Discover Oncology

Research

A bibliometric analysis of radiation-induced brain injury: a research of the literature from 1998 to 2023

Jinxin Lan[1,2] · **Yifan Ren**[2] · **Yuyang Liu**[3] · **Ling Chen**[1,4] · **Jialin Liu**[1,4]

Received: 2 April 2024 / Accepted: 6 August 2024

Abstract

Background Radiation-induced brain injury (RIBI) is a debilitating sequela after cranial radiotherapy. Research on the topic of RIBI has gradually entered the public eye, with more innovations and applications of evidence-based research and biological mechanism research in the field of that. This was the first bibliometric analysis on RIBI, assessing brain injury related to radiation articles that were published during 1998–2023, to provide an emerging theoretical basis for the future development of RIBI.

Methods Literature were obtained from the Web of Science Core Collection (WOSCC) from its inception to December 31, 2023. The column of publications, author details, affiliated institutions and countries, publication year, and keywords were also recorded.

Results A total of 2543 journal articles were selected. The annual publications on RIBI fluctuated within a certain range. Journal of Neuro-oncology was the most published journal and Radiation Oncology was the most impactful one. LIMOLI CL was the most prolific author with 37 articles and shared the highest h-index with BARNETT GH. The top one country and institutions were the USA and the University of California System, respectively. Clusters analysis of co-keywords demonstrated that the temporal research trends in this field primarily focused on imaging examination and therapy for RIBI.

Conclusion This study collects, visualizes, and analyzes the literature within the field of RIBI over the last 25 years to map the development process, research frontiers and hotspots, and cutting-edge directions in clinical practice and mechanisms related to RIBI.

Keywords Radiation-induced brain injury · Bibliometric analysis · Clinical practice · Mechanisms · Hotspots

Abbreviations

CNS	Central nervous system
AVM	Arteriovenous malformations
RIBI	Radiation-induced brain injury

Jinxin Lan, Yifan Ren and Yuyang Liu contributed equally.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12672-024-01223-6.

✉ Ling Chen, chen_ling301@163.com; ✉ Jialin Liu, Liu_00174@163.com | [1]Department of Neurosurgery, The First Medical Center, The Chinese PLA General Hospital, Beijing 100853, China. [2]Present Address: School of Medicine, Nankai University, Tianjin 300071, China. [3]Department of Neurosurgery, The 920th Hospital of Joint Logistics Support Force, Kunming 650032, Yunnan, China. [4]Chinese PLA General Hospital, Chinese PLA Institute of Neurosurgery, 28 Fuxing Road, Haidian District, Beijing 100853, China.

WOSCC	Web of science core collection
SSCI	Social sciences citation index
SCI	Science citation index
H-index	High-citation index
SRS	Stereotactic radiosurgery
NF-κB	Nuclear factor-kappa B
TNF	Tumor necrosis factor
COX	Cyclooxygenase
BBB	Blood–brain barrier
ECM	Extracellular matrix
T1WI	T1-weighted image
T2WI	T2-weighted image
FLAIR	Fluid-attenuated inversion recovery sequence
DWI	Diffusion-weighted imaging
ASL	Arterial spin labeling
PWI	Perfusion weighted imaging
rCBV	Cerebral blood volume
PET	Positron emission tomography
BMSCs	Bone marrow mesenchymal stem cells
EGb	Ginkgo biloba extract

1 Introduction

The incidence of all brain and other central nervous system (CNS) tumors was 24.83 per 100,000 population [1]. Radiotherapy is an effective and primary treatment of residual tumor and tumor recurrence following the surgical resection and is a backbone of first-line treatment in brain tumor [2]. Additionally, radiotherapy is also extensively used to treat intracranial benign disease [3], such as arteriovenous malformations (AVM) [4], meningioma [5], capillary hemangioma [6], vestibular schwannomas [7], pituitary adenomas [8], craniopharyngiomas [9], especially the lesion is not amenable to surgical resection.

Unfortunately, irradiated areas always contain the normal tissue surrounding the tumor, and consequently, any patients undergo progressive and irreversible side effects. Radiation-induced brain injury (RIBI), such as neuronal architecture alteration, inducing neuroinflammation, suppressing adult neurogenesis, vascular impairment, and neurological disorders, which lead ultimately to declination of cognitive capacity [10], is frequently developed in about 30% of patients receiving radiotherapy for head and neck cancer [11]. The consistent progress of RIBI can eventually cause cerebral herniation and death [12]. The incidence rate of RIBI varies with radiotherapy modality, total dose, and dose fractionated regimen [2]. The earliest description of RIBI was reported in a 45-year-old man who received X-ray radiation of the scalp in 1930 [13]. In the 1980s, Sheline et al. classified RIBI further into three distinct types based principally on the time frame from radiotherapy, namely acute injury which develops during the radiotherapy period, early delayed injury also namely pseudoprogression which develops within 12 weeks after radiotherapy, and late delayed injury which develops few months to years following radiotherapy [13, 14]. However, there is a different standard for the three phases of RIBI, as follow: acute injury occurring in days to weeks, early delayed injury occurring from 1 to 6 months, late delayed injury occurring at times greater than 6 months after irradiation [15]. The necrosis is the ultimate state of RIBI in late delayed injury [15], also named radionecrosis. Even though with the stereotactic precision, Gamma Knife and CyberKnife® procedures also produce scattered radiation to normal cerebral tissue outside the targeted areas [10]. Since brain injury induced by radiation is hardly avoided following radiotherapy, the research on exploring the underlying mechanisms, early diagnosis, and management of RIBI are particularly important. Here, we summarized the development process and cutting-edge trends of RIBI through bibliometric analysis.

Bibliometrics is a branch of informatics that has been used for describing the relationships between published works through conducting a quantitative and qualitative analysis of the metadata of scientific literature [16]. Although this type of report has been widely proposed in other fields, to our knowledge, there is still no bibliometric study on RIBI. To fill the knowledge gap, a bibliometric study of the current scholarly literature of RIBI would be of interest.

2 Method

2.1 Data acquisition and search strategy

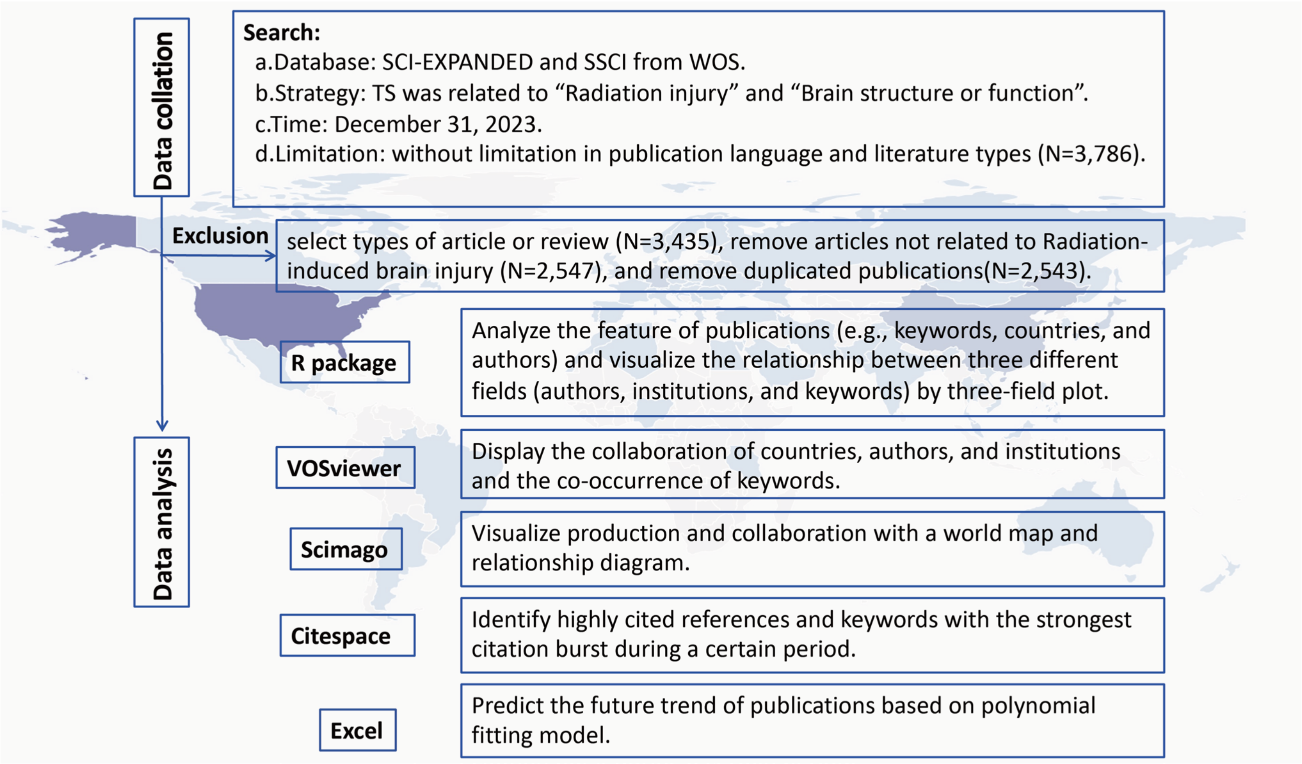
Two authors independently retrieved literature from the Science Citation Index Expanded (SCI-EXPANDED) and Social Sciences Citation Index (SSCI) in the Web of Science Core Collection (WoSCC) from its inception to December 31, 2023 (Fig. 1). WoSCC is one of the most commonly used academic database sources, which covers multiple disciplines, ensuring the comprehensiveness of our search. And it has a strong citation analysis function, which is very suitable for bibliometric analysis [17, 18]. The search strategy was set referred the previous studies (written in the supplemental file). The literature type was limited to article and review. No limitation in publication language. Relevant articles were exported and stored in the form of plain.txt (including full record and cited references) for further analyses.

2.2 Data analysis

This Bibliometric analysis was performed by five software, namely, R version 4.3.2 [19], VOSviewer [20], CiteSpace [21], Scimago, and Excel 2010 (Fig. 1).

Bibliometrix is an R package (version 4.3.2) containing a series of functions for scientometric quantitative research. Biblioshiny is a web-based tool that helps scholars import, gather, filter, and analyze data from bibliometrix. In this study, it was used to (1) analyze the production of all the countries, institutions, journals, and authors involved; (2) calculate the cooperation frequency among countries; (3) identify the hotspot of RIBI-related research by displaying cumulative occurrences of the top keywords, documents, and reference; (4) evaluate the influence of authors by h-, g-, m-index and citations; and (5) use three-field plot to visualize the relationship between three different fields [19].

