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Bibliometric Analysis of the Literature on Carbon Ion Therapy Using VOSviewer Software and Dimensions Database

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ABSTRACT

This study aims to carry out a bibliometric assessment of the worldwide research literature and historical research results on carbon ion therapy for cancer treatment. To carry out this work, we used the VOSviewer software and the Dimensions database. The VOSviewer software tool examined 2,500 publications exported from the Dimensions database. The results show a notable upward trajectory in academic research on carbon ion therapy since 1994, with 2020 showing the highest volume of publications. “Biomedical and Clinical Sciences”, “Physical Sciences”, “Oncology and Carcinogenesis”, and “Medical and Biological Physics” are the most important research categories. “Physics in Medicine and Biology” and “Medical Physics” are the leading journals for research publications on carbon ion therapy. Scrutiny based on term occurrences demonstrates the shift in research interest towards carbon ion radiation therapy. The analysis of bibliographic couplings concerning different countries revealed that Japan is the most dynamic and prolific country based on the number of publications (659) and citations (13734), followed by Germany with 590 publications and 19679 citations. These analytical studies provide a thorough overview of academic publications dedicated to using carbon ions for tumor treatment. This data is anticipated to be highly valuable for researchers seeking to pinpoint the most recent developments and emerging trends in this field of research.

INTRODUCTION

In 1895, Wilhelm Röntgen broke new ground by using a vacuum tube to project electrons accelerated by an electric field onto a tungsten target. This breakthrough gave rise to the mysterious radiation known as X-rays. This discovery subsequently paved the way for the development of external radiotherapy. Today, radiotherapy is divided into two main categories: conventional radiotherapy, which uses photons (X-rays or gamma radiation), and hadronic radiotherapy, which uses particles such as neutrons, protons, and heavy ions like helium and carbon, as projectiles. Research is also underway to explore the use of oxygen in this field [1-3]. Despite advances in conventional radiation technology, the major challenge remains the lack of effective treatment for certain tumors that are resistant to X-rays or gamma rays due to their low sensitivity to these types of radiation. To remedy this situation, a solution has been suggested, consisting of using charged particles, particularly carbon ions. In 1946, the famous scientist Robert R. Wilson, known for his contributions to the development of particle accelerators, was the pioneer in considering using protons in medicine as a possible therapy for cancer [4]. From 1954 until the accelerator's closure in 1992, the Lawrence Berkeley Laboratory employed protons and other heavy ions as a method for cancer treatment [5].

In 1994, Japan established its inaugural carbon ion hadron therapy research facility in Chiba, drawing upon the research undertaken at Berkeley.

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This pioneering medical accelerator, known as the Heavy Ion Medical Accelerator in Chiba (HIMAC), was the first of its kind in the country [6]. The initiation of carbon ion radiotherapy (CIRT) in Germany by Gesellschaft für Schwerionenforschung (GSI) in 1997 led to the development of a clinical center for CIRT, the Heidelberger Ionenstrahl-Therapiezentrum (HIT), in 2009. In 2001, the first proton and carbon facility, the Hyogo Ion Beam Medical Center (HIBMC), was established in Hyogo, Japan, marking the construction of a second clinical center in the region. In 2006, the Institute of Modern Physics (IMP) in China initiated clinical trials, followed by the clinical application of proton and carbon ion beams at the Shanghai Proton Heavy Ion Center (SPHIC) in 2014. In Japan, owing to technological advancements, three carbon facilities of reduced size were constructed: the Heavy Ion Medical Center at Gunma University in 2010, the SAGA Heavy Ion Medical Accelerator in 2013, and the Kanagawa Cancer Center (iROCK) in 2015 in Tosu. In Italy, the National Center of Oncological Hadrontherapy (CNAO) installed a medical accelerator for proton and carbon treatment in 2011. In 2016, MedAustron commenced clinical investigations in Austria and subsequently administered Carbon ion radiotherapy (CIRT) to patients in 2019. In 2018, the Osaka Heavy Ion Therapy Center in Japan started CIRT. The smallest institution in the world, East Japan (HIC) at Yamagata University Hospital, initiated CIRT in 2021. Most recently, Taiwan Veterans General Hospital in Taipei began employing C ions in 2022. Many institutions around the world use protons or heavy ions to treat persistent tumors. Table 1 provides a comprehensive list of carbon ion hadrontherapy centers, with only 14 centers currently operational. A further six C-ion therapy centers are currently under construction.

