Observational Study

Medicine

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Knowledge domain and dynamic patterns in multimodal molecular imaging from 2012 to 2021

A visual bibliometric analysis

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Abstract

Multimodal molecular imaging technologies have been widely used to optimize medical research and clinical practice. Bibliometric analysis was performed to identify global research trends, hot spots, and scientific frontiers of multimodal molecular imaging technology from 2012 to 2021. The articles and reviews related to multimodal molecular imaging were retrieved from the Web of Science Core Collection. A bibliometric study was performed using CiteSpace and VOSviewer. A total of 4169 articles and reviews from 2012 to 2021 were analyzed. An increasing trend in the number of articles on multimodal molecular imaging technology was observed. These publications mainly come from 417 institutions in 92 countries, led by the USA and China. K. Bailey Freund published the most papers amongst the publications, while R.F. Spaide had the most co-citations. A dual map overlay of the literature shows that most publications were specialized in physics/materials/chemistry, and molecular/biology/immunology. Synergistic therapy in cancer, advanced nanotechnology, and multimodal imaging in ophthalmology are new trends and developing areas of interest. A global bibliometric and visualization analysis was used to comprehensively review the published research related to multimodal molecular imaging. This study may help in understanding the dynamic patterns of multimodal molecular imaging technology research and point out the developing areas of this field.

Abbreviations: CT = computed tomography, IF = impact factor, JCR = journal citation reports, OCTA = optical coherence tomography angiography.

Keywords: bibliometric analysis, Citespace, molecular imaging, multimodal imaging, visualization, VOSviewer

1. Introduction

In clinical research, various modern imaging technologies have been used to monitor structural, functional, and molecular changes in tissues, including optical imaging (either by bioluminescence or fluorescence), computed tomography (CT), magnetic resonance imaging, positron emission tomography, single-photon emission CT, and ultrasound (US).[1–4] Each imaging modality has its own unique strengths and intrinsic limitations (such as spatial/depth resolution and sensitivity), which can make achievement of precise and consistent information at disease sites difficult. To compensate for these limitations, multimodal molecular imaging techniques have been researched in recent years.[5] Multimodal molecular imaging combines 2 or more kinds of detection technologies to create new methods of imaging to identify living biological processes at the cellular and molecular levels in a noninvasive manner.[5,6] Currently, multimodal molecular imaging is being widely used to optimize medical research and clinical practice, such as in drug discovery and development,[7] tumor diagnosis and treatment,[8] cardiovascular diseases,[9] neurological disorders,[10] and ophthalmic diseases.[11] The development of this field has been a breakthrough in medical imaging and molecular biology. However, no comprehensive and impartial assessment on the trends of published outputs, influential countries/regions, institutions, or authors, and their collaboration, knowledge base, hotspots, and frontiers in research related to multimodal molecular imaging technology is available.

Bibliometric research is a new method for summarizing progress in a target research field and further identifying hotspots, landmarks, pivots, or rising patterns in the research area by creating science mappings.[12,13] Many researchers have used bibliometric analysis in various fields of medicine. For example, Zhang et al[14] analyzed the research hotspots and trends of peripheral nerve injuries, and Li et al[15] reported the research hotspots and frontiers in post-stroke pain. Zhang et al[16] analyzed research trends on cholangiocarcinoma using machine learning.

The present study explored the hotspots and frontiers in multimodal molecular imaging technology over the past 10 years and generated the corresponding knowledge maps using CiteSpace and VOSviewer. This study provided insights on the

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The datasets generated during and/or analyzed during the current study are publicly available.

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latest progress, evolution paths, frontier research hotspots, and future research trends in multimodal molecular imaging for basic research, clinical prevention, and treatment.

2. Materials and Methods

2.1. Data source and retrieval strategy

The Web of Science Core Collection bibliographic database developed by Thomson Scientific was used to perform scientometric analysis. The following parameters were used for document retrieval: TS = "multi-modal molecular imaging" OR "multimodal imaging" OR "multimodal molecular imaging" OR "molecular imaging." Document retrieval was conducted in 1 day (June 25, 2022) to avoid deviation error. Two researchers (ZZW and FZG) independently searched the original data, then discussed possible differences, and the final agreement level reached 0.95, showing substantial consistency. We ultimately analyzed 4169 articles. Figure 1 shows the detailed filtering process.

