Review Article

The 100 most cited papers on bone metastasis: A bibliometric analysis

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Abstract

Background: Over the past few decades, a vast number of articles focused on bone metastasis have been published. Bibliometric analysis is helpful to determine the qualities and characteristics and to reveal the influential articles in this field.

Methods: All the databases in Web of Science were utilized to identify articles published from 1961 to 2020. The top 100 most cited articles on bone metastases were involved for degree centrality analysis and analyses on publication time and citations, journals, authors, geographical distribution, research institutions, and research keywords.

Results: The selected articles were published mainly from 1986 to 2015. The 100 most cited articles were selected from a total of 67,451 citations out of 90,502 publications with a density of 50.239 citations/year. Citations per article ranged from 357 to 2167. The leading country was USA, followed by Canada and United Kingdom. The most frequently studied themes were clinical management of bone metastasis from different malignancy origins. A co-authorship analysis revealed an intense collaborative activity between countries and institutions.

Conclusions: This study identified the top 100 most cited articles on bone metastasis. Publication time, area, and theme distribution were thoroughly analyzed. The present study highlighted some of the most influential contributions to the field. Clinical and academic communities have shown a sustained interest in the management of bone metastasis.

1. Introduction

Bone metastasis is a result of the complex interactions between tumor cells and bone cells. It is common in the advanced cancer, such as breast and prostate, with high clinical relevance [1,2]. According to the diagnosis time for bone metastasis, it is divided into synchronous bone metastasis and unsynchronous bone metastasis. For patients diagnosed with synchronous bone metastasis, cardiovascular and cerebrovascular diseases were the leading non-cancer cause of death, followed by COPD, septicemia, infectious and parasitic diseases, etc [3]. In this analysis, bone metastasis is a general concept without detailed distinction. Skeletal-related events (SREs), including bone pain, hypercalcemia, bone fracture, and spinal cord compression, are common complications of bone metastasis, all of these can significantly impact a patient’s life quality [4,5].

In the research field of cancer, metastatic process is a complex process, requiring adequate dissemination and homing. The concept of metastatic niche has been gradually developing and accepting. Upon arrival, primary cancer cells established interactions with various bone-resident cells during the process of colonization. Preparation of niche...
**Table 1**

List of the 100 most-cited articles.

