

Global Trends and Research Hotspots in Lung Cancer Radiomics: A Bibliometric Analysis From 2015 to 2025

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Background: Radiomics in lung cancer has experienced rapid development in recent years, yet its global research landscape and emerging hotspots remain insufficiently characterized. This study aims to systematically describe the development trends, contribution patterns, hotspot evolution, and emerging directions of lung cancer radiomics using bibliometric methods.

Methods: Literature related to “lung cancer radiomics” published between January 1, 2015, and December 31, 2025, was retrieved from the Web of Science Core Collection. Bibliometric analysis was conducted using the CiteSpace and R package bibliometrix. Metrics included annual publication output, national and institutional contributions, collaborative networks, author productivity, keyword clustering, co-citation networks, and hotspot evolution.

Results: A total of 2116 publications (376 reviews and 1740 articles) from 2015 to 2025 were included. China contributed the largest number of publications, whereas the United States showed the highest H-index and citation impact. Shandong First Medical University was the most productive institution, and Robert J. Gillies was the most prolific author. High-frequency keywords formed five clusters, summarizing four major research themes: diagnostic imaging modalities (computed tomography, positron emission tomography), application directions (classification, diagnosis), imaging indicators (textural features, signatures), and prognosis (survival, pulmonary nodules, prognostic value). Recent research hotspots focus on artificial intelligence-based computer-aided clinical applications and precision oncology.

Conclusion: Radiomics in lung cancer is undergoing rapid expansion, with research focus shifting toward artificial intelligence and bioinformatic imaging features. Enhancing research quality and international collaboration, particularly in China, is crucial for advancing the clinical translation of radiomics.

Keywords: lung cancer; radiomics; bibliometrics; Web of Science; CiteSpace

Introduction

Lung cancer is the most common malignancy in terms of both new cases and deaths worldwide [1,2,3]. Statistics indicate that in 2022 alone, there were 2.5 million new lung cancer diagnoses, accounting for approximately 12.4% of all new cancer cases globally, and resulting in about 1.8 million deaths (18.7%) [4]. Despite continuous advancements in lung cancer treatment strategies—including radiotherapy [5], targeted drugs [6], and immunotherapy [7]—which have elevated the 5-year survival rate for stage IA non-small cell lung cancer (NSCLC) patients to 73% [8,9], the survival rate for stage IV advanced patients remains only 13% [10]. Evidence indicates that early screening for lung cancer positively impacts patient prognosis [11,12]. Through the implementation of early screening measures, the proportion of Chinese lung cancer patients diagnosed at an early stage (Stage I) has increased from 46.3% to 65.6%, with the five-year survival rate rising to 90.4% [13].

Medical imaging technologies are widely applied in clinical settings for screening and diagnosing various dis-

eases, and play a crucial role in early screening and auxiliary diagnosis of patients with lung cancer [14,15]. With the advancement of high-throughput image analysis, radiomics has gained significant attention in recent years by extracting quantitative features from medical images, thereby providing new technical approaches for precise diagnosis, prognosis prediction, and treatment response evaluation of lung cancer [16,17,18,19]. Mark M Hammer [20] studied the detection of pulmonary nodules via chest computed tomography (CT) and found that solid nodules <6 mm carry a very low risk of malignancy. Wanling Li et al. [21] employed chest spiral CT technology and Shukun software to perform three-dimensional reconstruction of lesions, surrounding lung tissue, and trachea in patients. Their results demonstrated a sensitivity of 82.86% and specificity of 88.46% for diagnosing early-stage lung cancer. However, despite the growing number of related studies, significant variations persist across research projects in terms of image acquisition, feature extraction, model construction, and validation strategies. This leads to limitations in research reproducibility and clinical applicability. Concur-

rently, the research hotspots, development pathways, and global research landscape of radiomics in lung cancer have not yet been systematically summarized. Currently, there is a lack of comprehensive bibliometric research analyzing the overall trends, key contributors, collaborative networks, research themes, and future directions within this field.

This study conducts a systematic bibliometric analysis of lung cancer radiomics-related literature from 2015 to 2025 based on the Web of Science database. It aims to provide researchers with a better understanding of current research hotspots in this field, identify future development directions, support the academic community in optimizing resource allocation, and provide a theoretical foundation for technology transfer and industrial innovation.