VOSviewer is a Java application, which is widely used for science mapping, which visualizes the collaborative relationships between countries, authors, institutions, and the research topics in the field of RIBI. It can assign a set of closely related nodes into several clusters, where the same color indicates higher correlations of nodes. Additionally, VOSviewer also supports the overlay visualization map. In this study, it was used with Scimago. Scimago is an



Search:
a.Database: SCI-EXPANDED and SSCI from WOS.
b.Strategy: TS was related to “Radiation injury” and “Brain structure or function”.
c.Time: December 31, 2023.
d.Limitation: without limitation in publication language and literature types (N=3,786).

select types of article or review (N=3,435), remove articles not related to Radiation-induced brain injury (N=2,547), and remove duplicated publications(N=2,543).

Analyze the feature of publications (e.g., keywords, countries, and authors) and visualize the relationship between three different fields (authors, institutions, and keywords) by three-field plot.

Display the collaboration of countries, authors, and institutions and the co-occurrence of keywords.

Visualize production and collaboration with a world map and relationship diagram.

Identify highly cited references and keywords with the strongest citation burst during a certain period.

Predict the future trend of publications based on polynomial fitting model.

Fig. 1 Detailed process for literature screening information visualization tool whose aim is to reveal the structure of science to show the distribution and interconnection of the different countries intuitively. VOSviewer and Scimago were used to display: (1) the collaboration between corresponding authors' countries on the world map. (2) the co-occurrence network that reflected the associations between authors' keywords, and (3) the co-authorship network that explored the authors' and their institutions' collaboration networks [20].

CiteSpace is also a Java application, which is usually used to reflect the evolution of the bibliometric network over time. In this study, it was specially used to identify highly cited references and keywords with the strongest citation burst during a certain period [21].

Excel is used to summarize the annual and cumulative number of publications and predict the future trend of publications in RIBI in the coming decade based on the polynomial fitting model.

3 Result

3.1 Types and trends of publications

From January 1, 1998, to December 31, 2023, the topic of RIBI has published 2543 articles. Research articles (n = 2035, 80.0% of the total) constitute most of the published items and the rest items were reviews (n = 394, 15.5%), book chapter (n = 2, 0.8%), and proceedings paper (n = 88, 3.5%). In descending order by year, the highest number of documents were published, in 2023 (n = 178), 2022 (n = 175), 2021 (n = 170), 2018 (n = 161), 2020 (n = 158), and 2017 (n = 155), signaling a growth in the research of RIBI in recent year (Fig. 2a). Before 2008, the number of annual productions increased slowly, however, with the continuous development and wide application of radiotherapy and medical imaging, this field has received extensive attention (Fig. 2a). Since 2008, the volume of published documents has blown up. The annual number of publications identified a positive relation to the year of publication, with the correlation coefficient R [2] of 0.8871. Figure 2b showed the rate of article volume increase, revealing that 2013–2014 owned the most rapid onset rate with 45.54%. The general elevated trend in the number of articles published dissected that RIBI was an active research field and aroused the interest of scholars.

3.2 Analysis of published articles

3.2.1 Analysis of authors

So far, about 13,543 authors have been performing RIBI studies, and 11 of them have published more than 20 articles. According to the high-citation index (H-index) statistic of the top 20 authors, we found that the nationality of the top 20 authors mainly concentrated in the United States, which further clarified that the leading position of American

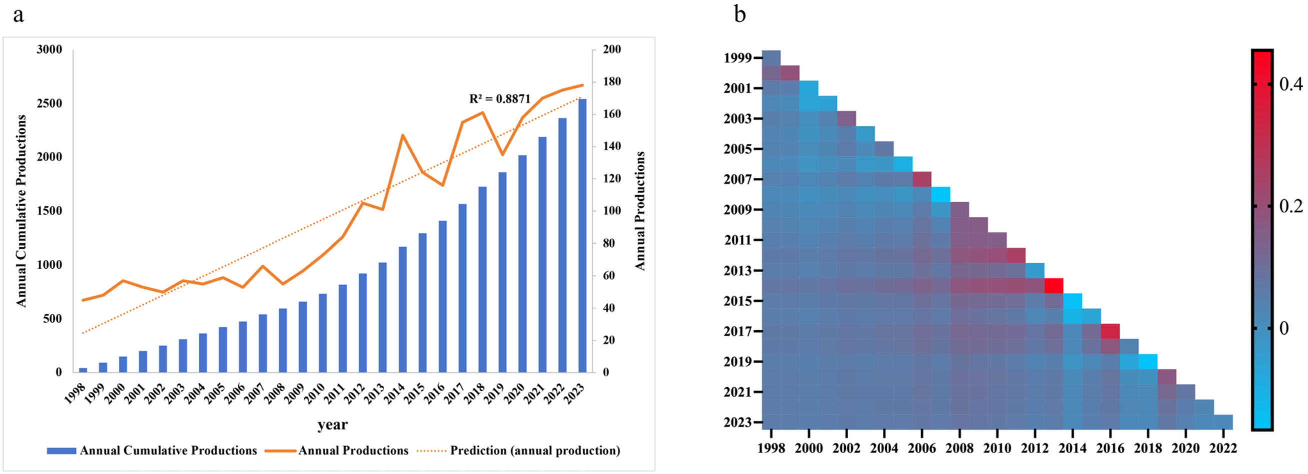


Fig. 2 **a** Annual publication volume and accumulation of RIBI from 1998 to 2023. **b** Heatmap of increase rate of published documents

Table 1 Top 20 authors with the highest influence

Name	Articles	h_index	g_index	m_index	TC	Country	Affiliation
Barnett GH	34	24	34	1.000	1526	USA	Cleveland Clinic
Limoli CL	37	24	37	1.143	2286	USA	University of California
Acharya MM	28	22	28	1.375	1676	USA	University of California
Robbins ME	24	20	24	1.111	1345	USA	Northwestern University Feinberg School of Medicine
Mohammadi AM	20	17	20	1.545	820	USA	Cleveland Clinic
Suh JH	22	17	22	0.708	1162	USA	Cleveland Clinic
Chao ST	22	16	22	0.667	1087	USA	Cleveland Clinic
Lunsford LD	22	16	22	0.593	1439	USA	University of Pittsburgh Medical Center
Kondziolka D	23	15	23	0.556	1431	USA	University of Pittsburgh
Pollock BE	20	15	20	0.577	1511	USA	Mayo Clinic School of Medicine
Vogelbaum MA	16	15	16	0.789	829	USA	Moffit Cancer Center
Fike JR	15	14	15	0.519	2154	USA	University of California
Galldiks N	18	14	18	1.167	875	Germany	University of Cologne
Giedzinski E	15	14	15	0.667	1019	USA	University of California
Allen BD	14	13	14	1.3	978	USA	University of California
Flickinger JC	14	13	14	0.481	1260	USA	University of Pittsburgh Medical Center
Langen KJ	16	13	16	1.3	800	Germany	Research Center Juelich
Ahluwalia MS	19	12	19	1	686	USA	Cleveland Clinic
Baulch JE	13	12	13	1.2	578	USA	University of California Irvine
Debus J	22	12	22	0.444	914	Germany	University Hospital Heidelberg

scholars in the field of RIBI. 5 scholars were affiliated with the Cleveland Clinic, indicating the high-performance research level of the Cleveland Clinic on research on RIBI. The most influential and productive authors were Limoli CL and Barnett GH according to the indicator of h-index (Table 1) (24). Those two scholars were the only two with more than 30 publications and Limoli CL was the only one with more than 2000 total citations, which implied their outstanding academic contribution in the field of TIBI.

3.2.2 Analysis of published journals

In terms of publication volume, we sorted the top 10 journals (Table 2). These journals had a larger possibility in accepting articles regarding RIBI, given their largest publication volume of relevant topics. Among them, the *Journal of Neuro-oncology* ranked the first with 130 publications, followed by the *International Journal of Radiation Oncology Biology Physics* with 113 publications, and the tenth was *Neuro-oncology*, with the number of publications reaching 35. Among the top ten journals, 40% are published by Elsevier. Among the top 10 journals, *Neuro-oncology* exhibited the highest impact factor (15.9 in 2022) and CiteScore (22.5%), which was first published in 1999 and now is one of the leading journals in the field.

It has been explained previously that *the Journal of neuro-oncology* occupies the first position based on publication volume, but the *International Journal of Radiation Oncology Biology Physic* not only has the highest h-index, g-index, and m-index but also has the highest total citation. This could reflect the high impact of this journal. At the same time, other 9 journals have also been endorsed by scholars in the fields of neuro-oncology and radiology.

3.2.3 Analysis of source affiliation

A total of 8,452 institutions published articles about RIBI. The top 10 productive affiliations are demonstrated in Table 3. A total of 8452 different institutions published articles related to RIBI. 7 institutions met the criteria of publishing at least 120 articles. As can be seen from the figure, the distribution of contributing institutions in this field was obviously uneven, and the top effect was very significant, with only the University of California System (the USA) accounting for 1/6 of the field's publications. We used VOSviewer to visualize the institutions with production of more than or equal to 10

Table 2 Top 10 journals with the most production in the field of RIBI

Journal	IF(2022)	CiteScore (2022)	JCR	Country	Articles	h_index	g_index	m_index	TC	Publishers
Journal Of Neuro-Oncology	3.9	7.3%	Q2	United States	130	35	55	1.296	3877	Springer Nature
International Journal of Radiation Oncology Biology Physics	7	11.0%	Q1	United States	113	52	94	1.926	9050	Elsevier
Journal of Neurosurgery	4.1	8.1%	Q1	United States	88	39	66	1.444	4536	American Association of Neurological Surgeons
Neurosurgery	4.8	7.4%	Q1	United States	64	36	65	1.333	4265	Lippincott Williams & Wilkins
Radiation Research	3.4	5.0%	Q2	United States	64	24	41	1.043	1829	Elsevier
World Neurosurgery	2	15.0%	Q3	United States	47	14	21	1.167	549	Elsevier
Radiation Oncology	3.6	6.6%	Q2	United Kingdom	45	19	38	1.056	1483	Springer Nature
Cancers	5.2	9.6%	Q2	Switzerland	43	8	15	0.800	268	MDPI (Basel, Switzerland)
Radiotherapy and Oncology	5.7	10.5%	Q1	Netherlands	39	18	35	0.667	1242	Elsevier
Neuro-Oncology	15.9	22.5%	Q1	United States	35	24	35	1.412	1815	Oxford University Press

