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Trends in Stereotactic Radiosurgery for Intracranial and Spinal Pathologies: Analysis of the Top 100 Most Cited Articles

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Abstract

There is a plethora of papers on the role of stereotactic radiosurgery (SRS) in various benign and malignant intracranial tumors, and it is possible to overlook the most important and landmark studies. Thus, the necessity of citation analysis arises, which reviews the most cited articles and recognizes the impact made by these articles. Utilizing the 100 most cited articles describing the use of SRS for intracranial and spinal pathologies, this article aims to provide meaningful information regarding the historical trends and recent directions in which this field is headed. We performed a search of the Web of Science database using the keywords "stereotactic radiosurgery," "gamma knife," "GKRS," "gamma knife radiosurgery," "LINAC," and "Cyberknife" on May 14, 2022. Our search retrieved a total of 30,652 articles published between the years 1968 and 2017. The top 100 cited articles were arranged in descending order based on citation count (CC) and citation per year (CY). The journal with the largest number of publications as well as citation count was the *International Journal of Radiation Oncology Biology Physics* (*n* = 33), followed by *Journal of Neurosurgery (n* = 25). The most cited article was authored by Andrews, which was published in 2004 in *The Lancet* (1699 CC, 89.42 CY). Flickinger, with 25 papers and 7635 total citations, was the author with the highest impact. Lunsford, with 25 publications and total citations of 7615, was a close second. The USA was the leading country with the maximum number of total citations (*n* = 23,054). Ninety-two articles described the use of SRS for intracranial pathologies (metastases, *n* = 38; AVM, *n* = 16; vestibular schwannoma, *n* = 9; meningioma, *n* = 8; trigeminal neuralgia, *n* = 6; sellar lesion, *n* = 2; glioma, *n* = 2; functional, *n* = 1; and procedure related, *n* = 10). Eight studies describing spinal radiosurgery were included, out of which four were on spinal metastases. Citation analyses of the top 100 articles revealed that the focus of research in the field of SRS started with functional neurosurgery and progressed to benign intracranial tumors and AVMs. More recently, central nervous system (CNS) metastases have received the maximum attention with 38 articles, including 14 randomized controlled trials finding a place in the top 100 cited articles. Presently, the use of SRS is concentrated in developed countries. Efforts need to be made for more widespread use in developing nations to bring the maximum possible benefits of this focused noninvasive treatment to a wider population.

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Full Text

The term radiosurgery was first coined in 1951.[1] Two different technologies developed to deliver radiation to a stereotactically targeted intracranial lesion are Gamma Knife radiosurgery (GKRS) and linear accelerator (LINAC). GKRS is a form of stereotactic radiosurgery (SRS) that relies on three-dimensional imaging to deliver highly focused gamma radiations. Lars Leksell, a Swedish neurosurgeon, has been credited for the invention of the Gamma Knife.[2] GKRS is useful for lesions which are smaller than 3 cm (because of the perceived limitation of normal tissue tolerance),[3] surgically inaccessible lesions, and residual lesions after surgery or embolization.[4] Because it requires the target to be immobilized (either in a stereotactic frame or a face mask), the use of GKRS is primarily limited to cranial lesions.[1],[2] LINACs, a mainstay of standard fractionated therapy, move in multiple arc-shaped fashion to fire a photon beam at an isocenter.[5] Cyberknife, conceptualized by Dr. John Alder, uses a LINAC fitted over a robot to deliver non-isocentric beams from any desired angle.[6] As opposed to GKRS, LINAC and Cyberknife can also be used for spinal pathologies like metastasis and others.[5],[6] SRS is commonly utilized in intracranial vascular lesions (arteriovenous malformations),[7],[8] tumors (metastases,[9],[10] vestibular schwannoma,[11],[12],[13] meningioma, [14],[15] and pituitary adenomas[16]), and functional disorders like trigeminal neuralgia.[17],[18],[19] There is a plethora of papers on the role of SRS in various benign and malignant intracranial tumors, and it is possible to overlook the most important and landmark studies. Thus, the necessity of citation analysis arises which reviews the most cited articles and recognizes the impact made by these articles. It assesses the progress and contributions made at the level of individuals, institutions, countries, and journals. The number of citations received by an article is also an indirect index of the recent research trends in the field under study and can provide an overview to a new scholar where the field is headed.

Materials and Methods

Search strategy

A title-specific search of the Web of Science database was executed using the keywords "Stereotactic radiosurgery," "Radiosurgery," "gamma knife," "GKRS," "gamma knife radiosurgery," "LINAC," and 'Cyberknife' on May 14, 2022. All the abstracts were screened for suitable articles. The inclusion criteria were articles describing the use of SRS in intracranial and spinal pathologies and published in peer-reviewed journals. Only the articles which described clinical outcomes following the administration of SRS or society guidelines were included. The articles describing the technical aspects of the SRS technology were excluded. The 100 most cited articles were selected and reviewed by the authors.

Data extraction and analysis

The articles were arranged in descending order of the number of citations. The parameters assessed were the title of the articles, authors, corresponding authors, country of origin, journal of publication, year of publication, citation count, and the journal impact factor.

