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ORIGINAL RESEARCH

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The top 100 most cited manuscripts in breast-conserving surgery for breast cancer: a bibliometric analysis

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Abstract

Breast conserving surgery (BCS) for breast cancer is widely performed. This study aimed to identify the characteristics of the 100 most cited articles in BCS research. The 100 most cited articles were retrieved from the Web of Science datasbase. Using bibliometric tools, the contributions of countries, institutions, authors, and of research development were analyzed. The country with the highest number of manuscripts in the top 100 was the United States (n = 59). The Memorial Sloan Kettering Cancer Center and University of Pennsylvania each published 21 articles. Bartelink H, Harris JR, and Morrow M each published eight articles. Among the top 100 most cited articles, hotspots focused on breast-conserving margins, recurrence, distant metastases, radiotherapy, and some controlled trials. Surgical margin, recurrence, distant metastases, radiation therapy are the hot topics in these 100 articles. There may be new radiotherapy modalities to improve the efficacy of post-operative radiotherapy in the future. The results of this review provide breast surgeons with research highlights and hot spots in the field of BCS and predict the future.

Keywords

Breast-conserving surgery; Top 100; Top-cited; Bibliometric; Visualized study

1. Introduction

Although breast cancer is a predominantly female disease, it has now become the most common cancer [1, 2]. As research into breast cancer continues to advance, its treatment modalities are becoming more abundant, and significant scientific and social advances have been made in treatment outcomes. The prognosis of breast cancer is enhanced by an extensive combination of molecular features and clinical treatment, including immunohistochemical markers, genomic markers, and immunomarkers [3]. The main surgical treatments for breast cancer include modified radical and breast-conserving surgeries and some reconstructive surgeries. Breast-conserving surgery (BCS) was recommended in 1990 and has been used since then [4]. The first choice for patients with early breast cancer is BCS (mainly lumpectomy and sentinel lymph node biopsy), followed by breast radiotherapy [5, 6]. Moreover, BCS has a lower recurrence risk and a better survival rate [7–9]. Because cosmesis is better following BCS, it is associated with a better quality of life (*e.g.*, functional status and less frequent symptoms) than total mastectomy [10–13]. BCS has certain advantages in terms of psychological, marital, sexual, body image, and social adjustment and cancer-related fears and concerns.

Over time, many highly cited articles on BCS have emerged. The application of bibliometrics to qualitative and quantitative analyses of highly cited articles allows for the assessment of the scientific value of the quantitative literature [14–16]. This study identified the top 100 most frequently cited original research articles which represented the most influential papers in this field and analyzed their characteristics and research directions.

2. Materials and methods

A search of the Web of Science Core Collection (WOSCC) database using subject terms was conducted, and the results were limited to articles written in the English language. The search terms used to ensure that all relevant manuscripts were identified were as follows: "breast cancer" or "breast tumor*" or "breast neoplasm" or "breast carcinoma" and "conservation" or "conserving" or "partial mastectomy*" or "lumpectomy*".

The top 100 most cited manuscripts were identified based on citation rankings. Two authors excluded articles not relevant to the topic, and a final determination was made to verify the 100 articles.

The 100 articles were analyzed for subject, author, jour-

nal, annual volume, institution, and country of origin using the R language package (R-4.2.2, Academic Spin-Off of the University of Naples Federico II, Naples, Italy) to analyze the characteristics of highly cited articles in the field.

The impact factors for each published journal were obtained from the 2020 Journal Citation Report Dataset. To better assess the importance of future articles, the 100 articles were ranked in terms of citation rates. Citation rate, also known as the average number of citations per year, is defined as the number of citations divided by the number of years since publication. This method was validated to adjust for the bias generated by older manuscripts, which increased the number of citations over time.

3. Results

A WOSCC search was conducted on 15 June 2022, and 2425 manuscripts were excluded. There were three types of papers in the remaining 100 articles: 96 original articles, three review papers, and one editorial material. The top 100 most cited articles are shown in **Supplementary Table 1** (sorted by the number of citations), including author, title, and journal and year of publication. The most frequently cited (with a total of 4446 citations) and least frequently cited (with a total of 105 citations) manuscripts had a median citation rate of 179. The average citation frequency of each article was 311.87.

The top 100 most cited manuscripts related to BCS were published between 1984 and 2019. From 1994 onwards, the number increased, reaching its first peak in 2001 (n = 8) and its second peak in 2014 (n = 8). Top 100 cited articles' year and citation distribution are shown in Fig. 1. The publishing time of the top 100 most cited articles was mainly between 1998 and 2016.

The most historical paper was the one written by Montague, ED, describing BCS and radiotherapy for breast cancer; it was published in CANCER in 1984 and cited 121 times. The journals that published the top 10 manuscripts are listed in Table 1.

The JOURNAL OF CLINICAL ONCOLOGY published the most articles among all relevant journals (n = 22), with an impact factor of 44.54 in 2020; it was followed closely by the INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSIC (n = 14; impact factor 7.04 in 2020) and CANCER (n = 9; impact factor 6.68 in 2020). The NEW ENGLAND JOURNAL OF MEDICINE had the highest impact factor in 2020 (79.32). Four of the top 100 most cited manuscripts were published in this journal.

The distribution of articles by country and the cooperation between countries are illustrated in Fig. 2. The country with the highest number of manuscripts among the top 100 most cited articles was the United States (n = 59), followed by the Netherlands (n = 14), Canada (n = 11), and England (n = 11). The red line in the figure represents cooperation between countries, and it is obvious that the United States, Canada, Australia, and European countries cooperate frequently.

Several institutions have published more than one article. The Memorial Sloan Kettering Cancer Center and University of Pennsylvania each published 21 articles. Harvard University and the Netherlands Cancer Institute published 15 articles each. The top 20 institutions in terms of the number of published articles are listed in Fig. 3.

Bartelink H, Harris JR, and Morrow M published eight articles each. The top 20 authors in terms of the number of published articles are listed in Fig. 4. Authors with the highest production over time are shown in Fig. 5. Most of the highly cited authors and institutions were from the United States.

To avoid publication time bias, we analyzed the annual average citation frequency, which ranged from 3.45–212.05 for the top 100 articles. The top 10 citation rankings are listed in Table 2; seven manuscripts in the top 10 were ranked based on total citations and average annual citation frequency. However, the other three were replaced with more highly cited and recent articles on breast conservation, which is an addition to the highlighted literature.