| Rank | No. | Title of the article | Journal | Year | Citation No. | Citation/Year |
|------|-----|----------------------|---------|------|--------------|---------------|
| 1    | 10  | Tumour exosome integrins determine organotropic metastasis | NATURE | 2015 | 2167 | 433.4 |
| 2    | 11  | Metastasis to bone: Causes, consequences and therapeutic opportunities | NATURE REVIEWS CANCER | 2002 | 2023 | 112.4 |
| 3    | 12  | A multigenic program mediating breast cancer metastasis to bone | CANCER CELL | 2003 | 1884 | 110.8 |
| 4    | 13  | Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer | NEW ENGLAND JOURNAL OF MEDICINE | 2013 | 1849 | 264.1 |
| 5    | 14  | Endogenous human microRNAs that suppress breast cancer metastasis | NATURE | 2008 | 1585 | 132.1 |
| 6    | 15  | Mechanisms of disease: Mechanisms of bone metastasis | NEW ENGLAND JOURNAL OF MEDICINE | 2004 | 1552 | 97.0 |
| 7    | 16  | Osteonecrosis of the jaws associated with the use of bisphosphonates: A review of 63 cases | JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY | 2004 | 1367 | 85.4 |
| 8    | 17  | Clinical features of metastatic bone disease and risk of skeletal morbidity | CLINICAL CANCER RESEARCH | 2006 | 1340 | 95.7 |
| 9    | 18  | Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial | LANCET | 2011 | 1252 | 139.1 |
| 10   | 19  | Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study | J.N.I.-JOURNAL OF THE NATIONAL CANCER INSTITUTE | 2002 | 1208 | 67.1 |
| 11   | 20  | Metastatic bone disease: clinical features, pathophysiology and treatment strategies | CANCER TREATMENT REVIEWS | 2001 | 1204 | 63.4 |
| 12   | 21  | Metastatic Behavior of Breast Cancer Subtypes | JOURNAL OF CLINICAL ONCOLOGY | 2010 | 1178 | 117.8 |
| 13   | 22  | Skeletal complications of malignancy | CANCER | 1997 | 1129 | 49.1 |
| 14   | 23  | Bisphosphonate-associated osteonecrosis of the jaw: Report of a task force of the American Society for Bone and Mineral Research | JOURNAL OF BONE AND MINERAL RESEARCH | 2007 | 1122 | 86.3 |
| 15   | 24  | Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study | JOURNAL OF CLINICAL ONCOLOGY | 2010 | 969 | 96.9 |
| 16   | 25  | Surgical strategy for spinal metastases | SPINE | 2001 | 870 | 45.8 |
| 17   | 26  | Use of the stromal cell-derived factor-1/CXCR4 pathway in prostate cancer metastasis to bone | CANCER RESEARCH | 2002 | 844 | 46.9 |
| 18   | 27  | BISPHOSPHONATES PROMOTE APOPTOSIS IN MURINE OSTEOCLASTS IN VITRO AND IN VIVO | JOURNAL OF BONE AND MINERAL RESEARCH | 1995 | 821 | 32.8 |
| 19   | 28  | THE CLINICAL COURSE OF BONE METASTASES FROM BREAST-CANCER | BRITISH JOURNAL OF CANCER | 1987 | 818 | 24.8 |
| 20   | 29  | Osteonecrosis of the jaw in cancer after treatment with bisphosphonates: Incidence and risk factors | JOURNAL OF CLINICAL ONCOLOGY | 2005 | 808 | 53.9 |
| 21   | 30  | RANKL-RANK signaling in osteoestrogenesis and bone disease | TRENDS IN MOLECULAR MEDICINE | 2006 | 805 | 57.5 |
| 22   | 31  | Efficacy of pamidronate in reducing skeletal complications in patients with breast cancer and lytic bone metastases | NEW ENGLAND JOURNAL OF MEDICINE | 1996 | 782 | 52.6 |
| 23   | 32  | Percutaneous vertebroplasty for osteolytic metastases and myeloma: Effects of the percentage of lesion filling and the leakage of methyl methacrylate at clinical follow-up | RADIOLOGY | 1996 | 759 | 31.6 |
| 24   | 33  | TGF-beta signaling blockade inhibits PTHrP secretion by breast cancer cells and bone metastases development | JOURNAL OF CLINICAL INVESTIGATION | 1999 | 755 | 36.0 |
| 25   | 34  | Percutaneous vertebroplasty with polymethylmethacrylate - Technique, indications, and results | RADIOLOGIC CLINICS OF NORTH AMERICA | 1998 | 752 | 34.2 |
| 26   | 35  | American society of clinical oncology 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer | JOURNAL OF CLINICAL ONCOLOGY | 2003 | 729 | 42.9 |
| 27   | 36  | Randomized, Double-Blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma | JOURNAL OF CLINICAL ONCOLOGY | 2011 | 717 | 79.7 |
| 28   | 37  | Cancer to bone: a fatal attraction | JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION | 2011 | 709 | 78.8 |
| 29   | 38  | Clinical implications of the osteoprotegerin/RANKL/RANK system for bone and vascular diseases | JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY | 2004 | 708 | 44.3 |
| 30   | 39  | Bisphosphonates: The first 40 years | BONE | 2011 | 707 | 78.6 |
| 31   | 40  | Percutaneous vertebroplasty for pain relief and spinal stabilization | SPINE | 2000 | 698 | 34.9 |
| 32   | 41  | Bisphosphonates: From the laboratory to the clinic and back again | BONE | 1999 | 695 | 33.1 |
| 33   | 42  | Identification of a population of blood circulating tumor cells from breast cancer patients that initiates metastasis in a xenograft assay | NATURE BIOTECHNOLOGY | 2013 | 674 | 96.3 |
| 34   | 43  | Zoledronic acid versus pamidronate in the treatment of skeletal metastases in patients with breast cancer or osteolytic lesions of multiple myeloma: A phase III, double-blind, comparative trial | CANCER JOURNAL | 2001 | 664 | 34.9 |
| 35   | 44  | Long-term efficacy and safety of zoledronic acid compared with pamidronate disodium in the treatment of skeletal complications in patients with advanced multiple myeloma or breast carcinoma - A randomized, double-blind, multicenter, comparative trial | CANCER | 2003 | 649 | 38.2 |
| 36   | 45  | Reduction in new metastases in breast cancer with adjuvant clodronate treatment | NEW ENGLAND JOURNAL OF MEDICINE | 1998 | 625 | 28.4 |
| 37   | 46  | Evidence for a causal role of parathyroid hormone-related protein in the pathogenesis of human breast cancer-mediated osteolysis | JOURNAL OF CLINICAL INVESTIGATION | 1996 | 616 | 25.7 |
| 38   | 47  | Malignant bone pain: Pathophysiology and treatment | PAIN | 1997 | 600 | 26.1 |
| 39   | 48  | Spinal metastases: Indications for and results of percutaneous injection of acrylic surgical cement | RADIOLOGY | 1996 | 594 | 24.8 |
| 40   | 49  | Common variants on chromosomes 2q35 and 16q12 confer susceptibility to estrogen receptor-positive breast cancer | NATURE GENETICS | 2007 | 592 | 45.5 |
| 41   | 50  | Regulation of cancer cell migration and bone metastasis by RANKL | NATURE | 2006 | 581 | 41.5 |

(continued on next page)
### Table 1 (continued)