To gain a comprehensive understanding of the global trend in research development about the topic under examination, a thorough historical review and bibliometric analysis of research on carbon ion radiotherapy have been carried out in the scope of this study. Drawing on the extensive Dimensions database, this research will examine advances in the scientific literature from 1994 to 2023, with a particular focus on cancer treatment using carbon ions. For comparison, in a recent review article titled "More than Five Decades of Proton Therapy: A Bibliometric Overview of the Scientific Literature," published on November 23, 2023, in the journal Cancers [7], the authors present a bibliometric analysis of the scientific literature regarding proton therapy from 1946 to 2022, utilizing the Scopus database. A total of 7,335 documents, predominantly articles and journals, were identified. Approximately 84 % of these documents were published in the last 15 years (2008-2022), with a mean annual growth rate of 13 % during this period. The primary contributors were the United States, followed by Germany and Japan.

Table 1. Summary of carbon ion facilities in operation (last update: August 2023 from https://ptcog.site).

Country	Who, where	Start of treatment
Japan	HIMAC, QST, Chiba	1994; 2017
Japan	HIBMC, Hyogo	2002
Germany	HIT, Heidelberg	2009; 2012
Japan	GHMC, Gunma	2010
Italy	CNAO, Pavia	2012
Japan	SAGA-HIMAT, Tosu	2013
China	SPHIC – Shanghai	2014
Germany	MIT, Marburg	2015
Japan	i-Rock Kanagawa Cancer Center, Yokohama	2015
Japan	Osaka Heavy Ion Therapy Center, Osaka	2018
Austria	MedAustron, Wiener Neustadt	2019
China	Heavy Ion Cancer Treatment Center, Wuwei, Gansu	2019
Japan	East Japan HIC, Yamagata University Hospital, Yamagata	2021
Taiwan	Taiwan Veterans General Hospital, Taipei	2022

METHODOLOGY

Collecting data

The data was extracted from the Dimensions database (https://www.dimensions.ai/, accessed on August 17, 2023), which has extensive coverage and is considered one of the largest bibliometric databases available, surpassing both Scopus and Web of Science [8-10]. The Dimensions database relies on multiple sources, including Crossref, PubMed, and Open Citation, for populating its database. This bibliometric database was released by Digital Sciences [11] in January 2018 and contains a vast array of scholarly works, including papers, chapters, books, policy documents, grants, patents, and clinical trials.

Our research exclusively concentrated on chapters, articles, preprints, and proceedings. The criteria for our search were as follows: Period (1994 to 2023 inclusive), Type of publication (articles, chapters, proceedings, and preprints), query date (conducted on August 17, 2023), Search terms employed ("Carbon AND ion AND therapy"), and the number of publications retrieved (an impressive tally of 2500 scholarly works).

Bibliometric evaluation using the VOSviewer program

The development of bibliometric data networks made up of researchers, journals, or individual articles, can be facilitated using VOSviewer [12], a software package designed for creation and visualization purposes. Building analyses through the utilization of bibliometric databases such as Scopus, Web of Sciences, or Dimensions can be achieved through the examination of citation, co-citation, bibliographic coupling, or Co-authorship relations. The utilization of such databases allows for the visualization of three distinct types of maps: network visualization, density visualization, and overlay visualization. In the current investigation, the most recent version of VOSviewer (Version 1.6.19), which was released on January 23, 2023, was employed. Using data retrieved from the Dimensions database as input into VOSviewer, we conducted a bibliometric mapping. The mapping process involved exporting 2,500 publications and extracting relevant terms from their respective titles and abstract fields. The visualization of the resulting map was carried out using VOSviewer, as illustrated in Fig. 1 [13].