2.2. Data analysis and visualization

We utilized CiteSpace (version 5.8.3) to perform collaboration network analysis (countries/regions, institutions, authors), co-citation analysis (authors, journals, and references), dual-map overlays, and citation burst detection for references. The specific parameters used in CiteSpace were set as follows: time slicing (from January 2012 to December 2021; years per slice = 1), text processing (title, abstract, author keywords, and keywords plus), node type (1 option chosen at a time from country, institution, author, co-cited journal, co-cited author, or co-cited reference), link strength (cosine), link scope (within slices), selection criteria (g-index, k = 25), and pruning (none). Other parameters were set to default. Betweenness centrality is an indicator of a node that considers the number of shortest paths from all vertices to all others that pass through the node. A node with a high value of betweenness centrality has a large influence on the transfer of information through the network. This indicator is used by CiteSpace to find and quantify the value of literature, and a purple circle is used to emphasize high-influence literature (or authors, journals, institutions, etc.).[17,18]

Developed by Leiden University, VOSviewer is used for map creation, visualization, and exploration based on network data.[19] VOSviewer (version 1.6.18) was used to create the keyword co-occurrence and cluster maps based on text data. We used natural language processing algorithms to extract terms from the fields of titles and abstracts, supplemented with VOSviewer corpus files.[17]

We obtained the journal citation reports (JCR), 2021 impact factor (IF), and JCR division of analyzed journals from the Web of Science.

2.3. Ethics and consent

This study involved no animal and human subjects; therefore, no ethical approval was required.

3. Results

3.1. Temporal distribution map of publications and citations

After the screening process, the retrieved publications on multimodal molecular imaging technology included 4169 related articles, which showed an annually increasing trend. The number of papers published on this topic steadily increased from 2012 to 2021. The lowest number of articles (148) and citations

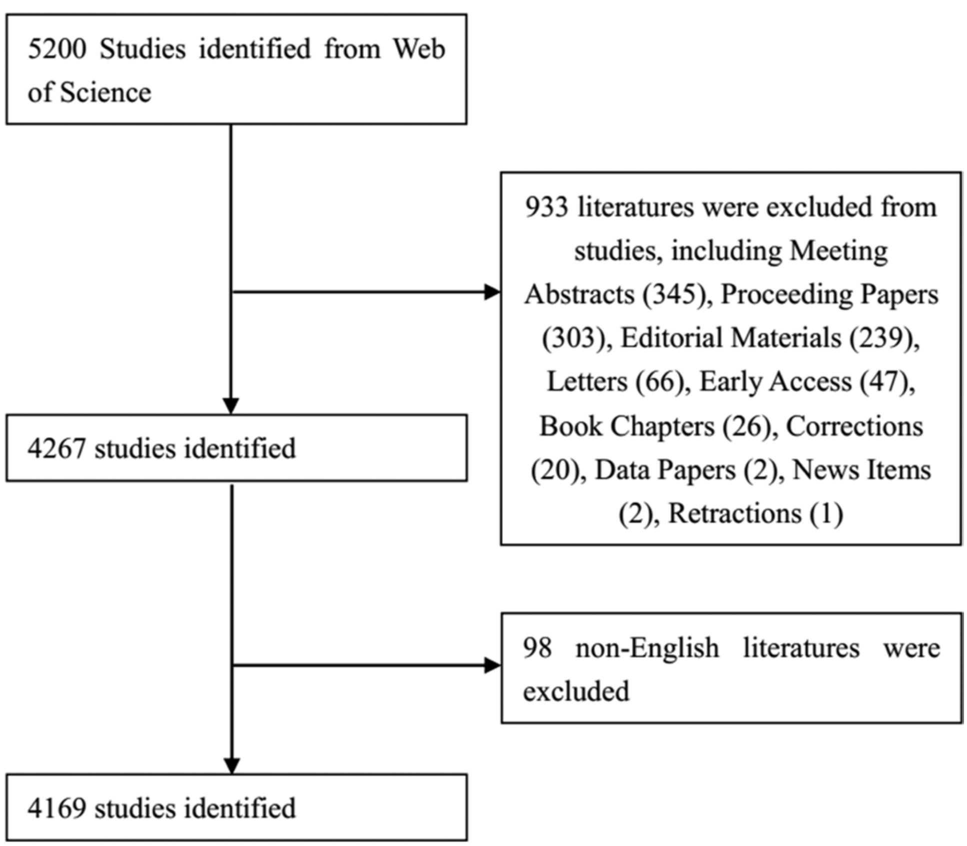

Figure 1. Flowchart of the screening process.

