Global Research Output of Lutetium-177 PSMA in Prostate Cancer: Bibliometric and Altmetric Analyses

Globale Forschungsergebnisse zu Lutetium-177-PSMA bei Prostatakrebs: bibliometrische und altmetrische Analysen

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ABSTRACT

Aim The integration of innovative radio-pharmaceutical agents targeting prostate-specific membrane antigen (PSMA) within nuclear medicine has transformed prostate cancer detection and management. This study aims to investigate the present landscape of [^{177}Lu]Lu-PSMA in prostate cancer, elucidating trends, global contributions, scholarly outlets, institutions, and thematic concentrations with an aim to inform forthcoming research endeavors.

Methods We systematically probed the Scopus repository for relevant [^{177}Lu]Lu-PSMA literature. An assessment of bibliometric and altmetric data was carried out. Finally, we assessed the correlation between the altmetric attention scores and the number of citations for the retrieved data.

Results Spanning January 2015 to July 2023, the study encompassed 466 articles concerning [^{177}Lu]Lu-PSMA therapy for prostate cancer. Predominant citation accolades gravitated towards metastatic castration-resistant prostate cancer investigations and assessments of [^{177}Lu]Lu-PSMA therapy's safety and efficacy. Further research encompassed adverse effects linked to [^{177}Lu]Lu-PSMA intervention, including xerostomia, thrombocytopenia, anemia, and fatigue. Germany emerged as the primary academic contributor, with The Journal of Nuclear Medicine dominating publications (n = 55). A moderate significant correlation was detected between the number of citations and altmetric attention scores .

Conclusion The findings highlight the growing interest and advancements in the utilization of [^{177}Lu]Lu-PSMA therapy in prostate cancer and offer a comprehensive global perspective on future research directions.

Introduction

Prostate cancer is a prevalent male health concern worldwide and is associated with age [1]. While it is uncommon in individuals under 40 years old, research indicates that approximately one-third of individuals over 80 years old have exhibited prostate neoplasms upon postmortem examination [2]. Globally, prostate cancer is the second most commonly diagnosed cancer in men and ranks as the fifth leading cause of cancer-related mortality [1]. Dispari-

ties in incidence rates across countries can be attributed to variations in the utilization of diagnostic screening methods [1].

In recent years, the utilization of PET agents labeled with ^{68}Ga and ^{18}F to specifically target PSMA has gained substantial importance, particularly in the context of imaging biochemically recurrent prostate cancer [3]. In addition, the utilization of PSMA ligand PET/CT is a clinically valuable tool for this purpose, supported by multiple studies that demonstrated its superior detection efficacy compared to standard-of-care imaging modalities [4, 5, 6].

The utilization of PSMA-ligand PET/CT has proven to be a valuable asset in the management of prostate cancer across multiple domains. PSMA-ligand PET/CT is utilized for the detection of non-metastatic prostate cancer that may not be discernible through traditional imaging methods, initial staging and assessment of disease progression, and the identification of recurrent or persistent tumors [7]. Furthermore, it is employed as a surrogate marker prior to PSMA-directed radioligand therapy, thereby assisting in the process of treatment planning [3, 8]. The utilization of PSMA-ligand PET/CT enables the visualization of metastatic prostate cancer and aids in the assessment of the efficacy of systemic treatments for patients with metastatic prostate cancer [3].

The concept of radionuclides targeting PSMA holds potential benefits not only for the diagnosis but also for the therapeutic management of patients with metastatic castration-resistant prostate cancer (mCRPC) [9]. This therapeutic approach is known as radioligand therapy (RLT), which involves the combination of PSMA-ligands for diagnostic and therapeutic radionuclides to selectively administer high doses of radiation to cancer cells, resulting in cellular death [10]. PSMA-ligands are typically labeled with beta-emitting radionuclides Lutetium-177 (^{177}Lu) and alpha-emitting radionuclides like Actinium-225 (^{225}Ac) [11, 12]. Alternatively, other radionuclides could be considered like Lead-212 (^{212}Pb), and Terbium-161 (^{161}Tb) radionuclides [12, 13, 14]. Each of the aforementioned radionuclides possess distinct physical and radiobiological characteristics [12].

Bibliometric analysis is a method employed to evaluate the scholarly output within a defined timeframe on a specific subject [15]. Research utilizing bibliometric analysis offers a comprehensive overview of the worldwide scientific contributions to the literature in a given field [16]. Such studies present condensed information, encompassing influential papers, countries with high productivity, prominent journals, as well as leading authors and institutions [17]. By utilizing the foundational insights gained from bibliometric analysis, areas that warrant further exploration in future research can be identified [18].

Due to the widespread use of the Internet and the increasing popularity of social media platforms, alternative article metrics known as altmetrics are now commonly used to assess the academic and social influence of articles [19, 20]. Online tools enable the swift tracking of a scientific publication's social impact by analyzing its shares on social media, comments on platforms like YouTube and Facebook, mentions on Twitter, as well as references in news outlets and academic platforms [21]. Bibliometric studies have been conducted in various fields, including radiotheranostics [22]. To our knowledge, there is no existing evidence of any bibliometric or altmetric analysis for [^{177}Lu]-PSMA acknowledged up to date. Therefore, we aimed to present the landscape of [^{177}Lu]Lu-PSMA in prostate cancer, by analyzing patterns, worldwide contributions, academic publications, institutions involved, and thematic focuses. The intention behind this investigation is to provide valuable insights for future research undertakings.

