Global Growth and Distribution of CyberKnife Stereotactic Radiosurgery: A Bibliometric Analysis

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BACKGROUND AND OBJECTIVES: CyberKnife (CK) is advanced stereotactic radiosurgery (SRS) technology indicated for brain metastases, arteriovenous malformations, functional disease, and a number of other neurosurgical conditions that combines a linear accelerator with a highly maneuverable robotic arm and real-time imaging, allowing for several advantages including the ability to deliver radiation from a wide variety of angles and frameless delivery of therapy. We seek to explore the current trend and evolution of publications related to CK SRS using bibliometric approach, with a particular focus on neurosurgical disease applications.

METHODS: The Web of Science database was queried for data collection, using keyword "CyberKnife". Network visualization figures representing exported Web of Science data were created using visualization of similarities viewer. Statistics were completed in R.

RESULTS: In total, 3980 articles from 12 077 authors were identified for analysis. Annual publication number has expressed growth from 1 article in 1996 to 263 articles in 2023. Most frequently reported conditions were brain metastases, followed by vestibular schwannoma and meningiomas. The top 5 most prolific authors in the field are Andrew Muacevic, Steven D. Chang, Oliver Blanck, Christian Baues, and John R. Adler. The top 3 most prolific institutions are the University of Cologne, Stanford University, and the University of Munich. Institutional collaboration is strongest between institutions within countries. Through authorial key word analysis, we identified that articles related to pituitary adenoma, brain metastases, meningioma, hemangioma, and cavernous sinus have increased. Through the same analysis, we noticed an increase in key words potentially associated with interdisciplinary applications of CK, such as immunotherapy, machine learning, and deep learning.

CONCLUSION: CK SRS is an emergent technology with increasingly more neurological conditions and diseases being researched for treatment options. The rise in academic focus on CK SRS has been spearheaded by international effort from the United States, Japan, and Italy. There remains significant potential for future international collaboration.

KEY WORDS: CyberKnife, Stereotactic radiosurgery, Bibliometrics

tereotactic radiosurgery (SRS) is a minimally invasive treatment modality in the field of neurosurgery that uses highly focused radiation with target and treats structural and functional abnormalities in the brain and spinal cord. CyberKnife (CK), developed by Accuray (Sunnyvale, CA) and first introduced in 1991, is currently one of the most advanced forms

of SRS that combines a linear accelerator with a highly maneuverable robotic arm and real-time imaging, allowing for several advantages including the ability to deliver radiation from a wide array of angles, treatment of nonbrain conditions, and frameless delivery of therapy. CK and other forms of SRS have replaced open neurosurgical procedures for a growing number of

ABBREVIATIONS: CK, CyberKnife; SRS, stereotactic radiosurgery.

conditions, including brain and spine metastases, trigeminal neuralgia, arteriovenous malformations (AVMs), and functional disease. ²⁻⁵ CK also serves as an alternative to whole brain radiotherapy for inoperable conditions. ¹ Given the rapid expansion of CK, we aim to quantify and assess its global emergence and reach with a particular focus on the technology's application in treating neurosurgical and neurological diseases. To date, there has been no assessment of the academic development of CK or radiosurgical technology on a global scale. Bibliometrics is a statistical approach that analyses publications to determine the evolution of scholarly fields and provides an avenue to objectively determine academic impacts and trends. ⁶ To elucidate CK's impact and identify potential opportunities for future growth and adoption, we conducted a bibliometric analysis of CK-related publications from its inception to the year 2023.

METHODS

The Clarivate Web of Science Core Collection database was queried for data collection using keyword "CyberKnife" on June 28th, 2024. Articles published in 2024 were initially excluded from the search results. Data tables were collected through the The Clarivate Web of Science Core Collection database "Analyze Results" feature in the categories "Publication Years," "Authors," "Citation Topics Meso," "Citation Topics Micro," "Affiliations," "Countries/Regions," and "Research Areas." Data tables provided the number of articles within a certain subcategory, as well as the percent makeup of each subcategory in the overall article pool. Visualization of Similarities viewer (Center for Science and Technology Studies, Leiden University) was used to create visual bibliometric networks through association of strength normalization, providing an avenue to interpret academic metrics that are otherwise impossible or tedious to discern from raw data.⁶

Distinct bibliometric networks were created to map the interactions and prominence of authors, institutions, nations, keywords, citations, and individual publications. Interactions were determined by coauthorship, citations, cocitations, co-occurrence, and bibliometric coupling, whereas prominence was determined by publication or citation count. Each bibliometric map was visualized through a network map and a temporal map, providing information about key bibliometric relationships and their evolution over time. Statistical analysis and summary figures were generated by the programming language R (The R Foundation) using the ggplot2 package (posit). Because this work is a bibliometric analysis and not a systematic review, this study was not registered on International Prospective Register of Systematic Reviews (PROSPERO) or other systematic review databases.

