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Research

Trends in focal therapy for localized prostate cancer: a bibliometric analysis from 2014 to 2023

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Abstract
Focal therapy, a minimally invasive strategy for localized prostate cancer, has been widely employed in the targeted treatment of localized prostate cancer in recent years. We analyzed 1312 relevant papers from the last decade using Web of Science Core Collection data. Our analysis covered countries, institutions, journals, authors, keywords, and references to offer a multifaceted perspective on the development of this field. The U.S. led in publications, contributing over half of the top 10 institutions. Emberton, M from University College London was the most published and cited author. "EUROPEAN UROLOGY" was the top journal by impact factor in 2022. Analysis of references and keywords suggests the prevalence of brachytherapy-related research, while high-intensity focused ultrasound (HIFU), cryotherapy, and irreversible electroporation (IRE) are emerging as new research focuses. Consequently, more high-quality evidence is necessary to evaluate the long-term effectiveness and safety of these novel therapeutic methods.

Keywords Focal therapy · Prostate cancer · High-intensity focused ultrasound · Cryotherapy · Irreversible electroporation · Bibliometric analysis

1 Introduction

For localized prostate cancer (PCa), the standard of care hinges on life expectancy and typically involves active surveillance (AS) or watchful waiting (WW). Additionally, clinicians often consider radical prostatectomy (RP) for intermediate-risk PCa patients [1], despite it may result in inevitable impairment of genitourinary function such as erectile dysfunction and urinary incontinence [2–4]. Focal therapy (FT) is a minimally-invasive procedure that aims to reduce toxicity and improve functional outcomes compared to radical treatment options [1]. Nevertheless, research over the past few decades has demonstrated that FT struggle to match the oncological outcomes of radical treatment, including biochemical recurrence (BCR), cancer-specific survival (CSS), metastasis-free survival (MFS) and overall survival (OS) [5–7]. FT is categorized based on various energy sources, including high-intensity focused ultrasound (HIFU), cryotherapy, photodynamic therapy (PDT), laser interstitial thermotherapy (LITT), brachytherapy, irreversible electroporation (IRE), and radiofrequency ablation (RFA) [6, 8, 9].

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Bibliometrics is a novel method that enables the evaluation of research outcomes, shedding light on research trends in specific sectors and serving as a valuable reference for clinical medical research. The approach provides researchers with both qualitative and quantitative insights into literature [10, 11], facilitating the identification of research hotspots in a given field. In this study, we employ the innovative methods to assess the research status of focal therapy in prostate cancer treatment over the past decade, as well as figure out the research focus and emerging topics.

2 Materials and methods

2.1 Search strategy

Eligible studies were searched in the Web of Science Core Collection (WoSCC) on September 15, 2023. We retrieved articles using search strategy: TI = ((prostat* AND (cancer* OR carcinoma* OR malignan* OR tumor OR tumors OR tumour* OR neoplas* OR intraepithelial OR adenocarc*)) AND ("Ablation Techniques" OR "Photochemotherapy" OR "Brachytherapy" OR Ablati* OR Brachytherap* OR Cryoablat* OR Cryotherap* OR Cryosurg* OR focal OR hemiablati* OR HIFU OR "high-intensity focused ultrasound" OR IRE OR "irreversible electroporation" OR "laser interstitial thermother*" OR LITT OR PDT OR "photodynamic therap*" OR RFA OR "therapeutic ultrasound" OR TULSA)) AND AB = ((prostat* AND (cancer* OR carcinoma* OR malignan* OR tumor OR tumors OR tumour* OR neoplas* OR intraepithelial OR adenocarc*)) AND ("Ablation Techniques" OR "Photochemotherapy" OR "Brachytherapy" OR Ablati* OR Brachytherap* OR Cryoablat* OR Cryotherap* OR Cryosurg* OR focal OR hemiablati* OR HIFU OR "high-intensity focused ultrasound" OR IRE OR "irreversible electroporation" OR "laser interstitial thermother*" OR LITT OR PDT OR "photodynamic therap*" OR RFA OR "therapeutic ultrasound" OR TULSA)). We have restricted our inclusion criteria to articles and review articles based on the bibliometric guideline [12], and the publication dates were limited to between January 1, 2014, and September 15, 2023. Selecting 2014 as the cut-off date was inspired by the findings of Valerio et al. [9], who highlighted the emergence of novel focal treatment methods after 2014, such as IRE. Two independent investigators (Zhi-Yu Xia and Si-Han Zhang) evaluate comprehensively each article based on abstract and title to ensure that only relevant articles were included in our analysis. In cases where there was any uncertainty or disagreement regarding the inclusion of an article, a third reviewer (Qi-Dong Xia) was engaged to provide the final decision. This process was designed to minimize the risk of including unrelated in our study and to maximize the validity of our findings. There is no language restriction on the retrieved literature.

2.2 Data collection

The retrieved literature information determined through the search query was downloaded from WoSCC on September 15, 2023. The literature details, including authorship, title, abstract, source, sponsorship, address, citation count, accession number, document type, and references cited, are available for download in both TXT and BibTex formats.

2.3 Statistical analyses

We analyzed the bibliometric data using VOSviewer (version 1.6.19), CiteSpace (version 6.2.R4), and bibliometrix package (version 4.1.3; https://cran.r-project.org/web/packages/bibliometrix/) based on R language (version 4.3.1). CiteSpace and VOSviewer are both powerful tools for creating collaborative maps. Each of them has its unique strengths, which can complement the other. CiteSpace employs a set-theoretic approach in standardizing data for measuring knowledge unit similarity. Leveraging similarity algorithms, it produces insightful time zone and timeline views, offering a lucid depiction of knowledge evolution over time and the historical trajectory of literature within specific clusters. This allows us to gain a better understanding of the development process and trends within a given field [13, 14]. On the other hand, VOSviewer opts for a probability-based approach to data normalization and offers multiple visualization views across various fields such as keywords, co-institution, and co-authorship. These include network visualization, overlay visualization, and density visualization, each of which features easy mapping and appealing image representation [15, 16]. Additionally, the bibliometrix package was executed on the R-studio to assess the quality of included literature, and we categorized them into "Excellent", "Good", "Acceptable", and "Poor" by calculating the missing proportion of essential components.

3 Results

3.1 Characteristics of recruited studies

A total of 1,312 documents were retrieved by PRISMA 2020 flow diagram [17] (Fig. 1), involving 67 countries/regions, 1,792 institutions, 241 journals, and 6,569 authors contributing to the publication of relevant literature. The majority of the documents were published in English (1272, 96.9%), followed by Spanish (15, 1.1%), French (14, 1.0%), and German (11, 0.8%). The proportion of missing essential components is within an acceptable range (Table 1). Figure 2 illustrates the annual publication count and the publishing trends of original articles and reviews over the past decade.