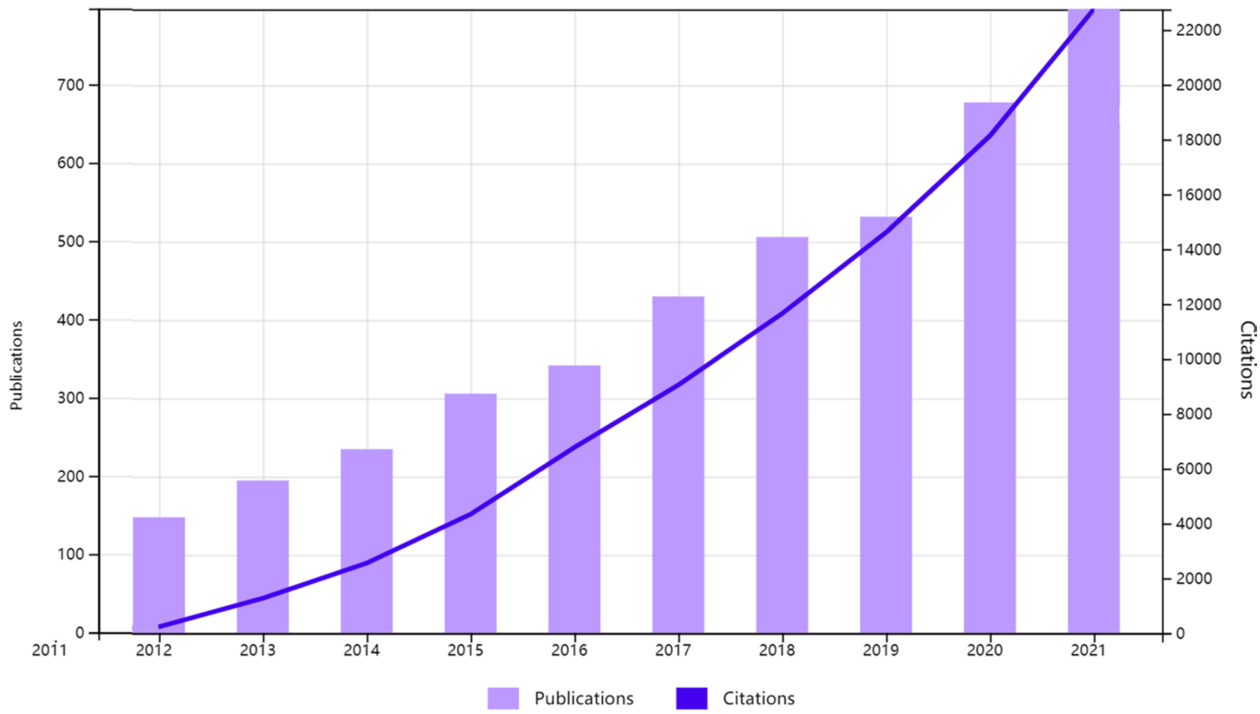

Figure 2. Temporal distribution map of publications and citations.

Table 1

Top 10 most productive countries/regions and institutions.

Rank	Country/Regions	Yr	Count (%)	Centrality	Institutions	Yr	Count (%)	Centrality
1	USA	2012	1362 (32.67)	0.48	Chinese Acad Sci	2012	160 (3.84)	0.09
2	Peoples R China	2012	952 (22.84)	0.03	Vitreous Retina Macula Consultants of New York	2012	105 (2.52)	0.08
3	Germany	2012	414 (9.93)	0.08	Univ Calif Los Angeles	2012	84 (2.01)	0.20
4	Italy	2012	352 (8.44)	0.10	Soochow Univ	2012	83 (1.99)	0.03
5	England	2012	300 (7.20)	0.18	New York Univ	2012	83 (1.99)	0.06
6	France	2012	286 (6.86)	0.08	Stanford Univ	2012	77 (1.85)	0.19
7	India	2012	184 (4.41)	0.11	Columbia Univ	2012	65 (1.56)	0.04
8	South Korea	2012	171 (4.10)	0.01	Manhattan Eye Ear & Throat Hosp	2012	57 (1.37)	0.04
9	Switzerland	2012	168 (4.03)	0.17	Harvard Med Sch	2016	57 (1.37)	0.09
10	Australia	2012	157 (3.77)	0.12	Sun Yat Sen Univ	2012	53 (1.27)	0.02

(228) were from 2012, and the highest number of articles (797) and citations (22,740) were from 2021 (Fig. 2).

3.2. Spatial distribution map of countries/regions and institutions

Overall, 417 institutions from 92 different countries/regions contributed to research related to multimodal molecular imaging technology. We ranked the 10 countries/regions and institutions with the highest productivity (Table 1). The USA (1362/32.67%) and China (952/22.84%) published the most articles, followed by Germany (414/9.93%), Italy (352/8.44%), and England (300/7.20%). In addition, the Chinese Academy of Sciences (160/3.84%) published the most articles, followed by the Vitreous Retina Macula Consultants of New York (105/2.52%) and University of California-Los Angeles (84/2.01%). Among the top 10 productive institutions, the USA was the home to most institutions, excluding Chinese Academy of Sciences, Soochow University, and Sun Yat Sen University in China. Additionally, several countries and institutions, such as the USA (0.48), England (0.18), Switzerland (0.17), Australia (0.12), University of California-Los Angeles (0.20), Stanford University (0.19), showed high centrality (Fig. 3A and B, encircled in purple). This finding suggests that these countries and institutions may play critical roles in multimodal molecular imaging technology. The lines connecting the circles represent international collaboration, and dense connections indicate active cooperation among those countries and affiliations (Fig. 3).

