Original Article

[^{18}F]sodium fluoride positron emission tomography: a systematic bibliometric review from 2008 to 2022

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Background: As a noninvasive diagnostic tool, fluorine-18-labelled sodium fluoride positron emission tomography ([^{18}F]NaF PET) has been increasingly applied in clinical practice due to its excellent imaging performance, attracting more attention from clinical practitioners. However, with the continuous development of technology and growth of knowledge, the field of [^{18}F]NaF PET is changing. Nevertheless, few studies have conducted quantitative analyses of the literature in this field. Therefore, in this study, we used bibliometric methods to analyze the trends, content distribution, and frontiers of this field from multiple perspectives, including social and international structure, conceptual structure, and intellectual structure.

Methods: This study used the Web of Science (WOS) core database as the data source and retrieved literature related to [^{18}F]NaF PET between 2008 and 2022. CiteSpace and VOSviewer software were then employed for bibliometric analysis. This study performed co-occurrence analysis and citation analysis to investigate the characteristics of [^{18}F]NaF PET in 3 aspects.

Results: A total of 682 articles related to [^{18}F]NaF PET were collected during the period from 2008 to 2022. The author, Alavi, had the highest number of publications (67 articles). In terms of institutions, the University of Edinburgh had the highest number of publications (64 articles). The United States (300 articles) was the country with the highest number of published articles. Keyword co-occurrence analysis revealed that [^{18}F]NaF PET-related technologies, bone metastasis (prostate cancer and breast cancer), and atherosclerosis were prominent research directions in this field. In terms of highly cited authors, Even-Sapir had the highest citation count (188 citations). Regarding highly cited journals, the *Journal of Nuclear Medicine* ranked as the most highly cited journal. The literature co-citation clustering and timeline graph showed that atherosclerotic plaques, bone metastasis, and the clinical applications of [^{18}F]NaF PET were topics of active research in this field.

Conclusions: There has been an increase in the literature published in the field of [^{18}F]NaF PET from 2008 to 2022. The United States holds a prominent position in the field of [^{18}F]NaF PET. Arteriosclerosis and bone metastasis are the main topics in this field and at the forefront of research.

Keywords: Fluorine-18-labelled sodium fluoride positron emission tomography ([^{18}F]NaF PET); bibliometrics; CiteSpace; VOSviewer

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Introduction

As a noninvasive diagnostic modality, fluorine-18-labelled sodium fluoride positron emission tomography ([^{18}F]NaF PET) has undergone several stages of development. Initially discovered by Blau *et al.*, [^{18}F]NaF was first used for the detection of skeletal lesions (1). However, due to the limitations of traditional gamma cameras, [^{18}F]NaF was quickly replaced by ^{99m}Tc-methyl diphosphonate (^{99m}Tc-MDP). Subsequently, with the development and widespread use of PET or PET-computed tomography (PET/CT), [^{18}F]NaF PET has regained attention due to its excellent imaging performance. The molecular mechanism of [^{18}F]NaF imaging involves the exchange of [^{18}F] ions with hydroxyl (OH^-) groups on the surface of hydroxyapatite matrix, followed by binding with the crystalline matrix, thereby enabling the labeling of bone lesions or calcified regions for the purpose of imaging (2). Furthermore, [^{18}F]NaF was initially used solely for detecting bone metastases. However, with advancements in technology and widespread clinical adoption, [^{18}F]NaF has also demonstrated notable accomplishments in the diagnosis and monitoring therapy of bone diseases, cardiovascular conditions, and other fields (3,4).

Bibliometrics is a scientific discipline that employs statistical methods and relies on published literature as a foundation to uncover the characteristics and trends of a particular field during a defined period of time (5,6). It is worth noting that literature reviews (7-9) related to [^{18}F]NaF PET have been conducted, but these have been limited to specific aspects of the technology and may not objectively and comprehensively cover the structural overview, developmental landscape, or the most active areas of the [^{18}F]NaF PET field. Furthermore, there is a scarcity of bibliometric studies on [^{18}F]NaF PET. Given the widespread clinical application of [^{18}F]NaF PET and the increasing publication of relevant literature, bibliometric analysis of this field appears warranted.

The aim of this study was thus to characterize the main content, developmental overview, and the most active areas of [^{18}F]NaF PET by analyzing its social and international structure, conceptual structure, and intellectual structure. Given this, we sought to answer the following 3 principal research questions:

(I) What is the social and international structure of the [^{18}F]NaF PET field?
(II) What is the conceptual structure of the [^{18}F]NaF PET field?
(III) What is the intellectual structure of the [^{18}F]NaF PET field?

Methods

Materials

The Web of Science (WOS) Core Collection database, renowned for its wealth of high-quality and influential scientific articles, serves as both a citation database and a pivotal bibliographic resource encompassing the primary literature pertaining to [^{18}F]NaF PET. Consequently, we used this database as the primary data source for this study. We searched for articles published between January, 1 2008 and December 31, 2022, using the following search strategy: topic= ("sodium fluoride*" OR "NaF") AND topic= ("positron emission tomography" OR "PET") AND document type= (article OR review) AND language= (English). Then, 2 researchers independently screened the data and excluded irrelevant documents and added tags to the document according to radiological subspecialties. The radiological subspecialties were the central nervous system (CNS), the head and neck, the respiratory system, musculoskeletal system, circulation system, breast, digestive system, genitourinary system, and the miscellaneous. *Figure 1* shows the retrieval process. Finally, a total of 682 documents were extracted for further analysis.

Research methods

Research fields are socially, internationally, conceptually, and intellectually structured, and we could identify the most active areas of the [^{18}F]NaF PET field from these aspects (10):

(I) To clarify the social and international structure, we use the authors (co-authorship analysis) and the author's affiliations (co-country/region, co-institution analysis) to map co-authorship, co-

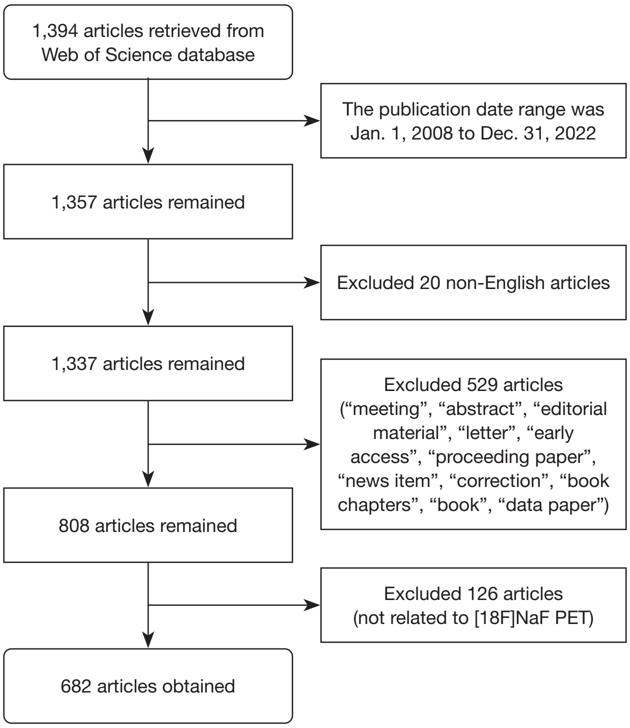

Figure 1 The retrieval process of the [^{18}F]NaF PET articles. [^{18}F]NaF PET, fluorine-18-labelled sodium fluoride positron emission tomography.

institution, and co-country/region networks in the [^{18}F]NaF PET field.

