Understanding the research trend and evolution in radiogenomics (2005-2023): A bibliometric analysis

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Abstract

Background: Radiogenomics has emerged as a field that links medical imaging (radiomics) with molecular pathology (genomics), including proteomics and metabolomics. It utilizes radiomics to improve disease diagnosis, predict prognosis, evaluate treatment efficacy, and analyze outcomes. This study aims to examine the current research status and highlight the dynamic changes in hotspots within radiogenomics research.

Objective: Radiogenomics has emerged as a field that links medical imaging (radiomics) with molecular pathology (genomics), including proteomics and metabolomics. It utilizes radiomics to improve disease diagnosis, predict prognosis, evaluate treatment efficacy, and analyze outcomes. This study aims to examine the current research status and highlight the dynamic changes in hotspots within radiogenomics research.

Methods: Visual software Vosviewer and Citespace were employed to analyze the data in this study. Vosviewer was used to assess the frequency of keywords, while Citespace was utilized to analyze countries, institutions, journals, co-citations, reference clusters, timeline views, and keyword bursts. The number of published documents was counted using Excel.

Results: The United States and China are the leading contributors to this field, with the largest number of co-citations and published articles, respectively. The co-occurrence map of keywords indicates a recent prevalence of machine learning, deep learning, and artificial intelligence. The reference co-citations resulted in 11 clusters, including radiomics, glioma, breast cancer, EGFR, radiotherapy, normal tissue toxicity, glioblastoma, rectal cancer, immunotherapy, oncologic imaging, and deep learning.

Conclusions: The United States and China are the leading contributors to this field, with the largest number of co-citations and published articles, respectively. The co-occurrence map of keywords indicates a recent prevalence of machine learning, deep learning, and artificial intelligence. The reference co-citations resulted in 11 clusters, including radiomics, glioma, breast cancer, EGFR, radiotherapy, normal tissue toxicity, glioblastoma, rectal cancer, immunotherapy, oncologic imaging, and deep learning.

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Understanding the research trend and evolution in radiogenomics (2005-2023): A bibliometric analysis

Abstract

Background: Radiogenomics is an emerging technology that integrates genomics and medical image-based radiomics. It is considered as a promising approach towards precision medicine.

Objective: This study aims to quantitatively analyze the research status, dynamic trend and evolutionary trajectory in radiogenomics field uing bibliometric methods.

Materials and Methods: The relevant literatures up to 2023 were retrieved from WoSCC. Excel was used to analyze the annual publication. VOSviewer was employed for constructing the keywords co-occurrence network, collaboration networks among countries and institutions, CiteSpace for conducting citation keywords burst analysis and references timeline view.

Results: A total of 3237 papers were included and exported in “plain text” format. The annual number of publications showed an increasing trend yearly. China and USA published the most papers, with the highest number of citations in USA and the highest average per item in Netherlands. Keyword burst analysis revealed that keywords such as big data, magnetic resonance spectroscopy, renal cell carcinoma, stage, temozolomide have shown citation burst in recent years. The timeline views demonstrated the references can be categorized into 8 clusters: lower-grade glioma, lung cancer histology, lung adenocarcinoma, breast cancer, radiation-induced lung injury, EGFR mutation, late radiotherapy toxicity and artificial intelligence.

Conclusion: The field of radiogenomics is attracting increasing attention from researchers worldwide, with the USA and Netherlands being the most influential country. Artificial intelligence method based on big data to predict the response of tumors to various treatment methods is the research hot topic in this field at present.

Keywords: bibliometric, radiogenomics, multi-omics, genomics, radiomics

Introduction

Radiogenomics is an emerging technology that combines radiomics and genomics, with the ultimate goal of improving the prognosis and outcomes[1]. It can investigate the relationship between imaging features and gene mutations and expression patterns[2-4]. Unlike traditional gene sequencing methods, which contain inherent drawbacks such as invasive and cost-expensive, radigenomics provides a non-invasive, convenient and cost-effective method by using quantitative imaging parameters extracted from the entire lesions[5,6]. Many scholars have demonstrated that radiogenomics may predict the pathologic type, prognosis, and outcome of cancers such as lung cancer and liver cancer based on pre-treatment multimodal imaging (CT or MRI)[7-10]. For non-tumor diseases, this technology has also been proposed as a biomarker for diagnosis, classification, and prognostic assessment in coronary heart disease[11].

Radiogenomics is an important potential tool for precision medicine. Some review articles summarized the routine process of radiogenomics and its various applications in disease[12,13]. However, they usually focus on presenting the research directions rather than analyzing the dynamic changes in the field, and they only analyzed the process and application status of radiogenomics. Bibliometrics can quantitatively analyze the country, institution, author, keyword and other information of all literatures in a specific field. It can also visually display the dynamic progress in the field through network mapping[14]. This study aims to summarize the research status and the dynamic changes of research hot topics over time by bibliometric methods, thus helping researchers gain a comprehensive understanding of radiogenomics.

Materials and Methods

Bibliometric Data Acquisition

The literatures on radiogenomics were retrieved from Web of Science Core Collection (WoSCC), the most widely used database in bibliometric analysis, at March 1, 2024[15]. The first relevant article was published in 2005 during initial search phase, hence, we restricted the publication phase to 2005-2023. The search term was: (TS= (Radiogenomics) OR TS= (Radiomics AND genomics) OR TS= ((Radiomics) AND (gene* OR DNA OR RNA OR expression OR mutation OR molecular subtype))) AND FPY= (2005-2023).

The literature retrieval and refining were carried out by one author, and the rest of the authors supervised the whole process. A total of 3669 documents were retrieved. The refine function of the WOS website was used to screen the language and document type of the retrieved documents sequentially. The exclusion criteria were as follows: ①document type is not article or review article(e.g. proceeding paper, meeting abstract editorial material). ②articles written in languages other than English (e.g. Japanese, Chinese). There were 420 papers excluded due to document type and 12 papers due to language. 3237 papers were remained and exported in “plain text” format. The corresponding countries, institutions, authors and journals information in WOS website were recorded. See supplementary materials 1 for the original data.

Data analysis and visualization

After detecting duplicate documents using CiteSpace (version 6.3.R1). Excel 2016, CiteSpace and VOSviewer (version 1.6.19.0) were used to conduct bibliometrics analysis. Excel was used to analyze the annual publications. VOSviewer was utilized to generate visualization networks of keywords co-occurrence, countries and institutions collaboration. The network conducted with keywords/countries/institutions as nodes. The thickness of the line connecting nodes indicated the strength of association. The betweenness centrality (BC) parameter was used to assess the importance of each node in the network. A higher BC value signifies greater importance in the network[16].