The most significant change in rank was that achieved by a study by Coles, titled "partial breast radiotherapy after BCS in patients with early breast cancer: 5-year results of a multicenter, randomized, controlled, phase 3 non-inferiority trial in 2017", which rose in citation rate from 28th (263) to 7th (43.83).

The keyword co-occurrence network is shown in Fig. 6. The high-frequency keywords used by the authors of the top 100 cited articles were BCS, brachytherapy, radiotherapy, follow-up, local recurrence, accelerated partial breast irradiation, mastectomy, quality of life, and local recurrence. Fig. 7 provides a thematic map of the subject keywords used in the articles on BCS for breast cancer on two axes—density (degree of development) and centrality (degree of correlation). In this map, the high-frequency theme of BCS appears in the form of bubbles in four quadrants. The basic topics include the follow-up of BCS for breast cancer, postoperative radiotherapy, and local recurrence. In addition, postoperative radiation therapy is the MOTOR theme with a good degree of development and high centrality in the upper right quadrant. Therefore, there may be some room for future research.

Figs. 8,9 show the conceptual structure and tree diagram of the top 100 most cited articles for BCS, consisting of two clusters. Each keyword was considered a topic, and the closest keywords were combined in the clustering phase with each combination transformed into a new cluster. Cluster 1, with four keywords—adjuvant breast, lobular carcinoma, dose-escalation, and locoregional recurrence—was small in conceptual structure and hierarchical graphical network.

There were 46 keywords in Cluster 2; it was considered to be the largest in this study. The main themes in this cluster were as follows: positive margins, local recurrence, follow-up, radical mastectomy, resistant metastases, randomized trial, follow-up, tumor recurrence, trial tamoxifen therapy, risk, radiotherapy, surgical radiation survival recurrence, postoperative radiotherapy, clinical trial, premenopausal women, mastectomy, lumpectomy, irradiation, dose rate brachytherapy, total mastectomy, axillary dissection, estrogen receptor, progesterone receptor, expression patterns, and prognosis. As shown in Figs. 8,9, of the top 100 most cited articles on BCS for breast cancer, most focused on breast-conserving margins, recurrence, distant metastases, radiotherapy, and some controlled trials.

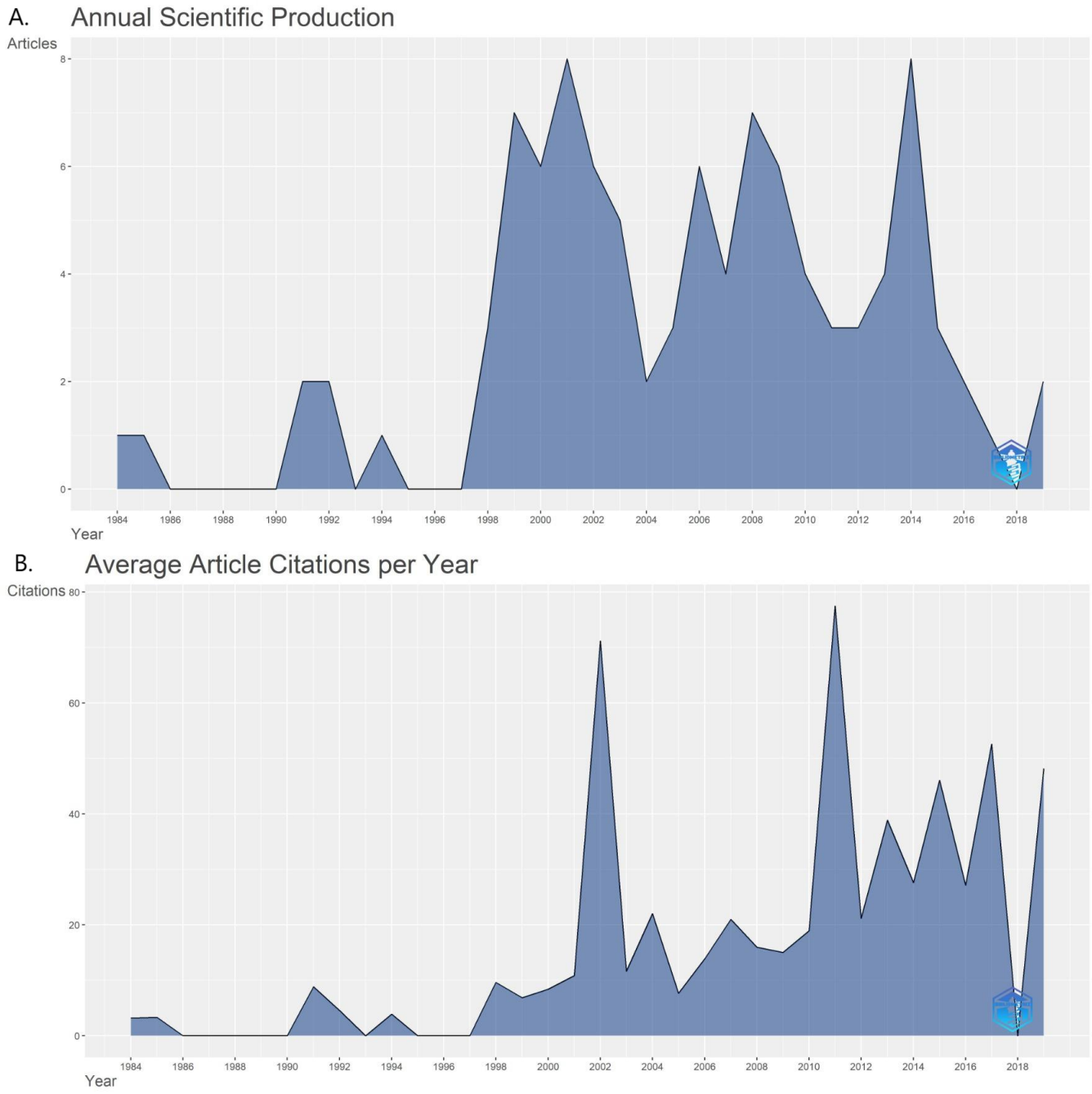

FIGURE 1. Top 100 cited articles' annual citation distribution. (A) Annual production distribution. (B) Average article citations distribution.