| Rank | Title of the article                                                                 | Journal                                           | Year | Citation No. | Citation/Year |
|------|--------------------------------------------------------------------------------------|---------------------------------------------------|------|--------------|---------------|
| 43   | The detection of bone metastases in patients with high-risk prostate cancer: Tc-99m-MDP planar bone scintigraphy, single- and multi-field-of-view SPECT, F-18-fluoride PET, and F-18-fluoride PET/CT [60] | JOURNAL OF NUCLEAR MEDICINE                       | 2006 | 575          | 41.1          |
| 44   | Palliative radiotherapy trials for bone metastases: A systematic review [61]          | JOURNAL OF CLINICAL ONCOLOGY                      | 2007 | 574          | 44.2          |
| 45   | Receptor activator of nuclear factor kappa B ligand and osteoprotegerin regulation of bone remodeling in health and disease [62] | ENDOCRINE REVIEWS                                 | 2008 | 565          | 47.1          |
| 46   | PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE [23] | INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY PHYSICS | 2011 | 544          | 60.4          |
| 47   | A module map showing conditional activity of expression modules in cancer [63]         | NATURE GENETICS                                   | 2004 | 540          | 33.8          |
| 48   | Zoledronic acid versus placebo in the treatment of skeletal metastases in patients with lung cancer and other solid tumors: A phase III, double-blind, randomized trial - The zoledronic acid lung cancer and other solid tumors study group [14] | JOURNAL OF CLINICAL ONCOLOGY                      | 2003 | 522          | 30.7          |
| 49   | Pamidronate to prevent bone loss during androgen-deprivation therapy for prostate cancer [64] | NEW ENGLAND JOURNAL OF MEDICINE                  | 2001 | 520          | 27.4          |
| 50   | Bisphosphonates inhibit breast and prostate carcinoma cell invasion, an early event in the formation of bone metastases [65] | CANCER RESEARCH                                  | 2000 | 517          | 25.9          |
| 51   | The seed and soil hypothesis revisited-The role of tumor-stroma interactions in metastasis to different organs [66] | INTERNATIONAL JOURNAL OF CANCER                  | 2011 | 512          | 56.9          |
| 52   | IDENTIFICATION OF ENDOTHELIN-1 IN THE PATHOPHYSIOLOGY OF METASTATIC THYROID-CARCINOMA OF THE PROSTATE [67] | NATURE MEDICINE                                  | 1995 | 508          | 20.3          |
| 53   | Randomized trial of short-versus long-course radiotherapy for palliation of painful bone metastases [68] | JNCI JOURNAL OF THE NATIONAL CANCER INSTITUTE     | 2005 | 505          | 33.7          |
| 54   | Pamidronate prevents skeletal complications and is effective palliative treatment in women with breast carcinoma and osteolytic bone metastases - Long term follow-up of two randomized, placebo-controlled trials [69] | CANCER                                           | 2000 | 505          | 25.3          |
| 55   | STRATIFICATION OF PATIENTS WITH METASTATIC PROSTATE-CANCER BASED ON EXTENT OF DISEASE ON INITIAL BONE-SCAN [70] | CANCER                                           | 1988 | 502          | 15.7          |
| 56   | Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients [71] | JOURNAL OF NEUROSURGERY                          | 2003 | 498          | 29.3          |
| 57   | Latent Bone Metastasis in Breast Cancer Tied to Src-Dependent Survival Signals [72] | CANCER CELL                                      | 2009 | 491          | 44.6          |
| 58   | Radiosurgery for spinal metastases - Clinical experience in 500 cases from a single institution [73] | SPINE                                            | 2007 | 486          | 37.4          |
| 59   | Denosumab and bone-metastasis-free survival in men with castration-resistant prostate cancer: results of a phase 3, randomized, placebo-controlled trial [74] | LANCET                                           | 2012 | 482          | 60.3          |
| 60   | Long-term efficacy and safety of zolendronic acid in the treatment of skeletal metastases in patients with nonsmall cell lung carcinoma and other solid tumors - A randomized, phase III, double-blind, placebo-controlled trial [75] | CANCER                                           | 2004 | 479          | 29.9          |
| 61   | Bisphosphonate inhibits angiogenesis in vitro and testosterone-stimulated vascular regrowth in the ventral prostate in castrated rats [77] | JOURNAL OF UROLOGY                               | 2003 | 470          | 27.6          |
| 62   | Bisphosphonates inhibit angiogenesis in vitro and testosterone-stimulated vascular regrowth in the ventral prostate in castrated rats [77] | CANCER Research                                  | 2002 | 468          | 26.0          |
| 63   | Long-term prevention of skeletal complications of metastatic breast cancer with pamidronate [78] | JOURNAL OF CLINICAL ONCOLOGY                     | 1998 | 468          | 21.3          |
| 64   | A Novel Classification System for Spinal Instability in Neoplastic Disease An Evidence-Based Approach and Expert Consensus From the Spine Oncology Study Group [24] | SPINE                                            | 2010 | 466          | 46.6          |
| 65   | Pamidronate reduces skeletal morbidity in women with advanced breast cancer and lytic bone lesions: A randomized, placebo-controlled trial [79] | JOURNAL OF CLINICAL ONCOLOGY                     | 1999 | 464          | 22.1          |
| 66   | SCORING SYSTEM FOR THE PREOPERATIVE EVALUATION OF METASTATIC SPINE TUMOR PROGNOSIS [80] | CANCER                                           | 1990 | 461          | 15.4          |
| 67   | Human prostate cancer metastases target the hematopoietic stem cell niche to establish footholds in mouse bone marrow [81] | JOURNAL OF CLINICAL INVESTIGATION                | 2011 | 458          | 50.9          |
| 68   | Frequency and risk factors associated with osteonecrosis of the jaw in cancer patients treated with intravenous bisphosphonates [82] | JOURNAL OF BONE AND MINERAL RESEARCH             | 2008 | 452          | 37.7          |
| 69   | Mechanisms of bone metastasis [83]                                                  | CANCER                                           | 1997 | 451          | 19.6          |
| 70   | DOUBLE-BIND CONTROLLED TRIAL OF ORAL CLORDONATE IN PATIENTS WITH BONE METASTASES FROM BREAST-CANCER [84] | JOURNAL OF CLINICAL ONCOLOGY                     | 1993 | 448          | 16.6          |
| 71   | The effect of a single fraction compared to multiple fractions on painful bone metastases: a global analysis of the Dutch Bone Metastasis Study [85] | RADIOTHERAPY AND ONCOLOGY                        | 1999 | 440          | 21.0          |
| 72   | RESULTS OF A RANDOMIZED PHASE-III TRIAL TO EVALUATE THE EFFICACY OF SR-99 ADJUVANT TO LOCAL FIELD EXTERNAL BEAM IRRADIATION IN THE MANAGEMENT OF ENDOCRINE RESISTANT METASTATIC PROSTATE-CANCER [86] | INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY PHYSICS | 1993 | 430          | 15.9          |
| 73   | Percutaneous vertebroplasty: State of the art [87]                                   | RADIOGRAPHICS                                    | 1998 | 428          | 19.5          |
| 74   | LONG-TERM RESULTS OF TREATMENT OF 283 PATIENTS WITH LUNG AND BONE METASTASES FROM DIFFERENTIATED THYROID-CARCINOMA [88] | JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM   | 1986 | 428          | 12.6          |
| 75   | Breast cancer cells interact with osteoblasts to support osteoclast formation [89] | ENDOCRINOLOGY                                    | 1999 | 427          | 20.3          |
| 76   | WNT/TCF Signaling through LEF1 and HOXB9 Mediates Lung Adenocarcinoma Metastasis [90] | CELL                                             | 2009 | 425          | 38.6          |
| 77   | Bone turnover markers as predictors of skeletal complications in prostate cancer, lung cancer, and other solid tumors [91] | JNCI JOURNAL OF THE NATIONAL CANCER INSTITUTE     | 2005 | 424          | 28.3          |
| 78   | Predictive value of bone resorption and formation markers in cancer patients with bone metastases receiving the bisphosphonate zoledronic acid [92] | JOURNAL OF CLINICAL ONCOLOGY                     | 2005 | 413          | 27.5          |
required the changes the constant cycle of bone matrix formation and degradation as the prerequisite, leading to the clinical phenotypes of lytic and sclerotic lesions. Meanwhile, the bone microenvironment may even influence primary cancer cells to subsequently metastasis, also known as secondary metastasis, which indicated intricate cancer-bone crosstalk [6].

