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Bibliometric analysis and visualization of research trends in radiation dermatitis in the past twenty years

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Abstract

Objectives This study aims to explore the most influential countries/regions, institutions, journals, authors, keywords, and trends in the study of the mechanism and treatments of radiation dermatitis (RD) from 2003 to 2023 using bibliometric analysis.

Methods The literature associated with RD was retrieved from the Web of Science Core Collection, only articles and reviews in English were included. Individual articles were reviewed to identify the authorship, published journal, journal impact factor, institution and country of origin, and year of publication.

Results A total of 6,453 authors from 1,605 institutions in 64 countries/regions published 1,062 RD-related literature. The United States was the most productive country. The Unicancer in France was the institution that published the majority of articles on RD. Edward Chow was the most productive author and *Supportive Care in Cancer* contributed the most articles. Advanced head and neck cancer is the most common cause of RD. The mechanism research mainly focused on nitric oxide, oxidative stress, and apoptosis in recent years, and Mepitel film, Mepilex Lite, and PBMT were the main preventive and therapeutic measures for RD.

Conclusion Our bibliometric studies provide a thorough overview of RD and valuable insights and ideas for scholars in this discipline.

Keywords Bibliometrics, Radiation dermatitis, Randomized controlled trial, Research trend

Introduction

With the extensive use of radiotherapy, the side effects have gradually attracted people's attention. Radiation dermatitis (RD) is one of the most common adverse reactions, of which about 95% of radiotherapy patients had varying degrees of RD [1]. RD can be manifested as skin pigmentation, pain, dry desquamation, wet desquamation, and even ulcers in severe cases [2, 3]. The pathophysiology of RD is complex. One of the mechanisms is the DNA damage of skin cells directly caused by radiation, followed by the subsequent changes in cell proliferation and differentiation, the production of

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pro-inflammatory markers, and reactive oxygen species (ROS) in the microenvironment [4, 5].

In recent years, there has been a rapid growth in the number of papers regarding RD, which presents a challenge to scholars who expect to recognize significant articles in RD research. Bibliometric analysis is the quantitative examination of a subject using mathematical and statistical methods, and it is vital for reflecting features and future developments [6]. In this study, we provided a comprehensive and systematic overview of the present research from 2003 to 2023, as well as to compensate for the lack of bibliometric analysis on this topic.

Methods

Literature sources and search strategy

The publications related to RD from 2003 to 2023 were obtained based on the Science Citation Index Expanded (SCIE) and Social Science Citation Index (SSCI) of the Web of Science Core Collection (WOSCC) on February 23, 2024. The retrieval topic was TS="*radiation dermatitis" OR "*radiation ulcer" OR "*radiation induced dermatitis" OR "*radiation induced ulcer" OR "*radiation skin injury" OR "radiodermatitis", only the "review" and "article" written in English were included in this study. A total of 1,062 targeted literature were obtained for the following analysis. The flow chart is shown in Fig. 1.

Visualization and statistical analysis

VOSviewer 1.6.18, CiteSpace 6.3.1, and R package Bibliometrix 4.1.2 were used to convert and analyze identified information. Information from each study including title, authors, keywords, institutions, nations and regions, total citation, year of publication, journal, impact factor, and other details. In short, the Bibliometrix package was utilized to visualize parameters such as the trend of annual publications and citations, institutions, authors, keywords, and collaboration networks. VOSviewer was used to analyze the collaboration network between journals and keywords, and CiteSpace tended to conduct visual analysis and generate the dual map. Scimago Graphica and GraphPad Prism 9.5 were also employed.

Results

Annual growth trend of publications and citations

The search strategy in Fig. 1 was implemented. A total of 1,062 publications published from 2003 to 2023 in WoS Core Collection focused on RD were included, comprising 906 articles and 156 reviews. The total number of citations with self-citations excluded reached 14,695.