4. Discussion

BCS and definitive radiation therapy have proven effective for early stage breast cancer [17, 18]. The safety of BCS is widely recognized, and its cosmetic effect is significantly better than that of total mastectomy. Cosmetic satisfaction with BCS is similar to that with mastectomy and reconstruction [19]. Breast-conserving surgery for breast cancer is an important surgical procedure, and its generalization is beneficial to the development of this technique. To the best of our knowledge, this is the first study to use bibliometric methods to analyze and interpret the 100 most cited and influential articles in the field of BCS for breast cancer. Of the 100 articles, many dealt with the surgical margin of BCS, and 15 of them addressed this issue alone. Approximately 30% or more of the top 100 most cited articles included studies related to postoperative radiotherapy.

The most cited article (4453 citations) was authored by Fisher *et al*. [20]. They reported a randomized trial comparing mastectomy, lumpectomy, and lumpectomy plus radiotherapy for breast cancer.

This original research article was published in the NEW ENGLAND JOURNAL OF MEDICINE in 2002. This study evaluated 20-year follow-up results of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer [20]. This study also ranked first in terms of the average number

TABLE 1. The top 10 journals with the top 100 most cited articles are ranked according to the number of articles published.

Rank	Title	2020 Impact Factor	Number of manuscripts in the top 100	Total number of citations
1	JOURNAL OF CLINICAL ONCOLOGY	44.54	22	6842
2	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSIC	7.04	14	2336
3	CANCER	6.68	9	1534
4	ANNALS OF SURGICAL ONCOLOGY	5.34	6	1218
5	EUROPEAN JOURNAL OF CANCER	9.16	5	887
6	LANCET	79.32	5	2719
7	LANCET ONCOLOGY	43.15	4	1316
8	NEW ENGLAND JOURNAL OF MEDICINE	95.12	4	8044
9	AMERICAN JOURNAL OF SURGERY	2.57	4	731
10	ANNALS OF SURGERY	12.97	3	486

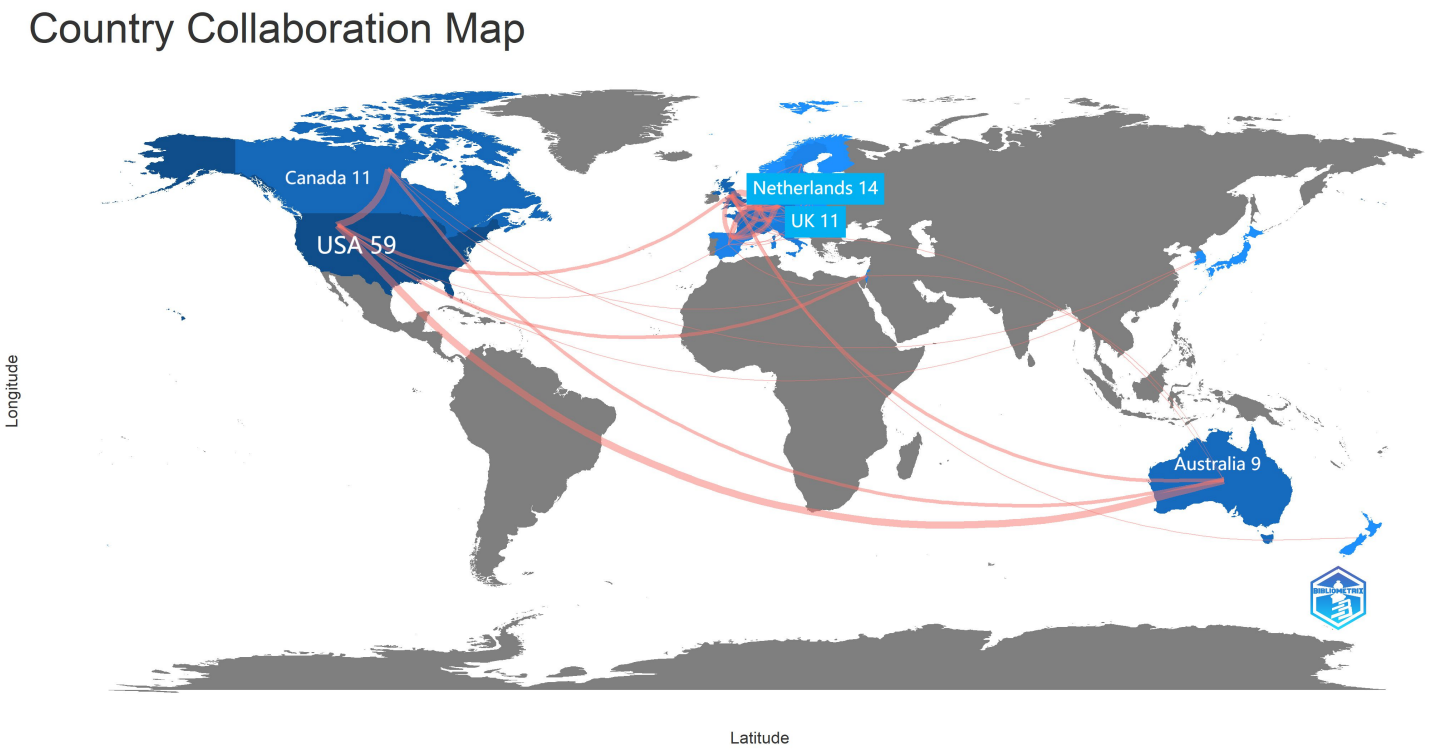

FIGURE 2. Map of the country cooperation network. The darker blue color represents the higher volume of articles issued by the country. The red line represents cooperation between countries, and it is clear that the United States, Canada, Australia and European countries not only publish more articles but also cooperate more frequently.