[*] IF, impact factor (2022–2023); †JCR-c, Journal Citation Report category; ‡TC, total citation

Table 3 Top 10 contributing institutions and production over time on Radiation-induced brain injury-related research

Affiliations	Most relevent affiliations
University of California System	416
Harvard University	278
Sun Yat Sen University	163
Helmholtz Association	160
Wake Forest University	153
University Of Texas System	126
University Of Toronto	124
UTMD Anderson Cancer Center	119
German Cancer Research Center (DKFZ)	114
UDICE-French Research Universities	105

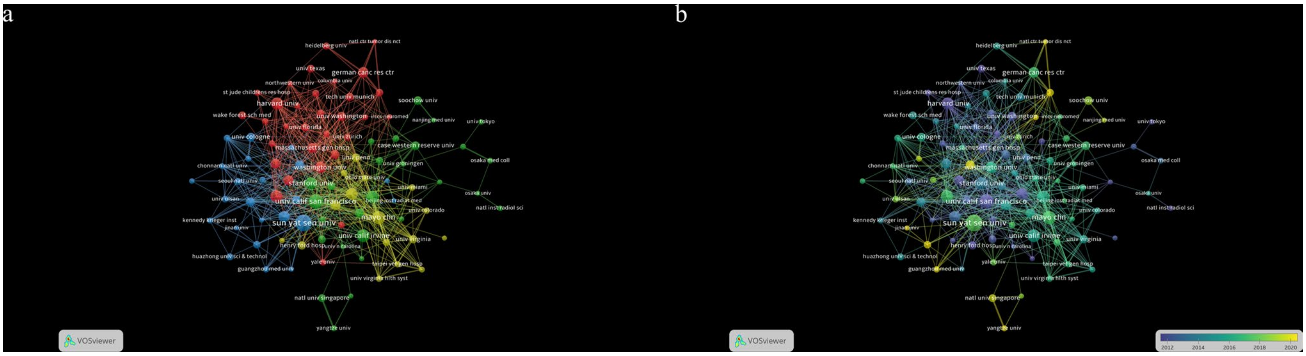


Fig. 3 The Network and Overlay visualization of institutions. **a** Cluster network diagram of cooperative analysis of institutions in the field of RIBI (Published periodical articles ≥ 10). **b** Time-dependent network diagram of cooperative analysis of institutions in the field of RIBI (Published periodical articles ≥ 10). Early research institutions are shown in purple and frontier institutions in yellow

articles, and the results were shown in Fig. 3a. Where the size of the nodes represented the number of publications, the link between two nodes depicted their connection, and the node colors represented the different clusters. 99 countries were included in the analysis, and the most productive University of California System was strongly associated with Stanford University; Harvard University was strongly associated with the University of Florida, and Sun Yat-sen University was strongly associated with Guangzhou Medical College and Huazhong University of Science and Technology. This probes that inter-institutional collaboration mostly occurred within countries. Institutions with more publications had more collaborations with other institutions, which suggested that collaboration between institutions and platforms can further promote the production of good works.

Figure 3b illustrated the overlay network, the color represents the average commencement year of publications in each institution. The visualization marked in purple reveals the average publication year of institutions that started earlier, while the green to yellow represents the average publication year of the institutions that began more recently. As we can see, institutions in the Americas and Europe, such as the University of California System and Harvard University, conducted research in this area earlier, and then institutions in Asia, such as Huazhong University of Science and Technology, Sun Yat-sen University, Nanjing University, National University of Singapore, Guangzhou Medical College, and Jinan University, have gradually invested in this area of research.

3.2.4 Analysis of most cited articles

Citation analysis is a valuable method to assess the most highly cited articles, citations can reveal the influence of publications in a specific research field [22]. Table 4 exhibited the 20 most cited articles. All of these top 20 most cited articles were published earlier than 2011. Of these articles, the top three were all the research articles. The most cited article

Table 4 The top 20 most cited articles in the field of RIBI

Article	DOI	Year	Local citations	Global citations	LC/GC Ratio (%)
Kumar AJ, 2000, Radiology [23]	10.1148/radiology.217.2.r00nv36377	2000	156	478	32.64
Levin VA, 2011, Int J Radiat Oncol [24]	10.1016/j.ijrobp.2009.12.061	2011	139	458	30.35
Rola R, 2004, Exp Neurol [25]	10.1016/j.expneurol.2004.05.005	2004	134	547	24.50
Mizumatsu S, 2003, Cancer Res [26]	–	2003	125	564	22.16
Minniti G, 2011, Radiat Oncol [27]	10.1186/1748-717X-6–48	2011	124	504	24.60
Ruben JD, 2006, Int J Radiat Oncol [28]	10.1016/j.ijrobp.2005.12.002	2006	117	330	35.45
Monje ML, 2003, Science [29]	10.1126/science.1088417	2003	115	1885	6.10
Gonzalez J, 2007, Int J Radiat Oncol [30]	10.1016/j.ijrobp.2006.10.010	2007	101	301	33.55
Giglio P, 2003, Neurologist [31]	10.1097/01.nrl.0000080951.78533.c4	2003	94	192	48.96
Ricci PE, 1998, Am J Neuroradiol [32]	–	1998	91	256	35.55
Hein PA, 2004, Am J Neuroradiol [33]	–	2004	90	311	28.94
Terakawa Y, 2008, J Nucl Med [34]	10.2967/jnumed.107.048082	2008	90	286	31.47
Blonigen BJ, 2010, Int J Radiat Oncol [35]	10.1016/j.ijrobp.2009.06.006	2010	89	340	26.18
Sugahara T, 2000, Am J Neuroradiol [36]	–	2000	88	288	30.56
Chao ST, 2013, Int J Radiat Oncol [13]	10.1016/j.ijrobp.2013.05.015	2013	81	194	41.75
Chao ST, 2001, Int J Cancer [37]	10.1002/ijc.1016	2001	79	256	30.86
Lawrence YR, 2010, Int J Radiat Oncol [38]	10.1016/j.ijrobp.2009.02.091	2010	75	491	15.27
Barajas RF, 2009, Am J Neuroradiol [39]	10.3174/ajnr.A1362	2009	73	169	43.20
MULLINS ME, 2005, Am J Neuroradiol [40]	–	2005	72	170	42.35
BARAJAS RF, 2009, Radiology [41]	10.1148/radiol.2532090007	2009	71	287	24.74

entitled "Malignant gliomas: MR imaging spectrum of radiation therapy- and chemotherapy-induced necrosis of the brain after treatment" in 2000 (IF:19.7) [23], which described the varying spatial and temporal patterns of radiation necrosis at MR imaging, addressed the frequent diagnostic dilemma of recurrent neoplasm versus radiation necrosis. The top 2 was "Randomized double-blind placebo-controlled trial of bevacizumab therapy for radiation necrosis of the central nervous system" in 2011 (IF:7.0) [24], which summarized the controlled trial of bevacizumab for the treatment of symptomatic radiation necrosis of the brain and provided the Class I evidence of bevacizumab efficacy from the present study in the treatment of central nervous system radiation necrosis which justified consideration of this treatment option for people with radiation necrosis secondary to the treatment of head-and-neck cancer and brain cancer. The third cited article entitled "Radiation-induced impairment of hippocampal neurogenesis is associated with cognitive deficits in young mice" in 2004 (IF:5.3) [25], was a fundamental research article, providing evidence that irradiation of young animals induced a long-term impairment of SGZ neurogenesis that was associated with hippocampal-dependent memory deficits.

3.3 Analysis of country performance

3.3.1 Contribution of different countries

Until the time node of article retrieval, a total of 69 countries/regions published articles about RIBI. The top 20 high-output countries/regions were ranked according to the accumulation of the number of publications (Table 5). Figure 4a displayed the publication distribution globally. USA published the most papers (1000, 39.3%), followed by China (405, 15.9%) and Japan (199, 7.8%). These data imply that the USA and China have a dominant position in the research field of RIBI. The number of citations was 51,606 for the USA, accounting for over half (56.25%) of the total, followed by China (6346, 6.92%) and Germany (5768, 6.29%). However, the Netherlands enjoyed the highest average article citations (55.30) (Table 6).

3.3.2 Country cooperation network

Through statistical analysis of publications of the specific field, it is possible to identify the key countries that have made a considerable contribution to promoting the development of this field and the cooperative relationship between them. To analyze the stable cooperative relationship between these countries/regions, the analysis of Scimago software was

Table 5 The Top 20 countries/regions with the highest number of publications

Country	Articles	SCP	MCP	Freq	MCP_Ratio
USA	1000	857	143	0.392	0.143
China	405	342	63	0.159	0.156
Japan	199	187	12	0.078	0.06
Germany	155	121	34	0.061	0.219
Italy	88	69	19	0.035	0.216
France	82	67	15	0.032	0.183
South Korea	73	68	5	0.029	0.068
Canada	70	48	22	0.027	0.314
United Kingdom	49	34	15	0.019	0.306
India	44	39	5	0.017	0.114
Netherlands	36	28	8	0.014	0.222
Turkey	28	26	2	0.011	0.071
Belgium	25	20	5	0.01	0.2
Switzerland	24	13	11	0.009	0.458
Australia	22	15	7	0.009	0.318
Sweden	22	12	10	0.009	0.455
Israel	21	18	3	0.008	0.143
Spain	19	18	1	0.007	0.053
Russia	16	12	4	0.006	0.25
Singapore	14	7	7	0.005	0.5