3.2 Leading countries/regions

Publications come from a total of 67 countries/regions, with 34 of them having published five or more papers. Table 2 summarizes the publishing landscape of the top 10 countries/regions over the past decade. The United States leads with 441 publications, followed by Canada (164), England (159), Japan (152), and France (136). In terms of total citations, the top five countries or regions are the United States (8541 citations), England (4094 citations), Canada (3388 citations), France (2750 citations), and the Netherlands (2541 citations), with the Netherlands having the highest average

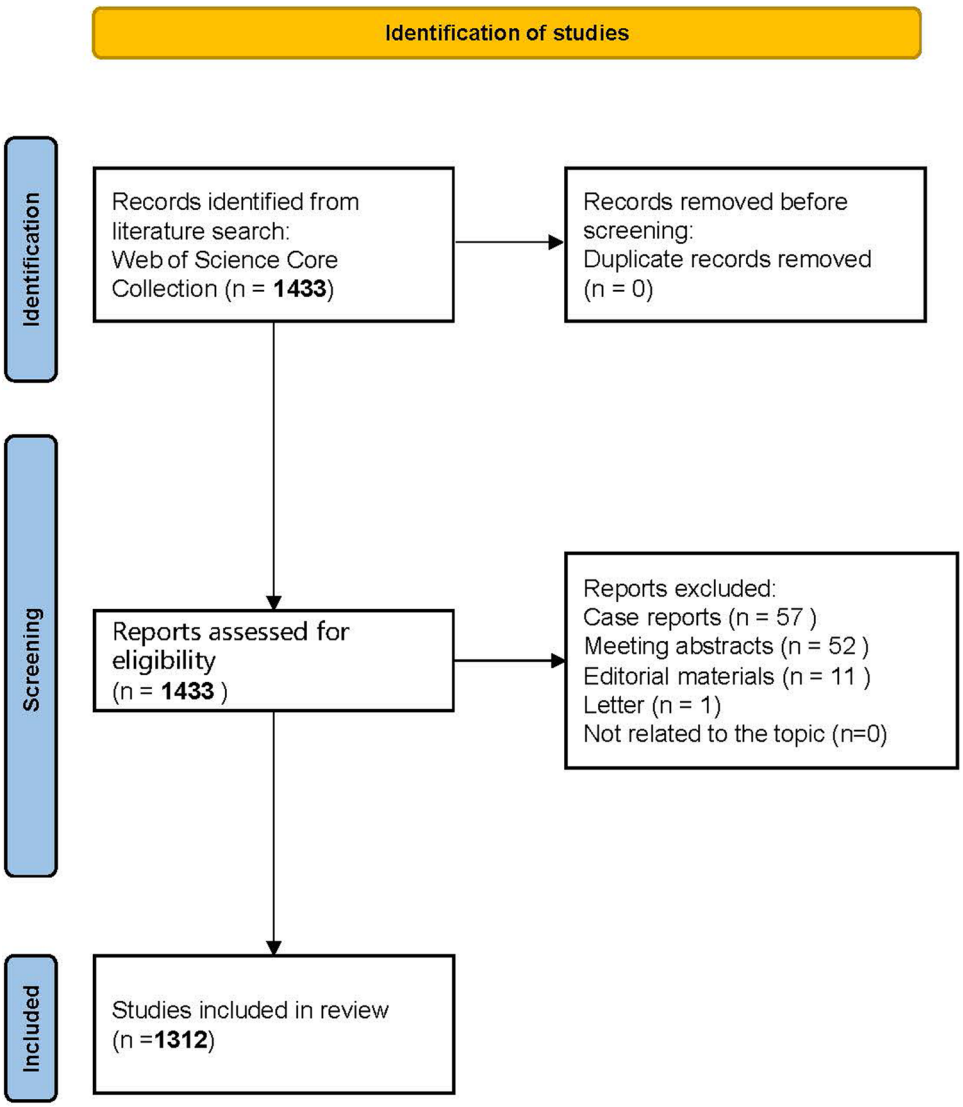


Fig. 1 The inclusion and exclusion of publications on focal therapy

Table 1 The quality assessment of 1312 included studies

Metadata	Description	Missing Counts	Missing %	Status
AB	Abstract	0	0	Excellent
AU	Author	0	0	Excellent
CR	Cited References	0	0	Excellent
DT	Document Type	0	0	Excellent
SO	Journal	0	0	Excellent
LA	Language	0	0	Excellent
NR	Number of Cited References	0	0	Excellent
PY	Publication Year	0	0	Excellent
WC	Science Categories	0	0	Excellent
TI	Title	0	0	Excellent
TC	Total Citation	0	0	Excellent
C1	Affiliation	1	0.08	Good
RP	Corresponding Author	1	0.08	Good
DI	DOI	31	2.36	Good
ID	Keywords Plus	53	4.04	Good
DE	Keywords	217	16.54	Acceptable

Excellent: No missing essential components; Good: ≤ 10% missing essential components. Acceptable: ≤ 20% missing essential components. Poor: > 20% missing essential components

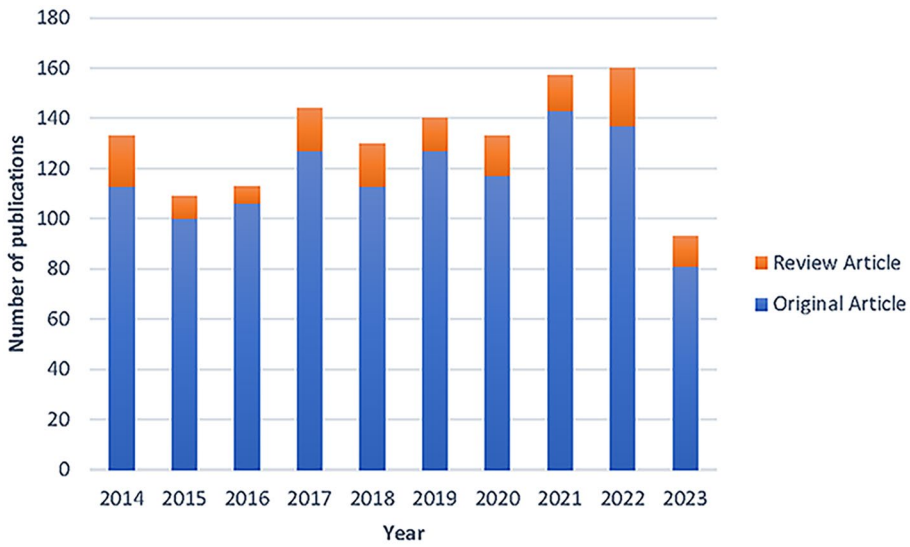


Fig. 2 Annual number of publications on focal therapy

citations. Collaborative networks among countries/regions are conducted using VOSviewer software (Fig. 3), where the lines between nodes represent collaborative relationships. Thicker lines indicate stronger relationships, reflecting higher total link strength (TLS).