Till now, bone metastasis has been remaining one of the trickiest clinical challenges that is closely related to a patient’s prognosis and life quality. A comprehensive understanding of the molecular mechanisms and clinical management advances in bone metastasis is crucial for providing optimal medical care. Further knowledge in this field is warrant to reveal the pathogenesis, characteristics, and clinical treatment landscape of bone metastasis. However, many open questions are remaining to be addressed to establish individually tailored management approaches.

Bibliometrics is a unique and useful tool for analyzing the quality and characteristics of published articles in a specific field. In 1987, the first bibliometrics analysis of classics from the Journal of the American Medical Association (JAMA) was first published. Recently, it has been widely used in various of different fields to investigate the most important publications or research trends [7]. The purpose of this study was to reveal the top 100 most cited publications in the field of bone metastasis, aiming to analyze the quality and characteristics and to highlight potential milestones as well as promising research direction of the most cited original papers of the past 6 decades.

2. Materials and Methods

Literature Search and Screening.

The literature search was systematically performed using the Web of Science (WOS) (Clarivate Analytics, USA) ‘All Databases’. To enhance the sensitivity, two reviewers (Li Huiyang and Li Shu.) independently identified the top 100 literatures used the same query terms (‘bone’ OR ‘skeletal’ OR ‘osseous’) AND (‘metastasis’ OR ‘metastases’ OR ‘metastatic’) without any literature type restrictions to search simultaneously. After filtering by language as “English”, 91,024 pieces of literature was listed. The selected articles were sorted in descending order according to the total citations (TC). Any disagreement between the 2 reviewers was resolved by consensus involving a third reviewer (Wu Haixiao). Finally, a unanimous decision was made on the list of the top 100 most-cited manuscripts.

2.1. Data extraction and bibliometric parameters

2.1.1. Data analyses and visualization

After identifying the top 100 most-cited articles, records including all
available information from the Web of Science all database, including article title, citation count, citation density, year of publication, authorship, contributing institution, journal of publication, and PMID, etc. From these data, parameters such as the number of times a particular author, institution or country published a T100 article and citation density were obtained. Citation density was calculated as the average number of citations per annum after the work was first published.

The “Visualization of Similarities (VOS) viewer software” is widely used to graphically illustrate the bibliometric parameters in mapping networks, which allow easy visualization of critical elements. The current study used VOS to represent a graphical mapping of keywords as

| Publishing Year | Number of Articles | Total Citations | Mean Citations |
|-----------------|-------------------|-----------------|----------------|
| 1986–1990       | 4                 | 2209            | 552.3          |
| 1991–1995       | 5                 | 2588            | 517.6          |
| 1996–2000       | 20                | 12,094          | 604.7          |
| 2001–2005       | 33                | 24,134          | 804.5          |
| 2006–2010       | 21                | 14,090          | 671.0          |
| 2011–2015       | 17                | 12,536          | 725.6          |

Fig. 1. Numbers of publications in top 100 by year of publication.

Fig. 2. Bubble plot of published year and citations on the top 100 cited articles. Note: X-axis: publication year; Y-axis: the total number of citations; bubble size: the average number of citations; colors: the number of articles.
identified bibliometric analysis to identify the focus of research in recent decades.

Visualization of Similarities (VOS) Viewer 1.6.17 (Leiden University, Leiden, Netherlands) is a software developed and widely used to graphically illustrate for building and visualizing bibliometric parameters in mapping networks. Here, we used it to visualize author collaborations, countries, and contributing institutions. “Full counting” was the counting method. In the visual map, different nodes represented authors, countries, institutions, and keywords. The node size represented the corresponding number or frequency of reference. The links between nodes represented cooperation and co-occurrence relationships. The colors of the nodes and lines represented different clusters or corresponding years or average references.

3. Results

3.1. Article analysis

A total of 90,502 articles were obtained in December 2020 as far back as January 1961. All articles were written in English. Of these, the top 100 articles according to their citation count were demarcated and were presented accordingly (Table 1). Table 2 showed the number of articles published in each 5-year interval. Less than five articles were published before 1990 for each interval, while more than 90 were published after 1995. The largest number of articles published in a single interval was 33, which occurred in 2001–2005. These included guidelines (2), recommendation (1), articles (51), reviews (21), systemic review or meta-analysis (2) and clinical trials (23).

When focus on the first 10 papers (T 10), we found that they brought a total of 16,309 citations, which represents 24.179% of the total citations. All publications included in the T 10 exceed 1200. These T 100 papers comprise a total of 67,451 citations, with a citation density of 50,239.

As noted in Fig. 1, the year that yielded the highest number of influential articles was 2005 (n = 9). Most included articles were published after 1995 (n = 91). Within the T100, the oldest work is from 1986 (#74) and the most recent which is also the most-cited work is from 2015 (#1). Fig. 2 showed the relationship of publication year (X-axis), the total number of citations (Y-axis), the average number of citations (bubble size), and the number of articles (different colors). In the data label, the former data are the Y value, and the latter is the value of the bubble size. The highest number of citations was in 2004 (n = 5439), and the lowest was in 1991 (n = 381). In terms of the average number of citations, the highest was 2,167 times in 2015 and the lowest was 381 times in 1991.

It is worth noting that the most cited article (2167 citations) was “Tumour exosome integrins determine organotropic metastasis,” by Hoshino et al., published in Nature in 2015. The article has received an average of 433.4 CY. The last in our list (357 citations) was “Update on the Systematic Review of Palliative Radiotherapy Trials for Bone Metastases,” by Chow et al., published in Clinical Oncology in 2012; it has received an average of 44.6 CY (Fig. 3).