The statistical analysis was performed using R (R Foundation for Statistical Computing, Vienna, Austria) employing the "bibliometrix" package.[20] The VOSviewer software (Van Eck and Waltman, Leiden University, Leiden, The Netherlands) was also used to plot network and overlay plots.[21]

Bibliometric parameters

The following statistical parameters were considered during the analysis:

Hirsch h-index: authors' number of publications and number of citations, reviewed in other articles.[22] g-index: It is a variant of h-index which gives credit for the most cited papers. It is the highest rank where the sum of the citations is larger than the square of rank.[22] m-index: It is another variant of the h-index which displays the h-index per year since the first publication.[22]Citation per year (CY): This is calculated by dividing the total number of citations by the total number of years.[22]

Results

Article analysis

Our search retrieved a total of 30,652 articles. Based on our inclusion criteria, the top 100 most cited articles were assorted and analyzed. These articles were published between the years 1968 and 2017, with an average of 21.1 years from publication. The main information regarding our citation analysis is summarized in [Table 1]. Eighty-six articles out of these 100 were original articles. There were 15 randomized controlled trials (RCTs), while there were seven review articles. The retrieved articles received 349.7 mean citations per document and 20.2 mean citations per document per year. These 100 articles were authored by 510 authors in total, and these authors had a total of 795 appearances in these 100 articles. {Table 1}

Year of publication

The publication of most cited articles on SRS for intracranial and spinal pathologies increased in the 1990s. Maximum number of these articles were published in 1996 and 2001 (seven articles each) [Figure 1]a. The mean total citation per article was highest in the year 2009 (1557). The highest mean total citation per year was 119 in 2016 and the lowest was three in the year 1968 [Supplementary Table 1].{Figure 1}[INLINE:1]

The average article citations per year increased gradually from the late 1980s and attained a peak in the year 2016 [Figure 1]b.

Top authors

The retrieved data showed that 510 authors contributed to these 100 most cited articles. JC Flickinger, with 25 papers and 7635 total citations, was the author with the highest impact. LD Lunsford, with 25 publications and total citations of 7615, was a close second. The author's h-index, g-index, and m-index (as per the 100 articles included in this analysis) were evaluated [Supplementary Table 2]. The individual author's impact visualized as h-index is shown in [Figure 2]a, while their academic output over time has been depicted in [Figure 2]b.{Figure 2}[INLINE:2]

Country of origin of articles

The USA had a maximum number of articles in these 100 articles, with 67 articles authored by corresponding authors belonging to the USA [Supplementary Table 3]. Eleven articles out of these 67 had authors from other countries as well. The collaborating ratio (multiple country publications [MCP] ratio) was the highest for Canada. [Figure 3]a shows the leading countries in publishing SRS-related articles in terms of the number of authors belonging to that country. It shows the dominance of the USA, with 278 out of 510 authors from these top 100 articles belonging to the USA followed by Japan (n = 60).[INLINE:3]{Figure 3}

[Supplementary Table 3] also shows the leading countries with the highest number of total citations. The USA was the leading country with the maximum number of total citations (n = 23,054) and the average number of citations per article being 344 [Figure 3]b. It was followed by Japan and Germany with 3025 and 1944 total citations, respectively. The average number of citations per article was the highest for the UK (680 citations per article).

The University of Pittsburgh in the USA had the highest number of author affiliations (n = 75), followed by

Harvard University (n = 20) [Figure 3]c.

Topic of articles

Ninety-two articles described the use of SRS for intracranial pathologies. The topics of these articles included metastases (n = 38), Arteriovenous malformation (AVM) (n = 16), vestibular schwannoma (n = 9), meningiomas (n = 8), trigeminal neuralgia (n = 6), sellar and suprasellar pathology (n = 2), glioma (n = 2), functional (n = 1), and procedure related (n = 10). Eight studies describing spinal radiosurgery were included, out of which four were on spinal metastases.

Most frequently encountered terms

The retrieved articles were searched for the most frequently encountered terms in the title of the article [Figure 4]a. The most found words were radiation therapy (n = 38) followed closely by surgery (n = 24). Cluster analysis among these keywords is depicted in the network graph in [Figure 4]b. There is a shift of the keywords from stereotactic radiosurgery and arteriovenous malformation in the late 1990s to Gamma Knife radiosurgery in the early 2000s.{Figure 4}

Most cited documents

The top 10 cited articles are summarized in [Table 2][23],[24],[25],[26],[27],[28],[29],[30],[31],[32] (top 100 articles listed in [Supplementary Table 4][SUPPORTING:1]). The most cited article ”Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: Phase III results of the RTOG 9508 randomized trial” was published in The Lancet in 2004.[23] It was authored by Andrews et al.[23] and has 1699 citations with 89.42 CY. The second most cited article “Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: A randomized controlled trial” was published in 2009 in Lancet Oncology.[24] It was authored by Chang et al.[24] and received 1557 citations with a CY of 111.21. Overall, the top 18 articles are “citation classics,” having received more than 400 citations each.{Table 2}

Most relevant sources

The journal with the largest number of publications as well as citation count was the International Journal of Radiation Oncology Biology Physics (n = 33, citation count 10,023) [Figure 5]a. It was followed closely by Journal of Neurosurgery (n = 25, citation count = 7079) and Neurosurgery (n = 15, citation count = 3625). The top three journals accounted for more than two-thirds of the total articles. The growth of the top five journals in terms of publishing top cited articles over time has been shown in [Figure 5]b. The bibliometric parameters (h-index, g-index, and m-index) were analyzed and are listed in [Supplementary Table 5].{Figure 5}[INLINE:4]

Discussion

There has been a rapid increase in the number of publications on SRS. The radiosurgery technologies have evolved over time, gradually becoming less time consuming and more patient as well as operator friendly. The original Gamma Knife (Model U, B, C, 4C) employed 201 cobalt-60 sources as the source of radiation.[33] The secondary collimators were external (helmet) and changed manually.[3] The position of the source was fixed in these models and the patient's position had to be changed manually during the treatment. The GK model PERFEXION (Elekta Instrument AB, Stockholm, Sweden), which was introduced in the year 2006, utilizes 192 cobalt-60 sources as a source of radiation with a fully internalized collimator.[34] The position of the source can move in this model, and the patient's position is changed automatically. The gamma knife ICON (Elekta Instrument AB) is the latest model which can perform single or fractionated frame-based or frameless SRS. It incorporates a cone-beam computed tomography (CT), allowing mask-based hypofractionation. Most of the highly cited publications on SRS have utilized GKRS. LINAC is still the most readily available source of SRS, but this is not reflected in the number of research publications or citations. This is perhaps because we studied

only cranial and spinal pathologies, for which GKRS is in use since a long time. Cyberknife, which utilizes a robotic arm, is used to deliver SRS without the need of immobilization of the head in a frame. The number of publications on Cyberknife is limited because it is the most recent SRS technology, is not as widely available as LINAC and GKRS, and is significantly more expensive.

