Research Paper

A global bibliometric and visualized analysis of the status and trends of bone metastasis in breast cancer research from 2002 to 2021

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HIGHLIGHTS

- Study examines global breast cancer bone metastasis research trends, highlighting leading contributors like the US and key journal.
- 7381 articles reviewed, revealing rising annual publications. US leads in citations and H-index; "Macrophage" and "skeletal related event" to trend.
- First systematic bibliometric assessment of breast cancer bone metastasis publications. Reveals current status, research focus, top researchers/institutions.
- Valuable resource for researchers to choose topics and directions. Enhances understanding of field's landscape and emerging trends.
- Unveils global bone metastasis of breast cancer research landscape, aiding academics in topic selection and confirming research path.

ARTICLE INFO

ABSTRACT

Bone metastasis of breast cancer considerably reduces not only overall survival but also health-related quality of life due to pain, fatigue, and skeletal-related events. Objective: This study aims to analyze the research hotspots and trends of global research on bone metastasis of breast cancer in the past 20 years to provide a reference for relevant personnel in this field to carry out academic research. Methods: The literature related to bone metastasis of breast cancer from 2002 to 2021 was retrieved from the Web of Science. The bibliometric research method and VOSviewer and CiteSpace were used to analyze the publications, and the research status and development direction in the last 20 years were visualized. Results: A total of 7381 articles were included. The number of global publications is increasing every year. The United States contributes the most to global research, with the most citations and the highest H-index. The journal *Cancer Research* published the most articles on this issue. "Macrophage" and "skeletal related event" will receive more attention and be the next popular hotspot in the future. Conclusion: There will be an increasing number of publications on bone metastasis of breast cancer based on current global trends. The United States made the largest contribution to this field. More focus will be placed on the mechanisms of metastasis research, which may be the next popular topic in bone metastasis of breast cancer.

1. Introduction

Breast cancer is the most common malignant tumor among women worldwide and the leading cause of cancer-related death [1]. Bone is the most common site of metastasis in patients with breast cancer, and up to 75% of patients with stage IV breast cancer have bone metastasis [2–4]. Bone metastases considerably reduce not only overall survival but also health-related quality of life due to pain, fatigue, and skeletal-related events [5–6]. To date, the clinical management of bone metastatic breast cancer includes systemic antitumor therapy and bone-targeted drugs designed to slow bone resorption and reduce the risk of bone-related events. However, their reliability and impact on patients' frailty remain a subject of debate [7–9]. This may be due to the lack of a complete understanding of the interaction between breast cancer circulating cells, the tumor microenvironment, muscle tissue and the bone microenvironment [10–14]. Due to the high mortality rate and the
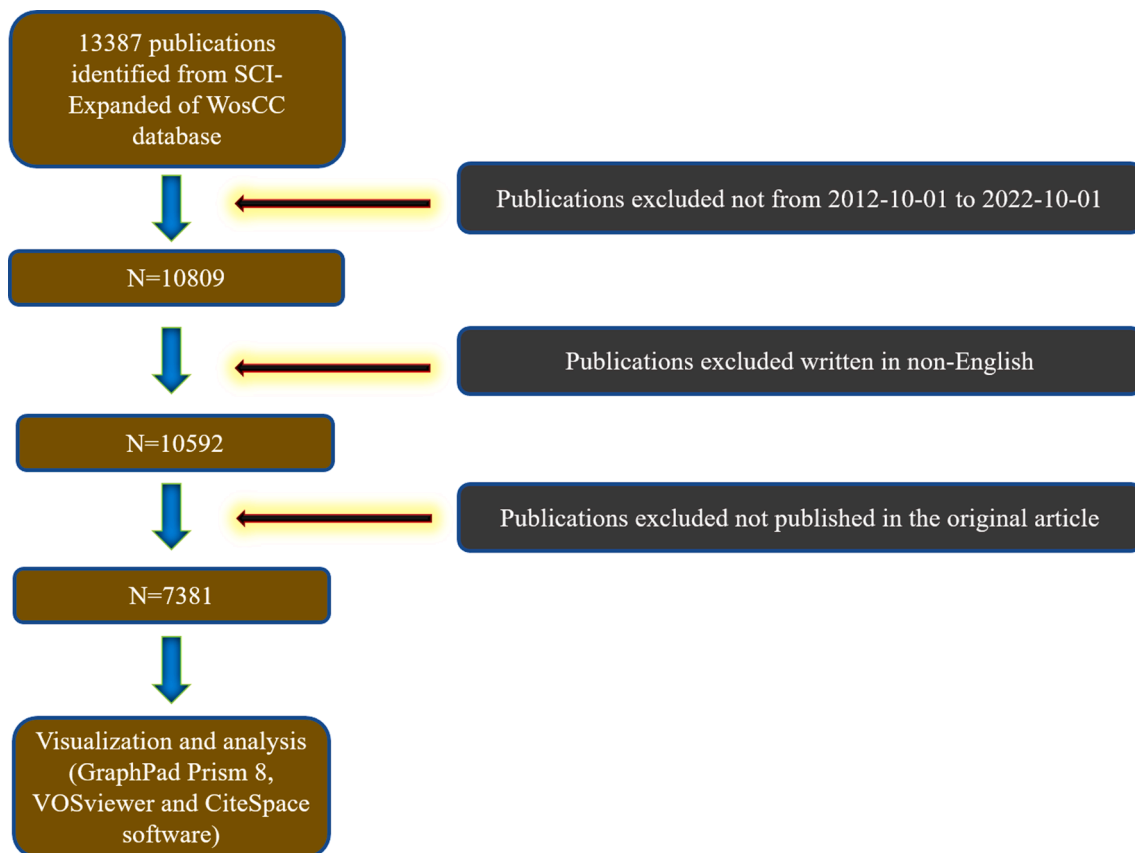
Fig. 1. Flowchart depicting the article selection process.

corresponding social pressure, it is necessary to have a deeper understanding of the development of bone metastasis in breast cancer. It contributes to researchers' investigation and macroscopic grasp of the etiology and clinical treatment.

In scientific research, publishing is a vital index to measure the contribution of scientific research. Bibliometric analysis can offer information based on bibliometric databases and bibliometric characteristics, which can be chosen to qualitatively and quantitatively analyze the trend of research activities over a period of time [15]. Bibliometric analysis is also performed to formulate policy and clinical practice guidelines [16]. It has been successfully used to analyze the research trends of arthritis [17], diabetes [18] and thyroid cancer [19]. However, to the best of our knowledge, the quantity and quality of bone metastasis in breast cancer research have not been reported. Hence, the purpose of this study is to evaluate the current landscape and future trends in the field of bone metastasis of breast cancer by bibliometric analysis.

2. Materials and methods

2.1. Ethics statement

This study was based on published papers and did not involve human or animal experiments. Therefore, this research did not require ethical approval.

2.2. Data source

Publication information is retrieved from the SCI-Expanded Web of Science (WoS), which is considered the optimal database for bibliometrics [20].

2.3. Search strategy

All published papers were collected from WoS, and the expiration date of the database was set to 31 December 2021. In this study, the search terms were as follows: theme = neoplasm of the breast OR breast neoplasm OR carcinoma breast OR carcinoma of the breast OR breast cancer OR cancer of the breast OR breast cancer AND theme = bone metastasis OR metastatic carcinoma of bone OR metastatic tumor of bone OR metastatic cancer of bone AND publishing year = (2002.01.01–2021.12.31) AND Language = (English) AND Document types = (Article). Additionally, detailed information on certain countries or regions was refined by indexing countries/regions in the WoS.

