsten rat sarcoma viral oncogene homolog (KRAS) are frequently mutated or rearranged in lung adenocarcinoma, with distinct mutation patterns correlating with clinical characteristics such as smoking status, gender, and histopathological subtypes (Ma et al. 2020, 2024; Li et al. 2020). For instance, EGFR mutations are more prevalent in female non-smokers and are associated with well or moderately differentiated adenocarcinomas, whereas KRAS mutations are more common in male smokers and poorly differentiated tumors (Ma et al. 2024; Hsu et al. 2022). ALK rearrangements are often found in younger patients and are linked with specific histological features (Li et al. 2020). Although studies have explored the tumor genomics of invasive pulmonary adenocarcinoma manifested as solid nodules (Liu et al. 2024), GGNs provide a unique perspective for exploring early genetic events prior to invasive growth. Constructing a bridge between lung GGNs and genes using AI may help identify genomic alterations associated with tumor initiation and indolent progression. but also influence tumor biology and prognosis. The interplay between genetic alterations and tumor microenvironmental factors such as PD-L1 expression further modulates therapeutic responses, especially to immunotherapy (Takamochi et al. 2021; Liu et al. 2024). Despite the established significance of these mutations, the relationship between the genomic landscape and imaging phenotypes of lung adenocarcinoma, particularly GGNs, remains incompletely understood.

Artificial intelligence (AI), especially deep learning, has emerged as a transformative tool in medical imaging and genomics, offering the capability to analyze complex, high-dimensional data and uncover latent patterns that may elude human observers. In the context of lung GGNs and adenocarcinoma, AI technologies have been applied to enhance image interpretation, automate lesion detection, and predict pathological invasiveness and genetic mutation status from CT images (Li et al. 2025a). Deep learning-based radiomics models integrate clinical, radiographic, and imaging features to achieve high accuracy in differentiating invasive adenocarcinoma from pre-invasive lesions, thereby aiding in personalized treatment planning (Feng et al. 2023; Xiong et al. 2022). Moreover, AI facilitates the mining of large-scale genomic data, enabling the identification of novel biomarkers and the construction of predictive models that link imaging phenotypes with driver gene mutations (Li and Zhang 2025). The integration of AI with multimodal data—including imaging, histopathology, and genomics—holds promise for building a comprehensive bridge between CT imaging features of lung GGNs and the underlying molecular drivers of tumorigenesis.

Despite these advances, challenges remain in standardizing AI models, ensuring interpretability, and validating findings across diverse populations and clinical settings (Avanzo et al. 2024; Cobo et al. 2025). The "black-box" nature of many AI algorithms necessitates the development of explainable AI (XAI) frameworks to enhance transparency and clinical trustworthiness (Ghnemat et al. 2023; Velden et al. 2022). Furthermore, large-scale prospective studies and external validations are needed to confirm the clinical utility of AI-based approaches in lung adenocarcinoma diagnosis and management (Li et al. 2025a). Addressing these limitations will be critical for the successful translation of AI-driven insights into routine clinical practice.

In summary, Compared with solid nodules or part-solid nodules, pulmonary GGNs represent a unique and biologically early imaging phenotype of lung adenocarcinoma, characterized by complex radiological features and a heterogeneous molecular background defined by key driver gene mutations. The advent of AI technologies, particularly deep learning and radiomics, provides novel methodological foundations to systematically link CT imaging features with genomic alterations, potentially revolutionizing early diagnosis, prognostication, and personalized therapy. This review aims to comprehensively summarize the current research progress in constructing this bridge using AI, critically analyze the strengths and limitations of existing techniques, and explore future directions for integrating AI into the multidisciplinary management of lung GGNs and adenocarcinoma.

Main body

Analysis of CT imaging features of lung ground-glass nodule adenocarcinoma

See Fig. 1

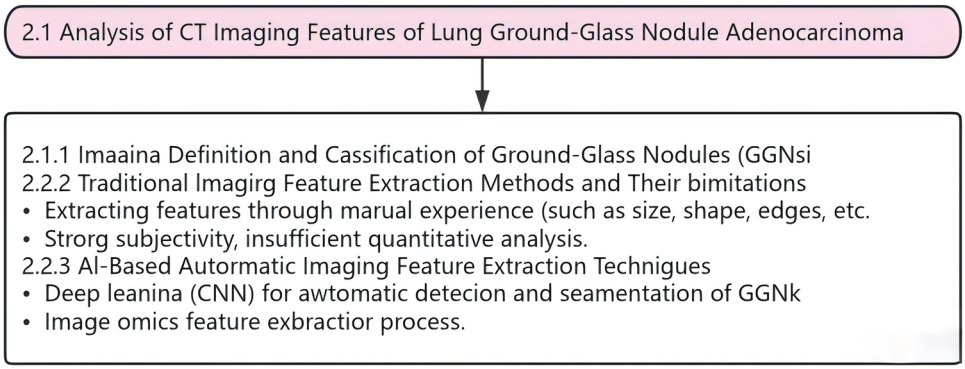

Fig. 1 Overview of the main content of this paragraph. The picture was created by Jinchun Chen

Imaging definition and classification of ground-glass nodules (GGNs)

Ground-glass nodules (GGNs) are a distinct radiological entity on computed tomography (CT) characterized by hazy areas of increased lung attenuation without obscuration of the underlying bronchial structures or pulmonary vessels. GGNs are broadly classified into two categories based on their CT appearance: pure ground-glass nodules (pGGNs) and mixed ground-glass nodules (mGGNs), also termed part-solid nodules. Pure GGNs exhibit homogeneous ground-glass opacity without any solid component, whereas mixed GGNs contain both ground-glass and solid elements within the same lesion. This distinction is clinically significant as it correlates with the pathological invasiveness and prognosis of lung adenocarcinomas. Studies have demonstrated that pGGNs often correspond to pre-invasive or minimally invasive adenocarcinomas, such as atypical adenomatous hyperplasia (AAH), adenocarcinoma in situ (AIS), or minimally invasive adenocarcinoma (MIA), while mGGNs are more frequently associated with invasive adenocarcinomas (IAC) (Zhong et al. 2024; Zhou et al. 2025; Wang et al. 2020).

High-resolution CT (HRCT) imaging is the primary modality for detecting and characterizing GGNs. The imaging features of GGNs include nodule size, shape, margin characteristics (lobulation, spiculation), presence of air bronchograms, vascular convergence, pleural indentation, and solid component size. Quantitative parameters such as the consolidation-to-tumor ratio (CTR), mean CT attenuation values, and intratumoral heterogeneity scores have been incorporated into classification schemas to enhance diagnostic accuracy and invasiveness prediction (Zuo et al. 2025; Wang et al. 2025a; Yu et al. 2022a). For instance, a CTR less than 0.5 in part-solid GGNs has been shown to have a high positive predictive value for primary lung cancer (Notsuda et al. 2024). Moreover, the size of the solid component within mGGNs is a critical determinant of pathological invasiveness, with larger solid components correlating with more aggressive disease (Lu et al. 2020).

The Lung Imaging Reporting and Data System (Lung-RADS) provides standardized criteria for classifying pulmonary nodules, including GGNs, to guide clinical management. The 2022 version of Lung-RADS introduced refinements in the categorization of GGNs, particularly regarding the size thresholds and the classification of suspected infectious or inflammatory findings, which often manifest as GGNs or tree-in-bud patterns. This update aims to reduce false-positive rates and unnecessary follow-ups by more accurately stratifying the risk associated with GGNs (Arora et al. 2025; Kastner et al. 2021; Song et al. 2023). Modified Lung-RADS incorporating GGN-vascular relationships has shown improved sensitivity and agreement rates for pGGNs compared to the original version, highlighting the importance of vascular and morphological features in classification (Song et al. 2023).

Advanced imaging techniques and computational methods, including three-dimensional reconstruction, radiomics, and deep learning algorithms, have been increasingly applied to the evaluation of GGNs. Radiomics analyses extract high-dimensional quantitative features from intra- and peri-nodular regions, enhancing the ability to predict invasiveness and guide individualized treatment strategies (Feng et al. 2023; Wu et al. 2020; Zhang et al. 2022a). Deep learning models, such as convolutional neural networks (CNNs), have been developed for automatic segmentation, detection, and classification of GGNs, achieving high accuracy in distinguishing benign from malignant nodules and differentiating invasive from non-invasive adenocarcinomas (Wang et al. 2020; Xiong et al. 2025; Ma et al. 2022). These AI-based approaches facilitate objective and reproducible assessments that complement radiologists' interpretations.

In summary, the imaging definition and classification of GGNs rely on detailed CT morphological and quantitative features, with pGGNs and mGGNs representing distinct pathological entities with different clinical implications. The integration of standardized classification systems, advanced imaging techniques, and artificial intelligence enhances the precision of diagnosis and prognostication, ultimately

guiding optimal management of patients with GGNs in lung adenocarcinoma.

Traditional imaging feature extraction methods and their limitations

Traditional imaging feature extraction methods for lung ground-glass nodules (GGNs), especially in the context of adenocarcinoma, primarily rely on qualitative and semi-quantitative assessments based on radiologists' experience. These methods focus on visually recognizable features such as nodule size, shape, margin characteristics, and internal components. Key features include nodule diameter, consolidation tumor ratio (CTR), presence and size of solid components, morphological signs like spiculation, lobulation, pleural indentation, air bronchogram, vascular changes, and cavitation. For instance, nodule size and the size of the solid component have been repeatedly identified as crucial indicators for differentiating invasive adenocarcinoma (IAC) from pre-invasive lesions such as adenocarcinoma in situ (AIS) or minimally invasive adenocarcinoma (MIA) (Lu et al. 2020; Wu et al. 2025). Morphological features such as spiculation, lobulation, pleural traction, and vascular abnormalities are also used to infer malignancy and invasiveness (Wu et al. 2025). The consolidation tumor ratio (CTR), which quantifies the proportion of the solid component within a GGN, is another commonly used metric, with higher CTR values correlating with increased invasiveness (Wang et al. 2024a; Wu et al. 2025).

These traditional approaches have been implemented through visual assessment and manual measurements on computed tomography (CT) images. For example, radiologists measure the maximum diameter of nodules and solid components and note the presence of features such as air bronchograms, pleural indentation, and cavitation (Wang et al. 2024a; Wu et al. 2025). Spectral CT imaging provides additional quantitative parameters such as water concentration and iodine concentration, which have been explored for differentiating inflammatory lesions, pre-invasive lesions, and invasive adenocarcinomas (Yu et al. 2021; Cao et al. 2023). However, these parameters are not yet widely adopted in routine clinical practice.

Despite their utility, traditional imaging feature extraction methods are limited by several factors. Firstly, they are heavily reliant on subjective interpretation and experience of radiologists, which introduces inter-observer variability and limits reproducibility (Digumarthy et al. 2020). The qualitative nature of morphological features and manual measurements can lead to inconsistencies, especially in subtle cases or small nodules. Secondly, conventional methods often lack sufficient sensitivity and specificity to reliably distinguish between different pathological subtypes of GGNs, particularly in differentiating AIS/MIA from invasive adenocarcinoma (Liu et al. 2022; Xu et al. 2020). For example, features like nodule size or solid component size alone may not fully capture the complex heterogeneity of tumor biology.

Another limitation is the challenge in quantifying features objectively and comprehensively. Traditional methods focus on a limited set of features and may overlook subtle textural or spatial variations within nodules. This limitation restricts the ability to capture tumor heterogeneity, which is crucial for accurate diagnosis and prognosis. Additionally, some features, such as the presence of vascular abnormalities or cavitation, can be ambiguous and overlap between benign and malignant lesions (Cao et al. 2020).

Moreover, the dynamic evolution of GGNs over time, which is important for assessing invasiveness and growth patterns, is difficult to quantify precisely with traditional methods. While volume doubling time and exponential growth models have been proposed, their clinical application is limited by measurement errors and the complexity of longitudinal imaging analysis (Margerie-Mellon et al. 2020; Zikri et al. 2019).

In summary, traditional imaging feature extraction methods based on radiologists' experience and manual measurements provide valuable but limited information for characterizing lung GGNs. Their subjective nature, limited quantitative capacity, and insufficient sensitivity for subtle pathological distinctions underscore the need for more advanced, objective, and reproducible approaches. These limitations have motivated the development of radiomics and artificial intelligence-based methods, which aim to extract high-dimensional quantitative features and improve diagnostic accuracy and consistency (Xu et al. 2020; Shi et al. 2021; Hu et al. 2021a).

AI-based automatic imaging feature extraction techniques

Deep learning, particularly convolutional neural networks (CNNs), has revolutionized the automatic detection and segmentation of ground-glass nodules (GGNs) in lung CT images by enabling end-to-end learning of hierarchical image features without manual intervention. CNN-based models, such as 3D U-Net architectures, have been successfully applied to segment GGNs with high accuracy, as demonstrated in ovarian cancer PET/CT segmentation studies that achieved Dice scores around 0.74, highlighting the robustness of 3D deep networks in volumetric medical image segmentation (Sadeghi et al. 2024). Similarly, multiscale CNN models incorporating Gaussian pyramid decomposition have improved lung nodule detection performance, including solid and pure ground-glass nodules, by enhancing feature representation across scales (Xiong

et al. 2025). The use of lightweight CNN architectures like MobileNetV2 has also been explored for efficient feature extraction, balancing computational cost and accuracy (Xie et al. 2024). These models often integrate advanced techniques such as transfer learning to overcome limited dataset sizes, improving generalizability in classifying GGNs as benign or malignant (Hu et al. 2021b). Moreover, CNNs have been combined with region-growing and segmentation algorithms to reconstruct intranodular vessels within GGNs, quantifying vascular features that correlate with tumor invasiveness (Zhao et al. 2023a). Deep learning models not only automate the segmentation process but also facilitate extraction of complex features reflecting tumor heterogeneity, which are critical for downstream predictive tasks. For example, deep learning-based segmentation followed by radiomics feature extraction has enabled accurate differentiation of pulmonary contusion from bacterial pneumonia, outperforming radiologists (Deng et al. 2025). The integration of CNN-extracted features with clinical and radiological data has further enhanced the prediction of tumor invasiveness and treatment outcomes in lung adenocarcinoma (Zhang et al. 2025a). However, challenges such as the need for large annotated datasets, variability in imaging protocols, and interpretability of deep learning models remain. To address these, explainable AI techniques like SHAP have been employed to elucidate feature contributions, fostering clinical trust and adoption (Zhang et al. 2025a). Overall, CNN-based deep learning models form the backbone of modern AI-driven automatic detection and segmentation of GGNs, enabling precise and reproducible imaging biomarker extraction essential for personalized lung cancer management.

Radiomics is a quantitative imaging analysis approach that extracts a large number of handcrafted features from medical images to characterize tumor phenotypes and microenvironment non-invasively. The radiomics workflow typically involves several key steps: image acquisition, lesion segmentation, feature extraction, feature selection, and model building. Initially, high-quality CT images are acquired, followed by precise delineation of regions of interest (ROIs) encompassing GGNs, often using semi-automated or AI-assisted segmentation tools to ensure reproducibility (Wang et al. 2024b). Subsequently, a comprehensive set of features is extracted, including first-order statistics (e.g., intensity histograms), shape descriptors, texture features derived from gray-level co-occurrence matrices (GLCM), gray-level run-length matrices (GLRLM), and higher-order features obtained through wavelet or Laplacian of Gaussian filters (Chen et al. 2025). Feature selection methods such as minimum redundancy maximum relevance (mRMR), least absolute shrinkage and selection operator (LASSO), and recursive feature elimination (RFE) are applied to reduce dimensionality and retain the most informative features (Chen et al. 2025; Hong et al. 2020). These selected features are then integrated into machine learning classifiers like support vector machines (SVM), random forests, gradient boosting, or deep neural networks to build predictive models for clinical endpoints including malignancy, tumor invasiveness, and genetic mutation status (Hu et al. 2021b; Chen et al. 2025). Radiomics offers several advantages: it enables high-throughput extraction of quantitative data beyond human visual assessment, captures intratumoral heterogeneity reflecting underlying pathophysiology, and facilitates non-invasive prediction of molecular and histopathological characteristics (Chen et al. 2025; Michalet et al. 2021). Moreover, radiomics can be combined with clinical and genomic data to improve diagnostic and prognostic accuracy, as seen in multimodal models predicting early-stage lung cancer invasiveness and treatment response (Zhang et al. 2025a; Liu et al. 2023a). The integration of radiomics with artificial intelligence enhances feature robustness and model performance, while explainability techniques help interpret feature importance (Zhang et al. 2025a). Despite its promise, radiomics faces challenges including standardization of image acquisition, segmentation variability, and need for large multicenter datasets for validation (Jia et al. 2022). Nonetheless, radiomics remains a powerful tool in the AI-driven imaging pipeline, bridging imaging phenotypes with clinical decision-making in pulmonary ground-glass nodules and lung adenocarcinoma.