Analysis of the bibliometric parameters showed that Flickinger, Lunsford, Kondziolka, and Pollock contributed to the majority of the publications. These authors had the maximum impact factor, which is evident from the h-index, g-index, and m-index. All these authors are from the USA. It is not surprising to see the dominance of developed nations in the field of SRS. This can be linked to high income and better health-care facilities. Analysis of the publications showed that the USA leads the list with more than two-thirds of the total publications. The USA is also the leader in the number of SRS-related publications with international collaborations. The GKRS was introduced in the USA in 1987, which is much earlier than most other countries.[2] This increases the number of citable years, and therefore, the highest citation count is as expected. However, Japan has an edge over the USA in terms of average citations per article. Presently, the use of SRS is concentrated in developed countries. Efforts need to be made for more widespread use in developing nations in order to bring the maximum possible benefits of this focused noninvasive treatment to a wider population.

The International Journal of Radiation Oncology Biology Physics had the largest share of articles on SRS (n = 33), followed by Journal of Neurosurgery (n = 25) and Neurosurgery (n = 15). These top three journals had the highest number of total citations, which is suggestive of the prestigious and influential nature of these journals in this field.

The most frequently encountered keyword was "radiation therapy" (n = 38). Radiation therapy is a general term and includes all forms of radiotherapy. Therefore, it is not surprising to see this term at the top of the list. This was closely followed by the term "surgery" (n = 24), which is specific to the search topic.

Research trends

The oldest article included in the list is a case report by Leksell outlining gamma thalamotomy for intractable pain, which was published in 1968.[35] The next few decades saw research being focused on intracranial tumors, namely, vestibular schwannoma and meningiomas including cavernous sinus meningiomas [Figure 6]a. Seminal publications related to the procedure and radiation dose–volume relationships were highly endorsed. The maximum research in the field was in the fields of AVMs and metastases, with this period seeing simultaneous and parallel growth in the number of publications on these topics. But the primary focus of global research in the last two decades has undoubtedly been cranial metastases. This is reflected in that six studies in the top 10 cited articles have been published after 2001, all focusing on intracranial metastases. An oft-quoted drawback of citation analysis is that it takes time for publications to accrue the number of citations needed to figure in the top of such lists, and thus, older publications have an unfair advantage when compared to newer, more impactful publications.[36] Indeed, many of the recent bibliometric analyses on various topics in neurosurgery have revealed that the decade between 1991 and 2000 had been the most productive in terms of citation count.[37],[38] This does not hold true here, thus portraying the attention radio surgeons have been paying to the treatment of cranial metastases. The result of this focus has been that high-quality evidence has been generated on this topic within a short time span. Analysis of the most cited documents revealed that "Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: Phase III results of the RTOG 9508 randomized trial" published in The Lancet received the highest count of total citations (n = 1699).[23] They concluded that WBRT and SRS improved functional outcomes for all patients and survival for patients with single unresectable brain metastasis. However, the article "Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: A randomized controlled trial" published in the Lancet Oncology received the highest citations per year (n = 111.21).[24] These are landmark trials, and the high citation counts truly show the influence in the field of radiotherapy. This is an index of both patient's and physician's confidence of the value of this technique to prolong the median survival rates in cancer-afflicted patients. {Figure 6}

There are 15 RCTs included in the top 100 cited articles. Notably, 14 out of 15 were related to the role of SRS in intracranial metastases, while one was related to glioblastoma multiforme. This highlights the availability of

high-quality research and evidence in the field of intracranial metastases [Figure 6]b. Moreover, the decade wise distribution of RCTs shows that the evidence related to SRS is still evolving.

Limitations

Despite our best efforts, this study has certain limitations related to the bibliometric nature of the study. First, the search strategy was limited to a single database, which can possibly miss a highly cited article. The exclusion from the aforementioned list does not decrease the significance of those articles. Second, specific search terms were used to retrieve the articles related to SRS. Third, there could be the possibility of self-citations, in-house citations (authors share authorship as a collaboration), and omission bias (excluding articles that do not support their hypothesis).[39],[40],[41] Moreover, the reasons why an article is cited multiple times may be diverse and may not accurately reflect the influence of the study in question. Sole reliance on these indicators can lead to missing some of the papers reporting important results, as confirmed by experts' review. Some of the treatment regimens described in these top 100 cited articles may not be the standard of care in the current time.[42],[43],[44],[45]

Conclusion

The results of our study revealed that the research on SRS for intracranial and spinal pathologies has been slowly but steadily increasing. It can act as an insight for clinicians and researchers about the output of publications on SRS. The focus of research in the field of SRS started with functional neurosurgery and progressed to benign intracranial tumors and AVMs. More recently, central nervous system (CNS) metastases have received the maximum attention with 38 articles, including 14 RCTs finding a place in the top 100 cited articles. Focus also needs to be placed on the application of radiosurgery to other fields of neurosurgery. Presently, the use of SRS is concentrated in developed countries like the USA, Europe, and Japan. Efforts need to be made for more widespread use in developing nations in order to bring the maximum possible benefits of this focused noninvasive treatment to a wider population.