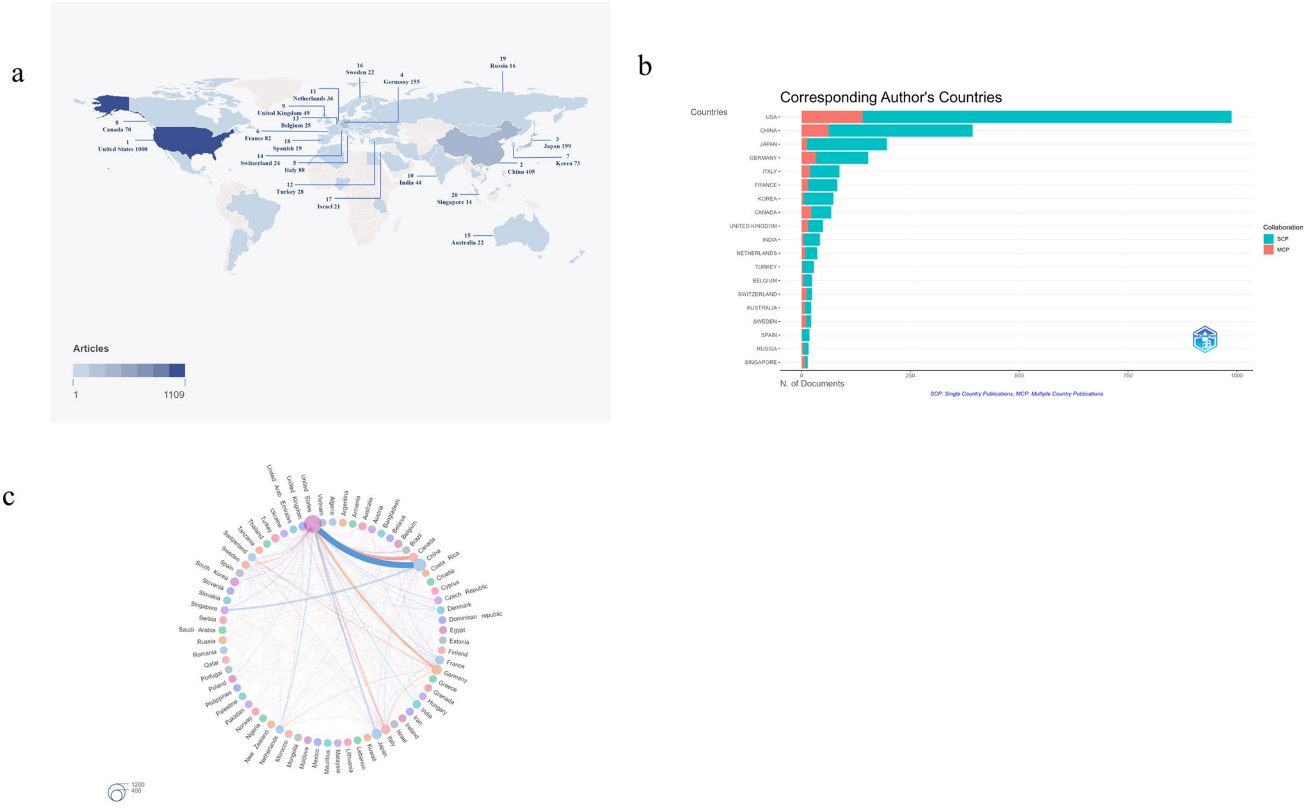


Fig. 4 The distribution of publications and collaboration between countries/regions. **a** A world map displays the publication counts of each country; **b** The national distribution and collaboration of the top 20 corresponding authors; **c** The top 20 collaborations between countries

Table 6 Top 20 countries/regions with the most total citations

Country	TC	Average article citations
USA	51606	51.60
China	6349	15.70
Germany	5768	37.20
Japan	5662	28.50
Canada	3544	50.60
Italy	2556	29.00
France	2218	27.00
Netherlands	1991	55.30
United Kingdom	1523	31.10
Korea	1464	20.10
Belgium	1157	46.30
Switzerland	987	41.10
Sweden	821	37.30
India	807	18.30
Australia	799	36.30
Turkey	520	18.60
Spain	441	23.20
Israel	385	29.60
Greece	276	30.70
Austria	274	22.80

conducted (Fig. 4c). The larger the node, the larger the number of publications, and the line between two nodes represents the cooperative relationship, the thicker the line, the stronger the collaboration. Related global cooperation was mainly concentrated in the USA and China, and the cooperation between other countries/regions was relatively weak. As illustrated in Table 4 and Fig. 4b, the USA had the highest number of internationally cooperative publications (143), but the rate of that is not high (14.3%) among the top 20 high-output countries/regions. While, with the 20th number of publications, Singapore had the highest rate of cooperative publication (50%), followed by Switzerland (45.8%) and Sweden (45.5%). In a word, these results highlighted that these key scholars had made a great impact and in-depth impression of the research area and their outstanding contributions served as a catalyst for the rapid development of this field.

3.4 Analysis of keywords

Keywords represent a research's principal ideas and theme concepts and also demonstrate certain research hotspots [42]. We identified words that appeared over 25 times as the keyword for further analysis and finally identified 164 keywords with strong bursts among 8292 keywords. The keyword co-occurrence networks are shown in Fig. 5. As demonstrated in Fig. 5a, the red bar represents the time span of citation bursts. "radiation injury" experienced the strongest burst (intensity = 9.32), followed by "gamma knife" (intensity = 7.78) and "arteriovenous malformation" (intensity = 6.13). The keywords "pituitary adenoma" and "brain tumor" received a great of attention in the first decade of the twenty-first century. The keywords, including "machine learning", laser interstitial thermal therapy", "brain metastasis", "lung cancer", "cognitive impairment" and "space radiation", remained in an explosive state in 2023 (Fig. 5a). Heatmap of keywords demonstrated that "radiotherapy", "stereotactic radiosurgery", "radiation necrosis", "radiation" and "glioma" were keywords occurring with the highest frequency (Fig. 5b).

A total of 3 clusters were organized as presented in Fig. 5c. The blue cluster concentrated on the causes, complications, and mechanisms of RIBI, and its main nodes were "radiation", "radiation-induced brain injury", "inflammation", "brain", "cognition", "apoptosis", "brain injury", "ionizing radiation", "microglia" and "DNA damage". The red cluster mainly focused on the treatment that caused RIBI, and the main nodes were "radiotherapy", "stereotactic radiosurgery", "gamma knife", "stereotactic radiotherapy" and "cyber knife". The green cluster highlighted the importance of imaging examination for the diagnosis of RIBI and the tumors that were caused by RIBI, and the main nodes were "radiation necrosis", "MRI", "glioma", "glioblastoma", "pet", "perfusion mri" and "pseudoprogression".

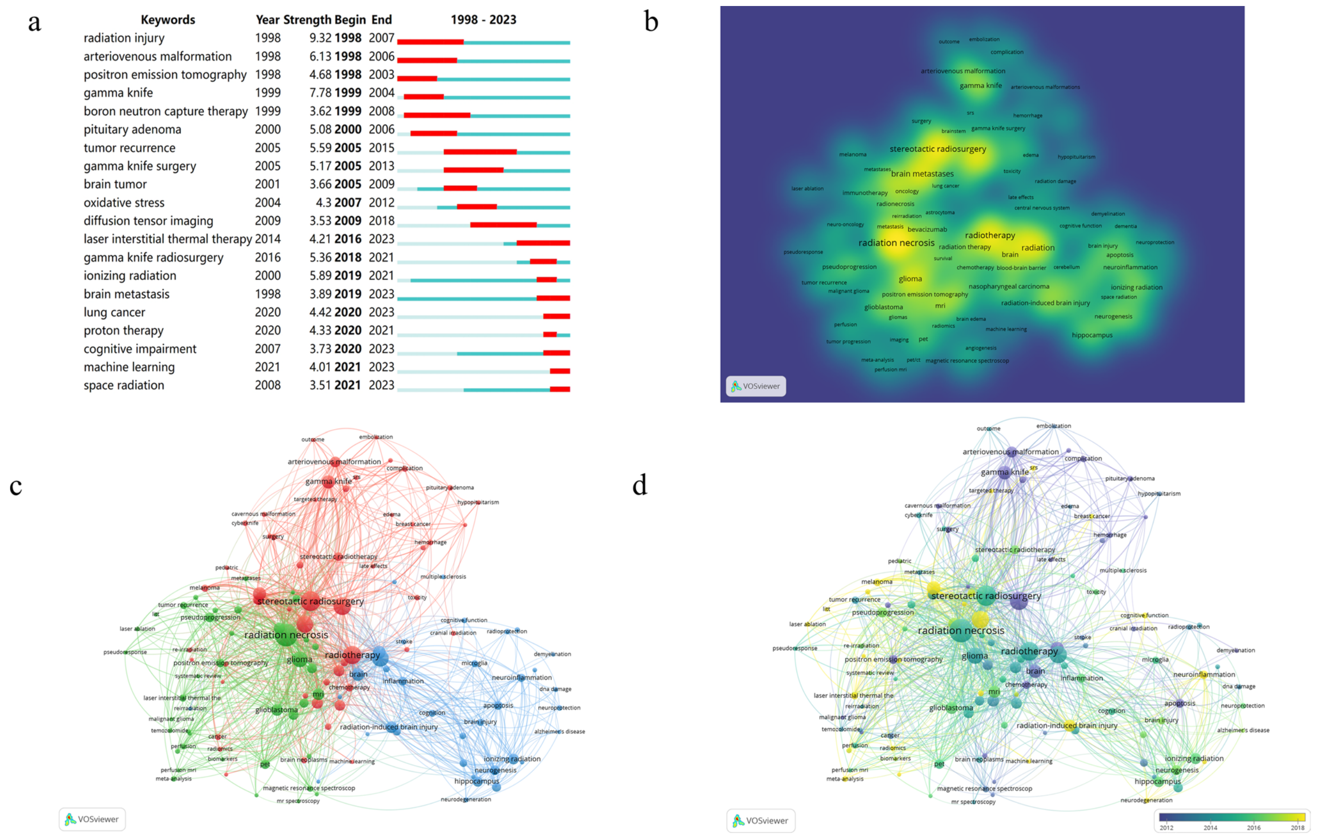


Fig. 5 The visualization of the analysis of keywords. **a** the top 20 keywords with the strongest citation bursts; **b** the density map of keywords based on occurrence frequency; **c** the cluster analysis graph of the 135 keywords appearing over 10 times; **d** the timeline of keywords occurrence

The current tendency of keywords by time overlay was shown in Fig. 5d. The terms marked in purple indicate that the publication year was 2010 or earlier, while those marked in luminous yellow appeared after 2018 (Fig. 5d). Keywords such as "arteriovenous malformation", "gamma knife", "hemorrhage", "cavernous malformation", "positron emission tomography" and "pituitary adenoma" were the main topics during the early stage. The keywords "melanoma", "meta-analysis", "cognitive function", "radiation-induced brain injury", "neurodegeneration", "targeted therapy", "srs", "neuroinflammation" and "melanoma" appeared relatively late in the period of RIBI study.

Figure 6 visualizes the relationships between authors, institutions, and keywords occurrence in the research field of RIBI. It is obvious that the majority of collaborations between institutions were confined within national boundaries, such as the University of California System and Cleveland Clinic Foundation in the US, with relatively fewer across countries. The most prominent across-countries collaboration of these observed was between the Sun Yat-sen University in China and the Mayo Clinic in the US.