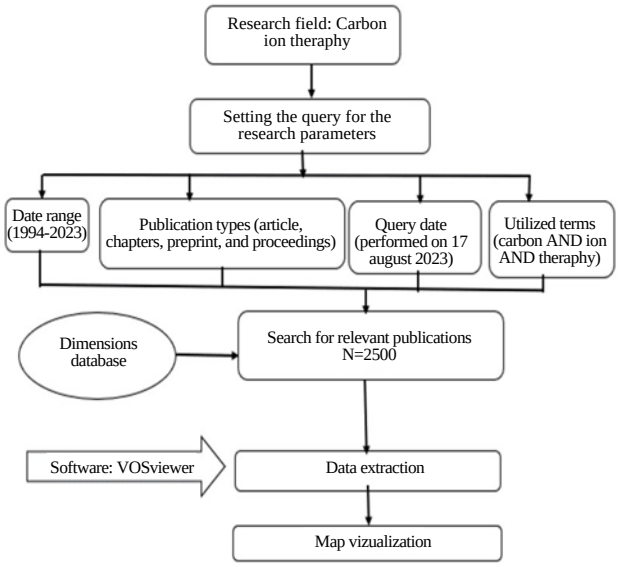

Fig. 1. Flowchart showing the steps involved in using the VOSviewer program to visualize a map.

The initial phase of producing a map using VOSviewer necessitates the selection of fields from which the terms will be extracted. We opted to extract the terms from the title and abstract fields. The subsequent phase involved excluding terms with an occurrence count below 20. Out of the 48,198 terms, only 678 satisfied the predetermined threshold. A relevance score was then computed for each of the 678 terms, and based on this score, the 407 most pertinent terms were chosen.

RESULTS AND DISCUSSION

Type of publications

Our examination of the Dimensions database revealed that most of the documents, specifically 90 % (N = 2916), were articles. Additionally, 5 % (N = 171) were chapters, while 3 % (N = 91) were proceedings, and 2 % (N = 89) were preprints (refer to Fig. 2 for a visual representation). During the period spanning from 1994 to 2022, a substantial amount of research about carbon ion therapy was disseminated, with most of it being featured in prominent academic journals such as "Physics in Medicine and Biology" (N=214), "Medical Physics" (N=195), "International Journal of Radiation Oncology, Biology, Physics" (N=179), and "Radiotherapy and Oncology" (N=137).

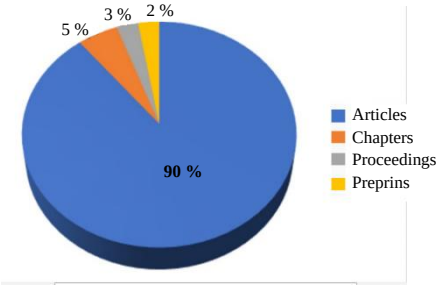

Fig. 2. Various types of publications and their respective percentages.

Search category

Figure 3 illustrates the main field of study for carbon ion therapy. The field of “Biomedical and Clinical Sciences” was the foremost field examined in connection with our exploration of “carbon AND ion AND therapy”, featuring 1929 publications and 44993 citations. It was succeeded by “Physical Sciences” with 1544 publications and 24667 citations, and “Oncology and Carcinogenesis” with 1396 publications and 28657 citations. This suggests a growing interest in examining both the biomedical and physical aspects of carbon ion therapy.