Mechanisms of oncogenic driver genes in lung adenocarcinoma

See Fig. 2

Major oncogenic driver genes and their mutation types

Lung adenocarcinoma (LUAD) is characterized by a diverse spectrum of oncogenic driver gene mutations, with EGFR, ALK, KRAS, and ROS1 being among the most prominent. The epidermal growth factor receptor (EGFR) gene mutation is the most frequently observed, particularly in Asian populations, with mutation rates ranging from approximately 48.9% to over 69.8% in older patients and real-world cohorts (Liu et al. 2023b; Lu et al. 2024; Li et al. 2025b). Predominant EGFR mutations include exon 19 deletions and the L858R substitution in exon 21, which together account for roughly 80–85% of EGFR-mutated cases (Liu et al. 2023b; Lu et al. 2024; Li et al. 2025b). These mutations primarily localize within the tyrosine kinase catalytic domain of the receptor, underscoring their functional significance in aberrant signaling activation (Liu et al. 2023b; Li et al. 2025b). Additionally, rare EGFR mutations, including

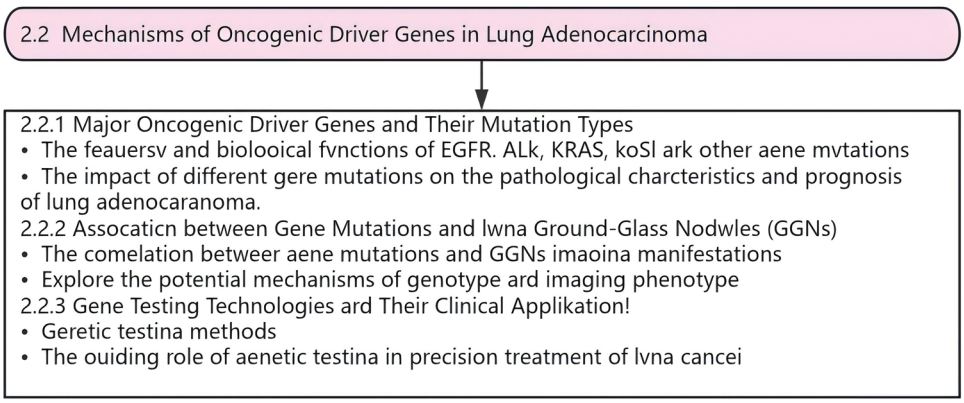

Fig. 2 Overview of the main content of this paragraph. The picture was created by Jinchun Chen

those in the cysteine-rich and receptor binding domains, have been identified, highlighting the genetic heterogeneity within this gene (Liu et al. 2023b; Lu et al. 2024). The anaplastic lymphoma kinase (ALK) gene rearrangements, though less frequent, are notable driver mutations occurring in approximately 2.5 to 6.6% of LUAD patients, often detected in younger, non-smoking populations (Ma et al. 2020; Liu et al. 2023b; Hu et al. 2020). Similarly, ROS1 rearrangements are observed in about 0.7 to 3% of cases and are associated with larger tumor diameters and distinct clinical features (Liu et al. 2023b; Lu et al. 2024). KRAS mutations, prevalent in approximately 6–16% of LUAD patients, tend to occur more frequently in male smokers and are associated with poorer differentiation and aggressive histopathological subtypes (Ma et al. 2024; Liu et al. 2023b; Lu et al. 2024). The mutation spectrum of KRAS includes hotspot mutations such as G12C and G12D, which have implications for targeted therapy development (Lin et al. 2025). Other driver genes such as HER2, BRAF, RET, MET, and PIK3CA have been identified with lower mutation frequencies but contribute to the complexity of LUAD molecular profiles (Lu et al. 2024; Lin et al. 2025; Zhang et al. 2020a). Notably, HER2 exon 20 insertions, though rare (~1.7%), represent actionable mutations with emerging targeted therapies (Zhang et al. 2020a). Co-occurrence of multiple driver mutations has been documented, particularly involving EGFR and PIK3CA, which may influence therapeutic response and prognosis (Ma et al. 2020; Zhao et al. 2021). The mutation landscape also varies with demographic factors; EGFR mutations are more common in females and non-smokers, whereas KRAS mutations predominate in males and smokers (Ma et al. 2024; Liu et al. 2023b; Hu et al. 2020). Ethnic differences further modulate mutation frequencies and prognostic implications, with East Asian populations exhibiting higher EGFR mutation rates and distinct signaling pathway alterations compared to Caucasians (Gu et al. 2020). Emerging studies employing multi-omics and machine learning approaches have identified novel candidate driver genes beyond the classical mutations, expanding the understanding of LUAD molecular pathogenesis (Yuan et al. 2025). Collectively, the mutation types in these key driver genes predominantly involve point mutations, small insertions/deletions (e.g., exon 19 deletions in EGFR), and gene rearrangements or fusions (e.g., ALK and ROS1 fusions), each contributing uniquely to oncogenic signaling and tumor behavior.

The biological functions of these driver genes are central to LUAD tumorigenesis. EGFR encodes a receptor tyrosine kinase that, upon ligand binding, activates downstream pathways such as RAS-RAF-MEK-ERK and PI3K-AKT, promoting cell proliferation and survival. Mutations in EGFR lead to constitutive activation of these pathways, driving oncogenesis and rendering tumors sensitive to EGFR tyrosine kinase inhibitors (TKIs) (Liu et al. 2023b; Lu et al. 2024). ALK rearrangements result in fusion proteins with constitutive kinase activity, similarly activating proliferative and anti-apoptotic signaling cascades (Liu et al. 2023b; Hu et al. 2020). KRAS mutations activate the RAS-RAF-MEK-ERK pathway independently of upstream receptor signals, often conferring resistance to EGFR-targeted therapies and correlating with more aggressive tumor phenotypes (Ma et al. 2024; Lu et al. 2024). ROS1 fusions function analogously to ALK rearrangements, driving oncogenic signaling via constitutive kinase activation (Liu et al. 2023b; Lu et al. 2024). HER2 mutations, particularly exon 20 insertions, activate receptor tyrosine kinase signaling, contributing to tumor growth and representing emerging therapeutic targets (Zhang et al. 2020a). These driver gene mutations influence tumor biology, including histopathological differentiation, metastatic potential, and response to targeted therapies.

The impact of these driver mutations on pathological features and prognosis is significant and multifaceted. EGFR mutations are predominantly associated with invasive non-mucinous adenocarcinoma (INMA) histology and are more frequent in early clinical stages, correlating with better prognosis and responsiveness to EGFR TKIs (Ma et al. 2024; Liao et al. 2021). Conversely, KRAS mutations

are enriched in invasive mucinous adenocarcinoma (IMA) and poorly differentiated tumors, often linked to smoking history and worse clinical outcomes (Ma et al. 2024; Lu et al. 2024). ALK and ROS1 rearrangements tend to occur in younger patients and are associated with distinct histopathological patterns and favorable responses to specific inhibitors (Liu et al. 2023b; Hu et al. 2020). HER2 and BRAF mutations, though less common, are associated with particular histological subtypes such as micropapillary adenocarcinoma and may portend variable prognoses (Ma et al. 2024). Importantly, co-mutations and complex mutation patterns can adversely affect prognosis; for example, the coexistence of EGFR mutations with other driver mutations like PIK3CA has been linked to shorter overall survival (Zhao et al. 2021). Moreover, the presence of certain mutations influences tumor behavior, such as the higher frequency of KRAS mutations in poorly differentiated tumors and the association of EGFR mutations with non-smoking status and female gender (Ma et al. 2024; Liu et al. 2023b). Prognostic implications also vary by stage, with TP53 and STK11 mutations modulating survival outcomes in resected early-stage LUAD (Liao et al. 2021). These findings underscore the necessity of comprehensive genotyping to inform prognosis and guide personalized treatment strategies in LUAD patients.

Association between gene mutations and lung ground-glass nodules (GGNs)

The correlation between gene mutations and the imaging characteristics of lung ground-glass nodules (GGNs) has been extensively investigated in recent literature, revealing important insights into the molecular underpinnings of these lesions and their radiologic manifestations. A significant body of evidence highlights the frequent involvement of driver gene mutations, particularly in the receptor tyrosine kinase (RTK)/RAS signaling pathway, including EGFR, KRAS, BRAF, ERBB2, and MAP2K1, in GGN-associated lung adenocarcinomas. For instance, a comprehensive genomic study of 334 resected pulmonary nodules presenting as GGO from 262 patients demonstrated that 88% of GGNs harbored at least one mutation in these RTK/RAS pathway genes, with alterations being mutually exclusive, suggesting distinct oncogenic drivers for different nodules (Yu et al. 2022b). Notably, nodules with ERBB2, BRAF, or MAP2K1 mutations tended to exhibit more indolent behavior compared to those with EGFR or KRAS mutations, which were associated with more aggressive features and distinct immune microenvironment profiles, such as increased infiltration of CD4+and CD8+T cells in KRAS-mutant GGNs (Yu et al. 2022b).

The epidermal growth factor receptor (EGFR) mutation status has been closely linked to specific radiologic features of GGNs. Studies have shown that nodules harboring EGFR mutations tend to be larger and more frequently exhibit the vacuole or honeycomb sign on high-resolution computed tomography (HRCT), which can independently predict EGFR mutation status with moderate sensitivity and specificity (Zhu et al. 2021). Furthermore, the presence of ground-glass opacity (GGO) or mixed GGO on CT is more commonly associated with EGFR mutations, particularly in nonsmoking female patients with multiple primary lung adenocarcinomas (Han et al. 2020). Quantitative and qualitative three-dimensional CT parameters, including bronchial sign, pleural indentation, vascular bundle sign, maximum nodule diameter, nodule volume, average CT value, and solid compartment proportion, have also been demonstrated to correlate significantly with EGFR mutations and ALK rearrangements in GGO-associated lung adenocarcinoma, underscoring the potential of imaging biomarkers to infer underlying genetic alterations (Liu et al. 2025).

Beyond EGFR, other gene mutations have been implicated in GGN pathogenesis and radiologic phenotypes. For example, bronchial adenomas, a rare benign lung tumor presenting as GGNs or mixed nodules, exhibit distinct mutation profiles with proximal-type adenomas frequently harboring BRAF V600E mutations and distal-type adenomas associated with KRAS mutations, reflecting their differing histopathological and imaging characteristics (Xu et al. 2025a). Similarly, rare germline mutations such as EGFR R776H have been identified in patients with multifocal lung adenocarcinomas presenting as multiple GGNs, highlighting the role of hereditary predisposition in GGN development (Wang et al. 2024c).

The evolutionary trajectory of GGNs from preinvasive to invasive lesions is also associated with dynamic changes in gene mutations and expression patterns. Integrated whole-exome and transcriptome sequencing studies have revealed that EGFR and RBM10 mutations are significantly involved in the progression from adenocarcinoma in situ (AIS) to invasive adenocarcinoma (IAC), accompanied by upregulation of pathways related to cell migration and invasion and downregulation of angiogenesis pathways (Zhou et al. 2024). Additionally, stepwise genomic analyses of subsolid lung adenocarcinomas manifesting as pure, heterogeneous, and part-solid GGNs have demonstrated increasing tumor mutation burden, genomic alterations, and intra-tumor heterogeneity along this continuum, with EGFR mutation as a key early event followed by mutations in RBM10 or TP53 driving further progression (Li et al. 2022).

The immune microenvironment associated with different driver mutations also influences the radiologic and biological behavior of GGNs. Multi-omics analyses have shown

that KRAS-mutant GGNs exhibit higher immune cell infiltration and stronger immune inhibitory signals compared to EGFR-mutant nodules, which may contribute to their distinct clinical outcomes (Yu et al. 2022b). Moreover, the immunosuppressive microenvironment characterized by increased regulatory T cells and exhausted immune cells has been implicated in the development and progression of multiple pulmonary lung cancers presenting as GGNs (Zhang et al. 2024a).

In summary, the existing literature establishes a robust association between specific gene mutations and the imaging phenotypes of lung GGNs. EGFR mutations are predominantly linked with larger nodules, vacuole/honeycomb signs, and ground-glass or mixed GGO appearances, while other mutations such as KRAS, BRAF, and ALK rearrangements correspond to distinct radiologic and pathological features. The underlying mechanisms likely involve the influence of these driver mutations on tumor proliferation, invasion, and interaction with the immune microenvironment, which collectively shape the radiologic manifestations of GGNs. These findings underscore the potential of integrating genomic profiling with advanced imaging analysis to improve the diagnosis, prognostication, and personalized management of patients with lung GGNs.

Gene testing technologies and their clinical applications

Gene testing technologies such as next-generation sequencing (NGS) and polymerase chain reaction (PCR) have revolutionized molecular diagnostics and personalized medicine, particularly in oncology. NGS enables high-throughput sequencing of multiple genes or even whole exomes/genomes simultaneously, allowing comprehensive detection of mutations, insertions, deletions, copy number variations, and gene rearrangements across a broad panel of genes. This capability is critical in diseases like lung adenocarcinoma, where multiple driver mutations (e.g., EGFR, ALK, KRAS, HER2) influence therapeutic decisions. For instance, NGS-based panels have been widely adopted to identify actionable mutations that guide targeted therapies and immunotherapies, improving treatment efficacy and patient outcomes (Zhang et al. 2024b; International Medical Society et al. 2022). Moreover, NGS has been standardized to accommodate dynamic expansion of detection ranges as new clinically relevant biomarkers emerge, ensuring adaptability in clinical practice (Zhang et al. 2024b). Complementing NGS, PCR-based methods, including quantitative PCR and loop-mediated isothermal amplification (LAMP), offer rapid, sensitive, and cost-effective detection of specific gene mutations or resistance genes. LAMP assays, for example, have demonstrated high specificity and sensitivity in detecting bacterial resistance genes, highlighting their utility in infectious disease diagnostics and potentially in oncology for rapid mutation screening (Lin et al. 2022). In lung cancer, PCR remains a valuable tool for detecting hotspot mutations such as EGFR exon 19 deletions and L858R point mutations, facilitating timely therapeutic decisions (Xue et al. 2022). Clinically, gene testing plays a pivotal role in precision oncology by enabling molecular subtyping, prognostic stratification, and therapeutic monitoring. Multigene panel testing informs the selection of targeted agents, as seen in breast and lung cancers, where assays like the 21-gene Recurrence Score guide adjuvant chemotherapy decisions, reducing overtreatment without compromising survival (International Medical Society et al. 2022; Bae et al. 2021). In advanced lung adenocarcinoma, gene testing of circulating tumor DNA (ctDNA) complements tissue biopsy, overcoming limitations of tissue availability and enabling real-time monitoring of mutation dynamics and resistance mechanisms (Xue et al. 2022; Zhao et al. 2023b). Furthermore, gene testing facilitates the identification of rare or germline mutations, such as EGFR R776H germline variants, which have implications for familial risk assessment and targeted therapy selection (Wang et al. 2024c). The integration of gene testing into clinical workflows enhances diagnostic accuracy, informs prognosis, and personalizes treatment strategies, underscoring its indispensable role in modern oncology care.

Application of AI in the integration of radiomics and genomics

See Fig. 3

Multimodal data fusion techniques

Multimodal data fusion techniques in lung adenocarcinoma research aim to integrate heterogeneous data sources such as imaging data (e.g., CT scans) and genomic or clinical data to improve diagnostic accuracy and prediction of molecular characteristics. Two primary fusion strategies are commonly employed: feature-level fusion and decision-level fusion. Feature-level fusion involves combining raw or processed features extracted from different modalities into a unified representation before model training. This approach enables the model to learn complex interactions between modalities directly. For example, combining radiomic features derived from CT images with clinical variables such as serum tumor markers or patient demographics can provide a more comprehensive characterization of the tumor microenvironment and biological behavior. Decision-level fusion, on the other hand, integrates the outputs or predictions from separate unimodal models, using methods such as voting schemes or ensemble learning, to achieve a final classification or

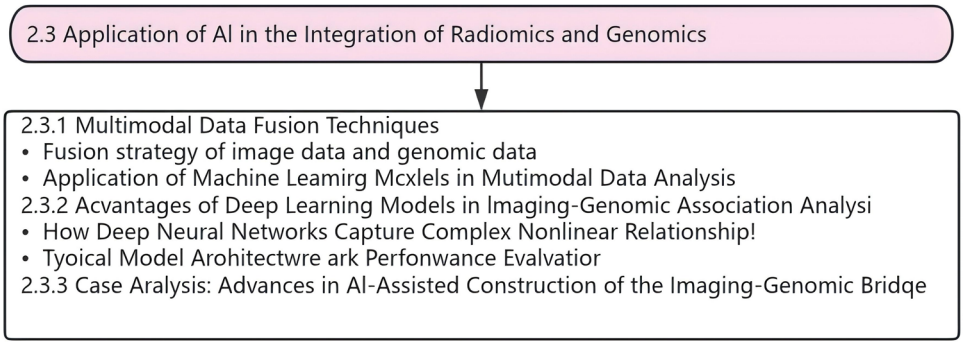

Fig. 3 Overview of the main content of this paragraph. The picture was created by Jinchun Chen

prediction. This strategy allows leveraging the strengths of individual models specialized for each modality while mitigating their weaknesses. Recent studies have demonstrated the effectiveness of both approaches in lung adenocarcinoma, particularly in predicting invasiveness and genetic mutations such as EGFR status. For instance, a multimodal data fusion model that combined CT images, patient general data, and serum tumor markers using a residual learning architecture and attention mechanisms achieved superior accuracy (88.5%) and AUC (0.957) in distinguishing invasive adenocarcinoma from non-invasive ground-glass nodules, outperforming senior radiologists (Huang et al. 2022). This highlights the value of feature-level fusion in integrating complementary data types to enhance predictive performance.