Materials and Methods

Objectives

This bibliometric analysis aims to review the current research status in the field of [^{177}Lu]Lu-PSMA and prostate cancer. In addition, an attempt to identify trends, country contributions, journals, institutions, and focus areas was explored to guide the future research direction. The research trends from the start of January 2015 to the 5th of July 2023 are the focus of this study.

Search Analysis in Scopus

We searched the Scopus database for articles that discussed the use of [^{177}Lu]Lu-PSMA in prostate cancer. The retrieved articles were restricted to the last nine years (2015–2023). The search results were obtained from the Scopus database by employing a combination of keywords. These included "LU177 PSMA", "LU-177 PSMA", "Lutetium-177 PSMA", "Lutetium PSMA", "177Lu-PSMA", "177Lu PSMA", and "prostate cancer". All 466 documents resulted from the previous search were extracted.

Bibliometric Analysis by VOSviewer

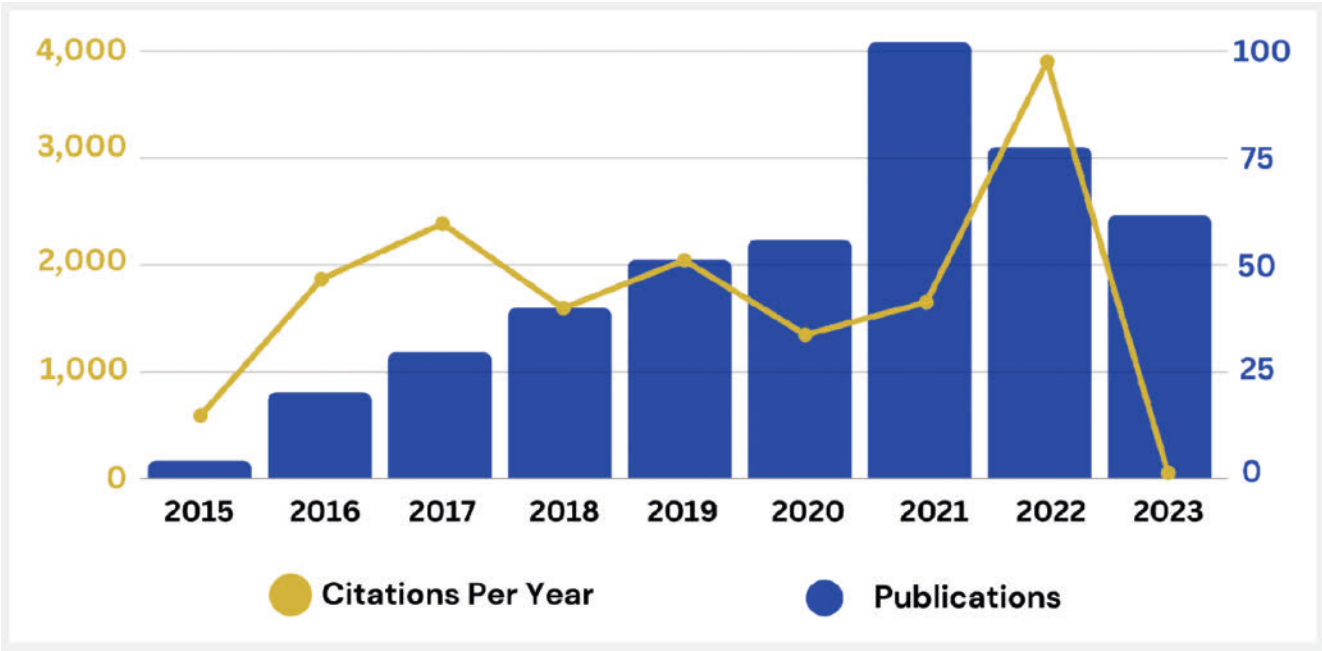
Using VOSviewer version 1.6.19, we analyzed annual trends, top-contributing countries and institutions, top-publishing journals, most occurred keywords, and top cited articles. These were summarized and visually presented using tables and figures. The most frequently occurring keywords were studied by limiting them to a minimum of 40 occurrences, then we manually removed the non-specific keywords that implied the study design and demographic data, such as "clinical article", "review", "middle aged", "human", "male", "female", "adult", etc. We also removed synonyms like "lutetium", lutetium 177", and "psma-617" to reduce redundancy.

Altmetric Analysis

The Altmetric database was accessed through the altmetric website (https://www.altmetric.com) in order to obtain altimetric attention scores for the data being analyzed.