2.4. Data collection

The inclusion criteria of publication were as follows: (1) The manuscript focused on the theme of bone metastasis of breast cancer; (2) The document types were article and review. (3) The papers must be written in English. The exclusion criteria were as follows: (1) The themes were not related to bone metastasis of breast cancer; (2) Articles were briefings, news, meeting abstracts, etc. All the records of publications, including year of publication, title, author names, affiliations, countries/regions, abstract, keywords, and name of publishing journals, were downloaded and saved as.txt files from the SCI-Expanded database and then imported into Excel 2019. Finally, GraphPad Prism 8.0 and Origin 2021 were chosen to analyze the data. Any problem that emerged in the present study has been solved by consulting experts.

2.5. Bibliometric analysis

The intrinsic function of WoS was to characterize the basic features of eligible publications. In addition, total publications of each year

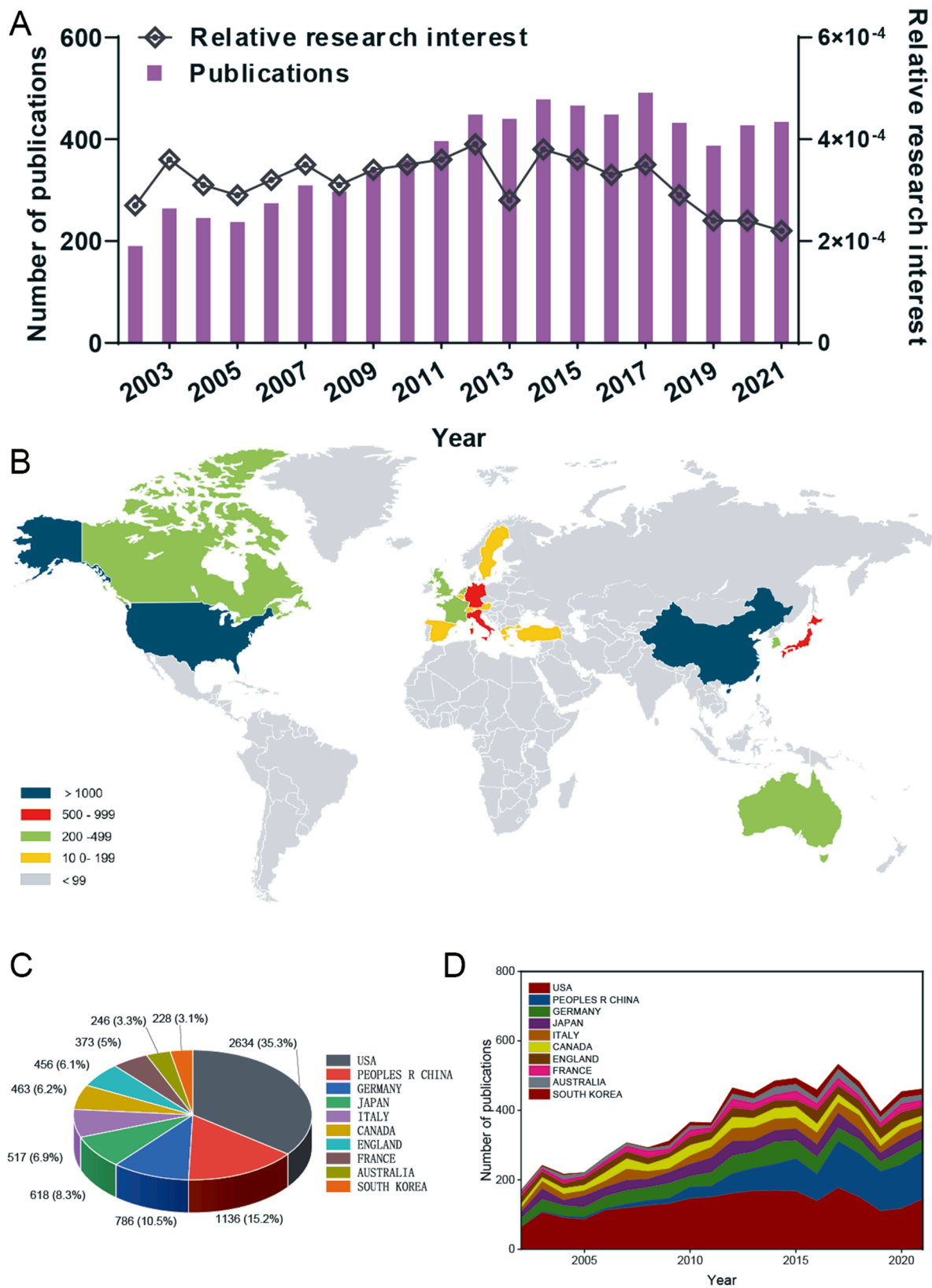**Fig. 2.** Global trends and countries/regions contributing to the research field regarding bone metastasis of breast cancer from 2002 to 2021. (A) The annual number of publications related to bone metastasis of breast cancer. (B) A world map depicting the distribution of bone metastasis of breast cancer. The total number (C) and annual number (D) of publications in the top 10 most productive countries from 2002 to 2021.

Table 1

The top 10 productive countries/regions related to bone metastasis of breast cancer.

Rank	Country/region	Article counts	Percentage (n = 7381)
1	USA	2634	35.69
2	Peoples R China	1136	15.39
3	Germany	786	10.65
4	Japan	618	8.37
5	Italy	517	7.01
6	Canada	463	6.27
7	England	456	6.18
8	France	373	5.05
9	Australia	246	3.33
10	South Korea	228	3.09

acquired from SCI-Expanded were first pictured by GraphPad Prism 8.0, and the relative research interest (RRI) was defined as the number of publications in one certain field by all field publications per year. The world map was generated by R software including python + numpy + scipy + matplotlib, and the time curve of publications was depicted according to a previous article [21]. The data of publications from the top 25 countries/regions were analyzed by GraphPad Prism 8.0. In addition, the total citations, average citations and H-index level were also evaluated by GraphPad Prism 8.0. The H-index, indicating that a scholar has published H papers and they have been cited at least H times, was created to measure the impact of scientific research. Hence, it reflects both the number of publications and corresponding citations [22]. Finally, high-contribution journals, institutions, funds and authors of global publications about bone metastasis of breast cancer were also analyzed by Origin 2021.

2.6. Visualized analysis

VOSviewer (Leiden University, The Netherlands) is a powerful software tool for mapping and visualizing bibliometric networks and thus was used for visualization in the present study. These networks include journals, authors, countries and individual publications, and they can be constructed based on bibliographic couplings, cocitations, coauthorship relationships and cooccurrence of keywords. CiteSpace (6.1. R2) was used to detect burst cited journals/authors, references, and keywords for forecasting the possible hotspots and research frontiers in the future.

3. Results

3.1. Overall performance of global literature

According to the search criteria, a total of 10,809 publications were collected from 2002 to 2021. Second, 10,592 publications were identified, excluding non-English articles. Finally, 7381 original articles were identified (Fig. 1). As shown in Fig. 2A, the trend of global literature experienced a steady increase almost year by year. The number of total global studies rose from 191 (2002) to 435 (2021). In the past decade, the year most studies (492) were published was 2017 (Fig. 2A). In addition, the relative interest in this field has declined over the past few years (Fig. 2A).

Generally, 90 countries/regions have made contributions to the literature in this field according to VOSviewer. As shown in Fig. 2B-D, the USA published the most papers (2634), followed by China (1136), Germany (786), Japan (618) and Italy (517). It is shown in Fig. 2C and Table 1 that the United States proceeds much more in the number of publications of the top 10 countries/regions, accounting for 35.3% of the total number of publications.