These high-impact most-cited articles were published in 44 different scientific journals. When these articles were compared, Journal of Clinical Oncology was the one with the most publications (n = 17), followed by Cancer (n = 9). Only 3 Journals in this category belongs to Q3 (Quartile in Category) (Table 3).

For the T100 citations, we summarized the topics and classification of these citations roughly according to article type and specific details, including disease focus, basic or clinical medical research, review, etc. (shown in Table 4).

3.2. Countries or Regions, Institutions, and Authors

In analyzing countries (or regions) and institutions of the authors, the 100 most cited articles were originated from 16 countries or regions, led by USA (n = 53), followed by the United Kingdom (n = 10), Canada (n = 9), and so on. The distribution was illustrated on the world map (Fig. 4). The authors from USA contributed greater than 10 articles. Considering the continents, authors from North America (n = 62) published the most articles, followed by Europe (n = 31), Asia (n = 6) and Oceania (n = 1). None of them was published in Africa or South America.

The cooperation among different countries/regions, institutions, and authors is a critical driving force to promote the development of most successful large-scale trials. To this point, there seemed to be close cooperation among different institutions from various countries and regions, especially in North America (Figs. 5-6).

Moreover, authors were classified into greater than 10 clusters in the authors’ collaboration network analysis; several major research teams were identified, mainly including Seam, Lipton, Coleman, etc. (shown in Fig. 7).

4. Discussion

Metastasis is the single most catastrophic complication of human malignancy, while the great avidity for bone always causes painful and untreatable consequences. This bibliometric analysis thoroughly
suggested that the clinical community kept the interest focus in bone metastasis. Characteristics of published articles were explored based on specific and reliable parameters. In fact, there has been a relatively rare publications per year before 1995. After 1996, there has been a gradually increased papers involved in bone metastasis until 2015. Another indication of this interest is that all top 10 most cited articles were found to be with more than 1200 citations.

It is a fact that older papers had more chance to be cited [8], and even the most cited papers may had seldom citation after they were published [9]. Here, we presented a study providing a detailed bibliometric analysis of the top 100 most cited articles in bone metastasis, which may pave the way for further research. These articles were published between 1961 and 2020. Most articles focused on the medical management of different originated bone metastasis, including surgery, radiation therapy and drugs clinical trials mostly.

The top 1 most cited article was published in 2015, entitled *Tumour exosome integrins determine organotropic metastasis*, with 2197 citations [10]. This article provided insight into the possibility of targeting exosome integrins interventions, which may be candidates for blockade of organ-specific metastasis combination therapies. Deciphering the mystery of tumour organotropism apparently has drawn a lot of interest from scholarship worldwide, in the important role of tumour-derived exosomes in determining and mediating future organ-specific metastasis to form favourable niche processes. The top 2 most cited article was published in 2002, entitled *Metastasis to bone: Causes, consequences and therapeutic opportunities*, with 2023 citations [11]. This article provided a thorough overview of the specific cancer avidity for bone, the molecular mechanisms responsible for how they alter the skeletal system physiology, and new potential molecular targets for future drug development.

The top 3 most cited article was published in 2003, entitled *A multigenic program mediating breast cancer metastasis to bone*, with 1884 citations [12]. This article aimed to investigate the molecular basis for osteolytic bone metastasis by in vivo selection of highly metastatic breast expression signature in high metastatic cells cancer. Transcriptional profiles were compared of cells with different metastatic potentials in order to identify genes that differ functionally validation of genes overexpressed in these cells was also carried out. This article provided a conceptual framework and experimental evidence for a specific set of genes that mediated the breast cancer cells to metastases to bone. What’s more, from the most frequently occurring keywords analysis we can learn that the connection between “bone metastasis” with “breast cancer” and “bone metastasis” with “bisphosphonates” is deep and tight, and these topics have always been the focus of research.

Bisphosphonates are a class of pyrophosphate analogs with a high binding affinity to mineralized bone surfaces, moderating osteoblast-mediated bone production and osteoclast-mediated bone resorption. Typical examples of bisphosphonates are zoledronate, pamidronate, and so on. These bone-specific anti-resorptive agents are often chosen as first-line therapy for patients with diseases of bone loss, such as osteoporosis and cancers that cause osteolysis [11,13]. Clinical trials have made up a relatively important part of the T 100 list. We noticed that 11 clinical trial papers focus on zoledronic acid among the 23 papers reporting clinical trial findings. Among them, the most common topic is the long-term efficacy and safety of zoledronic acid for treating skeletal-related events in patients with bone metastases. Zoledronic acid, denosumab and pamidronate are the most common topic of these articles. Zoledronic acid is the first new-generation bisphosphonate with highly potent demonstrating efficacy in patients with bone metastases from solid tumors not only restricted to breast cancer, such as prostate cancer and non-small-cell lung cancers [14–16].

Denosumab is a human immunoglobulin G2 (IgG2) antibody, with a molecular weight of about 147,000 Da [17]. By targeted inhibiting the action of receptor activator of nuclear factor-kappaB ligand (RANKL), denosumab reduces the biofunction of osteoclasts, thereby moderating bone resorption and increasing bone mineral density, mirroring the action of endogenous osteoprotegerin [18,19]. Pamidronate is a bisphosphonate class of medication, which is a valuable agent in managing hypercalcemia of malignancy, osteolytic bone metastases of breast cancer, and osteoporosis [20]. Radium-223 (223Ra) is a bone-targeted alpha-emitter radionuclide which has been studied as a new treatment option for hormone-refractory prostate patients with bone metastases [21]. Comparative study between zolendronic acid and other drugs, including denosumab (3 papers) and pamidronate (1 paper). While, the efficacy of pamidronate (3 papers), radium-223 (2 papers), and pamidronate (2 papers) cover most of the remaining clinical trials’ findings. From the above articles, we can see that factors that may influence scientific interests include not only the