3.3 Active institutions and authors

A total of 1792 institutions actively engaged in the application of focal therapy to prostate cancer, including 186 institutions with ≥ 5 publications. Table 3 outlines the publications of the top 10 institutions in the past 10 years, with the top 3 institutions being "University of Toronto", "University College London" and "Memorial Sloan Kettering Cancer

Table 2 The top 10 most productive countries in terms of focal therapy research

Rank	Country	Publications n (%)	Total citations	Average citations	Centrality
1	United States	441 (29.6)	8541	19.37	0.38
2	Canada	164 (11.0)	3388	20.66	0.52
3	England	159 (10.7)	4094	25.75	0.41
4	Japan	152 (10.2)	1220	8.03	0.13
5	France	136 (9.1)	2750	20.22	0.43
6	Germany	131 (8.8)	2100	16.03	0.31
7	Netherlands	96 (6.4)	2541	26.47	0.11
8	China	78 (5.2)	660	8.46	0.08
9	Italy	71 (4.8)	1134	15.97	0.08
10	Spain	64 (4.3)	736	11.50	0.03

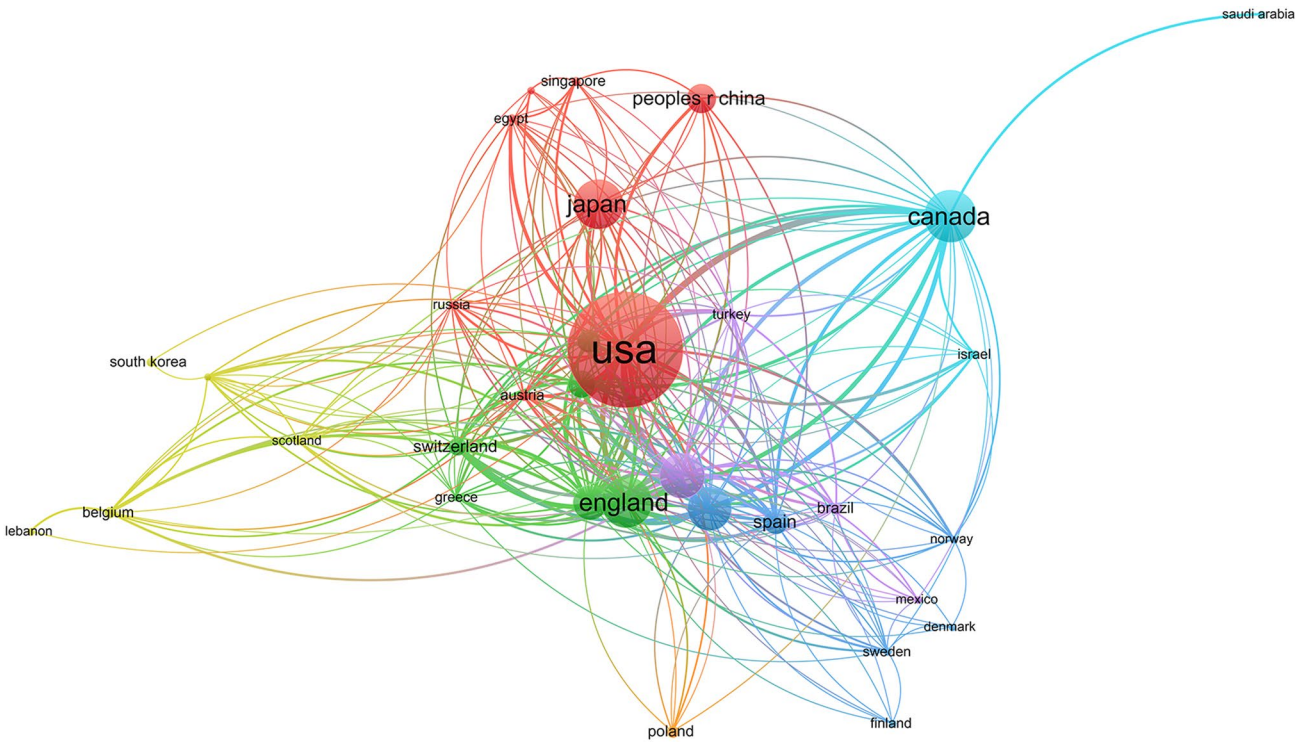


Fig. 3 The clustering of collaboration among countries/regions. The nodes represent countries/regions. The size of nodes represents the number of published documents, the more published documents, the larger the nodes. The connection between nodes represents the cooperation between countries/regions, the density of the lines represents the Total Link Strength (TLS). Thicker lines indicate stronger relationships, reflecting a higher TLS

Center", contributing 69, 63 and 36 publications respectively. Utilizing the VOSviewer software, the collaborative network map was generated for institutions with ≥ 5 publications (Fig. 4), and the top 3 institutions with TLS were the "University College London", "University of Toronto" and the "Memorial Sloan Kettering Cancer Center." Collaborative centrality is a measure of node importance, and the institutions with high centrality (> 0.1) such as "University of Toronto" (0.18), "University College London" (0.18), and "Memorial Sloan Kettering Cancer Center" (0.20) play a pivotal role in this field.

The field of focal therapy for prostate cancer involved 6930 authors and 11,603 co-cited authors. Table 4 presents the top 10 most prolific authors, with Emberton, M. leading with the highest number of publications (41), followed by Ahmed, HU (38) and Sánchez-Salas, RE (24), and Emberton, M. of the University College London shows the highest H-index of 79. Figure 4B displays the annual output of the top 10 most productive authors. The network of collaboration between authors and the mapping of the co-citation of authors are shown in Fig. 4.

Table 3 The top 10 most productive institutions in terms of focal therapy research

Rank	Institution	Country	Publications n (%)	Total citations	Average citations	Centrality
1	University of Toronto	United States	69 (19.3)	2127	30.83	0.18
2	University College London	England	63 (17.6)	2145	34.05	0.18
3	Memorial Sloan Kettering Cancer Center	United States	36 (10.1)	1039	28.86	0.20
4	The University of Texas MD Anderson Cancer Center	United States	32 (8.9)	618	19.31	0.09
5	University of California, Los Angeles	United States	31 (8.7)	740	23.87	0.02
6	Imperial College London	England	27 (7.5)	707	26.19	0.08
7	University Medical Center Utrecht	Netherlands	27 (7.5)	550	20.37	0.02
8	Imperial College Healthcare NHS Trust	England	25 (7.0)	652	26.08	0.05
9	University of California, San Diego	United States	24 (6.7)	326	13.58	0.05
10	Institut Mutualiste Montsouris	French	24 (6.7)	223	9.29	0.08