Statistical Analysis

Statistical descriptive analysis was conducted using Microsoft Excel 2019 to analyze the relationship between publication years and total citations. We analyzed the annual trends by examining the number of publications each year, and number of citations per year. The mean ± standard deviation (SD) for the number of citations for all the documents in each year were calculated. Additionally, we used Stata software version 17 (College Station, TX, USA) to analyze correlation between altmetric data and citation values using Spearman's rank correlation test (Spearman's rho). Spearman's rho score less than 0.250 was considered to indicate a weak correlation, while scores between 0.250 and 0.499 were



▶ **Fig. 1** Annual publication and citation trends of [177Lu]Lu-PSMA articles in the field of prostate cancer. The data were extracted from the start of 2015 to 5th of july-2023.

▶ **Table 1** Annual publications and citations of [^{177}Lu]Lu-PSMA articles in the field of prostate cancer. The data were extracted from the start of 2015 to the 5th of july-2023. SD = Standard Deviation.

Year	Articles (n = 466)	Citations/year (n = 11859)	Cited by	
			Mean (SD)	Median
2015	4 (0.86 %)	582	16.2 (17.6)	10.5
2016	21 (4.51 %)	1862	11.1 (16.4)	3
2017	31 (6.65 %)	2381	11.0 (17.9)	4
2018	42 (9.01 %)	1588	6.30 (9.06)	2
2019	54 (11.6 %)	2038	7.54 (11.7)	3
2020	59 (12.7 %)	1340	5.67 (8.46)	2
2021	108 (23.2 %)	1644	5.04 (21.3)	1
2022	82 (17.6 %)	3901	2.27 (3.32)	1
2023	65 (13.9 %)	43	0.61 (1.23)	0

categorized as moderate. Whereas, scores between 0.500 and 0.749 were classified as strong, and scores equal to or greater than 0.750 were considered to represent a very strong correlation. A p-value less than 0.05 ($p < 0.05$) was deemed to be statistically significant for all the analyses conducted.

Results

The analysis incorporated a comprehensive set of 466 research papers derived from the initial search. Predominantly, these consisted of journal articles (n = 340 journal articles). Supplementary research outputs encompassed a diversity of formats. The remaining papers included 3 book chapters, 2 conference papers, 6 editorial pieces, 2 erratum, 17 letters, 14 notes, 80 reviews, and 2 short surveys. Within this corpus, a substantial proportion of 422 articles were composed in English, while 15 were in German, and 5 in Dutch. The remainder of the documents were written in different languages.

Annual Trends

The examination of annual data highlights a gradual increase in publication metrics. In 2015, only four articles were identified, accounting for approximately 0.86 % of the overall pool. This was fol-

▶ **Table 2** Publications and citations of the top-contributing countries. The data were extracted from the start of 2015 to the 5th of july-2023.

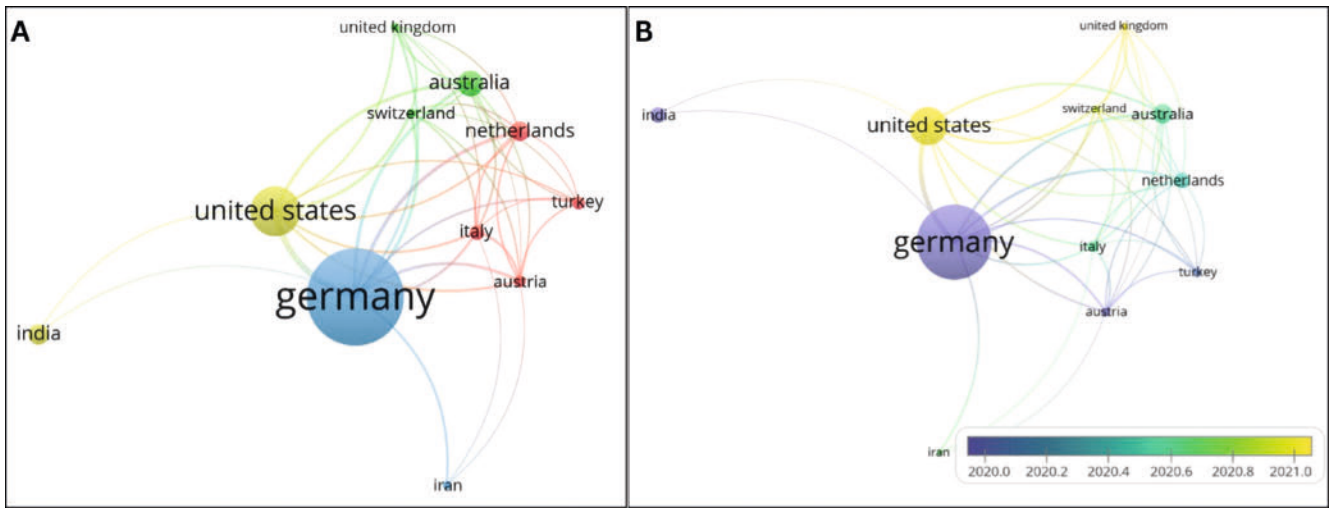
Country	Publications	Citations	Total Link Strength
Germany	188	7646	156
United States	97	2487	125
Australia	50	2086	63
India	39	610	3
Netherlands	39	771	53
Italy	29	644	56
Turkey	25	874	29
Austria	24	777	57
Switzerland	17	1164	60
Iran	16	65	10
United Kingdom	16	744	41
China	15	143	8
Canada	14	728	13
France	14	677	32
South Africa	9	296	14
Sweden	7	141	18
Belgium	7	147	20
Finland	7	242	16
Denmark	6	201	14
Japan	5	139	6
Russian Federation	5	54	7
Singapore	5	132	4
Spain	5	208	23