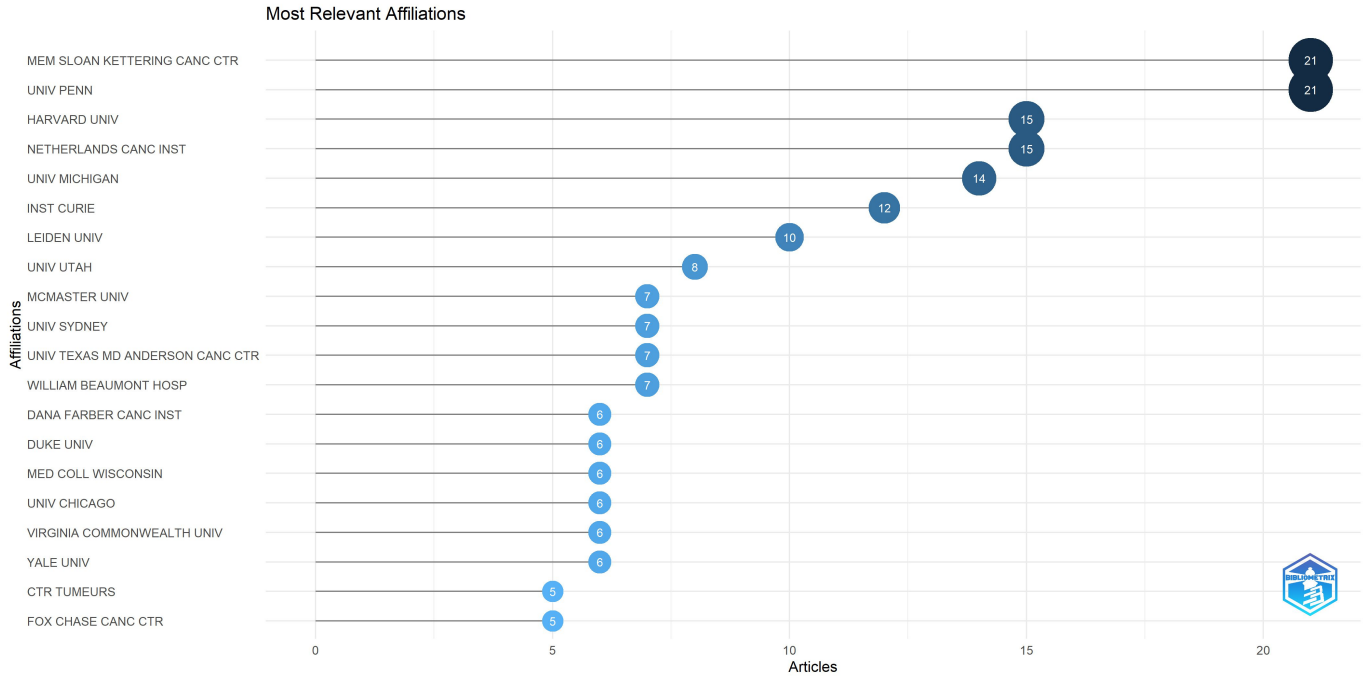

FIGURE 3. Top 20 institutions with the highest number of published articles.

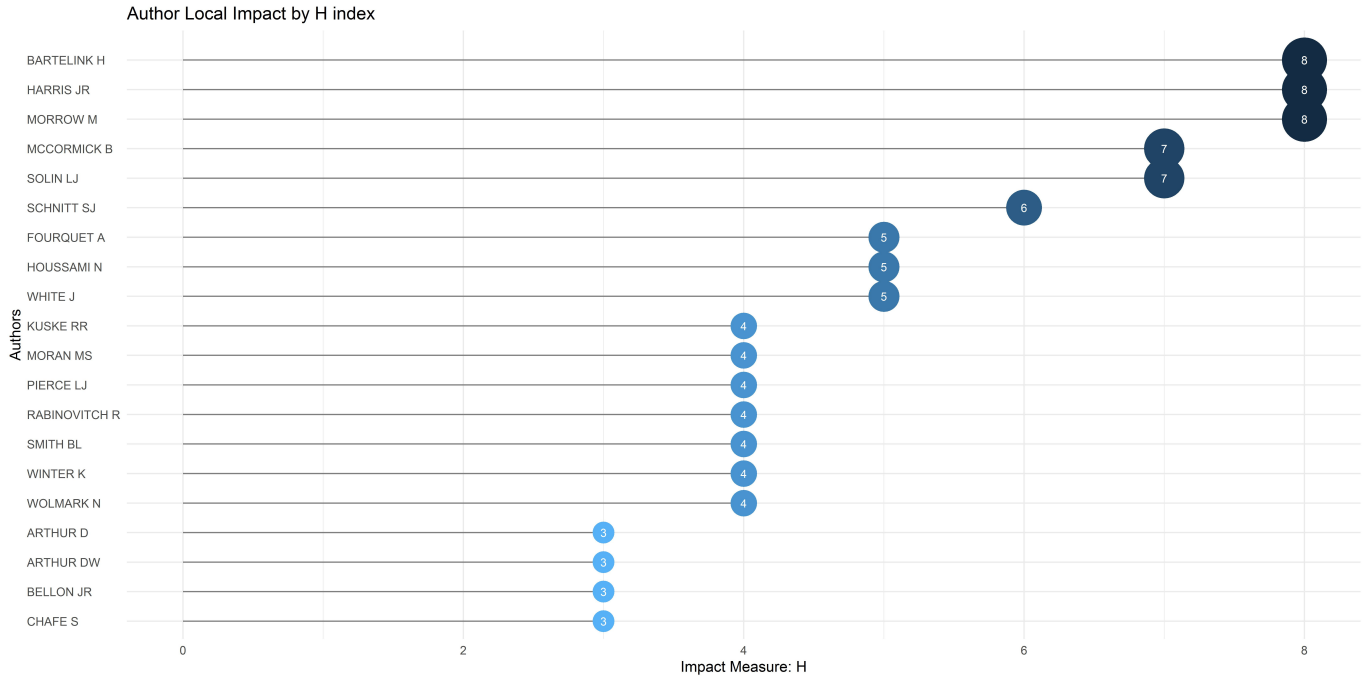

FIGURE 4. Top 20 authors in published articles.

of citations per year. After 20 years of follow-up, it was found that overall survival rate of patients with breast cancer who underwent BCS plus radiotherapy did not reduce as long as the surgical margins were negative [21].