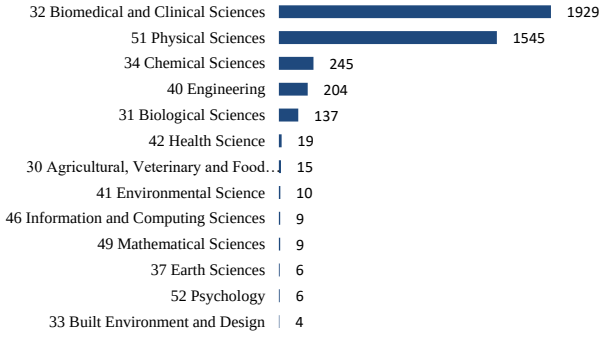

Fig. 3. Comparison between the number of publications and their respective search categories. (Image imported on August 17, 2023 from www.dimensions.ai).

Figure 4 shows a significant upward trend in the volume of publications devoted to carbon ion therapy between 1994 and 2023, indicating a sustained interest in the subject. The peak in publications was recorded in 2020, with a total of 264 publications. Our investigation divulged that the fields of biomedical and clinical sciences and physical sciences were the most explored areas of study for the search query “carbon ion therapy”. Between 1994 and 2023, there was a significant increase in scientific output from 7 to 245 documents, with an annual growth rate of 34 %. The relevance of physics in investigating the interaction between charged particles and matter in the realm of cancer treatment explains the popularity of these fields, playing a crucial role as a bridge between carbon ions and radiotherapy.

A group of editors has established themselves as leading experts through their engagement in writing scientific articles on carbon ion therapy. Their frequent scientific contributions have considerably enriched the medical literature and kept the international medical community informed of innovative results in this rapidly evolving field. These authors include Jürgen Debus of Heidelberg University Hospital, Germany (234 publications and 6,995 citations), Tadashi Kamada of the Kanagawa Prefectural Hospital Organization, Japan (161 publications and 5,283 citations), Oliver Jäkel from the German Cancer Research Center, Germany (155 publications and 5,795 citations), Hiroshi Tsuji from the National Institutes for Quantum and Radiological Science and Technology, Japan (124 publications and 3,407 citations), Katia Parodi from Ludwig -Maximilians-Universität München, Germany (114 publications and 3,796 citations), and Marco Durante of the GSI Helmholtz Center for Heavy Ion Research, Germany (106 publications and 3,387 citations). Based on VOSviewer integrated into the Dimensions database, and on Co-authorship analysis, we obtained a network visualization of 494 researchers in the field of carbon ion therapy: In total, the researchers were grouped into 15 clusters in the form of coloured circles linked by 6195 links (see Fig. 5).

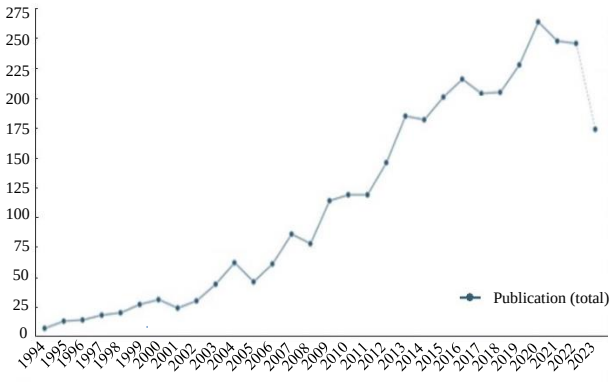

Fig. 4. Publications on carbon ion therapy published from 1994 to 2023. (Figure imported on August 17, 2023 from www.dimensions.ai).

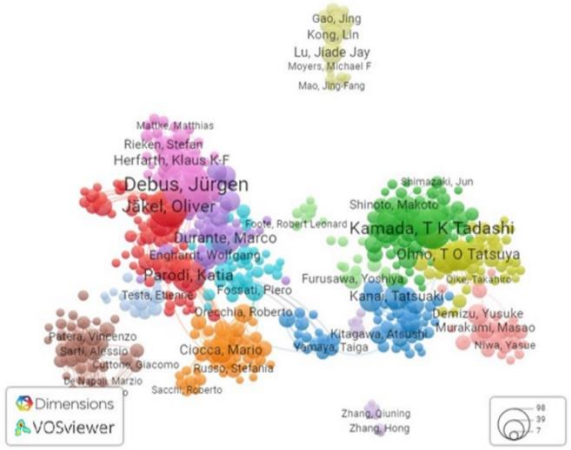

Fig. 5. Network visualization showing researchers related to areas of carbon ion therapy.