4 Discussion

To our best knowledge, it was the first time that a comprehensive bibliometric analysis of publications related to RIBI was conducted to investigate the research dynamics and hot spots. The annual scientific productivity is the indicator of the development trend of a specific research field [43–45]. Drawing on data from the WOS database from 1998 to 2023, there are 2543 articles related to RIBI published by 13,543 authors from 8452 institutions in 69 countries/regions in 700 academic journals.

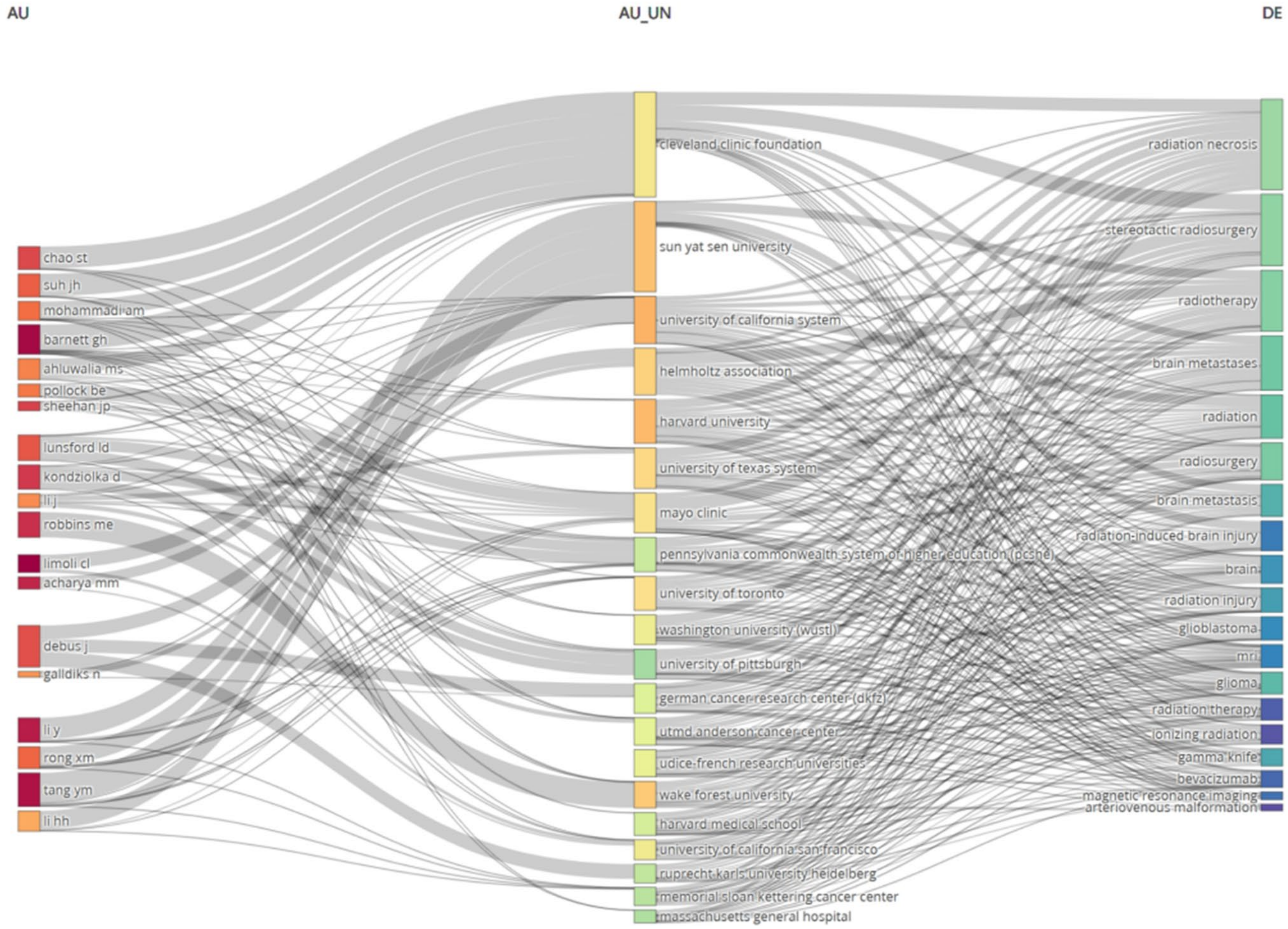


Fig. 6 Thematic evolution plot (Sankey graph) of RIBI-related research

4.1 General analysis

Our results demonstrated a steady increase trend in the volume of annual publications on RIBI. Over four times as many publications were delivered in 2023 as in 1998, illustrating the growing interest and exploratory research in the field of RIBI. The expansion of research may be due to RIBI has become an increasingly important side effect affecting the prognosis of brain tumor patients after radiotherapy [46]. One underlying reason might relate to a randomized double-blind placebo-controlled trial that demonstrated bevacizumab was an effective therapy for brain radiation necrosis, which caused a minor burst in 2014 [24]. Another factor might be the promotion and application of stereotactic radiosurgery (SRS), and several studies reported the clinical data of RIBI and reviewed the RIBI [27, 38, 47]. Afterward, annual scientific productivity demonstrated a much slower growth during 2018–2023 (average rate of growth: 2.03%). This phenomenon suggested that current research encountered some bottlenecks and required breakthroughs in the explorations.

The *h*-index, *g*-index, and *m*-index can partly represent the academic impact of a scholar. H-index is a mixed quantitative index, which can be used to evaluate the quantity and quality of academic output of a researcher or journal, and is one of the indicators reflecting influence. Based on the *h*-index, the *g*-index takes into account the very high citations of a single article by one researcher, while based on the *g*-index, the *m*-index adds the influence of research years of researchers on influence [45, 48, 49]. As mentioned before, Barnett GH and Limoli CL took over the leading position in these indexes. Limoli CL was a professor of the Department of Radiation Oncology at the University of California, Irvine. He devoted himself to research on oxidative stress, hippocampal neurogenesis, stem cells, transplantation, chemo-brain, memory, irradiation, and cognitive dysfunction and has produced impactful research achievements with Nelson GM (Loma Linda University), Fike JR (University of California), and Baure J (University of California) [50–53]. Research in his lab was focused on the mechanisms by which stem cells regulated stress responses in compromised tissue beds, and how stem cells can be used to lessen the severity of radiation-induced normal tissue injury in the brain [54–56]. Barnett GH was co-ranked first author with Limoli CL on the h-index, who was the Director of Cleveland Clinic's Brain Tumor and Neuro-Oncology Center and Health System Gamma Knife Center. He had authored more than 600 articles published in leading medical journals with 37,498 citations and majored in the areas of neuro-oncology [57, 58], computer-assisted surgery [59], and stereotactic radiosurgery [60–62]. It is worth pointing out that Dr. Barnett created the Center for Computer-Assisted Neurosurgery at Cleveland Clinic in the late 1980s [63]. In addition, he had served on several editorial boards and was a reviewer for several neurosurgery journals. In a word, these key scholars had a great impact on this research area and their outstanding contributions catalyzed the development of this field.

In terms of the above index, *the International Journal of Radiation Oncology Biology physic* was the highest-impact journal in this field. It is a journal, known in the field as the Red Journal, dedicated to research and application of radiation oncology, radiation biology, and medical physics, which are popular among medical scientific workers related to radiology. The IF is also a crucial indicator that represents the influence of a journal [64]. This IF of *the International Journal of Radiation Oncology Biology physic* has steadily increased in recent years, which reflects the journal's increasingly high academic status and influence in the field of radiation.

The USA, with the most articles published, has made great contributions to the study of RIBI. For example, the USA had more than twice as many publications as the country ranked second. The total citation of the USA was over eight times than those of the second country. Moreover, 5 of the top 10 productive institutions were from the USA, including the University of California System, Harvard University, Wake Forest University, the University of Texas System, and UTMD Anderson Cancer Center. According to the overlay visualization of institutions, the institutions in the USA started early in the research field of RIBI, while other countries gradually devoted themselves to RIBI-related research in recent years. These findings not only indicated that brain necrosis had drawn much attention in the United States research institutions in the field of radiotherapy but also owed to the strong support and well-established research infrastructure of the United States for academic research.

International collaboration can lead to the sharing of knowledge and expertise, and the cooperative efforts of multiple platforms and resources can lead to more excellent research. As far as it stands, international collaborations in RIBI-related research are strongly centered in the United States. This could also explain why the United States has the highest influence in this area of research. Therefore, other countries should also strengthen cooperation between domestic and foreign institutions. By analyzing the publications and cooperation of countries and institutions, our findings can help researchers quickly find the most relevant institutions in this field so that more communications and collaborations can take place, which could produce more high-quality results in the RIBI-related field.

4.2 Major finding

Based on keyword analysis, we summarized three main clusters for classification. To systemically understand RIBI and insight into the new directions for further study.

4.2.1 Induction factor of RIBI

Microglial cells resident in the cerebral parenchyma are the main cellular clusters involved in innate immune response [65]. It is well recognized that multiple inflammatory reactions were induced after ionizing radiation via microglia [66]. This process may be triggered by DNA double-strand breaks in microglia, leading to nuclear factor-kappa B (NF-κB) pathway-induced release of pro-inflammatory mediators and cytokines [67], including IL(interleukin-1α, IL-6, IL-10, IL-18, IL-1β, CCL-2 (MCP-1), tumor necrosis factor (TNF) α and cyclooxygenase (COX)-2 [68–71]. In addition, IR could induce oxidative stress in microglia under both 0.5Gy and 8Gy γ rays which activated the inflammatory response via MEK-ERK1/2 kinase cascade [68, 72].

The blood–brain barrier (BBB) disruption and perfusion changes played a key part in the initiation and development of RIBI [11]. Although a series of studies reported that hypoperfusion was related to the severity of TIBI [73], elevated perfusion was also identified in some cases of RIBI [74]. Though BBB was leaked and plasma-containing fibronectin was exudated into parenchyma after radiation [75], the extracellular matrix (ECM) was remodeled by cerebrovascular endothelial and vascular smooth muscle cells secreting fibronectin [75]. The formation of perivascular fibrous extracellular matrix (ECM) without a corresponding increase in microvascular density impaired nutrition diffusion to the parenchyma and contributed to the observed cognitive decline in late-delayed RIBI [75].