From a temporal perspective, there was a slight decline in the annual number of publications in all countries during 2017–2019, which has increased in the past two years (Fig. 2D). Overall, research on bone metastasis of breast cancer has attracted increasing attention from
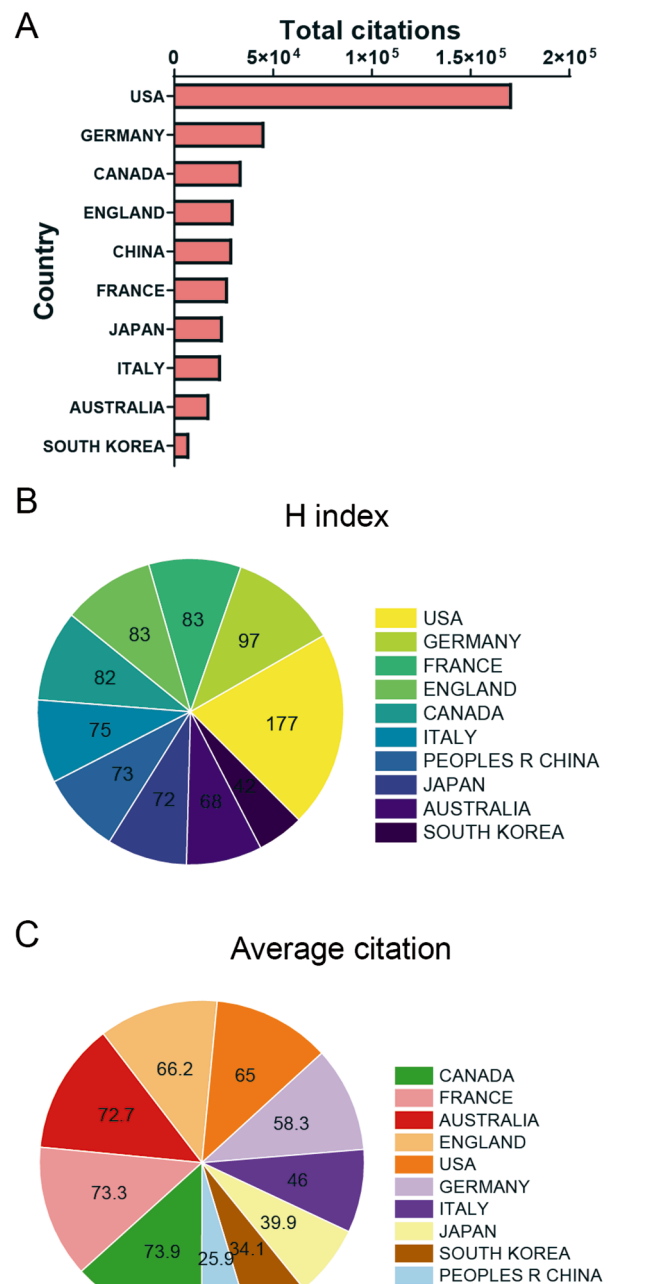

Fig. 3. (A) The top 10 countries/regions of total citations related to bone metastasis of breast cancer. (B) The top 10 countries/regions of the publication H-index related to bone metastasis of breast cancer. (C) The top 10 countries/regions of the average citations per publication related to bone metastasis of breast cancer.

researchers and has reached a stage of rapid development.

3.2. Analysis of countries

As shown in Fig. 3A, publications from the USA had the highest total citation frequencies (170588). Germany ranked second in total citation frequencies (45723), followed by Canada (34124), England (30154) and China (29451). Additionally, the USA (177) dominated in this field in the relative publications of the H-index, followed by Germany (97), France (83), England (83) and Canada (82) (Fig. 3B). Interestingly, in terms of average citation frequency, publications from Canada had the
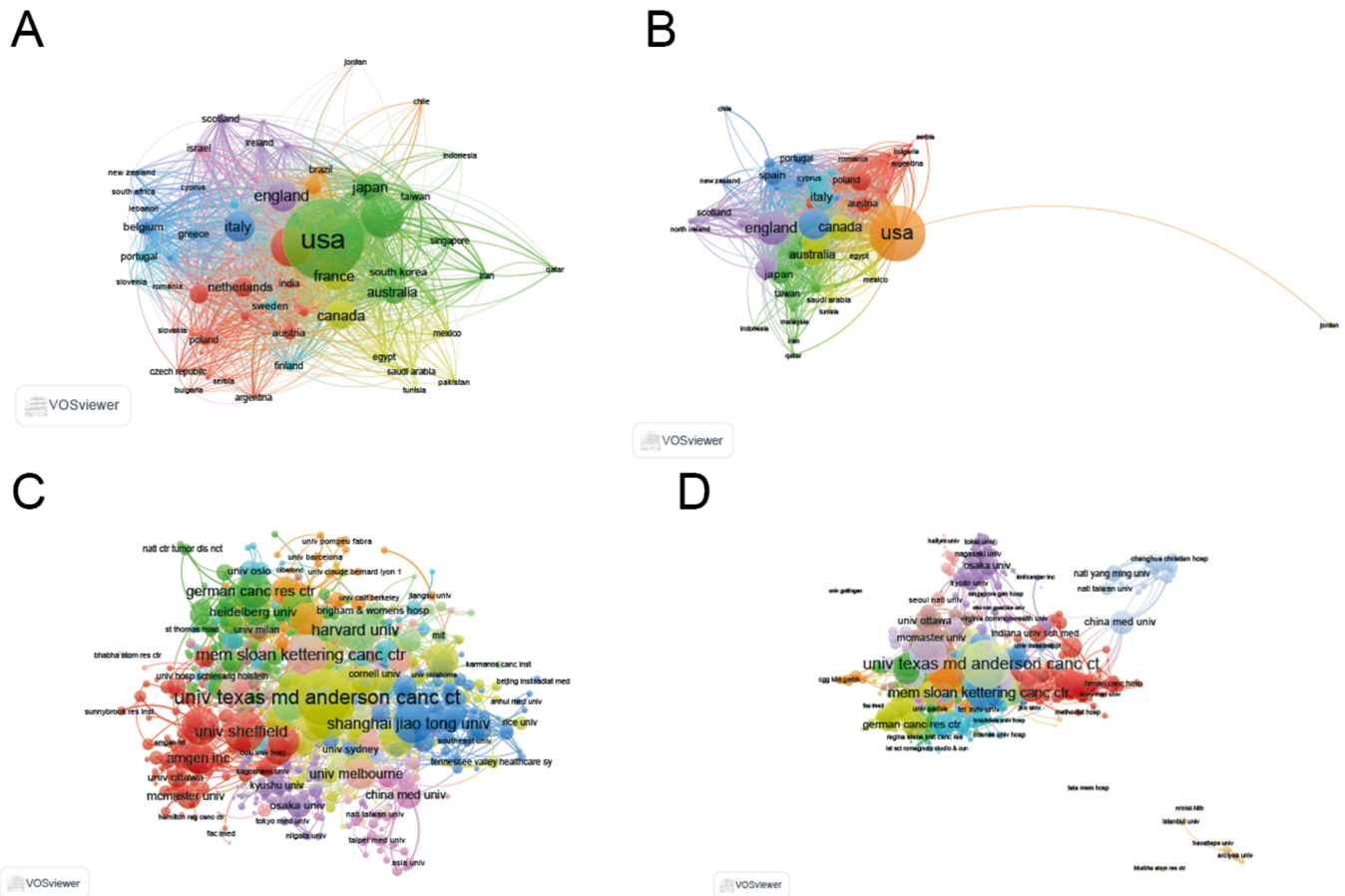
Fig. 4. Mapping of countries/regions and institutions associated with bone metastasis of breast cancer. (A) Country/regional collaboration analysis based on Vosviewer. (B) The authorship-country collaboration analysis via Vosviewer. (C) Institutional collaboration analysis based on Vosviewer. (D) The authorship-institution collaboration analysis via Vosviewer. The nodes represent countries/regions or institutions, and the lines connect them. The number of publications grows proportionally to the size of the nodes. The lines between the nodes represent the cooperation relationship, and the thickness of the connecting lines represents the strength of their cooperation; the closer the cooperation, the thicker the connecting lines.

Table 2
The top 10 institutions published literature related to bone metastasis of breast cancer.