Material and Methods

Source of Information

A systematic literature search was conducted in the Web of Science Core Collection (WoSCC) to identify studies related to lung cancer radiomics published between January 1, 2015, and December 31, 2025. The search strategy combined lung cancer-related terms (“lung cancer” OR “lung carcinoma” OR “lung tumor” OR “lung neoplasm” OR “cancer of lung” OR “carcinoma of lung” OR “tumor of lung” OR “neoplasm neoplasm”) with radiomics-related terms (“radiomics” OR “omics of radiation” OR “omics in radiation”) using the Topic field. Only English-language articles and reviews were included. All records, including full records and cited references, were exported in plain text format on February 6, 2026.

The inclusion criteria were as follows: (1) studies involving lung cancer; (2) studies related to radiomics; (3) publications written in English. The exclusion criteria were: (1) conference papers or data-only papers; (2) retracted publications; (3) studies without accessible full text; (4) publications lacking essential information, such as authors, keywords, or references. The literature retrieval and screening process was independently performed by three researchers. Articles were excluded if at least two reviewers agreed that they did not meet the inclusion criteria.

Literature Data Analysis

Literature data analysis was performed using R software (<https://www.r-project.org/>, Version 4.5.1) to conduct basic statistical analyses of publications meeting the inclusion and exclusion criteria. The bibliometrix R package (Version 4.3.2), accessed via the Bibliometric online analysis platform (<http://bibliometric.com/>), was used to analyze overall publication output, international collaboration networks, citation networks, and high-frequency authors and journals, followed by graphical visualization. In addition, CiteSpace software (Version 6.4.R1, <https://citespace.e.podia.com/>) was applied to perform co-occurrence analysis of institutions (with ≥ 5 publications), as well as key-

word co-occurrence, clustering, and burst analyses, and reference burst detection [22,23]. Network centrality values were calculated using CiteSpace [24], and the interpretation of the silhouette coefficient followed previously published methodological references [25]. Furthermore, VOSviewer (<https://www.vosviewer.com/>, Version 1.6.20) and the R package ggplot2 (Version 4.0.1) were used for additional visualization. Only institutions, authors, and keywords with an occurrence frequency greater than five were included in the analysis.

Results

Overall Characteristics of Posts

Through preliminary literature retrieval, a total of 2574 literature records were exported from the WoSCC database into EndNote 20 software. After excluding correspondence, conference abstracts, editorials, conference papers, revised manuscripts, news items, retracted manuscripts, books, and other document types, 2116 records were ultimately included. These comprised 376 reviews and 1740 articles. First, we conducted statistical analyses of the national and annual distributions of publications among all retrieved documents. Results revealed that 67 countries or regions published literature on lung cancer radiomics research (**Supplementary Table 1**). China led with 998 publications (47.16%), followed by the United States with 342 publications (16.16%). The third to fifth positions were occupied by Italy (150 publications, 7.09%), Korea (62 papers, 2.93%), and Canada (60 papers, 2.84%) (Fig. 1A). From 2015 to 2025, the total number of publications related to radiomics research in lung cancer showed an overall upward trend, with an annual growth rate of 43.1% (Fig. 1B).

Academic Influence Analysis

The H-index is a composite quantitative metric used to evaluate both the quantity and quality of a researcher’s academic output. Fig. 2 shows the H-index and citation frequency of the top ten countries in terms of published literature on lung cancer radio-omics research. In the WOS database literature search, the United States significantly outperformed other nations with an H-index of 83 and 29024 citations. China followed with an H-index of 53 and 13090 citations, while Italy ranked third with an H-index of 36 and 4449 citations.

Journals were ranked by publication volume and analyzed for impact factor (2024–2025), H-index, and Journal Citation Reports (JCR) quartile. Thirteen journals published ≥ 30 papers, accounting for 746 publications or 35.25% of the total literature (Table 1). The top three journals by publication volume were *Frontiers in Oncology* (172 papers), *Cancers* (93 papers), and *Scientific Reports* (65 papers). Eight journals are classified as Q1 in the JCR, with one each in Q2 and Q3. The *European Journal of Nu-*