4.1 Surgical margin of BCS

Moran *et al.* [22] conducted a systematic review of 33 studies (including 28,162 patients) that examined cut margins and ipsilateral breast tumor recurrence and found that positive margins (invasive or ductal carcinoma) were twice as common as negative cut margins in terms of the risk for ipsilateral tumor recurrence. This increased risk was not mitigated by good biology, endocrine therapy, or radiation stimulation [22]. In 2014, Buchholz *et al.* [23] published a consensus on surgical margins, and the absence of cancer cells at the surgical margins as a surgical margin criterion for invasive cancer led to a lower rate of ipsilateral breast tumor recurrence, reducing the incidence of reoperation and medical costs. Therefore, insufficient surgical margins are a high-risk factor for poor clinical outcomes in breast-conserving therapy for early-stage breast cancer [24, 25]. Higher recurrence rates were associated with positive or indeterminate margins than with negative

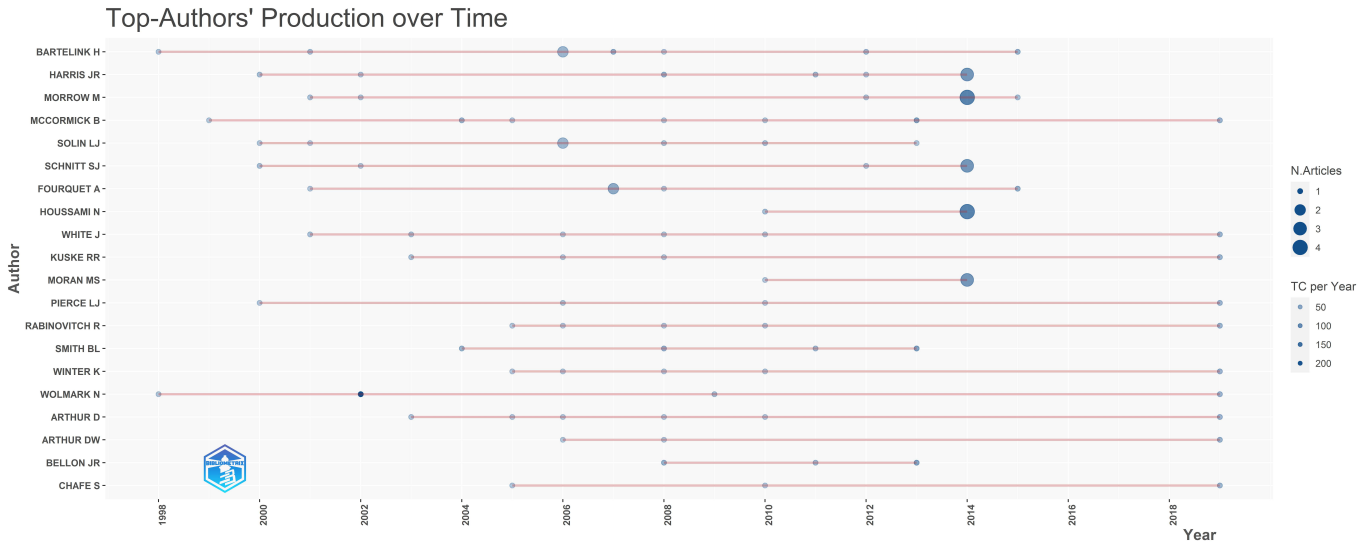

FIGURE 5. Top-authors' production authors over time. TC: Total citation.

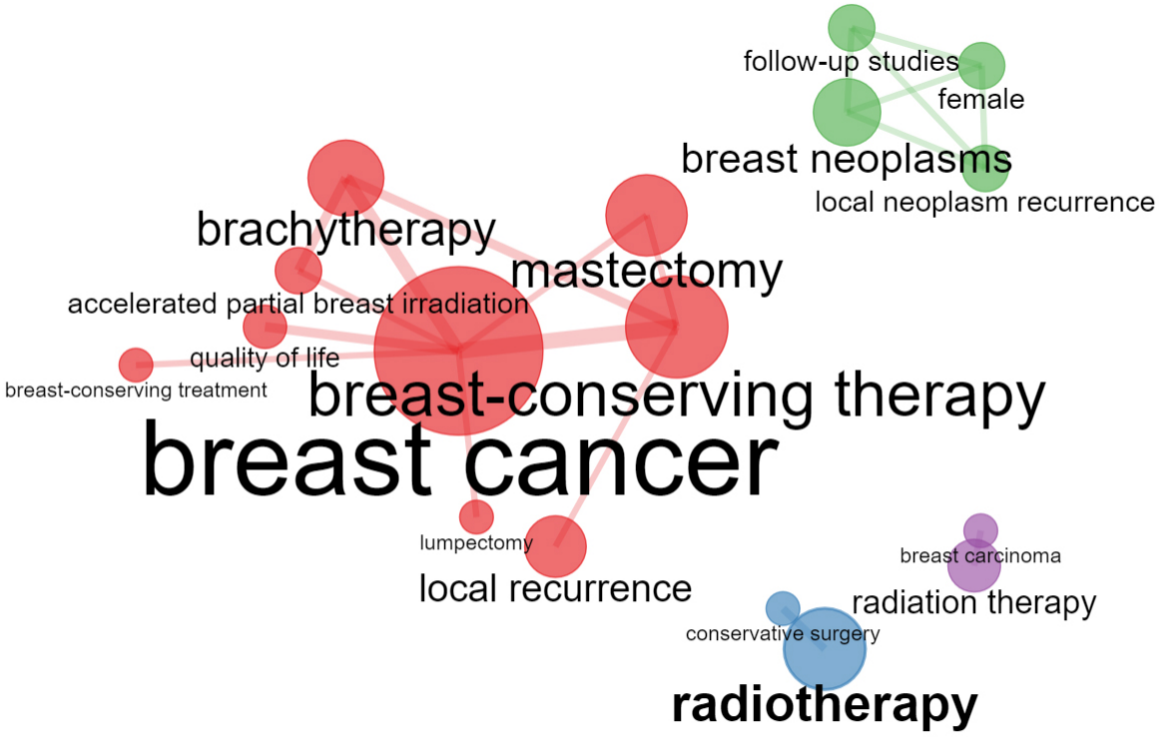

FIGURE 6. Top keyword co-occurrence mapping. The same color represents the same category, and the size of the circles represents the number of occurrences. The thickness of the connecting lines represents the frequency of co-occurrence.

pathological margins [26]. Under the premise of ensuring negative pathological margins, whether the threshold distance for negative margins is as large as possible is still a question worthy of discussion. Many researches have already confirmed that the reduced odds of local recurrence was not significantly associated with the increase of distance for defining negative margins [27–30]. Appropriate margin assessment techniques are the key to ensuring negative margins in breast-conserving surgery. Cendan *et al.* [31] from the University of Florida used intraoperative frozen section analysis (FSA) to assess the margins of lumpectomy, and they found that the accuracy of FSA was 84%, thereby improving breast conservation. Emerging techniques such as hyperspectral imaging, 3D tomosynthesis specimen radiograph, pegulicianine fluorescence-guided system and so forth for the assessment of intraoperative surgical margin not only have excellent specificity and sensitivity but also save more time and effort compared to FSA [32–34].