CiteSpace was utilized to conduct citation burst of keywords and timeline of references by keywords. The burst detection can detect the citation burst of a specific keyword (or document) within a certain field at least within a short phase of time during the time frame[17]. Keywords with a burst of occurrences are indicators of hot topics. According to the instructions of CiteSpace (How to Use CiteSpace, Chaomei Chen), the timeline of reference clusters is an analysis based on references for the exported literature. CiteSpace can extract noun phrases from the titles, keyword lists, or abstracts of articles that cited the particular cluster. The automatically selected labels will be displayed and the clusters are numbered in the descending order of the cluster size, starting from the largest cluster #0, the second largest #1, and so on. The network characterizes the development of the field over time, showing the most important footprints of the related research activities.

Certain data, including the number of publications, impact factor (IF), H-index and average per item of journals, countries and authors, was retrieved from the WOS website. The H-index and average per item were used in the country, institution, and author analyses. H-index was introduced by Jorge Hirsch and used as a scientific contribution metric corresponding to the number of times papers cited[18]. The average per item is calculated by dividing the total number of citations by the number of publications, resulting in the average number of citations per publication.

Synonym substitution of keywords

The keywords with the same meaning were merged by synonym substitution. For example, terms like computed tomography, computed tomography (ct), computed-tomography, ct and ct images were uniformly labeled as CT. More details were shown in supplementary materials 2. For a workflow of the analytical procedures (Figure 1).

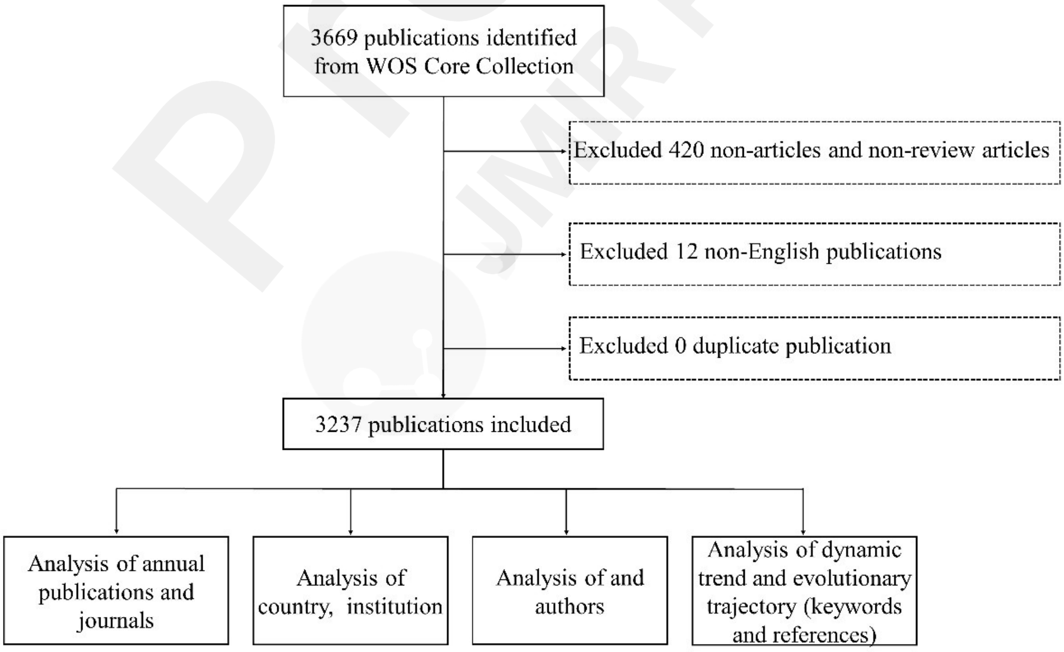


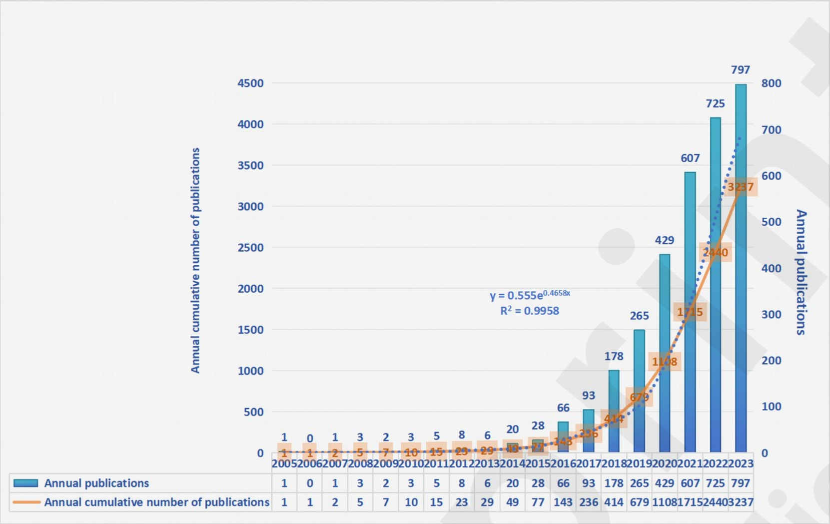
Figure 1. Workflow of the analytical procedures

Results

Analysis of Annual Publications

A total of 3237 papers were included for the final analysis. No duplicate literature was found. There has been a clear upward trend in research on radiogenomics since 2013 (Figure 2).

Figure 2. Global trend of publications on radiogenomics from 2005-2023



Analysis of journals

Table 1 presents the top 15 journals with the most publications on radiogenomics. Frontiers in Oncology, Cancers, and European Radiology were the top three journals with 284, 196, and 135 papers, respectively. Radiology got the most citations.

Table 1. Top 15 journals with the most publications on radiogenomics.