| Journal                                      | No. of articles | Citation count | Impact factor | Quartile in Category |
|----------------------------------------------|-----------------|----------------|---------------|----------------------|
| Journal of Clinical Oncology                 | 17              | 9619           | 44.544        | Q1                   |
| Cancer                                       | 9               | 4883           | 6.86          | Q1                   |
| New England Journal of Medicine              | 5               | 5328           | 91.245        | Q1                   |
| Spine                                        | 5               | 2981           | 3.468         | Q1/Q2                |
| International Journal of Radiation Oncology  | 4               | 1709           | 7.038         | Q1/Q1                |
| Physics                                      |                 |                |               |                      |
| Journal of Clinical Investigation            | 4               | 2208           | 14.808        | Q1                   |
| Cancer Cell                                  | 3               | 2757           | 31.743        | Q1/Q1                |
| Cancer Research                              | 3               | 1829           | 12.701        | Q1                   |
| Onco-journal of the National Cancer Institute| 3               | 2137           | 13.506        | Q1                   |
| Journal of Bone and Mineral Research         | 3               | 2395           | 6.741         | Q1                   |
| Lancet                                       | 3               | 3024           | 79.321        | Q1                   |
| Nature                                       | 3               | 4333           | 49.962        | Q1                   |
| Nature Reviews Cancer                        | 3               | 3138           | 60.716        | Q1                   |
| Bone                                         | 2               | 1402           | 4.398         | Q2                   |
| Clinical cancer research                     | 2               | 1704           | 12.531        | Q1                   |
| Nature Genetics                              | 2               | 1132           | 38.33         | Q1                   |
| Radiology                                    | 2               | 1353           | 11.105        | Q1                   |
| Annals of Oncology                           | 3               | 411            | 32.976        | Q1                   |
| Blood                                        | 1               | 361            | 22.114        | Q1                   |
| British Journal of Cancer                    | 1               | 818            | 7.64          | Q1                   |
| Cancer Journal                               | 1               | 664            | 3.36          | Q3                   |
| Cancer Treatment Reviews                     | 1               | 1204           | 12.111        | Q1                   |
| Cell                                         | 1               | 425            | 41.582        | Q1/Q1                |
| Clinical Oncology                            | 1               | 357            | 4.126         | Q3                   |
| Endocrine Reviews                            | 1               | 565            | 19.871        | Q1                   |
| Endocrinology                                | 1               | 427            | 4.736         | Q2                   |
| International Journal of Cancer              | 1               | 512            | 7.396         | Q1                   |
| Jama-journal of the American Medical Association | 1             | 708            | 56.722        | Q1                   |
| Journal of Clinical                          | 1               | 428            | 5.958         | Q1                   |
| Endocrinology & Metabolism                   |                 |                |               |                      |
| Journal of Neurosurgery                      | 1               | 498            | 5.115         | Q1/Q1                |
| Journal of Nuclear Medicine                  | 1               | 575            | 10.057        | Q1                   |
| Journal of Oral and                          | 1               | 1367           | 1.893         | Q1                   |
| Maxillofacial Surgery                        |                 |                |               |                      |
| Journal of Urology                           | 1               | 470            | 7.45          | Q1                   |
| Lancet Oncology                              | 1               | 361            | 41.316        | Q1                   |
| Nature Biotechnology                         | 1               | 674            | 54.908        | Q1                   |
| Nature Medicine                              | 1               | 506            | 53.44         | Q1/Q1                |
| Nature Reviews Drug Discovery                | 1               | 376            | 84.694        | Q1                   |
| Pain                                         | 1               | 600            | 6.961         | Q1                   |
| Proceedings of the National Academy of Sciences of the United States of America | 1 | 407 | 11.205 | Q1 | |
| Radiographics                                | 1               | 428            | 5.333         | Q1                   |
| Radiologic Clinics of North                  | 1               | 752            | 2.303         | Q3                   |
| America                                      |                 |                |               |                      |
| Radiology and Oncology                       | 1               | 440            | 6.28          | Q1/Q1                |
| Science Signaling                            | 1               | 378            | 8.192         | Q1/Q1                |
| Trends in Molecular Medicine                 | 1               | 805            | 11.951        | Q1/Q1                |

*Data from the 2020 edition of Journal Citation Reports.*
### Table 4
Rough summary of topics and classification of the TOP 100 citations.

| rank | type  | basic medical research | specific field | clinical medical research | biology of metastasis | disease focus | imaging | clinical trail | clinical guidelines | recoocomendation | consensus | review | meta-analysis | systemic review |
|------|-------|------------------------|----------------|---------------------------|----------------------|---------------|---------|----------------|---------------------|------------------|-----------|-------|---------------|-----------------|
| T1   | article ✓ | tumour exosome ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T2   | review | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T3   | article ✓ | osteonecrosis of the jaws ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T4   | clinical trail | alpha emitter radium-223 ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T5   | article ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T6   | review | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T7   | article ✓ | clinical features and risk ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T8   | review | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T9   | clinical trail | direct decompressive surgical resection ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T10  | clinical trail | denosumab and zoledronic acid ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T11  | clinical trail | zoledronic acid ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T12  | review | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T13  | article ✓ | metastatic breast cancer ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T14  | review | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T15  | recommendation | bisphosphonate-associated osteonecrosis of the jaw ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T16  | clinical trail | denosumab and zoledronic acid ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T17  | article ✓ | spinal metastases ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T18  | article ✓ | prostate cancer metastases to bone ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T19  | article ✓ | bisphosphonates ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T20  | article ✓ | bisphosphonates and osteonecrosis of the jaws ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T21  | article ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T22  | review | RANKL-RANK signaling pathway ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T23  | article ✓ | pamidronate ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T24  | article ✓ | Percutaneous vertebroplasty ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T25  | article ✓ | pamidronate ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T26  | review | RANKL-RANK signaling pathway ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T27  | guideline | bisphosphonates and bone health ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| T28  | clinical trail | denosumab and zoledronic acid ✓ | ✓ | ✓ | ✓ | breast cancer metastasis to bone | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