(II) Using co-word analysis to visualize the conceptual structure, we drew a keyword occurrence knowledge map.

(III) We selected authors, journals, and documents as units of the co-citation for characterizing the intellectual structure.

CiteSpace and VOSviewer, widely recognized as essential software tools for visual analysis in the realm of bibliometrics, were employed in this study to offer a more comprehensive and intuitive depiction of the research landscape pertaining to [^{18}F]NaF PET. VOSviewer, devised by Nees Jan van Eck and Ludo Waltman at the Center for Scientific and Technological Research, Leiden University, and CiteSpace, developed by Chaomei Chen of Drexel University, were critical to completing this research. For the purpose of this study, VOSviewer version 1.6.19 (released January 23, 2023) and CiteSpace version 6.2 R2 were used.

The PET density data used in this study were sourced from OECD Statistics (https://stats.oecd.org/). It should be noted that comprehensive data for Germany and the United Kingdom are not available in this database. For these countries, we obtained range data from the International Atomic Energy Agency (IAEA) (https://humanhealth.iaea.org/HHW/DBStatistics/IMAGINEMaps4.html). Additionally, the PET data for China were obtained from the survey report of the Nuclear Medicine Branch of the Chinese Medical Association (https://chinanm.cma.org.cn/col/col1385/index.html), and population data were sourced from the CIA World Factbook (https://www.cia.gov/the-world-factbook/countries/china/).

Results

Overall distribution

There was an overall increasing trend in the number of publications, from 4 in 2008 to 75 in 2022 (*Figure 2A*). The main application areas of [^{18}F]NaF PET were the musculoskeletal system (59%) and the circulation system (34%) (*Figure 2B*). These documents were cited 13,287 times, an average of 19.48 times per article. Although the total number of documents was only 682, the annual number of publications and the frequency of citations showed an increasing trend, indicating that this field is an area of growing research activity.

Social and international structure of the [^{18}F]NaF PET field

Co-authorship analysis

To identify key authors and their collaborations, we created a co-authorship network map of the [^{18}F]NaF PET domain via using CiteSpace. To improve the readability of the network map, we used a network pruning method (pathfinder + pruning the merged network) to form a network including 520 nodes and 1,098 connections. *Figure 3* shows the largest subnetwork, and *Table 1* lists the top 10 most prolific authors. Alavi (67 papers) was the author with the highest number of publications.

Co-institution analysis

To identify the core institutions and their partnerships, we constructed a co-institution network map using CiteSpace with all parameters kept as default, resulting in a network with 357 nodes and 699 connections. *Figure 4* presents the largest subnetwork.

The number of institutional publications reflects

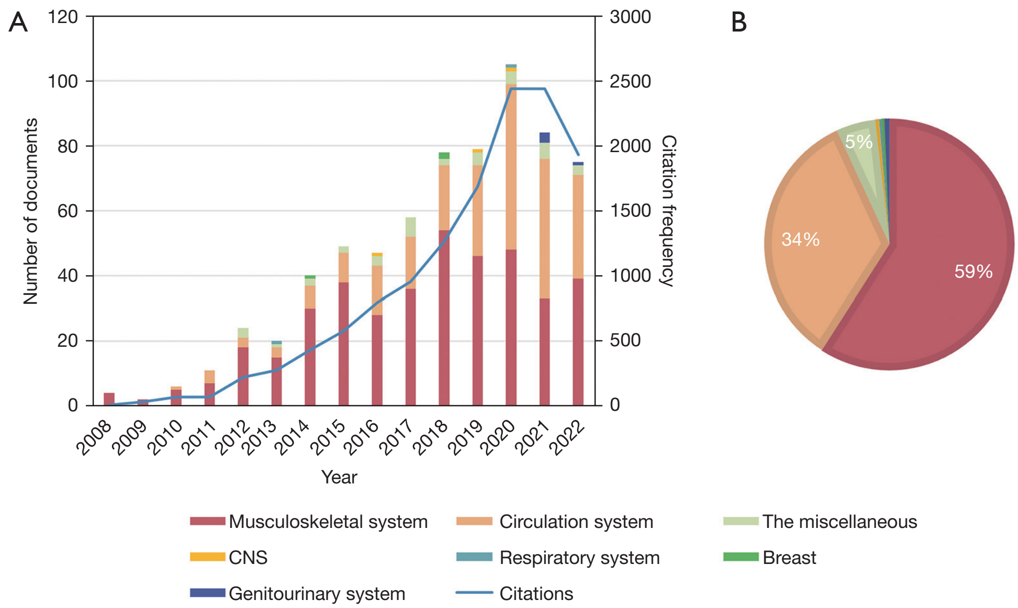

Figure 2 Annual publication trends and subspecialty distribution in the field of [18F]NaF PET. (A) Distribution of [18F]NaF PET documents from 2008 to 2022. (B) The overall distribution of [18F]NaF PET documents in different radiological subspecialties. [18F]NaF PET, fluorine-18-labelled sodium fluoride positron emission tomography; CNS, central nervous system.

Figure 3 Co-authorship network. Each node represents a corresponding author, the node's size is proportional to the number of articles published by the author, and the width of the link between 2 nodes is proportional to the closeness of the collaboration between the corresponding 2 authors. The closer the color is to dark purple, the earlier the author's posting time. The nodes covered by the purple circles exhibit high centrality (greater than or equal to 0.1).

Table 1 Top 10 authors in terms of the number of publications

Rank	Count	Centrality	Author
1	67	0.08	Alavi, Abass
2	52	0.11	Dweck, Marc R
3	50	0.08	Newby, David E
4	50	0.01	Hoilund-Carlsen, Poul F
5	41	0.02	Werner, Thomas J
6	27	0.01	Raynor, William Y
7	25	0.01	Gerke, Oke
8	21	0	Slomka, Piotr J
9	21	0.02	Borja, Austin J
10	20	0.01	Kwiecinski, Jacek

the level of research in the field. In all, 357 institutions produce articles related to [^{18}F]NaF PET in the WOS core collection database, and the top 10 institutions in terms of the number of publications are listed in *Table 2*. In addition, there were 5 institutions with a betweenness centrality greater than 0.1: University of Pennsylvania (USA), Cedars Sinai Medical Center (USA), University of Edinburgh (UK), Hospital of the University of Pennsylvania (USA), and Stanford University (USA).

Co-country/region analysis

To identify the core countries/regions in the [^{18}F]NaF PET field, we mapped the co-country/region network using CiteSpace and with the help of pathfinding network clipping. *Figure 5* shows the leading national/regional cooperative network, with 45 nodes and 207 links. A total of 682 publications in the WOS core database were published by 45 countries/regions, and the major countries/regions in the field showed close cooperation. *Table 3* lists the top 10 countries in terms of the number of publications, with the United States being first (300 articles), followed by the United Kingdom (132 articles), and Denmark (81 articles).