Rank	Institution	Article counts	percentage (n = 7381)	H-index	Total citations	Average citation
1	University of Texas System	318	4.31	76	26,533	83.44
2	Utmd Anderson Cancer Center	218	2.95	65	16,738	76.78
3	Udice French Research Universities	210	2.85	66	18,905	90.02
4	Harvard University	201	2.72	68	18,897	94.01
5	University of California System	174	2.36	56	14,642	84.15
6	Institut National De La Sante Et De La Recherche Medicale Inserm	168	2.28	59	11,729	69.82
7	University of Toronto	162	2.20	44	11,262	69.52
8	Pennsylvania Commonwealth System of Higher Education Pcshe	160	2.17	56	10,676	66.73
9	Unicancer	157	2.13	55	14,967	95.33
10	University of Hamburg	148	2.01	53	14,836	100.24

highest average citation frequencies (73.9). France ranked second in average citation frequency (73.3) prior to Australia (72.7), England (66.2) and the USA (65) (Fig. 3C).

3.3. Analysis of country/region and institution collaboration

Regarding the global collaboration network analysis, the collaboration of the 31 countries is visualized in Fig. 4A-B. Fig. 4A-B shows that the USA (link strength 1761), England (link strength 828) and Germany (link strength 761) have the most frequent international collaborations. In addition, the majority of international partners of the USA are Australia and Canada.

Regarding institutions, the top 10 contributing institutions are listed in Table 2, and the collaboration of the institutions is visualized in Fig. 4C-D. Based on Vosviewer in Fig. 4C-D and Table 2, the most frequent international collaborating institution is The University of Texas MD Anderson Cancer Center (link strength 373), followed by Mem Sloan Kettering Cancer Center (link strength 252) and Amgen Inc. (link strength 251).

3.4. Analysis of research areas and journals

A list of research orientations is summarized in Table 3. In detail, the most prevalent research fields are Oncology, Cell Biology, Radiology

Table 3
The top 10 well-represented research areas.

Rank	Research Areas	Records	Percentage (n = 7381)
1	Oncology	3943	53.43
2	Cell Biology	694	9.40
3	Radiology Nuclear Medicine Medical Imaging	527	7.14
4	Biochemistry Molecular Biology	516	6.99
5	Science Technology Other Topics	434	5.88
6	Research Experimental Medicine	410	5.56
7	Pharmacology Pharmacy	380	5.15
8	Surgery	297	4.02
9	Endocrinology Metabolism	265	3.59
10	General Internal Medicine	221	3.00

Nuclear Medicine Medical Imaging and Biochemistry Molecular Biology. The main research orientation points out the current research focus and potential.

Table 4 lists the top 10 productive journals involved in this study. In addition, a dual-map overlay of journals was used to analyze the association of subject categories between citing and cited journals. The spline wave from left to right describes the citation path, and this interaction illustrates the linkage of different research areas. Four critical citation paths marked in orange and green indicate that papers published in journals in the area of Molecular/Health usually cited papers published in Molecular/Medicine journals (Figure 5A). The journal *Cancer Research* published the most, with 193 publications. There were 176 publications in *Breast Cancer Research and Treatment*, 161 publications in *PLOS One*, 154 publications in *Clinical Cancer Research* and 137 articles in *Clinical Experimental Metastasis*. Bibliographic coupling was used to analyze the similarity relationship between documents (Figure 5B). There are 294 identified journals that appeared in total link strength, which are shown in Figure. 5B. The top 3 journals with larger total link strength were as follows: *Cancer Research* (total link strength = 12305), *Journal of Clinical Oncology* (total link strength = 11456) and *Clinical Cancer Research* (total link strength = 6989 times). Concerning the analysis of journals of cocitation using VOSviewer, the journal with a minimum number of citations over 20 was defined. As plotted in Figure 5C, journals are shown in the total link strength. The top 3 journals with larger total link strength were as follows: *Cancer Research* (total link strength = 12305.6), *Journal of Clinical Oncology* (total link strength = 11457.6) and *Clinical Cancer Research* (total link strength = 6989.36), as shown in Table 5. Journals with intense citation bursts in a short period can act as a sensitive indicator to reflect journals in which important results are published. In Figure 5D, a clear transition of cited journals with time from 2002 to 2022 has been displayed, predicting a possible transfer of academic centers. According to Fig. 5D, it seems that during 2002-2022, burst cited journals transfer from *Journal of the National Cancer Institute* to *Nature Reviews Clinical Oncology* and then to *Sarcoma*.

3.5. Analysis of authors

In general, a total of 823 authors in this field that have more than 5 articles are considered and calculated by VOSviewer and CiteSpace. Table 6 lists the top 10 most productive authors involved in this study. Based on VOSviewer (Figure 6A), the visualization of author collaboration shows that there exist some collaboration circles of researchers, the central authors of which are Pantel K, Clezardin P and Clemons M. Coauthorship analysis was performed to evaluate the item relatedness based on the total number of coauthored publications. A total of 823 authors with over 5 publications were analyzed using VOSviewer, and the results are shown in Figure. 6B. The top 3 authors with larger total link strength were as follows: Pantel K (total link strength = 187), Ibrahim T (total link strength = 122) and Lipton A (total link strength = 115). Concerning the analysis of author cocitation using VOSviewer, the

author with a minimum number of citations over 20 was defined. As plotted in Figure 6C and Table 7, authors are shown in the total link strength. The top 3 authors with larger total link strength were as follows: Coleman, Re (total link strength = 2132.49), Mundy, Gr (total link strength = 881.46) and Braun, S (total link strength = 854.1). In Figure 6D, a clear transition of cited authors with time from 2002 to 2022 is displayed. It seems that during 2002-2022, burst cited author transfer from Hillner BE to Therasse P and then to Shiozawa Y.

3.6. Analysis of references and funds

The top 5 most cited documents are shown in Table 8. There were 2653 citations for "Tumor exosome integrins determine organotropic metastasis", followed by "Mesenchymal stem cells within tumor stroma promote breast cancer metastasis", with 2370 citations. The third-ranked article with the largest number of citations was "A multigenic program mediating breast cancer metastasis to bone", with 1909 citations. Moreover, to show the most influential literature, cocited references were analyzed by VOSviewer (Fig. 7A). The references with a minimum number of citations over 20 were defined. The top 3 references with larger total link strength were as follows: *Mundy JR, 2002, Nat Rev Cancer, v2, p584* (total link strength = 594), *Kang YB, 2003, Cancer Cell, v3, p537* (total link strength = 480) and *Roodman GD, 2004, New Engl J Med*, v305 (total link strength = 394).

In addition, citation burst is a valuable indicator that reflects the references of interest to researchers in a particular domain in a period. In our study, the top 25 references with the strongest citation bursts were identified by CiteSpace and are presented in Fig. 7B, which shows the citation burst for the duration of references. The article published by Stopeck An in 2010 maintains the strongest citation burst with a strength of 48.57, lasting from 2011 to 2015.

A list of the funds for bone metastasis of breast cancer is summarized in Table 9. The United States Department of Health Human Services supports the most articles with 1344 articles, followed by the National Institutes of Health Nih Usa with 1337 articles and the Nih National Cancer Institute Nci with 1041 articles. Interestingly, the first three funds that support most articles are funds from the USA, which is consistent with previous analyses of countries.

3.7. Keyword and hotspot analysis

The objective of co-occurrence analysis is to investigate popular directions and areas of research, and it also plays a vital role in monitoring developments in scientific research. Keywords, which were defined as words used more than 20 times in titles/abstracts in all papers, were chosen and analyzed via VOSviewer. As shown in Fig. 8A, the 606 identified keywords were roughly classified into 4 clusters. In the center of the co-occurrence map, the keywords, including expression, survival, therapy, zoledronic acid and prostate cancer, were shown more prominently with higher weight. Thus, further high-quality studies on bone metastasis of breast cancer in these directions are still needed. Additionally, keywords were coded with different colors by VOSviewer based on average times they appeared in all the published papers (Fig. 8B). The color in purple meant that the keywords appeared earlier, whereas the color in yellow indicated a later appearance.