On the other hand, the journal "Physics in Medicine and Biology" is considered the primary source for publications related to carbon ion therapy. Its contents cover a wide range of topics, including Physical Sciences, Medical and Biological Physics, Synchrotrons and Accelerators, and Nuclear and Plasma Physics. The trajectory of publications on carbon ion therapy from 1994 to 2023 is visually represented in Fig. 6. Notably, the year 2017 recorded a remarkable tally of 21 publications. Researchers Katia Parodi and Oliver Jäkel have made significant contributions to this journal, with 42 and 24 publications respectively, making them influential within this context.

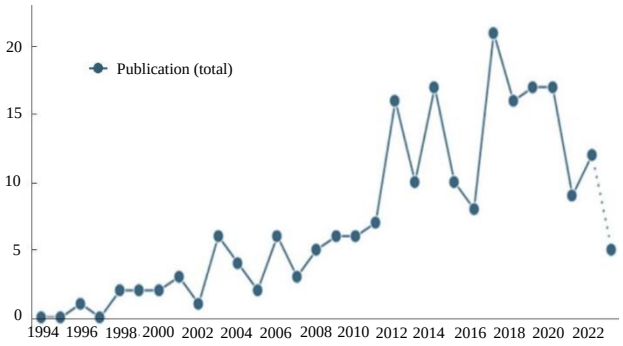

Fig. 6. The number of publications related to carbon ion therapy published between 1994 and 2023 in the "Physics in Medicine and Biology" Journal. (Image imported on August 17, 2023, from www.dimensions.ai).

Network visualization based on text data

A total of 2,500 papers were selected from a corpus of 3412 publications spanning the years 1994 to 2023. These papers were sorted based on their relevance to the search query: "Carbon AND ion AND therapy" and were extracted from the Dimensions database. The visualization map was generated using these selected papers. The establishment of co-occurrence links between terms through the utilization of natural language processing algorithms within text data allowed for the creation of a network [14]. The diagram depicted in Fig. 7 displays three clusters comprised of 407 keywords that are visually represented by coloured circles. These circles are interconnected by a total of 25030 links, resulting in an overall link strength of 230707.

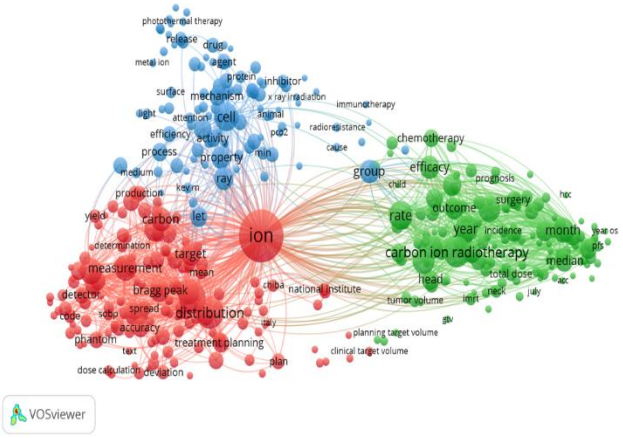

Fig. 7. Visualization map with weighted publications. The number of published papers connected to the search term or keywords determines the size of each circle. (Produced by VOSviewer 1.6.19).