4.2.2 Examination for RIBI

Conventional MRI examination can reveal specific changes: the early stage of radioactive brain injury is manifested as brain swelling in the irradiated area of the damaged tissues, edema in the white matter of the brain in a "finger-like" distribution, low signal in the T1-weighted image (T1WI), and high signal in the T2-weighted image (T2WI). When necrosis occurs with the progression of the lesion, enhancement of the damaged area can be seen on enhanced scanning due to the disruption of the blood–brain barrier in the necrotic area. In advanced lesions, liquefaction necrosis occurs, and the liquefaction necrosis part of the T1WI signal is lower and the T2WI signal is higher, which is similar to the cerebrospinal fluid cystic degeneration area of the lesion is a low-signal non-enhanced area. Fluid-attenuated inversion recovery sequence (FLAIR) scans can show the extent of cerebral edema in the lesion and help to determine the extent of cystic degeneration in the lesion [76, 77].

Several models were developed for early detection of RIBI and clinical intervention [78, 79]. The incorporation of diffusion-weighted imaging (DWI) and arterial spin labeling (ASL) improved the diagnostic performance in RIBI [80]. DWI is more sensitive to radiation brain injury and can be used as one of the methods of early monitoring, and also assists in the differentiation between radiation brain injury and tumors. Radiation injury lesions show a low signal on DWI and a high signal on ADC maps, while tumors show a high signal on DWI and a low signal on ADC maps [81].

As perfusion changes were considered to be a character of RIBI, perfusion-weighted imaging (PWI) measures local cerebral blood volume (rCBV), which helps to differentiate between tumor recurrence and RIBI; radiological brain necrosis has a reduced rCBV, whereas tumor recurrence tends to have an elevated rCBV [82, 83].

In addition, positron emission tomography (PET) is good at showing the difference between radiation injury and tumor recurrence. PET has a sensitivity of 80%-90% and a specificity of 50%-90% for distinguishing radiation brain injury from tumor recurrence [84].

4.2.3 Therapy for RIBI

Corilagin, which suppressed the NF-κB pathway, inhibited radiation-induced microglia activation and relieved RIBI [67]. PPARα agonists also significantly prevented radiation-induced pro-inflammatory response [85]. RIBI could be mitigated by the blockade of voltage-gated Kv1.3 potassium channel with a selective inhibitor named shK-170 [86]. A fluorescent small molecule dye named IR-780 alleviated the neuroinflammation, promoted the recovery of BBB function in RIBI, and reduced the level of oxidative stress in vascular endothelial cells [87].

A phase 2 clinical trial (NCT03208413) of thalidomide was performed and nearly half of patients with RIBI experienced a clinical improvement [11].

Stem cells were used to treat various brain injuries due to its ability of tissue repair ability via secreting several neuroprotective factors, facilitating nerve regeneration and survival [88]. Stem cell therapy was an alternative therapy for RIBI and a study reported that intravenous injection of bone marrow mesenchymal stem cells (BMSCs) protected the integrity of neural structures and improved cognitive function after irradiation [88].

Ginkgo biloba extract (EGb) attenuated irradiation-induced oxidative organ injury [89] and the effect was proved in intestinal injury [90], indicating that EGb may have a therapeutic potentiality for RIBI.

Corticosteroids are the conventional therapy for RIBI because they effectively inhibit the proinflammatory response which propagates necrosis and reduces leakage from the blood–brain barrier (BBB). Then symptoms will be relieved by reducing edema. However, long-term application of glucocorticoids can lead to gastric ulcers, glucose intolerance, osteopenia, steroid myopathy, and iatrogenic Cushing’s syndrome [91].

Surgery is another important conventional method for managing progressive resectable radionecrotic lesions, with the main advantage of which being the relief of any mass effect and histological confirmation. Removal of the nidus of necrotic tissue causing peri-lesion edema will provide symptomatic relief for the patient and allow weaning off steroids. Tissue diagnosis can be used to rule out tumor progression by biopsy. However, brain edema may persist for several weeks even after surgical resection and thus requiring close monitoring [92].

RIBI tissues have elevated levels of VEGF, so Bevacizumab, an anti-VEGF antibody, is now being used in the treatment of RBN. Several clinical trials have shown that bevacizumab improves neurological symptoms and cognitive function in patients with RIBI, and two randomized controlled trials have shown that bevacizumab treatment is more efficacious than placebo or corticosteroids and has a better safety profile [93].

The overlay visualization of keywords and the citation burst analysis of Keywords and References can reflect the research hotspots in different stages, and even indicate the future research directions. In this study, we found that the research on the mechanisms of RIBI, distinguishing from brain tumors and therapy for RIBI attracted increasing attention, and would be a research hotspot for the present and the future.

This is despite the fact that with the development of radiation therapy for brain disorders, radiation-induced brain injury is becoming more common, and more research is being done on this subject. It is still difficult for readers to understand the current development status and hotspots of RIBI in numerous literatures, and to find a suitable research direction. Our study was the first bibliometric study in the field of RIBI up to 2023, which objectively and systematically presented the current status and trends of research, analyzed the reasons for the current situation, and pointed out the possible future directions of research in this field, which could facilitate academic development and guide researchers toward under-explored areas. However, our study still has many limitations: (1) because CiteSpace is limited in the selection of databases, we only selected WoS for retrieval to obtain more comprehensive analysis results. Though WoS remains one of the oldest and most widely recognized databases, covering a broad range of fields. And it is known for its authority and the quality of the journals it includes. There may still be small studies, locally limited articles, etc. that are not included, resulting in an incomplete search and publication bias. (2) all the literature was obtained from WOS' SCI and SSCI databases and filtered according to the criteria mentioned earlier. However, it should be noted that the manual selection process involved subjective judgments, as we filtered literature based on relevance to our research focus while excluding entirely unrelated content. This subjectivity could introduce bias when attempting to replicate our analysis. (3) while most of the results in this study were based on machine algorithms and were slightly deficient in manual generalization. Therefore, this study maintains the reliability of the research results to a certain extent, and we suggest that more databases should be combined for a more comprehensive analysis in the subsequent research process.

5 Conclusion

Our results provide more understanding of RIBI, and perhaps, opportunities for scholars to identify a research direction in the field of RIBI, which may facilitate further research. The contribution of this article may be summarized in several ways. Firstly, Eastern Asia, North America, and Europe are the most impactful regions of the world in this field, with a spotlight on the USA. Secondly, outstanding articles with the highest citations have driven the research field's progress greatly. Thirdly, the changing pattern of the research theme reflects the current status and potential theoretical basis for future investigation on RIBI. Besides, from 1998, the analysis showed that research on RIBI mainly concentrated on the inducement, imaging, and clinical manifestation but less on mechanisms and effective treatment. Therefore, based on the bibliometric analysis of the co-occurrence keywords, the concrete mechanism and effective treatment of RIBI may be a future research direction.

Author contributions Jinxin Lan: Conceptualization; Writing Original Draft. Yifan Ren: Conceptualization; Writing Review & Editing; Data curation. Yuyang Liu: Investigation; Methodology. Jialin Liu: Funding acquisition; Supervision. Ling Chen: Supervision; Project administration. All authors reviewed the manuscript.

Funding This work was supported by the National Natural Science Foundation of China (grant numbers 82172680).

Data availability All the raw literature used in this study were retrieved from the Science Citation Index Expanded (SCI-EXPANDED) and Social Sciences Citation Index (SSCI) in the Web of Science Core Collection (WoSCC).

Code availability All the raw code used in this study could be obtained by contacting the corresponding author (Email: chen_ling301@163.com).