lowed by a significant growth in scholarly production in subsequent years. The peak of this trend was reached in 2021, with the emergence of 108 articles, constituting roughly one-fourth of all observed publications (▶ **Fig. 1**). After this peak, there was a gradual decline in research efforts, as evidenced by the presence of 82 articles in 2022, representing 17.6 % of the comprehensive compilation. From 2023 until the end of our analysis, a cumulative total of 65 articles were published, accounting for 14 % of the total. The pattern of annual citations showed noticeable fluctuations, with significant oscillations in earlier years and more stable metrics in later periods. Notably, the highest number of citations, totaling 3901, was recorded in 2022. The total number of citations accumulated to 11,859, resulting in an average of 2.49 citations per article. The mean, along with its SD were examined (▶ **Table 1**).

Countries

Of 69 countries, 22 met the threshold of five minimum number of publications on [^{177}Lu]Lu-PSMA in prostate cancer. We observed that the majority of publications were conducted by institutes from Germany, with a total of 188 documents and highest number of 7646 citations. Other notable contributors in terms of publications and citations included United States (n = 97, citations 2487), Australia (n = 50, citations 2086), India (n = 39, citations 610), the Netherlands (n = 39, citations 771), and Italy (n = 29, citations 644) (▶ **Table 2**).

We identified four main clusters in the network analysis of the top contributing countries. The largest cluster consisted of Austria, Turkey, Netherlands, and Italy. The second cluster included Australia, Switzerland, and the United Kingdom, while the third cluster was dominated by Germany and Iran, and the last cluster included India and the United States. An overlay presentation of the top publishing countries according to the average publication year was examined. This was visually overlayed by VOSviewer along with the international contribution (▶ **Fig. 2**).



▶ **Fig. 2** (**A**) Network visualization of the top-contributing countries and their connections, grouped in 4 clusters. Countries included in the same cluster are displayed in the same color. Larger circles indicate that the country had more publications. The distance between the 2 circles shows the degree of connection between two countries. (**B**) Overlay presentation of the top publishing countries, the color of a term indicates the average publication year for each country. A color bar is shown in the bottom right corner of the visualization, that indicate the publication years range.

▶ **Table 3** Top-contributing institutions according to the number of publications. The data were extracted from the start of 2015 to the 5th of july-2023.

Author	Documents	Publications	Citations
Technical University of Munich	Germany	46	2628
Münster University Hospital	Germany	40	2622
University Hospital Essen	Germany	37	1571
German Cancer Research Center	Germany	36	2037
University Hospital of the Technical University Munich	Germany	36	2060
Peter MacCallum Cancer Centre	Australia	34	1769
University Hospital of Bonn	Germany	32	1338
University of Melbourne	Australia	25	775
University Hospital Heidelberg	Germany	22	1654
University of California	United States	21	1012
The Sir Peter MacCallum Department of Oncology	Australia	20	1080
David Geffen School of Medicine at UCLA	United States	19	779
Zentralklinik Bad Berka	Germany	19	1425
Ludwig Maximilian University of Muich	Germany	19	1266
Radboud University Medical Center	Netherlands	17	393
University of Duisburg-Essen	Germany	16	762
Klinikum der Universität München	Germany	15	342
Weill Cornell Medicine	United States	15	820
St. Vincent's Hospital Sydney	Australia	14	462
The University Hospital of the Saarland	Germany	12	349
University Medical Center Utrecht	Netherlands	12	187
Memorial Sloan-Kettering Cancer Center	United States	11	798
Tulane University School of Medicine	United States	11	617
Bhabha Atomic Research Centre	India	11	90
Homi Bhabha National Institute	India	11	80
Garvan Institute of Medical Research	Australia	10	378
Medical University of Innsbruck	Austria	10	388
The University of Sydney	Australia	10	418

Institutions

In terms of the overall number of published works, the Technical University of Munich in Germany was the leading institution with 46 publications. In succession, the Münster University Hospital in Germany achieved 40 publications. Afterwards, the University Hospital Essen in Germany rendered 37 publications. Other notable contributors included the German Cancer Research Center, with 36 publications. This was followed by the University Hospital of the Technical University Munich in Germany with 36 publications and the Peter MacCallum Cancer Centre in Australia with 34 publications. It is important to note that the departments responsible for these publications were primarily from the fields of nuclear medicine, urology, and radiology (▶ **Table 3**).

Authors

A total of 159 authors were included in our analysis. Among them, 28 authors had at least 10 publications on [^{177}Lu]Lu-PSMA in prostate cancer. The top five authors were Eiber M., Rahbar K., Ahmadzadehfar H., Hofman M.S., and Essler M.; they published at least 24 publications on this topic, and their articles were from the top cited studies (▶ **Table 4**).