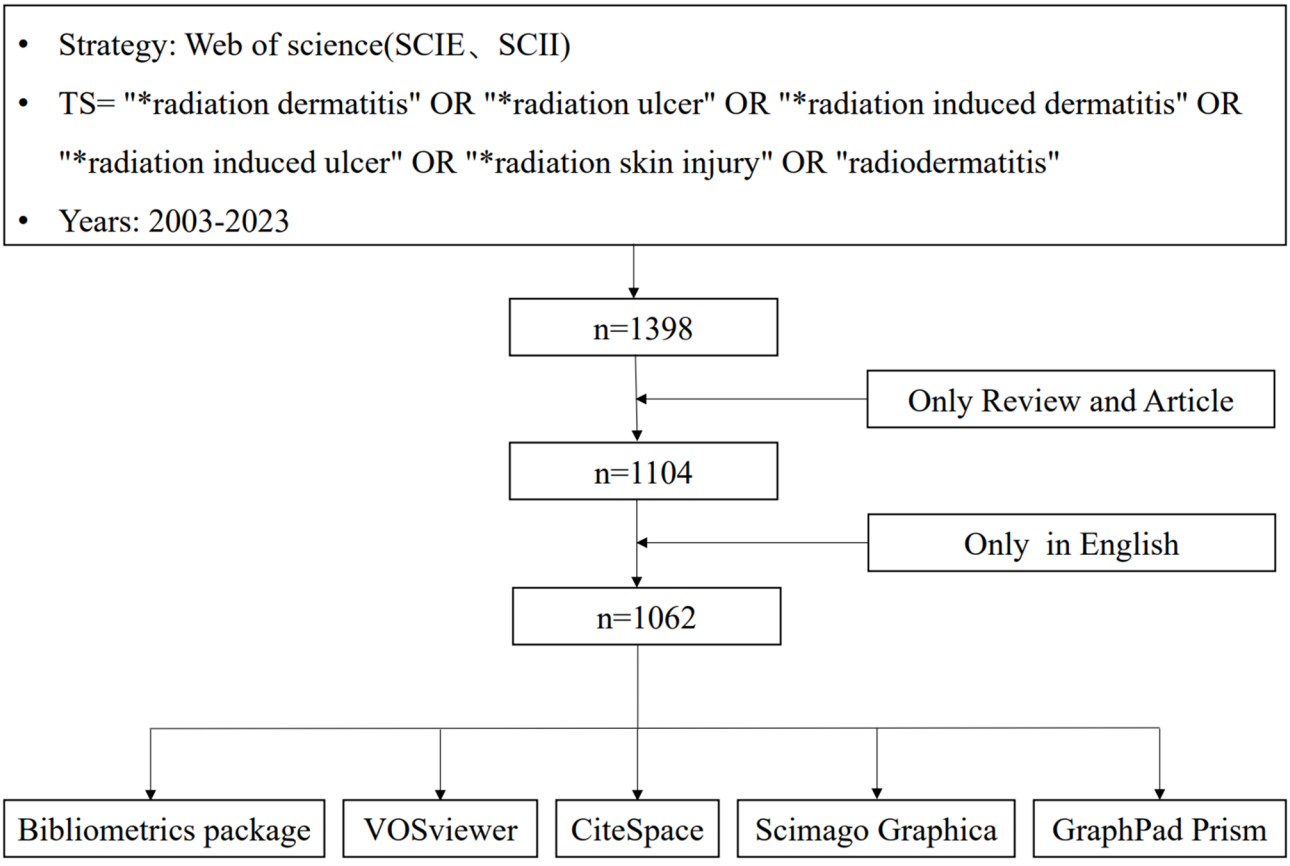

Fig. 1 Flow diagram of the searching process

The annual number of published papers is an important indicator that reflects the development of a certain subject and presents the trend of the field. Although a slight downward trend has been present in several years, such as 2014, 2018, and 2020, a consistent increase can be seen in Fig. 2A. Notably, 456 articles, accounting for 42.94% of the total amount, were published in the last five years, indicating RD's global study attention as a common complication of radiation therapy. As a whole, the number of citations was consistent with the trend of the number of published papers. Statistically significant linear correlation between the year and the number of publications can be found (R^2=0.9150, Y = 4.673* X-9356, Fig. 2B). In summary, RD research has garnered increasing interest in the past few decades.

Major contributing countries/regions and institutions

Overall, the literature included in the analysis came from 64 different countries or regions. According to the visual analysis (Fig. 3A), the top five countries/regions with the highest number of publications were the United States (299 literature), China (184 literature), Japan (106 literature), Germany (91 literature), and Italy (81 literature). In terms of citations (Fig. 3B), the top five most-cited countries were the United States (10,538 times), China(2,716 times), France (2,670 times), Canada (2,549 times), and Italy (2,327 times). The Collaborative Network World map showed the partnerships between countries. As shown in Fig. 3C, the United States worked most closely with others in this area of research, such as China, Canada, Italy, and the Netherlands. We also noticed that the cooperation between countries was dominated by developed countries.

A total of 1,605 institutions contributed publications, among which Unicancer in France published the most articles (88 articles), followed by University of Toronto (50 articles), University of Rochester (47 articles), University of Texas System (45 articles), and UTMD Anderson Cancer Center (42 articles) (Fig. 4A). The top 10 institutions published 456 articles, accounting for 42.94% of the overall count. Despite having the second-highest number of total publications, none of the top 10 institutions were located in China. This may be due to the dispersed research among institutions. The cooperation among institutions was also analyzed. Most institutions prefer domestic rather than international cooperation (Fig. 4B). However, collaborations among the influential research institutions in different countries were also observed.

Major contributing authors

Based on the collected information, we listed the top 10 most published researchers in their field (Fig. 5A), which included Edward Chow (30 publications), Tara Behroozian (20 publications), Pierluigi Bonomo (20 publications), Julie Ryan Wolf (18 publications), Saverio Caini (15 publications), Jolien Robijns (15 publications), Corina van den Hurk (14 publications), Paul Bulens (13 publications), Rene Jean Bensadoun (12 publications), and Henry Lam (12 publications). Annual publications and annual citations of the above researchers were analyzed (Fig. 5B). Among these authors, Edward Chow from Sunnybrook Health Sciences Centre, who was the most prolific author, one of his articles published in 2023 (DOI: https://doi.org/10.1016/S1470-2045(23)00067-0 IF: 41.6 Q1 B1) summarized the opinions of 42 international experts on the care for RD and expounded the function of Mepilex Lite dressings for the management of acute radiation dermatitis [7]. Moreover, Rene Jean Bensadoun has constantly studied RD since 2008 and presented the opinion that low-level light therapy or vascular lasers may effectively control RD symptoms [8]. Accordingly, his research received 192 citations in total.

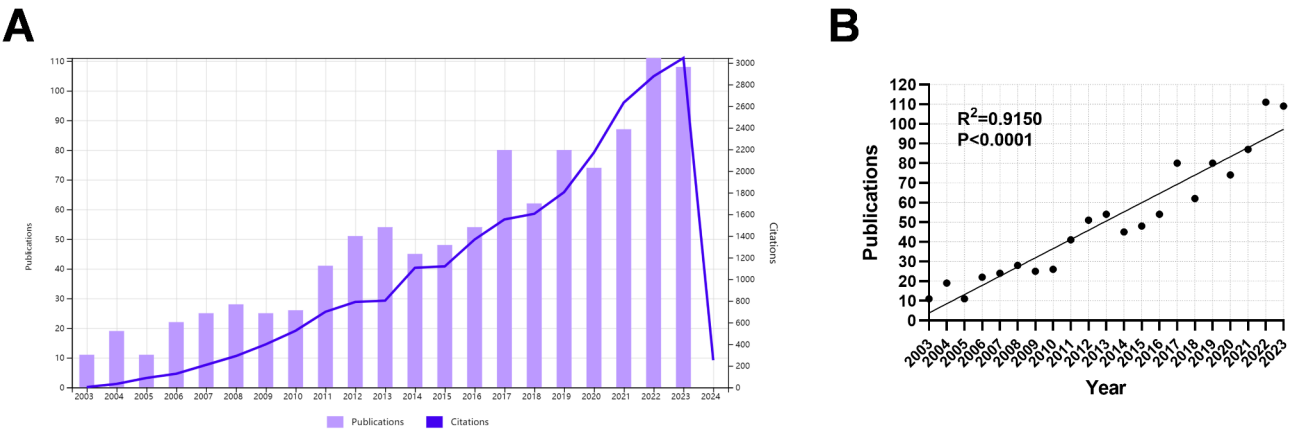

Fig. 2 Overall publication trends from 2003–2023. **(A)** Publication and citation number from 2003 to 2023 of the papers on RD. **(B)** The trend curve fitted according to the number of publications