Rank	Journal	Documents	IF (2022)	Citations	
				Journal	IF (2022)
1	Frontiers in Oncology	284	4.7003	Radiology	19.7005
2	Cancers	196	5.5999	European Radiology	5.9003
3	European Radiology	135	5.9003	Scientific Reports	4.6
4	Scientific Reports	103	4.6	Frontiers in Oncology	4.7003
5	Diagnostics	73	3.5999	Clinical Cancer Research	11.5003
6	Medical Physics	63	3.800	Journal of Clinical	45.3008

			1	Oncology	
7	Journal of Magnetic Resonance Imaging	60	4.3997	Plos One	3.7001
8	European Journal of Radiology	57	3.3	Journal of Magnetic Resonance Imaging	4.3997
9	Academic Radiology	50	4.8003	International Journal of Radiation Oncology Biology Physics	6.9997
10	Physics in Medicine And Biology	49	3.5	New England Journal of Medicine	158.4985
11	British Journal of Radiology	45	2.6002	Radiotherapy and Oncology	5.6998
12	Radiology	41	19.7005	Medical Physics	3.8001
13	European Journal of Nuclear Medicine and Molecular Imaging	40	9.1005	European Journal of Nuclear Medicine and Molecular Imaging	9.1005
14	Abdominal Radiology	34	2.4002	Journal of Nuclear Medicine	9.2994
15	BMC Medical Imaging	33	2.7001	Neuro-oncology	15.9004

Analysis of Country and Institution

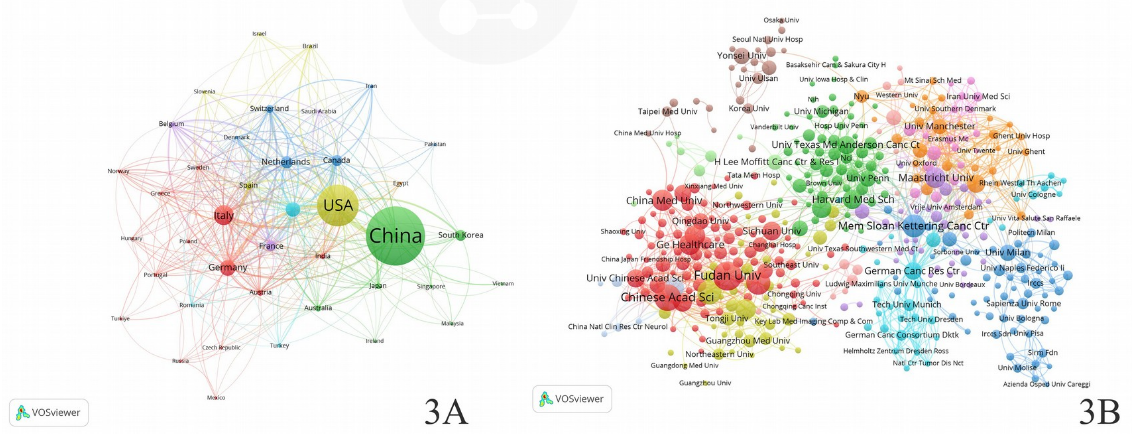
A total of 71 countries have published articles related to radiogenomics. Table 2 highlights the top 10 countries in terms of number of publications. China ranks first with 1470 articles, followed by the United States of America (USA) with 891, and Italy with 326. USA obtained the highest citation count and the second highest average citation per item. Only three countries, Netherlands(99.86) , USA(52.11) and Canada(51.46), have average citations per item >50, with the Netherlands in particular significantly higher than other countries. Six countries, including USA, England, Italy, Canada, China, and Netherlands, have a high BC value (≥0.1).

Table 2 Top 10 productive countries with the most publications

Rank	Total link strength	BC	Countries	Count	H-index	Times Cited	Average Per Item
1	329	0.11	China	1470	68	25319	17.22
2	820	0.36	USA	891	87	46426	52.11
3	311	0.13	Italy	326	41	7327	22.48
4	353	0.06	Germany	233	39	7966	34.19
5	418	0.19	England	209	37	6185	29.59
6	328	0.1	Netherlands	161	37	16077	99.86
7	54	0.01	South korea	142	31	4296	30.25
8	248	0.12	Canada	140	36	7204	51.46
9	223	0.08	France	128	32	4099	32.02
10	181	0.01	Switzerland	88	23	1893	21.51

*BC, betweenness centrality; USA, United States of America

A total of 71 countries/regions have contributed to radiogenomics research, 40 of them published≥5 documents. Figure 3A presents the visualization of the countries co-authorship network. A total of 3523 institutions have contributed to radiogenomics research, 432 institutions published ≥5 documents. Figure 3B presents the visualization of the institions co-authorship network. There is more cooperation between developed countries and their institutions.



3A 3B

Figure 3. Countries (3A) and institutions (3B) collaboration network in the field of radiogenomics. * The size of the nodes corresponds to the number of published documents, while the line width between nodes indicates the strength of co-authorship. Thicker lines indicate a higher frequency of cooperation.

Analysis of Authors

A total of 17,727 authors had contributed to radiogenomics. Table 3 presents the top 10 productive authors and most cited authors. The authors with the most publications are Lambin Philippe (33papers), West Catharine M (32papers) and Gillies Robyn (32papers). Three of the top 10 productive authors, including Lambin Philippe (Netherlands), Gillies Robyn (Australia) , and Aerts Hugo (USA) obtained top 3 citation times.

Table 3. Top 10 productive and cited authors on radiogenomics

	Publications					Citations		
Rank	Author	Count	Country	H-index	Average Per Item	Author	Citations	Country
1	Lambin, Philippe	33	Netherlands	21	358.06	Lambin, Philippe	1573	Netherlands
2	West, Catharine M	32	England	17	44.78	Gillies, Robyn	1109	Australia
3	Gillies, Robyn	32	Australia	24	486.13	Aerts, Hugo	965	USA
4	Sala, Evis	26	Italy	17	35.92	Van Griethuysen, jjm	720	USA
5	Dekker, Andre	25	Netherlands	12	448.4	Zwanenburg, Alex	597	Germany
6	Tian, Jie	25	China	14	48.04	Parmar, Chintan	448	USA
7	Sarah L. Kerns	25	USA	17	44.72	Louis, David N.	429	USA
8	Aerts, Hugo	24	USA	21	526.42	Kickingereder, Philip	390	Germany
9	Duan, Shaofeng	24	China	11	12.67	Yan-Qi Huang	382	China
10	Lee, Seung-Koo	22	South Korea	10	23.91	Vinod Kumar	376	India

Analysis of keywords

There were 7624 keywords in this study and 466 keywords appeared more than 9 times. Figure 4 presents an overlay visualization map of the co-occurrence keywords.