Declarations

Competing interests All authors declare that they have no competing interests. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Ostrom QT, Price M, Neff C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the UNITED STATES in 2016–2020. Neuro Oncol. 2023;25(Supplement_4):iv1–99. https://doi.org/10.1093/neuonc/noad149.
2. Ali FS, Arevalo O, Zorofchian S, et al. Cerebral radiation necrosis: incidence, pathogenesis, diagnostic challenges, and future opportunities. Curr Oncol Rep. 2019;21(8):66. https://doi.org/10.1007/s11912-019-0818-y.
3. Wu H, Wang C, Liu J, et al. Evaluation of a tumor electric field treatment system in a rat model of glioma. CNS Neurosci Ther. 2020;26(11):1168–77. https://doi.org/10.1111/cns.13441.
4. Milano MT, Grimm J, Niemierko A, et al. Single- and multifraction stereotactic radiosurgery dose/volume tolerances of the brain. Int J Radiat Oncol Biol Phys. 2021;110(1):68–86. https://doi.org/10.1016/j.ijrobp.2020.08.013.
5. Chen WC, Perlow HK, Choudhury A, et al. Radiotherapy for meningiomas. J Neurooncol. 2022;160(2):505–15. https://doi.org/10.1007/s11060-022-04171-9.
6. Morace R, Marongiu A, Vangelista T, et al. Intracranial capillary hemangioma: a description of four cases. World Neurosurg. 2012;78(1–2):191 e115-121. https://doi.org/10.1016/j.wneu.2011.09.017.
7. Murphy ES, Suh JH. Radiotherapy for vestibular schwannomas: a critical review. Int J Radiat Oncol Biol Phys. 2011;79(4):985–97. https://doi.org/10.1016/j.ijrobp.2010.10.010.
8. Chanson P, Dormoy A, Dekkers OM. Use of radiotherapy after pituitary surgery for non-functioning pituitary adenomas. Eur J Endocrinol. 2019;181(1):D1–13. https://doi.org/10.1530/EJE-19-0058.
9. Iannalfi A, Fragkandrea I, Brock J, Saran F. Radiotherapy in craniopharyngiomas. Clin Oncol (R Coll Radiol). 2013;25(11):654–67. https://doi.org/10.1016/j.clon.2013.07.005.
10. Gorbunov NV, Kiang JG. Brain damage and patterns of neurovascular disorder after ionizing Irradiation. Complications in radiotherapy and radiation combined injury. Radiat Res. 2021;196(1):1–16. https://doi.org/10.1667/RADE-20-00147.1.
11. Cheng J, Jiang J, He B, et al. A phase 2 study of thalidomide for the treatment of radiation-induced blood-brain barrier injury. Sci Transl Med. 2023;15(684):eabm6543. https://doi.org/10.1126/scitranslmed.abm6543.
12. Shi Z, Yu P, Lin WJ, et al. Microglia drive transient insult-induced brain injury by chemotactic recruitment of CD8(+) T lymphocytes. Neuron. 2023;111(5):696-710 e699. https://doi.org/10.1016/j.neuron.2022.12.009.
13. Chao ST, Ahluwalia MS, Barnett GH, et al. Challenges with the diagnosis and treatment of cerebral radiation necrosis. Int J Radiat Oncol Biol Phys. 2013;87(3):449–57. https://doi.org/10.1016/j.ijrobp.2013.05.015.
14. Sheline GE, Wara WM, Smith V. Therapeutic irradiation and brain injury. Int J Radiat Oncol Biol Phys. 1980;6(9):1215–28. https://doi.org/10.1016/0360-3016(80)90175-3.
15. Tofilon PJ, Fike JR. The radioresponse of the central nervous system: a dynamic process. Radiat Res. 2000;153(4):357–70. https://doi.org/10.1667/0033-7587(2000)153[0357:trotcn]2.0.co;2.
16. Wei N, Xu Y, Li Y, et al. A bibliometric analysis of T cell and atherosclerosis. Front Immunol. 2022;13:948314. https://doi.org/10.3389/fimmu.2022.948314.
17. AlRyalat SAS, Malkawi LW, Momani SM. Comparing bibliometric analysis using pubmed, scopus, and web of science databases. J Vis Exp. 2019. https://doi.org/10.3791/58494.
18. Falagas ME, Pitsouni EI, Malietzis GA, Pappas G. Comparison of PubMed, scopus, web of science, and google scholar: strengths and weaknesses. FASEB J. Feb2008;22(2):338–42. https://doi.org/10.1096/fj.07-9492LSF.
19. Aria M, Cuccurullo C. An R-tool for comprehensive science mapping analysis. J Informetr. 2017;11(4):959–75. https://doi.org/10.1016/j.joi.2017.08.007.
20. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010;84(2):523–38. https://doi.org/10.1007/s11192-009-0146-3.
21. Synnestvedt MB, Chen C, Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. AMIA Annu Symp Proc. 2005;2005:724–8.
22. Gao Q, Zhang C, Wang J, et al. The top 100 highly cited articles on osteoporosis from 1990 to 2019: a bibliometric and visualized analysis. Arch Osteoporos. 2020;15(1):144. https://doi.org/10.1007/s11657-020-0705-z.
23. Kumar AJ, Leeds NE, Fuller GN, et al. Malignant gliomas: MR imaging spectrum of radiation therapy- and chemotherapy-induced necrosis of the brain after treatment. Radiology. 2000;217(2):377–84. https://doi.org/10.1148/radiology.217.2.r00nv36377.
24. Levin VA, Bidaut L, Hou P, et al. Randomized double-blind placebo-controlled trial of bevacizumab therapy for radiation necrosis of the central nervous system. Int J Radiat Oncol Biol Phys. 2011;79(5):1487–95. https://doi.org/10.1016/j.ijrobp.2009.12.061.
25. Rola R, Raber J, Rizk A, et al. Radiation-induced impairment of hippocampal neurogenesis is associated with cognitive deficits in young mice. Exp Neurol. 2004;188(2):316–30. https://doi.org/10.1016/j.expneurol.2004.05.005.
26. Mizumatsu S, Monje ML, Morhardt DR, Rola R, Palmer TD, Fike JR. Extreme sensitivity of adult neurogenesis to low doses of X-irradiation. Cancer Res. 2003;63(14):4021–7.
27. Minniti G, Clarke E, Lanzetta G, et al. Stereotactic radiosurgery for brain metastases: analysis of outcome and risk of brain radionecrosis. Radiat Oncol. 2011;6:48. https://doi.org/10.1186/1748-717X-6-48.

28. Ruben JD, Dally M, Bailey M, Smith R, McLean CA, Fedele P. Cerebral radiation necrosis: incidence, outcomes, and risk factors with emphasis on radiation parameters and chemotherapy. Int J Radiat Oncol Biol Phys. 2006;65(2):499–508. https://doi.org/10.1016/j.ijrobp.2005.12.002.
29. Monje ML, Toda H, Palmer TD. Inflammatory blockade restores adult hippocampal neurogenesis. Science. 2003;302(5651):1760–5. https://doi.org/10.1126/science.1088417.
30. Gonzalez J, Kumar AJ, Conrad CA, Levin VA. Effect of bevacizumab on radiation necrosis of the brain. Int J Radiat Oncol Biol Phys. 2007;67(2):323–6. https://doi.org/10.1016/j.ijrobp.2006.10.010.
31. Giglio P, Gilbert MR. Cerebral radiation necrosis. Neurologist. 2003;9(4):180–8. https://doi.org/10.1097/01.nrl.0000080951.78533.c4.
32. Ricci PE, Karis JP, Heiserman JE, Fram EK, Bice AN, Drayer BP. Differentiating recurrent tumor from radiation necrosis: time for re-evaluation of positron emission tomography? AJNR Am J Neuroradiol. 1998;19(3):407–13.
33. Hein PA, Eskey CJ, Dunn JF, Hug EB. Diffusion-weighted imaging in the follow-up of treated high-grade gliomas: tumor recurrence versus radiation injury. AJNR Am J Neuroradiol. 2004;25(2):201–9.
34. Terakawa Y, Tsuyuguchi N, Iwai Y, et al. Diagnostic accuracy of 11C-methionine PET for differentiation of recurrent brain tumors from radiation necrosis after radiotherapy. J Nucl Med. 2008;49(5):694–9. https://doi.org/10.2967/jnumed.107.048082.
35. Blonigen BJ, Steinmetz RD, Levin L, Lamba MA, Warnick RE, Breneman JC. Irradiated volume as a predictor of brain radionecrosis after linear accelerator stereotactic radiosurgery. Int J Radiat Oncol Biol Phys. 2010;77(4):996–1001. https://doi.org/10.1016/j.ijrobp.2009.06.006.
36. Sugahara T, Korogi Y, Tomiguchi S, et al. Posttherapeutic intraaxial brain tumor: the value of perfusion-sensitive contrast-enhanced MR imaging for differentiating tumor recurrence from nonneoplastic contrast-enhancing tissue. AJNR Am J Neuroradiol. 2000;21(5):901–9.
37. Chao ST, Suh JH, Raja S, Lee SY, Barnett G. The sensitivity and specificity of FDG PET in distinguishing recurrent brain tumor from radionecrosis in patients treated with stereotactic radiosurgery. Int J Cancer. 2001;96(3):191–7. https://doi.org/10.1002/ijc.1016.
38. Lawrence YR, Li XA, el Naqa I, et al. Radiation dose-volume effects in the brain. Int J Radiat Oncol Biol Phys. 2010;76(3 Suppl):S20-27. https://doi.org/10.1016/j.ijrobp.2009.02.091.
39. Barajas RF, Chang JS, Sneed PK, Segal MR, McDermott MW, Cha S. Distinguishing recurrent intra-axial metastatic tumor from radiation necrosis following gamma knife radiosurgery using dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. AJNR Am J Neuroradiol. 2009;30(2):367–72. https://doi.org/10.3174/ajnr.A1362.
40. Mullins ME, Barest GD, Schaefer PW, Hochberg FH, Gonzalez RG, Lev MH. Radiation necrosis versus glioma recurrence: conventional MR imaging clues to diagnosis. AJNR Am J Neuroradiol. 2005;26(8):1967–72.
41. Barajas RF Jr, Chang JS, Segal MR, et al. Differentiation of recurrent glioblastoma multiforme from radiation necrosis after external beam radiation therapy with dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. Radiology. 2009;253(2):486–96. https://doi.org/10.1148/radiol.2532090007.
42. Lin F, Chen Y, Mo W, et al. A bibliometric analysis of autophagy in lung diseases from 2012 to 2021. Front Immunol. 2022;13:1092575. https://doi.org/10.3389/fimmu.2022.1092575.
43. Durieux V, Gevenois PA. Bibliometric indicators: quality measurements of scientific publication. Radiology. 2010;255(2):342–51. https://doi.org/10.1148/radiol.09090626.
44. Kokol P, Kokol M, Zagoranski S. Machine learning on small size samples: a synthetic knowledge synthesis. Sci Prog Jan-Mar. 2022;105(1):368504211029777. https://doi.org/10.1177/00368504211029777.
45. Song Q, Tan Y. Knowledge mapping of the relationship between norepinephrine and memory: a bibliometric analysis. Front Endocrinol (Lausanne). 2023;14:1242643. https://doi.org/10.3389/fendo.2023.1242643.
46. Liu Q, Huang Y, Duan M, Yang Q, Ren B, Tang F. Microglia as therapeutic target for radiation-induced brain injury. Int J Mol Sci. 2022. https://doi.org/10.3390/ijms23158286.
47. Rahmathulla G, Marko NF, Weil RJ. Cerebral radiation necrosis: a review of the pathobiology, diagnosis and management considerations. J Clin Neurosci. 2013;20(4):485–502. https://doi.org/10.1016/j.jocn.2012.09.011.
48. Ali MJ. Understanding the "g-index" and the "e-index." Semin Ophthalmol. 2021;36(4):139. https://doi.org/10.1080/08820538.2021.1922975.
49. Hirsch JE. An index to quantify an individual's scientific research output. Proc Natl Acad Sci U S A. 2005;102(46):16569–72. https://doi.org/10.1073/pnas.0507655102.
50. Fishman K, Baure J, Zou Y, et al. Radiation-induced reductions in neurogenesis are ameliorated in mice deficient in CuZnSOD or MnSOD. Free Radic Biol Med. 2009;47(10):1459–67. https://doi.org/10.1016/j.freeradbiomed.2009.08.016.
51. Rola R, Zou Y, Huang TT, et al. Lack of extracellular superoxide dismutase (EC-SOD) in the microenvironment impacts radiation-induced changes in neurogenesis. Free Radic Biol Med. 2007;42(8):1133–45. https://doi.org/10.1016/j.freeradbiomed.2007.01.020.
52. Acharya MM, Christie LA, Lan ML, et al. Human neural stem cell transplantation ameliorates radiation-induced cognitive dysfunction. Cancer Res. 2011;71(14):4834–45. https://doi.org/10.1158/0008-5472.CAN-11-0027.
53. Acharya MM, Christie LA, Lan ML, et al. Rescue of radiation-induced cognitive impairment through cranial transplantation of human embryonic stem cells. Proc Natl Acad Sci U S A. 2009;106(45):19150–5. https://doi.org/10.1073/pnas.0909293106.
54. Leavitt RJ, Limoli CL, Baulch JE. miRNA-based therapeutic potential of stem cell-derived extracellular vesicles: a safe cell-free treatment to ameliorate radiation-induced brain injury. Int J Radiat Biol. 2019;95(4):427–35. https://doi.org/10.1080/09553002.2018.1522012.
55. Smith SM, Limoli CL. Stem cell therapies for the resolution of radiation injury to the brain. Curr Stem Cell Rep. 2017;3(4):342–7. https://doi.org/10.1007/s40778-017-0105-5.
56. Benderitter M, Caviggioli F, Chapel A, et al. Stem cell therapies for the treatment of radiation-induced normal tissue side effects. Antioxid Redox Signal. 2014;21(2):338–55. https://doi.org/10.1089/ars.2013.5652.
57. Rahmathulla G, Recinos PF, Kamian K, Mohammadi AM, Ahluwalia MS, Barnett GH. MRI-guided laser interstitial thermal therapy in neuro-oncology: a review of its current clinical applications. Oncology. 2014;87(2):67–82. https://doi.org/10.1159/000362817.
58. Silva D, Sharma M, Juthani R, Meola A, Barnett GH. Magnetic resonance thermometry and laser interstitial thermal therapy for brain tumors. Neurosurg Clin N Am. Oct2017;28(4):525–33. https://doi.org/10.1016/j.nec.2017.05.015.