Abbreviations

GK: Gamma Knife, GKRS: Gamma Knife radiosurgery, SRS: stereotactic radiosurgery, CY: citation per year, CC: citation count, SCP: single country publications, MCP: multiple country publications, RCT: randomized controlled trial, RTOG: Radiation Therapy Oncology Group, WBRT: whole brain radiation therapy.

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Conflicts of interest

There are no conflicts of interest.

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Figure 1: (a) Line graph showing number of articles published in different years. (b) Line graph showing total citation count per year

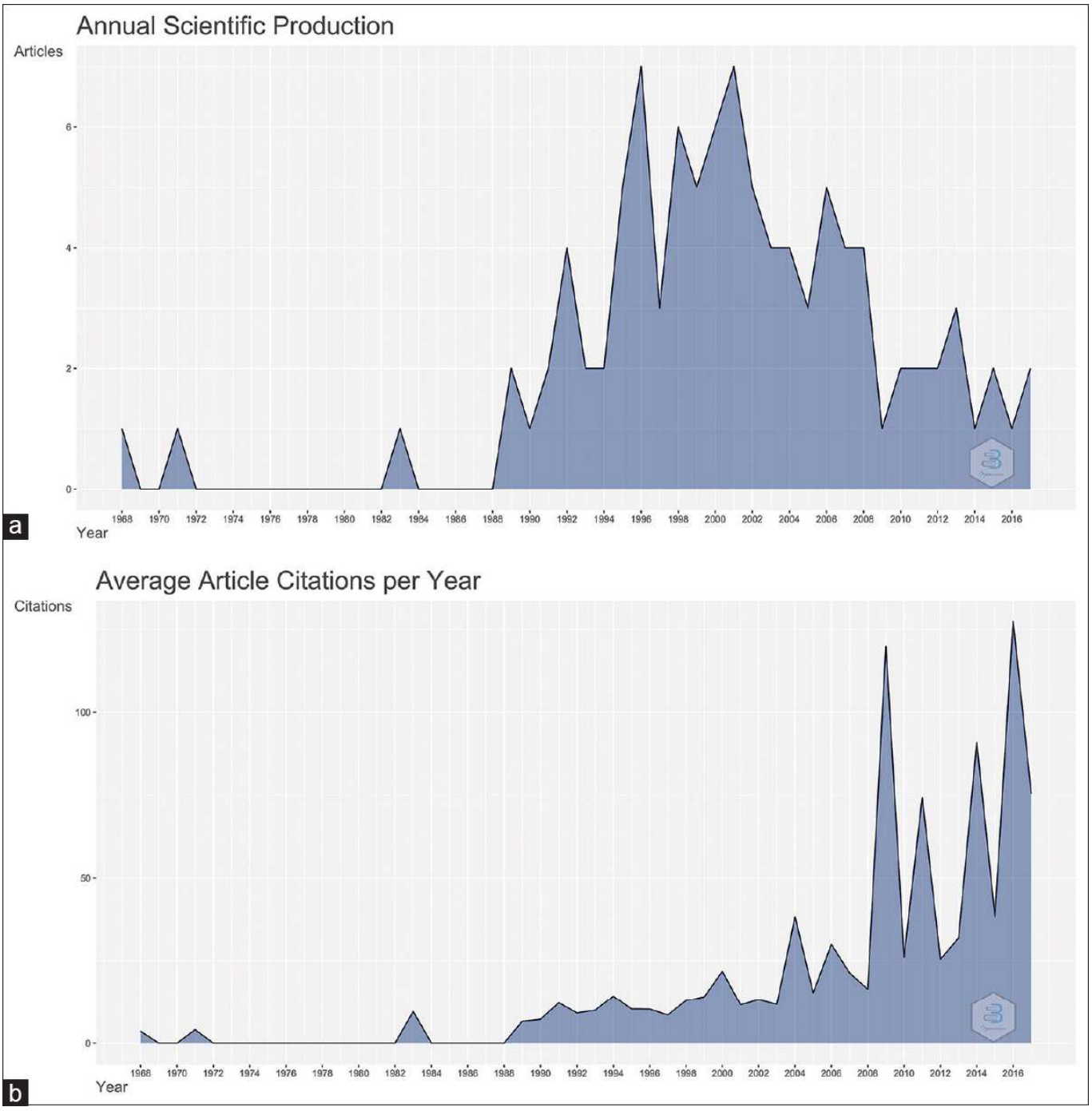

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Figure 2: (a) Graph showing authors' impact factors. (b) Top authors' academic production over time