4.2 Recurrence and metastases after BCS

Nguyen *et al.* [35] compared the five-year recurrence rate after BCS for different subtypes of breast cancer and found that the local recurrence rate of the luminal A subtype was

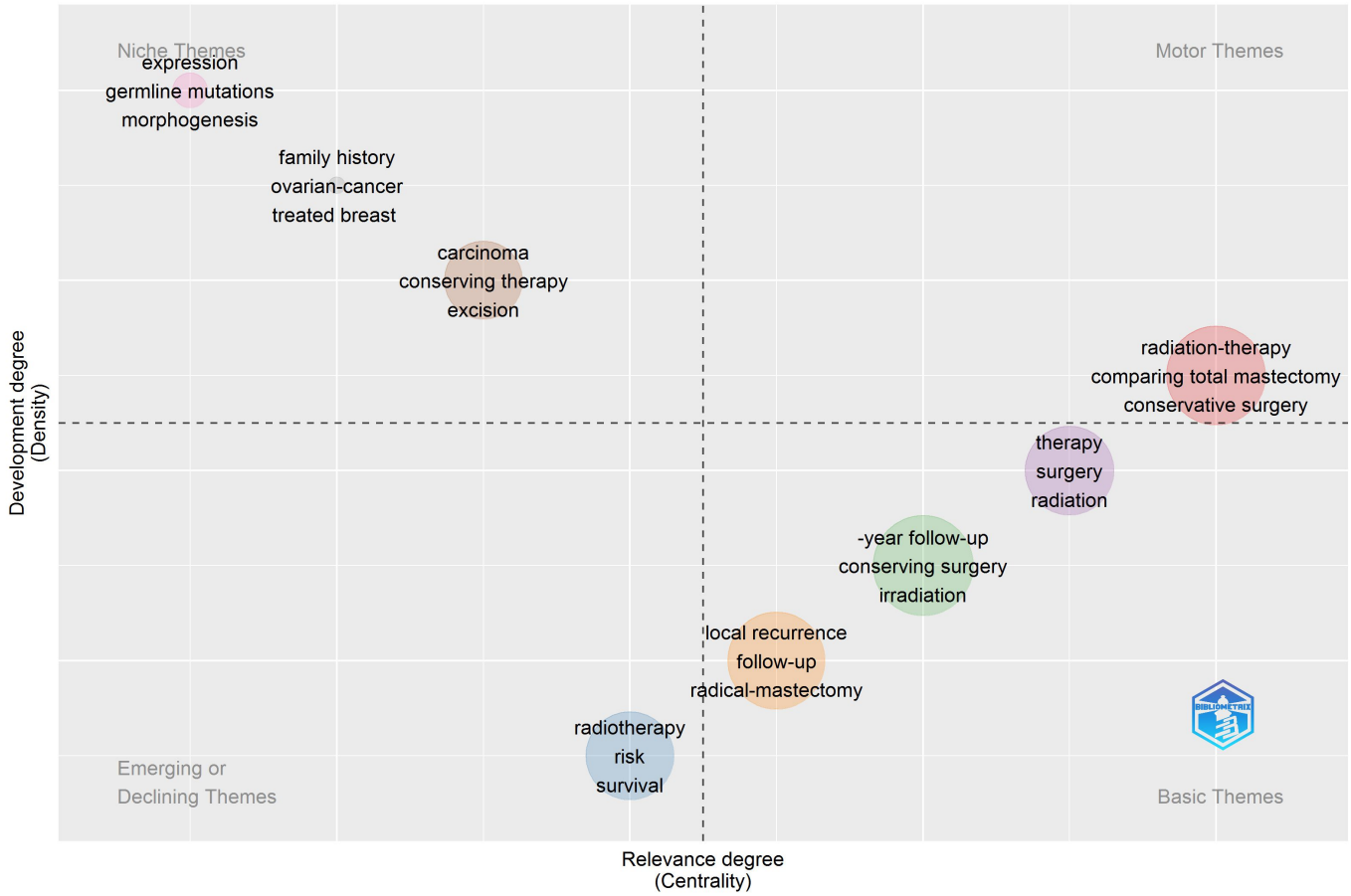

FIGURE 7. Thematic map. The visual map of the subject keywords used in the articles on BCS for breast cancer on two axes—density (degree of development) and centrality (degree of correlation). In this map, the high-frequency theme of BCS appears in the form of bubbles in four quadrants. Topics in the lower right quadrant are the underlying themes include: follow-up of breast cancer BCS, postoperative radiotherapy, and local recurrence. The themes in the upper right quadrant are motor themes with a good degree of centrality and development.

particularly low; however, the local recurrence rate of all subtypes was less than 10% after five years [35]. For patients with triple-negative breast cancer with tumors less than 5 cm in diameter and no lymph node metastases, the no locoregional recurrence rate for BCS plus radiotherapy was 96%; it was 90% for the modified radical treatment group (p = 0.027) [36]. Therefore, BCS is an excellent treatment option for patients with early-stage triple-negative breast cancer [37]. Patients with estrogen receptor-negative breast cancer with non-negative margins have a higher rate of local recurrence than those with estrogen receptor-positive tumors, regardless of the margin status [38]. Bollet, MA *et al.* [39] found that age was the important prognostic factor for loco-regional recurrence in young (<40 years) women treated with BCS. However, some studies have confirmed that the prognosis of breast-conserving surgery is not significantly different or even better than that of total mastectomy in young women [40, 41]. Therefore, breast-conserving surgery may be the preferred operation for young patients with breast cancer. In terms of metastases, patients with infiltrative local recurrences greater than 1 cm are at a high risk of developing distant disease. Patients with recurrences ≤1 cm have a higher rate of distant disease-free survival, which may indicate that early detection can improve treatment outcomes [42]. Komoike *et al.* [43] conducted a study of recurrence and metastasis after BCS in Japan. They found that young age, positive surgical margins, and lack of radiation therapy appeared to be important factors associated with local recurrence. Patients with positive lymph nodes at initial surgery or local recurrence shortly after surgery are at a particularly high risk of developing distant metastases [43]. However, the underlying mechanisms remain unclear. Chemotherapy is a treatment to prevent postoperative recurrence and metastasis. Literature suggests that neoadjuvant chemotherapy combined with breast-conserving surgery can increase the probability of axillary preservation and improve 5-year disease-free survival.