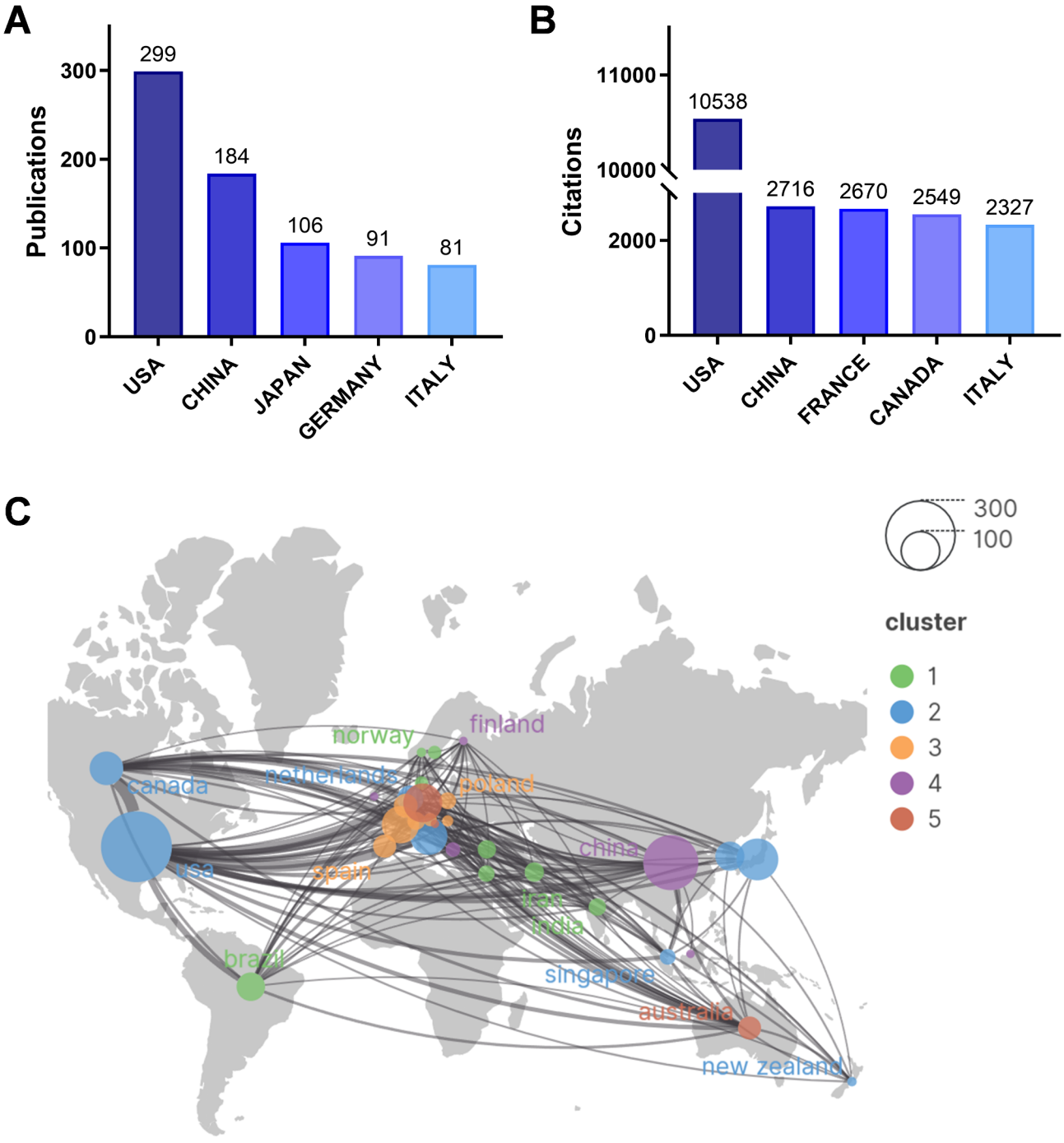

Fig. 3 Analysis of countries/regions engaged in RD research. **(A)** Top 5 countries/regions with the largest number of publications. **(B)**Top 5 countries with the largest number of citations over time. **(C)** Visualization world map of publications and collaboration relationship

Analysis of journals and co-cited journals

Academic journals serve as a channel for scholars to disseminate their discoveries, and act as an important role in reflecting research quality. According to the data, 395 scholarly journals had been mentioned. Among them, 50 journals with five or more publications were chosen to ensure a thorough mapping study. In Fig. 6A, the size of the dots correlated to the number of publications, line width denoted association strength. Besides, Tables 1 and 2 listed the top 5 journals based on the publication or citation number. *The Supportive Care in Cancer* had the most published articles (46 articles), equivalented to 4.3% of the total, and was also one of the most cited journals. Followed by *The International Journal of Radiation Oncology Biology Physics* (44 articles), which also ranks top in terms of citations. *The New England Journal of*