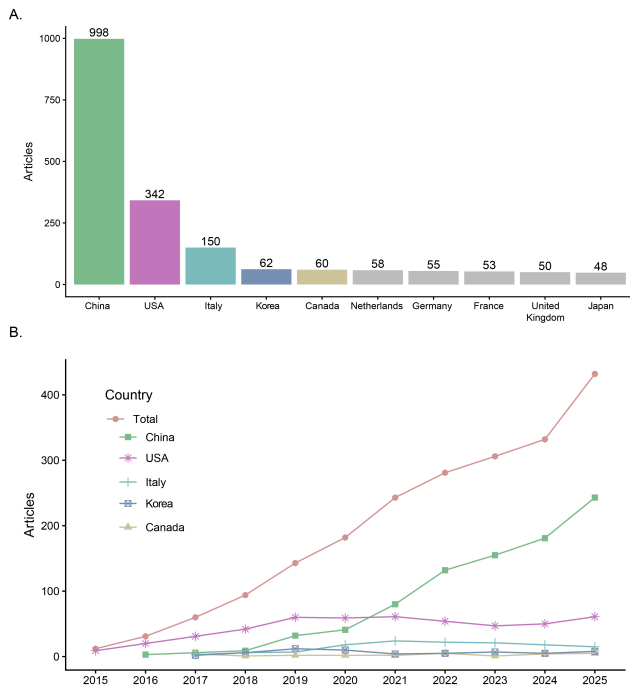


Fig. 1. National Publication Trends from 2015 to 2025. (A) Publication counts for the top ten countries. (B) Publication volume trends over time for the top five countries. Visualized using the R package “ggplot2”.

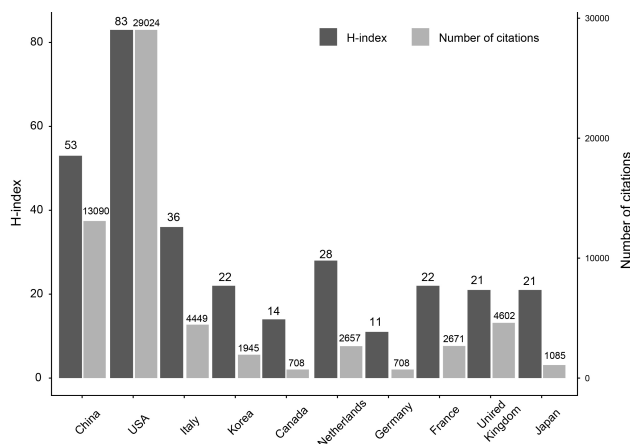


Fig. 2. Top 10 Countries by H-Index and Citation Frequency in Relevant Literature Publications from 2015 to 2025, visualized using the R package “ggplot2”.

clear Medicine and Molecular Imaging holds the highest impact factor (7.6). A co-citation analysis of journals using CiteSpace revealed that the top three journals in terms of centrality within this field were Radiology (0.06), Journal of Magnetic Resonance Imaging (0.06), and European Radiology (0.06).

Academic Cooperation Network

In the CiteSpace software, Nodetypes were set as Country and Institute, with a time span of 2015–2025, a

time slice of 1 year, and a Top 25 filter criterion. This yielded a visualization map of national/institutional collaborations in lung cancer radiomics research (Fig. 3). Results indicate relatively close collaboration among nations. The top three centrality rankings in this field are held by the United States (0.44), Italy (0.21), and the Netherlands (0.20), while China ranks seventh (0.13) (Fig. 3A). Institutional collaboration network analysis revealed Maastricht University (0.25), Stanford University (0.20), University of Texas System (0.11), University of London (0.11), and University of Pennsylvania (0.10) as core institutions with relatively dense collaborative networks (Fig. 3B). The top three institutions by publication volume were Shandong First Medical University (China, 88 papers), Maastricht University (Netherlands, 76 papers), and the University of Texas System (the United States, 69 papers) (Fig. 4A). Concurrently, the top three authors in this field by publication output are Robert J Gillies from H. Lee Moffitt Cancer Center and Research Institute (30 papers), Hugo J W L Aerts from Maastricht University (29 papers), and Matthew B Schabath from H. Lee Moffitt Cancer Center and Research Institute (29 papers) (Fig. 4B).