(continued on next page)
| rank | type | basic medical research | specific field | clinical medical research | biology of metastasis | disease focus | imaging | clinical trail | clinical guidelines | recoomendation | consensus | review | meta-analysis | systemic review |
|------|------|------------------------|----------------|--------------------------|-----------------------|--------------|---------|----------------|-------------------|---------------|-----------|---------|----------------|------------------|
| T29  | review | ✓                      |                |                         |                       | myeloma metastasis to bone | ✓                  |                  |                  |               |           |         |                |                  |
| T30  | review | ✓                      |                |                         | osteoprotegerin/RANKL/RANKL/RANK system |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T31  | review | ✓                      |                |                         | bisphosphonates       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T32  | article | ✓                      |                |                         | Percutaneous vertebroplasty |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T33  | review | ✓                      |                |                         | bisphosphonates       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T34  | article | ✓                      |                |                         |                       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T35  | clinical trial | ✓          |                |                         | zoledronic acid and pamidronate |                       | ✓                  |                  | breast cancer or osteolytic lesions of multiple myeloma metastasis to skeleton | ✓             |           |         |                |                  |
| T36  | clinical trial | ✓          |                |                         | zoledronic acid and pamidronate |                       | ✓                  |                  | breast cancer or osteolytic lesions of multiple myeloma metastasis to skeleton | ✓             |           |         |                |                  |
| T37  | article | ✓                      |                |                         | adjuvant clodronate treatment |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T38  | article | ✓                      |                |                         | breast cancer-mediated osteolysis |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T39  | review | ✓                      |                |                         | pathophysiology and treatment |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T40  | article | ✓                      |                |                         | vertebroplasty of spinal metastases |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T41  | article | ✓                      |                |                         | chromosomal variants in estrogen receptor-positive breast cancer |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T42  | article | ✓                      |                |                         | RANKL and bone metastasis |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T43  | article | ✓                      |                |                         | high-risk prostate cancer |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T44  | systemic review | ✓                  |                |                         | palliative radiotherapy trials for bone metastases |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T45  | review | ✓                      |                |                         | RANKL and osteoprotegerin |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T46  | guideline | ✓                      |                |                         | palliative radiotherapy for bone metastases |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T47  | article | ✓                      |                |                         |                       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T48  | clinical trial | ✓          |                |                         | zoledronic acid       |                       | ✓                  |                  | lung cancer and other solid tumors metastasis to skeleton | ✓             |           |         |                |                  |
| T49  | article | ✓                      |                |                         | pamidronate and prostate cancer |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T50  | article | ✓                      |                |                         |                       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T51  | review | ✓                      |                |                         | endothelin-1 in the pathophysiology of metastatic prostate cancer |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T52  | article | ✓                      |                |                         |                       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| T53  | clinical trial | ✓          |                |                         | radiotherapy for palliation of bone pain |                       | ✓                  |                  | breast or prostate cancer metastasis to bone | ✓             |           |         |                |                  |
| T54  | clinical trial | ✓          |                |                         | pamidronate       |                       | ✓                  |                  |                  |               |           |         |                |                  |
| rank | type | basic medical research | specific field | clinical medical research | biology of metastasis | disease focus | imaging | clinical trail | clinical guidelines | recoomendation | consensus | review | meta-analysis | systemic review |
|------|------|------------------------|----------------|--------------------------|-----------------------|---------------|---------|--------------|-------------------|---------------|-----------|--------|---------------|----------------|
| T55  | article | ✓                      |         |               |         |               | breast cancer and osteolytic bone metastases |
| T56  | article | ✓                      |         |               |         |               |
| T57  | article | ✓                      |         |               |         |               |
| T58  | article | ✓                      |         |               |         |               |
| T59  | clinical trail |         | denosumab | ✓                      | castration-resistant prostate cancer non-small cell lung carcinoma and other solid tumor metastasis to skeleton |
| T60  | clinical trail |         | zoledronic acid | ✓                      | bone loss in nonmetastatic prostate cancer patient with hormone therapy |
| T61  | clinical trail |         | zoledronic acid | ✓                      | advanced breast cancer and lytic bone lesions |
| T62  | article | ✓                      | bisphosphonates |         |               | breast cancer metastasis to bone |
| T63  | clinical trail |         | pamidronate | ✓                      | breast cancer metastasis to bone |
| T64  | article | ✓                      | a novel classification system for spinal instability in neoplastic disease |         |               |
| T65  | clinical trail |         | pamidronate | ✓                      | advanced breast cancer and lytic bone lesions |
| T66  | article | ✓                      | bisphosphonates and osteonecrosis of the jaws |         |               |
| T67  | article | ✓                      |         |               |         |               |
| T68  | article | ✓                      | bisphosphonates and osteonecrosis of the jaws |         |               |
| T69  | review |         | clodronate | ✓                      | breast cancer metastasis to bone |
| T70  | clinical trail |         | clodronate | ✓                      | breast cancer metastasis to bone |
| T71  | article |         | fraction on painful bone metastases | ✓                      | endocrine resistant metastatic prostate-cancer |
| T72  | clinical trail |         | SR-89 adjuvant to local field external beam irradiation | ✓                      | endocrine resistant metastatic prostate-cancer |
| T73  | review |         | percutaneous vertebroplasty | ✓                      | endocrine resistant metastatic prostate-cancer |
| T74  | article |         | differented thyroid carcinoma | ✓                      | endocrine resistant metastatic prostate-cancer |
| T75  | article | ✓                      | lung adenocarcinoma metastasis |         |               |
| T76  | article | ✓                      | lung adenocarcinoma metastasis |         |               |
| T77  | article |         | bone metastases and zoledronic acid | ✓                      |               |
| T78  | article |         | bone metastases and zoledronic acid | ✓                      |               |
| T79  | clinical trail |         | incidence, risk factors, and outcomes of osteonecrosis of the jaw | ✓                      | osteonecrosis of the jaw |