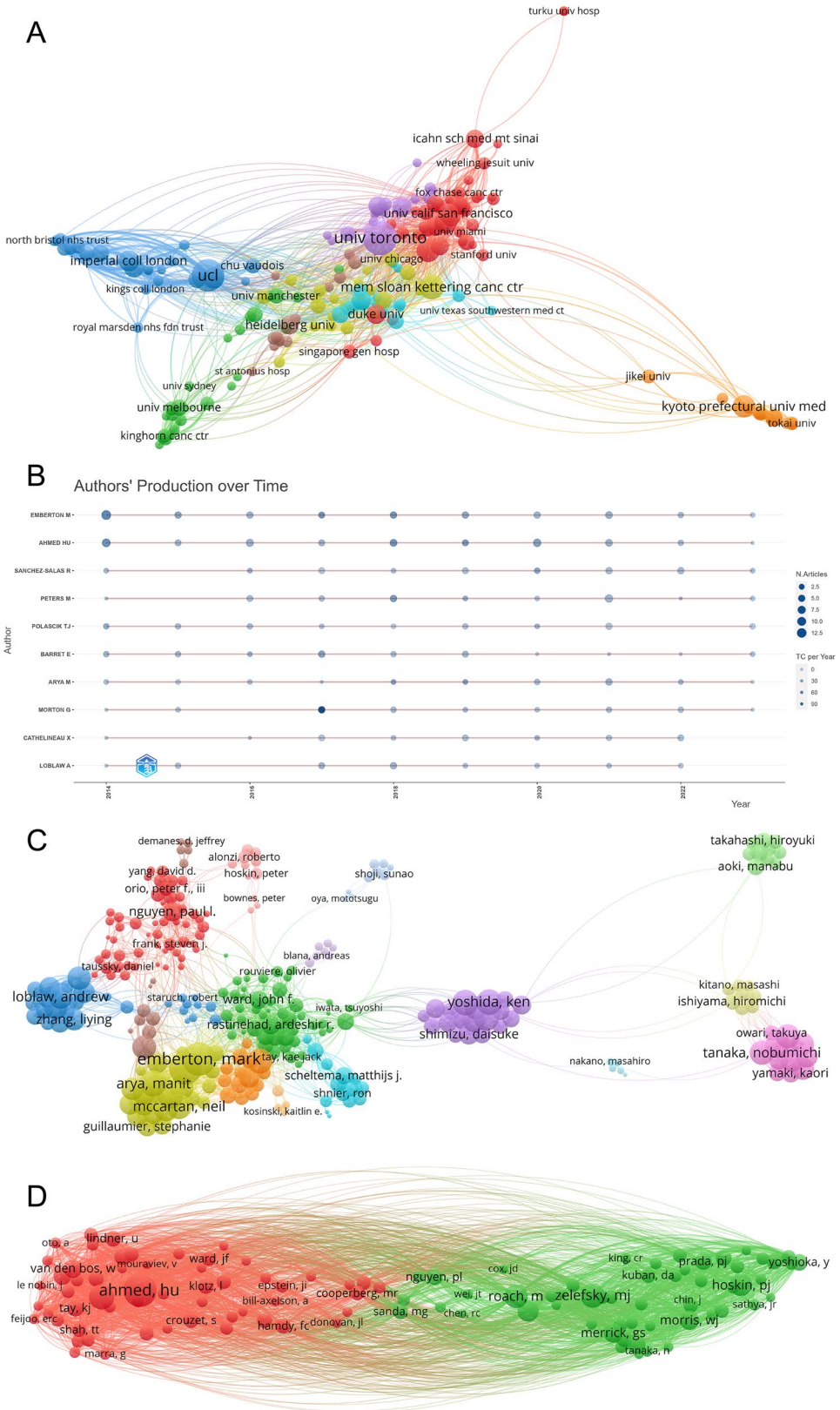


Fig. 4 The bibliometric analysis of active institutions and authors. **A** The clustering of collaboration among institutions. Nodes: Represent institutions. Node size indicates the number of published documents, with larger nodes representing a higher publication count. Lines: Represent collaborative relationships between institutions. Thicker lines indicate stronger relationships, reflecting a higher TLS. Arrows: Point towards institutions with a higher TLS, indicating the dominant institution in the collaboration; **B** annual output of the top 10 most productive authors; **C** the mapping of the co-citation of authors, and **D** the clustering of collaboration among authors

3.4 Core journals and references

Table 4 The top 10 most productive authors in terms of focal therapy research

Rank	Author	Institution	Country	Publications n (%)	Total Citations	Average ciations	H-index	Centrality
1	Emberton, M	University College London	England	41 (17.2)	1672	40.78	79	0.10
2	Ahmed, Hashim Uddin	Imperial College Healthcare NHS Trust	England	38 (15.9)	1417	37.29	59	0.08
3	Sánchez-Salas, Rafaël Ernesto	Université McGill	Canada	24 (10.0)	518	21.58	33	0.01
4	Peters, Max	University Medical Center Utrecht	Netherlands	23 (9.6)	543	23.61	19	0.01
5	Polascik, Thomas J	Duke Cancer Institute	United States	21 (8.8)	451	21.48	55	0.06
6	Nguyen, Paul L	Harvard Medical School	United States	19 (7.9)	508	26.74	66	0.12
7	Yoshida, Ken	Kansai Medical University	Japan	19 (7.9)	240	12.63	23	0.01
8	Barret, E	L'Institut Mutualiste Montsouris	France	18 (7.5)	748	41.56	40	0.04
9	Loblaw, Andrew	University of Toronto Faculty of Medicine	Canada	18 (7.5)	364	20.22	56	0.00
10	Morton, Gerard C	University of Toronto Faculty of Medicine	Canada	18 (7.5)	1048	58.22	39	0.00

Table 5 The top 10 core journals in terms of focal therapy research

Rank	Journal	Publications n (%)	Total citations	Average citations	2022 JCR category quartile	2022 IF
1	BRACHYTHERAPY	139 (26.0)	1585	11.40	Q3	1.9
2	RADIOTHERAPY AND ONCOLOGY	68 (12.7)	1223	17.99	Q2	5.7
3	Journal of Contemporary Brachytherapy	66 (12.4)	433	6.56	Q4	1.4
4	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	47 (8.8)	1635	34.79	Q1	7.0
5	BJU INTERNATIONAL	44 (8.2)	978	22.23	Q1	4.5
6	JOURNAL OF UROLOGY	43 (8.1)	1331	30.95	Q1	6.6
7	WORLD JOURNAL OF UROLOGY	42 (7.9)	700	16.67	Q2	3.4
8	UROLOGIC ONCOLOGY-SEMINARS AND ORIGINAL INVESTIGATIONS	30 (5.6)	299	9.97	Q3	2.7
9	EUROPEAN UROLOGY	28 (5.2)	1844	65.86	Q1	23.4
10	INTERNATIONAL JOURNAL OF UROLOGY	27 (5.1)	151	5.59	Q3	2.6

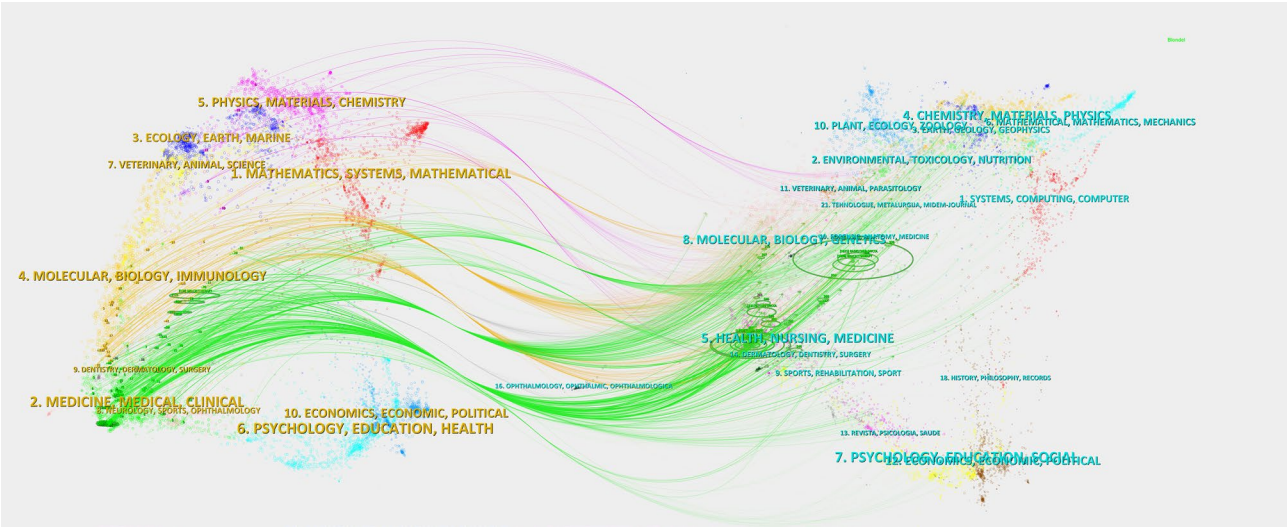


Fig. 5 The dual-map overlay of citing and citied journals publishing studies on focal therapy. Citing journals are on the left, cited journals are on the right, and lines represent the citation relationship. Two primary citation paths: publications in Health/Nursing/Medicine journals are predominantly cited by those in Medicine/Medical/Clinical journals. Publications in Molecular/Biology/Genetics journals are mostly cited by publications in Dentistry/Dermatology/Surgery journals