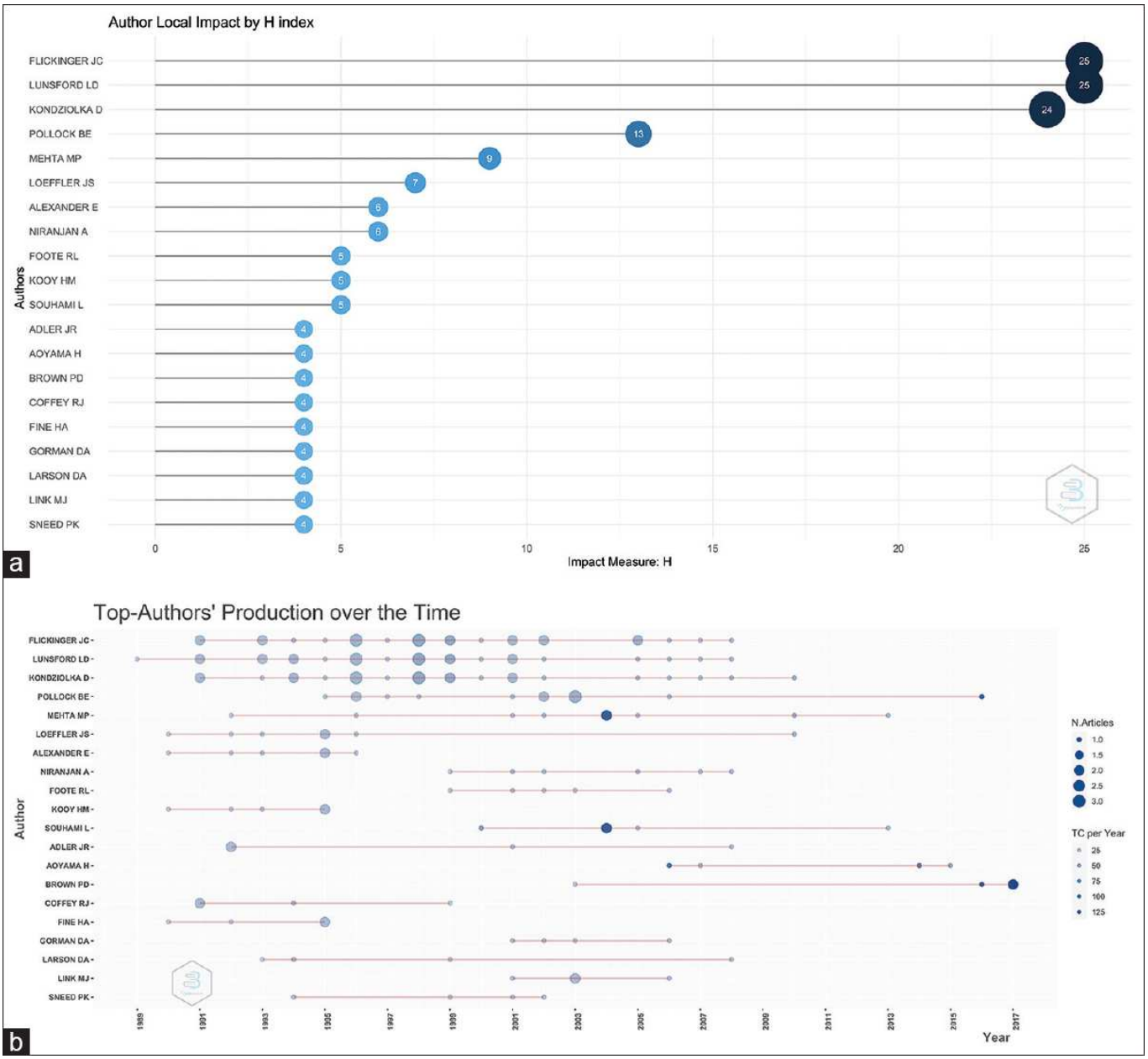

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Figure 3: (a) World map by country-specific publications. (b) Bar graph showing the most cited countries. (c) Graph showing most relevant affiliations

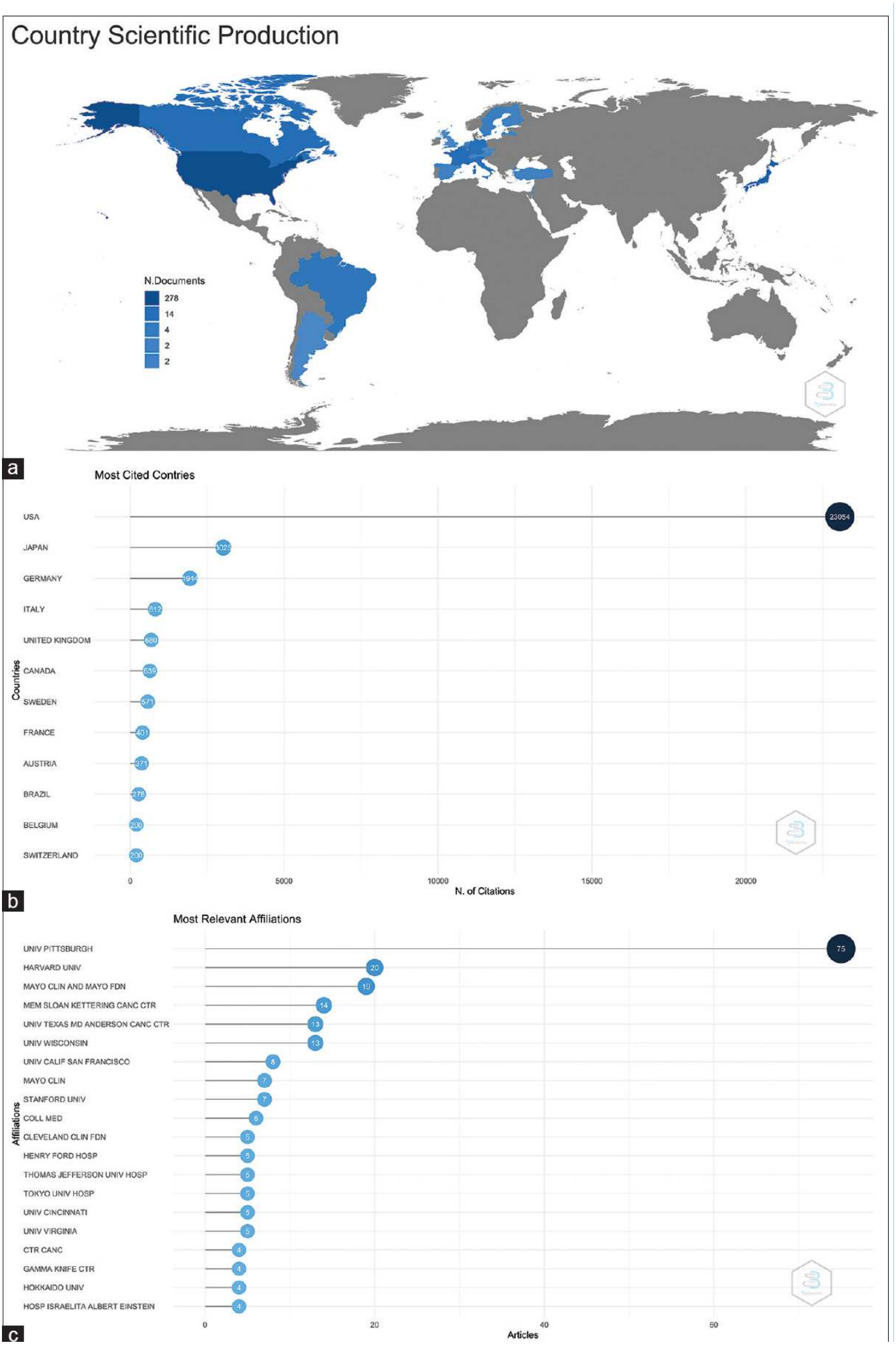
Country Scientific Production
N.Documents
278
14
4
2
2
a
Most Cited Contries
USA
JAPAN
GERMANY
ITALY
UNITED KINGDOM
CANADA
SWEDEN
FRANCE
AUSTRIA
BRAZIL
BELGIUM
SWITZERLAND
23054
3029
1944
812
680
639
571
401
371
278
200
200
Countries
0
5000
10000
15000
20000
N. of Citations
b
Most Relevant Affiliations
UNIV PITTSBURGH
HARVARD UNIV
MAYO CLIN AND MAYO FDN
MEM SLOAN KETTERING CANC CTR
UNIV TEXAS MD ANDERSON CANC CTR
UNIV WISCONSIN
UNIV CALIF SAN FRANCISCO
MAYO CLIN
STANFORD UNIV
COLL MED
CLEVELAND CLIN FDN
HENRY FORD HOSP
THOMAS JEFFERSON UNIV HOSP
TOKYO UNIV HOSP
UNIV CINCINNATI
UNIV VIRGINIA
CTR CANC
GAMMA KNIFE CTR
HOKKAIDO UNIV
HOSP ISRAELITA ALBERT EINSTEIN
75
20
19
14
13
13
8
7
7
6
5
5
5
5
5
5
4
4
4
4
Affiliations
0
20
40
60
Articles
c