RESULTS

Primary Results on CK Publications and Highest Cited CK Papers

In total, 3980 articles from 12 077 authors were identified for analysis (Table 1). Annual publication number has increased from 1 article in 1996 to 291 articles in 2021. There has been a slight decrease in annual publication count since 2021, with 259 articles

TABLE 1. Summary Statistics	
Timespan	1996:2023
Included article count	3937
Source count	659
Author count	12 194
Country count	80
Institution count	3048
Condition count	176
Subfield count	96
Conference count	244
First article date	1996
Article count of earliest year	1
Article count of latest year	263

in 2022, and 263 articles in 2023 (r = 0.97) (Figure 1A). The most cited documents in the field of CK radiosurgery are presented in Table 2, with exclusion criteria for publications not directly related to CK specifically. ⁷⁻¹¹ Bibliometric network visualization by citation demonstrates 8 primary clusters, with nodes of the greatest size being the most highly cited. The largest clusters are individually dominated by Chang et al (2015), ⁷ Goldbrunner et al (2016), ¹² Gerszten et al (2007), ⁸ Das et al (2008), ¹³ Fowler et al (2010), ¹⁴ Adler et al (1997), ⁹ King et al (2013), ¹⁰ and Kang et al (2012). We identify these highly cited, cluster-defining documents as foundational works in the field of CK radiosurgery (Figure 1B; Table 3).

Trends in Top Journals of CK Publications

The journals that have published the most articles on CK radiosurgery were "Medical Physics," "Radiotherapy and Oncology," "International Journal of Radiation Oncology Biology Physics," "Strahlentherapie Und Onkologie," "Cureus Journal of Medical Science," "Frontiers in Oncology," "Radiation Oncology," "Journal of Applied Clinical Medical Physics," "Neurosurgery," and "Technology in Cancer Research Treatment," "Medical Physics" has produced 392 CK articles to date, and these articles make up nearly 10% of all CK publications. Of the top 4 journals, "Radiotherapy and Oncology" and "Strahlentherapie Und Onkologie" demonstrate strong increases in CK publication count with time (r > 0.85) (Figure 1C). Journals within the same specialty of medicine were clustered together and tended to cocite frequently. Examples include cocitations between "Neurosurgery, " "World Neurosurgery," and "Clinical Neurology and Neurosurgery," as well as "Medical Physics," "Journal of Medical Physics," and "Physics in Medicine and Biology" (Figure 1D).

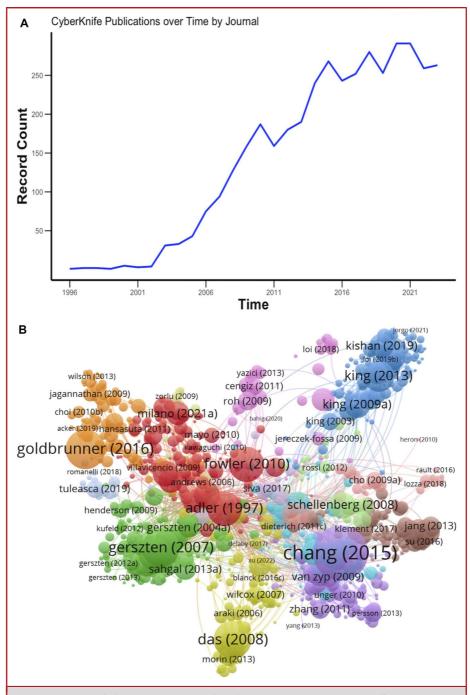
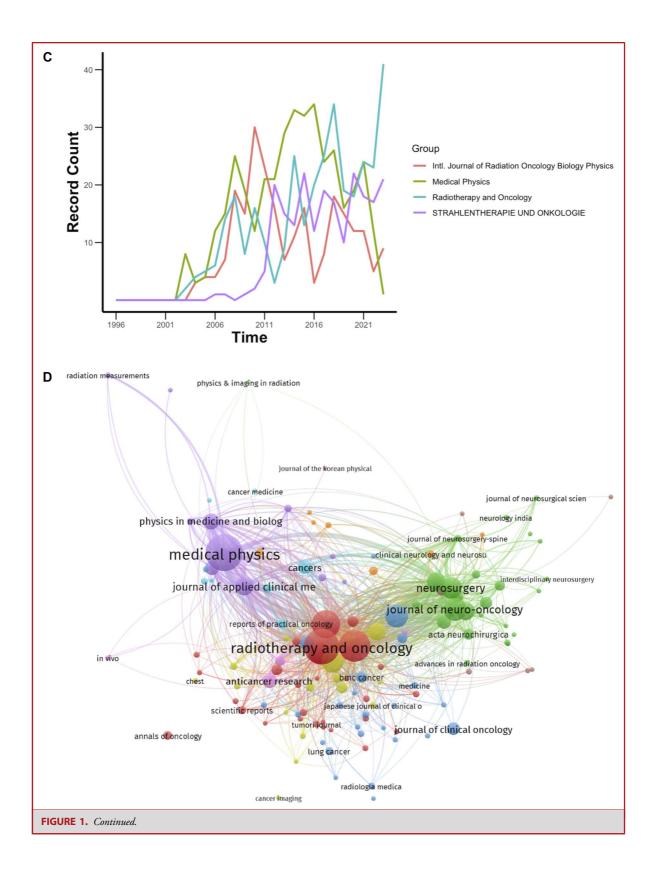