Machine learning models, especially deep learning architectures, have been extensively applied to multimodal data analysis in lung adenocarcinoma. These models are capable of capturing complex nonlinear relationships and interactions between imaging features and genomic or clinical variables. For example, a deep learning-based multimodal feature interaction-guided fusion (DL-MFIF) framework was developed to integrate macroscopic CT radiomic features with microscopic whole-slide image features, achieving high AUC values (0.856 internal, 0.817 external) for predicting EGFR mutations in advanced lung adenocarcinoma patients (Xu et al. 2025b). This approach leverages deep learning to model feature interactions across scales and modalities, improving mutation status prediction which is critical for targeted therapy decisions. Another innovative application involves graph neural networks (GNNs) that fuse multimodal features by representing clinical, semantic, and imaging data as nodes and edges in a graph structure. This method, combined with an edge-generation network, enhanced interpretability and achieved competitive performance in lung adenocarcinoma classification, demonstrating the potential of advanced machine learning techniques in multimodal fusion (Li et al. 2023).

Moreover, multimodal fusion strategies have been extended to integrate imaging data with electronic health records and lesion annotations. A multimodal deep neural network incorporating CT images, lesion bounding boxes, and clinical data employed contrastive learning and attention-based feature fusion modules to generate a unified representation, resulting in a high validation accuracy of 81.42% and AUC of 0.9120 for adenocarcinoma subtype classification (Wang et al. 2025b). This exemplifies how combining spatial imaging context with clinical information through sophisticated fusion mechanisms can improve subtype discrimination, which is essential for personalized treatment planning. Additionally, fusion of radiomic and deep learning features extracted from intratumoral and peritumoral regions using soft voting ensemble methods yielded robust prediction of EGFR mutation status with AUCs up to 0.925 internally and 0.889 externally, outperforming single-modality models (Huang et al. 2025a). This confirms that multimodal fusion not only enhances predictive accuracy but also provides a more holistic tumor characterization by capturing diverse biological and spatial information.

In summary, multimodal data fusion techniques integrating CT imaging, genomic, and clinical data via feature-level and decision-level fusion strategies have demonstrated significant potential in improving lung adenocarcinoma diagnosis, molecular characterization, and prognostication. Machine learning models, particularly deep learning and graph neural networks, play a pivotal role in effectively capturing complex inter-modality relationships, thereby bridging the gap between radiological phenotypes and oncogenic driver gene status. These advances facilitate precision medicine by enabling more accurate, non-invasive prediction of tumor invasiveness and mutation profiles, ultimately guiding tailored therapeutic interventions. Continued development and validation of such multimodal fusion frameworks are essential for their translation into clinical practice.

Advantages of deep learning models in imaging-genomic association analysis

Deep learning models, particularly deep neural networks (DNNs), have demonstrated remarkable advantages in capturing complex nonlinear relationships between imaging features and genomic data, which are often elusive to

traditional statistical or machine learning methods. The intrinsic hierarchical architecture of deep neural networks enables them to learn multi-level representations of input data, facilitating the extraction of subtle and high-dimensional patterns embedded within medical images such as CT scans, MRI, or histopathological slides. This capacity is critical when linking radiographic phenotypes, such as lung ground-glass nodules (GGNs), to underlying oncogenic driver mutations, where the relationship is inherently nonlinear and multifactorial. Unlike handcrafted radiomic features that may only capture shallow or low-order image characteristics, deep learning-derived features can encode richer tumor heterogeneity and microenvironmental information, leading to stronger and more biologically meaningful correlations with genomic profiles (Liu and Hu 2023). Moreover, deep learning models can integrate multimodal data, including imaging, genetic variants, and clinical parameters, through architectures such as convolutional neural networks (CNNs) combined with transformers or graph neural networks, thereby enhancing the modeling of complex genotype–phenotype interactions (Li et al. 2025c; Bi et al. 2022).

Typical deep learning architectures employed in imaging-genomic association studies include CNNs for spatial feature extraction from images, autoencoders for unsupervised phenotype representation learning, and hybrid models that fuse imaging and genomic features for joint analysis. For instance, 3D ResNet and 3D Xception networks have been used to extract volumetric features from CT images, which, when combined with clinical data in support vector machines, achieve robust classification performance in disease subtyping (Li et al. 2025d). Autoencoder-based frameworks, such as cineMAE, have been developed to learn unsupervised deep image phenotypes from cardiac MRI, enabling genome-wide association studies (GWAS) to uncover novel genetic loci linked to cardiac morphology (You et al. 2025). In the context of histological images, deep CNNs pretrained on natural images or domain-specific datasets have been fine-tuned to predict gene expression patterns or molecular subtypes, revealing image quantitative trait loci (imageQTLs) and differentially expressed genes associated with morphological features (Meng et al. 2025a, 2025b).

Performance evaluation of these models typically involves metrics such as area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, specificity, and concordance indices for survival prediction. Deep learning models have consistently outperformed traditional handcrafted radiomic feature-based classifiers. For example, MRI-based deep radiomic features achieved AUCs greater than 0.9 in predicting breast cancer clinical characteristics and showed stronger associations with genomic factors compared to conventional radiomic features (Liu and Hu 2023). Similarly, integrated deep learning frameworks combining imaging and genomic data have demonstrated high accuracy (e.g., AUCs exceeding 0.85) in predicting molecular subtypes, gene mutation status, and clinical outcomes across various cancers, including gliomas, lung cancer, and breast cancer (Zuo et al. 2022; Zhang et al. 2024c, 2025b). Furthermore, the application of transfer learning and multi-task learning strategies enhances model generalizability and interpretability, enabling the extraction of biologically relevant features that bridge imaging phenotypes and gene expression profiles (Phan et al. 2021; Zhang et al. 2020b).

In summary, deep learning models offer significant advantages in imaging-genomic association analysis by effectively capturing complex nonlinear relationships, enabling multimodal data integration, and providing biologically interpretable features. These capabilities facilitate the discovery of novel imaging biomarkers linked to genetic drivers and hold promise for advancing precision medicine through non-invasive genomic inference from medical images.

Case analysis: advances in AI-assisted construction of the imaging-genomic bridge

Recent representative studies have demonstrated significant progress in leveraging artificial intelligence (AI) to effectively link computed tomography (CT) imaging features of lung adenocarcinoma (LUAD) with oncogenic driver gene mutations, thus constructing a robust imaging-genomic bridge. For instance, a study involving 164 primary LUAD patients undergoing surgery analyzed the correlation between CT imaging characteristics and epidermal growth factor receptor (EGFR) gene mutations. The findings revealed significant associations between EGFR mutations and clinical factors such as sex, smoking history, and pulmonary nodule morphology, as well as specific CT signs including cavity, hair prick, and chest depression signs. Notably, pathological subtypes, particularly the micropapillary subtype, exhibited the highest EGFR mutation rate (44.44%). Moreover, vascular convergence signs on CT correlated with EGFR mutations, whereas pleural effusion and related signs did not show significant association. This study underscores AI's capacity to discern subtle imaging features predictive of gene mutation status, offering valuable insights for intelligent medicine and personalized treatment strategies (Zhou et al. 2022).

Complementing this, advanced deep learning models have been developed to predict gene mutation status from histopathological images in LUAD. A ResNeXt101-based framework trained on cohorts from both a Chinese medical center and The Cancer Genome Atlas (TCGA) demonstrated

high accuracy, with area under the curve (AUC) values ranging from 0.85 to 1.0 for multiple gene mutations. Importantly, the model maintained predictive performance even on metastatic cancer datasets, highlighting AI's generalizability in mutation status inference from imaging data. Such AI models facilitate non-invasive, rapid, and accurate molecular profiling, thereby advancing precision oncology in LUAD management (Yu et al. 2025).

Beyond lung cancer, AI has shown promise in integrating imaging and genomic data across various solid tumors. A systematic review of AI applications in histopathologic image-based gene mutation prediction revealed that AI models achieved satisfactory AUCs for driver gene mutations, such as 0.79 for EGFR in lung cancers, although average performance across all mutations remains suboptimal (mean AUC ~ 0.64). This indicates the potential and current limitations of AI in predicting gene mutations from imaging, emphasizing the need for larger datasets and further validation before clinical implementation (Alam et al. 2023).

Radiogenomics, the interdisciplinary field combining imaging phenotypes with genomic data, has been propelled by AI advancements. Reviews highlight radiogenomics' capacity to non-invasively infer gene expression patterns and mutation status from imaging modalities, enabling precision medicine. AI facilitates the extraction of high-dimensional imaging features and their integration with multi-omics data, improving biomarker discovery and clinical risk stratification. Challenges such as tumor heterogeneity and the need for multi-modal data integration are being addressed through AI-driven workflows, expanding radiogenomics' applicability in oncology (Guo et al. 2025).

Recent methodological innovations also include hybrid neural networks like THItoGene, which predict spatial transcriptomics from histological images by adaptively sensing molecular signals. This approach exemplifies AI's ability to bridge high-resolution pathology phenotypes with gene expression regulation, offering spatially resolved insights into tumor biology that can enhance diagnostic and therapeutic decision-making (Jia et al. 2023).

Furthermore, AI-assisted imaging analyses have demonstrated improved accuracy over traditional methods. For example, AI-based medical imaging of pulmonary nodules achieved an average accuracy increase of 3.88% compared to conventional imaging, while correlating imaging features with multiple driver gene mutations. Although some correlations with metabolic values were non-significant, these findings affirm AI's role in enhancing early LUAD diagnosis and molecular characterization (Yin et al. 2023).

Collectively, these studies illustrate AI's transformative role in constructing the imaging-genomic bridge in lung adenocarcinoma. By extracting nuanced imaging features and integrating them with genomic data, AI enables non-invasive prediction of oncogenic driver mutations, facilitating personalized diagnosis and treatment. Continued advancements in AI algorithms, larger multimodal datasets, and rigorous external validations are essential to translate these promising research outcomes into routine clinical practice, ultimately improving patient management and precision oncology outcomes.

Artificial intelligence-assisted diagnosis and prognostic evaluation of lung ground-glass nodule adenocarcinoma

See Fig. 4

AI in early lung cancer screening

Artificial intelligence (AI) has become a transformative tool in early lung cancer screening, particularly in the detection and characterization of ground-glass nodules (GGNs), which are critical imaging features often associated with early-stage lung adenocarcinoma. Although low-dose computed tomography (LDCT) screening has been proven to

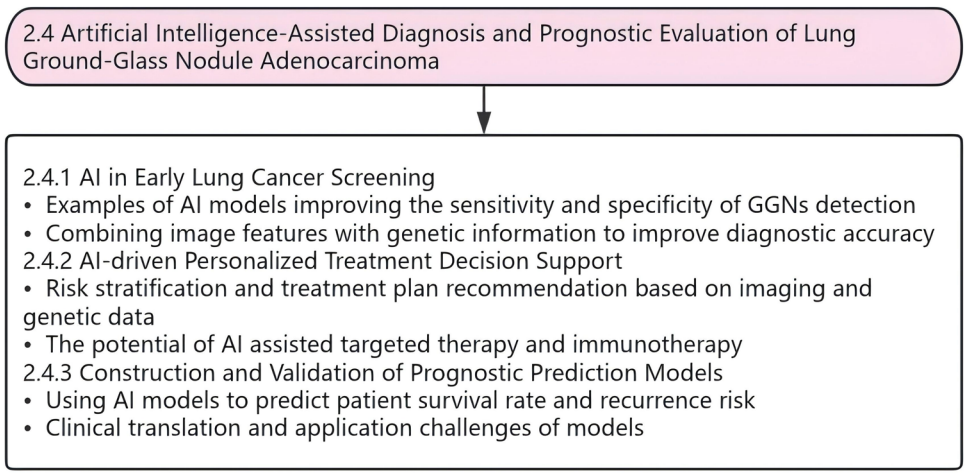

Fig. 4 Overview of the main content of this paragraph. The picture was created by Jinchun Chen

reduce lung cancer mortality, the screening compliance rate is generally low worldwide. Recent discussions on lung cancer screening in Asia have highlighted concerns about overdiagnosis, as overly aggressive screening may lead to overdiagnosis, and delayed follow-up may result in missed diagnoses, adversely affecting survival outcomes (Hsin-Hung et al. 2024). Therefore, integrating AI technology into the entire process of lung cancer screening should not only focus on optimizing nodule detection performance but also aim to improve overall screening coverage, compliance, and cost-effectiveness.

Numerous studies have demonstrated that AI models significantly improve the sensitivity and specificity of GGN detection on computed tomography (CT) scans, addressing one of the major challenges in early lung cancer diagnosis. For instance, large-scale clinical trials embedding AI algorithms into CT screening workflows have reported sensitivity improvements of up to 20.7%, with overall detection sensitivity rising from approximately 67.7 to 88.4% for various nodule sizes, including GGNs that are traditionally difficult to identify by radiologists (Chao et al. 2023). Moreover, AI-assisted systems have achieved sensitivity rates exceeding 95% with high area under the curve (AUC) values (>0.88) for nodule detection, outperforming or matching experienced radiologists while reducing false positives (Zhang et al. 2021). Deep learning models such as DenseNet and WOANet have shown exceptional accuracy in detecting GGNs, with accuracies near 99%, coupled with high sensitivity and specificity, underscoring the potential of AI to serve as a reliable adjunct in lung cancer screening programs (Shah et al. 2025).

Beyond mere detection, AI enhances the classification and risk stratification of GGNs by extracting quantitative radiomic features that correlate with malignancy risk. For example, AI-based vessel suppression and automated detection algorithms improve the differentiation of subsolid nodules into ground-glass and part-solid nodules, which have distinct prognostic implications (Singh et al. 2021). Radiomics combined with AI has been used to noninvasively predict early recurrence risk in clinical stage IA lung cancer, utilizing imaging features such as solid part size and volume ratios extracted via AI software (Shimada et al. 2022). Additionally, AI-driven radiomic analysis integrated with quantum machine learning models has achieved high accuracy (up to 89.23%) and interpretability in classifying pulmonary GGNs, facilitating early and precise diagnosis (Huang et al. 2025b).

The integration of imaging features with genetic information represents a cutting-edge advancement that further elevates diagnostic accuracy. AI models have been developed to predict oncogenic driver mutations, such as epidermal growth factor receptor (EGFR) mutations, directly from CT images of lung nodules, enabling non-invasive molecular profiling that guides targeted therapies (Batra et al. 2024). The combination of AI-based imaging analysis with clinical and genomic data has demonstrated area under the curve (AUC) values up to 0.91 for EGFR mutation prediction, suggesting that AI can bridge radiological phenotypes with underlying tumor genotypes (Batra et al. 2024). Moreover, AI-assisted liquid biopsy approaches utilizing circulating biomarkers alongside imaging data have shown promise in early lung cancer detection, offering a complementary strategy to improve screening specificity and reduce unnecessary invasive procedures (Habbab et al. 2025; Wei et al. 2025).

Clinical implementation of AI in lung cancer screening has also been explored in diverse populations, including underserved and high-risk groups. Mobile low-dose CT units equipped with AI diagnostic systems have demonstrated cost-effectiveness and feasibility in rural settings, achieving lung cancer detection rates around 0.7% and reducing health disparities (Huang et al. 2025c). LDCT screening can help save lives by detecting lung cancer early, especially in people at high risk, but some challenges need to be carefully managed (Mathew et al. 2025). Furthermore, AI models have been validated to improve workflow efficiency by shortening detection times and increasing diagnostic concordance when compared to manual readings or multidisciplinary team assessments (Du et al. 2022b).These advancements indicate that AI has the potential to expand screening coverage and improve participation among high-risk populations by optimizing resource allocation, reducing the workload of radiologists, and supporting primary healthcare institutions in conducting preliminary screenings.

Despite these promising advances, challenges remain in standardizing AI models, ensuring external validation, and integrating multi-omic data into clinical practice. Limitations include heterogeneity in AI algorithms, variability in imaging protocols, and the need for large annotated datasets to train robust models (Zhang et al. 2021; Ayasa et al. 2025). Ethical considerations, transparency, and clinical accountability must also be addressed to facilitate widespread adoption. Nonetheless, the current evidence supports that AI-enhanced imaging, particularly when combined with genetic and biomarker information, substantially improves the early detection and characterization of GGNs, thereby enabling more accurate diagnosis and personalized management of early lung adenocarcinoma (Li et al. 2025a; Gandhi et al. 2023). This integration marks a pivotal step toward precision medicine in lung cancer screening, with the potential to reduce mortality through timely intervention.

AI-driven personalized treatment decision support

The integration of artificial intelligence (AI) with imaging and genomic data holds transformative potential for personalized treatment decision-making in lung adenocarcinoma presenting as ground-glass nodules (GGNs). AI algorithms can leverage quantitative imaging features derived from computed tomography (CT) scans, such as nodule size, volume, density, and morphological characteristics, combined with genetic mutation profiles, to stratify patients by risk and recommend tailored therapeutic strategies. For instance, AI-based radiomics models have demonstrated robust capability in distinguishing pathological subtypes of GGNs—including atypical adenomatous hyperplasia (AAH), adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), and invasive adenocarcinoma (IAC)—by analyzing multidimensional CT parameters such as solid component size, mean CT attenuation values, and three-dimensional volumetric measurements (Wu et al. 2025; Fang et al. 2022). These imaging biomarkers correlate significantly with oncogenic driver mutations, notably epidermal growth factor receptor (EGFR) mutations, which are prevalent in certain adenocarcinoma subtypes and influence responsiveness to targeted therapies (Zhong et al. 2024). AI models incorporating both imaging and genetic data can thus provide a refined risk stratification framework that informs the likelihood of nodal metastasis and tumor invasiveness, critical factors in determining the extent of surgical resection and the necessity for adjuvant treatment (Shimada et al. 2023; Tsuchiya et al. 2025).