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Figure 4: (a) Graph showing the most relevant keywords. (b) Network visualization map for keyword analysis

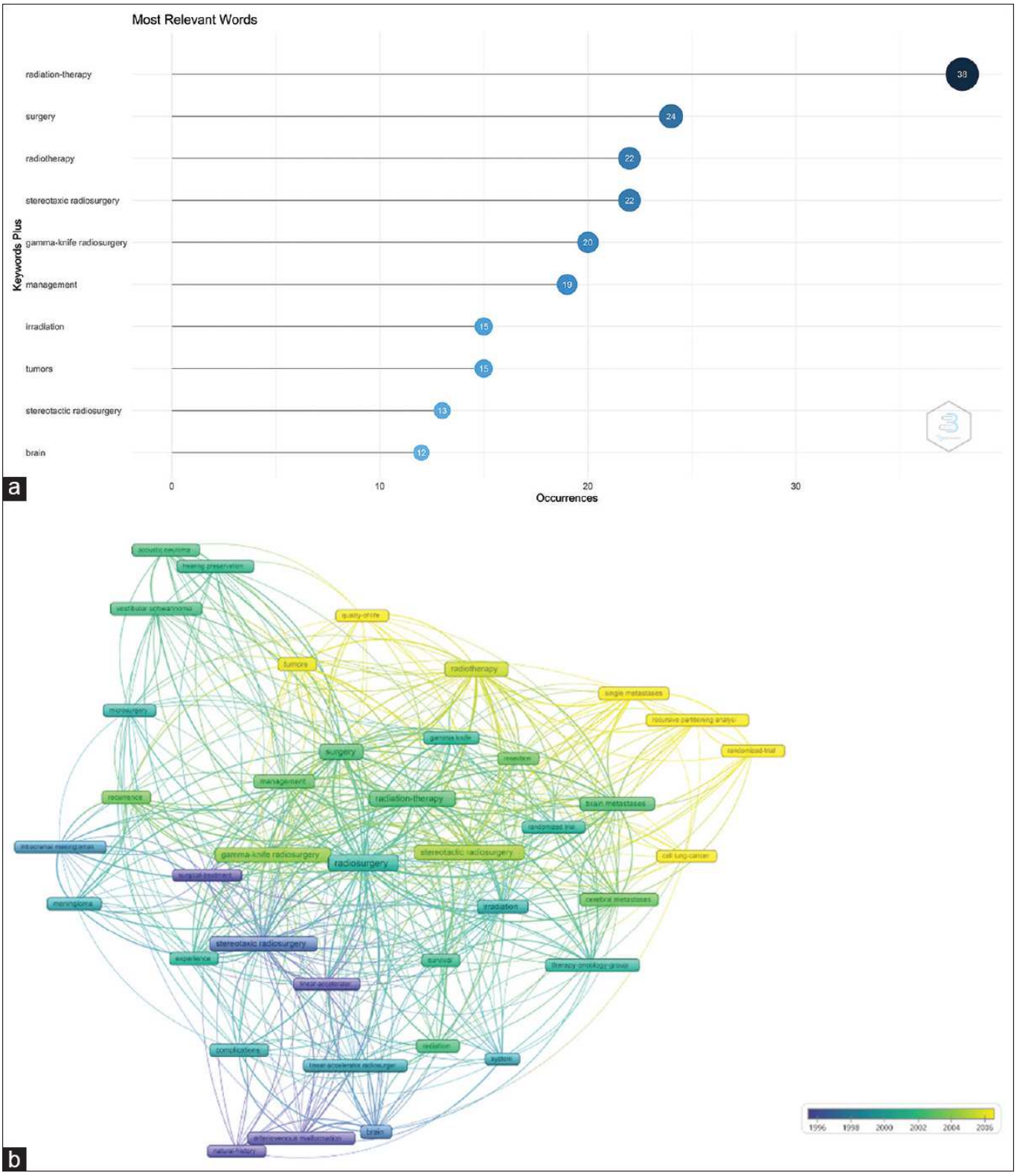

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Figure 5: (a) Graph showing the most relevant journal sources. (b) Growth of the top five journals in terms of publishing top cited articles over time