3.3. Visual analysis of authors and co-cited authors

In total, 555 authors and 834 co-cited authors were associated with multimodal molecular imaging technology. The top ten productive authors are listed in Table 2. K. Bailey Freund of the Vitreous Retina Macula Consultants of New York was the most productive, with the highest number of publications (n = 81), followed by Giuseppe Querques (n = 48), Francesco Bandello (n = 45), and David Sarraf (n = 36). Co-cited authors refer to 2 or more authors cited by another or several papers simultaneously, constituting a co-cited relationship.[17] Among the top 10 co-cited authors, 4 authors have been cited more than 200 times. R.F. Spaide (350) from the Vitreous Retina Macula Consultants of New York was the most frequently co-cited author, followed by L. Cheng (238), J. Kim (235), and

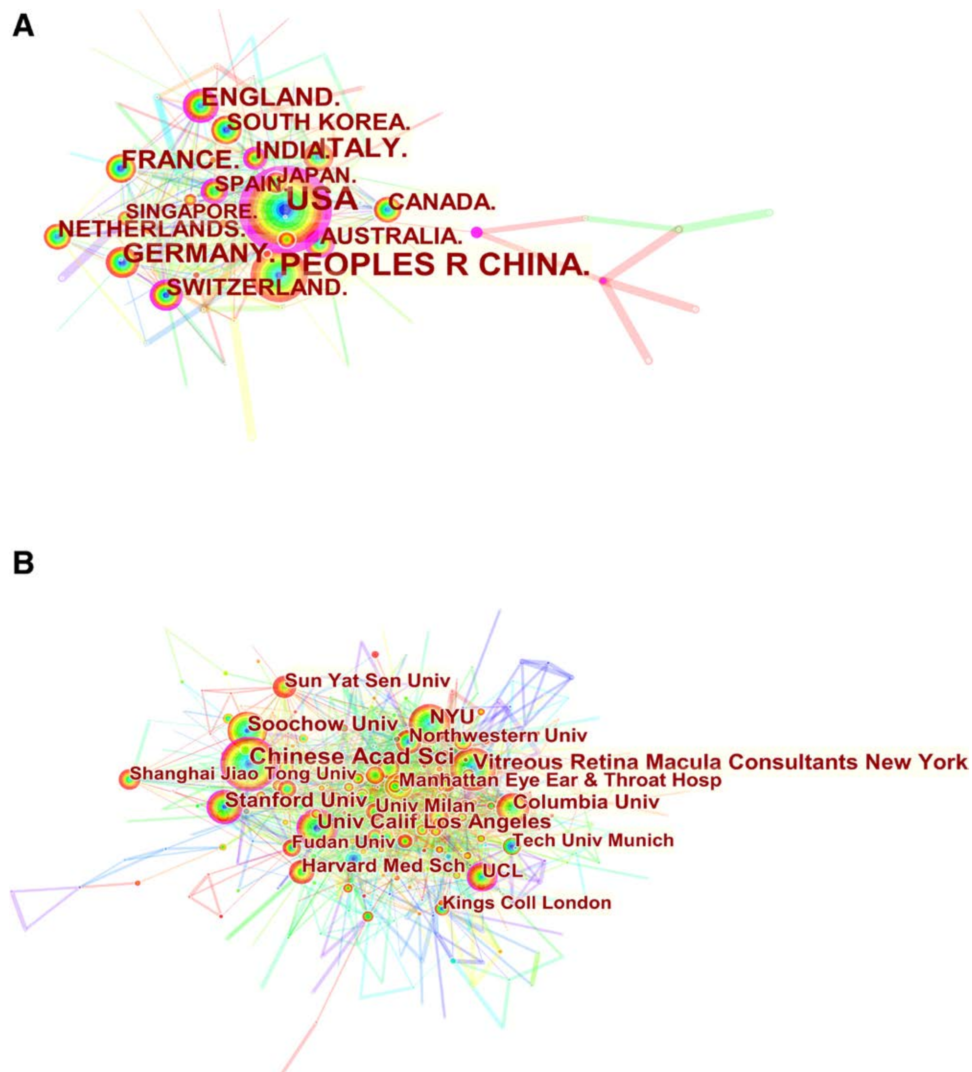

Figure 3. Spatial distribution map of countries/regions (A) and institutions (B). Each circle in the diagram represents a nation/institution, with the size of the circle indicating the published outputs of the country/institution. The lines that connect the circles represent international collaboration, and the broader the lines, the tighter the cooperation. The color of the node and line represent different years, and the warmer the color, the more recent time of the publication.

Table 2

Top 10 journals and co-cited journals.

Rank	Journal	Count	JCR	IF (2021)	Co-cited journals	Citations	JCR	IF (2021)
1	Retina	135	Q2	3.975	Proceedings of the National Academy of Sciences of the United States of America	1128	Q1	12.779
2	ACS Applied Materials Interfaces	79	Q2	10.83	ACS Nano	1054	Q1	18.027
3	Ophthalmic Surgery Lasers Imaging Retina	64	Q4	1.296	PLOS One	1054	Q3	3.752
4	Scientific Reports	64	Q3	4.996	Biomaterials	1025	Q1	15.304
5	Biomaterials	62	Q1	15.304	Journal of the American Chemical Society	978	Q1	16.383
6	European Journal of Ophthalmology	60	Q4	1.922	Angewandte Chemie	914	Q1	16.823
7	Nanoscale	59	Q2	8.307	Advanced Materials	894	Q1	32.086
8	ACS Nano	58	Q1	18.027	Science	844	Q1	63.714
9	Advanced Functional Materials	50	Q1	19.924	Ophthalmology	825	Q1	14.277
10	Theranostics	46	Q1	11.600	American Journal of Ophthalmology	823	Q2	5.488

JCR = journal citation reports, IF = impact factor.