Conceptual structure of the [^{18}F]NaF PET field

Co-occurring keywords analysis

Keywords are specialized terms that express the core and highly summarized content of a research article. By analyzing the co-occurrence of keywords, we could uncover the main research topics in the field of [^{18}F]NaF PET. To this end, we employed VOSviewer software to create a keyword co-occurrence network and density graph and listed the top 20 keywords by co-occurrence frequency (*Table 4*). *Figure 6* illustrates the co-occurrence network of keywords with a frequency greater than or equal to 3 after merging of synonymous terms. To provide a more intuitive visualization of the research topics in this field, we also created a keyword density graph (*Figure 7*).

Intellectual structure of the [^{18}F]NaF PET field

Author co-citation analysis

This portion of the study aimed to evaluate the influence and contributions of authors in the field of [^{18}F]NaF PET by analyzing their citation frequency. It should be emphasized that highly cited authors are not necessarily experts in the field, but their contributions are of great significance to the development of the field. Author co-citation refers to the relationship between 2 authors when they are both cited in the same reference (11). In summary, author citation analysis is a crucial means to understanding the academic achievements of various authors in the academic community and is also part of the knowledge foundation of this field.

With parameters in CiteSpace kept at their default settings, we employed the network pruning method (pathfinder + pruning the merged network) to illustrate the clear structure of the co-citation network map of authors. Ultimately, a network map containing 617 nodes and 1,157 links was obtained, with *Figure 8* showing its largest subnetwork. We ranked the co-cited authors based on their citation frequency and betweenness centrality, with the top 10 being listed in *Table 5*. In addition, to analyze the characteristics of highly cited authors in this field, we determined the annual citation frequency distribution of the top 5 most highly cited authors (*Figure 9*).

Journal co-citation analysis

Journal co-citation analysis involves identifying the co-citation patterns among journals by examining which journals are cited together in the same articles and by calculating the co-occurrence frequency of their citations. This analysis helps to understand the co-citation patterns and relationships between journals. By conducting journal co-citation analysis, we could identify core journals and influential journals within a specific academic field, revealing the academic influence and interactions among journals. In this portion of the study, we first conducted an analysis of the literature sources and then used the visualization of

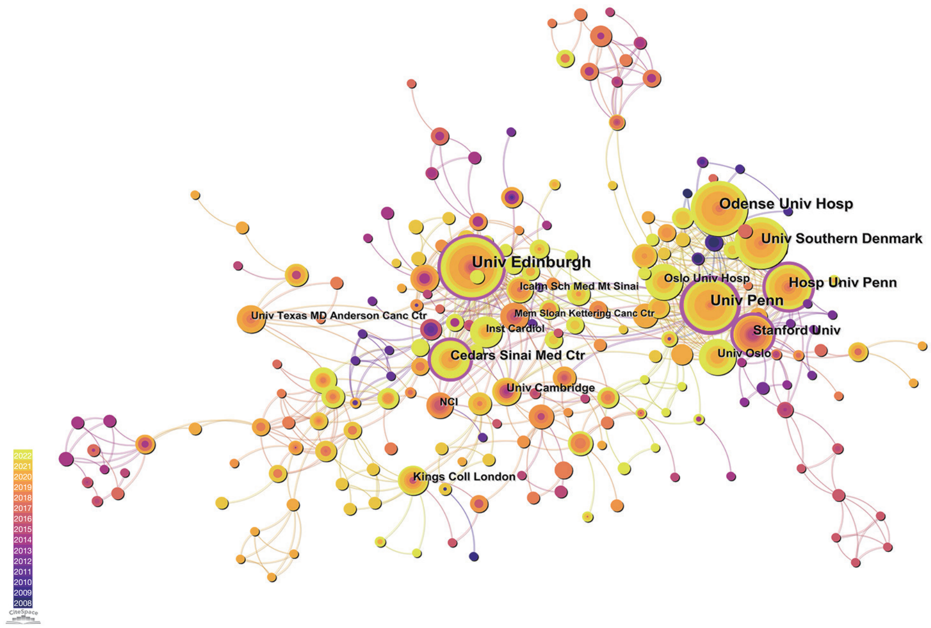

Figure 4 Co-institution network. Each node represents an institution, with the size of the node proportional to the volume of publications produced by that institution. The thickness of the links between nodes reflects the strength of collaboration between corresponding institutions. The darker the color of the node is, the earlier the institution's publications. Furthermore, the nodes covered by the purple circles in the figure indicate high centrality (greater than or equal to 0.1). Univ Edinburgh, University of Edinburgh; Odense Univ Hosp, Odense University Hospital; Univ Penn, University of Pennsylvania; Hosp Univ Penn, Hospital of the University of Pennsylvania; Univ Southern Denmark, University of Southern Denmark; Stanford Univ, Stanford University; Cedars Sinai Med Ctr, Cedars Sinai Medical Center; Oslo Univ Hosp, Oslo University Hospital; Univ Oslo, University of Oslo; Kings Coll London, King's College London; Univ Cambridge, University of Cambridge; Inst Cardiol, Institute of Cardiology – Poland; NCI, National Cancer Institute; Univ Texas MD Anderson Canc Ctr, University of Texas MD Anderson Cancer Center; Icahn Sch Med Mt Sinai, Icahn School of Medicine at Mount Sinai; Mem Sloan Kettering Canc Ctr, Memorial Sloan Kettering Cancer Center.

Table 2 The top 10 institutions in terms of the number of publications

Rank	Count	Centrality	Institution (country)
1	64	0.12	University of Edinburgh (UK)
2	51	0.02	Odense University Hospital (Denmark)
3	47	0.29	University of Pennsylvania (USA)
4	41	0.11	Hospital of the University of Pennsylvania (USA)
5	41	0.02	University of Southern Denmark (Denmark)
6	31	0.11	Stanford University (USA)
7	29	0.14	Cedars Sinai Medical Center (USA)
8	19	0	Oslo University Hospital (Norway)
9	19	0	University of Oslo (Norway)
10	17	0.06	King's College London (UK)

the journal co-citation network to identify the journals that have made significant contributions to the field. To some extent, the number of citations received by a journal is also a knowledge foundation in the academic field. We used the default settings of CiteSpace software and employed the pruning network method (pathfinder + pruning the merged network) to render the journal co-citation network map clearer and more readable. The resulting journal co-citation network map included 488 nodes and 929 edges, with *Figure 10* displaying the largest subnetwork.

Table 6 presents the distribution of literature sources extracted from the WOS report. A total of 682 articles were included, which were published in 219 different journals. The top 3 journals in terms of publication volume in this field were the *Journal of Nuclear Cardiology*, the *Journal of Nuclear Medicine*, and the *European Journal of Nuclear Medicine and Molecular Imaging*. Together, these 3 journals

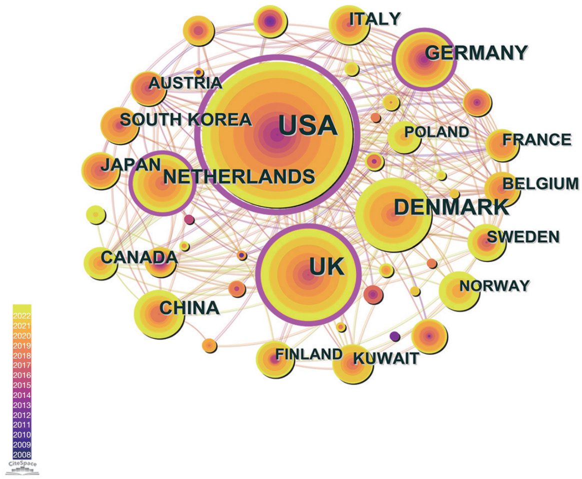

Figure 5 Co-country/region network. Each node represents a country/region, and the size of the node is proportional to the number of publications from that country/region. The thickness of the links between nodes corresponds to the strength of collaboration between the corresponding countries/regions. The darker the color of the node is, the earlier the country's/ regional first publication. The nodes covered by the purple circles in the graph indicate high centrality (greater than or equal to 0.1).