FIGURE 1. A, Trend of CK manuscript counts from the years 1996 to 2023. Pearson coefficient r=0.97. **B,** Network visualization of CK publications. Clusters of articles are represented spatially and with different colors. Article prominence in the field is represented by the size of the bubble. The most prominent articles in each cluster are explicitly labeled. **C,** Trend of CK manuscript counts stratified for top journals over Time. Medical Physics (r=0.65), Radiotherapy and Oncology (r=0.87), International Journal of Radiation Oncology Biology Physics (r=0.54), Strahlentherapie und Onkologie (r=0.86). **D,** Network visualization of journal citations of CK publications. Clusters of citations are repented spatially and with different colors. Journal prominence in the field is represented by the size of the bubble. The most prominent journals in each cluster are explicitly labeled. CK, CyberKnife.



Through temporal analysis, international journals such as "Neurology India" and "Radiologica Medica" were increasingly featured in cocitations following 2020 and in recent years (Figure 2A).

Trends in Conditions and Medical Subspecialties Featured in CK Publications

The most prominent neurosurgical conditions featured in CK publications included brain metastases (4.698%), vestibular schwannoma (2.186%), meningiomas (2.11%), glioblastoma (1.834%), and AVMs (1.53%). Most conditions featured in CK articles were neurosurgical, with a greater number of brain conditions than spine. All of the most prominent neurosurgical conditions demonstrated strong increases in record count with time (r > 0.7). Brain metastases featured the greatest domination of the field, as evidenced by the greater number of CK records featuring brain metastases compared with other neurosurgical conditions in 2023 and the high Pearson coefficient of brain metastases publications over time (r = 0.89) (Figure 2B). The top 5 non-neurosurgical conditions featured in CK publications included prostate cancer (5.839%), hepatocellular carcinoma (1.752%), head and neck cancer (1.650%), uveal melanoma (1.472%), and endometrial cancer (1.295%). The most prominent medical subspecialties of CK publications were oncology (50.8%), radiology (48.1%), clinical neurology (12.049%), and surgery (11.7%). Oncology and radiology have risen consistently over time, whereas surgery and clinical neurology reached a peak before 2010 and are on the decline (Figure 2C).

Trends in Authors of CK Publications

The most prolific scientists in the field of CK research by publication count are Alexander Muacevic (121 publications, h-index 44), Steven Daniel Chang (110 publications, h index 70), Oliver Blanck (108 publications, h index 31), John R. Adler (84 publications, h index 28), and Simone Marnitz (82 publications, h index 31). For the top 3 authors, there are no strong correlations with publication count and time (r = 0.47, -0.13, 0.48) (Figure 2D). Coauthorship bibliometric visualization resulted in 27 clusters, with the most prolific authors in the field defining individual clusters, including Steven Daniel Chang, Oliver Blanck, and Alexander Muacevic (Figure 3A). Citation network visualization resulted in 11 distinct clusters, retaining Steven Daniel Chang, Oliver Blanck, and Christian Baues as cluster defining nodes, with Sean Collins and Lorenzo Livi defining new clusters. Steven Daniel Chang had the largest node and the most citations with 479 links to other authors. The cluster which Steven Daniel Chang defined was also the largest cluster in the network (Figure 3B).

Trends in Institution Production and Collaboration of CK Publications

In the field of CK research, the most prolific institutions are the University of Cologne, Stanford University, the University of

Munich, UNICANCER, and Georgetown University. Coauthorship network visualization yielded 15 clusters with Stanford University, University of Florence, University of Cologne, University of Pittsburgh, Osaka University, and Korea Institute of Radiological and Medical Science defining individual clusters. Stanford University was the largest node with 132 links to other nodes and a total link strength of 293. Institutional collaboration within the United States was prominent between Stanford University, the University of California—San Francisco, Hopkins University, and Harvard Medical School. Institutions outside the United States typically clustered together by country, whereas US institutions were dispersed between clusters, suggesting international institutional collaboration with the United States. Collaboration between US institutions and between Japanese institutions has decreased in recent years, whereas European and Chinese intrainstitutional collaboration has increased since the turn of the decade. The cluster defined by the University of Cologne has seen significant publication growth at the turn of the decade (Figure 4A and 4B). An analysis of citations identifies 14 clusters, with Stanford University, Accuray Inc., University of Cologne, University of Florence, and Georgetown University as cluster defining. Stanford University was the most prominent node with 457 links and a link strength of 48 370. Citations between institutions of the United States are the most common in the field but occurred most prominently in the past decade. Citations between European institutions (specifically German, French, Italian and Swiss institutions) are the second most common and have increased sharply in the past 5 years. Accuray was clustered with and cited most prominently with Italian and Australian institutions (Figure 4C and 4D).