Moreover, AI-driven decision support systems enhance the precision of therapeutic recommendations by predicting tumor behavior and treatment response. Deep learning frameworks have been developed to classify pulmonary nodules with high accuracy, distinguishing malignant from benign lesions and further differentiating histopathological subtypes, thereby reducing unnecessary interventions and optimizing follow-up protocols (Wang et al. 2022; Margerie-Mellon and Chassagnon 2023). The ability of AI to analyze complex imaging-genomic datasets facilitates the identification of high-risk patients who may benefit from more aggressive treatment modalities, including sublobar resections or lymph node dissection, versus those suitable for conservative management (Kudo et al. 2024). These systems also support clinicians in evaluating the metastatic potential of small solid nodules, which are often challenging to assess preoperatively, by integrating AI-derived confidence scores with clinical and pathological data (Kudo et al. 2024).

In the context of targeted therapy and immunotherapy, AI holds promise in predicting molecular alterations and the tumor immune microenvironment from non-invasive imaging features, thus guiding personalized treatment selection. For example, AI algorithms have been used to infer EGFR mutation status and other driver gene alterations from CT radiomics signatures, enabling early identification of candidates for tyrosine kinase inhibitors without the need for invasive biopsy (Zhong et al. 2024; Margerie-Mellon and Chassagnon 2023). Additionally, AI-based analyses of tumor-associated macrophage remodeling and immune microenvironment evolution provide insights into the immunosuppressive milieu of early lung adenocarcinoma, potentially informing immunotherapeutic strategies (Li et al. 2025e). Currently, research on targeted therapy and immunotherapy that can objectively reflect (such as tumor shrinkage) or long-term outcomes for patients (such as mortality rate, incidence) is still limited. Therefore, there are challenges in associating imaging biomarkers of lung GGNs with complex immunotherapy responses. Future studies need to prospectively validate the ability of AI models to predict their true clinical endpoints in order to fully realize their potential in guiding immunotherapy decisions.

Overall, AI-driven personalized treatment decision support systems represent a critical bridge between imaging phenotypes and oncogenic driver gene profiles in lung adenocarcinoma with GGNs. These systems improve risk stratification accuracy, optimize therapeutic recommendations, and facilitate the implementation of precision oncology approaches. However, challenges remain in clinical translation, including the need for large, diverse datasets to enhance model generalizability, transparency of AI decision-making processes, and integration into clinical workflows. Continued development and validation of AI tools that combine imaging and genomic data will be essential to realize their full potential in guiding individualized treatment and improving patient outcomes in lung adenocarcinoma.

Construction and validation of prognostic prediction models

The construction of prognostic prediction models utilizing artificial intelligence (AI) has become a pivotal advancement in forecasting patient survival and recurrence risk in lung adenocarcinoma presenting as ground-glass nodules (GGNs). AI models integrate multidimensional data, including CT imaging features, molecular biomarkers, and clinical parameters, to generate accurate survival predictions and stratify patients by risk, thereby guiding personalized treatment strategies. For instance, a nomogram combining novel biomarkers CST1 and GIMAP1-GIMAP5, derived from RNA sequencing and CT imaging data, demonstrated robust predictive power for lung adenocarcinoma in GGNs with an area under the curve (AUC) exceeding 0.8, underscoring the utility of molecular-imaging integration in prognosis

(Li and Zhang 2025). Similarly, radiomics-based models leveraging high-resolution CT features have effectively differentiated invasive adenocarcinomas from pre-invasive or minimally invasive lesions, with AUCs reaching up to 0.92 in independent cohorts, enabling noninvasive assessment of tumor aggressiveness and prognosis (Chen et al. 2022). Moreover, advanced machine learning algorithms applied to dual-layer spectral detector CT parameters combined with clinical data have yielded high AUCs (~0.95) for invasiveness prediction, facilitating risk stratification and surgical decision-making (Wan et al. 2025). Deep learning approaches, such as 3D convolutional neural networks, have also been employed to quantify tumor size, volume, and mass from CT images, outperforming manual measurements in prognostic accuracy for early-stage lung adenocarcinoma (Zhu et al. 2023). Beyond imaging, AI-driven pathological scoring systems assessing tumor-infiltrating lymphocytes have independently predicted overall and disease-free survival, highlighting the prognostic value of integrating histopathological data (Pan et al. 2022). Despite these promising developments, clinical translation faces challenges including model generalizability, interpretability, and integration into routine workflows. Many studies lack external validation or are limited by retrospective designs and single-center data, which may restrict applicability across diverse populations (Margerie-Mellon and Chassagnon 2023). Furthermore, the "black-box" nature of some AI models raises concerns regarding transparency and clinical accountability, necessitating explainable AI frameworks and multidisciplinary collaboration for effective implementation (Margerie-Mellon and Chassagnon 2023). Addressing these challenges, recent efforts have focused on developing interpretable multimodal fusion models that combine histology, genomics, and transcriptomics, enhancing prognostic precision even with incomplete data (Gao et al. 2025). In summary, AI-based prognostic models for lung adenocarcinoma with GGNs demonstrate significant potential to predict survival and recurrence risk by integrating imaging, molecular, and clinical data. Continued validation, methodological rigor, and user-friendly interfaces are essential to bridge the gap between research and clinical application, ultimately improving patient outcomes through personalized prognostication and management.

Challenges and solutions of artificial intelligence technology

See Fig. 5

Data quality and sample size limitations

The quality of data and the size of sample cohorts represent critical challenges in the application of artificial intelligence (AI) to the analysis of lung ground-glass nodules (GGNs) and their association with oncogenic driver genes. Data heterogeneity arises from variations in imaging protocols, reconstruction algorithms, and annotation standards across institutions, which can significantly affect the consistency and reliability of AI models. For instance, phantom studies have demonstrated that different computed tomography (CT) scanning parameters, such as tube voltage and current, influence the measured size and density of pulmonary nodules, including GGNs, thereby impacting the ground truth data used for AI training (Meng et al. 2024). Moreover, the use of various image reconstruction techniques, including filtered back projection (FBP), iterative reconstruction (IR), and deep learning image reconstruction (DLIR), alters image noise, spatial resolution, and nodule detectability, further contributing to data variability (Yao et al. 2022; Greffier et al. 2022). This heterogeneity complicates the development of generalized AI models capable of robust performance across diverse clinical settings.

Annotation quality is another pivotal factor; accurate and consistent labeling of nodules, including delineation of solid

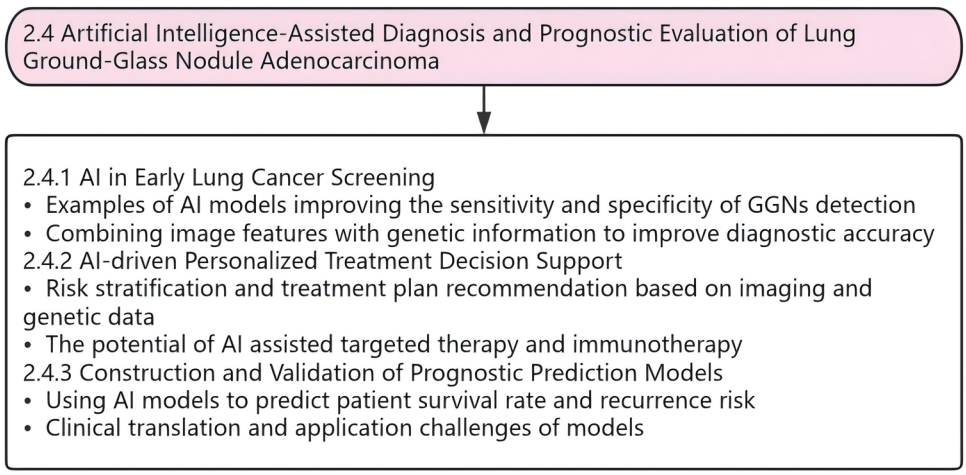

Fig. 5 Overview of the main content of this paragraph. The picture was created by Jinchun Chen

and ground-glass components, is essential for supervised learning. Studies have shown interobserver variability in the detection and characterization of GGNs, especially for small or part-solid nodules, which can introduce noise into training datasets (Digumarthy et al. 2020; Solomon et al. 2021). Training AI systems on such data without sufficient quality control may lead to suboptimal model performance and reduced clinical applicability.

Sample size limitations also restrict AI development. Although large datasets improve model generalizability, the availability of well-annotated, high-quality datasets for GGNs remains limited. Many studies rely on retrospective cohorts with relatively small numbers of cases, which may not capture the full spectrum of nodule characteristics or genetic heterogeneity (Feng et al. 2023; Wu et al. 2020). This scarcity is particularly pronounced for rare nodule subtypes or specific driver gene mutations, which are critical for personalized medicine approaches.

To mitigate these challenges, data augmentation and transfer learning techniques have been employed. Data augmentation artificially expands training datasets by applying transformations such as rotation, scaling, and noise addition, enhancing model robustness to variations (Margerie-Mellon and Chassagnon 2023). Transfer learning leverages pretrained models on large, general datasets and fine-tunes them on smaller, domain-specific datasets, thus reducing the need for extensive labeled data (Feng et al. 2023). For example, radiomics-based models incorporating both clinical-radiographic features and AI-extracted imaging features have demonstrated improved predictive performance for invasiveness in GGNs despite limited sample sizes (Feng et al. 2023; Xiong et al. 2022).

Furthermore, the integration of multi-institutional data and standardization of imaging protocols and annotation criteria are essential to reduce heterogeneity and improve data quality. Collaborative efforts to establish large, annotated databases with harmonized imaging and clinical data will facilitate the development of more reliable AI models. Additionally, advanced image reconstruction algorithms, such as spectral photon-counting CT and dual-layer spectral detector CT, offer improved image quality and nodule characterization, potentially enhancing the quality of input data for AI applications (Si-Mohamed et al. 2022; Kang et al. 2025).

In conclusion, addressing data quality and sample size limitations through standardized imaging protocols, rigorous annotation, data augmentation, transfer learning, and collaborative data sharing is fundamental to advancing AI applications in the analysis of lung GGNs and their underlying molecular drivers. These strategies will enable the construction of robust, generalizable AI models that can bridge imaging phenotypes with genetic alterations, ultimately improving early diagnosis and personalized treatment of lung adenocarcinoma.

Model interpretability and clinical trustworthiness

AI model "Black Box" issue and its impact on clinical application Artificial intelligence (AI) models, particularly those based on deep learning, have demonstrated remarkable capabilities in analyzing CT images of pulmonary ground-glass nodules (GGNs) and predicting lung adenocarcinoma characteristics, including malignancy risk, pathological subtypes, and invasiveness. However, a critical challenge limiting their widespread clinical adoption is the so-called "black box" problem, where the internal decision-making processes of AI systems are opaque and difficult for clinicians to interpret. This lack of transparency raises concerns about the reliability and safety of AI-driven diagnostic tools in clinical workflows. Clinicians are hesitant to fully trust AI outputs without understanding the rationale behind predictions, especially when these decisions influence critical management strategies such as surgical planning or biopsy necessity. For example, while AI algorithms like DeepLN have achieved high accuracy in classifying pulmonary nodules and predicting pathological subtypes based on CT imaging features, the inability to explain how specific image characteristics contribute to the final classification limits their acceptance in routine practice (Wang et al. 2022). Moreover, the variability in CT imaging protocols and patient heterogeneity further complicates the interpretability of AI predictions. The "black box" nature also poses regulatory challenges, as clinical validation and risk assessment require clear understanding of model behavior. Consequently, addressing the interpretability issue is essential to bridge the gap between AI research advances and real-world clinical implementation, ensuring that AI tools can be safely integrated into diagnostic workflows and trusted by healthcare providers.

Current development status of explainable AI technologies In response to the interpretability challenge, explainable AI (XAI) techniques have been actively developed to elucidate the decision-making processes of AI models applied to lung nodule analysis. These techniques aim to provide visual or quantitative explanations that highlight the imaging features or regions contributing most to the AI's prediction, thereby enhancing clinician trust and facilitating model validation. For instance, saliency maps and heatmaps can localize areas within CT images that influence malignancy risk assessment or subtype classification, allowing radiologists to verify whether AI focuses on relevant pathological features such as nodule size, density, spiculation, or

vascular convergence (Fang et al. 2022; Xia et al. 2020). Additionally, combining AI-derived quantitative parameters with traditional radiological signs has been shown to improve diagnostic performance while maintaining interpretability. Studies have demonstrated that integrating AI parameters like nodule diameter, volume, and mass with CT morphological features enables construction of predictive nomograms with clear clinical relevance, which can be more readily understood and trusted by clinicians (Long et al. 2025; Li et al. 2024). Furthermore, hybrid models that fuse deep learning features with radiomics and clinical data enhance both accuracy and transparency by linking AI outputs to established imaging biomarkers (Xia et al. 2020). Advances in multimodal imaging analysis, including PET/CT and spectral CT, combined with AI, have also contributed to more explainable models by correlating imaging phenotypes with pathological invasiveness (Ruan et al. 2025; Chang et al. 2023). Despite these promising developments, challenges remain in standardizing XAI methods, validating their clinical utility, and ensuring that explanations are both accurate and comprehensible to end-users. Ongoing research is focused on refining XAI frameworks to provide actionable insights, reduce interobserver variability, and ultimately foster greater clinical trust in AI-assisted diagnosis of lung adenocarcinoma manifesting as GGNs.

Regulations, ethics, and privacy protection

Medical data privacy protection regulations The application of artificial intelligence (AI) in the analysis of lung ground-glass nodules (GGNs) and their correlation with oncogenic driver genes necessitates stringent adherence to medical data privacy protection regulations. Medical imaging data, particularly CT scans used for detecting and characterizing GGNs, constitute sensitive personal health information. Regulatory frameworks such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States, the General Data Protection Regulation (GDPR) in the European Union, and similar laws worldwide impose rigorous requirements on the collection, storage, processing, and sharing of such data. These regulations mandate that patient identifiers be anonymized or pseudonymized before data utilization in AI model training or validation to prevent unauthorized re-identification. The complexity increases when integrating multi-modal data, such as genetic profiles linked to imaging phenotypes, since genetic data are inherently identifiable and require elevated protection standards. Moreover, compliance with these regulations involves implementing secure data transmission protocols, access controls, audit trails, and data encryption. The challenge is compounded by the need for large, diverse datasets to develop robust AI models for GGN analysis, which often entails cross-institutional or international data sharing. Therefore, establishing standardized data governance policies and employing federated learning techniques, where AI models are trained locally without transferring raw data, have emerged as promising approaches to reconcile data privacy with AI development. In the context of lung GGN research, ensuring that CT imaging and genetic data are handled in compliance with privacy laws is critical to protect patient confidentiality and maintain public trust, which ultimately facilitates the ethical advancement of AI applications in precision oncology (Ge et al. 2025; Liang et al. 2025).

Ethical considerations of AI technology in clinical applications The integration of AI technologies into clinical workflows for lung GGN evaluation and management raises profound ethical considerations that extend beyond data privacy. One primary concern is the transparency and interpretability of AI algorithms, especially when they influence diagnostic and therapeutic decisions. Clinicians must understand the rationale behind AI-generated predictions or classifications to ensure informed decision-making and maintain accountability. The risk of algorithmic bias is another ethical challenge; AI models trained on datasets lacking diversity may perform suboptimally in underrepresented populations, potentially exacerbating health disparities. For instance, variations in imaging characteristics or genetic profiles of GGNs across different ethnic groups could lead to biased AI outputs if not properly addressed during model development. Furthermore, the potential for overdiagnosis and overtreatment of GGNs, already a clinical issue, may be amplified by AI systems that detect subtle imaging features without adequate clinical context, leading to unnecessary interventions and patient anxiety (Liang et al. 2025). Ethical deployment of AI also requires rigorous validation to ensure safety and efficacy, as erroneous AI recommendations could cause harm. Informed consent processes should explicitly address the use of AI in patient care, including potential benefits and limitations. Additionally, the responsibility for errors or adverse outcomes related to AI-assisted decisions must be clearly delineated among clinicians, developers, and institutions. Finally, the continuous monitoring and updating of AI systems are essential to adapt to evolving clinical knowledge and maintain ethical standards. Collectively, these ethical considerations underscore the necessity for multidisciplinary collaboration among clinicians, ethicists, data scientists, and policymakers to establish guidelines that safeguard patient welfare while

harnessing AI's potential in lung GGN management (Ge et al. 2025; Liang et al. 2025).