Journals

In terms of the number of publications, the Journal of Nuclear Medicine had the highest number of publications with (n = 55). Followed closely by Clinical Nuclear Medicine (n = 46), and European Journal of Nuclear Medicine and Molecular Imaging (n = 43). In a consecutive manner, EJNMMI Research published a total of 14 research papers (▶ **Table 5**).

▶ **Table 4** Top publishing authors. The data were extracted from the start of 2015 to the 5th of july-2023.

Author	Documents	Citations
Eiber M.	39	1971
Rahbar K.	37	2606
Ahmadzadehfar H.	32	1787
Hofman M.S.	24	1222
Essler M.	24	1342
Fendler W.P.	22	1601
Baum R.P.	20	1781
Kratochwil C.	19	2123
Herrmann K.	19	809
Kulkarni H.R.	16	1695
Wester H.J.	15	1790
Tauber R.	15	692
Calais J.	14	362
Emmett L.	14	462
Gafita A.	13	447
Czernin J.	13	443
Bögemann M.	13	949
Bartenstein P.	12	877
Weber W.A.	11	351
Nagarajah J.	11	93
Ezziddin S.	11	347
Sandhu S.	11	692
Singh A.	10	697
Murphy D.G.	10	422
Böning G.	10	270
Sartor O.	10	626
Giesel F.L.	10	1110
Violet J.	10	903

▶ **Table 5** Top publishing journals and citation. The data were extracted from the start of 2015 to the 5th of july-2023. EJNMMI = European Journal of Nuclear Medicine and Molecular Imaging.

Author	Publications	Citations
Journal of Nuclear Medicine	55	3920
Clinical Nuclear Medicine	46	576
EJNMMI[1]	43	1898
EJNMMI Research	14	436
Prostate	12	117
Cancers	9	51
European Urology	9	311
Nuklearmedizin	8	135
Theranostics	8	292
Annals of Nuclear Medicine	7	34
Frontiers in Oncology	7	27
Nuclear Medicine and Molecular Imaging	7	17
Oncotarget	6	469
European Urology Focus	5	55
Journal of Nuclear Medicine Technology	5	4
Nuclear Medicine Communications	5	58
Urologe	5	37
Seminars in Nuclear Medicine	4	204
British Journal of Radiology	4	187
European Urology Oncology	4	131
Diagnostics	4	119
Medical Physics	4	22

In terms of citation count, the Journal of Nuclear Medicine garnered the highest number of citations (n = 3920), trailed by the European Journal of Nuclear Medicine and Molecular Imaging (n = 1898), the New England Journal of Medicine (n = 579), and Clinical Nuclear Medicine (n = 576). Afterwards, a comprehensive total of 469 citations was identified for the Oncotarget Journal (▶ **Table 6**).

Research Focus

Of 2920 keywords, 98 met the threshold of minimum 40 occurrences. The tope occurring keywords were retrieved after excluding the nonspecific keywords and the duplicates such as “human”, “male”, “lutetium”, and ”lutetium 177” (▶ **Table 7**).

Three clustered groups were visualized when assessing the top specific keywords that represents a field of interest when using [177Lu]Lu-PSMA in prostate cancer. Cluster number one is prostate cancer diagnosis, include items such as: “castration-resistant prostate cancer”, “prostate specific antigen”, “Positron Emission Tomography-Computed Tomography”, “cancer staging”, and “tumor volume”. Cluster number 2 is related to the systemic therapies for prostate cancer, includes keywords such as: “Enzalutamide”, “Docetaxel”, “Cabazitaxel”, and “Abiraterone”. Cluster number 3 is related to the side effects associated with [^{177}Lu]Lu-PSMA treatment in prostate cancer. It includes items such as: “drug safety”, “drug efficacy”, “xerostomia”, “thrombocytopenia”, “anemia”, and “fatigue”. This was visually represented along with the top occurred keywords and their interconnections (▶ **Fig. 3**).

Most Cited Documents

The article titled “Lutetium-177-PSMA-617 for mCRPC,” authored by O. Sartor et al., has received an impressive 579 citations, demonstrating its prominence in the academic community [23]. The year 2021 saw the publication of this notable work in the esteemed New England Journal of Medicine. Importantly, a study led by Rahbar K. et al., titled “German multicenter study investigating

▶ **Table 6** Top contributing journals table, ranked by citations. The data were extracted from the start of 2015 to the 5th of july-2023. EJNMMI = European Journal of Nuclear Medicine and Molecular Imaging.

Author	Documents	Citations
Journal of Nuclear Medicine	55	3920
EJNMMI[1]	43	1898
New England Journal of Medicine	2	579
Clinical Nuclear Medicine	46	576
Oncotarget	6	469
EJNMMI Research	14	436
European Urology	9	311
Theranostics	8	292
Radiographics	1	202
Seminars in Nuclear Medicine	4	197
Journal of Medical Radiation Sciences	1	195
British Journal of Radiology	4	179
Journal of Urology	3	147
Nuklearmedizin	8	135
European Urology Oncology	4	127
Molecular Imaging	1	121
Prostate	12	117
BJU International	3	115
Clinical Genitourinary Cancer	1	115
Diagnostics	4	114

177Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients," has received 544 citations [24]. In 2017, this research work was published in the esteemed Journal of Nuclear Medicine. In addition, an article by Kratochwil C. et al. entitled "PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with 177Lu-labeled PSMA-617" has garnered 405 citations [25]. In 2016, this significant contribution was published in the Journal of Nuclear Medicine. The top 10 cited articles have been examined to show their imminent contribution to literature in this field (▶ **Table 8**).