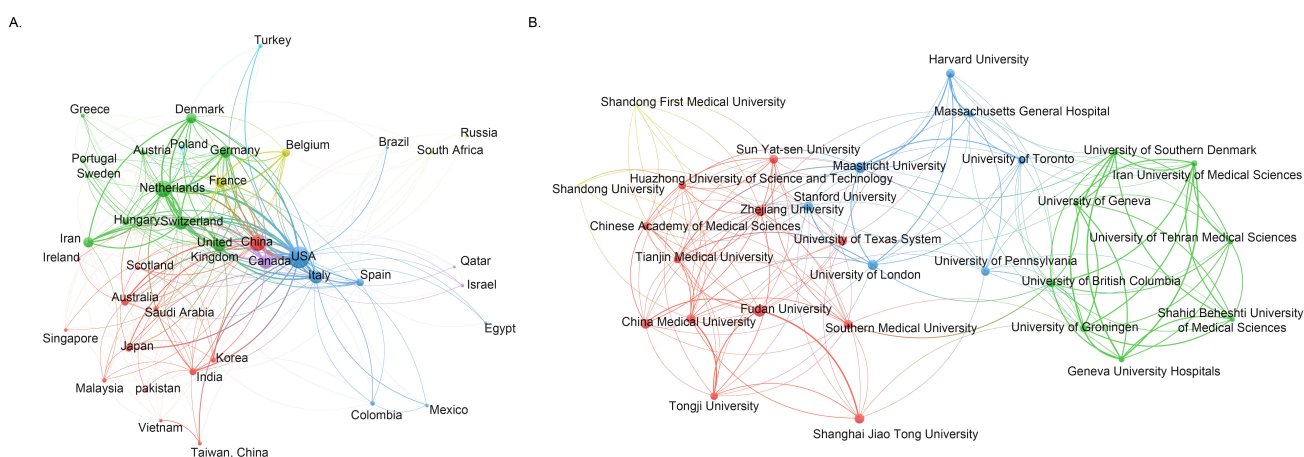
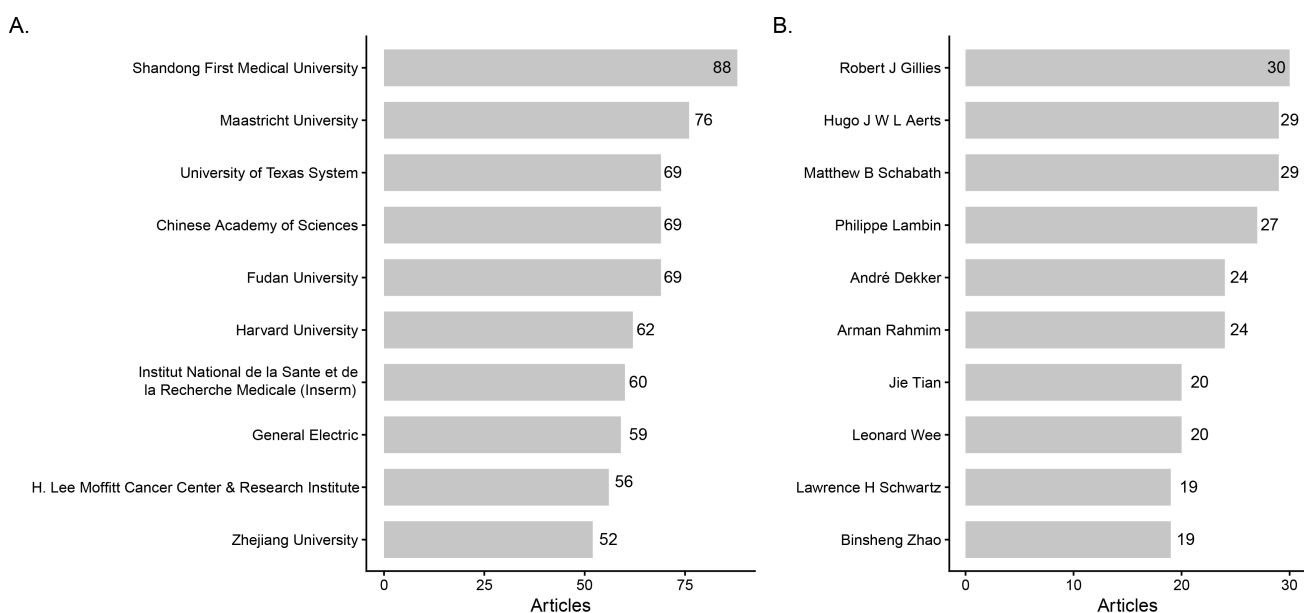
Keyword Co-Occurrence and Clustering

Co-occurrence keyword analysis reflects research hotspots in lung cancer radiomics. Setting “Node types” as keywords, with a time span of 2015–2025, annual time slices, and a top 30 selection criterion, yields a co-occurrence visualization of keywords related to lung cancer radiomics research. The results, as shown in Fig. 5A, indicate high levels of attention in this field toward diagnostic imaging modalities (computed tomography, positron emission tomography), application directions (classification, diagnosis), imaging indicators (textural features, signature, imaging biomarkers), and prognosis (survival, pulmonary nodules, prognostic value).