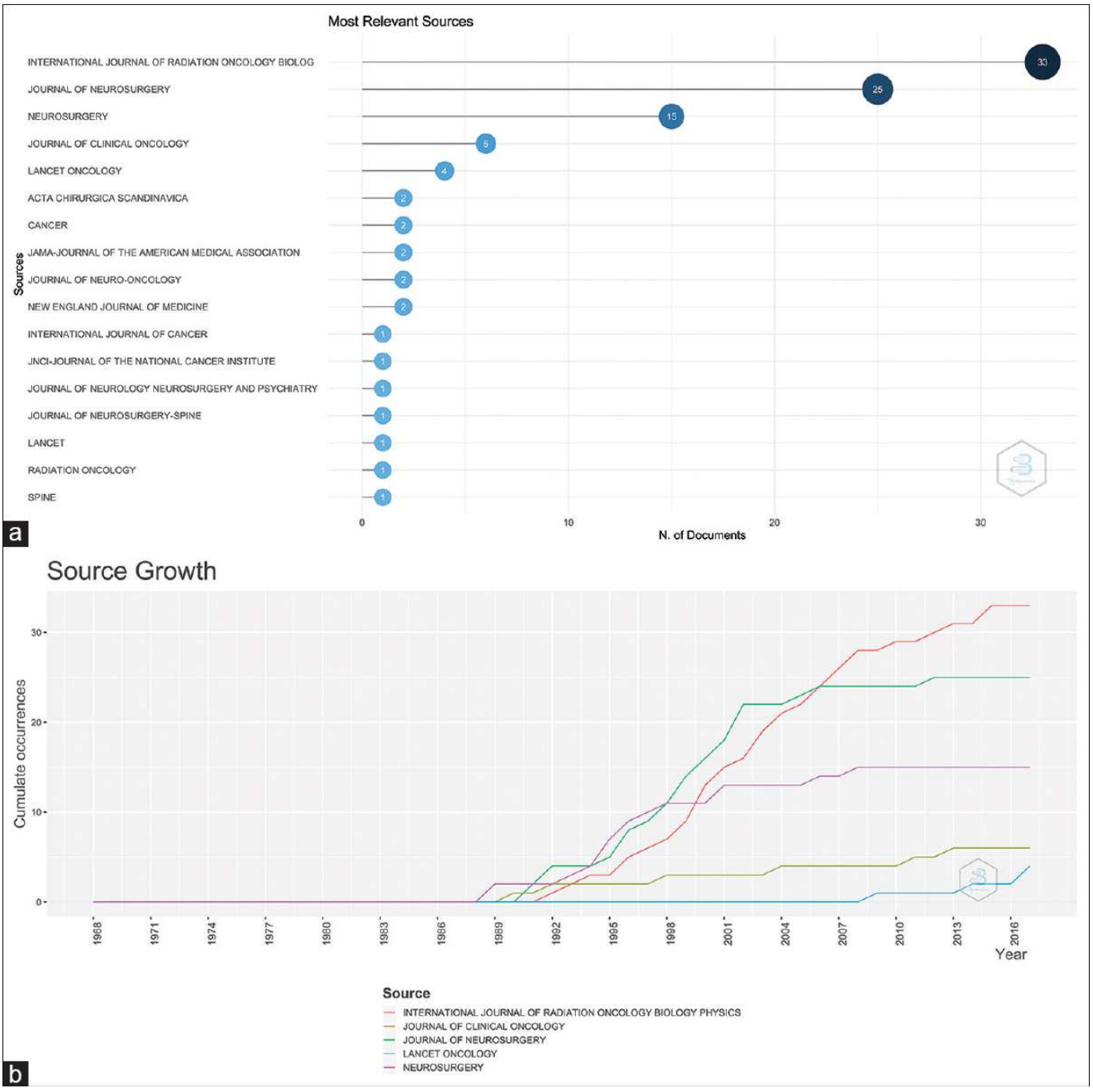

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Figure 6: (a) Trends in the publication of the top 100 cited articles based on pathology. (b) Trends in the publication of top cited RCTs. RCT = randomized controlled trial