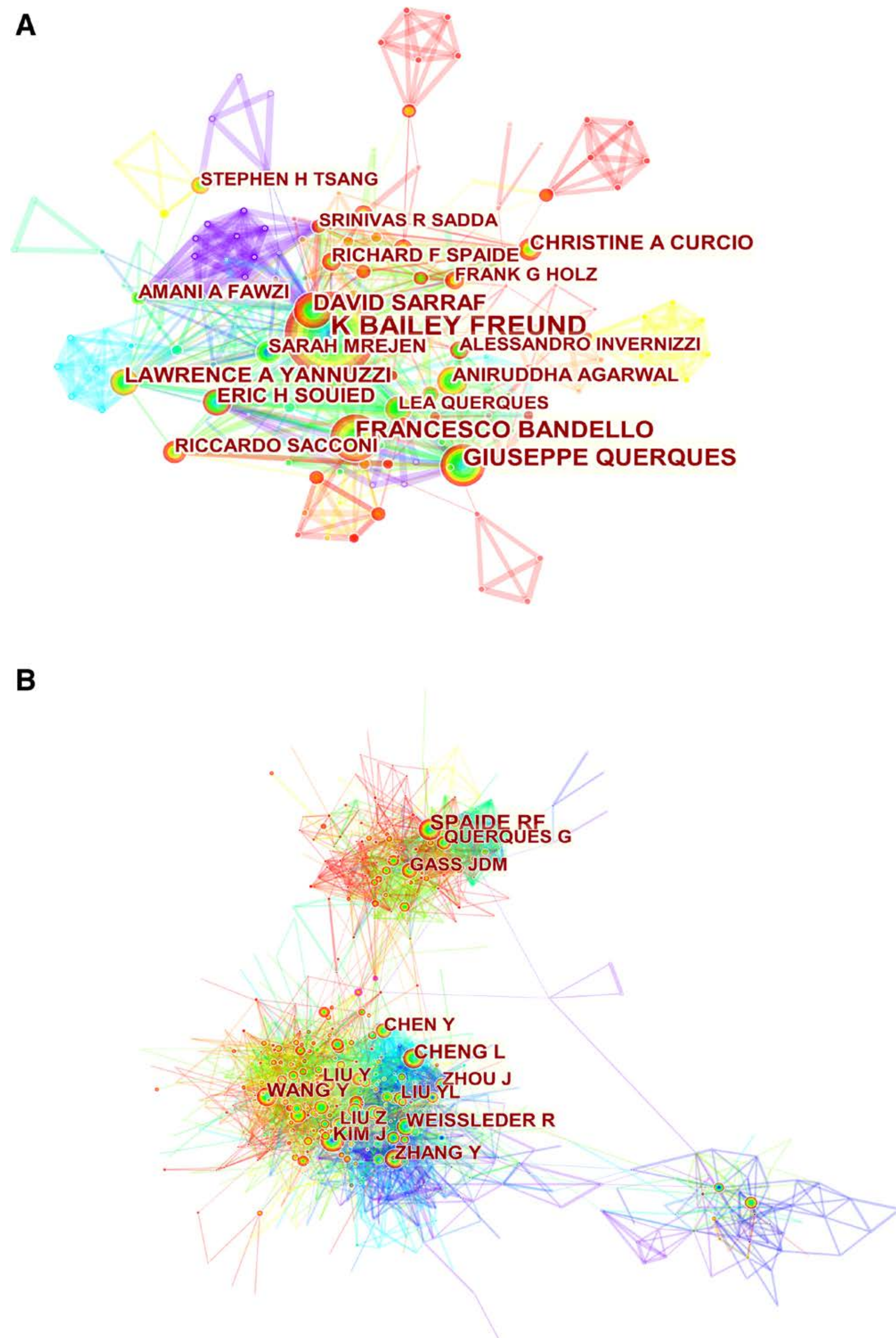

Figure 4. Visual analysis of authors (A) and co-cited authors (B). The node size represents the number of studies published by the author, with larger nodes representing more published papers. The closer the collaboration between the 2 writers is, the shorter the distance between the 2 nodes. The purple nodes represent early published articles, while the red nodes represent recently published articles.

Y. Wang (220). However, the co-cited authors have relatively low centralities (<0.05). Figure 4 shows the relatively interconnected network of communication and cooperation among authors and co-cited authors in this research field since 2012.