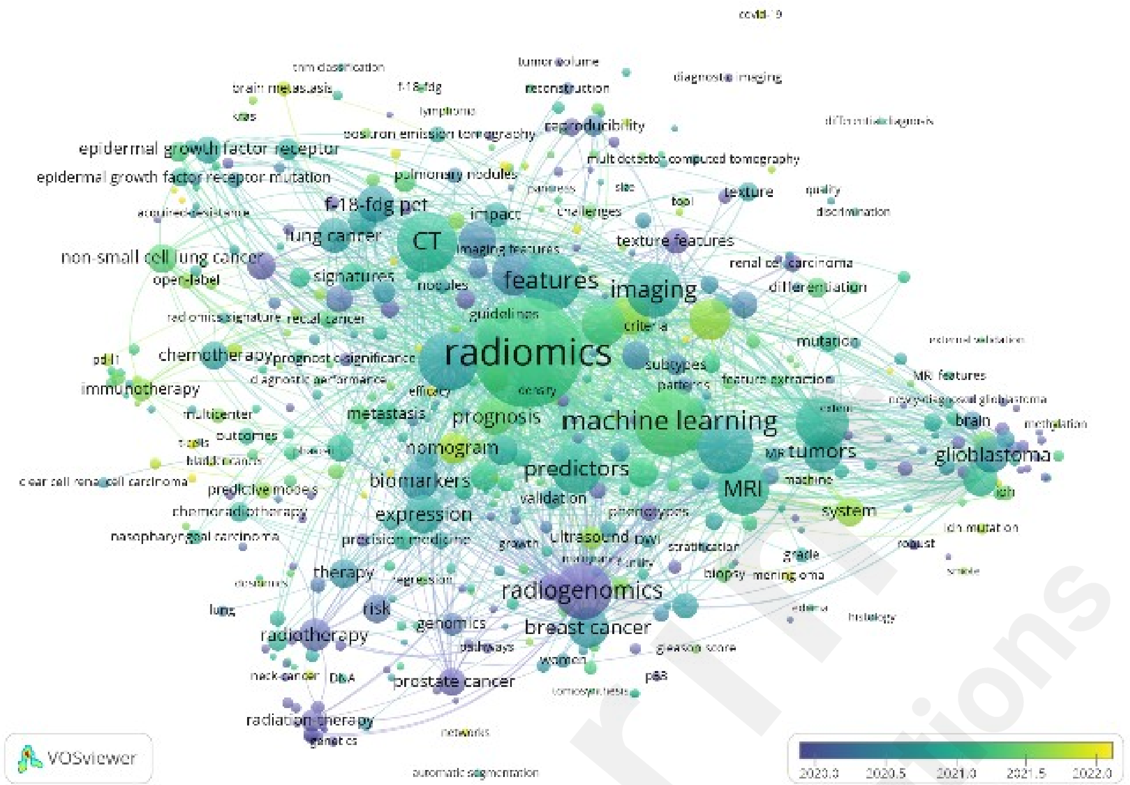


Figure 4. Overlay visualization map of keywords. *The node size indicates the frequency of keyword occurrences, while the color represents the average publication year of the identified keywords.

Table 4 presented the top 30 keywords based on their occurrence frequency. Apart from "radiomics" and "radiogenomics", the most frequent keyword is " machine learning " (n = 779), followed by " CT " (n = 580) and " carcinoma " (n = 569).

Table 4. The top 30 keywords with the highest frequency on radiogenomics

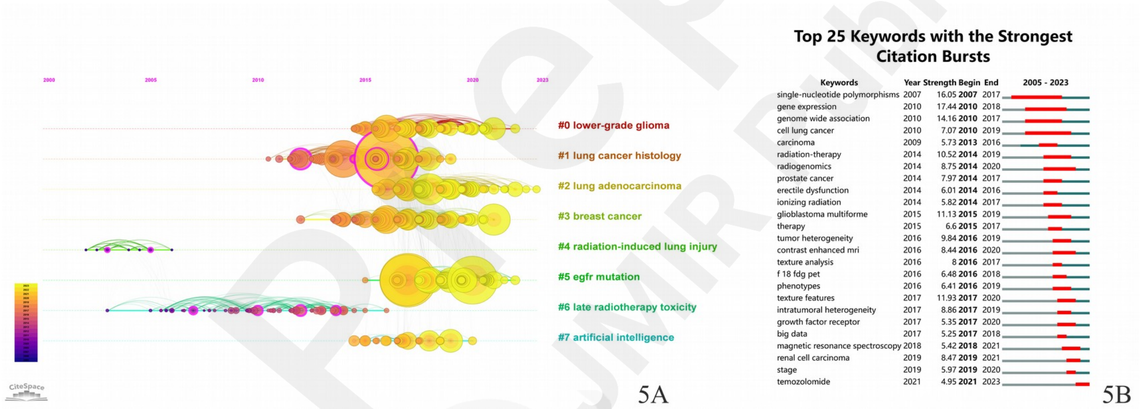
Rank	Keywords	Total Link Strength	Frequency	Rank	Keywords	Total Link Strength	Frequency
1	radiomics	13538	1918	16	breast cancer	1958	260
2	machine learning	5816	779	17	artificial intelligence	2074	254
3	CT	4300	580	18	expression	1906	242
4	carcinoma	4250	569	19	biomarkers	1906	240
5	features	4279	538	20	heterogeneity	1902	227
6	radiogenomics	4102	535	21	f-18-fdg pet	1874	225
7	survival analysis	3984	500	22	prognosis	1670	219
8	imaging	3650	478	23	glioblastoma	1806	212
9	classification	3367	439	24	gliomas	1611	198
10	MRI	3323	423	25	lung cancer	1485	193
11	predictors	3427	416	26	radiotherapy	1258	175
12	diagnosis	2247	310	27	nomogram	1228	167
13	texture analysis	2489	303	28	models	1083	152
14	deep learning	2076	273	29	recurrence	1329	152
15	tumors	2095	271	30	system	983	144

Analysis of keywords burst and References cluster

The top 25 keywords with the strongest citation bursts are depicted in Figure 5A.

The top 3 keywords with strongest citation bursts were gene expression (17.44), single nucleotide polymorphism (16.05) and genome-wide association (14.16). The keywords including big data, magnetic resonance spectroscopy, renal cell carcinoma, stage, temozolomide show citation burst in recent years. Figure 5B illustrates the reference clusters along horizontal timelines. CiteSpace generated 8 clusters, #0 lower-grade glioma , #1 lung cancer histology, #2 lung adenocarcinoma, #3 breast cancer, #4 radiation-induced lung injury, #5 EGFR mutation, #6 late radiotherapy toxicity , #7 artificial intelligence.