Trends in International Production and Collaboration of CK Publications

Although CK was developed in the United States, a bibliometric analysis of international prominence, collaboration, and cocitation demonstrates the technology's permeation into healthcare systems across the globe. The countries producing the most CK-related publications are the United States of America (32.687%), Germany (16.157%), Italy (11.310%), China (7.308%), and Japan (7.035%). The most common conditions featured in the top 3 countries were identified through subgroup analysis. In the United States, prostate cancer (8.5%), brain metastases (5.53%), vestibular schwannoma (3.3%), and trigeminal neuralgia (2.4%) were the most common conditions featured. In Germany, brain metastases (5.9%), endometrial cancer (3.94%), uveal melanoma (3.7%), and lymphoma (3.26%) were the most common featured. In Italy, prostate cancer (8.1%), meningioma (4.825%), lymphedema (4.167%), glioblastoma (3.95%), and brain metastases (2.85%) were the most common. From clustering analysis, the United States has most prominently collaborated with South Korea, Mexico, and Thailand. Germany has most prominently collaborated with Switzerland and the Netherlands, and Japan has collaborated with

Source	Title	Journal (most recently reported impact factor)	Citation count
Chang et al, ⁷ 2015	Stereotactic ablative radiotherapy versus lobectomy for operable stage I non–small-cell lung cancer: a pooled analysis of two randomized trials	Lancet Oncology (41.6)	1068
Gerszten et al, ⁸ 2007	Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution	Spine (2.7)	524
Adler et al, ⁹ 1997	The CyberKnife: a frameless robotic system for radiosurgery	Stereotactic and Functional Neurosurgery (1.9)	432
King et al, ¹⁰ 2013	Stereotactic body radiotherapy for localized prostate cancer: pooled analysis from a multi-institutional consortium of prospective phase II trials	Radiotherapy and Oncology (4.9)	351
Hoogeman et al, ¹¹ 2009	Clinical accuracy of the respiratory tumor tracking system of the CyberKnife: assessment by analysis of log files	International Journal of Radiation Oncology Biology Physics (6.4)	265

Hungary, Belgium, and Singapore. The U.A.E, Turkey, Pakistan, and Singapore are emergent nations to the field that are involved in coauthorships increasingly following 2020 (Figure 5A and 5B). Cocitations between the United States, Canada, Saudi Arabia, Israel, and Singapore occur heavily, whereas cocitations between Germany, Japan, and Italy are also prominent. The U.A.E, Hungary, Norway, Pakistan, and Singapore have been cocited increasingly following 2020 (Figure 5C and 5D).

Trends in Topics and Terms

Publications in all major databases are tagged with keywords. Such keywords are also linked to authors based on the type of publications they produce. The co-occurrence of author keywords in records published between 1996 and 2023 was analyzed. The resulting 16 clusters groups keywords belonging to similar areas of research and clinical practice. For example, "image guidance," "linac," "spine radiosurgery," "frameless," and "radiosurgery"

Source	Title	Journal (IF)	Citation count
Chang et al, ⁷ 2015	Stereotactic ablative radiotherapy versus lobectomy for operable stage I non–small-cell lung cancer: a pooled analysis of 2 randomized trials	Lancet Oncology (41.6)	1068
Goldbrunner et al, ¹² 2021	European Association of Neuro-Oncology (EANO) guidelines for the diagnosis and treatment of meningiomas	Lancet Oncology (41.6)	564
Gerszten et al, ⁸ 2007	Radiosurgery for spinal metastases–Clinical experience in 500 cases from a single institution	Spine (2.7)	524
Das et al, ¹³ 2008	Small fields: nonequilibrium radiation dosimetry	Medical Physics (3.2)	515
Fowler et al, ¹⁴ 2010	21 years of biologically effective dose	British Journal of Radiology (2.7)	442
Adler et al, ⁹ 1997	The CyberKnife: a frameless robotic system for radiosurgery	Stereotactic and Functional Neurosurgery (1.9)	432
King et al, ¹⁰ 2013	Stereotactic body radiotherapy for localized prostate cancer: Pooled analysis from a multi-institutional consortium of prospective phase II trials	Radiotherapy and Oncology (4.9)	351
Kang et al, ¹⁵ 2012	Stereotactic body radiation therapy for inoperable hepatocellular carcinoma as a local salvage treatment after incomplete transarterial chemoembolization	Cancer: An International Interdisciplinary Journal of the American Cancer Society (6.1)	258