Table 3 Top 10 countries by publishing volume

Rank	Count	Centrality	Country	PET density	Contribution level
1	300	0.74	USA	5.75	52.17
2	132	0.24	UK	1–2	66–132
3	81	0.02	Denmark	8.85	9.15
4	51	0.17	Germany	1–2	25.5–51
5	48	0.19	The Netherlands	5.42	8.86
6	40	0.06	China	0.3	133.33
7	31	0.06	Italy	3.67	8.45
8	28	0.01	Japan	4.71	5.94
9	27	0.02	Canada	1.52	17.76
10	27	0.01	South Korea	3.46	7.80

PET density refers to the number of PET devices per 1 million population. Contribution level is the ratio of the number of publications in the field by each country to the PET density. PET, positron emission tomography.

accounted for approximately 18% of all literature in this field, indicating that they are high-productivity journals in this area. The references in this field mainly originated from 488 journals. *Table 7* lists the top 10 most frequently cited journals, with the top 3 being the *Journal of Nuclear Medicine*, *European Journal of Nuclear Medicine and Molecular Imaging*, and *Clinical Nuclear Medicine*. Only the *American Journal of Roentgenology* had a betweenness centrality index greater than 0.3.

Document co-citation analysis

The purpose of the co-citation analysis of literature is to characterize the knowledge base and research frontier (12) of the [^{18}F]NaF PET field. Co-citation analysis refers to the formation of a co-citation relationship between 2 articles when they both appear in the reference list of a third citing article (13). The literature is taken as the analysis unit for co-citation analysis, and a visual citation network map of the field is obtained through clustering. In CiteSpace

Table 4 The top 20 keywords by co-occurrence frequency

Keyword	Occurrence	Keyword	Occurrence
^{18}F-NaF	292	Calcification	44
PET	263	MRI	43
PET/CT	127	Inflammation	33
CT	106	Molecular imaging	32
Atherosclerosis	92	Breast cancer	25
Bone metastases	84	PET/MRI	20
^{18}F-FDG	83	Bone	18
Prostate cancer	68	Microcalcification	17
[^{18}F]NaF PET/CT	59	Standardized uptake value	17
[^{18}F]NaF PET	49	Vascular calcification	17

^{18}F-NaF, [^{18}F]sodium fluoride; ^{18}F-FDG, [^{18}F]Fluorodeoxyglucose; PET, Positron emission tomography; CT, computed tomography; MRI, magnetic resonance imaging.

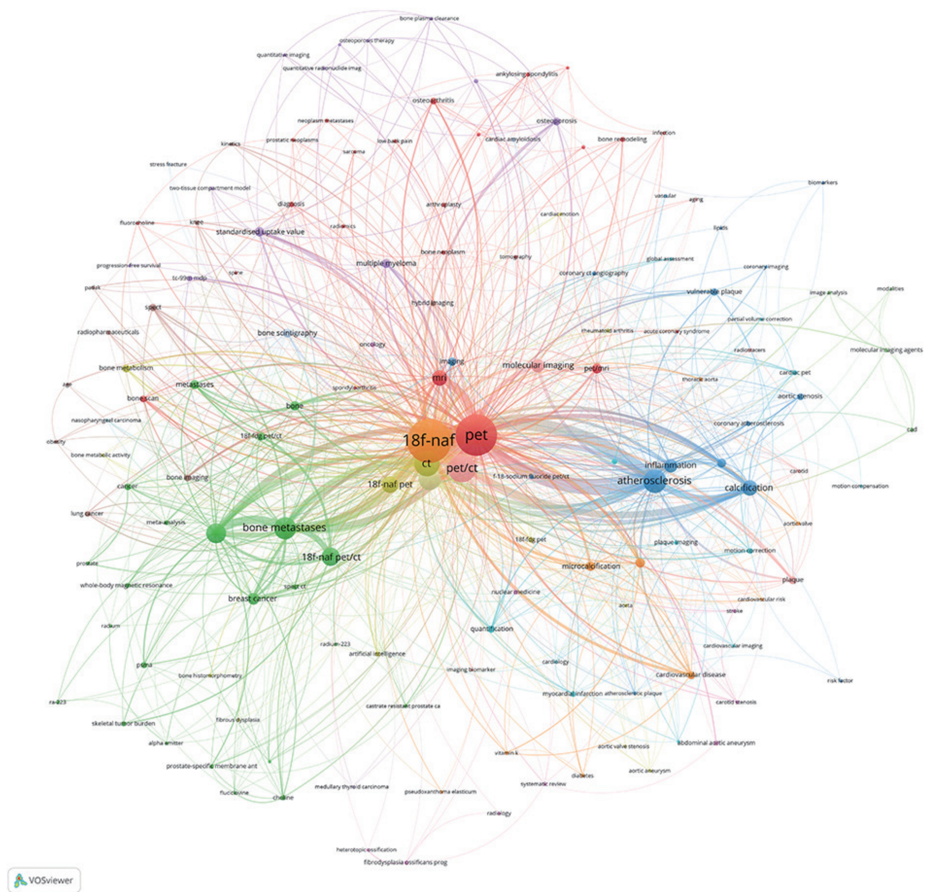

Figure 6 Keyword co-occurrence network. Each node represents a key phrase, with larger nodes indicating higher frequency of occurrence. The thickness of the edges connecting the nodes indicates the strength of the correlation between the 2 key phrases, as measured by the frequency of co-occurrence in the same document. Node color indicates different clusters.