Based on the comprehensive analysis of the above two figures (Figure 5A and 5B), the time frame from 2005 to 2023 can be artificially segmented into distinct phases based on the evolution of hot topic. The first phase is approximately 2005-2010, and its keywords include radiation-induced lung injury, late radiotherapy toxicity and single nucleotide polymorphism. The second phase is approximately 2011-2017, the keywords include lung cancer histology, breast cancer, tumor heterogeneity, contrast enhanced MRI, F-8FDG PET. The third phase is probably after 2018, and the keywords include phenotypes, big data, magnetic resonance spectroscopy, renal cell carcinoma, stage, EGFR mutation, temozolomide and artificial intelligence.



Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2005 - 2023
single-nucleotide polymorphisms	2007	16.05	**2007**	2017	
gene expression	2010	17.44	**2010**	2018	
genome wide association	2010	14.16	**2010**	2017	
cell lung cancer	2010	7.07	**2010**	2019	
carcinoma	2009	5.73	**2013**	2016	
radiation-therapy	2014	10.52	**2014**	2019	
radiogenomics	2014	8.75	**2014**	2020	
prostate cancer	2014	7.97	**2014**	2017	
erectile dysfunction	2014	6.01	**2014**	2016	
ionizing radiation	2014	5.82	**2014**	2017	
glioblastoma multiforme	2015	11.13	**2015**	2019	
therapy	2015	6.6	**2015**	2017	
tumor heterogeneity	2016	9.84	**2016**	2019	
contrast enhanced mri	2016	8.44	**2016**	2020	
texture analysis	2016	8	**2016**	2017	
f 18 fdg pet	2016	6.48	**2016**	2018	
phenotypes	2016	6.41	**2016**	2019	
texture features	2017	11.93	**2017**	2020	
intratumoral heterogeneity	2017	8.86	**2017**	2019	
growth factor receptor	2017	5.35	**2017**	2020	
big data	2017	5.25	**2017**	2018	
magnetic resonance spectroscopy	2018	5.42	**2018**	2021	
renal cell carcinoma	2019	8.47	**2019**	2021	
stage	2019	5.97	**2019**	2020	
temozolomide	2021	4.95	**2021**	2023	

5B

Figure 5. Timeline view of reference clustering analysis on radiogenomics (5A) and Top 25 keywords with the strongest citation bursts (5B).

Discussion

The concept of precision medicine has propelled the attention towards radiogenomics, a fusion of genomics and radiomics to achieve personalized treatment, owing to its potential to noninvasive predict treatment responses. This study analyzed 3,237 relevant documents published between 2005-2023 from WoSCC. The increasing number of annual publications, especially the extremely high growth rate after 2017, indicating how interest in radiogenomics research in the clinical field has been increasing from year to year.

Current status of countries and authors

China has the highest number of publications, but the total citations is lower than USA, with the average citation number per item lower than other top 10 countries. Netherlands, USA and Canada obtained the highest average per item. It can be concluded that USA and Netherlands performed reasonably well both in terms of the number and quality of published documents, demonstrating their strong influence. Lambin Philippe, one of the authors comes from Netherlands, ranked the first in both publications and citations, indicating his contributions in this field.

The dynamic trend and evolutionary trajectory

The time frame can be artificially segmented into three phases according to the evolution of hot topics. In the first phase (2005 to 2010), radiogenomics primarily focused on the genetic variation associated with the response to radiation therapy in radiation oncology[12]. Radiation therapy plays a crucial role in tumor treatment, accounting for 50% of all tumor therapies worldwide[19]. However, individuals with similar tumors often exhibit significant differences in radiosensitivity, and many patients experience various types of adverse reactions, including radiation-induced lung injury, and late radiotherapy toxicity after radiation therapy[20,21]. In order to develop precise and personalized treatments that achieve the best efficacy with minimal adverse reactions, researchers have been searching for biomarkers that can predict treatment outcomes. Through the analysis of the complete genome using techniques such as genome-wide association, particularly focusing on single nucleotide polymorphism markers, researchers have identified numerous genomic variation sites associated with the response to radiotherapy[22,23].

In the second phase (2011 to 2017), the concept of radiogenomics expanded. Studies incorporating medical imaging features and biological parameters beyond genomics were also included in radiogenomics[24]. It is believed that the medical images features such as MRI, CT and PET CT of lesions are closely related to tumor heterogeneity. Therefore, the researchers extracted the features (including semantic features/texture analysis features) of the tumors, and adopted radiomics for differentiation diagnosis, such as histological subtype identification. Doshi AM et al found that MRI-based first-order texture metrics can help discriminate between type 1 and type 2 papillary renal cell carcinoma[25]. From the late second phase onwards, the purpose of radiogenomics is not limited to prediction of the radiotherapy side effects or differential diagnosis, but analyzing the relationship between gene expression and imaging. For example, through the analysis of quantitative features of enhanced MRI, Yeh AC analyzed quantitative features of enhanced MRI and found that partial features were correlated with the expression levels of JAK/STAT and VEGF pathway in breast cancer[26].

The distinction between the second and third phase is indistinct, with some of the hot topics beginning during the second phase and continuing beyond 2018. In the third phase, the scope of radiogenomics has gradually expanded and become more in-depth. From the view of raw data, apart from conventional images, some functional imaging such as magnetic resonance spectroscopy were used for radigenomics analysis[27]. Moreover, with the use of PACS system, the storage and re-extraction of medical data are more convenient, which promotes the progress of big data research and improves the credibility of radiogenomics. From the research purposes perspective, more and more therapeutic methods (e.g. neoadjuvant, chemoarterial chemoembolizatio, transcatheter arterial chemoembolization) have been developed and applied to clinic. The researchers are beginning to explore the use of radiogenomics to identify the patients who may not sensitive to certain therapies reducing unnecessary treatment so as to avoid side effects[28]. From the view of research methods, the study in the previous phase tended to screen for the quantitative features (most manually extracted) associated with gene expression status. At present, many studies use machine learning algorithms, even combined with deep learning algorithms that can automatically segment lesions to achieve higher performance[25].

Limitations

Our study has the following limitations: (1) Only articles and review articles published in English from WoSCC were included in this study, potentially introducing language, publication type and database biases. (2) This research focuses on the in-depth analysis of the dynamic trend and evolutionary trajectory based on the keywords and reference. There are other analyses that could have been considered to understand the evolution of radiogenomics as a subject, such as more comparative analyses of the different factors including authors/country/keywords/journals. (3) Our study found that radiogenomics is currently applied mostly in cancer. Bibliometrics may overlook such non-hot topic topics. After all, keywords related to non-oncologic diseases, such as mental illness, do not appear in the tables and figures.