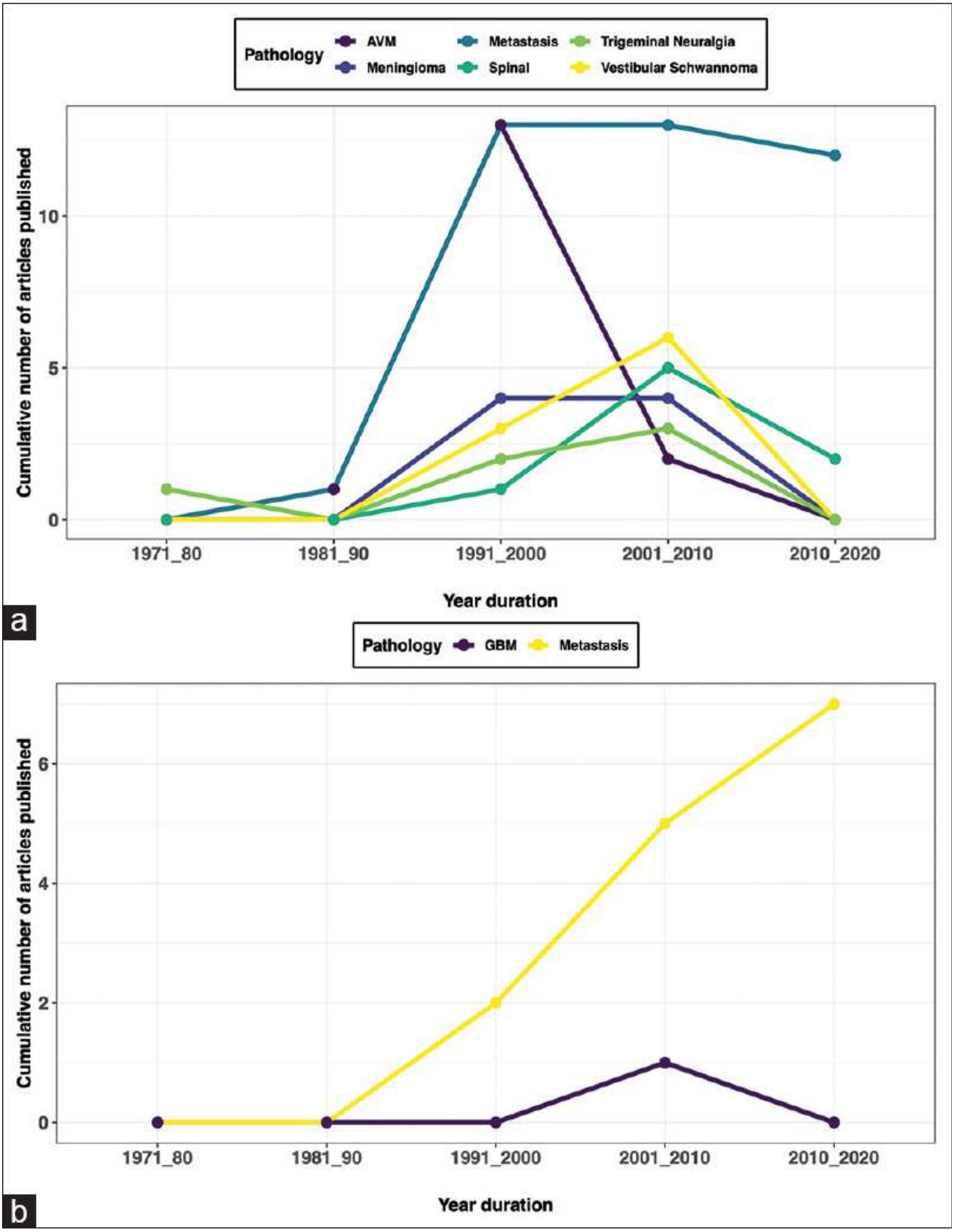

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Table 1: Main information about data

Description	Results
Main information about data	
Timespan	1968-2017
Sources (journals, books, etc.)	17
Documents	100
Average years from publication	21.1
Average citations per documents	349.7
Average citations per year per doc	20.2
References	2018
Document types	
Article	86
Article; proceedings paper	10
Note	1
Review	3
Document contents	
Keywords plus (ID)	249
Author's keywords (DE)	139
Authors	
Authors	510
Author appearances	795
Authors of single-authored documents	2
Authors of multi-authored documents	508
Authors' collaboration	
Single-authored documents	4
Documents per author	0.196
Authors per document	5.1
Co-authors per document	7.95
Collaboration index	5.29

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Table 2: The top 10 most cited articles

Rank	Title	DOI	Authors, year	Journal	Study design	Cranial/ spinal	Total citations	TC per year
1	Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: Phase III results of the RTOG 9508 randomised trial	10.1016/ S0140-6736 (04) 16250-8	Andrews *et al.*,[23] 2004	Lancet	RCT	Cranial	1699	89.42
2	Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: A randomised controlled trial	10.1016/ S1470-2045 (09) 70263-3	Chang *et al.*,[24] 2009	Lancet Oncol	RCT	Cranial	1557	111.21
3	Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases: A randomized controlled trial	10.1001/jama. 295.21.2483	Aoyama *et al.*,[25] 2006	Ama-J Am Med Assoc	RCT	Cranial	1497	88.06
4	Adjuvant whole-brain radiotherapy versus observation after radiosurgery or surgical resection of one to three cerebral metastases: Results of the EORTC 22952-26001 study	10.1200/ JCO.2010.30.1655	Kocher *et al.*,[26] 2011	J Clin Oncol	RCT	Cranial	1234	102.83
5	Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: Final report of RTOG protocol 90-05	10.1016/ S0360-3016 (99) 00507-6	Shaw *et al.*,[27] 2000	Int J Radiat Oncol	RCT	Cranial	1030	44.78
6	Effect of radiosurgery alone vs radiosurgery with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: A randomized clinical trial	10.1001/jama. 2016.9839	Brown *et al.*,[28] 2016	Jama-J Am Med Assoc	RCT	Cranial	764	109.14
7	Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): A multi-institutional prospective observational study	10.1016/ S1470-2045 (14) 70061-0	Yamamoto M,[29] 2014	Lancet Oncol	Prospective	cranial	726	80.67
8	Stereotactic radiosurgery plus whole brain radiotherapy versus radiotherapy alone for patients with multiple brain metastases	10.1016/ S0360-3016 (99) 00198-4	Kondziolka *et al.*,[30] 1999	Int J Radiat Oncol	RCT	Cranial	698	29.08
9	A simple scoring ratio to index the conformity of radiosurgical treatment plans	10.3171/ jns. 2000.93. supplement_3.0219	Paddick,[31] 2000	J Neurosurg	Technical note	Cranial	680	29.57
10	Stereotactic radiosurgery for arteriovenous malformations of the brain	10.3171/jns. 1991.75.4.0512	Lunsford *et al.*,[32] 1991	J Neurosurg	Prospective	Cranial	547	17.09

DOI=Digital Object Identifier, RCT=randomized controlled trial, TC=Total citations