By clustering the cocited documents, insight into the topology of documents was provided. Therefore, we performed cocitation analysis of bone metastasis of breast cancer to explore its historical developments and scientific landscapes. As a result, 10 main clusters were generated and labeled by phrase extracted from the abstracts (Fig. 8C).

Keyword with intense bursts in a short period can act as a sensitive indicator to reflect the research focus. Recent burst keywords provide researchers with possible research frontiers in the short term. A keyword burst map was generated by CiteSpace where the strength and the beginning or ending year of the burst are shown (Fig. 8D). The strength reveals the burst intensity and the burst year indicates the
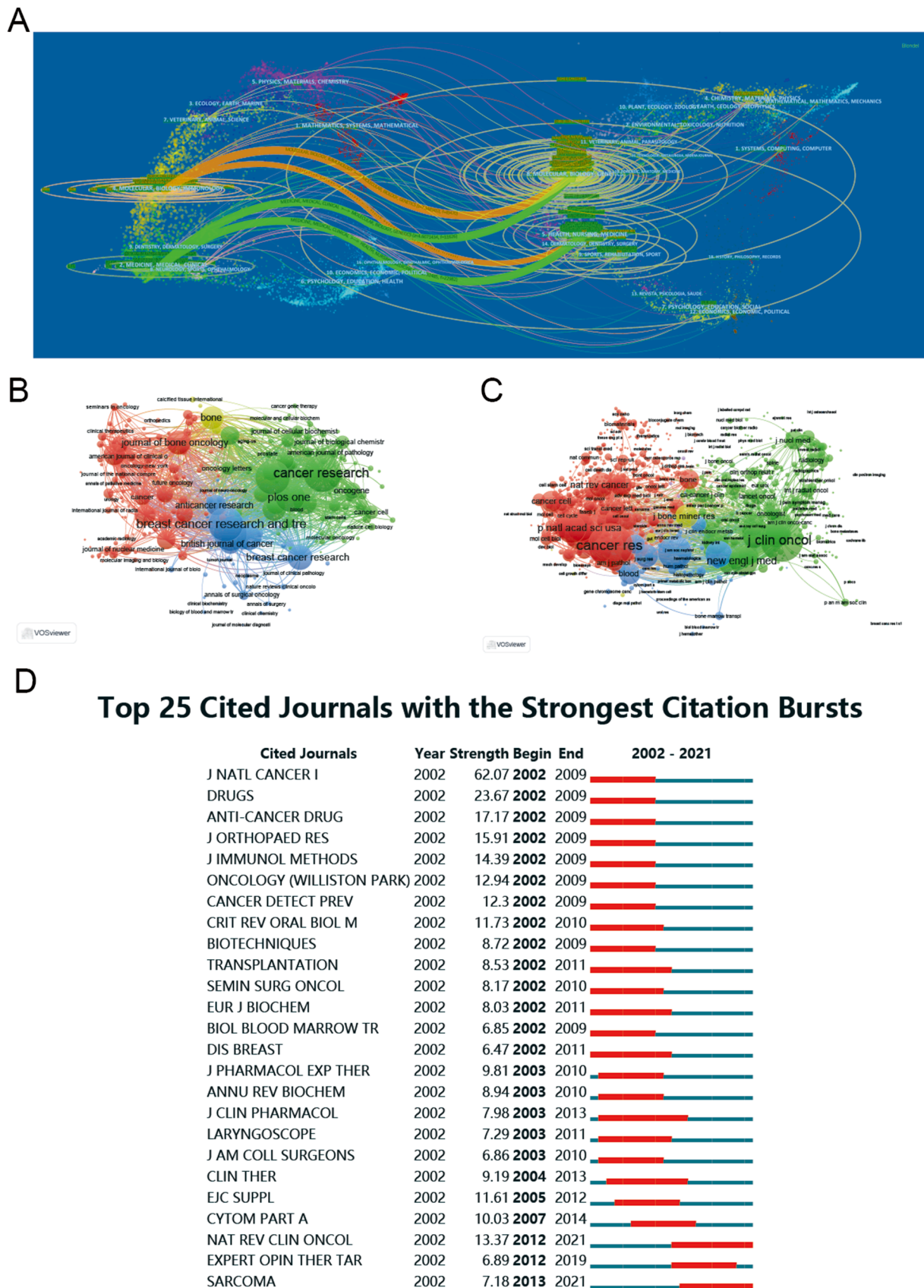
Fig. 5. Articles published in different journals on bone metastasis of breast cancer. (A) The dual-map overlay of journals related to bone metastasis of breast cancer. (B) Bibliographic coupling analysis of journals based on Vosviewer. (C) Network map of journals that were cocited in more than 50 citations based on Vosviewer. (D) Top 25 cited journals with the strongest citation bursts of publications related to bone metastasis of breast cancer. Lines in red represent the burst detection years. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Top 25 Cited Authors with the Strongest Citation Bursts

Cited Authors	Year	Strength	Begin	End	2002 – 2021
HILLNER B	2002	35.55	2002	2010	
FLEISCH H	2002	28.74	2002	2009	
ROGERS M	2002	25.05	2002	2009	
SENARATNE S	2002	24.97	2002	2010	
POWLES T	2002	22.76	2002	2010	
FISHER B	2002	21.5	2002	2009	
ARGUELLO F	2002	20.5	2002	2010	
GREEN J	2002	20.3	2002	2009	
SHIPMAN C	2002	20.19	2002	2010	
CONTE P	2002	19.48	2002	2009	
MAJOR P	2002	19.43	2002	2009	
HIRAGA T	2002	14.74	2002	2009	
MORONY S	2002	13.76	2002	2010	
SAARTO T	2002	13.67	2002	2010	
CLOHISY D	2002	13.45	2002	2009	
KAKONEN S	2002	17.38	2003	2011	
PAVLAKIS N	2002	22.48	2004	2011	
THERASSE P	2002	14.57	2006	2014	
NEVILLE-WEBBE H	2002	13.98	2006	2013	
MENG S	2002	17.33	2007	2014	
FEHM T	2002	21.31	2008	2015	
KARNOUB A	2002	17.78	2010	2017	
STOPECK A	2002	18.64	2011	2021	
WEILBAECHER K	2002	33.54	2013	2021	
SHIOZAWA Y	2002	19.51	2013	2021	