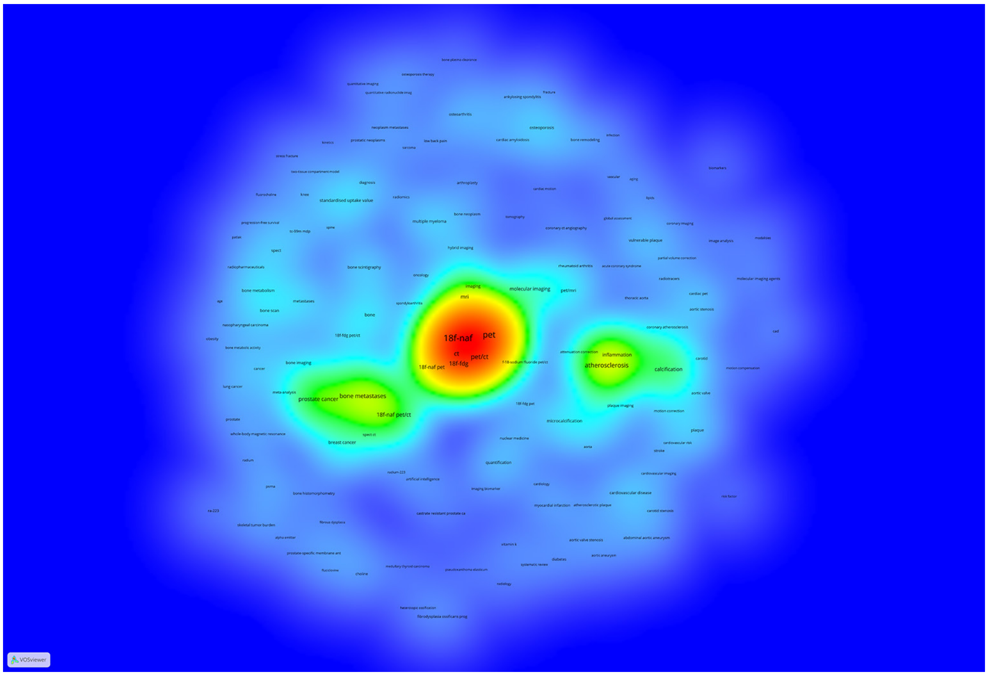

Figure 7 Keyword density graph. The progression from cool to warm colors represents an increasing frequency of the co-occurrence of keywords.

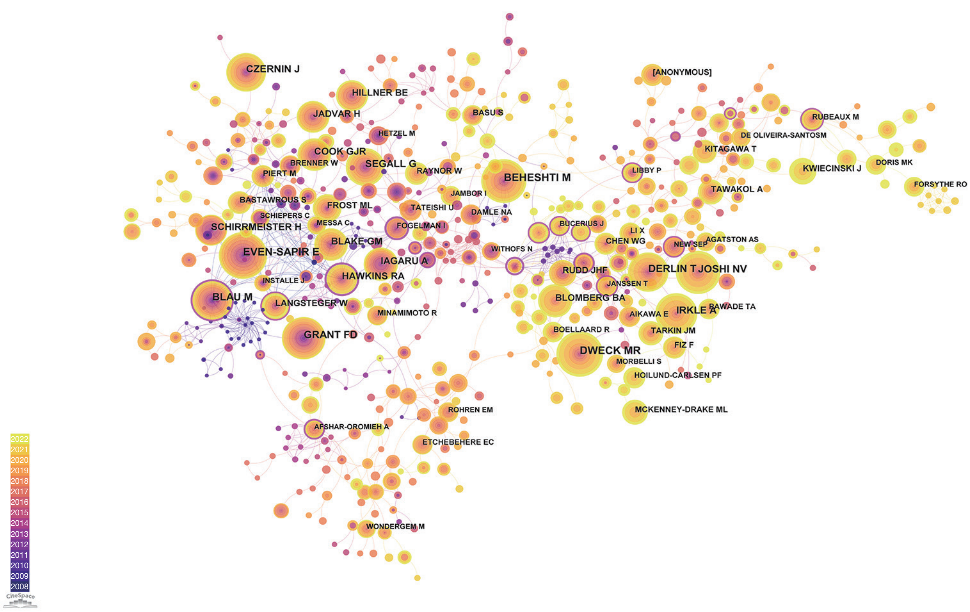

Figure 8 Author co-citation network. Each node in the graph represents a cited author, and the size of the node reflects the frequency of citations for that author. The thickness of the links between nodes is proportional to the strength of co-citation between the 2 authors represented by the nodes. Nodes with a betweenness centrality greater than or equal to 0.1 are identified by a purple circle. The color depth of each node indicates the temporal order of the author's publication.

Table 5 The top 10 authors ranked by both citation frequency and centrality

Rank	Ranked by citation frequency				Ranked by centrality			
	Cited author	Count	Centrality	Country	Cited author	Centrality	Count	Country
1	Even-Sapir E	188	0.02	Israel	Ben-Haim S	0.72	26	Israel
2	Dweck MR	170	0.01	UK	Fogelman I	0.48	40	USA
3	Beheshti M	167	0	USA	Hawkins RA	0.41	101	UK
4	Grant FD	162	0.01	USA	Blau M	0.3	136	Germany
5	Joshi NV	157	0	UK	Virmani R	0.24	29	USA
6	Derlin T	145	0.01	Germany	Afshar-Oromieh A	0.2	31	Switzerland
7	Blau M	136	0.3	Germany	Nakahara T	0.15	22	Japan
8	Czernin J	127	0.01	USA	Baum RP	0.15	4	Germany
9	Segall G	126	0	USA	Libby P	0.14	31	USA
10	Irkle A	126	0.01	UK	Bucerius J	0.14	30	Germany

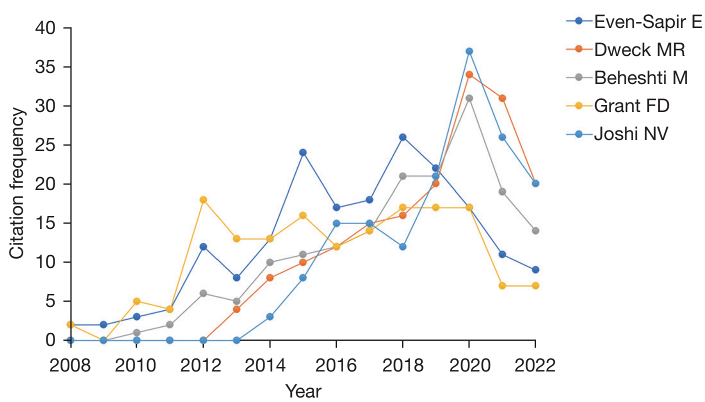

Figure 9 The citation distribution for the 5 most frequently cited authors.

software, with default parameters and clustering conducted by topic, a total of 15,430 valid cited documents and 682 citing documents were identified as the basis for co-citation analysis. The clustering result included 698 nodes and 3,286 edges, with the top 10 clusters being shown in *Figure 11*. It should be noted that since the amount of cited literature within each cluster in the [18F]NaF PET field is relatively low, the cluster labels automatically selected by the software may not accurately represent the themes of the citing literature. Therefore, we manually selected relatively reasonable cluster names by reading the citing literature reflected in each cluster and combining the labels extracted with the Latent Semantic Indexing (LSI), Log-Likelihood Ratio (LLR), and Mutual Information (MI) algorithms. This approach maintained the objectivity of co-citation analysis while making the labels more relevant to the themes of the literature. Pieces of literature within the same cluster show strong similarities, while those in different clusters have greater differences, and each cluster's title represents a specific theme. Furthermore, the clustering result's quality was measured by both the S and Q values, with higher Q and S values indicating better clustering performance and homogeneity within the clusters. The Q value of the [18F]NaF PET field's co-citation network map was 0.7327, which was greater than 0.3, indicating a significant network structure, while the S value was 0.886, which was greater than 0.7, indicating reasonable clustering results with high credibility. Additionally, by using the *timeview* function of CiteSpace, we created a timeline of the co-cited literature network (*Figure 12*), which reflects the time characteristics