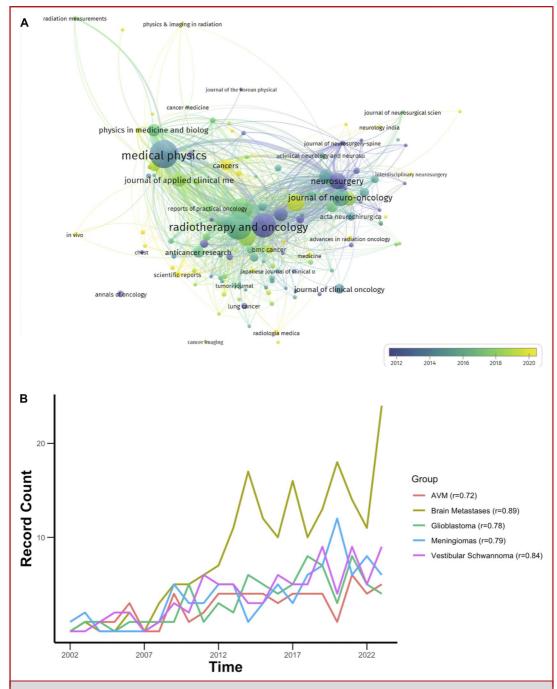
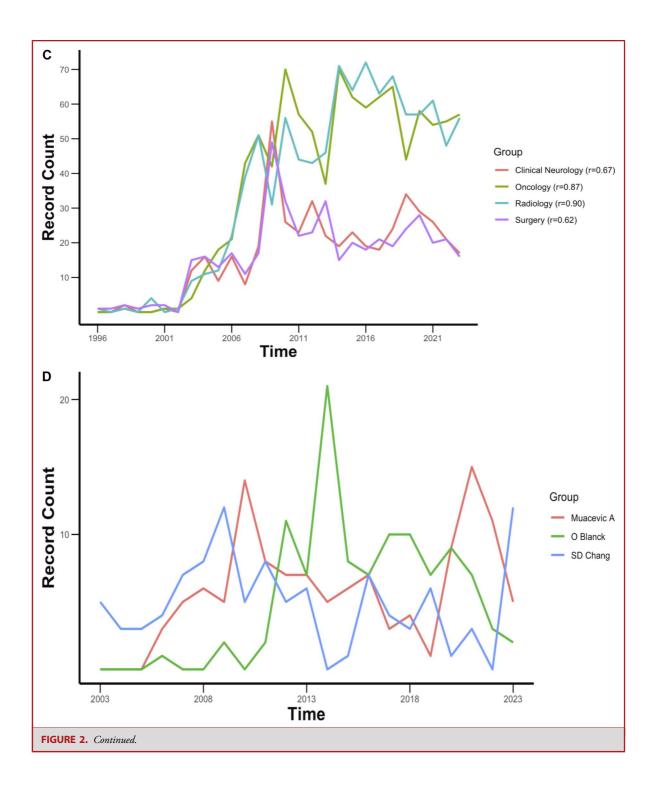


FIGURE 2. A, Temporal visualization of journal citations of CK publications. Clusters are represented spatially and citations within and between clusters are given different colors based on recency of the collaboration. Journal prominence in the field is represented by the size of the bubble. The most prominent journals in each cluster are explicitly labeled. B, Trend of CK manuscripts for the top 6 neurosurgical conditions over time from 1996 to 2023. Brain metastases (r = 0.889), glioblastoma (r = 0.764), meningiomas (r = 0.791), atrioventricular malformations (r = 0.719), and vestibular schwannoma (r = 0.839). C, Trend of CK manuscripts for the top 4 medical specialties over time from 1996 to 2023. Clinical neurology (r = 0.69), oncology (r = 0.866), radiology (r = 0.897), and surgery (r = 0.62). D, Trend of CK manuscript authors over time. Alexander Muacevic (r = 0.47), Steven Daniel Chang (r = -0.13), and Oliver Blanck (r = 0.49). AVM, arteriovenous malformation; CK, CyberKnife.



belonged the same cluster. Author keywords provided further evidence of specific conditions prominent in CK publications. The size of nodes representing brain metastases, vestibular schwannoma, and "neurosurgery" demonstrate the prominence

these conditions have in the field, as well as the dominance of neurosurgical conditions in the literature. Visualization of Similarities clustering provides insight into brain metastases primary sites and potentially non-neurological conditions that are being

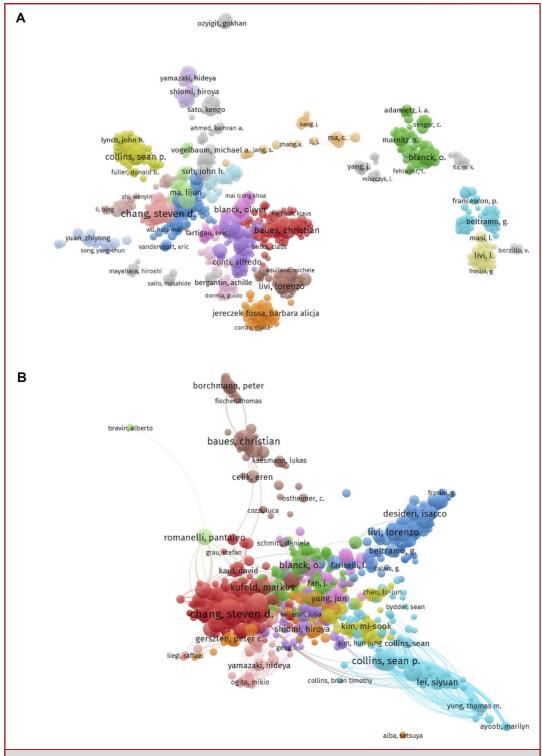


FIGURE 3. A, Network visualization of author coauthorship of CK publications. Clusters of coauthorship are repented spatially and with different colors. Author prominence in the field is represented by the size of the bubble. The most prominent authors in each cluster are explicitly labeled. B, Network visualization of author citations of CK publications. Clusters of cited authors are represented spatially and with different colors. Author prominence in the field is represented by the size of the bubble. The most prominent authors in each cluster are explicitly labeled. CK, CyberKnife.