Cluster analysis of high-frequency keywords enables dimensionality reduction and integration of research directions, facilitating rapid identification of research hotspots. Cluster analysis of keywords using CiteSpace software identified five clusters with the largest ranges, displayed in Fig. 5B. Detailed classifications are provided in Table 2. Cluster 1 encompasses various diagnostic imaging techniques (e.g., FDG-PET, F-18-FDG PET, positron-emission-tomography); Cluster 2 primarily involves drugs used in combination radiotherapy (e.g., nivolumab, docetaxel, pembrolizumab); Cluster 3 focuses on prognosis and prognostic factor analysis in radiotherapy, involving patient survival, gene expression, biomarkers, and texture analysis; Cluster 4 relates to radiotherapy failure phenomena such as recurrence, invasion, and metastasis; Cluster 5 pertains to the application (e.g., diagnosis, management) and methodologies (e.g., artificial intelligence, feature selection, computer-aided diagnosis) of radio-omics.

Table 1. Top 10 Journals by Publication Volume in Lung Cancer Radiomics Research from 2015 to 2025.

Journal	Nation	Number of articles published	Impact factor (2024–2025)	H-index	JCR partition
Frontiers in Oncology	Switzerland	172	3.3	60	Q1
Cancers	Switzerland	93	4.4	53	Q1
Scientific Reports	The United Kingdom	65	3.9	149	Q1
Medical Physics	USA	61	3.2	159	Q1
Academic Radiology	USA	52	3.9	87	Q1
European Radiology	Germany	50	4.7	134	Q1
Translational Lung Cancer Research	Hong Kong, China	43	3.5	-	Q1
Journal of Thoracic Disease	China	40	1.9	45	Q3
Diagnostics	Poland	38	3.3	-	Q2
European Journal of Nuclear Medicine and Molecular Imaging	Germany	36	7.6	153	Q1

**Fig. 3. National and Institutional Collaboration Networks for WOS Lung Cancer Radiomics Research Literature from 2015 to 2025. (A) National collaboration network. (B) Institutional collaboration network. Networks were visualized using VOSviewer software.****Fig. 4. Publication Output of Institutions and Authors in WOS Lung Cancer Radiomics Research from 2015 to 2025. (A) Publishing Institutions. (B) Publishing Authors. Visualization was performed using the R package “ggplot2”.**