Altmetric Attention Scores

According to the altmetric database, "Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer" published in New England Journal of Medicine in 2021 has received the highest altmetric attention score (n = 763) [23]. This was followed by "Developing a Patient-Reported Outcome Measure for Radionuclide Therapy for Prostate Cancer" published in Journal of Nuclear Medicine in 2023 (n = 249) [26], and "PSMA-Targeted Radionuclide Therapy of Metastatic Castration-Resistant Prostate Cancer with 177Lu-Labeled PSMA-617" published in Journal of Nuclear Medicine in 2016 (n = 183) [25]. It's noteworthy that the top 7 journal articles have received an overall altmetric score exceeding 100 (▶ **Table 9**).

Citations and altmetric scores were studied and a significant moderate correlation was found between the number of citations and altmetric scores ($p < 0.001$, rho = 0.469).

Discussion

Prostate cancer constitutes a significant source of morbidity in men on a global scale, necessitating a comprehensive expansion of our knowledge regarding the underlying disease mechanisms [2]. Such expansion is crucial to enhance the diagnosis of aggressive tumors and foster the development of more efficacious therapeutic approaches [2]. Recent studies have firmly established that the utilization of [^{177}Lu]Lu-PSMA has led to notable improvements in overall survival and a delayed progression based on imaging assessments among patients diagnosed with prostate cancer [23].

In our study, we aimed to offer a comprehensive global perspective on the utilization of [^{177}Lu]Lu-PSMA therapy in prostate cancer and assess the significance of published literature in this field. To our knowledge, there is a lack of existing bibliometric and altmetric studies specifically focusing on [^{177}Lu]Lu-PSMA therapy in prostate cancer.

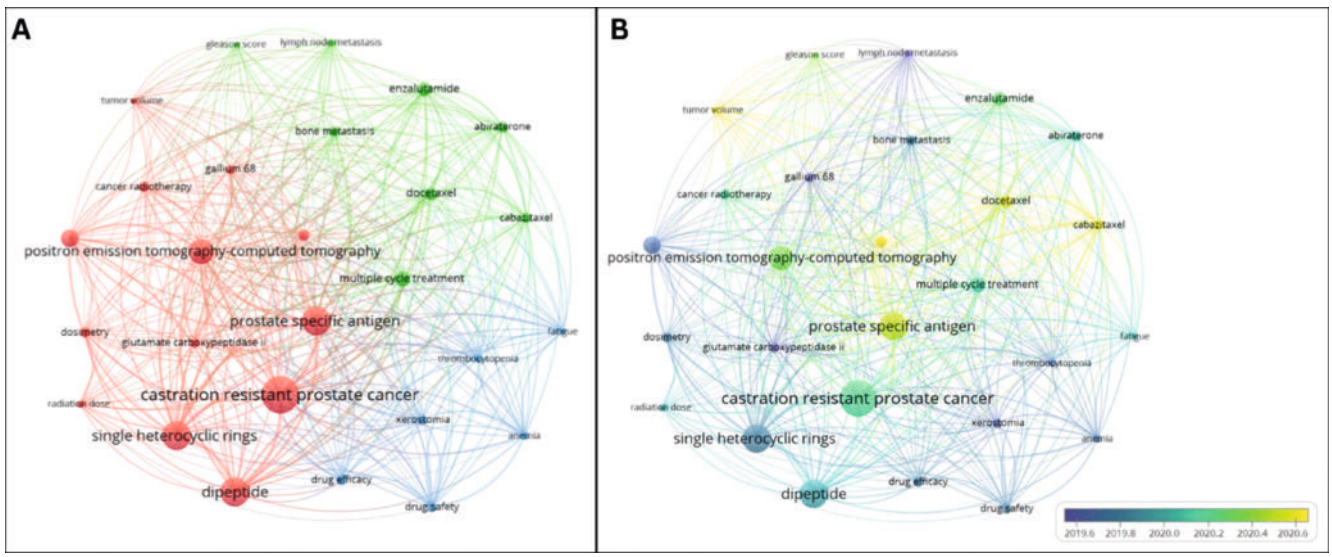
Our bibliometric analysis encompasses a total of 466 relevant articles from the start of January 2015 to 5th of July 2023. A noticeable upward trajectory in publications related to [^{177}Lu]Lu-PSMA therapy has been observed since 2015, signifying a growing interest in the utilization of this innovative radioligand therapy. The peak in publication output was reached in 2021; however, a slight decrease in the number of articles was observed in subsequent years. Notably, this decline coincided with the Federal Drug Agency (FDA) approval of [^{177}Lu]Lu-PSMA-617 (Pluvicto) in March 2022 as well as the rise of [^{177}Lu]Lu-PSMA research output in the United States during the same year [27].