Future development directions and research trends

See Fig. 6

Deep integration and analysis of multi-omics data

The deep integration and analysis of multi-omics data—encompassing radiomics, genomics, proteomics, and other molecular layers—have become pivotal in constructing comprehensive models that elucidate the complex biological underpinnings of diseases such as lung adenocarcinoma with ground-glass nodules. Integrative frameworks like iModMix exemplify biology-agnostic approaches that leverage data-driven module construction without reliance on prior pathway annotations, enabling the discovery of novel associations across heterogeneous omics datasets including transcriptomics, proteomics, and metabolomics (Narváez-Bandera et al. 2024). Such methods preserve the distinctiveness of each omics layer while facilitating horizontal integration through eigenfeatures, thereby enhancing interpretability and uncovering cross-modality relationships. Multi-staged data-integrated multi-omics (MS-DIMO) analyses further demonstrate the power of combining multiple omics domains within a single study to provide a holistic view of molecular mechanisms, which can refine mechanistic hypotheses and identify therapeutic targets more effectively than single-omics approaches (Harris et al. 2021). This is particularly relevant in lung cancer research, where the interplay between imaging phenotypes and driver gene mutations demands a systemic view. From a systems biology perspective, the integration of multi-omics data enables the construction of heterogeneous multi-layered networks (HMLNs) that represent biological hierarchies and interactions, such as protein–protein interactions and gene regulatory networks, facilitating the inference of causal genotype–phenotype associations (Lee et al. 2019). Advanced computational models, including multi-scale multi-hop graph AI models like M3NetFlow, have been developed to analyze these complex networks, allowing both hypothesis-guided and generic multi-omic analyses that identify biomarkers and core signaling pathways with high predictive accuracy and interpretability (Zhang et al. 2025c, 2023). Deep learning-based approaches have also been increasingly applied to multi-omics integration, employing architectures such as graph convolutional neural networks and variational autoencoders to handle heterogeneous data types and missing modalities, thus improving performance in classification, prediction, and clustering tasks (Ballard et al. 2024). Moreover, integrative analyses that combine multi-omics data with imaging (radiomics) and clinical information through artificial intelligence frameworks have shown promise in enhancing early cancer detection, prognosis prediction, and treatment response monitoring, underscoring the importance of comprehensive data fusion (Camps et al. 2025). Tools like iSODA provide user-friendly platforms for interactive visualization and functional analysis of single- and multi-omics data, facilitating exploratory and hypothesis-driven research (Olivier-Jimenez et al. 2025). Despite these advances, challenges such as data heterogeneity, high dimensionality, missing data, and privacy concerns remain. Federated analysis frameworks that adhere to FAIR principles have been proposed to enable secure, privacy-preserving integration and reuse of multi-omics data across institutions (Liao et al. 2024). In sum, the deep fusion of multi-omics data through sophisticated computational and AI-driven methodologies offers a powerful avenue to unravel the molecular complexity of lung adenocarcinoma and other cancers from a systems biology perspective, enabling the development of integrative models that bridge imaging phenotypes with oncogenic drivers and ultimately inform precision medicine strategies.

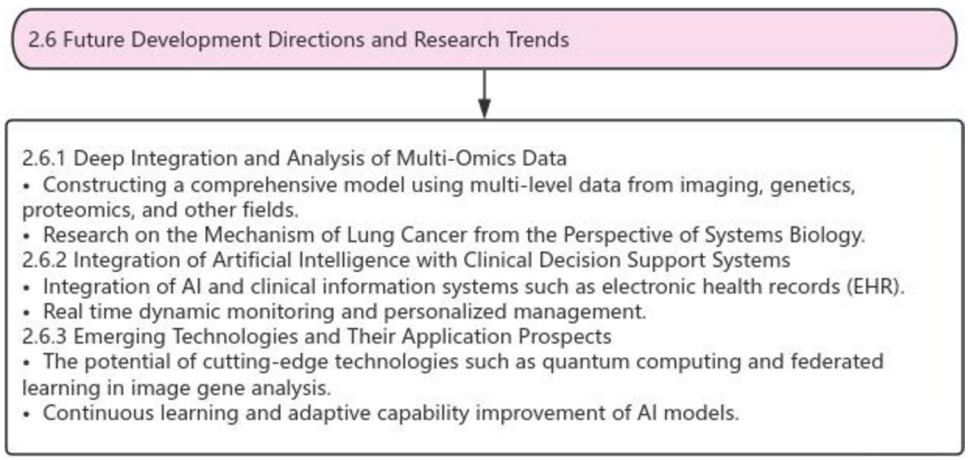

Fig. 6 Overview of the main content of this paragraph. The picture was created by Jinchun Chen

Integration of artificial intelligence with clinical decision support systems

The integration of artificial intelligence (AI) with electronic health records (EHR) and other clinical information systems represents a pivotal advancement in clinical decision support systems (CDSS). AI-augmented CDSS leverage the wealth of data stored in EHRs, including patient demographics, laboratory results, imaging data, and treatment histories, to provide personalized, evidence-based recommendations that enhance clinical decision-making. For instance, AI models have been developed to retrieve and analyze similar cases from medical databases, thereby enabling comparative diagnostics that improve accuracy and efficiency without requiring extensive manual segmentation of imaging data (Iglesias et al. 2024). In oncology, AI-driven CDSS such as Watson for Oncology (WfO) have been integrated into multidisciplinary teams, demonstrating improved adherence to clinical guidelines and positively influencing treatment decisions and patient satisfaction (Lee and Lee 2020; You et al. 2020; Yao et al. 2020). These systems utilize advanced machine learning algorithms to synthesize heterogeneous clinical data, facilitating precise risk stratification, therapy selection, and prognostic predictions. Moreover, AI-CDSS have been applied in various specialties, including cardiovascular diseases and geriatrics, where integration with clinical information systems supports risk assessment, early warning, and personalized management (Bozyel et al. 2024; Skuban-Eiseler et al. 2023). The seamless incorporation of AI into EHR platforms enhances real-time data accessibility and decision support, but challenges remain in interoperability, data standardization, and ensuring clinical reliability. Addressing these challenges through robust system design and validation is essential to realize the full potential of AI-integrated CDSS in routine clinical workflows (Shaikh et al. 2021; Gomez-Cabello et al. 2024).

Real-time dynamic monitoring powered by AI-enhanced clinical decision support systems enables continuous assessment of patient status and facilitates personalized management strategies tailored to individual risk profiles and disease trajectories. AI algorithms can analyze streaming data from various sources, including wearable devices, continuous monitoring systems, and imaging modalities, to detect subtle changes indicative of disease progression or complications. For example, in type 1 diabetes management, AI-CDSS integrate data from continuous glucose monitors, insulin pumps, and lifestyle trackers to provide predictive insights and personalized treatment recommendations, thereby optimizing glycemic control and resource allocation (Nimri and Phillip 2025). In intensive care settings, AI-based monitoring systems are being developed to interpret complex physiological data, supporting timely clinical decisions and improving care quality, although widespread bedside implementation is still evolving (Montomoli et al. 2022). Furthermore, AI-driven CDSS have demonstrated efficacy in enhancing diagnostic accuracy and urgency assessment in triage processes, as exemplified by cloud-based decision tree algorithms in ophthalmology, which improve referral accuracy and standardize care pathways (Tanya et al. 2023). The dynamic nature of AI-CDSS allows for adaptation to patient-specific changes, promoting proactive interventions and individualized care plans. However, successful deployment requires integration with existing clinical workflows, user-friendly interfaces, and continuous validation to maintain trust and usability among healthcare professionals (Tun et al. 2025; Ouanes and Farhah 2024). Ethical considerations, including preserving patient autonomy and ensuring equitable access, are also critical in the design and application of AI-driven personalized management systems (Skuban-Eiseler et al. 2023). Collectively, these advances underscore the transformative potential of AI-enhanced real-time monitoring and personalized management in improving patient outcomes and healthcare delivery efficiency.

Emerging technologies and their application prospects

Emerging technologies like quantum computing and federated learning hold promising potential to revolutionize the integration of imaging and genomic data in lung adenocarcinoma, particularly in the context of ground-glass nodules (GGNs). Quantum computing, with its ability to process complex, high-dimensional data exponentially faster than classical computers, could significantly accelerate the analysis of large-scale imaging-genomic datasets. This is crucial given the intricate relationship between CT imaging features of lung adenocarcinomas and their underlying driver gene mutations, such as EGFR mutations, which have been successfully predicted using AI-based deep learning models on CT images (Yoon et al. 2022; Wu et al. 2023). The computational demands of extracting radiomic features and correlating them with genomic profiles for thousands of nodules could be efficiently managed by quantum algorithms, enabling more rapid and precise biomarker discovery and risk stratification.

Federated learning, another cutting-edge approach, offers a secure and privacy-preserving framework for collaborative AI model training across multiple institutions without sharing raw patient data. This is particularly relevant in lung cancer imaging-genomics research, where data heterogeneity and privacy concerns limit large-scale multi-center studies. Federated learning can facilitate the aggregation of diverse CT imaging and genomic datasets from different centers, enhancing model generalizability and robustness. For instance, multi-center studies employing AI to predict

invasiveness and driver mutations in GGNs have demonstrated improved diagnostic accuracy when combining imaging features with genetic sequencing (Long et al. 2025; Zhang et al. 2022b). By enabling decentralized learning, federated approaches could overcome current limitations related to data sharing and allow continuous model refinement with new data from varied populations.

Moreover, the continuous learning and adaptive capabilities of AI models are critical for maintaining and improving diagnostic performance over time. Current AI frameworks, such as DeepLN and other convolutional neural networks, have shown competitive performance in classifying pulmonary nodules and predicting pathological subtypes (Wang et al. 2022). However, these models often rely on static training datasets and may suffer from performance degradation when exposed to new imaging protocols, scanner types, or patient demographics. Incorporating continuous learning mechanisms allows AI models to update their parameters dynamically as new data become available, adapting to shifts in data distribution and improving resilience against domain shifts. This capability is essential for clinical deployment, where imaging conditions and patient populations evolve.

Adaptive AI models can also integrate multi-modal data streams, including longitudinal CT imaging, radiomics, and genomic information, to provide personalized risk assessments and treatment guidance. For example, nomogram models combining AI-derived quantitative imaging parameters with clinical and genetic biomarkers have demonstrated superior predictive accuracy for invasiveness and prognosis in lung adenocarcinoma presenting as GGNs (Li and Zhang 2025; Li et al. 2024). Continuous learning frameworks could further enhance these models by incorporating follow-up imaging and molecular data, refining predictions and supporting dynamic clinical decision-making.

In summary, frontier technologies such as quantum computing and federated learning offer transformative potential for imaging-genomic analysis in lung adenocarcinoma, enabling faster computation and collaborative model development while preserving data privacy. Concurrently, enhancing AI models with continuous learning and adaptability is vital to sustain and improve their clinical utility in the dynamic environment of lung cancer diagnosis and management. These advances collectively pave the way for more precise, personalized, and scalable AI-driven solutions bridging CT imaging features and oncogenic driver genes in pulmonary ground-glass nodules.

Conclusion

The integration of artificial intelligence (AI) technology in the study of ground-glass nodules (GGNs) and adenocarcinoma of the lung represents a significant transformation in thoracic oncology. By driving the connection between imaging phenotypes and carcinogenic driver gene profiles, AI facilitates the deep integration of radiomics and genomics, which not only deepens our understanding of tumor biology but also paves the way for precise clinical applications. AI-assisted multimodal data analysis demonstrates significant potential in enhancing the accuracy of early diagnosis of adenocarcinoma of the lung, promoting personalized treatment and prognosis assessment, and helping to address tumor heterogeneity, thereby improving patient outcomes and prognosis.

However, the field still faces key challenges such as data quality and heterogeneity, insufficient algorithm interpretability, and lagging ethical and regulatory frameworks. The representativeness and reliability of data directly affect the performance of AI models, while the “black box” issue hinders the establishment of clinical trust. At the same time, issues related to patient privacy, data security, and equitable access urgently need to be addressed through cross-disciplinary collaboration to establish clear guidelines and standards.

Looking ahead, the development of AI technologies such as deep learning and multi-omics analysis is expected to fundamentally change the diagnosis and management landscape of pulmonary GGNs. Achieving this vision relies on close collaboration among multiple disciplines, including radiology, genomics, clinical oncology, and ethics, and effective validation through large-scale prospective clinical trials. Ultimately, these advancements will drive lung cancer management towards a more intelligent, precise, and personalized direction, ushering in a new era of smart healthcare. See Fig. 7.

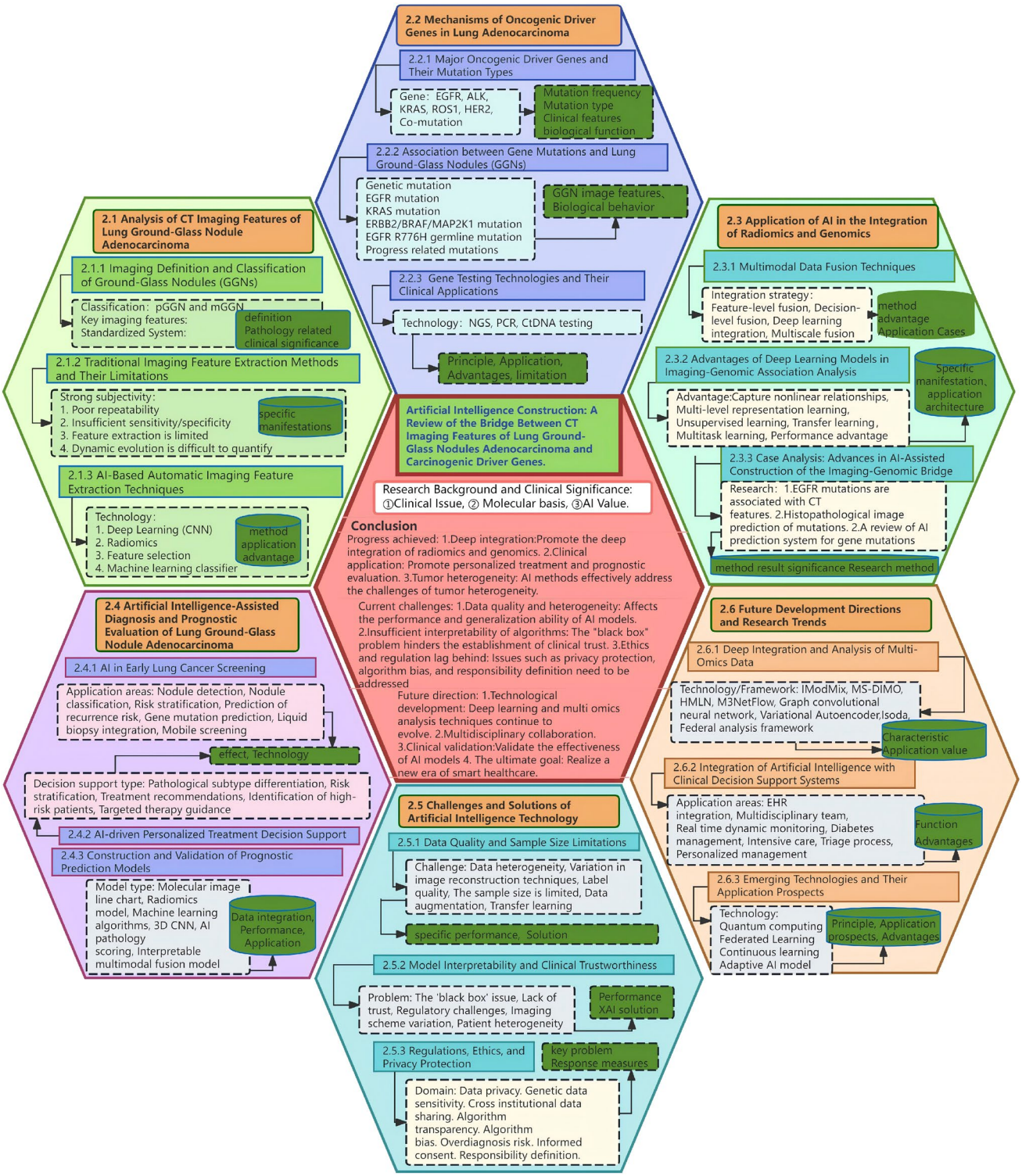

Fig. 7 This paragraph presents a panoramic view of the articlewas created by. Jinchun Chen

Author contributions Conceptualization: All authors. Writing original draft: Weikuan Xue. Writing review and editing: All authors. Image production: Jinchun Chen,

Data availability This is a clinical medical review. Due to the lack of creation or analysis of new data in this study, data availability is not applicable to this article. Full Text Sources: BioMed, Central PubMed Central, Europe PubMed Central

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval and consent to participate Not applicable.