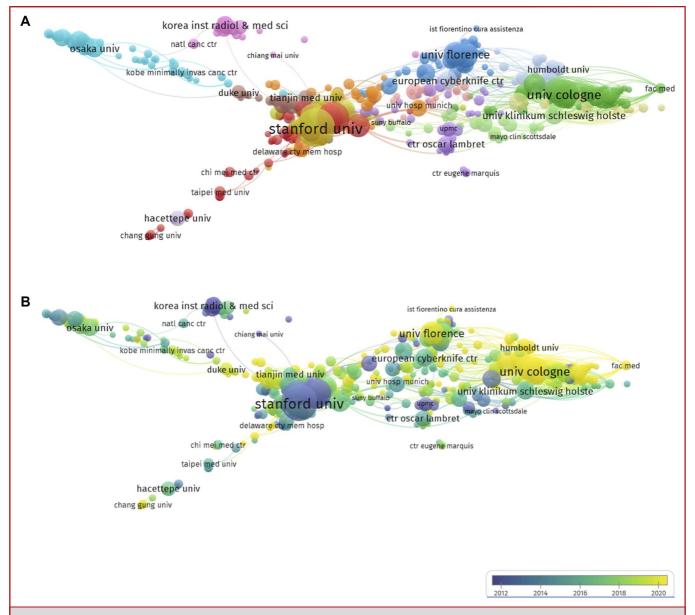
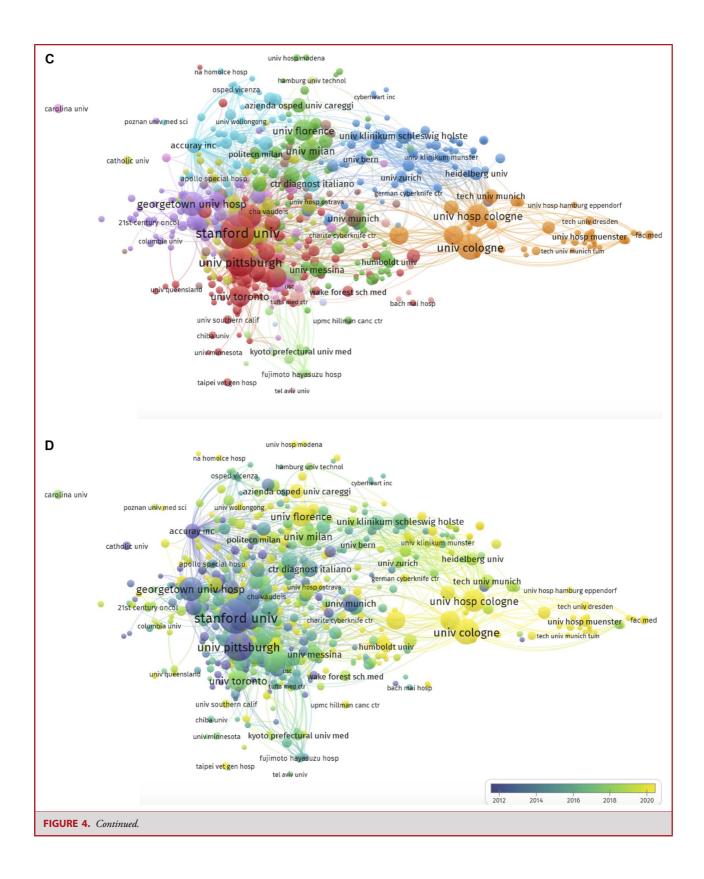


FIGURE 4. A, Network visualization of institutional coauthorship from CK publications. Clusters of coauthorship between institutions are represented spatially and with different colors. Institution prominence is represented by the size of the bubble. The most prominent institutions in each cluster are explicitly labeled. B, Temporal visualization of institutional coauthorship from CK publications. Clusters are represented spatially and institutional coauthorship within and between clusters are given different colors based on recency of the collaboration. Institution prominence is represented by the size of the bubble. The most prominent institutions in each cluster are explicitly labeled. C, Network visualization of institutional cocitation from CK publications. Clusters of institutions are represented spatially and with different colors. Institution prominence is represented by the size of the bubble. The most prominent institutions in each cluster are explicitly labeled. D, Temporal visualization of institutional cocitation from CK publications. Clusters are represented spatially, and institutional cocitation within and between clusters are given different colors based on recency of the citation. Institution prominence is represented by the size of the bubble. The most prominent institutions in each cluster are explicitly labeled. CK, CyberKnife.