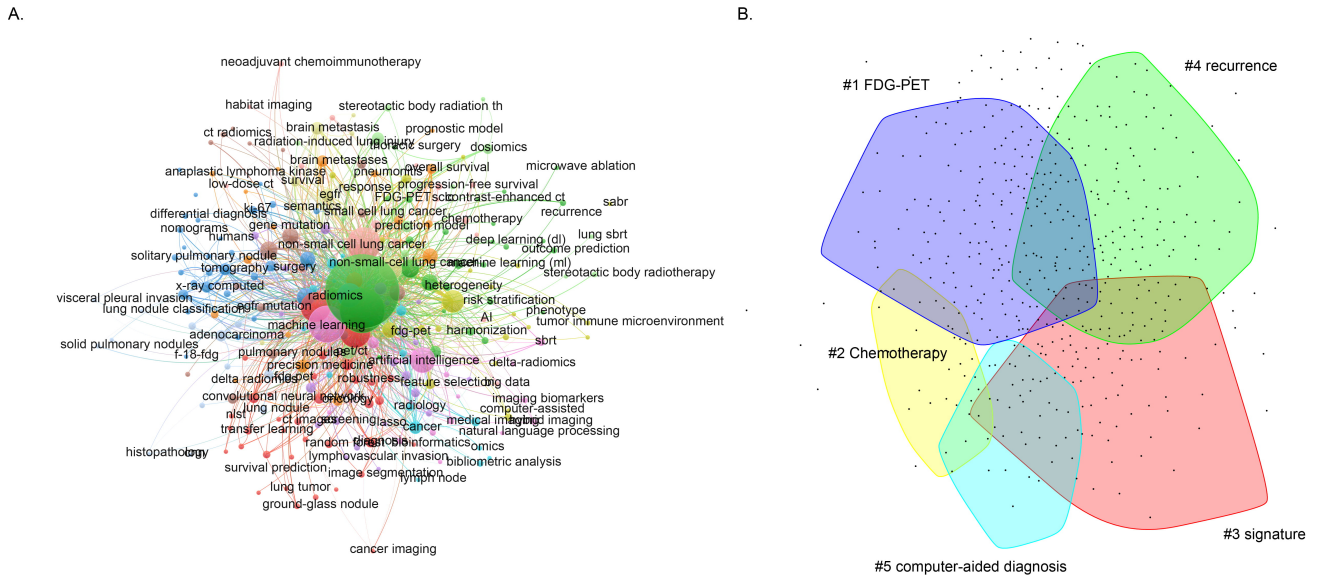


Fig. 5. Knowledge map of co-occurring keywords and five major clusters in WOS lung cancer radiomics research literature from 2015 to 2025. (A) Keyword co-occurrence network. (B) Five keyword clusters. Visualization was performed using CiteSpace and VOSviewer software.

Table 2. Five primary clusters of co-occurring keywords.

Clusters	Cluster size	Conformity coefficient (Silhouette)	Label (Log-Likelihood Ratio, LLR)
1	135	0.9684	FDG-PET; positron-emission-tomography; F-18-FDG PET; textural features
2	26	0.9534	Chemotherapy; nivolumab; docetaxel; pembrolizumab; crizotinib
3	173	0.9167	texture analysis; expression; biomarker; outcomes; signature; survival; imaging biomarkers
4	65	0.9235	recurrence; differentiation; resection; tumor spread; invasion
5	99	0.8110	Diagnosis; management; segmentation; machine learning feature-selection; computer-aided diagnosis; artificial-intelligence

Note: The silhouette coefficient ranges from −1 to 1. The closer the value is to 1, the clearer the theme of the cluster and the more similar the content of the clustered articles.

Research Hot Spots and Evolutionary Trends

The lung cancer radiomics research keyword timeline partially reflects shifts in related studies (Table 3). Based on the median year of keyword occurrence in publications, no significant keyword hotspots were observed in 2015 and 2016. In 2017, the field was in its initial stage, with primary focus on the three keywords: image features, fractal analysis, and learning health-care. In 2018, the hot keywords were CT texture and FDG-PET. Between 2019 and 2020, academic activities were increasingly concentrated on F-18-FDG PET, tumor heterogeneity, and texture analysis. During 2021–2022, the four keywords—features, images, CT, and survival—were widely mentioned. In 2023, machine learning emerged as the most prominent hotspot. In 2024, greater attention shifted toward the combined application of PET and CT. From 2025 to the present, key research areas have included the clinical application of computer-aided approaches represented by artificial intelligence and precision oncology.

The analysis of highly cited literature also reflects a notable shift in research interests within the field of lung cancer radiomics. The top 20 highly cited references from 2015 to 2025 are listed in Fig. 6. Among these, “Decoding tumor phenotype by noninvasive imaging using a quantitative radiomics approach” exhibits the highest citation intensity (80.1314) [26]. This work explored the association between radiomics features and tumor molecular/-pathological phenotypes, developing a quantitative analytical framework to noninvasively decode tumor phenotypes through imaging. We also note that three papers concerning FDG-PET: one addressed test-retest variability and inter-observer variability of radiomics features [27]; another investigated the prognostic value of 18F-FDG PET texture features for treatment response (RECIST criteria) and survival outcomes (OS, PFS, LPFS) in NSCLC patients following chemoradiotherapy [28]; and a third demonstrated that SUV discretization methods significantly impact the stability and clinical predictive value of FDG-PET texture

Table 3. Timeline of relevant research keywords in lung cancer radiomics research.