Fig. 6. Visualization of author analysis regarding bone metastasis of breast cancer. (A) Bibliographic coupling analysis of authors by Vosviewer. (B) Network visualization diagram of authorship-author analysis based on Vosviewer. (C) Author cocitation analyzed by Vosviewer. (D) Top 25 cited authors with the strongest citation bursts of publications related to bone metastasis of breast cancer. Authors are indicated by the node. The collaboration relationship is indicated by the line connecting the nodes. The node area grows as the number of collaborations increases. Author cocitations are indicated by the node. The cocitation relationship is indicated by the line connecting the nodes. The node area grows as the number of cocitations increases. Lines in red represent the burst detection years. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
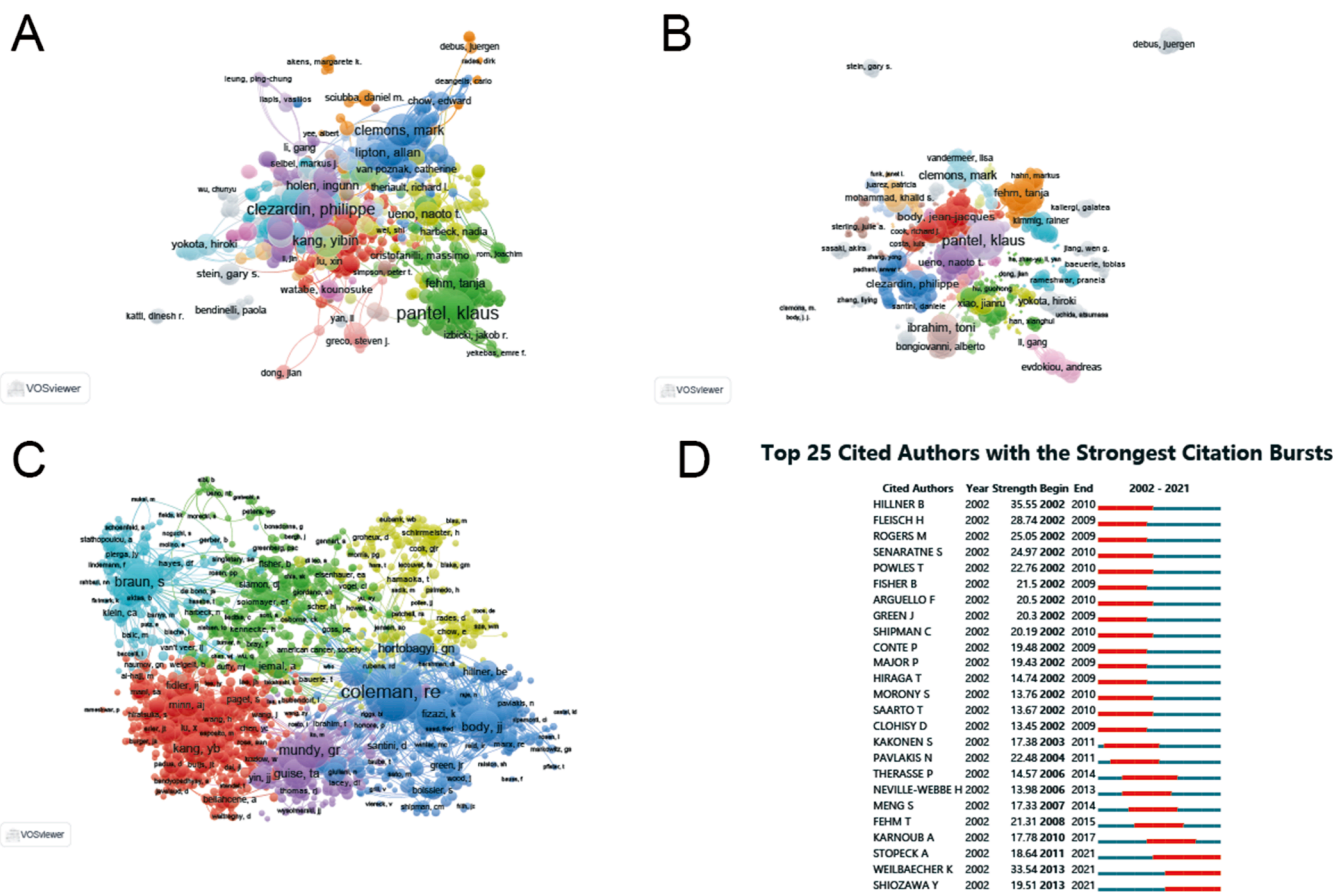
transformation of the research focus and its duration. The most intense keyword was polymerase chain reaction (strength = 35.65) followed by skeletal complication (26.52) and bone marrow transplantation (22.74). The keyword with the longest burst time was nitrogen-containing bisphosphonate which lasted 11 years from 2002 to 2013. More meaningfully the keywords "macrophage" and "skeletal-related event" had outbreak citations most recently (2013–2021) which implied that macrophage- and skeletal-related events will be research hotspots in the future.

In addition, the time dynamic evolution of keyword clusters is presented in Fig. 7E. In total, 10 clusters were identified, namely, expression, bone scintigraphy, zoledronic acid, bone marrow, metastatic breast cancer, estrogen receptor, T cell, breast carcinoma, cell coculture and ATF3. The year of appearance for ATF3 was most recent, 2020.

4. Discussion

Bibliometrics and visual analysis can reveal the current situation in the search field and make predictions [21]. Therefore, the purpose of this research is to evaluate bone metastasis of breast cancer in the field of open access from the aspects of authors, donor countries, journal, institutions and research focus. Over the past 20 years, the progress of bone metastasis of breast cancer has become an exciting and steadily developing research field [23–24].

4.1. Trends in bone metastasis of breast cancer research

As shown in this study, there has been a steady increase in the number of publications published each year from 2002 to 2021 despite a slight decrease in 2019. This could be attributed to the global epidemic of COVID-19 [25]. Therefore, in the past few years, related research interest has declined. Based on the present data, we believe that more in-depth bone metastasis studies of breast cancer will be published in the coming years. The current optimistic results will also allow researchers to conduct further high-quality studies.

4.2. The quality and standing of global publications

The total citations and H-index represent the academic influence and publishing quality of one county [26]. As shown in Fig. 2C, D and Fig. 3, based on the total number of published papers, the total number of citations and the H-index, the USA makes the largest contribution to global research, and it is arguably the leader in this area. Interestingly, Canada ranked first in terms of average citations, followed by France and Australia. Regarding the top 10 total publications, it can be argued that France, ranking eighth in the number of publications, is still making significant progress in this field. Considering that China ranked the second largest number of total publications, it showed a weaker performance in average citations, ranking only tenth, which means a low acceptance in the global academic research field of bone metastasis of breast cancer. The contradiction between the quantity and quality of
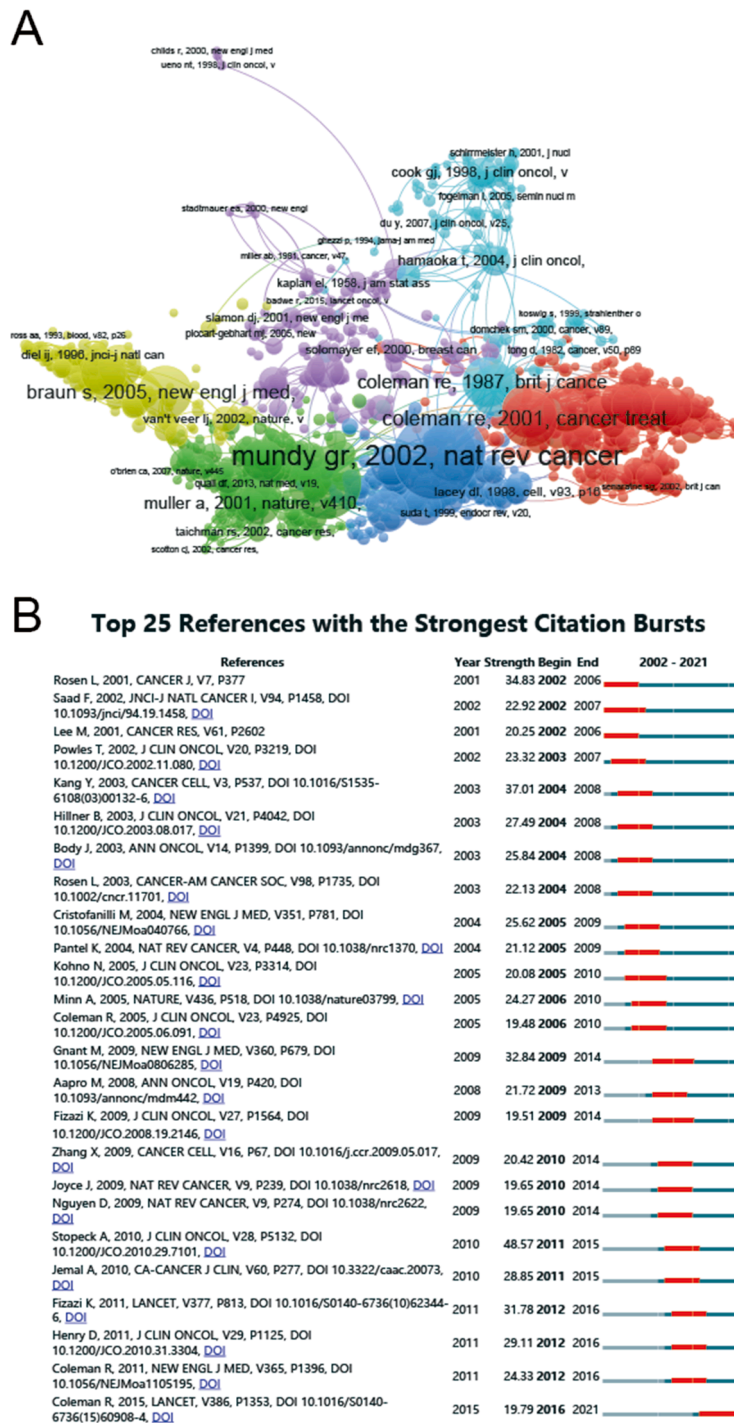
Fig. 7. Mapping of references in studies on bone metastasis of breast cancer. (A) Network map of publishing document analysis based on Vosviewer. (B) Top 25 references with the strongest citation bursts of publications related to bone metastasis of breast cancer.