In addition, Germany emerges as the leading contributor, with 188 articles and 7646 citations. Following closely, the United States and Australia secure the second and third positions, respectively, with 97 and 50 papers, as well as 2487 and 2086 citations. This notion finds support in the origin of PSMA-617, which can be traced back to its initial development by the German Cancer Research Center and University Hospital Heidelberg in Germany [27].

The articles that received the highest number of citations in early 2015 discussed first proof-of-concept human studies and pre-therapeutic dosimetry [28]. The first original work on this subject was published in the same year [29]. Subsequently, there was a shift towards investigating the targeting of mCRPC and the evaluation of associated side effects in 2016 [25]. In 2017, the emphasis shifted to comparing the safety and effectiveness of [^{177}Lu]Lu-PSMA with other third-line systemic therapies for mCRPC [24]. This was followed by studies in 2019 that explored the correlations between pre-treatment imaging, overall tumor dosage, and treatment outcomes [30], and a subsequent survival analysis in 2021 [31]. More recently, researchers have begun comparing the integration of PSMA-targeted therapies with standard

▶ **Table 7** Highest occurring keywords.

Keywords	Occurrences	Keywords	Occurrences
Castration Resistant Prostate Cancer	260	Drug Safety	72
Prostate Specific Antigen	201	Dosimetry	70
Dipeptides	198	Gallium 68	67
Single Heterocyclic Rings	197	Procedures	67
Positron Emission Tomography-Computed Tomography	173	Xerostomia	65
Pathology	136	Antineoplastic Agent	64
Metastatic Castration Resistant Prostate Cancer	128	Glutamate Carboxypeptidase ii	64
Diagnostic Imaging	124	Thrombocytopenia	62
177Lu-psma-617	121	Anemia	61
Multiple Cycle Treatment	110	Cancer Chemotherapy	56
Enzalutamide	97	Radiation Dose	55
Docetaxel	94	Fatigue	50
Radioisotopes	94	Cancer Staging	48
Vipivotide Tetraxetan lutetium Lu 177	82	Lymph Node Metastasis	48
Abiraterone	79	Theranostics	46
Metabolism	78	Tumor Volume	44
Drug Efficacy	76	Androgen Deprivation Therapy	43



▶ **Fig. 3** (**A**) Network visualization of the top-occurred keywords and their interconnections, grouped into 3 clusters, each color represents a cluster of related items. Keywords included in the same cluster are displayed in the same color. Larger circles indicate that the keyword appears more frequently. The distance between the 2 circles shows the de-gree of connection between two keywords. (**B**) Overlay presentation of the top occurred keywords and their inter-connections across the years. The color of a term indicates the average publication year. A color bar is shown in the bottom right corner of the visualization, that indicate the publication years range.

treatment approaches to improve treatment effectiveness, as well as examining the predictive value of post-treatment [^{68}Ga]Ga-PSMA PET/CT and [^{18}F]Fluorodeoxyglucose PET/CT in patients with mCRPC [32, 33].

Our finding of "castration-resistant prostate cancer" being the most frequently occurring keyword and a research focus in [^{177}Lu]Lu-PSMA and prostate cancer studies, can be attributed to the limited approval of [^{177}Lu]Lu-PSMA therapy for patients specifically diagnosed with PSMA-positive mCRPC, particularly those

▶ **Table 8** Top 10 most cited articles. The data were extracted from the start of 2015 to the 5th of july-2023. NEJM = New England Journal of Medicine; JNM = Journal of Nuclear Medicine; JMIRS = Journal of Medical Radiation Sciences.

Author	Title	Year	Journal	Citations
Sartor O.	Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer	2021	NEJM[1]	579
Rahbar K.	German multicenter study investigating 177Lu-PSMA-617 Radioligand therapy in advanced prostate cancer patients	2017	JNM[2]	544
Kratochwil C.	PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with 177Lu-Labeled PSMA-617	2016	JNM	405
Weineisen M.	68Ga-and 177Lu-labeled PSMA I and T: Optimization of a PSMA-targeted theranostic concept and first proof-of-concept human studies	2015	JNM	364
Baum R.P.	177Lu-labeled prostate-specific membrane antigen radioligand therapy of metastatic castration-resistant prostate cancer: Safety and efficacy	2016	JNM	356
Kratochwil C.	Targeted a-therapy of metastatic castration-resistant prostate cancer with 225Ac-PSMA-617: Dosimetry estimate and empiric dose finding	2017	JNM	296
Hofman M.S.	Prostate-specific membrane antigen PET: Clinical utility in prostate cancer, normal patterns, pearls, and pitfalls	2018	Radiographics	202
Ahmadzadehfar H.	Therapeutic response and side effects of repeated radioligand therapy with 177Lu-PSMA-DKFZ-617 of castrate-resistant metastatic prostate cancer	2016	Oncotarget	202
Violet J.	Dosimetry of 177Lu-PSMA-617 in metastatic castration-resistant prostate cancer: Correlations between pretherapeutic imaging and whole-body tumor dosimetry with treatment outcomes	2019	JNM	198
Emmett L.	Therapeutic response and side effects of repeated radioligand therapy with 177Lu-PSMA-DKFZ-617 of castrate-resistant metastatic prostate cancer	2017	JMIRS[3]	195

▶ **Table 9** Top 10 articles according to the altmetric attention score. AAS = Altmetric Attention Score.