Term	Frequency	Year (Q1)	Year (Median)	Year (Q3)
Image features	9	2017	2017	2018
Fractal analysis	8	2016	2017	2019
Learning health-care	5	2017	2017	2017
CT texture	15	2018	2018	2021
FDG-PET	15	2017	2018	2019
Textural features	84	2018	2019	2020
Reproducibility	83	2018	2019	2021
F-18-FDG PET	77	2018	2019	2021
Texture analysis	199	2019	2020	2022
Heterogeneity	161	2019	2020	2023
Tumor heterogeneity	104	2018	2020	2022
Features	364	2020	2021	2023
Images	338	2020	2022	2023
CT	311	2020	2022	2023
Survival	300	2020	2022	2024
Machine learning	325	2021	2023	2025
PET/CT	76	2020	2024	2025
Efficacy	10	2023	2025	2025
Artificial Intelligence (AI)	9	2024	2025	2025
Precision oncology	9	2025	2025	2025

features [29]. Furthermore, recent studies, “The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping Introduction” [30] and “Introduction to Radiomics” [16] focus on establishing a comprehensive system encompassing technical specifications, quality control, and cross-center collaboration. These studies systematically address standardization challenges in radiomics research and outline a full-chain methodology from image acquisition and feature analysis to clinical application. The aforementioned references also reflect the current hot topics in lung cancer radiomics research.

Discussion

Global Publication Trends and Academic Influence

This study indicates that from 2015 onward, the field of lung cancer radiomics research entered a phase of rapid growth, following a period of very limited output prior to 2015. The annual number of publications has shown a sustained upward trend, reflecting the expanding research interest in this domain. This growth is closely associated with the widespread adoption of low-dose CT screening, increased availability and sharing of imaging data, and the extensive application of artificial intelligence and machine learning methods. It also underscores the substantial global attention devoted to lung cancer radiomics research over the past decade.

China and the United States have consistently been the leading contributors worldwide, publishing 998 (47.16%) and 342 (16.16%) papers, respectively, accounting for a

substantial proportion of the total output. However, analysis of the H-index and citation frequency reveals a noticeable disparity in academic influence. The United States achieved an H-index of 83 with 29,024 citations, whereas China had an H-index of 53 with 13,090 citations. Although Chinese scholars have produced a considerable volume of publications, there is still room to improve their citation impact and overall global academic influence. Future efforts should therefore emphasize not only publication quantity but also research quality, methodological rigor, and international collaboration.

Differences in Academic Cooperation Patterns and Research Ecology

With the advancement of international academic exchange, collaborative research has increasingly emerged among diverse countries and institutions. Network analysis reveals a relatively well-established international cooperation framework within the field of lung cancer radiomics. At the national level, the United States, Italy, and the Netherlands demonstrate the highest centrality within the collaborative network, indicating their prominent roles in cross-center cooperation and global research connectivity. Although China ranks first in publication output, its collaborative centrality is relatively lower (0.13), suggesting that research activities may rely more heavily on domestic collaboration than extensive international partnerships. Strengthening international cooperation may further enhance its global academic influence and translational impact.



Fig. 6. The top 20 citations for research related to lung cancer radiomics research in WOS from 2015 to 2025, visualized by the R package “ggplot2”.

At the institutional level, Maastricht University, Stanford University, the University of Texas System, the University of London, and the University of Pennsylvania serve as core collaborative nodes within the global network. In terms of publication output, Shandong First Medical University (88 papers), Maastricht University (76 papers), and the University of Texas System (69 papers) rank among the leading institutions. The most productive authors include Robert J. Gillies from H. Lee Moffitt Cancer Center and Research Institute (30 papers), Hugo J. W. L. Aerts from Maastricht University (29 papers), and Matthew B. Schabath from H. Lee Moffitt Cancer Center and Research Institute (29 papers), all of whom have made sustained contributions to the methodological development and clinical translation of radiomics research.

High-output institutions exhibit distinct research orientations, reflecting differences in technological resources and scientific priorities. Shandong First Medical University has mainly focused on the prognostic application of radiomics in lung cancer, including studies exploring imaging heterogeneity to predict treatment response after microwave ablation [31]. Maastricht University has emphasized algorithm development and imaging-based pathological classification [32,33], whereas the University of Texas System has concentrated more on predicting therapeutic benefit and clinical outcomes using radiomics models [34].

These diverse research strategies demonstrate how methodological refinement combined with clinical translation continues to shape the advancing research landscape of lung cancer radiomics.