researched in the field as well: melanoma, non–small-cell lung cancer, prostate cancer, renal cell carcinoma, and liver cancer are prominent nodes in the bibliometric map. When analyzing specific clusters, CK-related methods and treatments administered

with CK may be discerned for each condition. For example, clustered with "Brain Metastases" are "whole brain radiotherapy," "radiation necrosis," and "local recurrence" (Figure 6A). Furthermore, when temporal analysis was conducted, the evolution of



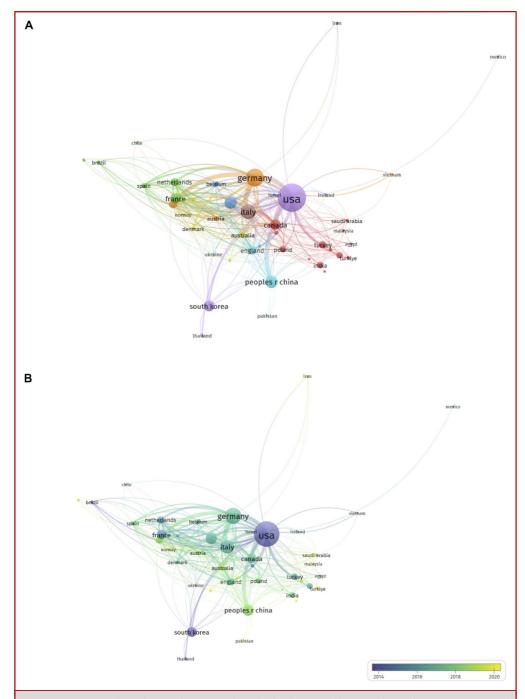
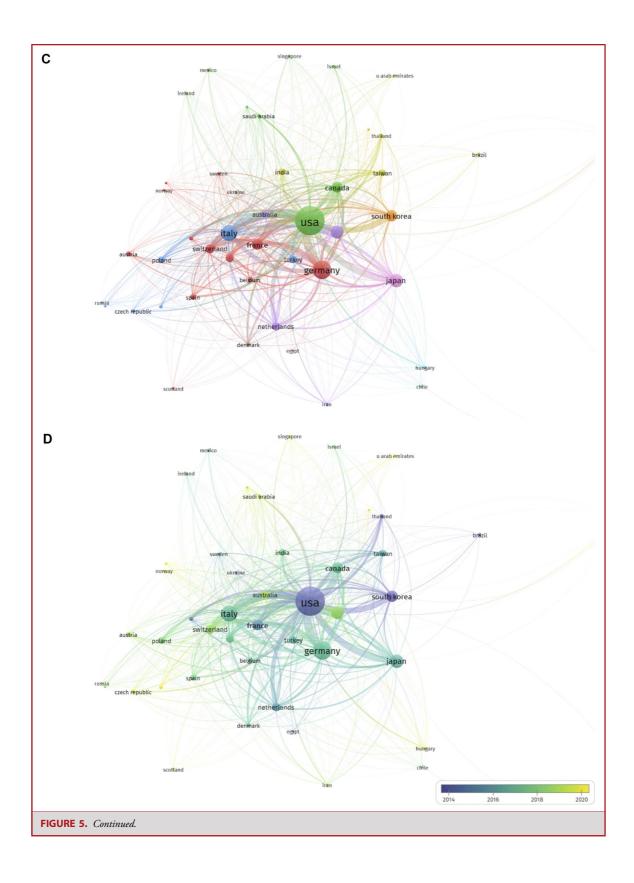


FIGURE 5. A, Network visualization of international coauthorship from CK publications. Clusters of countries are represented spatially and with different colors. Country prominence is represented by the size of the bubble. The most prominent countries in each cluster are explicitly labeled. B, Temporal visualization of international collaboration from CK publications. Clusters are represented spatially and collaboration within and between clusters are given different colors based on recency of the citation. Country prominence is represented by the size of the bubble. The most prominent countries in each cluster are explicitly labeled. C, Network visualization of international cocitation from CK publications. Clusters of countries are represented spatially and with different colors. Country prominence is represented by the size of the bubble. The most prominent countries in each cluster are explicitly labeled. D, Temporal visualization of international cocitation from CK publications. Clusters are represented spatially and citations within and between clusters are given different colors based on recency of the citation. Country prominence is represented by the size of the bubble. The most prominent countries in each cluster are explicitly labeled. CK, CyberKnife.