Title	AAS[1]	Journal	Year
Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer	763	New England Journal of Medicine	2021
Developing a Patient-Reported Outcome Measure for Radionuclide Therapy for Prostate Cancer	249	Journal of Nuclear Medicine	2023
PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with 177Lu-Labeled PSMA-617	183	Journal of Nuclear Medicine	2016
The use of Lutetium-177 PSMA radioligand therapy with high dose rate brachytherapy for locally recurrent prostate cancer after previous definitive radiation therapy: a randomized, single-institution, phase I/II study (ROADSTER).	134	BMC Cancer	2023
Nomograms to predict outcomes after 177Lu-PSMA therapy in men with metastatic castration-resistant prostate cancer: an international, multicentre, retrospective study	130	The Lancet Oncology	2021
Theranostic radiopharmaceuticals: Established agents in current use	112	British Journal of Radiology	2018
German multicenter study investigating 177Lu-PSMA-617 Radioligand therapy in advanced prostate cancer patients	109	Journal of Nuclear Medicine	2017
Prostate-specific membrane antigen ligands for imaging and therapy	82	Journal of Nuclear Medicine	2017
Targeted a-therapy of metastatic castration-resistant prostate cancer with 225Ac-PSMA-617: Dosimetry estimate and empiric dose finding	80	Journal of Nuclear Medicine	2017
Novel Framework for Treatment Response Evaluation Using PSMA PET/CT in Patients with Metastatic Castration-Resistant Prostate Cancer (RECIP 1.0): An International Multicenter Study	79	Journal of Nuclear Medicine	2022

who have undergone prior treatment modalities [27]. However, in a recent prospective pilot study involving ten patients diagnosed with low-volume Hormone-Sensitive Metastatic Prostate Cancer, [^{177}Lu]Lu-PSMA demonstrated feasibility and safety as a treatment modality [34]. These findings highlight the importance of conducting additional trials to reassess the effectiveness of [^{177}Lu]Lu-PSMA therapy at various stages of the disease, including in low-volume metastatic disease, and its potential role in hormone-sensitive prostate cancer [34].

Another rising research focus was [^{177}Lu]Lu-PSMA side effects, such as xerostomia, thrombocytopenia, anemia, and fatigue, which were from the [^{177}Lu]Lu-PSMA treatment-related toxicity occurring up to 12 weeks after treatment cessation and were self-limiting and not affecting quality of life [30]. These findings were further substantiated by another study conducted in hormone-sensitive prostate cancer patients, where no treatment-related adverse events affecting laboratory parameters such as hematology, kidney function, or liver function were observed during the weekly blood evaluations of all ten patients [34].

The article with the highest citation was "Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer" by Sartor O. et al., published in the New England Journal of Medicine in 2021 [23]. Along with other top-cited articles, this highlights that the field of mCRPC has emerged as a prime domain for the development of this radioligand therapy [10, 23]. Despite significant progress, there are still numerous unresolved inquiries regarding [^{177}Lu]Lu-PSMA-617. These include determining the optimal dosage and administration schedule, refining selection criteria based on imaging outcomes, assessing the role of predictive biomarkers such as PSMA uptake, ensuring long-term safety, and evaluating the efficacy of combination therapy alongside standard of care treatments [35].

Our study findings indicate that [^{177}Lu]Lu-PSMA research outcomes focused on mCRPC; still, other studies debate whether there is potential for exploring PSMA radioligand therapy in specific solid cancers such as salivary gland cancer, glioblastoma, thyroid cancer, liver cancer, and clear cell renal cell cancer, where PSMA expression is detected on tumor cells [36].

In addition, we have provided current altmetric data insights, primarily derived from social media platforms, news sources, policy documents, and blogs. Consequently, this data primarily reflects the impact of individual users rather than that of professional researchers. This can explain the moderate correlation between altmetric score and citation numbers. Nonetheless, it is advisable to consider altmetric values and standard bibliometric analyses as complementary factors in order to comprehensively assess the overall impact of articles.

Similar to other bibliometric and altmetric studies, our research has some limitations. Specifically, our search was conducted exclusively on the Scopus database, without including the Web of Science Core Collection or Google Scholar potentially resulting in the omission of some articles on prostate cancer using this approach. However, Scopus include other search engines such as Embase and Cochrane library, offers extensive coverage across multiple disciplines and is able to generate a paramount volume of relevant publications when used in bibliometric analysis [37].

Conclusion

The surge in attention towards PSMA-based radioligand therapy for prostate cancer can be attributed to the significant rise in the quantity of published works and citations on this subject since 2015, emphasizing the potential advantages of this treatment with minimal toxic side effects. This bibliometric and altmetric analyses offer a comprehensive summary of the current research output and key areas of interest in this field. Moreover, this review enhances the existing research on [^{177}Lu]Lu-PSMA in prostate cancer by offering bibliometric and altmetric analyses, thereby providing valuable references for scholars and policymakers in this domain.

Conflict of Interest

The authors declare that they have no conflict of interest.

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