3.4. Visual analysis of journals and co-cited journals

The results showed that the 4169 articles were published in 200 academic journals. As shown in Table 2, *Retina* (135 publications, IF: 3.975) published the most articles concerning multimodal molecular imaging technology, followed by *ACS Applied Materials Interfaces* (79 publications, IF: 10.83) and *Ophthalmic Surgery Lasers Imaging Retina* (64 publications, IF: 1.296). Among the top ten journals, 4 were in the Q1 JCR division, and 6 had an IF of more than 5.0 (Table 2). Through analysis of periodical co-citations, we can see the contribution of each periodical to this field. Among the 944 co-cited journals, 4 journals had citations totaling over 1000. As presented in Table 2, *Proceedings of the National Academy of Sciences of*

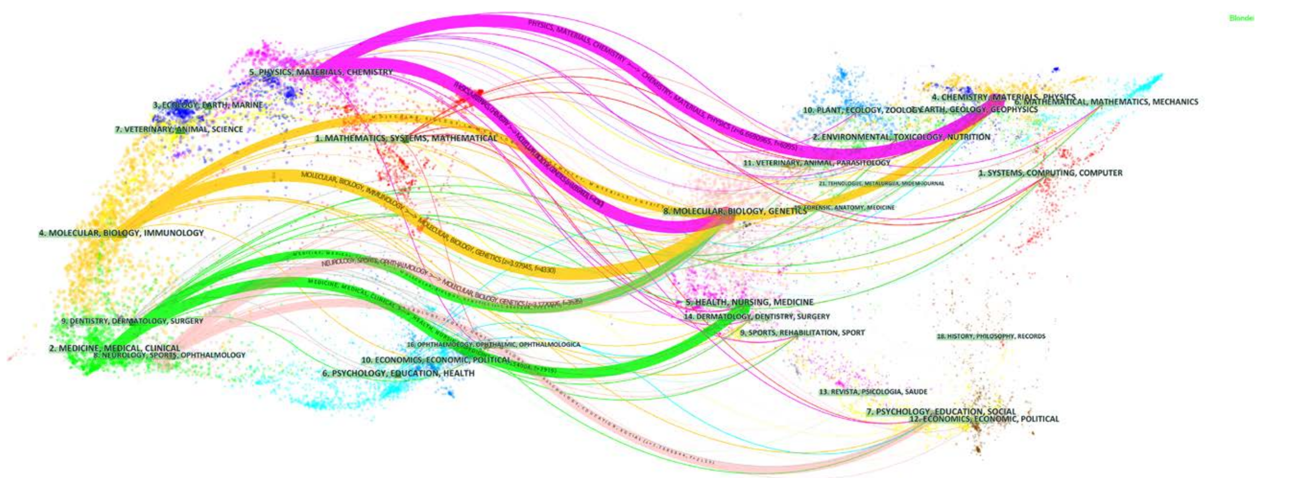

Figure 5. A dual-map overlay of the science mapping literature. The citing journals are on the left, the cited journals are on the right, and the colored path represents the citation relationship. Citation trajectories are distinguished by the colors of the citing regions. The thickness of these trajectories is proportional to the z-score-scaled frequency of citations.

the United States of America had the most co-citations (citations: 1128, IF: 12.799), followed by *ACS Nano* (citations: 1054, IF: 18.027), *PLOS One* (citations: 1054, IF: 3.752), and *Biomaterials* (citations: 1025, IF: 15.304). According to the 2021 journal citation reports, 90% were in the Q1/2 JCR division except for *PLOS One*. Eight of the top ten co-cited journals had an IF of more than ten, with the highest IF from *Science* (IF = 63.714).

A dual-map overlay renders a domain-level view of the growth of the literature and concentration of citations through their reference paths. Figure 5 shows a dual map overlay concerning articles related to multimodal molecular imaging technology published between 2012 and 2021. The papers published in Chemistry/Materials/Physics and Molecular/Biology/Genetics journals are often cited by Physics/Materials/Chemistry and Molecular/Biology/Immunology journals. Papers published in Molecular/Biology/Genetics and Health/Nursing/Medicine journals are often cited by Medicine/Medical/Clinical journals, and papers published in Molecular/Biology/Genetics and Psychology/Education/Social journals are often cited by Neurology/Sports/Ophthalmology journals.

3.5. Visual analysis of co-citation, clustering networks, and citation burst

Figure 6A displays co-citations of the 856 citing articles, the first author, and the publication year of the top 10 most cited references. More information on the top 10 references cited is presented in Table 3. The most co-cited reference was a review published in *Chemical Society Reviews* by Lee D.E. et al[20] titled, "Multifunctional nanoparticles for multimodal imaging and theragnosis, followed by an article titled, "Multimodality imaging probes: design and challenges."[21]

Through CiteSpace, an hierarchical clustering network is generated if 2 publications have many similar references and are suggested to be homogeneous.[17] The 10 largest clusters extracted from the references of the 856 citing articles are shown in Figure 6B. The cluster labels are well-known noun phrases extracted from the title of citing articles using a logarithmic likelihood ratio algorithm, including theranostic agents (#0), synergistic therapy (#1), translational research (#2), recent advances (#3), biomedical nanomaterial (#4), drug delivery (#5), age-related macular degeneration (#6), optical coherence tomography angiography (OCTA) (#7), reticular pseudodrusen (#8), and targeting alpha v beta (#9). The total Q-value was 0.7536, and each cluster had a weighted mean silhouette of 0.8866, suggesting that the cluster quality was reasonable. Purple nodes represent early clustering labels which included biomedical nanomaterial and targeting alpha v beta, while red nodes represent recent clustering labels such as synergistic therapy, recent advances, and age-related macular degeneration.