Conclusion

In conclusion, radiogenomics has attracted substantial attention in recent years. USA and Netherlands are the leading country in this field, obtaining the highest total citations and average per item, respectively. Radiogenomics has been utilized to explore the genetic factors associated with radiotherapy-induced toxicity before 2010. Subsequently, it has evolved to encompass the combination of radiomics and genomics, enabling the prediction of cancer histology, gene mutations and expression status based on the tumor heterogeneity information from medical imaging. More and more researchers tend to explore the fisible for radiogenomics to predict the response of various tumor treatments such as neoadjuvant chemotherapy. The application of artificial intelligence method based on big data is the research hot topic in this field at present.

Acknowledgments

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Conflict of Interest

The authors have no conflicts of interest to declare.

Author Contributions

Meng Wang: Formal analysis, Validation, Investigation, Visualization, Data curation, Writing - original draft, Writing - review & editing.

Yun Peng: Methodology, Software, Formal analysis, Validation, Visualization, Supervision, Resources,Writing - original draft, Writing - review & editing.

Ya Wang: Methodology, Software, Formal analysis, Validation, Visualization, Supervision, Writing - original draft, Writing - review & editing.

Dehong Luo: Conceptualization, Validation, Formal analysis, Supervision, Project administration, Data curation, Writing - review & editing.

Disclosure of using artificial intelligence tools

AI was not used in preparing this manuscript.

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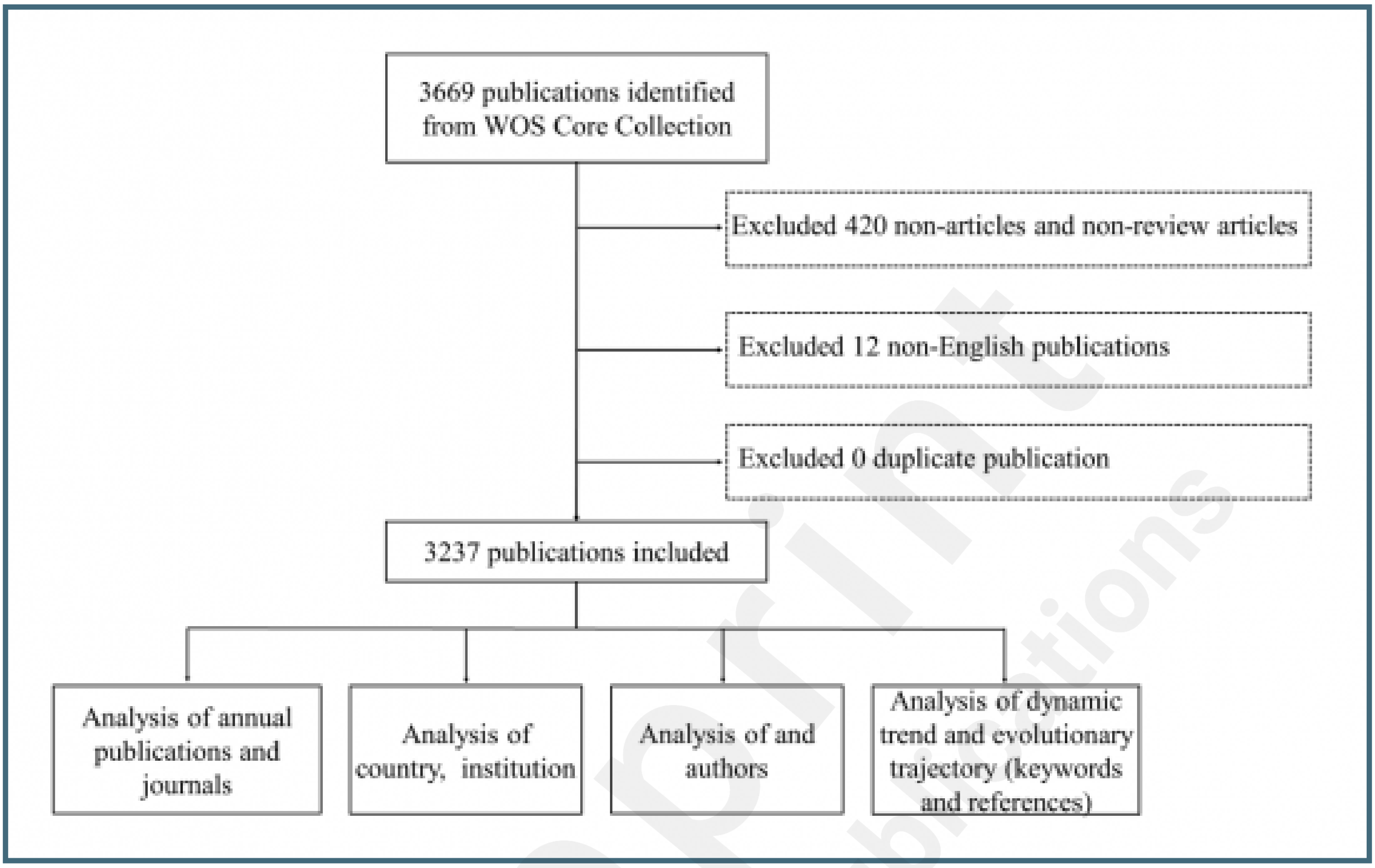
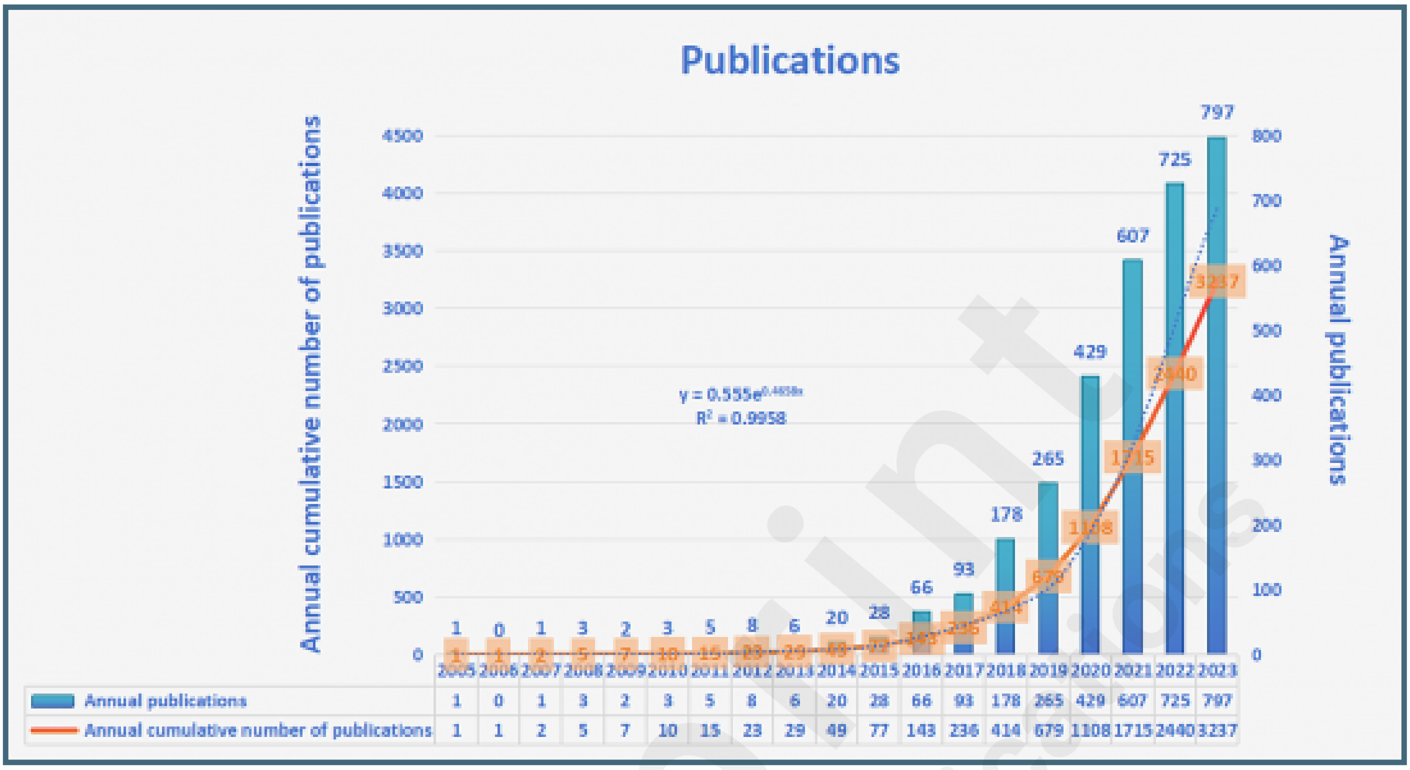
Supplementary Files