publications in China also indicates that China requires more in-depth studies.

In this study, a similar relationship among countries, institutions, journals and authors is established by bibliographic coupling analysis. Bibliographic coupling is defined as two works citing a common third work in their bibliography. These data show that the USA is the most relevant country, while the University of Texas MD Anderson Cancer Center is the leading institution in this field (Fig. 4A, C). Coauthorship analysis was used to assess collaboration among countries, institutions and authors. The one with greater total link strength suggested that the

country/institution/author would be more likely to cooperate with others. The top 2 research institutes with the largest number of articles are the leading organizations in bone metastasis of breast cancer research, which is consistent with the leadership of the USA in global publications.

In addition, the top 10 research orientations are composed of oncology, cell biology, radiology nuclear medicine medical imaging and surgery, which means it is a multidisciplinary field of deep intersection. More research on bone metastasis of breast cancer has been published in *Cancer Research*, *Breast Cancer Research and Treatment* and *PLOS One*
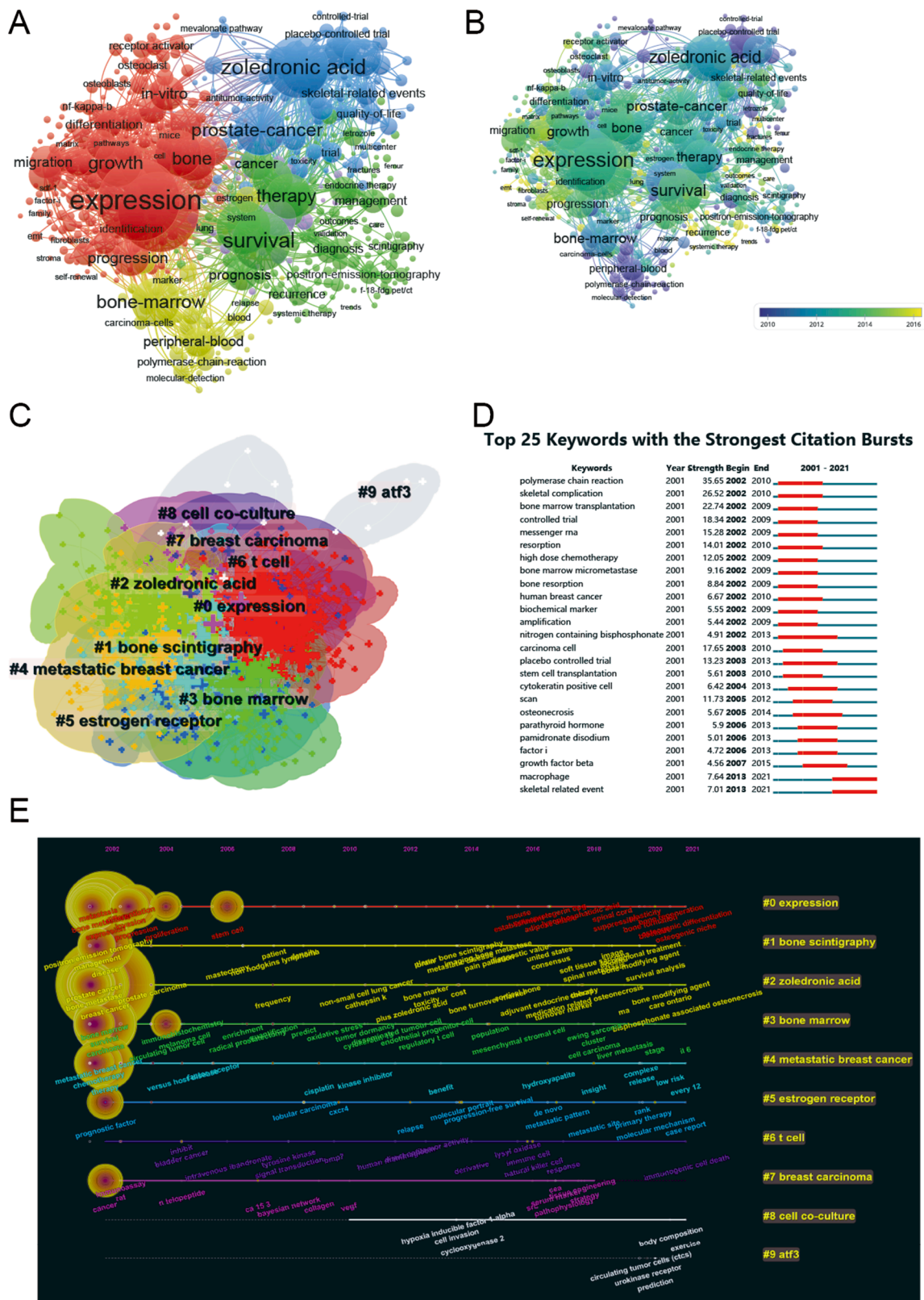
Fig. 8. Mapping of keywords in studies on bone metastasis of breast cancer. (A) Co-occurrence visualization of keywords based on Vosviewer. (B) Distribution of keywords according to the mean frequency of appearance; keywords in yellow appeared later than those in blue. (C) Keyword clustering visualization from 2012 to 2022 based on CiteSpace. (D) Top 25 keywords with the strongest citation bursts of publications related to bone metastasis of breast cancer based on CiteSpace. (E) Keyword timeline visualization from 2002 to 2021 based on CiteSpace. In the timeline view, the keywords on the same horizontal line belong to the right cluster. The colors of lines and keywords in the view correspond to the colors of the time slice at the top. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 4
The top 10 productive journals related to bone metastasis of breast cancer.

Rank	Journal	Article counts	Percentage (n = 7381)
1	Cancer Research	193	2.62
2	Breast Cancer Research and Treatment	176	2.39
3	Plos One	161	2.18
4	Clinical Cancer Research	154	2.09
5	Clinical Experimental Metastasis	137	1.86
6	Oncotarget	123	1.67
7	Anticancer Research	122	1.65
8	Bmc Cancer	120	1.63
7	International Journal of Cancer	92	1.25
10	Breast Cancer Research	90	1.22

Table 5
The top 10 cocited journals related to bone metastasis of breast cancer.