1312 studies were published in 241 journals, of which 61 journals published ≥ 5 volumes. The most productive journal was "Brachytherapy" (n = 139, 26.0%), followed by "Radiotherapy and Oncology" (n = 68, 12.7%) and "Journal of Contemporary Brachytherapy" (n = 66, 12.4%). Additionally, EUROPEAN UROLOGY garnered the highest number of citations at 1844 and achieved the highest impact factor in 2022 (23.4). The top three journals with average citations in the 2022 Journal Citation Reports (JCR) are Q1, and the top 10 journals collectively released 534 studies, constituting 40.7% of the overall publications, as detailed in Table 5. The dual-map overlay in Fig. 5 reveals intricate inter-domain connections between journals. The journals on the left are the citing journals, and the right side represents the cited journals, with lines indicating the citation relationships between them. Two primary citation paths were identified. Publications in Health/Nursing/Medicine journals were predominantly cited by those in Medicine/Medical/Clinical journals. On the other hand, publications in journals of Molecular/Biology/Genetics were mostly cited by publications in journals of Dentistry/Dermatology/Surgery.

There are a total of 17,950 references, among which 279 references have been cited ≥ 20 times. The top 10 most cited references are presented in Table 6. The most cited reference is the work titled "Defining biochemical failure following

radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: Recommendations of the RTOG-ASTRO Phoenix Consensus Conference" authored by Roach et al. (270 citations) [18]. Following this is the publication by Morris et al., titled "Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy" (133 citations) [19], and the paper by Hoskin et al., titled "Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localized prostate cancer" (132 citations) [20]. Figure 6A shows the top 25 references with the strongest citation bursts, with 11 of them still frequently cited, suggesting that the exploration of focal therapy in prostate cancer will remain a research hotspot in the coming years. Figure 6B displays the clustering of the top 50 cited-references.

3.5 Analysis of keywords

There are a total of 2970 keywords, with 110 keywords appearing ≥ 20 times. Table 7 presents the basic details of the top 10 keywords in terms of frequency. The top 50 keywords co-occurrence network map was generated using VOSviewer (Fig. 7A), where each color represents a cluster. The keywords are categorized into three clusters:

- Red cluster: Focuses on radiotherapeutic treatment, involving keywords such as brachytherapy, dose-rate brachytherapy, rate interstitial brachytherapy, etc.
- Green cluster: Active therapeutic options outside radiotherapy, featuring keywords such as intensity focused ultrasound, cryosurgery, irreversible electroporation, radical prostatectomy, etc.
- Blue cluster: Prognosis for patients with prostate cancer, involving keywords such as recurrence, failure, biochemical recurrence, etc.

Figure 7B presents an overlay network map of keywords, illustrating the evolving trends in keyword usage over time. Yellow nodes represent emerging keywords, signifying potential research hotspots. The graph indicates that in the past years, keywords such as "intensity focused ultrasound", "dose-rate brachytherapy", "irreversible electroporation", "ASCENDE-RT", and "focal therapy" have frequently appeared and may become future research hotspots.

4 Discussion

This study employed three bibliometric analysis tools, including VOSviewer, CiteSpace, and bibliometrix package based on R language, to conduct a visual analysis. We elaborate on the research status, development trend, and future research hotspots of focal therapy of PCa, offering researchers a better understanding of research dynamics.

The United States stands out with significantly higher publications compared to other countries/regions. Among the top 10 publishing institutions, 5 are based in the United States, underscoring the substantial contribution of the U.S. in the realm of localized PCa treatment. Notably, the University of Toronto leads in both the quantity of publications and collaborative centrality, highlighting its significant influence in this field and extensive cooperation with other institutions. Emberton, from the University College London, has been the most prolific in terms of publishing papers and citations over the last decade, coupled with the highest H-index. This underscores his remarkable contributions and exceptional influence in the field of localized PCa treatment. In the past decade, institutions and scholars in Europe and the United States have shown widespread interest in the focal treatment of PCa, possibly due to the higher detection rate of low-risk PCa in this region [21–23]. Focal treatment has potential, considering that it has less impact on genito-urinary function compared to surgical treatment for localized PCa.

The top five journals with the highest average citation rates are EUROPEAN UROLOGY (2022 IF = 23.4, JCR Q1), INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS (2022 IF = 7.0, JCR Q1), JOURNAL OF UROLOGY (2022 IF = 6.6, JCR Q1), RADIOTHERAPY AND ONCOLOGY (2022 IF = 5.7, JCR Q2), and WORLD JOURNAL OF UROLOGY (2022 IF = 3.4, JCR Q2). These journals are considered highly influential in the field. The citing journals predominantly belong to two areas (Health/Nursing/Medicine and Molecular/Biology/Genetics), mirroring the two primary fields of the journals being cited (Medicine/Medical/Clinical and Dentistry/Dermatology/Surgery). This implies that research in localized PCa treatment necessitates interdisciplinary collaboration.

The top 5 cited references all related to radiotherapy for PCa [2, 18–20, 24], suggesting that with the continuous development and progress of emerging treatment technologies such as image-guided radiation therapy [25–27], stereotactic

Table 6 The top 10 references on focal therapy with the highest number of citations

Rank	First author	Title	Journal	Year of publication	Total citations
1	Roach M	Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: Recommendations of the RTOG-ASTRO Phoenix Consensus Conference	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2006	270
2	Morris WJ	Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (the ASCENDE-RT Trial)	INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY BIOLOGY PHYSICS	2017	133
3	Hoskin PJ	Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer	RADIOTHERAPY AND ONCOLOGY	2012	132
4	D'Amico AV	Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer	JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	1998	120
5	Hamdy FC	10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer	NEW ENGLAND JOURNAL OF MEDICINE	2016	116
6	Valerio M	New and Established Technology in Focal Ablation of the Prostate: A Systematic Review	EUROPEAN UROLOGY	2017	111
7	Ahmed HU	Focal therapy for localised unifocal and multifocal prostate cancer: a prospective development study	LANCET ONCOLOGY	2012	104
8	Donaldson IA	Focal Therapy: Patients, Interventions, and Outcomes-A Report from a Consensus Meeting	EUROPEAN UROLOGY	2015	98
9	Guillaumier S	A Multicentre Study of 5-year Outcomes Following Focal Therapy in Treating Clinically Significant Nonmetastatic Prostate Cancer	EUROPEAN UROLOGY	2018	96
10	Valerio M	The Role of Focal Therapy in the Management of Localised Prostate Cancer: A Systematic Review	EUROPEAN UROLOGY	2014	93