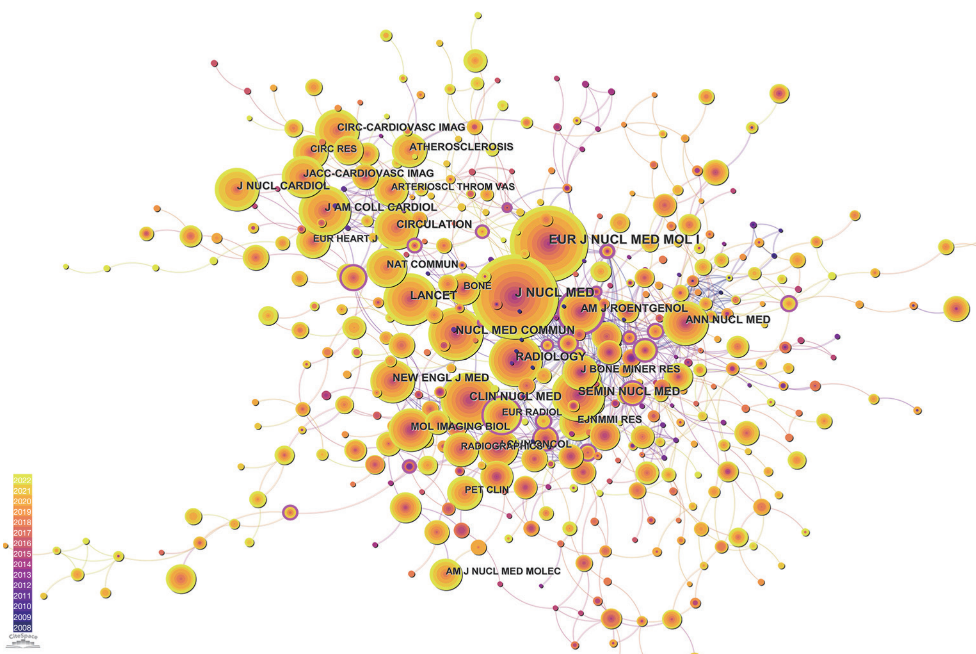

Figure 10 Journal co-citation network. Each node represents a journal, and the size of the node reflects the number of citations received by the journal. The thickness of the edges represents the strength of co-citation between the corresponding journals. Journals with betweenness centrality greater than or equal to 0.1 are encircled by purple circles. The color of the node reflects the time when the journal published its articles, with darker colors indicating earlier publication dates.

Table 6 Top 10 journals with the most articles published in the [^{18}F]NaF PET field

Rank	Count	Source	Country
1	44	*Journal of Nuclear Cardiology*	USA
2	44	*Journal of Nuclear Medicine*	USA
3	32	*European Journal of Nuclear Medicine and Molecular Imaging*	Germany
4	29	*Pet Clinics*	USA
5	28	*Nuclear Medicine Communications*	UK
6	17	*American Journal of Nuclear Medicine and Molecular Imaging*	USA
7	13	*Clinical and Translational Imaging*	Italy
8	12	*Clinical Nuclear Medicine*	USA
9	12	*Seminars in Nuclear Medicine*	USA
10	11	*Annals of Nuclear Medicine*	Japan

[^{18}F]NaF PET, fluorine-18-labelled sodium fluoride positron emission tomography.

of the research field, including its emergence, prosperity, and decline.

Table 8 presents detailed information for the 10 clusters, including cluster ID, size, silhouette value, start-stop time, duration, and mean year. All 10 clusters had a silhouette value greater than 0.7, indicating that the clustering results were reasonable and highly reliable. In terms of persistence, 6 of the 10 clusters had a duration of more than 10 years, including atherosclerotic plaque, bone metastases, F-18 NaF, coronary atherosclerosis, clinical application, and

Table 7 The top 10 most highly cited journals

Rank	Count	Centrality	Cited journals	Country
1	616	0	*Journal of Nuclear Medicine*	USA
2	497	0	*European Journal of Nuclear Medicine and Molecular Imaging*	Germany
3	285	0.06	*Clinical Nuclear Medicine*	USA
4	270	0.02	*Nuclear Medicine Communications*	UK
5	259	0.03	*Seminars in Nuclear Medicine*	USA
6	251	0	*Radiology*	USA
7	245	0	*Lancet*	UK
8	235	0	*Journal of the American College of Cardiology*	USA
9	197	0.02	*Circulation*	USA
10	186	0.32	*American Journal of Roentgenology*	USA

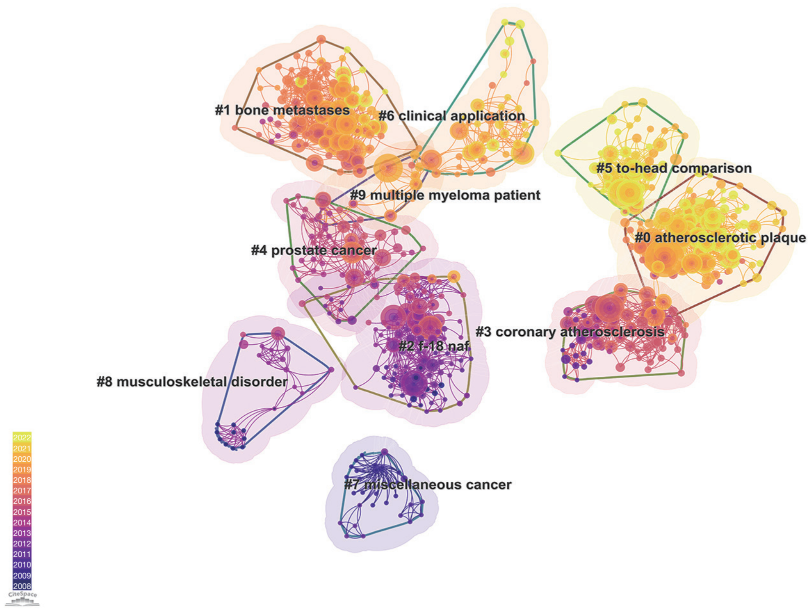

Figure 11 Visualization network of co-citation clustering in the literature. A label represents a clustering topic, where each node corresponds to a single document. Node size is proportional to the frequency of document citation while the thickness of the lines between nodes reflects the strength of co-citation relationships. Node color indicates the publication date of the document, with darker colors indicating earlier publication times.

musculoskeletal disorder, with atherosclerotic plaque having the longest duration of 14 years. Additionally, in terms of activity, 4 clusters have remained active in the last 3 years, including atherosclerotic plaque, bone metastases, head-to-head comparison, and clinical application, which constitute the research focus in this field.