We set the burst duration to at least 2 years in CiteSpace, from which we detected 30 of the most "bursty" references (Fig. 7). Figure 7 shows that the first co-citation burst began in 2012, titled, "Multimodality imaging probes: design and challenges." Seven references (23.33%) were in the burst stage until 2021, which implies that the research related to multimodal molecular imaging may continue to explode in the future.

A timeline view can visualize the evolution and progress of research hotspots over time.[22] As indicated in Figure 8, clusters #2 (translational research), #4 (biomedical nanomaterial), and #5 (drug delivery) started earlier but ceased in 2016, while clusters #1 (synergistic therapy), #3 (recent advances), and #6 (age-related macular degeneration) are still ongoing, which can be considered as the frontiers.

3.6. Keyword analysis of trending research topic

Author keywords extracted from titles and abstracts were analyzed using VOSviewer. A total of 15,358 keywords were extracted, of which 626 keywords appeared more than ten times, and 98 keywords appeared more than fifty times. As presented in Figure 9A and Table 4, multimodal imaging was the most important term with 996 co-occurrences, followed by nanoparticles, in vivo, optical coherence tomography, magnetic resonance imaging, and drug-delivery. In the keywords co-occurrence visualization diagram, author keywords are marked with different colors according to their average publication years. "OCT angiography," "fundus autofluorescence," "nanoparticles," "photodynamic therapy," and others are highlighted in yellow indicating more recent publications.

Figure 9B shows the timeline of 40 keywords, showing the evolution of the research topic over time.[23] The progress of the research field may divide into 2 stages. From 2012 to 2016, studies mainly focused on multimodal imaging, photothermal therapy, mice, indocyanine green angiography, risk factor, etc, indicating that researchers paid attention to the technology and related basic research. From 2017 to 2021, the representative burst keywords were diabetic retinopathy, photoacoustic microscopy, natural history, tumor microenvironment, pathogenesis, etc, suggesting the transition from basic to clinical research.