A

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2014 - 2023
Hoskin PJ, 2012, RADIOTHER ONCOL, V103, P217, DOI 10.1016/j.radonc.2012.01.007, DOI	2012	14.64	**2014**	2017	
Ahmed HU, 2012, LANCET ONCOL, V13, P622, DOI 10.1016/S1470-2045(12)70121-3, DOI	2012	12.23	**2014**	2017	
Wilt TJ, 2012, NEW ENGL J MED, V367, P203, DOI 10.1056/NEJMoa1113162, DOI	2012	12.05	**2014**	2016	
Bahn D, 2012, EUR UROL, V62, P55, DOI 10.1016/j.eururo.2012.03.006, DOI	2012	11.69	**2014**	2017	
Grimm P, 2012, BJU INT, V109, P22, DOI 10.1111/j.1464-410X.2011.10827.x, DOI	2012	11.42	**2014**	2017	
Ahmed HU, 2011, J UROLOGY, V185, P1246, DOI 10.1016/j.juro.2010.11.079, DOI	2011	11.34	**2014**	2016	
Demanes DJ, 2011, INT J RADIAT ONCOL, V81, P1286, DOI 10.1016/j.ijrobp.2010.10.015, DOI	2011	9.31	**2014**	2016	
Yamada Y, 2012, BRACHYTHERAPY, V11, P20, DOI 10.1016/j.brachy.2011.09.008, DOI	2012	9.02	**2014**	2017	
Yoshioka Y, 2011, INT J RADIAT ONCOL, V80, P469, DOI 10.1016/j.ijrobp.2010.02.013, DOI	2011	8.9	**2014**	2016	
Valerio M, 2014, EUR UROL, V66, P732, DOI 10.1016/j.eururo.2013.05.048, DOI	2014	9.12	**2015**	2019	
Donaldson IA, 2015, EUR UROL, V67, P771, DOI 10.1016/j.eururo.2014.09.018, DOI	2015	9.45	**2016**	2019	
Ahmed HU, 2015, EUR UROL, V68, P927, DOI 10.1016/j.eururo.2015.01.030, DOI	2015	8.9	**2017**	2020	
Hamdy FC, 2016, NEW ENGL J MED, V375, P1415, DOI 10.1056/NEJMoa1606220, DOI	2016	16.85	**2018**	2021	
Mottet N, 2017, EUR UROL, V71, P618, DOI 10.1016/j.eururo.2016.08.003, DOI	2017	10.33	**2018**	2021	
Guillaumier S, 2018, EUR UROL, V74, P422, DOI 10.1016/j.eururo.2018.06.006, DOI	2018	20.52	**2019**	2023	
van der Poel HG, 2018, EUR UROL, V74, P84, DOI 10.1016/j.eururo.2018.01.001, DOI	2018	13.45	**2019**	2023	
Kishan AU, 2018, JAMA-J AM MED ASSOC, V319, P896, DOI 10.1001/jama.2018.0587, DOI	2018	11.13	**2019**	2023	
Shah TT, 2019, EUR UROL, V76, P98, DOI 10.1016/j.eururo.2018.12.030, DOI	2019	14.82	**2020**	2023	
Stabile A, 2019, BJU INT, V124, P431, DOI 10.1111/bju.14710, DOI	2019	12.86	**2020**	2023	
Morris WJ, 2017, INT J RADIAT ONCOL, V98, P275, DOI 10.1016/j.ijrobp.2016.11.026, DOI	2017	11.65	**2020**	2023	
Tourinho-Barbosa RR, 2020, J UROLOGY, V203, P320, DOI 10.1097/JU.0000000000000506, DOI	2020	9.5	**2020**	2023	
Oishi M, 2019, J UROLOGY, V202, P1188, DOI 10.1097/JU.0000000000000456, DOI	2019	8.79	**2020**	2023	
Morton G, 2020, RADIOTHER ONCOL, V146, P90, DOI 10.1016/j.radonc.2020.02.009, DOI	2020	10.64	**2021**	2023	
Lebastchi AH, 2020, EUR UROL, V78, P371, DOI 10.1016/j.eururo.2020.05.018, DOI	2020	10.53	**2021**	2023	
Widmark A, 2019, LANCET, V394, P385, DOI 10.1016/S0140-6736(19)31131-6, DOI	2019	9.65	**2021**	2023	

B

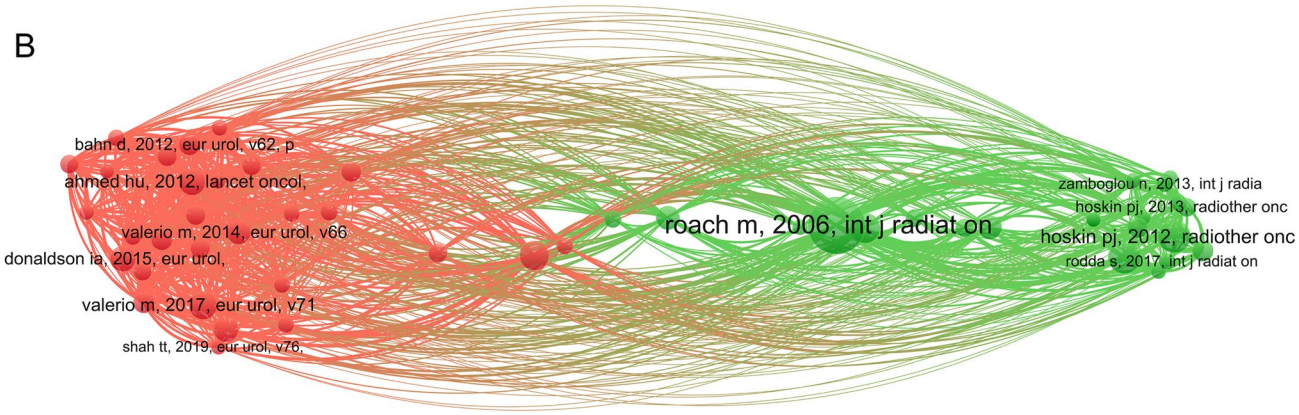


Fig. 6 The bibliometric analysis of co-cited references. **A** The top 25 references with the strongest citation burst. The red segments represent the periods when references burst out, and the longer the red segment, the more prolonged the duration of its popularity; **B** the clusters of top 50 references related to focal therapy on prostate cancer. Nodes: Represent references. Node size indicates the number of citations, with larger nodes representing a higher citation count

radiation therapy [28–30], and proton therapy [31–33], PCa radiation therapy has entered a new era of precision treatment. The precision radiation therapy aims to effectively eliminate tumor cells while minimizing damage to surrounding normal tissues, significantly enhancing the clinical efficacy of PCa radiation treatment [34, 35]. Notably, brachytherapy stands out as an additional curative treatment method for localized PCa, complementing external beam radiation therapy and radical prostatectomy. Its established effectiveness and minimal invasiveness make it an up-and-coming alternative to radical prostatectomy. This approach can find broad application in clinical practice, especially suitable for elderly PCa patients who cannot tolerate radical prostatectomy [19, 36]. For locally advanced PCa patients, consideration of

Table 7 The top 10 most common keywords

Rank	Keyword	Cluster	Occurrence
1	Prostate cancer	1	708
2	Brachytherapy	1	335
3	Radical prostatectomy	2	318
4	Radiotherapy	1	318
5	Focal therapy	2	275
6	Outcome	2	266
7	Radiation-therapy	1	242
8	Therapy	2	241
9	Men	2	219
10	External-beam radiotherapy	1	143

combining brachytherapy and hormonal therapy may have the potential to extend patient survival and improve quality of life [20, 37].