Figures

Workflow of the analytical procedures.

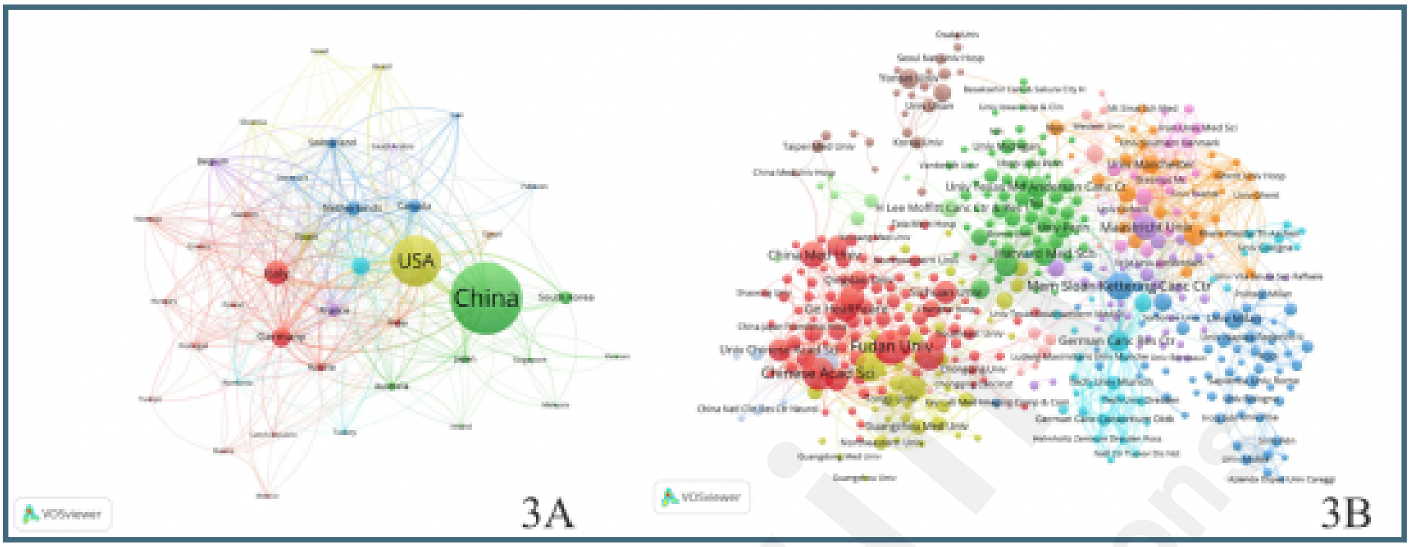


Global trend of publications on radiogenomics from 2005-2023.