(continued on next page)
Table 4 (continued)

| rank | type  | basic medical research | specific field | clinical medical research | biology of metastasis | disease focus | imaging | clinical trail | clinical guidelines | reccomendation | consensus | review | meta-analysis | systemic review |
|------|-------|------------------------|----------------|-------------------------|----------------------|--------------|---------|----------------|---------------------|---------------|-----------|-------|----------------|------------------|
| T80  | article | ✓ | Breast cancer bone metastasis | | | | | | | | | | | | |
| T81  | review | | | | | | | | | | | | | |
| T82  | article | | Pathologic fractures and malignant bone disease | | | | | | | | | | | | |
| T83  | article | | Ablation therapy for painful bone metastases | | | | | | | | | | | | |
| T84  | clinical trial | | Denosumab | | | | | | | | | | | | |
| T85  | review | | Bone imaging | | | | | | | | | | | | |
| T86  | clinical trial | | Zoledronic acid | | | | | | | | | | | | |
| T87  | article | | Detection of bone metastases in breast cancer | | | | | | | | | | | | |
| T88  | article | ✓ | Pathophysiology and treatment | | | | | | | | | | | | |
| T89  | review | | | | | | | | | | | | | | |
| T90  | article | ✓ | OPG-RANK-RANKL and denosumab | | | | | | | | | | | | |
| T91  | article | ✓ | Palliative radiotherapy for bone metastases | | | | | | | | | | | | |
| T92  | review | | | | | | | | | | | | | | |
| T93  | meta analysis | | OPG-RANK-RANKL and denosumab | | | | | | | | | | | | |
| T94  | article | | Zoledronic acid | | | | | | | | | | | | |
| T95  | clinical trial | | Osteonecrosis | | | | | | | | | | | | |
| T96  | article | | Denosumab | | | | | | | | | | | | |
| T97  | clinical trial | | Alpha-emitter radium-223 | | | | | | | | | | | | |
| T98  | article | ✓ | Radiotherapy for metastatic spinal lesions | | | | | | | | | | | | |
| T99  | article | ✓ | | | | | | | | | | | | | |
| T100 | review | | Palliative radiotherapy trials for bone metastases | | | | | | | | | | | | |
clinical need to solve problems in the real world but also the advances and development of the pharmaceutical industry nowadays.

It is noteworthy that the guideline published in 2003 entitled American society of clinical oncology 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer (27#), recommending a management algorithm for patients diagnosed non-metastatic breast cancer. Meanwhile, this guideline also emphasized the supportive, albeit expensive and non-life-prolonging, benefit of bisphosphonates to patients diagnosed with bone metastases [22]. Beyond the drug management for bone metastases, radiotherapy is also a successful and time-efficient option to palliate pain and/or prevent morbidity. Article #41 published an evidence-based guideline from American Society for Radiation Oncology (ASTRO) focused on palliative radiotherapy for bone metastases. According to published evidence and expert opinions, it defined the proper use of radiotherapy for patients and physicians regarding the management of bone metastases [23]. Before 2010, neoplastic spinal instability was poorly defined and lacked guidelines in defining the degree of spinal instability. Article #64 generated a consensus of best evidence through a modified Delphi technique to develop a classification system to define neoplastic spinal instability. Based on patient symptoms and radiographic criteria of the spine, a comprehensive classification system was developed aiming to be helpful in predicting spine stability of neoplastic lesions [24].

In our analysis, the involved 100 articles were published in 44 journals, with an impact factor range of 1.895 to 91.245. 90.91% of the journals were categorized in Q1 and Q2 quartile. Only 4 journals were
36% of the most cited articles were published in top 4 journals, including Journal of Clinical Oncology (IF = 44.544), followed by Cancer (IF = 6.86), New England Journal of Medicine (IF = 91.245) and Spine (IF = 3.468). It is not surprising that researchers preferred to submit high-quality articles to journals with high impact factors. On the other side, articles published in high-impact factor journals tended to get more citations.

We identified authors from 14 different countries in the top 100 most cited articles. Oncologists all over the world participated in rosacea research, especially in North America and Europe. Scholar from Africa and South America seems not much interested in bone metastasis. Massachusetts General Hospital, Texas State University, and Memorial Sloan-Kettering Cancer Center reflected a great interest in bone metastasis research. Professor Robert E Coleman from the University of Sheffield published the most articles (13 publications, 9847 total citations). From the countries, institutions, and even authors analyses, we could easily find the authoritative scholarships and key institutions attributed to bone metastasis. The above finding could be attributed to an enhanced opportunity for a general understanding of bone metastasis for new readers about the natural history and trends within the bone metastasis field.

Undoubtedly, there are also some limitations to our analysis. First, as publications are filtered according to citations number, publications in recent years may be of great significance in the field but have a great chance to be ignored and out of the present list for now. Second, this analysis included not only published articles, but also other papers like reviews, meta-analyses, and clinical guidelines or recommendations, which may lead to omission bias. Third, we only included publications in English recorded on the Web of Science, and language and/or database limits may have been omitted.

5. Conclusions

In conclusion, this bibliometric article highlights the top 100 most cited articles in the bone metastasis field over the past 30 years (1986–2015), in terms of their publishing time and citations, journals, authors, geographical distribution, research institutions, and research keywords. We addressed the top 100 cited papers, regardless of publication type. From the aspect of the research theme, we found that clinical management of bone metastasis was one of the issues of global concern. Clinical trials and basic laboratory research are still of great significance and warrant deeper and broader exploration. This data-driven analysis provided a key advantage of a bibliometric review and may be of help in paving the way for further research on bone metastasis. In summary, the research field of bone metastasis looks promising.

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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