Rank	Journal	Total citations	total link strength	IF
1	Cancer Res	13,409	12305.6	13.312
2	J Clin Oncol	13,216	11457.6	50.717
3	Clin Cancer Res	7389	6989.36	13.801
4	New Engl J Med	5455	5204.38	176.079
5	Nature	5260	5013.76	69.504
6	P Natl Acad Sci Usa	5067	4884.31	12.779
7	J Biol Chem	5029	4687.7	5.486
8	Brit J Cancer	4484	4343.19	9.075
9	Breast Cancer Res Tr	4115	3959.85	4.624
10	Nat Rev Cancer	4048	3926.41	69.800

Table 6
The top 10 authors with the most publications on bone metastasis of breast cancer.

Rank	High Published Authors	Article counts	Percentage (n = 7381)
1	Pantel K	81	1.10
2	Clemons M	61	0.83
3	Clezardin P	55	0.75
4	Lipton A	55	0.75
5	Zhang Y	51	0.69
6	Body JJ	50	0.68
7	Coleman RE	50	0.68
8	Zhang J	45	0.61
9	Wang Y	43	0.58
10	Liu J	41	0.56

Table 7
The top 10 cocited authors on bone metastasis of breast cancer.

Rank	High Cocited Authors	Total Citations	Total Link Strength
1	Coleman, Re	2248	2132.49
2	Mundy, Gr	894	881.46
3	Braun, S	914	854.1
4	Lipton, A	866	834.85
5	Body, Jj	789	727.02
6	Rosen, Ls	704	670.25
7	Pantel, K	695	655.86
8	Kang, Yb	650	641.77
9	Guise, Ta	620	602.76
10	Hortobagyi, Gn	610	595.65

Table 8
The top 5 publications with the most citations in the field of bone metastasis of breast cancer.

Rank	Title	Journal	IF	Publication year	Total citations
1	Tumor exosome integrins determine organotropic metastasis	Nature	69.504	2015	2653
2	Mesenchymal stem cells within tumor stroma promote breast cancer metastasis	Nature	69.504	2007	2370
3	A multigenic program mediating breast cancer metastasis to bone	Cancer Cell	38.585	2003	1909
4	Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer	Journal of Clinical Oncology	50.739	2008	1898
5	Tumor cells circulate in the peripheral blood of all major carcinomas but not in healthy subjects or patients with nonmalignant diseases	Clinical Cancer Research	13.801	2004	1856

Table 9
The top 10 funds related to bone metastasis of breast cancer.

Rank	Journal	Article counts	Percentage (n = 7381)
1	United States Department of Health Human Services	1344	18.21
2	National Institutes of Health Nih Usa	1337	18.12
3	Nih National Cancer Institute Nci	1041	14.11
4	National Natural Science Foundation of China Nsfc	481	6.52
5	European Commission	263	3.56
6	United States Department of Defense	205	2.78
7	Ministry of Education Culture Sports Science and Technology Japan Mext	139	1.88
8	German Research Foundation Dfg	124	1.68
7	Nih National Institute of Arthritis Musculoskeletal Skin Diseases Niams	123	1.67
10	Amgen	117	1.59

with 13,409 citations. Moreover, the strongest citation bursts of publications indicated that *Nature Reviews Clinical Oncology* and *Sarcoma* published authoritative research results in the past ten years.

Regarding authors, the top-ranked authors listed in Table 6 with the most publications were relatively earlier entrants and might have been given prior attention to obtaining new advancements in bone metastasis of breast cancer. Additionally, the collaboration analysis in Fig. 6B shows that the research relationship among authors in different countries is relatively scattered, indicating a lack of academic connection and communication among authors. Therefore, authors in different countries and institutions may strengthen their cooperation in this field jointly. For cocitation frequency, as shown in Fig. 6C and Table 7, Coleman, Re, Mundy, Gr and Braun, S might be the top authors with the highest cocitation frequency, which represents the international attention and recognition of these researchers in this field. Moreover, the strongest citation bursts of authors indicated that Hillner B published authoritative research results in 2002, and the works of Stopeck A,

(Table 4). Meanwhile, the related journals only occupy a limited percentage, and articles are relatively scattered in different journals without aggregations. The journals in the list are likely to be the main publishing channels for future discoveries in this area. Further research in this area may appear at the top of the list. Furthermore, cocitation analysis based on journals was conducted to investigate the impacts of publications by analyzing the total number of citations. Fig. 5C and Table 5 show that *Cancer Res* made the best contributions in this field,

Weilbaecher K and Shiozawa Y have gained more attention in recent years.

The impact of published literature was evaluated in the citation analysis of documents (Fig. 7A) and the citation bursts of publications analysis (Fig. 7B). Table 8 shows that the most cited article is "Tumor exosome integrins determine organotropic metastasis" [27], which may be the beacon light for bone metastasis of breast cancer research. Another study reported that mesenchymal stem cells within the tumor stroma promote breast cancer metastasis [28]. Among the top five most cited articles, most types of literature are of the basic research type, focusing on cancer metastasis mechanisms and clinical therapy.

Notably, cocitation and citation burst analysis of references can determine which publications have made the best contributions in this field. As shown in Fig. 7A, "Metastasis to bone: causes, consequences and therapeutic opportunities" [29]' authored by Gregory R Mundy, is the top reference with the highest cocitation strength. In Fig. 7B, the top 25 references with the strongest citation bursts showed the ladder depth of the findings in this research field.

4.3. The research focus and future trends of bone metastasis of breast cancer

The analysis of keywords can indirectly reveal various key research topics and characteristics in the research field. On the basis of co-occurrence analysis, we found the development direction and hot topic in this field. All the keywords of the publications were analyzed to create a map of the co-occurrence network. Four research directions can be observed from the co-occurrence map (Fig. 8A). Although this result is consistent with common sense in this field, this study can clarify future research directions. At the center of the cooccurrence map, as is shown obviously, keywords including "expression", "zoledronic acid", "survival" and "prostate-cancer", etc., have a greater weight. The overlay visualization map was assigned colors by VOSviewer based on the average number of times the keywords appeared in the papers. This method is of great significance to the research direction of monitoring. In the overlay visualization shown in Fig. 8B, the color represents the year of publication. Combined with document cocitation analysis with cluster timeline visualization (Fig. 8C, E), we detected that the earliest research clusters of bone metastasis of breast cancer were "expression", "zoledronic acid" and "bone marrow", followed by "breast carcinoma". Moreover, in recent years, research on "cell coculture" and "ATF3" has gradually increased and may attract much attention in the future.

Burst keywords reveal the research hotspots and their transformation from surgery to mechanisms of metastasis. In particular, burst keywords that continue to the present indicate the potential trends and possible frontiers in the field of bone metastasis of breast cancer (Fig. 8D). The latest burst keywords include "macrophage" and "skeletal related event". Therefore, studies on these aspects might indicate the frontier of the research field.

4.4. Strengths and limitations

The publications derived from SCI-expanded WoS were explored in the present study to acquire reliable and objective results. Bibliometric and visualized analyses were achieved by a variety of software (including Prism 8, Origin 2021, VOSviewer and CiteSpace), and we evaluated the status and trends of studies on corneal tissue engineering reliably and objectively. However, several limitations still exist in our study. It is well known that publications from different databases, such as WoS, PubMed, Embase and the Cochrane Library, are varied. Therefore, we may have missed some publications due to database bias. In addition, due to the limitation of the search strategy in English from the SCI-expanded database, non-English language literature could have been omitted, leading to language bias. Owing to the constant updates of the target database, slight differences may exist in the real world and the present results. Finally, there is no uniform standard for parameter

settings in the VOS viewer; thus, the outputs of cluster analysis may differ slightly under different settings.

5. Conclusion

This study showed the global status and trends in bone metastasis of breast cancer. The USA was the largest contributor to studies and had the leading position in global research in this field. The journal *Cancer Research* attracted the most publications related to this area. We predicted that more research about bone metastasis of breast cancer will be published in the coming years. An overall analysis of this field from the perspective of "cell coculture" and "ATF3" might be the latest research directions. In particular, "macrophages" and "skeleton-related events" might receive more attention and be the next popular hotspot in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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