The primary co-occurrence of the key terms within the red cluster, which consists of 153 items, includes "Ion" (with an occurrence of 1219), "beam" (with an occurrence of 455), "distribution" (with an occurrence of 464), "measurement" (with an occurrence of 305), "energy" (with an occurrence of 291), "target" (with an occurrence of 245), and "Bragg peak" (with an occurrence of 228). These particular terms have been mentioned in numerous studies, such as "The History of Ion Beam Therapy in Germany" [15], as well as "Review of the Existing Relative Biological Effectiveness Models for Carbon Ion Beam Therapy" [16]. The terms associated with this cluster group pertain to the deposition of energy and encompass the utilization of both Monte Carlo simulation and measurement techniques in the treatment involving carbon ion beams [17,18].

The Green cluster, comprising 149 items, encompasses the carbon ion radiotherapy aspects. Key terms within this cluster include "carbon ion radiotherapy" (mentioned 4015 times), "rate" (mentioned 347 times), and "year" (mentioned 323 times). In the visualization map, the term "carbon ion radiotherapy" is associated with 380 links. These links connect "carbon ion radiotherapy" with terms such as "ion," "cell", "beam", "distribution", "ray", and "Bragg peak". This association underscores the strong connection between carbon ion radiotherapy and the treatment of tumors.

The blue cluster consists of 105 items and focuses on the presence of "cells" and "cancer therapy" in the field of carbon ion therapy. The term "cell" appears frequently with a high occurrence of 362, followed by "ray" (221), and "property" (219). These numbers reflect the increasing interest in cancer therapy. The substantial frequency of the term "cell" is a critical parameter for defining, measuring, and studying the amount of energy deposited in the target volume required to treat hypoxic tumors [19,20].

All three clusters primarily encompass subjects related to carbon ion therapy and the planning of treatment for hypoxic cells.

Overlay and density visualization based on text data

The Overlay map is quite similar to the visualization map, primarily differing in the allocation of color to the various items. In Fig. 8, each item is characterized by its score and depicted using a specific color scheme, wherein the default color gradient spans from the lowest score (blue) to

the highest score (red). The overlay map offers a comprehensive view of the average citations, with blue terms denoting citations that average below 20, cyan terms hovering around an average of 30 citations, green terms showcasing an average of approximately 35 citations, yellow keywords possessing an average of 40 citations, and red keywords attaining an average of 50 citations or higher. It is discernible that the term "release" exhibits the highest average citations (78.83).

The Density visualization of the 407 terms and three groups is shown on the thermal distribution cards in Fig. 9. Notably, the regions with high densities are depicted in hot red hues, while the regions with low densities are shown in various shades of green. The number and significance of nearby terms determine the degree of phrase density. It's interesting to note that terms with high densities include "ion," "carbon ion therapy," “distribution”, “cell”, and “measurement”. It follows that these terms cover all the key terms that are important in the field of carbon ion therapy.

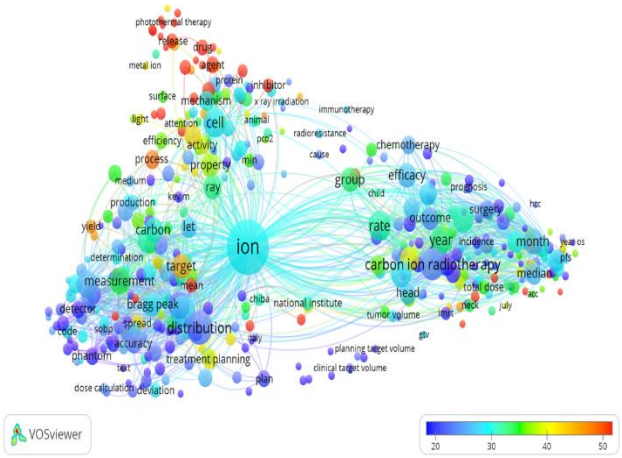

Fig. 8. Overlay graphic displaying each item's typical number of citations. Red denotes the highest score, while blue is the lowest. (Produced by VOSviewer 1.6.19).