Through keyword clustering analysis, the top 50 keywords can be grouped into three categories: "Red cluster: Focuses on radiotherapeutic treatment," "Green cluster: Active therapeutic options outside radiotherapy," and "Blue cluster: Prognosis for patients with PCa." The green cluster primarily includes emerging local treatment methods for PCa, such as high-intensity focused ultrasound (HIFU), irreversible electroporation (IRE), and cryotherapy. According to the overlay network map of keywords, the number of papers involving the aforementioned three keywords experienced rapid growth during the period from 2019 to 2023. The HIFU, IRE, and cryotherapy may emerge as the primary directions for the future focal therapy of PCa.

High-Intensity Focused Ultrasound (HIFU) stands out as one of the most commonly employed local treatment modalities. During the procedure, an ultrasound probe is positioned within the rectum, measuring the prostate volume and creating images. Clinicians delineate therapeutic targets on these images and then deliver precise, focused ultrasound to the target cancer tissue via HIFU. Within 2 to 3 s, the cancer tissue temperature rapidly ascends to nearly 100 °C, inducing coagulative necrosis [38–40]. Between 2005 and 2020, a multi-institute 15-year analysis was conducted on 1379 patients from 13 UK centers [41]. The median age was 66 years (range 60–71 years), and the median PSA level was 6.9 ng/ml (range 4.9–9.4). Based on the D'Amico risk classification, 65% (896/1379) of patients had intermediate-risk cancer and 28% (386/1379) had high-risk cancer. The overall median follow-up duration was 32 months (range 17–58). The Kaplan–Meier 7-year freedom from biochemical failure (FFS) rate was 69% (95% CI 64%–74%). For intermediate-risk and high-risk cancers, the 7-year FFS rates were 68% (95% CI 62%–75%) and 65% (95% CI 56%–74%), respectively. However, despite these encouraging results, several challenges and limitations remain. Firstly, the long-term oncological outcomes of HIFU are still unclear. While the survival rates reported in another large retrospective study were impressive [42], with 99%, 97%, and 97% survival at 24, 60, and 96 months respectively, the rates of detection of clinically significant cancer after treatment increased over time, reaching 46% at 96 months. This suggests that while HIFU may be effective in the short term, its long-term oncological control remains uncertain. Furthermore, the precision and accuracy of HIFU treatment depend heavily on the ability of the operator to accurately target the tumor while minimizing damage to surrounding healthy tissue. This adds a level of complexity and potential variability to the treatment process. Together, long-term oncological outcomes, operator dependency, and the need for further research are all crucial factors that need to be taken into account to ensure the successful integration of HIFU into the armamentarium of PCa treatments.

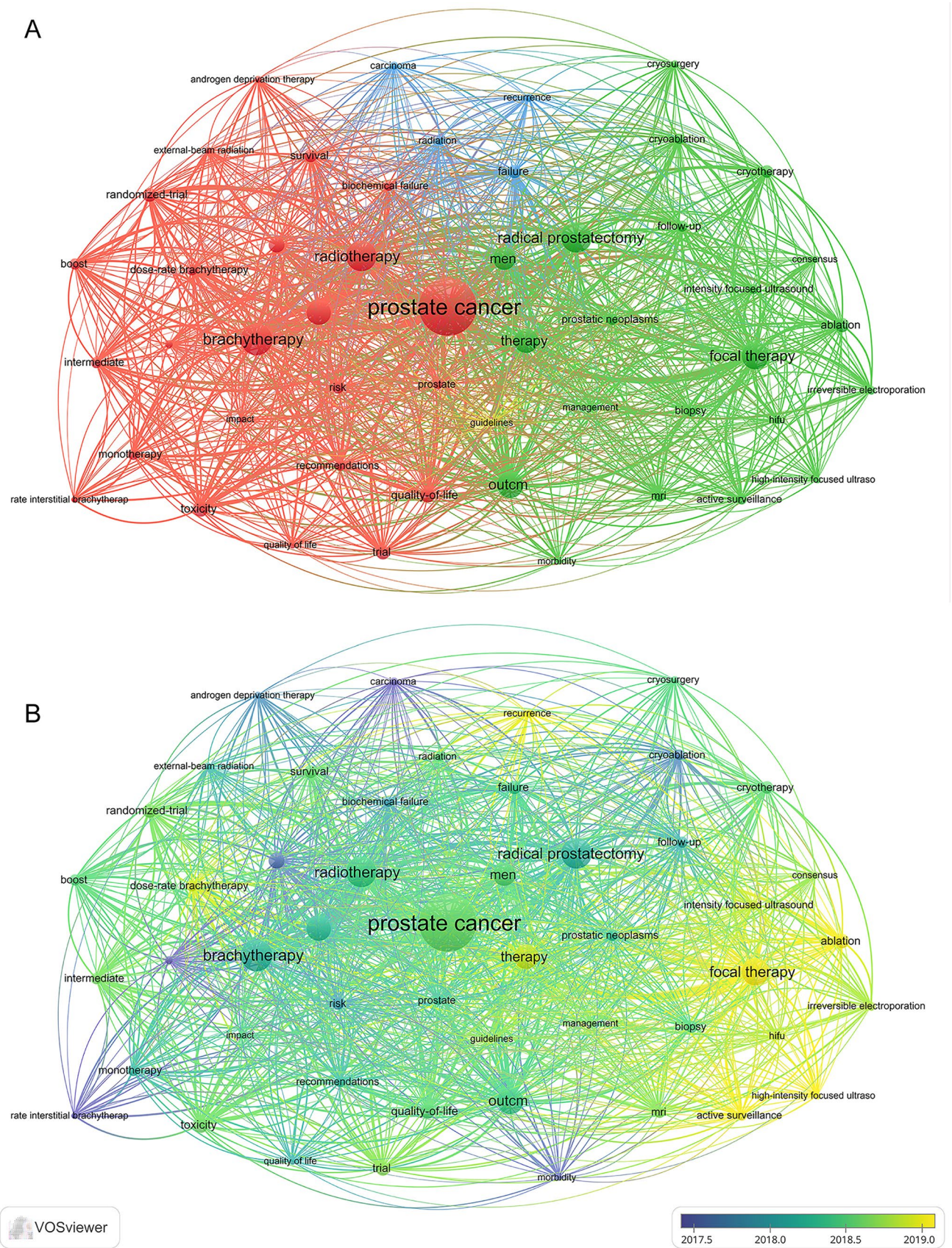
Cryotherapy primarily involves rapid freezing, slow thawing, and the repetition of freeze–thaw cycles [43]. There are two main mechanisms of prostate tumor tissue destruction by cryotherapy: the first is cellular damage caused by freeze–thaw cycles, and the second is vascular stasis leading to the progressive failure of tissue microcirculation [44, 45]. Aker et al. [46] conducted MRI-guided biopsy on 136 patients at 6 months after cryotherapy treatment. Among these patients, 76% (103/136) showed no evidence of cancer upon biopsy. Of these 103 patients, 71 subsequently underwent comprehensive biopsies over the next 18 months, and 65% (46/71) still did not have cancer upon the second biopsy. Additionally, the serum PSA levels of all patients significantly decreased from 6.9 to 2.5 ng/mL, and PSA density decreased from 0.15 to 0.07, while prostate volume decreased from 42 to 34 cc ($p < 0.01$). Based on the EPIC-CP questionnaire, these patients' urination function was only mildly affected, while their sexual function was moderately affected. In PCa treatment, the temperature of the frozen tissue should reach − 50 °C, but there is no consensus on the optimal duration of freezing [47]. This lack of standardization can make it difficult to compare results