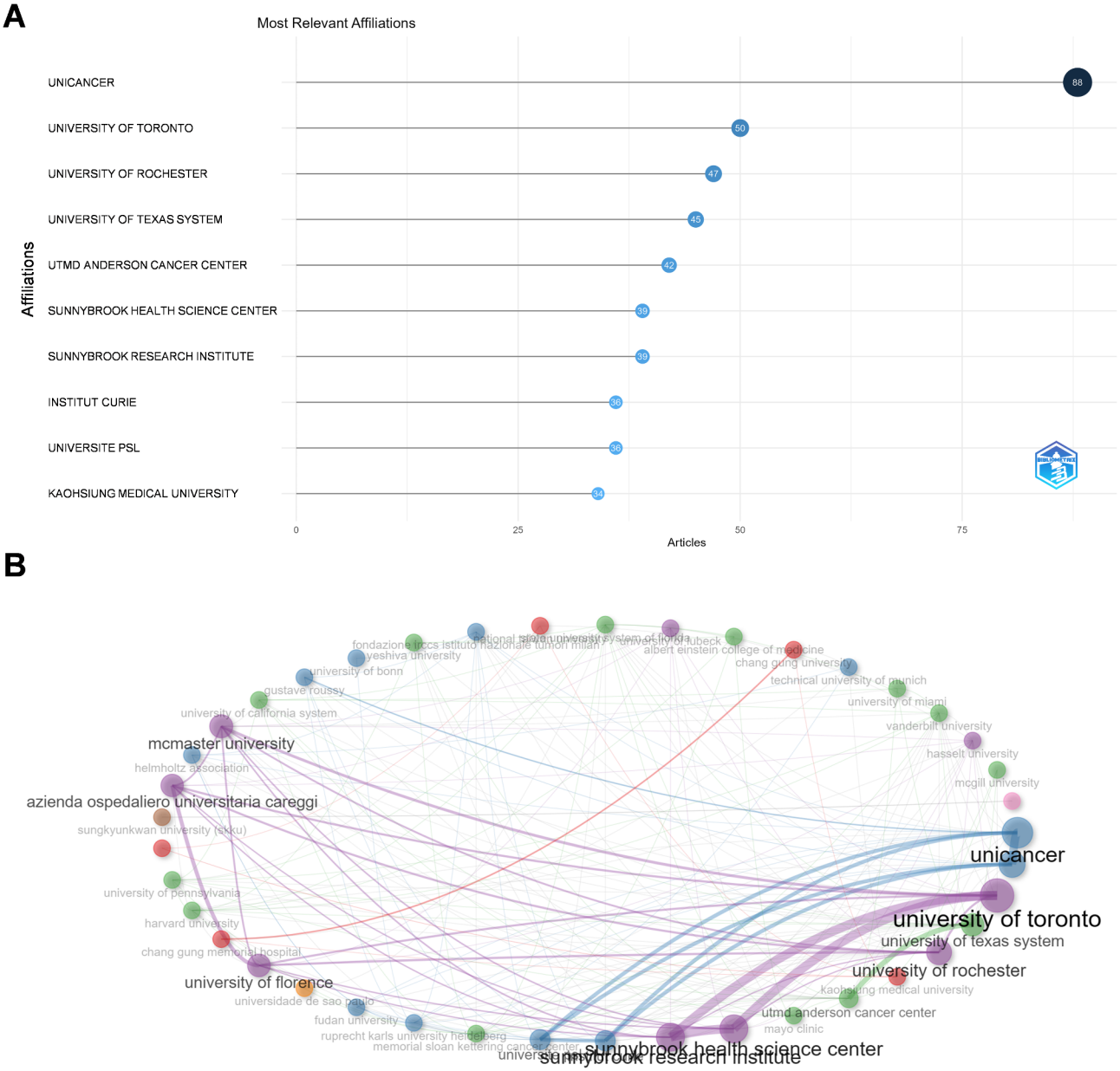

Fig. 4 Analysis of institutions engaged in RD research. **(A)** The 10 institutions with the largest number of publications. **(B)** Institutional cooperation network in top 50 institutions

Medicine and *The Journal of Clinical Oncology* were two of the comprehensive medical journals, which demonstrated their impact on this field.

The double map overlay of the journals often used to show the location of the research topic relative to the major research disciplines. As shown in Fig. 6B, each point on the map represented a journal, the distribution of journals containing the citing literature was on the left, while the corresponding cited literature was on the right, and the connection curve was the citation line. In radiotrauma, there were two main colors of major citation paths, molecular/biology/immunology and medicine/medical/clinical journals studies were primarily cited and cross-referenced by molecular/biology/genetics and health/nursing/ medicine associated journals.

Keywords analysis

Keywords are used to condense the core and essence of a paper, and keyword co-occurrence analysis can identify research hotspots in this field. We used VOSviewer to draw a network view of keyword co-occurrence of 1,062 articles and selected 100 critical keywords with frequencies more than 15 times for visualization. The results are shown in Fig. 7A. The size of the dots represented the