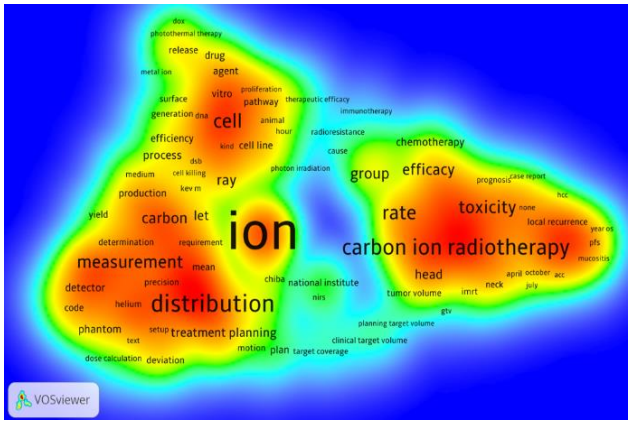

Fig. 9. Items density visualization map of 407 terms. (Produced by VOSviewer 1.6.19).

Density map based on bibliographic data

We generated maps using bibliographical data to facilitate bibliographic coupling analysis, which allowed us to assess the significance of connections between publications and track the publication rate trends across different countries. Considering this approach, we employed bibliographic coupling analysis to determine the number of publications associated with our search query, excluding countries with fewer than five publications. Of the 67 countries analyzed, 36 meet our criteria, as shown in Fig. 10. Our analysis revealed the presence of seven distinct clusters, with the size of each circle in the diagram directly proportional to the number of publications. Different colors were used to represent these clusters, illustrating their interconnections. Countries within the same clusters exhibited a higher frequency of citing each other.

The total link strength calculated through bibliographic coupling analysis pointed to Japan as the leading country in the field of carbon ion therapy, with 659 publications and 13,734 citations, followed closely by Germany, which had 590 publications and 19,679 citations. These findings confirm the observations we discussed in the introduction regarding the global landscape of carbon ion therapy facilities.

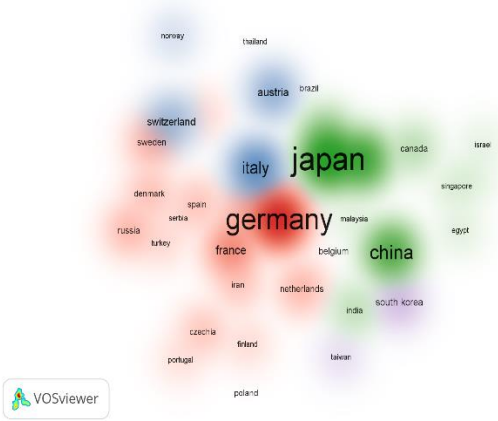

Fig. 10. Analysis of country-specific bibliographic coupling based on document weight (density visualization). (Produced by VOSviewer 1.6.19).

CONCLUSION

Carbon ion treatment bibliometric analysis using VOSviewer provides unique insights into the development of this vibrant field of study. The scientific community’s growing interest in carbon ion therapy is evident from the exponential growth in publications. This analysis technique allows us to map important contributors, significant research institutes, and new research trends. It is obvious from the analysis's findings that carbon ion therapy

offers a promising path toward the treatment of cancer and other diseases. Significant progress has been made in this area of study, particularly in terms of treatment accuracy and minimizing harm to healthy tissue. However, it's equally critical to take note of the research gaps and openings that this analysis has shown. In conclusion, the VOSviewer-based bibliometric analysis of carbon ion therapy demonstrates the expanding significance of this topic of study in the medical industry. It is a field that is continually developing, and the future holds many intriguing possibilities. We may anticipate seeing carbon ion therapy play an increasingly significant role in the treatment of disease, enhancing patients' quality of life, and paving the path for new medical advances by continuing to monitor trends and fostering cooperation between researchers and institutions.

AUTHOR CONTRIBUTION

The main authors of this study were H. El Bekkouri and E. Al Ibrahmi, who each contributed equally. The final draft of the manuscript was read and approved by all authors.

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