Discussion

Distribution of documents

The number of papers in a field and their trends can reflect the different stages of development in the field. We artificially divided the [^{18}F]NaF PET field into 3 stages

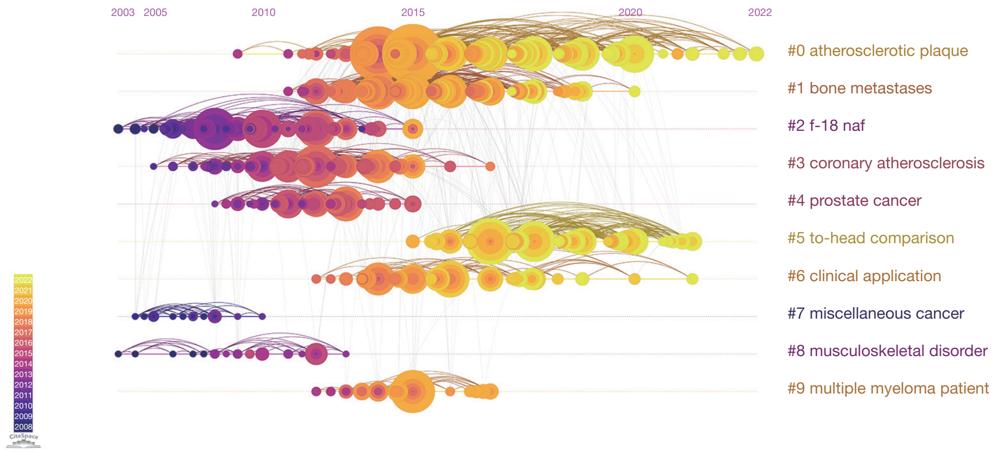

Figure 12 A visual representation of 10 clustered timelines. Documents with the same clustering are arranged on the same horizontal line. Each node represents a document, with node size proportional to the document's citation frequency. Document publication time is represented by color, with darker colors indicating earlier publication times.

Table 8 Detailed information on the top 10 clusters

Cluster ID	Size	Silhouette	Start	Stop	Duration	Mean	Label
0	115	0.856	2009	2022	14	2017	Atherosclerotic plaque
1	114	0.83	2011	2020	10	2015	Bone metastases
2	102	0.78	2003	2015	13	2009	F-18 NaF
3	77	0.965	2005	2017	13	2011	Coronary atherosclerosis
4	57	0.897	2008	2015	8	2011	Prostate cancer
5	51	0.949	2015	2021	7	2019	Head-to-head comparison
6	39	0.929	2012	2021	10	2016	Clinical application
7	31	0.997	2004	2010	7	2006	Miscellaneous cancer
8	24	1	2003	2013	11	2008	Musculoskeletal disorder
9	15	0.985	2012	2017	6	2014	Multiple myeloma patient

F-18 NaF, fluorine-18–labelled sodium fluoride.

based on the annual number of documents and the growth rate. The initial phase was from 2008 to 2010, with around 10 documents per year. Scholars in this period focused on applying the technique to the musculoskeletal system, and there was only 1 paper (14) published on the circulatory system. The 2011–2017 period was the growth phase; the number of documents grew more steadily but did not exceed 60 articles, as the technique was still mainly used in the musculoskeletal system during this period; however, its use in the circulatory system showed an increasing trend year by year. In the 2018–2022 period, the relative maturity stage, the growth rate of literature further increased, and the number of articles peaked in 2020 (105 articles); the average annual number of articles was greater than 70, with the field developing more rapidly during this period. The main fields of application of this technology are the musculoskeletal system and circulatory system, and the number of publications of both is almost equal. The application of this technology in the circulatory system will become increasingly widespread.

Social and international structure of the [^{18}F]NaF PET field

Through co-authorship, co-institution, and co-country/region analysis, we found that the social and international structure of the [^{18}F]NaF PET field exhibits the following characteristics.

In terms of social structure, 2 primary author collaborative groups formed the field, with Dweck, Newby, and Alavi, and Werner at the core (*Figure 3*). Collaboration within the 2 collaborative groups has been relatively intensive, but cooperation between them could be more frequent. Alavi was the most prolific authors in the field of [^{18}F]NaF PET. In 2008, he and Grant, among others, suggested that [^{18}F]NaF PET is superior to ^{99m}Tc-diphosphonate single-photon emission computerized tomography (SPECT) in terms of accuracy in identifying skeletal lesions and that [^{18}F]NaF should be reconsidered as a routine bone imaging agent (15). In addition, only Dweck showed a betweenness centrality value greater than 0.1, indicating that his work is highly promising or of great interest to people. His study demonstrated that [^{18}F]NaF can be a potential marker of valve calcification activity and that disease progression could be predicted by comparing the correlation between aortic valve histological features and [^{18}F]NaF uptake (16).

Publications in field of [^{18}F]NaF PET were found to be dominated by 2 major groups of publishers, centered on the University of Edinburgh and the University of Pennsylvania. These 2 groups maintain a relatively close collaborative relationship between and within each other. The University of Edinburgh ranked first in terms of the number of articles published that focused on [^{18}F]NaF PET and the cardiovascular system, for example, those covering the identification, localization, and assessment of plaques at high risk of atherosclerosis (17) and assessment of the degree of vascular inflammation and calcification (18).

There were several interesting findings concerning the international structure of the [^{18}F]NaF PET field. Regarding country distribution, the most active regions were Europe and the United States; among the top 10 countries in terms of publication volume, only China is a developing country, with the rest being developed countries. Betweenness centrality represents the importance of critical nodes in a network. The United States ranked first in terms of publication quantity and centrality, well ahead of the second-ranked country, the United Kingdom, indicating that the United States holds a prominent position in the field of [^{18}F]NaF PET. Furthermore, in terms of contribution level, China ranked first when the standardized conversion of population and PET quantity was considered.

Conceptual structure of the [^{18}F]NaF PET field

By conducting keyword co-occurrence analysis, we characterized the conceptual structure of the [^{18}F]NaF PET field. The main research topics in this field can be summarized into 3 categories (*Figure 6*, *Figure 7*, *Table 4*): [^{18}F]NaF PET-related technologies, bone metastasis (prostate cancer and breast cancer), and atherosclerosis.

Atherosclerosis is a disease characterized by the deposition of lipids, fibers, and arterial calcification (19). The rupture of an unstable atherosclerotic plaque can lead to compromised blood supply to the associated organ, resulting in severe consequences. Studies have shown that microcalcifications decrease plaque stability (20,21), but current CT imaging is unable to detect these microcalcifications (22), highlighting the critical need for a specific *in vivo* imaging technique for microcalcifications. Irkle *et al.* discovered that [^{18}F]NaF can specifically bind to microcalcification regions and thus can be used to identify high-risk plaques and their rupture locations, potentially reducing the occurrence of clinical acute events (23).

Bone metastasis is a common complication of various malignant tumors, with bone metastasis present in 70% of cases with metastatic prostate and breast cancer (24). Bone metastasis can cause bone pain, fractures, and other bone-related events, which not only negatively affect the physical and mental health of patients but also shorten their survival time. Therefore, early diagnosis and treatment of bone metastasis are of crucial significance for the quality of life of patients. Jambor *et al.* studied 26 breast cancer and 27 prostate cancer patients at high risk of bone metastasis and subjected them to ^{99m}Tc-hydroxymethane diphosphonate planar bone scintigraphy (^{99m}Tc-HDP BS), ^{99m}Tc-HDP SPECT, ^{99m}Tc-HDP SPECT/CT, [^{18}F]NaF PET/CT, and whole body magnetic resonance imaging combined with diffusion weighted imaging (wbMRI + DWI) examinations. They found that [^{18}F]NaF PET/CT and wbMRI + DWI had similar diagnostic accuracy for bone metastasis and were superior to the other 3 detection methods (25). The National Oncologic PET Registry (NOPR) conducted a study aimed at evaluating the effectiveness of [^{18}F]NaF PET in identifying bone metastatic disease, specifically in patients with prostate cancer. The results supported the significant impact of NaF PET in the initial staging of prostate cancer, diagnosis of first suspected bone metastasis, and expected management of known bone metastases. Overall variations in expected management, when divided into therapeutic and nontherapeutic categories, ranged from 44% to 52% and 12% to 16%, respectively. Additionally, approximately 70–80% of patients were able to avoid additional noninvasive imaging studies after undergoing [^{18}F]NaF PET examination (26).