Research Hotspot Evolution and Topic Structure

Keyword and cluster analyses indicate that lung cancer radiomics research primarily encompasses four major directions: diagnostic imaging modalities, application domains, imaging metrics, and prognostic value. The evolution of research themes demonstrates a clear developmental trajectory. Early-stage studies mainly focused on the exploration of imaging features, including CT texture and fractal analysis. Subsequent research expanded to the application of FDG-PET, with particular emphasis on textural features and reproducibility, followed by increased attention to tumor heterogeneity and the combined application of PET/CT technologies. In recent years, research hotspots have increasingly concentrated on the clinical integration of radiomics with computer-aided approaches represented by artificial intelligence and machine learning.

Methodological Challenges and Future Directions

The development of FDG-PET holds significant importance for radiomics research. This technology, formally known as 2-deoxy-2[18F]-fluoro-D-glucose positron

emission tomography/computed tomography (18F-FDG PET/CT), is widely applied across multiple radiomics domains, including lung cancer staging, treatment response evaluation, and minimally invasive endoscopic biopsy [28, 35]. The paper “Stability of FDG-PET Radiomics Features: An Integrated Analysis of Test-Retest and Inter-Observer Variability” by Ralph T. H. Leijenaar and colleagues [27] has been extensively cited. This study emphasizes that when utilizing FDG-PET imaging for treatment monitoring, prognostic prediction, or imaging biomarkers, the robustness and reliability of the metrics must be considered. Selecting more stable features from repeated PET imaging sessions yields greater stability in clinical applications [27].

The integration of artificial intelligence has significantly advanced lung cancer radiomics, enhancing not only feature extraction efficiency but also the predictive performance of models. Ashley Elizabeth Prosper and colleagues [36] noted in a review that AI can assist in analyzing medical images, aiding clinicians in lung cancer diagnosis. Annarita Fanizzi et al. [37] utilized radiological features from CT images of 535 lung cancer patients, combined with AI algorithms, to construct a predictive model for metastasis risk in lung cancer, achieving an accuracy rate of 0.78. However, the clinical adoption of AI remains constrained by multiple factors, including data heterogeneity, insufficient cross-center reproducibility, weak model interpretability, inadequate external validation, and algorithmic black-box issues. Alessia Artesani et al. [38] argue that limited data availability, accessibility, and interoperability may hinder the integration of AI-driven tools into clinical workflows. Furthermore, the opacity of AI models makes their decision-making processes challenging for healthcare professionals to understand and explain.

Research Limitations and Prospects

This study has certain limitations: First, the literature included in the analysis was retrieved solely from the Web of Science Core Collection (WOSCC) database, excluding other academic databases such as Google Scholar, Embase, and Scopus, which may have resulted in incomplete literature retrieval. Second, only English-language publications were included, which may introduce language bias.

In addition, there are methodological limitations inherent to bibliometric analysis. Analysis results from CiteSpace and Bibliometrix depend on parameter selection (e.g., thresholds, slice length), and these different settings may yield minor variations. Furthermore, differences in software versions may also influence calculated metrics, including centrality measures and clustering performance. Although standardized parameters were applied in this study to ensure reproducibility, minor variations may occur under different analytical conditions.

Moreover, bibliometric analysis is primarily based on quantitative indicators, such as publication counts, citation frequency, and centrality metrics, which cannot fully

reflect research quality, methodological rigor, or clinical applicability. Future research could integrate multiple databases, incorporate qualitative assessment approaches, and combine bibliometric analysis with systematic reviews to achieve a more comprehensive understanding of the field.

Conclusion

In summary, this bibliometric study systematically analyzed the development trends, research hotspots, and collaborative patterns in lung cancer radiomics from 2015 to 2025. The field has evolved from early exploration of imaging features to broader integration of FDG-PET applications, tumor heterogeneity analysis, and combined PET/CT technologies, with recent emphasis on artificial intelligence-assisted clinical applications and precision oncology. Although rapid growth in publications reflects increasing global interest, challenges such as standardization, reproducibility, and multi-center validation remain. Strengthening methodological consistency and international collaboration will be essential to enhance the clinical translation of lung cancer radiomics.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

HFQ: Conceptualization, Formal analysis, Investigation, Methodology, Software, Visualization, Writing—original draft. JKZ: Resources, Data curation, Validation, Supervision, Writing—review & editing. Both authors gave final approval of the version to be published. Both authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.24976/Descov.Med.202638213.243>.

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