Fig. 7 The bibliometric analysis of keywords. **A** Clustering of the top 50 keywords with the highest number of occurrences. Three clusters: ▶ Red cluster: Focuses on radiotherapeutic treatment, involving keywords such as brachytherapy, dose-rate brachytherapy, rate interstitial brachytherapy, etc. Green cluster: Focuses on active therapeutic options outside radiotherapy, featuring keywords such as intensity focused ultrasound, cryosurgery, irreversible electroporation, radical prostatectomy, etc. Blue cluster: Focuses on prognosis for patients with prostate cancer, involving keywords such as recurrence, failure, biochemical recurrence, etc.; **B** the overlay network map of top 50 keywords. The color of the nodes represents the chronological occurrence of keywords. Nodes closer to yellow indicate later appearances of keywords, reflecting the recent research hotspots and frontiers

between different studies and clinics, hindering the widespread acceptance of cryotherapy as a standard treatment option. Additionally, there is a need for further research and clinical trials to fully evaluate the long-term effectiveness and safety of cryotherapy. While short-term results may be encouraging, longer-term follow-up studies are crucial to assess the durability of the treatment response and the potential for recurrence. Standardization of treatment protocols, reduction of side effects and complications, cost considerations, further research, and appropriate patient selection are all crucial factors that need to be addressed to ensure the widespread acceptance of this therapy.

Irreversible electroporation (IRE) refers to the application of pulsed electric fields leading to increased membrane permeability in PCa cells [48]. In a nonrandomized controlled trial involving 109 patients (27 [24.8%] low risk and 82 [75.2%] intermediate risk) from 4 centers [49], with a median PSA value of 9.0 ng/ml (range 6.0–12.7) were treated with IRE therapy. Among the 100 patients who underwent biopsy at 6 months, the incidence of clinically significant PCa (ISUP grade ≥ 2) was found to be 6%. Compared to historical controls using other energy platforms, where the incidence of 6-month clinically significant PCa was around 20%, Wang et al. [49] reported that IRE ablation had a significantly lower incidence, with minimal impact on functional outcomes. Additionally, Zhang et al. [50] conducted a multicenter randomized clinical trial to compare focal and extended IRE ablation therapy for localized low- or intermediate-risk PCa. After 6 months of IRE therapy, focal ablation group showed a recurrence rate of 56.3% (27 out of 48), while the extended ablation group showed a recurrence rate of 43.4% (23 out of 53). Clinically significant PCa was detected in 18.8% (9 out of 48) of patients in the focal ablation group and 13.2% (7 out of 53) of patients in the extended ablation group. There was no significant difference in oncology outcomes between focal and extended IRE ablation therapy. IRE induces cell death by creating irreversible nanopores on the cell membrane without triggering thermal effects [51–53]. Theoretically, IRE may be more effective in eliciting immune responses than thermal ablation, attributed to its superior preservation of protein antigens and vascular structures pivotal for immune cell infiltration [54]. PCa has historically been regarded as an immunotherapy desert, and IRE is expected to bridge the gap from local therapy to immunotherapy, offering a promising alternative to conventional treatment paradigms. Firstly, IRE's non-thermal mechanism of action ensures that protein antigens and other cellular components are preserved during the ablation process. This preservation of antigens is fundamental for stimulating an effective immune response against the cancer cells. As the necrotic cancer cells release their antigens, they activate the immune system, triggering a cascade of immune reactions that can lead to the elimination of residual cancer cells. Secondly, IRE's precision allows for the targeted ablation of specific tumor areas while minimizing damage to surrounding healthy tissue and vital structures such as blood vessels and nerves. This precision not only enhances the safety of the treatment but also preserves the functionality of adjacent organs, thereby improving the overall quality of life for patients. Furthermore, the combination of IRE with immunotherapy agents or strategies could lead to synergistic effects. By using IRE to ablate the primary tumor, it may create an environment that is more conducive to the infiltration and activation of immune cells. Simultaneously, Burbach et al. [55] discovered that administering immunotherapy agents, specifically anti-CTLA-4 immune checkpoint inhibitors (ICIs), following IRE can promote robust expansion of tumor specific CD8+ T cells in blood, tumor, and non-lymphoid tissues (NLTs), further enhancing the anti-cancer effects. Notably, the full potential of IRE in immunotherapy for PCa has yet to be fully explored. Rigorous clinical studies and further research are needed to validate its effectiveness and safety in this context. Additionally, the optimal combination of IRE with immunotherapy agents or strategies needs to be carefully evaluated to ensure maximum therapeutic benefit for patients. If original research can validate this above theory, IRE will be further advocated for adoption and promotion.

Although we conducted a comprehensive analysis of articles on focal therapy for PCa from 2014 to 2023, there are still some limitations. Firstly, the data collection was finalized on September 15, 2023, and this limitation may affect the completeness of our findings and highlights the need for future studies to incorporate more recent publications. Secondly, our article collection was limited to the WOSCC, potentially resulting in the omission of articles from other repositories.


A
carcinoma
cryosurgery
androgen deprivation therapy
recurrence
external-beam radiation
survival
radiation
cryoablation
failure
cryotherapy
randomized-trial
biochemical-failure
follow-up
radical prostatectomy
radiotherapy
men
consensus
boost
dose-rate brachytherapy
intensity focused ultrasound
prostate cancer
prostatic neoplasms
ablation
brachytherapy
therapy
intermediate
focal therapy
risk
prostate
irreversible electroporation
management
biopsy
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guidelines
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monotherapy
recommendations
high-intensity focused ultraso
outcm
quality-of-life
mri
rate interstitial brachytherap
active surveillance
toxicity
quality of life
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morbidity
B
carcinoma
cryosurgery
androgen deprivation therapy
recurrence
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survival
failure
cryotherapy
biochemical-failure
randomized-trial
follow-up
radical prostatectomy
radiotherapy
men
consensus
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intensity focused ultrasound
prostate cancer
prostatic neoplasms
ablation
brachytherapy
therapy
intermediate
focal therapy
risk
prostate
irreversible electroporation
management
biopsy
impact
guidelines
hifu
monotherapy
recommendations
high-intensity focused ultraso
outcm
quality-of-life
mri
rate interstitial brachytherap
active surveillance
toxicity
quality of life
trial
morbidity
VOSviewer
2017.5
2018.0
2018.5
2019.0

5 Conclusion

Over the past decade, the United States has emerged as the leading country in focal therapy for PCa, with over half of the top 10 prolific institutions from the U.S. The brachytherapy has been extensively researched in the past. Looking forward, HIFU, cryotherapy, and IRE have the potential to become novel research hotspots in the field of localized PCa treatment.

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Declarations

Ethics approval and consent to participate Not applicable.

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