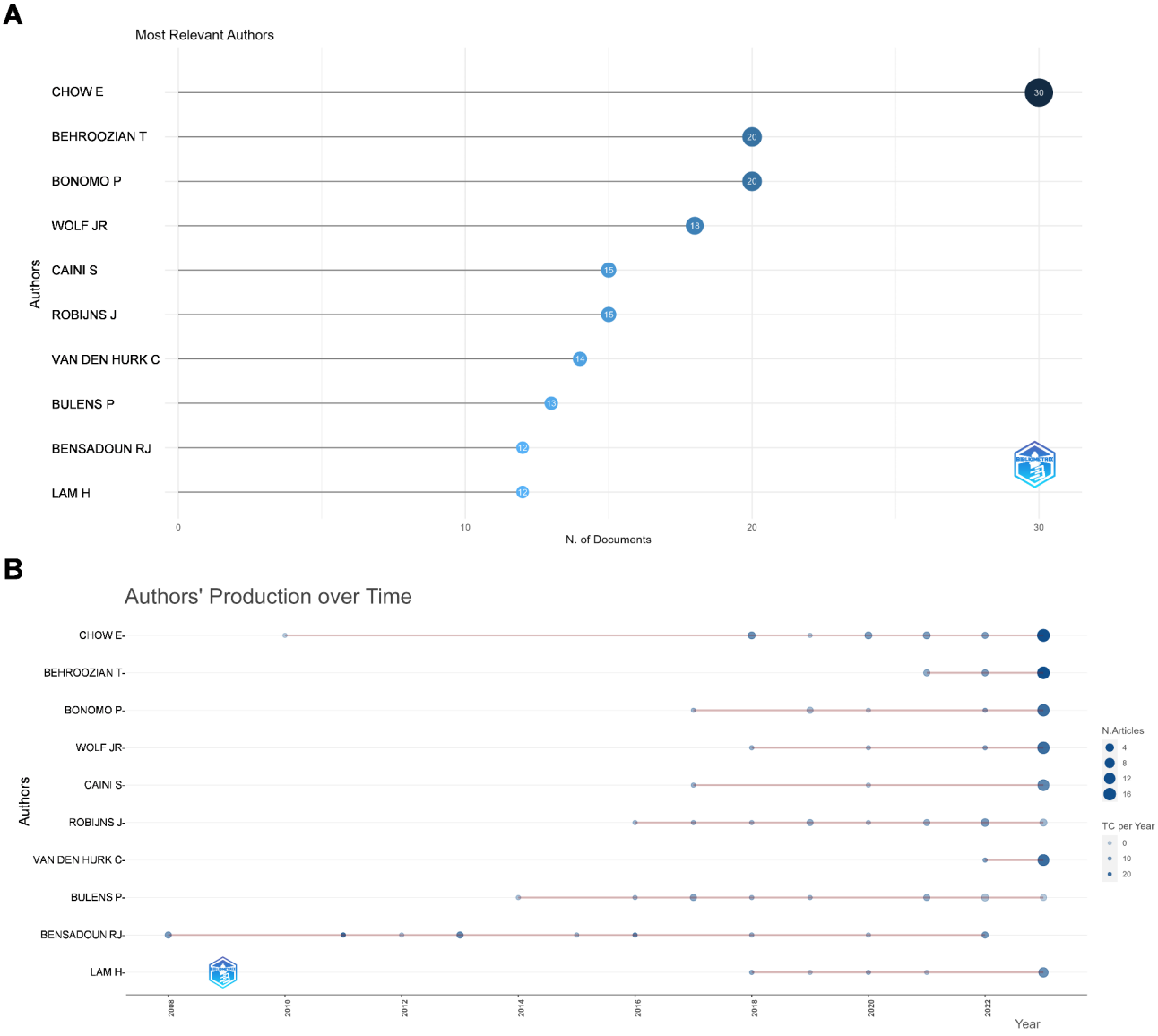

Fig. 5 Analysis of authors engaged in RD research. **(A)** The 10 authors with the largest number of publications. **(B)** The top 10 authors' published article over time

frequency of a certain keyword and also indicated the focus of this particular field. The thickness of the line between dots indicated the strength of the correlation. We found that the keywords with the largest node, the highest density, and the highest frequency include: radiation therapy, radiation dermatitis, breast cancer, cancer, management, toxicity. As can be observed in Fig. 7B, the top terms with the highest clustering information and citation frequency were grouped into ten clusters.

Two structural metrics are utilized to assess cluster quality: the Q score and the S score. The Q score indicates the network's modularity and represents the degree to which a network can be segmented into modules [9]. The S score, on the other hand, means silhouette score, is a technique for analyzing and verifying consistency among data clusters [10]. The Q score ranges from 0 to +1, and the S score ranges from −1 to +1. Basically, values of $Q > 0.3$ and $S > 0.5$ indicate considerable clustering inside the network, with our results showing consistent literature within each grouped topic ($Q = 0.7939$, $S = 0.9303$). In terms of etiology, advanced head and neck cancer were the most common underlying cause of RD. The most popular study approach for RD was randomized controlled trial (RCT) research, which is the gold standard in evidence-based medicine. In addition, photobiomodulation therapy (PBMT) has garnered a lot of interest in recent years.

In the time trend chart of keywords (Fig. 7C), at the early stages, researchers primarily concentrated on the primary condition of radiation dermatitis. However, in