References

Alam MR, Seo KJ, Abdul-Ghafar J, Yim K, Lee SH, Jang HJ, Jung CK, Chong Y (2023) Recent application of artificial intelligence on histopathologic image-based prediction of gene mutation in solid cancers. Brief Bioinform 24(3):bbad151. https://doi.org/10.1093/bib/bbad151

Arora S, Hammer MM, Byrne SC (2025) Real-world use and outcomes of Lung-RADS v1.1 category 4B versus Lung-RADS v2022 category 0 for suspected infectious or inflammatory findings on lung cancer screening CT. AJR Am J Roentgenol 225(5):e2533279. https://doi.org/10.2214/AJR.25.33279

Avanzo M, Stancanello J, Pirrone G, Drigo A, Retico A (2024) The Evolution of Artificial Intelligence in Medical Imaging: From Computer Science to Machine and Deep Learning. Cancers (Basel) 16(21):3702. https://doi.org/10.3390/cancers16213702.-DOI-PubMed

Ayasa Y, Alajrami D, Idkedek M, Tahayneh K, Akar FA (2025) The Impact of Artificial Intelligence on Lung Cancer Diagnosis and Personalized Treatment. Int J Mol Sci. https://doi.org/10.3390/ijms26178472

Bae SJ, Ahn SG, Ji JH, Chu C, Kim D, Lee J, Cha YJ, Jeong J (2021) Application of the 21-gene recurrence score in patients with early HR-positive/HER2-negative breast cancer: chemotherapy and survival rate according to clinical risk. Cancers (Basel) 13(16):403. https://doi.org/10.3390/cancers13164003

Ballard JL, Wang Z, Li W, Shen L, Long Q (2024) Deep learning-based approaches for multi-omics data integration and analysis. BioData Min 17(1):38. https://doi.org/10.1186/s13040-024-00391-z

Batra U, Nathany S, Nath SK, Jose JT, Sharma T, Pasricha S, Sharma M, Arambam N, Khanna V, Bansal A, Mehta A, Rawal K (2024) AI-based pipeline for early screening of lung cancer: integrating radiology, clinical, and genomics data. Lancet Reg Health Southeast Asia. 14(24):100352. https://doi.org/10.1016/j.lansea.2024.100352

Bi XA, Mao Y, Luo S, Wu H, Zhang L, Luo X, Xu L (2022) A novel generation adversarial network framework with characteristics aggregation and diffusion for brain disease classification and feature selection. Brief Bioinform. https://doi.org/10.1093/bib/bbac454

Bozyel S, Şimşek E, Koçyiğit Burunkaya D, Güler A, Korkmaz Y, Şeker M, Ertürk M, Keser N (2024) Artificial intelligence-based clinical decision support systems in cardiovascular diseases. Anatol J Cardiol 28(2):74–86. https://doi.org/10.14744/AnatolJCardiol.2023.3685

Camps J, Jiménez-Franco A, García-Pablo R, Joven J, Arenas M (2025) Artificial intelligence-driven integration of multi-omics and radiomics: a new hope for precision cancer diagnosis and prognosis. Biochimica Biophysica Acta Mol Basis Dis 1871(6):167841. https://doi.org/10.1016/j.bbadis.2025.167841

Cao L, Wang Z, Gong T, Wang J, Liu J, Jin L, Yuan Q (2020) Discriminating between bronchiolar adenoma, adenocarcinoma in situ and minimally invasive adenocarcinoma of the lung with CT. Diagn Interv Imaging 101(12):831–837. https://doi.org/10.1016/j.diii.2020.05.005

Cao X, Hu HG, Shen M, Deng K, Wu N (2023) Correlation between quantitative spectral CT parameters and Ki-67 expression in lung adenocarcinomas manifesting as ground-glass nodules. Curr Med Imaging 19(9):1052–1062. https://doi.org/10.2174/1573405619666221230120528

Chang Y, Xing H, Shang Y, Liu Y, Yu L, Dai H (2023) Preoperative predicting invasiveness of lung adenocarcinoma manifesting as ground-glass nodules based on multimodal images of dual-layer spectral detector CT radiomics models. J Cancer Res Clin Oncol 149(17):15425–15438. https://doi.org/10.1007/s00432-023-05311-y

Chao HS, Tsai CY, Chou CW, Shiao TH, Huang HC, Chen KC, Tsai HH, Lin CY, Chen YM (2023) Artificial intelligence assisted computational tomographic detection of lung nodules for prognostic cancer examination: a large-scale clinical trial. Biomedicines Basel 11(1):147. https://doi.org/10.3390/biomedicines11010147

Chen X, Yao B, Li J, Liang C, Qi R, Yu J (2022) Feasibility of using high-resolution computed tomography features for invasiveness differentiation of malignant nodules manifesting as ground-glass nodules. Can Respir J 2022(17):2671772. https://doi.org/10.1155/2022/2671772

Chen R, Zhang H, Huang X, Han H, Jian J (2025) CT radiomics-based machine learning approach for the invasiveness of pulmonary ground-glass nodules prediction. Eur J Radiol Open 23(15):100680. https://doi.org/10.1016/j.ejro.2025.100680

Cobo M, Corral Fontecha D, Silva W, Lloret IL (2025) Physical foundations for trustworthy medical imaging: A survey for artificial intelligence researchers. Artif Intell Med 11(169):103251. https://doi.org/10.1016/j.artmed.2025.103251.-DOI-PubMed

de Margerie-Mellon C, Chassagnon G (2023) Artificial intelligence: A critical review of applications for lung nodule and lung cancer. Diagn Interv Imaging 104(1):11–17. https://doi.org/10.1016/j.diii.2022.11.007

de Margerie-Mellon C, Ngo LH, Gill RR, Monteiro Filho AC, Heidinger BH, Onken A, Medina MA, VanderLaan PA, Bankier AA (2020) The growth rate of subsolid lung adenocarcinoma nodules at chest CT. Radiology 297(1):189–198. https://doi.org/10.1148/radiol.2020192322

Deng T, Feng J, Le X, Xia Y, Shi F, Yu F, Zhan Y, Liu X, Li C (2025) Automatic recognition and differentiation of pulmonary contusion and bacterial pneumonia based on deep learning and radiomics. BMC Med Imaging 25(1):234. https://doi.org/10.1186/s12880-025-01802-1

Digumarthy SR, Gullo RL, Levesque MH, Sayegh K, Rao S, Raymond SB, Otrakji A, Kalra MK (2020) Cause determination of missed lung nodules and impact of reader training and education: simulation study with nodule insertion software. J Cancer Res Ther 16(4):780–787. https://doi.org/10.4103/jcrt.JCRT_312_17

Du W, Yu M, Luo X, Chen M (2022a) Application value of spectral CT imaging in quantitative analysis of early lung adenocarcinoma. J Oncol 16(2022):2944473. https://doi.org/10.1155/2022/2944473

Du W, He B, Luo X, Chen M (2022b) Diagnostic value of artificial intelligence based on CT image in benign and malignant pulmonary nodules. J Oncol 2022(24):5818423. https://doi.org/10.1155/2022/5818423

Fang W, Zhang G, Yu Y, Chen H, Liu H (2022) Identification of pathological subtypes of early lung adenocarcinoma based on artificial intelligence parameters and CT signs. Biosci Rep. https://doi.org/10.1042/BSR20212416

Feng H, Shi G, Xu Q, Ren J, Wang L, Cai X (2023) Radiomics-based analysis of CT imaging for the preoperative prediction of invasiveness in pure ground-glass nodule lung adenocarcinomas. Insights Imaging 14(1):24. https://doi.org/10.1186/s13244-022-01363-9

Gandhi Z, Gurram P, Amgai B, Lekkala SP, Lokhandwala A, Manne S, Mohammed A, Koshiya H, Dewaswala N, Desai R, Bhopalwala H, Ganti S, Surani S (2023) Artificial intelligence and lung cancer: impact on improving patient outcomes. Cancers. https://doi.org/10.3390/cancers15215236

Gao F, Ding J, Gai B, Cai D, Hu C, Wang FA, He R, Liu J, Li Y, Wu XJ (2025) Interpretable multimodal fusion model for bridged histology and genomics survival prediction in pan-cancer. Adv Sci 12(17):e2407060. https://doi.org/10.1002/advs.202407060

Ge X, Hu J, Li Y, Wang L, Luo Y, Hua B, Liu R (2025) Risk assessment and interventions for malignant ground-glass lung nodules. Crit Rev Oncol Hematol 11(215):104856. https://doi.org/10.1016/j.critrevonc.2025.104856

Ghnemat R, Alodibat S, Abu A-H (2023) Explainable Artificial Intelligence (XAI) for Deep Learning Based Medical Imaging Classification. J Imaging 9(9):177. https://doi.org/10.3390/jimaging9090177.-DOI-PubMed

Gomez-Cabello CA, Borna S, Pressman S, Haider SA, Haider CR, Forte AJ (2024) Artificial-intelligence-based clinical decision support systems in primary care: a scoping review of current clinical implementations. Eur J Investig Health Psychol Educ 14(3):685–698. https://doi.org/10.3390/ejihpe14030045

Greffier J, Si-Mohamed S, Frandon J, Loisy M, de Oliveira F, Beregi JP, Dl D (2022) Impact of an artificial intelligence deep-learning reconstruction algorithm for CT on image quality and potential dose reduction: A phantom study. Med Phys 49(8):5052–5063. https://doi.org/10.1002/mp.15807

Gu W, Wang N, Gu W, Qiu Y, Zhang H, Liang J, Zhou T, Ma L, Cai W, Feng W, Chen L (2020) Molecular gene mutation profiles, TMB and the impact of prognosis in Caucasians and east Asian patients with lung adenocarcinoma. Transl Lung Cancer Res 9(3):629–638. https://doi.org/10.21037/tlcr-20-457

Guo Y, Li T, Gong B, Hu Y, Wang S, Yang L, Zheng C (2025) From Images to Genes: Radiogenomics Based on Artificial Intelligence to Achieve Non-Invasive Precision Medicine in Cancer Patients. Adv Sci (Weinh) 12(2):e2408069. https://doi.org/10.1002/advs.202408069.-DOI-PubMed

Habbab FM, Bédard ELR, Joy AA, Alam Z, Abraham AG, Roa WHY (2025) Early detection of lung cancer: a review of innovative milestones and techniques. J Clin Med 14(21):7812. https://doi.org/10.3390/jcm14217812

Han X, Fan J, Gu J, Li Y, Yang M, Liu T, Li N, Zeng W, Shi H (2020) CT features associated with EGFR mutations and ALK positivity in patients with multiple primary lung adenocarcinomas. Cancer Imaging 20(1):51. https://doi.org/10.1186/s40644-020-00330-1

Harris CS, Miaskowski CA, Dhruva AA, Cataldo J, Kober KM (2021) Multi-staged data-integrated multi-omics analysis for symptom science research. Biol Res Nurs 23(4):596–607. https://doi.org/10.1177/10998004211003980

Hong D, Xu K, Zhang L, Wan X, Guo Y (2020) Radiomics signature as a predictive factor for EGFR mutations in advanced lung adenocarcinoma. Front Oncol 31(10):28. https://doi.org/10.3389/fonc.2020.00028

Hsin-Hung C, En-Kuei T, Yun-Ju W, Fu-Zong W (2024) Impact of annual trend volume of low-dose computed tomography for lung cancer screening on overdiagnosis, overmanagement, and gender disparities. Cancer Imaging 24(1):73

Hsu J, Annunziata JF, Burns E, Bernicker EH, Olsen RJ, Thomas JS (2022) Molecular signatures of KRAS-mutated lung adenocarcinoma: analysis of concomitant EGFR, ALK, STK11, and PD-L1 status. Clin Pathol 23(15):2632010X221102054. https://doi.org/10.1177/2632010X221102054

Hu M, Zhang T, Yang Y, Che N, Li J, Liu Z, Li B (2020) Driver gene alterations in lung adenocarcinoma: demographic features of 2544 Chinese cases. Int J Biol Markers 35(4):44–50. https://doi.org/10.1177/1724600820967015

Hu F, Huang H, Jiang Y, Feng M, Wang H, Tang M, Zhou Y, Tan X, Liu Y, Xu C, Ding N, Bai C, Hu J, Yang D, Zhang Y (2021a) Discriminating invasive adenocarcinoma among lung pure ground-glass nodules: a multi-parameter prediction model. J Thorac Dis 13(9):5383–5394. https://doi.org/10.21037/jtd-21-786

Hu X, Gong J, Zhou W, Li H, Wang S, Wei M, Peng W, Gu Y (2021b) Computer-aided diagnosis of ground glass pulmonary nodule by fusing deep learning and radiomics features. Phys Med Biol 66(6):065015. https://doi.org/10.1088/1361-6560/abe735

Huang H, Zheng D, Chen H, Wang Y, Chen C, Xu L, Li G, Wang Y, He X, Li W (2022) Fusion of CT images and clinical variables based on deep learning for predicting invasiveness risk of stage I lung adenocarcinoma. Med Phys 49(10):6384–6394. https://doi.org/10.1002/mp.15903

Huang L, Xu L, Wang X, Zhang G, Gao X, Niu L, Wen L (2025a) Prediction of EGFR mutations in lung adenocarcinoma via CT images: a comparative study of intratumoral and peritumoral radiomics, deep learning, and fusion models. Acad Radiol 32(8):4880–4892. https://doi.org/10.1016/j.acra.2025.04.029

Huang X, Xu F, Zhu W, Yao L, He J, Su J, Zhao W, Hu H (2025b) An integrated strategy based on radiomics and quantum machine learning: diagnosis and clinical interpretation of pulmonary ground-glass nodules. BMC Med Imaging 25(1):279. https://doi.org/10.1186/s12880-025-01813-y

Huang F, Lin X, Hong Y, Li Y, Li Y, Chen WT, Chen W (2025c) The feasibility and cost-effectiveness of implementing mobile low-dose computed tomography with an AI-based diagnostic system in underserved populations. BMC Cancer 25(1):345. https://doi.org/10.1186/s12885-025-13710-2

Iglesias G, Talavera E, Troya J, Díaz-Álvarez A, García-Remesal M (2024) Artificial intelligence model for tumoral clinical decision support systems. Comput Methods Programs Biomed 253:108228. https://doi.org/10.1016/j.cmpb.2024.108228

International Medical Society, Chinese Anti-Cancer Association, Breast Cancer Group, Branch of Oncologist, Chinese Medical Doctor Association (2022) Consensus of Chinese experts on hot issues in genetic testing of advanced breast cancer. Chinese J Oncol 44(1):60–67. https://doi.org/10.3760/cma.j.cn112152-20211111-00837

Jia X, Chen L, Liang J, Ma X, Zhou H, Zhang Y (2022) [Progress in precision medicine of radiomics in abdominal tumors practice]. Chin J Med Devices 46(2):187–190. https://doi.org/10.3969/j.issn.1671-7104.2022.02.015

Jia Y, Liu J, Chen L, Zhao T, Wang Y (2023) THItoGene: a deep learning method for predicting spatial transcriptomics from histological images. Brief Bioinform 25(1):464. https://doi.org/10.1093/bib/bbad464

Kang S, Zhang H, Lei L, Xie X, Duan H, Han D, Jing W, Zhang X, Tian Y, Lv F (2025) Dual-layer spectral detector CT electron density imaging: impressive technology for imaging characteristics of ground-glass nodules. Quant Imaging Med Surg 15(8):7441–7452. https://doi.org/10.21037/qims-2024-2923

Kastner J, Hossain R, Jeudy J, Dako F, Mehta V, Dalal S, Dharaiya E, White C (2021) Lung-RADS version 1.0 versus Lung-RADS version 1.1: comparison of categories using nodules from the National Lung Screening Trial. Radiology 300(1):199–206. https://doi.org/10.1148/radiol.2021203704

Kudo Y, Nakamura T, Matsubayashi J, Ichinose A, Goto Y, Amemiya R, Park J, Shimada Y, Kakihana M, Nagao T, Ohira T, Masumoto J, Ikeda N (2024) AI-driven Characterization of Solid Pulmonary Nodules on CT Imaging for Enhanced Malignancy Prediction in Small-sized Lung Adenocarcinoma. Clin Lung Cancer 25(5):431–439. https://doi.org/10.1016/j.cllc.2024.04.015

Lee K, Lee SH (2020) Artificial intelligence-driven oncology clinical decision support system for multidisciplinary teams. Sensors Basel. https://doi.org/10.3390/s20174693

Lee B, Zhang S, Poleksic A, Xie L (2019) Heterogeneous multi-layered network model for omics data integration and analysis. Front Genet 28(10):1381. https://doi.org/10.3389/fgene.2019.01381

Li Y, Zhang Q (2025) A Nomogram Combining Two Novel Biomarkers for Predicting Lung Adenocarcinoma in Ground-Glass Nodule Patients. Hum Mutat 2025(11):8647969. https://doi.org/10.1155/humu/8647969.-DOI-PubMed

Li D, Ding L, Ran W, Huang Y, Li G, Wang C, Xiao Y, Wang X, Lin D, Xing X (2020) Status of 10 targeted genes of non-small cell lung cancer in eastern China: A study of 884 patients based on NGS in a single institution. Thorac Cancer 11(9):2580–2589. https://doi.org/10.1111/1759-7714.13577.-DOI-PubMed

Li H, Sun Z, Xiao R, Qi Q, Li X, Huang H, Wang X, Zhou J, Wang Z, Liu K, Yin P, Yang F, Wang J (2022) Stepwise evolutionary genomics of early-stage lung adenocarcinoma manifesting as pure, heterogeneous and part-solid ground-glass nodules. Br J Cancer 127(4):747–756. https://doi.org/10.1038/s41416-022-01821-7

Li R, Zhou L, Wang Y, Shan F, Chen X, Liu L (2023) A graph neural network model for the diagnosis of lung adenocarcinoma based on multimodal features and an edge-generation network. Quant Imaging Med Surg 13(8):5333–5348. https://doi.org/10.21037/qims-23-2

Li H, Luo Q, Zheng Y, Ding C, Yang J, Chen L, Liu X, Guo T, Fan J, Han X, Shi H (2024) A nomogram for predicting invasiveness of lung adenocarcinoma manifesting as ground-glass nodules based on follow-up CT imaging. Transl Lung Cancer Res 13(10):2617–2635. https://doi.org/10.21037/tlcr-24-492