4.3 Radiotherapy after BCS

Radiotherapy after BCS is an important treatment for breast cancer patients and can reduce the risk of recurrence and death from breast cancer. Postoperative radiation therapy is the MOTOR theme with a good degree of development and high centrality.

Coles *et al.* [44] found that low-dose radiotherapy after BCS for selected cases of breast cancer was comparable to standard whole-breast radiotherapy in terms of 5-year recurrence rates and had comparable or fewer adverse effects in normal tissues.

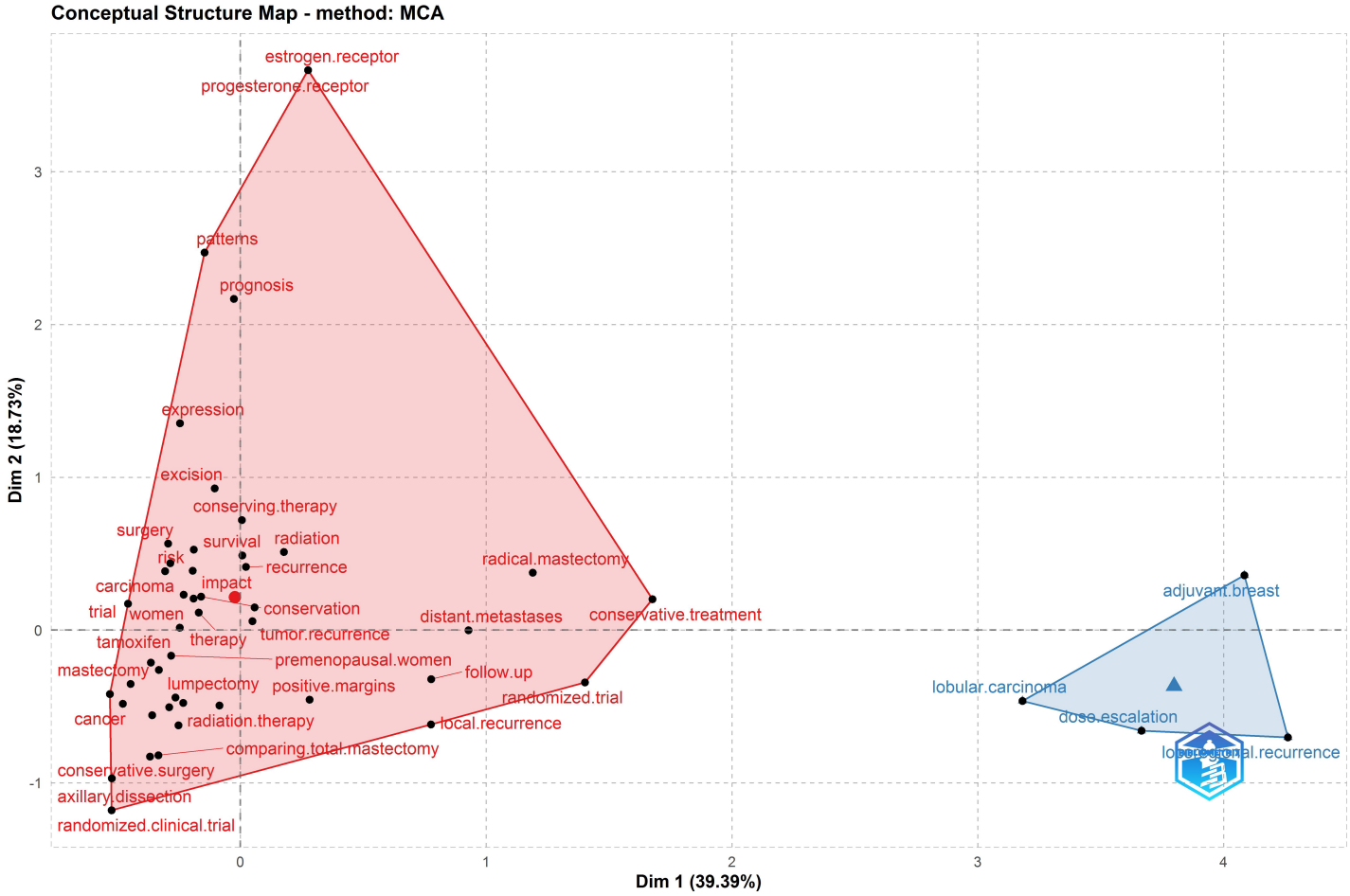

FIGURE 8. Conceptual structure diagram of the top 100 most cited articles in the BCS. MAC: Multiple cluster analysis.