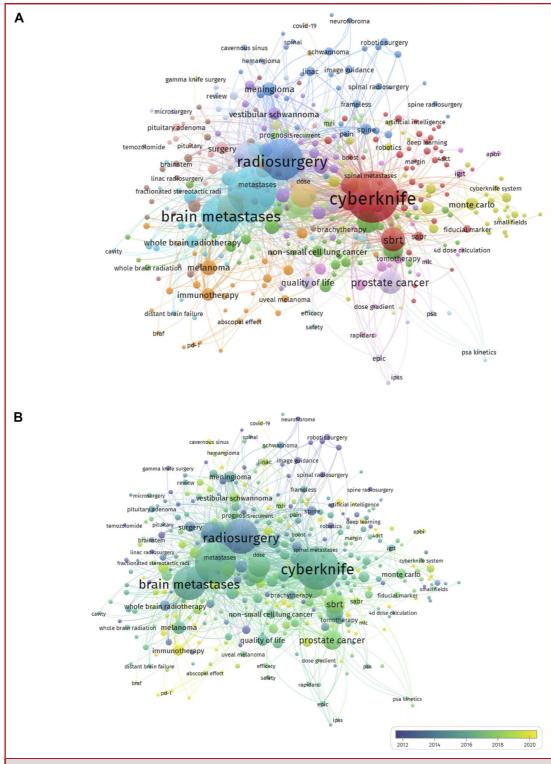


FIGURE 6. A, Network visualization of author keywords from CK publications. Clusters of co-occurring keywords are represented spatially and with different colors. Key word prominence is represented by the size of the bubble. The most prominent words in each cluster are explicitly labeled. B, Temporal visualization of author keywords from CK publications. Clusters are represented spatially and co-occurrence within and between clusters are given different colors based on recency of the citation. Key word prominence is represented by the size of the bubble. The most prominent words in each cluster are explicitly labeled. CK, CyberKnife.

modern approaches to CK research was apparent. Keywords pertaining to novel techniques and applications formed co-occurrences in the past 5 years—"immunotherapy," "pd-1," "small field dosimetry," "intercranial," "cervical cancer." Skull base approaches ("skull base," "cavernous sinus") and brain tumors such as meningiomas and gliomas also formed recent co-occurrences. Interestingly, "postoperative" has not co-occurred in recent years, but "neoadjuvant" and "preoperative" have. The same trend was noticed for cutting-edge technologies and their application to CK—"machine learning, motion tracking, radiomics, deep learning" co-occurred after 2020 (Figure 6B).

DISCUSSION

This study offers a semiquantitative assessment of the global growth of CK as a method of radiosurgical treatment through the analysis of academic publications. We provide a thorough assessment of the landscape of CK research, with insight into foundational publications, and productive authors, institutions, and countries, while simultaneously elucidating trends in global, institutional and individual collaboration, citation, and shared research focus.

CK publications stemming from Europe have dramatically increased since 2020. These publications stem from Germany, Swiss, French, and Italian institutions, including the University of Florence, The University of Cologne, the University of Munich, and UNICANCER. US collaborations with these institutions are limited but growing. While US institutions have collaborated internationally in the past, there has not been a growth of these collaborations in recent years—we, therefore, identify a significant opportunity in facilitating international collaborations. This is especially pertinent as countries such as Saudia Arabia, Singapore, Hungary, Pakistan, and the Czech Republic gain access to CK and begin to invest in clinical and translational radiosurgical research. The differences in primary conditions researched between countries suggest that research focus may be affected by local incidence and presence of diseases.

The results from this study demonstrate strong trends in annual document count for the top conditions in CK research, particularly brain metastases, vestibular schwannoma, and atrioventricular malformations. We further demonstrate that newer advances in CK research are related to exploring further neurological and neurosurgical conditions that may benefit from frameless SRS, particularly further forms of brain metastases, gliomas, meningiomas, and skull base tumors.

In the past 10 years, SRS as a monotherapy has emerged as the standard of care for newly diagnosed brain metastases and is the first line of treatment of oligometastatic brain metastases with lesions under 3 cm in maximal diameter. SRS is also increasingly being used for brain metastases larger than 3 cm and for patients with greater than 4 metastases. Neoadjuvant SRS before surgical resection is also a newly discussed treatment option. 16,17 For

vestibular schwannoma, SRS is the most favored treatment to minimize complications and prevent tumor growth compared with any microsurgical procedures. CK in particular has demonstrated highly effective results in vestibular schwannoma with strong preservation of hearing after radiosurgical treatment. SRS is increasingly being used to manage atrioventricular malformations and has shown significant efficacy in smaller AVM lesions. SRS is an emerging treatment modality for trigeminal neuralgia and may be used to support other treatment options such as microvascular decompression.

SRS for gliomas, particularly glioblastoma, is an emerging treatment option, both in adjuvant and neoadjuvant forms, as well as for recurrent glioblastoma. Skull base conditions have increasingly benefited from SRS, and recent work demonstrates further progress in the field, particularly for skull base metastases and meningiomas. Combination therapies for SRS with immunotherapy are also emerging, particularly the possibility of promoting an antitumor immune response by radiation, followed by traditional immunotherapy. 22,23

Limitations

This analysis must be interpreted in the context of its methodology. Included in this analysis are any publications containing the word 'cyberknife'. Additional screening was not performed, to ensure a broad capture of any documents that either focus on, or reference the technology. Furthermore, beyond cluster counts, link counts, and link strength, much of the VOS viewer analysis was qualitative in nature. Repeats due to different spellings and languages were identified in VOS Viewer, and qualitative analysis was performed accounting for such instances.

CONCLUSION

CK SRS is an emergent technology with increasingly more neurological conditions and diseases being researched for treatment options. The rise in academic focus on CK SRS has been spearheaded by international effort from the United States, Japan, and Italy. There remains significant potential for future international collaboration. ¹⁷

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