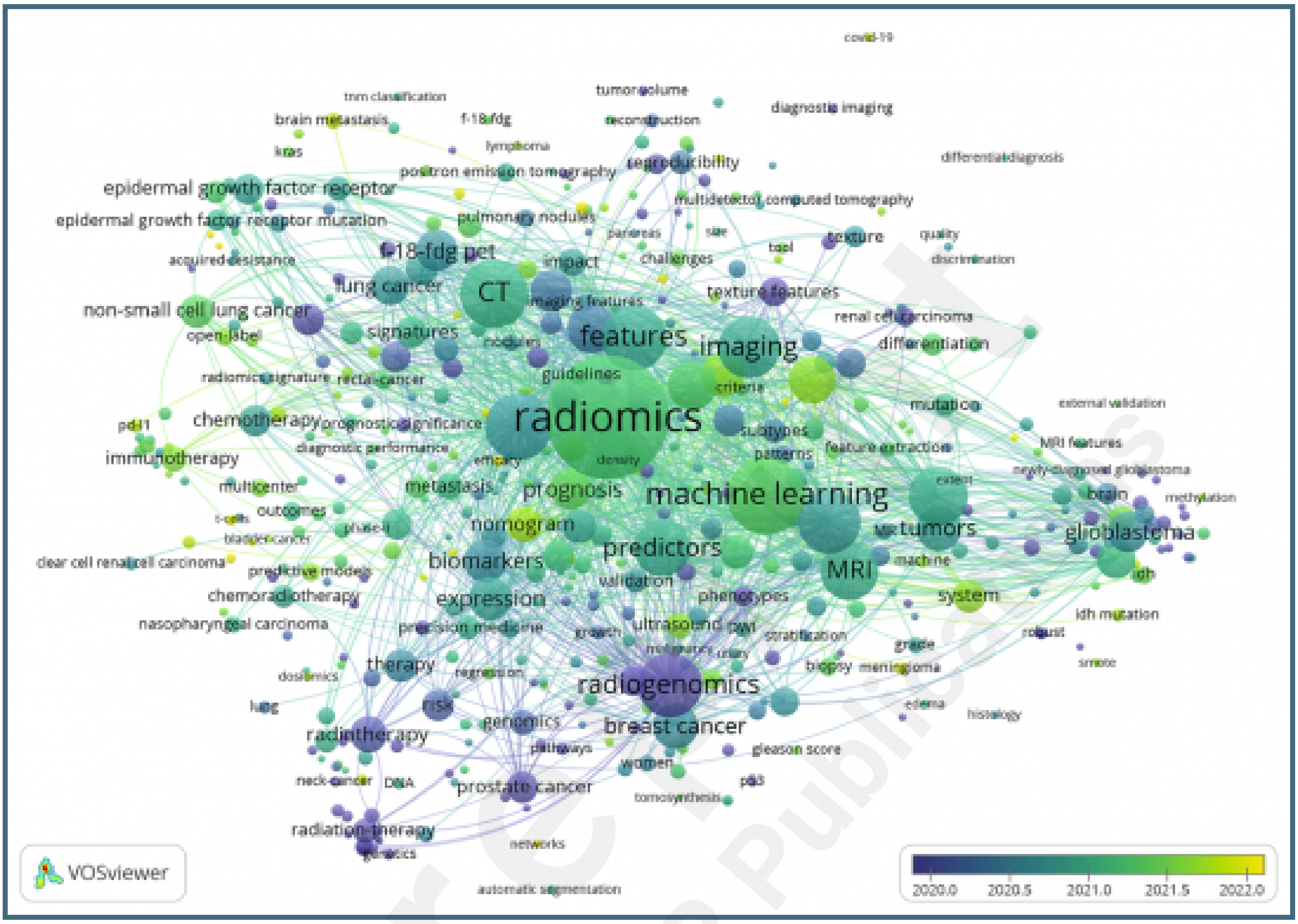


	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Annual publications	1	0	1	3	2	3	5	8	6	20	28	66	93	178	265	429	607	725	797
Annual cumulative number of publications	1	1	2	5	7	10	15	23	29	49	77	143	236	414	679	1108	1715	2440	3237

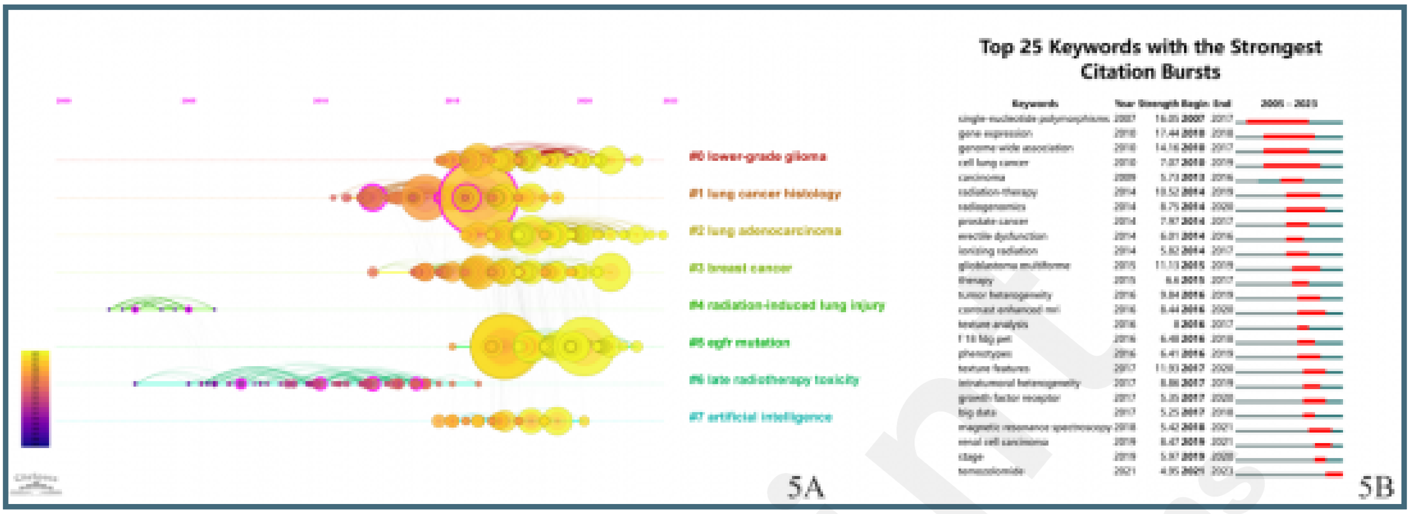
Countries (3A) and institutions (3B) collaboration network in the field of radiogenomics. * The size of the nodes corresponds to the number of published documents, while the line width between nodes indicates the strength of co-authorship. Thicker lines indicate a higher frequency of cooperation.



Overlay visualization map of keywords. *The node size indicates the frequency of keyword occurrences, while the color represents the average publication year of the identified keywords.



Timeline view of reference clustering analysis on radiogenomics (5A) and Top 25 keywords with the strongest citation bursts (5B).



Multimedia Appendixes

Primary data downloaded as plain text files from the WoSCC database for analysis.
URL: http://asset.jmir.pub/assets/e4369059657cbc7c8deed0ed43ec3022.zip

Synonym substitution of keywords.
URL: http://asset.jmir.pub/assets/24ff9c99aeef07fd9a8d82bd6d8394dc.doc

A revised version of your manuscript with tracked changes.
URL: http://asset.jmir.pub/assets/aa6f0455b66336c76f04402982e34e7d.doc