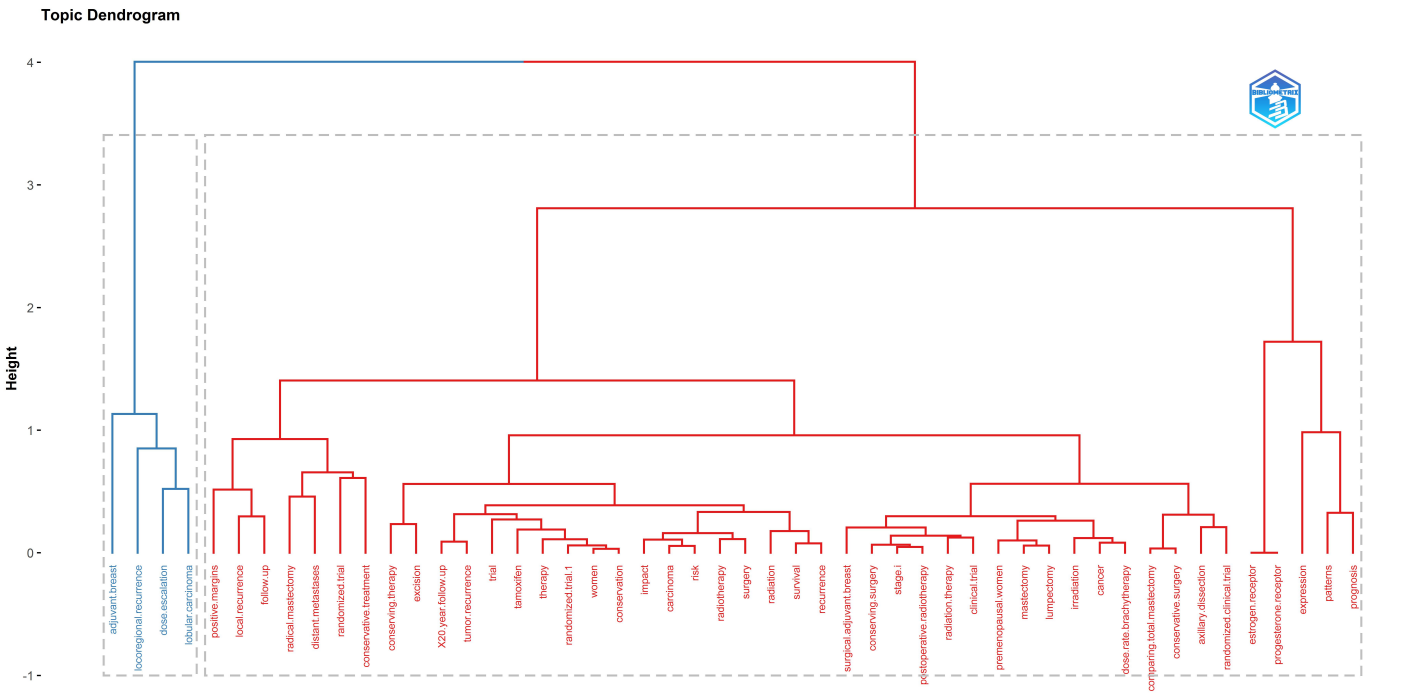

FIGURE 9. Tree diagram of the top 100 most cited articles in BCS, consisting of two clusters. Each keyword is considered as a topic, and in the clustering phase, the closest keywords are combined and each combination is transformed into a new cluster.

TABLE 2. Annual average citation (citation rate) of top ten articles.

Rank	Citation rate	Original rank	First Author	Title	Journal	Country	Date
1	211.9	1	Anderson, S [20]	Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer	NEW ENGLAND JOURNAL OF MEDICINE	USA	2002
2	168.75	3	Early Breast Canc Trialists Collab [17]	Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials	LANCET	UK	2011
3	132.57	2	Veronesi, U [21]	Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer	NEW ENGLAND JOURNAL OF MEDICINE	Italy	2002
4	65.9	6	Hughes, KS	Lumpectomy Plus Tamoxifen with or without Irradiation in Women Age 70 Years or Older with Early Breast Cancer: Long-Term Follow-Up of CALGB 9343	JOURNAL OF CLINICAL ONCOLOGY	USA	2013
5	60	9	Kunkler, IH [48]	Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial	LANCET ONCOLOGY	Scotland	2015
6	46.4	13	Cheung, KJ	Collective Invasion in Breast Cancer Requires a Conserved Basal Epithelial Program	CELL	USA	2013
7	45.38	4	Bartelink, H	Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial	JOURNAL OF CLINICAL ONCOLOGY	Netherlands	2007
8	43.83	28	Coles, CE [44]	Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial	LANCET	England	2017
9	42.63	18	Bartelink, H [46]	Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial	LANCET ONCOLOGY	Netherlands	2015
10	41.53	7	Nguyen, PL [35]	Breast cancer subtype approximated by estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after breast-conserving therapy	JOURNAL OF CLINICAL ONCOLOGY	USA	2008

Although the article authored by Coles *et al*. [44] ranked 28 in terms of citation rate, it ranked eighth in terms of citations in the LANCET and was published therein in 2017. This document is worthy of scholarly research. A cohort study in the Netherlands found that BCS plus radiation therapy improved 10-year overall survival compared with total mastectomy [45]. Radiation enhancement after whole-breast irradiation has no effect on long-term overall survival but improves local control and has the greatest absolute benefit in younger patients; it also increases the risk of moderate-to-severe fibrosis. For most patients aged over 60 years, additional radiation doses can be avoided [46]. There are also data suggesting that radiation therapy can be avoided in patients aged over 65 years and is an option for women aged 56–65 years who are lymph node-negative [47]. Kunkler *et al*. [48] conducted a randomized controlled trial and found that after BCS plus endocrine therapy, postoperative whole-breast radiotherapy reduced local recurrence in patients aged >65 years. However, they found that the recurrence rate of ipsilateral breast tumors within five years may be low, and some patients may not be considered for radiation therapy [48]. In 2008, some authors proposed the use of accelerated partial breast irradiation (APBI) with low or high dose brachytherapy to treat patients who had undergone BSC [49]. They found that the 5-year failure rates for breast, localized, and contralateral cancers were 6%, 0%, and 6%, respectively [49]. A systematic evaluation proposed APBI as a way of providing short-term radiation therapy for patients with early stage breast cancer, greatly avoiding the development of advanced radiation sickness in patients [50]. Through our analysis (Fig. 7) we found that radiation therapy after BSC is the MOTOR theme and there may be room for future development. There may be new radiotherapy modalities to improve the efficacy of post-operative radiotherapy in the future.

5. Limitations

First, publication time constraints caused delays in updating the citation counts of important articles. Second, despite the use of multiple search terms in database queries, a small percentage of manuscripts may have been missed. Third, a single WOS database was searched. However, these limitations did not affect our analysis of highly cited key studies regarding breast conservation.

In the future, more scholars should focus on BCS for oncoplastic surgery, and postoperative radiotherapy plans for different groups may be refined and differentiated [51–54].

6. Conclusions

This study highlights the top 100 most cited articles in the field of BCS, for which a comprehensive bibliometric analysis was performed including number of publications per year, number of citations, authors, journals, countries, and research topics. Fifty-nine of the 100 articles were from the United States, with some collaboration between the authors and institutions in other countries. Surgical margin, recurrence, distant metastases, radiation therapy are the hot topics in these 100 articles. Modification of postoperative radiation may appearances in the future. Despite the inherent limitations of bibliometric studies based on citation counts, the results of this review provide breast surgeons with research highlights and hot spots in the field of BCS and predict the future.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

YL—Writing original draft; PFL—Validation; PMF—Investigation; XCC—Methodology; PFL and YL—Software; PFL—Supervision; PFL and XCC—Project administration; YL, PFL and XCC—Review & editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.ejgo.net/files/article/1779754949881544704/attachment/Supplementary%20material.docx.

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