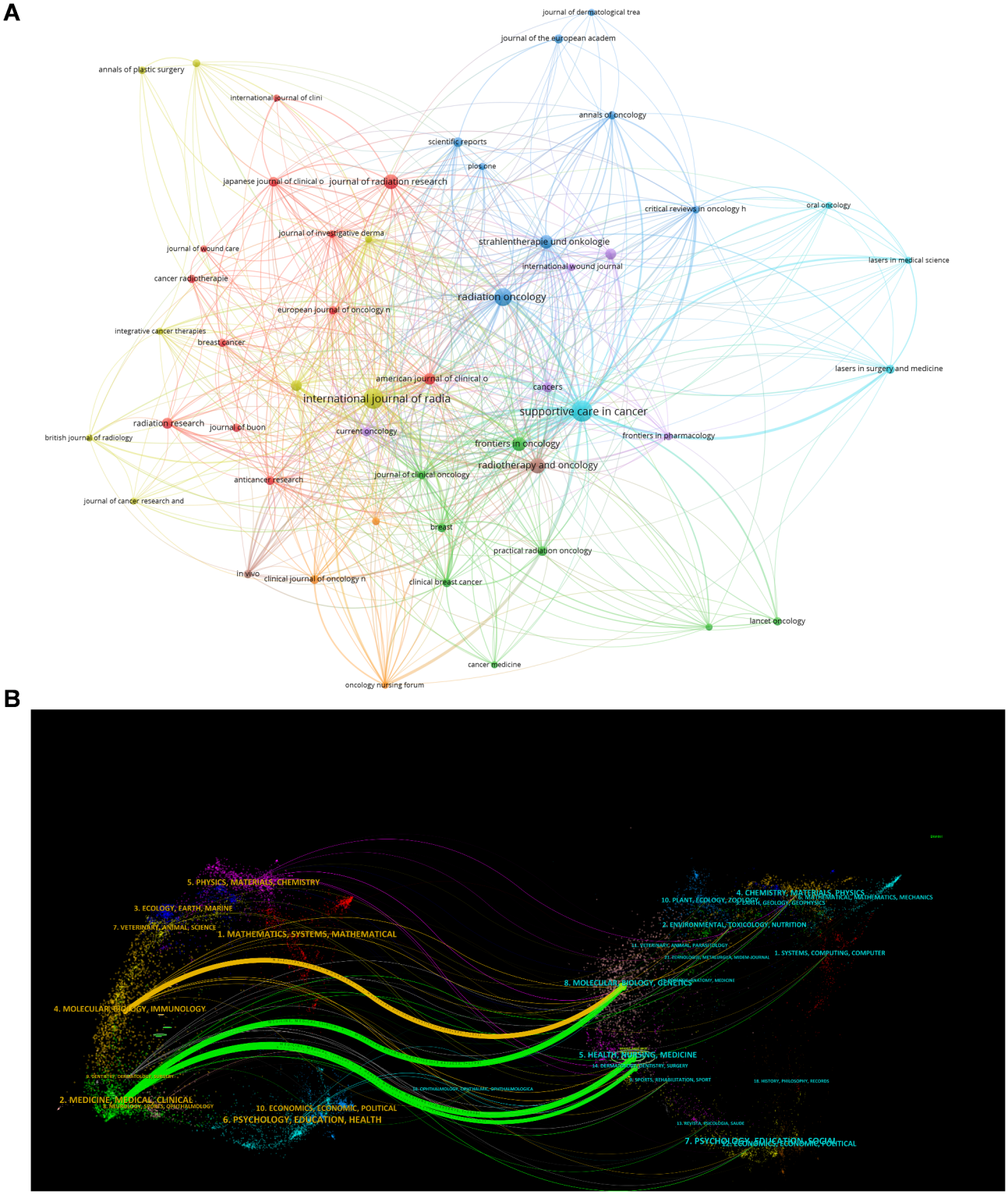

Fig. 6 Analysis of journals engaged in RD research. **(A)** Journal's cooperation network. **(B)** Dual map overlay for journals

Table 1 Top five productive journals

Journal	Count	IF (2023)	JCR (2023)
Supportive Care in Cancer	46	2.8	Q1
International Journal of Radiation Oncology Biology Physics	44	6.4	Q1
Radiation Oncology	33	3.3	Q1
Radiotherapy and Oncology	24	4.9	Q1
Journal of Radiation Research	22	1.9	Q2

Table 2 Top five highly co-cited journals

Co-cited Journal	Citation	IF (2023)	JCR (2023)
International Journal of Radiation Oncology Biology Physics	2982	6.4	Q1
Radiotherapy and Oncology	1585	4.9	Q1
Journal of Clinical Oncology	1517	42.1	Q1
Supportive Care in Cancer	657	2.8	Q1
New England Journal of Medicine	612	96.2	Q1

recent years, the development of clinical trials and the emergence of different biological nanomaterials have accelerated advancements in this field. Particularly, the emergence of barrier films and dressings, such as Mepitel film, demonstrated an effective function in preventing or reducing the occurrence of acute radiation dermatitis in several RCT studies [11, 12].

Discussion

Bibliometrics is a useful tool for summarizing current knowledge and forecasting future development trends. It utilizes statistical and mathematical expertise to summarize the state of knowledge at the moment and forecast future trends in development based on specific discipline perspectives. To the fullest of our understanding, this study is the first in this field to statistically assess all of the publications on RD published between 2003 and 2023 using bibliometrics. We analyzed these articles using VOSviewer, CiteSpace, and R package, to determine the countries/regions, institutions, authors, journals, keywords, and outbreak words. Both statistics and visualizations were performed to summarize and predict research hotspots for future topics.

The data analysis over the last 20 years showed that, despite some fluctuations in the annual number of publications, both the general trend and the number of citations have been growing. RD-related research was gaining more attention, it can be summarized for the following reasons. First, in clinical practice, RD still has a high incidence due to the widespread use of radiation therapy for patients. Specifically, the careless use of radiation can lead to radiation side effects in nations where there is a serious lack of nuclear medicine specialists and sophisticated imaging equipment needed for response, dosage, and treatment planning. Secondly, the signs and symptoms of RD vary depending on the kind and dosage of radiation. Most cases were mild cases, only represented by erythema, itching, burning feeling, etc. However, severe patients may have blisters, necrosis, and even ulcers. Fortunately, as more and more doctors become aware of RD, a growing number of people are being recognized and treated properly. Thirdly, apart from radiotherapy, other factors might also result in acute and chronic skin damage such as radiation nuclear accidents, radiation accidents, long-term occupational exposure to radiation, and nuclear war.

Regarding countries/regions analysis, the United States and China emerged as the leading entities in terms of publications and citations. We analyzed the potential reasons: Foremost among these was the relatively robust funding allocated to medical research in these nations. This financial backing enabled researchers to delve into in-depth basic research, conduct rigorous clinical studies, and foster interdisciplinary collaborations, thereby markedly enhancing the comprehensive understanding of RD. Secondly, the substantial populations of the United States and China resulted in a high incidence of new cancer cases annually. Meanwhile, the advanced medical technology and cancer screening methods facilitated earlier identification and diagnosis of cancers, leading to a significant number of patients receiving radiation therapy. Consequently, there was an urgent demand for effective prevention and treatment of RD, prompting researchers to explore innovative approaches to address this issue.

In terms of institutions, four of the top 10 institutions were located in France. Unicancer, an alliance of 18 comprehensive cancer treatment centers in France, ranked first among them. Unicancer publishes far more than other institutions, which explains why France had the second-highest number of articles cited in the world, only behind the United States. In addition, we observed that there is a greater frequency of collaboration and interactions between leading scientific research institutes, which promoted the growth of the subject.