Li X, Wei Q, Wang T, Rukonge PA, Sheng Y, Yu G (2025a) Narrative review of the application of artificial intelligence-related technologies in the diagnosis of pulmonary nodules with recommendations for clinical practice and future research. J Thorac Dis 17(8):6326–6338. https://doi.org/10.21037/jtd-2025-1512

Li J, Li X, Guo H, Zhou S, Ding H, Li B, Li W, Zhang B, Zou Y (2025b) Multi-gene panel sequencing reveals the relationship between driver gene mutation and clinical characteristics in lung adenocarcinoma. Discov Oncol 16(1):274. https://doi.org/10.1007/s12672-025-02008-1

Li Y, Niu D, Qi K, Liang D, Long X (2025c) An imaging and genetic-based deep learning network for Alzheimer's disease diagnosis. Front Aging Neurosci 21(17):1532470. https://doi.org/10.3389/fnagi.2025.1532470

Li J, Mao N, Aodeng S, Zhang H, Zhu Z, Wang L, Liu Y, Qi H, Qiao H, Lin Y, Qiu Z, Yang T, Zha Y, Wang X, Wang W, Song X, Lv W (2025d) Development and validation an integrated deep learning model to assist eosinophilic chronic rhinosinusitis diagnosis: a multicenter study. Int Forum Allergy Rhinol 15(10):1070–1081. https://doi.org/10.1002/alr.23595

Li Y, Jiang L, Liu X, Dai J, Liu Q (2025e) Functional remodeling of tissue-resident macrophages leads to distinct immune microenvironment evolution and clinical manifestations in lung adenocarcinoma. Clin Exp Med 25(1):223. https://doi.org/10.1007/s10238-025-01760-6

Liang X, Zhang C, Ye X (2025) Overdiagnosis and overtreatment of ground-glass nodule-like lung cancer. Asia Pac J Clin Oncol 21(1):108–114. https://doi.org/10.1111/ajco.14042

Liao H, Luo X, Liang Y, Wan R, Xu M (2021) Mutational status of main driver genes influences the prognosis of stage I-III lung adenocarcinoma patients underwent radical surgery. Transl Cancer Res 10(7):3286–3298. https://doi.org/10.21037/tcr-21-240

Liao X, Ederveen THA, Niehues A, de Visser C, Huang J, Badmus F, Doornbos C, Orlova Y, Kulkarni P, van der Velde KJ, Swertz MA, Brandt M, van Gool AJ, Hoen't PAC (2024) FAIR data cube, a FAIR data infrastructure for integrated multi-omics data analysis. J Biomed Semantics 15(1):20. https://doi.org/10.1186/s13326-024-00321-2

Lin M, Li Z, Lin Q, Wang P, Liu W, Yuan J, Hong Z, Chen Y (2022) Development and clinical application of a rapid and visual loop-mediated isothermal amplification test for tetM gene in *Clostridioides difficile* strains cultured from feces. Int J Infect Dis 9(122):676–684. https://doi.org/10.1016/j.ijid.2022.07.032. **(-DOI -PubMed)**

Lin YC, Yang TM, Wang TY, Fang YH, Lu MS, Lin CK, Jiang YY, Han CH, Lung J, Tsai YH, Hung MS (2025) The prevalence, distribution, and clinicopathological features of seven lung cancer actionable driver mutations in Taiwan. Thorac Cancer 16(14):e70138. https://doi.org/10.1111/1759-7714.70138

Liu Q, Hu P (2023) Radiogenomic association of deep MR imaging features with genomic profiles and clinical characteristics in breast cancer. Biomark Res 11(1):9. https://doi.org/10.1186/s40364-023-00455-y

Liu S, Liang B, Li Y, Xu J, Qian W, Lin M, Xu M, Niu L (2022) CT-guided percutaneous cryoablation in patients with lung nodules mainly composed of ground-glass opacities. J Vasc Interv Radiol 33(8):942–948. https://doi.org/10.1016/j.jvir.2022.04.021

Liu S, Liang W, Huang P, Chen D, He Q, Ning Z, Zhang Y, Xiong W, Yu J, Chen T (2023a) Multi-modal analysis for accurate prediction of preoperative stage and indications of optimal treatment in gastric cancer. Radiol Med 128(5):509–519. https://doi.org/10.1007/s11547-023-01625-6

Liu X, Jiang G, Sun X, Su G, Zhang X, Shen D, Yan N (2023b) Relationship between driver gene mutations and clinical pathological characteristics in older lung adenocarcinoma. Front Oncol 1(13):1275575. https://doi.org/10.3389/fonc.2023.1275575

Liu F, Zhang X, Lu M et al (2024) The association of genomic alterations with PD-L1 expression in Chinese patients with EGFR/ALK wild-type lung adenocarcinoma and potential predictive value of Hippo pathway mutations to immunotherapy. Cancer Med 13(3):e7038. https://doi.org/10.1002/cam4.7038.-DOI-PubMed

Liu X, Ren Y, Fei Z, Shi Q, Lu L (2025) Relationship between qualitative and quantitative parameters of three-dimensional computed tomography, EGFR gene mutation, and ALK gene rearrangement in GGO-associated lung adenocarcinoma and their prognostic value. Pathol Oncol Res 11(31):1612081. https://doi.org/10.3389/pore.2025.1612081

Long Y, Li Y, Zheng Y, Lin W, Qing H, Zhou P, Liu J (2025) Quantitative measures of pure ground-glass nodules from an artificial intelligence software for predicting invasiveness of pulmonary adenocarcinoma on low-dose CT: a multicenter study. Biomedicines 13(7):1600. https://doi.org/10.3390/biomedicines13071600

Lu J, Tang H, Yang X, Liu L, Pang M (2020) Diagnostic value and imaging features of multi-detector CT in lung adenocarcinoma with ground glass nodule patients. Oncol Lett 20(1):693–698. https://doi.org/10.3892/ol.2020.11631

Lu S, Guo A, Hu H, Ying X, Li Y, Huang Z, Xu W, Tao S, Hu X, Yan N, Zhang X, Shen D, Sasaki T, Arulananda S, Onodera K, He Z (2024) Correlation analysis between driver gene mutation and clinicopathological features in lung adenocarcinoma based on real-world cumulative clinical data. Transl Lung Cancer Res 13(6):1296–1306. https://doi.org/10.21037/tlcr-24-409

Ma Y, Du Y, Wang R, Ji X, Wu J, Liu Y, Guo X, Zhang Y (2020) Analysis of multigene detection in patients with advanced lung adenocarcinoma using cytological specimens. Pathol Res Pract 216(8):153036. https://doi.org/10.1016/j.prp.2020.153036

Ma H, Guo H, Zhao M, Qi S, Li H, Tian Y, Li Z, Zhang G, Yao Y, Qian W (2022) Automatic pulmonary ground-glass opacity nodules detection and classification based on 3D neural network. Med Phys 49(4):2555–2569. https://doi.org/10.1002/mp.15501

Ma XL, Jia RN, Han K, Zhang YX (2024) [Correlation between common driver gene variations and clinicopathological typing in lung adenocarcinoma]. Zhonghua Bing Li Xue Za Zhi 53(6):578–584. https://doi.org/10.3760/cma.j.cn112151-20231019-00277

Mathew S, Thangavel G, Pujar P, Pant A, Nath A (2025) An umbrella review of systematic evidence on the low dose computed tomography (LDCT) for lung cancer screening. Future Oncol 21(20):2649–2661

Meng D, Wang Z, Bai C, Ye Z, Gao Z (2024) Assessing the effect of scanning parameter on the size and density of pulmonary nodules: a phantom study. BMC Med Imaging 24(1):12. https://doi.org/10.1186/s12880-023-01190-4

Meng R, Zhu W, Cameron CJF, Ni P, Zhou X, Ulammandakh T, Gerstein MB (2025a) Machine-learning models based on histological images from healthy donors identify imageQTLs and predict chronological age. Proc Natl Acad Sci U S A 122(46):e2423469122. https://doi.org/10.1073/pnas.2423469122

Meng R, Zhu W, Cameron CJ, Ni P, Zhou X, Ulammandakh T, Gerstein MB (2525b) Machine learning models based on histological images from healthy donors identify ImageQTLs and predict chronological age. bioRxiv 9(4):674328. https://doi.org/10.1101/2025.09.04.674328

Michalet M, Azria D, Tardieu M, Tibermacine H, Nougaret S (2021) Radiomics in radiation oncology for gynecological malignancies: a review of literature. Br J Radiol 94(1125):20210032. https://doi.org/10.1259/bjr.20210032

Montomoli J, Hilty MP, Ince C (2022) Artificial intelligence in intensive care: moving towards clinical decision support systems. Minerva Anestesiol 88(12):1066–1072. https://doi.org/10.23736/S0375-9393.22.16739-8

Narváez-Bandera I, Lui A, Mekonnen YA, Rubio V, Sulman N, Wilson C, Ackerman HD, Ospina OE, Gonzalez-Calderon G, Flores E, Li Q, Chen A, Fridley B, Stewart P (2024) iModMix: Integrative Module Analysis for Multi-omics Data. bioRxiv. 11(12):623208. https://doi.org/10.1101/2024.11.12.623208

Nimri R, Phillip M (2025) Enhancing care in Type 1 diabetes with artificial intelligence driven clinical decision support systems. Horm Res Paediatr 98(4):384–395. https://doi.org/10.1159/000546713

Notsuda H, Oshio H, Onodera K, Hirama T, Watanabe Y, Watanabe T, Suzuki T, Oishi H, Niikawa H, Saito-Koyama R, Noda M, Tominaga J, Okada Y (2024) Morphological predictors of primary lung cancer among part-solid ground-grass nodules on high-resolution CT. Tohoku J Exp Med 263(1):35–42. https://doi.org/10.1620/tjem.2024.J016

Olivier-Jimenez D, Derks RJE, Harari O, Cruchaga C, Ali M, Ori A, Di Fraia D, Cabukusta B, Henrie A, Giera M, Mohammed Y (2025) iSODA: a comprehensive tool for integrative omics data analysis in single- and multi-omics experiments. Anal Chem 97(5):2689–2697. https://doi.org/10.1021/acs.analchem.4c04355

Ouanes K, Farhah N (2024) Effectiveness of artificial intelligence (AI) in clinical decision support systems and care delivery. J Med Syst 48(1):74. https://doi.org/10.1007/s10916-024-02098-4

Pan X, Lin H, Han C, Feng Z, Wang Y, Lin J, Qiu B, Yan L, Li B, Xu Z, Wang Z (2022) Computerized tumor-infiltrating lymphocytes density score predicts survival of patients with resectable lung adenocarcinoma. Iscience. https://doi.org/10.1016/j.isci.2022.105605

Phan NN, Huang CC, Tseng LM, Chuang EY (2021) Predicting breast cancer gene expression signature by applying deep convolutional neural networks from unannotated pathological images. Front Oncol 1(11):769447. https://doi.org/10.3389/fonc.2021.769447

Ruan D, Shi S, Guo W, Pang Y, Yu L, Cai J, Wu Z, Wu H, Sun L, Zhao L, Chen H (2025) Evaluation of locoregional invasiveness of early lung adenocarcinoma manifesting as ground-glass nodules via [68Ga]Ga-FAPI-46 PET/CT imaging. Eur J Nucl Med Mol Imaging 52(13):4788–4805. https://doi.org/10.1007/s00259-025-07361-5

Sadeghi MH, Sina S, Alavi M, Giammarile F, Yeong CH (2024) PET/CT-based 3D multi-class semantic segmentation of ovarian cancer and the stability of the extracted radiomics features. Phys Eng Sci Med 47(4):1739–1749. https://doi.org/10.1007/s13246-024-01485-y

Shah HP, Naqvi AS, Rajput P, Ambra H, Venkatesh H, Saleem J, Saravanan S, Wanjari M, Mittal G (2025) Artificial intelligence-based deep learning algorithms for ground-glass opacity nodule detection: a review. Narra J 5(1):e1361. https://doi.org/10.52225/narra.v5i1.1361

Shaikh F, Dehmeshki J, Bisdas S, Roettger-Dupont D, Kubassova O, Aziz M, Awan O (2021) Artificial intelligence-based clinical decision support systems using advanced medical imaging and radiomics. Curr Probl Diagn Radiol 50(2):262–267. https://doi.org/10.1067/j.cpradiol.2020.05.006

Shi L, Zhao J, Peng X, Wang Y, Liu L, Sheng M (2021) CT-based radiomics for differentiating invasive adenocarcinomas from indolent lung adenocarcinomas appearing as ground-glass nodules: asystematic review. Eur J Radiol 11(144):109956. https://doi.org/10.1016/j.ejrad.2021.109956

Shimada Y, Kudo Y, Maehara S, Amemiya R, Masuno R, Park J, Ikeda N (2022) Radiomics with artificial intelligence for the prediction of early recurrence in patients with clinical stage IA lung cancer. Ann Surg Oncol 29(13):8185–8193. https://doi.org/10.1245/s10434-022-12516-x

Shimada Y, Kudo Y, Maehara S, Fukuta K, Masuno R, Park J, Ikeda N (2023) Artificial intelligence-based radiomics for the prediction of nodal metastasis in early-stage lung cancer. Sci Rep 13(1):1028. https://doi.org/10.1038/s41598-023-28242-7

Si-Mohamed SA, Greffier J, Miailhes J, Boccalini S, Rodesch PA, Vuillod A, van der Werf N, Dabli D, Racine D, Rotzinger D, Becce F, Yagil Y, Coulon P, Vlassenbroek A, Boussel L, Beregi JP, Douek P (2022) Comparison of image quality between spectral photon-counting CT and dual-layer CT for the evaluation of lung nodules: a phantom study. Eur Radiol 32(1):524–532. https://doi.org/10.1007/s00330-021-08103-5

Singh R, Kalra MK, Homayounieh F, Nitiwarangkul C, McDermott S, Little BP, Lennes IT, Shepard JO, Digumarthy SR (2021) Artificial intelligence-based vessel suppression for detection of subsolid nodules in lung cancer screening computed tomography. Quant Imaging Med Surg 11(4):1134–1143. https://doi.org/10.21037/qims-20-630

Skuban-Eiseler T, Orzechowski M, Denkinger M, Kocar TD, Leinert C, Steger F (2023) Artificial intelligence-based clinical decision support systems in geriatrics: an ethical analysis. J Am Med Dir Assoc 24(9):1271-1276.e4. https://doi.org/10.1016/j.jamda.2023.06.008

Solomon J, Ebner L, Christe A, Peters A, Munz J, Löbelenz L, Klaus J, Richards T, Samei E, Roos JE (2021) Minimum perceivable size difference: how well can radiologists visually detect a change in lung nodule size from CT images? Eur Radiol 31(4):1947–1955. https://doi.org/10.1007/s00330-020-07326-2

Song F, Fu B, Liu M, Liu X, Liu S, Lv F (2023) Proposal of modified Lung-RADS in assessing pulmonary nodules of patients with previous malignancies: a primary study. Diagnostics 13(13):2210. https://doi.org/10.3390/diagnostics13132210

Takamochi K, Hara K, Hayashi T, Kohsaka S, Takahashi F, Suehara Y, Suzuki K (2021) Programmed death-ligand 1 expression and its associations with clinicopathological features, prognosis, and driver oncogene alterations in surgically resected lung adenocarcinoma. Lung Cancer 11(161):163–170. https://doi.org/10.1016/j.lungcan.2021.09.011.-DOI-PubMed

Tanya SM, Nguyen AX, Buchanan S, Jackman CS (2023) Development of a cloud-based clinical decision support system for ophthalmology triage using decision tree artificial intelligence. Ophthalmol Sci 3(1):100231. https://doi.org/10.1016/j.xops.2022.100231

Tsuchiya N, Kobayashi S, Nakachi R, Tomori Y, Yogi A, Iida G, Ito J, Nishie A (2025) Application of a pulmonary nodule detection program using AI technology to ultra-low-dose CT: differences in detection ability among various image reconstruction methods. Jpn J Radiol 43(8):1303–1312. https://doi.org/10.1007/s11604-025-01781-x

Tun HM, Rahman HA, Naing L, Malik OA (2025) Trust in artificial intelligence-based clinical decision support systems among health care workers: systematic review. J Med Internet Res 29(27):e69678. https://doi.org/10.2196/69678

van der Velden BHM, Kuijf HJ, Gilhuijs KGA, Viergever MA (2022) Explainable artificial intelligence (XAI) in deep learning-based medical image analysis. Med Image Anal 7(79):102470. https://doi.org/10.1016/j.media.2022.102470.-DOI-PubMed

Wan J, Lin X, Wang Z, Sun P, Gui S, Ye T, Fan Q, Liu W, Pan F, Yang B, Geng X, Quan Z, Yang L (2025) Dual-layer spectral detector computed tomography multiparameter machine learning model for prediction of invasive lung adenocarcinoma. Transl Lung Cancer Res 14(2):385–397. https://doi.org/10.21037/tlcr-24-822.-DOI-PubMed

Wang D, Zhang T, Li M, Bueno R, Jayender J (2020) 3D deep learning based classification of pulmonary ground glass opacity nodules with automatic segmentation. Comput Med Imaging Graph 5(88):101814. https://doi.org/10.1016/j.compmedimag.2020.101814