59. Rhoten RL, Luciano MG, Barnett GH. Computer-assisted endoscopy for neurosurgical procedures: technical note. Neurosurgery. 1997;40(3):632–7. https://doi.org/10.1097/00006123-199703000-00042.
60. Suh JH, Vogelbaum MA, Barnett GH. Update of stereotactic radiosurgery for brain tumors. Curr Opin Neurol. 2004;17(6):681–6. https://doi.org/10.1097/00019052-200412000-00007.
61. Suh JH, Barnett GH. Stereotactic radiosurgery for brain tumors in pediatric patients. Technol Cancer Res Treat. 2003;2(2):141–6. https://doi.org/10.1177/153303460300200210.
62. Barnett GH, Linskey ME, Adler JR, et al. Stereotactic radiosurgery–an organized neurosurgery-sanctioned definition. J Neurosurg. 2007;106(1):1–5. https://doi.org/10.3171/jns.2007.106.1.1.
63. Gomez H, Barnett GH, Estes ML, Palmer J, Magdinec M. Stereotactic and computer-assisted neurosurgery at the Cleveland clinic: review of 501 consecutive cases. Cleve Clin J Med. 1993;60(5):399–410. https://doi.org/10.3949/ccjm.60.5.399.
64. Clarivate. The Clarivate analytics impact factor. 2022. https://clarivate.com/webofsciencegroup/essays/impact-factor/.
65. Lumniczky K, Szatmari T, Safrany G. Ionizing Radiation-Induced Immune and Inflammatory Reactions in the Brain. Front Immunol. 2017;8:517. https://doi.org/10.3389/fimmu.2017.00517.
66. Kalm M, Fukuda A, Fukuda H, et al. Transient inflammation in neurogenic regions after irradiation of the developing brain. Radiat Res. 2009;171(1):66–76. https://doi.org/10.1667/RR1269.1.
67. Dong XR, Luo M, Fan L, et al. Corilagin inhibits the double strand break-triggered NF-kappaB pathway in irradiated microglial cells. Int J Mol Med. 2010;25(4):531–6.
68. Chen H, Chong ZZ, De Toledo SM, Azzam EI, Elkabes S, Souayah N. Delayed activation of human microglial cells by high dose ionizing radiation. Brain Res. 2016;1646:193–8. https://doi.org/10.1016/j.brainres.2016.06.002.
69. Hong JH, Chiang CS, Campbell IL, Sun JR, Withers HR, McBride WH. Induction of acute phase gene expression by brain irradiation. Int J Radiat Oncol Biol Phys. 1995;33(3):619–26. https://doi.org/10.1016/0360-3016(95)00279-8.
70. Hwang SY, Jung JS, Kim TH, et al. Ionizing radiation induces astrocyte gliosis through microglia activation. Neurobiol Dis. 2006;21(3):457–67. https://doi.org/10.1016/j.nbd.2005.08.006.
71. Wang J, Pan H, Lin Z, et al. Neuroprotective effect of fractalkine on radiation-induced brain injury through promoting the M2 polarization of microglia. Mol Neurobiol. 2021;58(3):1074–87. https://doi.org/10.1007/s12035-020-02138-3.
72. Deng Z, Sui G, Rosa PM, Zhao W. Radiation-induced c-Jun activation depends on MEK1-ERK1/2 signaling pathway in microglial cells. PLoS ONE. 2012;7(5): e36739. https://doi.org/10.1371/journal.pone.0036739.
73. Chan YL, Yeung DK, Leung SF, Lee SF, Ching AS. Dynamic susceptibility contrast-enhanced perfusion MR imaging in late radiation-induced injury of the brain. Acta Neurochir Suppl. 2005;95:173–5. https://doi.org/10.1007/3-211-32318-x_37.
74. Pruzincova L, Steno J, Srbecky M, et al. MR imaging of late radiation therapy- and chemotherapy-induced injury: a pictorial essay. Eur Radiol. 2009;19(11):2716–27. https://doi.org/10.1007/s00330-009-1449-8.
75. Andrews RN, Caudell DL, Metheny-Barlow LJ, et al. Fibronectin produced by cerebral endothelial and vascular smooth muscle cells contributes to perivascular extracellular matrix in late-delayed radiation-induced brain injury. Radiat Res. 2018;190(4):361–73. https://doi.org/10.1667/RR14961.1.
76. Romano A, Moltoni G, Blandino A, et al. Radiosurgery for brain metastases: challenges in imaging interpretation after treatment. Cancers (Basel). 2023. https://doi.org/10.3390/cancers15205092.
77. Salari E, Elsamaloty H, Ray A, Hadziahmetovic M, Parsai EI. Differentiating radiation necrosis and metastatic progression in brain tumors using radiomics and machine learning. Am J Clin Oncol. 2023;46(11):486–95. https://doi.org/10.1097/COC.0000000000001036.
78. Zhang B, Lian Z, Zhong L, et al. Machine-learning based MRI radiomics models for early detection of radiation-induced brain injury in nasopharyngeal carcinoma. BMC Cancer. 2020;20(1):502. https://doi.org/10.1186/s12885-020-06957-4.
79. Ding Z, Zhang H, Lv XF, et al. Radiation-induced brain structural and functional abnormalities in presymptomatic phase and outcome prediction. Hum Brain Mapp. 2018;39(1):407–27. https://doi.org/10.1002/hbm.23852.
80. Zhang J, Wu Y, Wang Y, et al. Diffusion-weighted imaging and arterial spin labeling radiomics features may improve differentiation between radiation-induced brain injury and glioma recurrence. Eur Radiol. 2023;33(5):3332–42. https://doi.org/10.1007/s00330-022-09365-3.
81. Taoka T, Ito R, Nakamichi R, et al. Evaluation of alterations in interstitial fluid dynamics in cases of whole-brain radiation using the diffusion-weighted image analysis along the perivascular space method. NMR Biomed. 2023. https://doi.org/10.1002/nbm.5030.
82. Lee J, Chen MM, Liu HL, Ucisik FE, Wintermark M, Kumar VA. MR perfusion imaging for gliomas. Magn Reson Imaging Clin N Am. 2024;32(1):73–83. https://doi.org/10.1016/j.mric.2023.07.003.
83. Alsulami TA, Hyare H, Thomas DL, Golay X. The value of arterial spin labelling (ASL) perfusion MRI in the assessment of post-treatment progression in adult glioma: a systematic review and meta-analysis. Neurooncol Adv. 2023;5(1):vdad122. https://doi.org/10.1093/noajnl/vdad122.
84. Santonocito OS, Grimod G, Di Stefano AL, et al. O-(2–18F- fl uoroethyl)-L-tyrosine (18F-FET) PET as a potential selection tool for second surgery in glioblastoma patients. J Neurosurg Sci. 2023. https://doi.org/10.23736/S0390-5616.23.06019-8.
85. Ramanan S, Kooshki M, Zhao W, Hsu FC, Robbins ME. PPARalpha ligands inhibit radiation-induced microglial inflammatory responses by negatively regulating NF-kappaB and AP-1 pathways. Free Radic Biol Med. 2008;45(12):1695–704. https://doi.org/10.1016/j.freeradbiomed.2008.09.002.
86. Peng Y, Lu K, Li Z, et al. Blockade of Kv1.3 channels ameliorates radiation-induced brain injury. Neuro Oncol. 2014;16(4):528–39. https://doi.org/10.1093/neuonc/not221.
87. Zhang C, Zheng J, Chen W, et al. Mitochondrial-targeting fluorescent small molecule IR-780 alleviates radiation-induced brain injury. Brain Res. 2023;1805:148285. https://doi.org/10.1016/j.brainres.2023.148285.
88. Liu Z, Xu K, Pan S, et al. Manganese-enhanced magnetic resonance assessment of changes in hippocampal neural function after the treatment of radiation-induced brain injury with bone marrow mesenchymal stem cells. Brain Res Bull. 2023;204:110795. https://doi.org/10.1016/j.brainresbull.2023.110795.

89. Sener G, Kabasakal L, Atasoy BM, et al. Ginkgo biloba extract protects against ionizing radiation-induced oxidative organ damage in rats. Pharmacol Res. 2006;53(3):241–52. https://doi.org/10.1016/j.phrs.2005.11.006.
90. Zhenkui Z, Jiarui H, Shuling J, Lulu H. Pretreatment with ginkgo biloba extract 50 alleviates radiation-induced acute intestinal injury in mice. Chin J Tissue Eng Res. 2021;25(23):3666–71. https://doi.org/10.12307/2021.037.
91. Chung C, Bryant A, Brown PD. Interventions for the treatment of brain radionecrosis after radiotherapy or radiosurgery. Cochrane Database Syst Rev. 2018;7(7):011492. https://doi.org/10.1002/14651858.CD011492.pub2.
92. Vellayappan B, Tan CL, Yong C, et al. Diagnosis and management of radiation necrosis in patients with brain metastases. Front Oncol. 2018;8:395. https://doi.org/10.3389/fonc.2018.00395.
93. Liao G, Khan M, Zhao Z, Arooj S, Yan M, Li X. Bevacizumab treatment of radiation-induced brain necrosis: a systematic review. Front Oncol. 2021;11:593449. https://doi.org/10.3389/fonc.2021.593449.