Regarding the author, radiation dermatitis expert Professor Edward Chow of Sunnybrook Health Sciences Centre is well-known and has authored numerous articles. He has been consistently publishing pertinent articles since 2010, and over the last five years, there has been a notable growth in the quantity of publications and citations. Furthermore, we found that author linkages are significantly more numerous than those between countries and organizations. As members of the MASCC Radiation Dermatitis Guidelines Working Group, Edward Chow, Tara Behroozian, Pierluigi Bonomo, Julie Ryan Wolf, and Corina van den Hurk published an educational article titled "Multinational Association of Supportive Care in Cancer (MASCC) clinical practice guidelines for the prevention and management of acute radiation

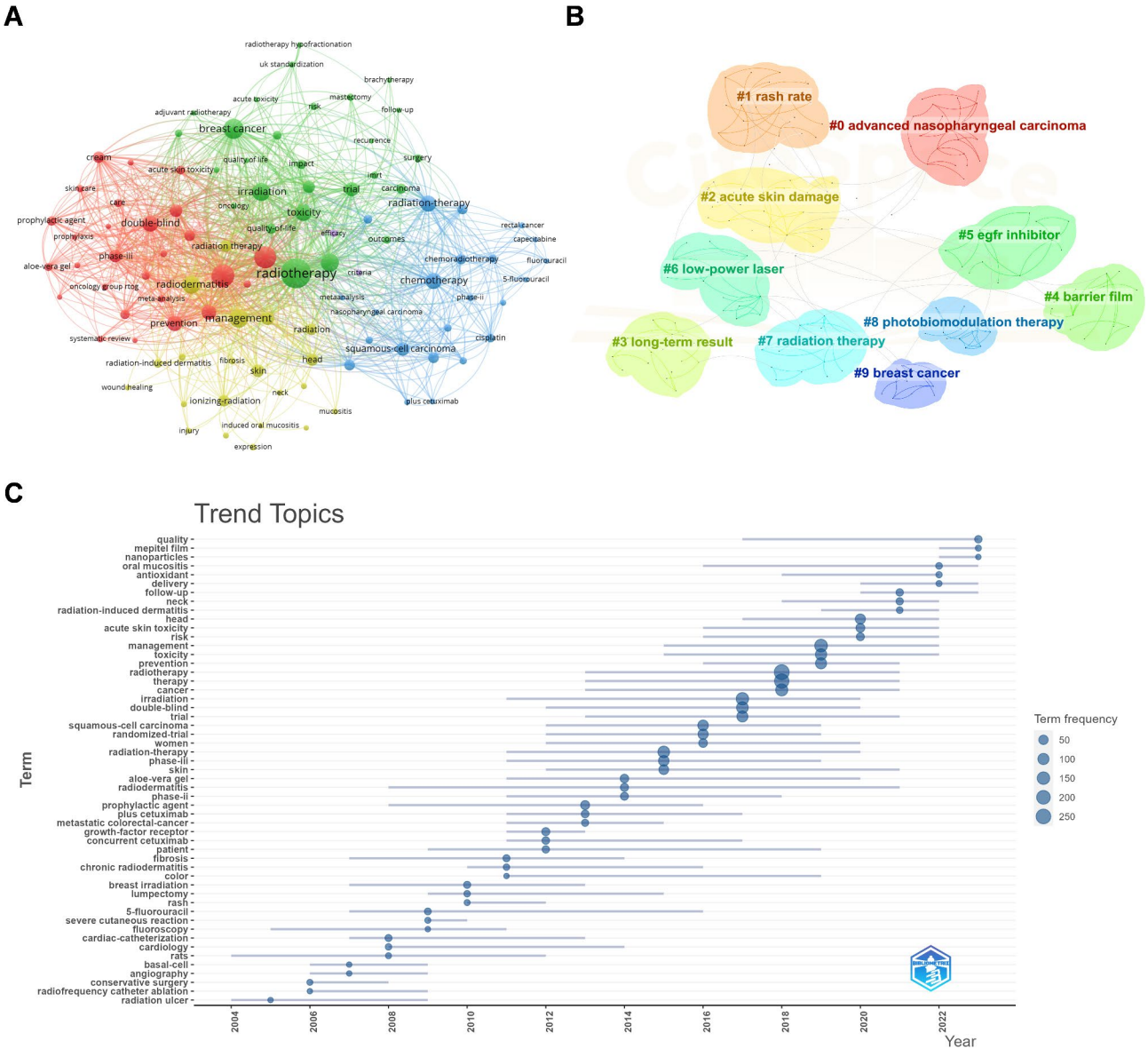

Fig. 7 Analysis of keywords engaged in RD research. **(A)** Keywords connection network. **(B)** Cluster analysis of keywords. **(C)** Timeline chart of the burst keywords

dermatitis: international Delphi consensus-based recommendations" in *The Lancet Oncology* online in April 2023. In this article, a comprehensive clinical practice guideline was developed, detailing both the prevention and early response strategies for acute radiation dermatitis.

When it comes to journals, scholars focused more on journals with more publications and citations to receive more timely information about the frontier of RD. In this article, we listed out the most published and cited journals on RD in order to save time for scholars to find the most appropriate journals and submit manuscripts. On the other hand, we also discovered that the absence of an academic journal dedicated to the study and publication of radiodermatitis, which may pose a barrier to its clinical advancement.