Intellectual structure of the [^{18}F]NaF PET field

Based on author, journal, and document co-citation analysis, we characterized the intellectual structure of the [^{18}F]NaF PET field.

First, the top 5 highly cited authors (*Table 5*) were Even-Sapir (188 times), Dweck (170 times), Beheshti (167 times), Grant (162 times), and Joshi (157 times). The overall trend, as shown in *Figure 9*, indicates that the citation frequencies of these authors exhibit an initial increase followed by a subsequent decline, with the year 2020 marking the peak. Even-Sapir is among the most highly cited authors in the field, with a keen interest in various areas such as bone metastasis, melanoma, and lymphoma. Despite his significant contributions to the field of [^{18}F]NaF PET, many of his publications predate 2008 and are thus not included in the co-authorship analysis. Joshi was the most highly cited academic author in the field in 2020, with 4 publications related to [^{18}F]NaF PET from 2012 to 2015. Each of his publications has received relatively high citation counts, and his first-author publications on the identification of coronary high-risk plaques (17) have been cited 644 times, demonstrating his profound academic influence in the field. Joshi's research interests are primarily focused on interventional therapies and diagnostic methods for cardiovascular disease. Dweck has been the most frequently cited scholar in the field over the past 3 years, with research primarily focused on imaging techniques for cardiovascular diseases such as coronary atherosclerosis and plaque rupture, as well as aortic valve stenosis. The highly cited papers authored by Beheshti primarily focus on prostate cancer, particularly in the area of bone metastases associated with this disease. Meanwhile, Grant's research interests center mainly around skeletal tumors and pediatric radiology. Regarding the metric of betweenness centrality, 5 scientists had a betweenness centrality score exceeding 0.2, indicating their significant influence in the development of the [^{18}F]NaF PET field. Moreover, authors with high citation frequency and betweenness centrality, such as Hawkins and Blau, may be regarded as possessing considerable impact on this domain.

Second, the *Journal of Nuclear Cardiology* and the *Journal of Nuclear Medicine* are the top-producing journals in the field, with a literature count of 44 each. Among them, the *Journal of Nuclear Medicine* is the most cited journal, with over 600 citations, indicating its significant contribution to the [^{18}F]NaF PET field and its high impact in this area. Additionally, *the American Journal of Roentgenology* had high betweenness centrality, indicating that it serves as a bridge connecting other journals and maintains close collaborative relationships with them.

Third, with the factors of size, activity, and the rationality of cluster labels being considered, the research areas of interest in the field of [^{18}F]NaF PET were found to mainly be concentrated in atherosclerotic plaque, bone metastases, and clinical application. Through reading core literature in this field, including highly cited references as the knowledge basis and representative citing papers as the research frontiers, we can gain a profound understanding of the meaning of these clusters.

The cluster concerning atherosclerotic plaque was the most cited and longest-enduring cluster in the [^{18}F]NaF PET field, with a total of 115 cited articles. Among them, a paper by Irkle as the first author was the most highly cited reference in this cluster. This paper revealed the precise molecular mechanism of vascular tissue uptake of [^{18}F]NaF in carotid atherosclerotic plaques. [^{18}F]NaF can specifically bind to calcified regions and distinguish between macrocalcification and microcalcification. Microcalcification, representing new and active plaques due to its large surface area and lack of diffusion barriers, shows higher uptake. Therefore, these authors believe that [^{18}F]NaF PET can noninvasively identify unstable atherosclerotic plaque (23). The second most highly cited reference in this cluster was a study by Joshi *et al.*, which demonstrated through clinical trials, that there is significant [^{18}F]NaF uptake in all ruptured carotid plaques, and that plaques with locally increased uptake of [^{18}F]NaF can be identified by intravascular ultrasound as having higher-risk features in stable angina patients. This supports [^{18}F]NaF PET/CT as a promising noninvasive technique for identifying and locating ruptured and high-risk coronary atherosclerotic plaques (17). The most representative citing article in the atherosclerotic plaque cluster (36 cited articles) was a paper by Raynor *et al.* This paper systematically summarizes the roles of NaF and fluorodeoxyglucose (FDG) in assessing the progression of atherosclerosis and suggests that NaF PET/CT has the potential to be a comprehensive detection method for the early evaluation of atherosclerosis (27).

The bone metastases cluster was the second largest cluster in the [^{18}F]NaF PET field, with 114 cited references. Among these, Hillner's 2 papers were among the most cited references, in which it was reported that [^{18}F]NaF PET plays an important role in the management of bone metastases in patients with cancer and their treatment monitoring (26,28). The most representative citing article in this cluster was the paper by Li *et al.* (29), which includes 24 cited references. In this study, Li *et al.* extensively examined the application of different tracers in PET/CT for prostate cancer, with [^{18}F]NaF PET showing high sensitivity and low specificity in the early stages of bone metastasis in prostate cancer, which may lead to misdiagnosis of benign degenerative and inflammatory lesions (29).

The clinical application cluster contained 39 cited articles, the seventh most among the clusters. In this cluster, Raynor's 2 articles are respectively the highly cited reference and the most representative citing papers. In 2 papers, the applications of [^{18}F]NaF PET in various diseases, including osteoporosis, vascular calcification, rheumatic diseases, bone metastasis, and back pain, are systematically introduced (30,31). Overall, the clinical applications of [^{18}F]NaF PET mainly center around musculoskeletal and cardiovascular diseases, which is reflected in the high proportion of publications in these 2 fields.

Study limitations

There are 3 limitations in this study. First, the data used in this study were limited to the WOS core dataset, and thus slight differences in the research results could have arisen if different databases, such as PubMed and Scopus, were used. This is mainly due to the variability in the fields covered by different databases and to software limitations. However, WOS is an extremely important academic literature database with a wide range of literature coverage. Second, the language of papers included in this study was limited to English, which might have led to some literature sources being missed. Nevertheless, we believe that the set of research data was representative, as English is a widely used language in academic fields. Third, due to the inherent focus of bibliometric analysis in exploring the more active aspects of a field, there is a tendency to overlook certain important developments and underestimate the diversity of clinical applications. This may occur, to some extent, because of the absence of key domain-specific keyword indexing or the low frequencies of certain keywords, which may prevent these aspects from being adequately highlighted.

Conclusions

The publication trend in the field of [^{18}F]NaF PET has shown a steady increase over the years. In terms of social and international structure, a relatively stable core group of authors and institutional collaborators has emerged, but the degree of collaboration between them needs to be improved. In terms of content structure, the field has mainly focused on [^{18}F]NaF PET-related technologies, bone metastasis, and atherosclerosis. In terms of intellectual structure, the research areas of concentration in the [^{18}F]NaF PET field are primarily concentrated on atherosclerotic plaques, bone metastasis, and its clinical applications.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-703/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All data were obtained through literature retrieval based on the canonical database. No medical institutions or patients were included, and thus ethical approval or informed consent was not applicable.

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