Wang C, Shao J, Xu X, Yi L, Wang G, Bai C, Guo J, He Y, Zhang L, Yi Z, Li W (2022) DeepLN: A Multi-Task AI Tool to Predict the Imaging Characteristics, Malignancy and Pathological Subtypes in CT-Detected Pulmonary Nodules. Front Oncol 11(12):683792. https://doi.org/10.3389/fonc.2022.683792

Wang H, Chen A, Wang K, Yang H, Wen W, Ren Q, Chen L, Xu X, Zhu Q (2024a) CT imaging features of lung ground-glass nodule patients with upgraded intraoperative frozen pathology. Discov Oncol 15(1):29. https://doi.org/10.1007/s12672-024-00872-x

Wang M, Wei Y, Zhu M, Yu H, Guo C, Chen Z, Shi W, Ren J, Zhao W, Yang Z, Chen LA (2024b) The value of topological radiomics analysis in predicting malignant risk of pulmonary ground-glass nodules: a multi-center study. Technol Cancer Res Treat 1(23):15330338241287088. https://doi.org/10.1177/15330338241287089

Wang T, Zheng Q, Deng C, Li X, Huang J, Fan J, Huang B, Zhang J, Chang X, Nie X (2024c) Identification of EGFR R776H germline mutations in a patient with multifocal lung adenocarcinoma: a case report and literature review. Respir Med Case Rep 27(50):102051. https://doi.org/10.1016/j.rmcr.2024.102051

Wang X, Cui Y, Wang Y, Liu S, Meng N, Wei W, Bai Y, Shen Y, Guo J, Guo Z, Wang M (2025a) Assessment of lung nodule detection and lung CT screening reporting and data system classification using zero echo time pulmonary MRI. J Magn Reson Imaging 61(2):822–829. https://doi.org/10.1002/jmri.29388

Wang C, Liu L, Fan C, Zhang Y, Mai Z, Li L, Liu Z, Tian Y, Hu J, Elazab A (2025b) Lung adenocarcinoma subtype classification based on contrastive learning model with multimodal integration. Sci Rep 15(1):30404. https://doi.org/10.1038/s41598-025-13818-2

Wei B, Wang W, Geng S, Wu W, Ding C, Zhu D, Cheng S, Zhao Q, Luan Y, Li S, Mao M (2025) An effective and affordable blood test for lung cancer early detection using four protein markers and artificial intelligence. Transl Lung Cancer Res 14(9):3444–3456. https://doi.org/10.21037/tlcr-2025-317

Wu L, Gao C, Xiang P, Zheng S, Pang P, Xu M (2020) CT-imaging based analysis of invasive lung adenocarcinoma presenting as ground glass nodules using peri- and intra-nodular radiomic features. Front Oncol 27(10):838. https://doi.org/10.3389/fonc.2020.00838

Wu N, Cao QW, Wang CN, Hu HG, Shi H, Deng K (2023) Association between quantitative spectral CT parameters, Ki-67 expression, and invasiveness in lung adenocarcinoma manifesting as ground-glass nodules. Acta Radiol 64(4):1400–1409. https://doi.org/10.1177/02841851221128213

Wu H, Zhang X, Zhong Z (2025) Exploration of CT-based discrimination and diagnosis of various pathological types of ground glass nodules in the lungs. BMC Med Imaging 25(1):119. https://doi.org/10.1186/s12880-025-01653-w

Xia X, Gong J, Hao W, Yang T, Lin Y, Wang S, Peng W (2020) Comparison and fusion of deep learning and radiomics features of ground-glass nodules to predict the invasiveness risk of Stage-I lung adenocarcinomas in CT scan. Front Oncol 31(10):418. https://doi.org/10.3389/fonc.2020.00418

Xie X, Liu Z, Wang Y, Fu H, Liu M, Zhang Y, Xu J (2024) Puppet dynasty recognition system based on MobileNetV2. Entropy 26(8):645. https://doi.org/10.3390/e26080645

Xiong Z, Jiang Y, Tian D, Zhang J, Guo Y, Li G, Qin D, Li Z (2022) Radiomics for identifying lung adenocarcinomas with predominant lepidic growth manifesting as large pure ground-glass nodules on CT images. PLoS ONE 17(6):e0269356. https://doi.org/10.1371/journal.pone.0269356

Xiong H, Lu Y, Qiu J, Wu T, Liu H, Fei Z, Fan C, Zhang P (2025) A novel method based on a multiscale convolution neural network for identifying lung nodules. Sci Rep 15(1):37632. https://doi.org/10.1038/s41598-025-21582-6

Xu F, Zhu W, Shen Y, Wang J, Xu R, Qutesh C, Song L, Gan Y, Pu C, Hu H (2020) Radiomic-based quantitative CT analysis of pure ground-glass nodules to predict the invasiveness of lung adenocarcinoma. Front Oncol 11(10):872. https://doi.org/10.3389/fonc.2020.00872

Xu QX, Ma TT, Xiang LQ, Hou YY, Lu SH, Yuan W (2025a) [Clinical and molecular characteristics of bronchial adenoma: an analysis of 88 cases]. Zhonghua Bing Li Xue Za Zhi 54(4):368–374. https://doi.org/10.3760/cma.j.cn112151-20240729-00480

Xu J, Feng B, Chen X, Wu F, Liu Y, Yu Z, Lu S, Duan X, Chen X, Li K, Zhang W, Dai X (2025b) Deep learning-based multimodal feature interaction-guided fusion: enhancing the evaluation of EGFR in advanced lung adenocarcinoma. Acad Radiol 32(9):5585–5595. https://doi.org/10.1016/j.acra.2025.04.071

Xue K, Luo B, Li X, Deng W, Zeng C, Zuo C (2022) Consistency evaluation of lung adenocarcinoma tissue and circulating tumor cells related gene mutation detection based on multi-site immunomagnetic beads. J Biomater Appl 36(9):1700–1711. https://doi.org/10.1177/08853282211065861

Yao S, Wang R, Qian K, Zhang Y (2020) Real world study for the concordance between IBM Watson for oncology and clinical practice in advanced non-small cell lung cancer patients at a lung cancer center in China. Thorac Cancer 11(5):1265–1270. https://doi.org/10.1111/1759-7714.13391

Yao Y, Guo B, Li J, Yang Q, Li X, Deng L (2022) The influence of a deep learning image reconstruction algorithm on the image quality and auto-analysis of pulmonary nodules at ultra-low dose chest CT: a phantom study. Quant Imaging Med Surg 12(5):2777–2791. https://doi.org/10.21037/qims-21-815

Yin Y, Lu J, Tong J, Cheng Y, Zhang K (2023) Relationship between early lung adenocarcinoma and multiple driving genes based on artificial intelligence medical images of pulmonary nodules. Front Genet 21(14):1142795. https://doi.org/10.3389/fgene.2023.1142795

Yoon HJ, Choi J, Kim E, Um SW, Kang N, Kim W, Kim G, Park H, Lee HY (2022) Deep learning analysis to predict EGFR mutation status in lung adenocarcinoma manifesting as pure ground-glass opacity nodules on CT. Front Oncol 12:951575. https://doi.org/10.3389/fonc.2022.951575

You HS, Gao CX, Wang HB, Luo SS, Chen SY, Dong YL, Lyu J, Tian T (2020) Concordance of treatment recommendations for metastatic non-small-cell lung cancer between Watson for oncology system and medical team. Cancer Manag Res 16(12):1947–1958. https://doi.org/10.2147/CMAR.S244932

You L, Zhao X, Xie Z, Patel KA, Chen C, Kitkungvan D, Mohammed KK, Narula N, Arbustini E, Cassidy CK, Narula J, Zhi D (2025) Uncovering genetic architecture of the heart via genetic association studies of unsupervised deep learning derived endophenotypes. bioRxiv 09(17):676827. https://doi.org/10.1101/2025.09.17.676827

Yu R, Hou JP, Ni XQ, Ya Y, Fan GH (2021) [Differential diagnosis of pure ground glass nodules in lung with spectral CT imaging]. Zhonghua Yi Xue Za Zhi 101(45):3742–3747. https://doi.org/10.3760/cma.j.cn112137-20210423-00972

Yu Z, Xu C, Zhang Y, Ji F (2022a) A triple-classification for the evaluation of lung nodules manifesting as pure ground-glass sign: a CT-based radiomic analysis. BMC Med Imaging 22(1):133. https://doi.org/10.1186/s12880-022-00862-x

Yu F, Peng M, Bai J, Zhu X, Zhang B, Tang J, Liu W, Chen C, Wang X, Chen M, Tan S, Sun Y, Liang Q, Li J, Hu Y, Liao A, Hu H, He Y, Xiao X, Wang B, Xing G, Xu Y, Chen R, Xia X, Chen X (2022b) Comprehensive characterization of genomic and radiologic features reveals distinct driver patterns of RTK/RAS pathway in ground-glass opacity pulmonary nodules. Int J Cancer 151(11):2020–2030. https://doi.org/10.1002/ijc.34238

Yu P, Chen W, Liu N, Yu Y, Guo H, Yuan Y, Guo W, Alatan Y, Zhao J, Su H, Nie S, Cui X, Miao Y (2025) Artificial Intelligence-Based Model Exploiting Hematoxylin and Eosin Images to Predict Rare Gene Mutations in Patients With Lung Adenocarcinoma. JCO Clin Cancer Inform 9(9):e2500093. https://doi.org/10.1200/CCI-25-00093.-DOI-PubMed

Yuan F, Huang F, Cao X, Zhang YH, Feng K, Bao Y, Huang T, Cai YD (2025) Integrative multi-omics machine learning reveals novel driver genes associations in lung adenocarcinoma. Biochim Biophys Acta Proteins Proteom 1874(1):141113. https://doi.org/10.1016/j.bbapap.2025.141113

Zhang X, Lv J, Wu Y et al (2020a) HER2 exon 20 insertion mutations in lung adenocarcinoma: case series and response to Pyrotinib. Front Oncol 31(10):1162. https://doi.org/10.3389/fonc.2020.01162

Zhang W, Li R, Zeng T, Sun Q, Kumar S, Ye J, Ji S (2020b) Deep model based transfer and multi-task learning for biological image analysis. IEEE Trans Big Data 6(2):322–333. https://doi.org/10.1109/tbdata.2016.2573280

Zhang H, Meng D, Cai S, Guo H, Chen P, Zheng Z, Zhu J, Zhao W, Wang H, Zhao S, Yu J, He Y (2021) The application of artificial intelligence in lung cancer: a narrative review. Transl Cancer Res 10(5):2478–2487. https://doi.org/10.21037/tcr-20-3398

Zhang T, Li X, Liu J (2022a) Prediction of the invasiveness of ground-glass nodules in lung adenocarcinoma by radiomics analysis using high-resolution computed tomography imaging. Cancer Control 1(29):10732748221089408. https://doi.org/10.1177/10732748221089408

Zhang DY, Liu J, Zhang Y, Ye JY, Hu S, Zhang WX, Yu DL, Wei YP (2022b) One-stage resection of four genotypes of bilateral multiple primary lung adenocarcinoma: a case report. World J Clin Cases 10(28):10301–10309. https://doi.org/10.12998/wjcc.v10.i28.10301

Zhang H, Goedegebuure SP, Ding L, DeNardo D, Fields RC, Chen Y, Payne P, Li F (2023) M3NetFlow: a novel multi-scale multi-hop graph AI model for integrative multi-omic data analysis. bioRxiv 6(15):545130. https://doi.org/10.1101/2023.06.15.545130

Zhang J, Zhou W, Li N, Li H, Luo H, Jiang B (2024a) Multi-omics analysis unveils immunosuppressive microenvironment in the occurrence and development of multiple pulmonary lung cancers. Npj Precis Oncol 8(1):155. https://doi.org/10.1038/s41698-024-00651-5

Zhang R, Wang D, Li JM (2024b) [Standardization of next-generation sequencing for detecting mutations associated with targeted therapy and immunotherapy based on dynamic pattern of expandable detection range]. Zhonghua Yi Xue Za Zhi 104(15):1211–1215. https://doi.org/10.3760/cma.j.cn112137-20240105-00032

Zhang X, Zhang G, Qiu X, Yin J, Tan W, Yin X, Yang H, Wang H, Zhang Y (2024c) Exploring non-invasive precision treatment in non-small cell lung cancer patients through deep learning radiomics across imaging features and molecular phenotypes. Biomark Res 12(1):12. https://doi.org/10.1186/s40364-024-00561-5

Zhang H, Miao L, Ma L, Sun X, Ouyang LN, Jing Y, Wang Y, Wang X, Wang P, Zhu L (2025a) Explainable machine learning for predicting invasiveness of pulmonary adenocarcinoma presenting as ground-glass nodules using CT images. Acad Radiol 10(22):S1076-6332(25)00960–2. https://doi.org/10.1016/j.acra.2025.10.004

Zhang R, Wang K, Wang S, Wang C, Cao T, Ci C, Xu M, Ge M (2025b) Multimodal deep learning model for prediction of breast cancer recurrence risk and correlation with oncotype DX. Breast Cancer Res 27(1):178. https://doi.org/10.1186/s13058-025-02129-z

Zhang H, Goedegebuure SP, Ding L, DeNardo D, Fields RC, Province M, Chen Y, Payne P, Li F (2025c) M3NetFlow: a multi-scale multi-hop graph AI model for integrative multi-omic data analysis. iScience 28(3):111920. https://doi.org/10.1016/j.isci.2025.111920

Zhao S, Cong X, Liu Z (2021) Mutation profile assessed by next-generation sequencing (NGS) of circulating tumor DNA (ctDNA) in Chinese lung adenocarcinoma patients: analysis of real-world data. Biomed Res Int 4(2021):8817898. https://doi.org/10.1155/2021/8817898

Zhao B, Wang X, Sun K, Kang H, Zhang K, Yin H, Liu K, Xiao Y, Liu S (2023a) Correlation between intranodular vessels and tumor invasiveness of lung adenocarcinoma presenting as ground-glass nodules: a deep learning 3-Dimensional reconstruction algorithm-based quantitative analysis on noncontrast computed tomography images. J Thorac Imaging 38(5):297–303. https://doi.org/10.1097/RTI.0000000000000731

Zhao C, Li J, Zhang Y, Han R, Wang Y, Li L, Zhang Y, Zhu M, Zheng J, Du H, Hu C, Zhou C, Yang N, Cai S, He Y (2023b) The rational application of liquid biopsy based on next-generation sequencing in advanced non-small cell lung cancer. Cancer Med 12(5):5603–5614. https://doi.org/10.1002/cam4.5410

Zhong W, Zhang W, Dai L, Chen M (2024) The clinical, radiological, postoperative pathological, and genetic features of nodular lung adenocarcinoma: a real-world single-center data. J Thorac Dis 16(5):3228–3250. https://doi.org/10.21037/jtd-24-510.-DOI-PubMed

Zhou G, Xu S, Liu X, Ge J, He Q, Cao W, Ding J, Kai X (2022) Relationship between the image characteristics of artificial intelligence and EGFR gene mutation in lung adenocarcinoma. Front Genet 4(13):1090180. https://doi.org/10.3389/fgene.2022.1090180

Zhou D, Li YQ, Liu QX, Deng XF, Chen L, Li MY, Zhang J, Lu X, Zheng H, Dai JG (2024) Integrated whole-exome and bulk transcriptome sequencing delineates the dynamic evolution from preneoplasia to invasive lung adenocarcinoma featured with ground-glass nodules. Cancer Med 13(11):e7383. https://doi.org/10.1002/cam4.7383

Zhou M, Wang J, Chen H, Tang W, Li C (2025) CT characteristics and their clinicopathological associations in ground-glass nodular multifocal lung adenocarcinoma. Medicine 104(17):e42145. https://doi.org/10.1097/MD.0000000000042145

Zhu P, Xu XJ, Zhang MM, Fan SF (2021) High-resolution computed tomography findings independently predict epidermal growth factor receptor mutation status in ground-glass nodular lung adenocarcinoma. World J Clin Cases 9(32):9792–9803. https://doi.org/10.12998/wjcc.v9.i32.9792

Zhu Y, Chen LL, Luo YW, Zhang L, Ma HY, Yang HS, Liu BC, Li LJ, Zhang WB, Li XM, Xie CM, Yang JC, Wang DL, Li Q (2023) Prognostic impact of deep learning-based quantification in clinical stage 0-I lung adenocarcinoma. Eur Radiol 33(12):8542–8553. https://doi.org/10.1007/s00330-023-09845-0.-DOI-PubMed

Zikri YKB, Helguera M, Cahill ND, Shrier D, Linte CA (2019) Toward an affine feature-based registration method for ground glass lung nodule tracking. VipIMAGE 10(34):247–256. https://doi.org/10.1007/978-3-030-32040-9_26.-DOI-PubMed

Zuo Z, Liu W, Zeng Y, Fan X, Li L, Chen J, Zhou X, Jiang Y, Yang X, Feng Y, Lu Y (2022) Multiparametric magnetic resonance imaging-derived deep learning network to determine ferroptosis-related gene signatures in gliomas. Front Neurosci 20(16):1082867. https://doi.org/10.3389/fnins.2022.1082867

Zuo Z, Zeng Y, Deng J, Lin S, Qi W, Fan X, Feng Y (2025) Intratumoral heterogeneity score enhances invasiveness prediction in pulmonary ground-glass nodules via stacking ensemble machine learning. Insights Imaging 16(1):209. https://doi.org/10.1186/s13244-025-02097-0