Based on keyword analysis, the most common disease linked to RD was breast cancer, followed by rectal cancer, head and neck squamous cell carcinomas, which may help prevent the occurrence of RD in these patients more efficiently. Regarding pathogenesis, scientists have focused on keywords like nitric oxide, oxidative stress, and apoptosis when exploring the etiology. High-energy rays cause cells to develop amounts of oxidative stress products, such as ROS. ROS is a collective term for a group of oxygen molecule derivatives, which may result in apurinic/apyrimidinic sites, single-strand breaks, DNA-protein crosslinking, and abnormal glycosylation

[13]. To remove ROS, scientists have carried out several research. Of them, Nrf2 is a crucial transcription factor for antioxidant proteins. Research has demonstrated that exogenous Nrf2 overexpression in rats prevents radiation-induced ROS, promotes DNA damage repair, and shields the endoplasmic reticulum and mitochondria from radiation damage [14]. Another literature reported that activating Nrf2 may represent a therapeutic target for preventing RD via inhibiting cell senescence and apoptosis [15]. Additionally, Nrf2 stimulates the production of p53-binding protein 1 (53BP1), which repairs DNA in NHEJ and shields cells from chromosomal abnormality [16]. Furthermore, chemotherapy medications like doxorubicin and cisplatin will aggravate the genotoxicities of ROS [5]. While it was well established that ROS production was a primary cause of RD, the molecular mechanisms remain uncertain. For instance, how radiation and ROS influence cell proliferation, differentiation, apoptosis, and other cellular processes of skin cells are not yet completely elucidated. Additionally, the potential interaction mechanisms among ROS production, inflammation, and angiogenesis require further exploration.

For prevention or mild RD, traditional topical medications were the preferred treatment options. Topical corticosteroids ointments and olive oil were commonly used to alleviated skin dryness and erythema [17, 18]. For wound that at risk of infection, antibiotic ointments can be applied [19]. In cases where the skin exhibits wet desquamation, barrier films and dressings were useful tools. Mepitel film, a silicone-based polyurethane film, which is characterized by creating a moist wound environment to promote reepithelization [20, 21]. In an RCT test, including 78 breast cancer patients, prophylactically used Mepitel film totally prevented moist desquamation and reduced skin responses by 92%, compared to the aqueous cream group [22]. Another RCT research demonstrated that Mepitel film can reduce the severity of acute RD responses in patients with head and neck cancer following radiation therapy [23]. For the treatment of acute RD, Mepilex Lite, a foam dressing, was suggested as a better option compared with Mepitel film [7, 24].

PBMT was also widely applied in RD therapy, this technology describes the application of visible red and/or near-infrared (NIR) light produced by laser diodes and/or light-emitting diodes (LEDs) to target cells and tissues in order to induce the photobiological alterations and the desired physiological changes in the body [25]. In mechanism, PBMT is mainly dependent on the absorption of light by cytochrome c oxidase (complex IV in the electron transfer chain). The photoexcitation of cytochrome c oxidase modifies electron transport, boosts adenosine triphosphate (ATP) generation, and triggers subsequent protein synthesis, secretion, and cell division [26]. An RCT test ($n = 120$) reported by Robijns [27] showed that PBMT was applied to breast cancer patients starting on the first day of radiation therapy (2 times a week, 808–905 nm, 4 J/cm^2). The outcomes showed that PBMT can successfully lower the incidence of ARD of RTOG grade 2 and above, while also improving the quality of life for patients. As a result, PBMT was preferred to be used for prevention rather than management of RD in clinical practice guidelines [7]. Researchers also have found that the incidence that irradiation-induced dermatitis may become higher when combined with chemotherapy medication, such as cetuximab [28, 29]. In terms of prevention, the explosive term, intensity modulated radiation (IMRT), gained attention in 2017. IMRT used beam-limiting devices to control the beam intensity that ensured the three-dimensional distribution of the dosage in the high-dose region matched the shape of the tumor [30]. Besides, to avoid RD developing in the surrounding skin, the dosage of the target area was also minimized as much as possible [31]. Existing treatments, including topical dressings or films and phototherapy, have demonstrated therapeutic effects, but they also had adverse consequences, such as allergic reactions, skin irritation, and infection risks. Future research could explore novel approaches and strategies, for instance, gene therapy, stem cell therapy, and nanomedicine delivery systems, to enhance treatment and improve patients' quality of life. Furthermore, clinicians ought to focus on metastatic colorectal cancer and head and neck squamous cell carcinoma, as these two types of cancer have recently emerged as high-risk factors of RD.

In addition, given the varying genetic backgrounds and radiotherapy regimens, the clinical manifestation existed individualized characteristics in RD. As a consequence, there should be a greater emphasis on individualized treatment and precision medicine-based prevention and treatment efforts.

Conclusion

Our comprehensive bibliometric analysis of RD research from 2003 to 2023 provides valuable insights into the evolution of this subject, including top countries/regions, institutions, authors, journals, and keywords analysis. Additionally, we described the current research hotspots, identified new research directions, and offered a thorough assessment of global RD research alliances and trends. We hope to give valuable conclusions for researchers, physicians, and policymakers to find feasible solutions.

Abbreviations

ATP	Adenosine triphosphate
IMRT	Intensity modulated radiation
LEDs	Light-emitting diodes
NIR	Near-infrared

PBMT	Photobiomodulation therapy
RCT	Randomized controlled trial
RD	Radiation dermatitis
ROS	Reactive oxygen species
SCIE	Science Citation Index Expanded
SSCI	Social Science Citation Index
WOSCC	Web of Science Core Collection
53BP1	P53-binding protein 1

Author contributions
Xinyi Zhang, Yuai Xiao, and Ang Li wrote the main manuscript text and prepared data collection and visualization.Yuchong Wang, Jianguo Xu, Kexin Chen, and Haoyuan Zheng participated in data management and visualization.Minliang Wu and Chunyu Xue participated in supervision and revision of the manuscript.All authors reviewed the manuscript.The first three authors: Xinyi Zhang, Yuai Xiao, and Ang Li contributed to the work equally and should be regarded as a co–first authors.Minliang Wu and Chunyu Xue should be regarded as co-corresponding authors.

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Data availability
The data that support the findings of this study are openly available in https://webofscience.clarivate.cn/wos/woscc/basic-search.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
Not applicable.

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