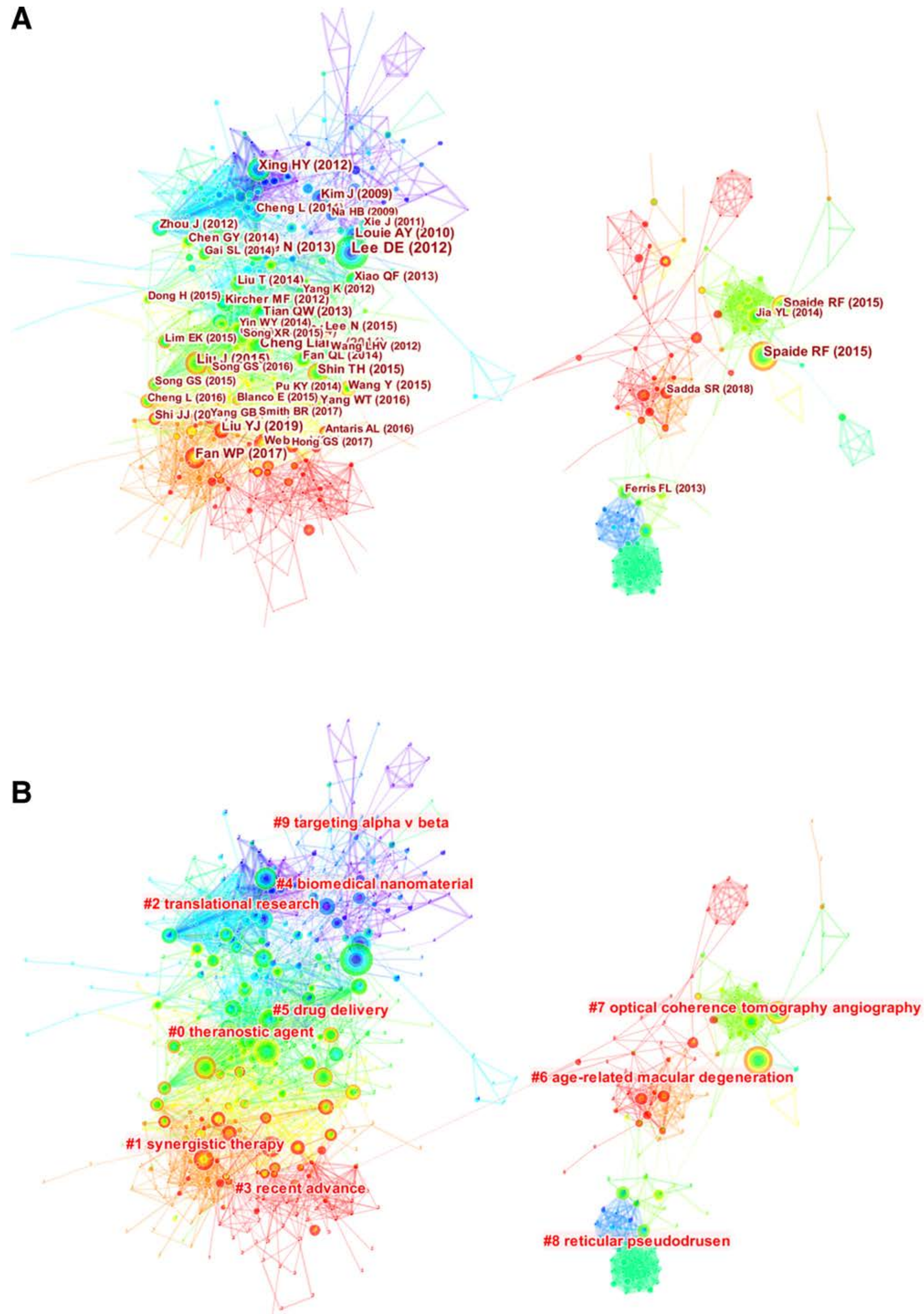

Figure 6. Visual analysis of co-citation (A) and clustering network (B). Each circle represents a reference. The size of the circle is proportional to the citation frequency. The link between the 2 circles represents 2 references cited in the same article among the articles (citing articles). Similarly, line thickness is positively correlated with co-citation frequency.

Keyword bursts are those that were cited significantly frequently over a period.[22] As shown in Figure 10, ray CT had the strongest bursts (strength = 9.84), followed by natural history, ranibizumab, and retinitis pigmentosa, etc 2021, suggesting that these domains may become a hot topic in future research.

4. Discussion

4.1. General information

This study is the first bibliometric analysis of the dynamic patterns in multimodal molecular imaging technology research. After the screening process, we determined that a total of 555 authors from 417 institutions in 92 countries have published 4169 papers in 200 academic journals related to multimodal molecular imaging technology in the last decade.

The spatial distribution map of countries/regions and institutions (Table 1 and Fig. 3) shows that the USA, China, and Germany were the top 3 high-yield nations in publishing studies on multimodal molecular imaging technology. The USA has the highest betweenness centrality (0.48), indicating that it plays a key bridge role in national cooperation networks worldwide. The Chinese Academy of Sciences published the most papers, and we discovered extensive connections among Vitreous

Table 3

Top 10 co-cited references.

Rank	Title	Journal	Co-citation	Centrality
1	Multifunctional nanoparticles for multimodal imaging and theragnosis	Chemical Society Reviews	80	0.05
2	Multimodality imaging probes: design and challenges	Chemical Reviews	56	0.01
3	PEGylated WS(2) nanosheets as a multifunctional theranostic agent for in vivo dual-modal CT/photoacoustic imaging guided photothermal therapy	Advanced Materials	55	0.11
4	Functional nanomaterials for phototherapies of cancer	Chemical Reviews	53	0.05
5	Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography	JAMA Ophthalmology	51	0
6	Bismuth sulfide nanorods as a precision nanomedicine for in vivo multi-modal imaging-guided photothermal therapy of tumor	ACS Nano.	44	0.07
7	Photothermal therapy and photoacoustic imaging via nanotheranostics in fighting cancer	Chemical Society Reviews	42	0.06
8	Multifunctional nanoprobes for upconversion fluorescence, MR and CT trimodal imaging	Biomaterials	41	0.03
9	Nanotechnology for Multimodal Synergistic Cancer Therapy	Chemical Reviews	41	0.04
10	Nano-sized CT contrast agents	Advanced Materials	41	0.04

CT = computed tomography.

Retina Macula Consultants of New York, Manhattan Eye Ear & Throat Hospital, Sun Yat Sen University, and other institutions, indicating significant collaborative contributions to multimodal molecular imaging technology.

We ranked the top ten productive authors and co-cited authors in Table 5 and Figure 4. K. Bailey Freund was the most productive author (81). He has been working on pachychoroid disorders and has published approximately ten related articles per year since 2012.[24–26] R.F. Spaide R.F. the most co-citations (350 citations), with the most cited article (613 citations) being a review titled, "Optical coherence tomography angiography," published in *Progress in Retinal and Eye Research* in 2018.[26] From Figure 4B, we can observe that the researchers seemed to be scattered into 3 main clusters, with relatively rare connections, indicating a lack of academic exchange between researchers from different countries.

As shown in Table 2, among the top ten journals, 4 were in the Q1 JCR division, and 6 had an IF of more than 5. Among 944 co-cited journals, 90% were in the Q1/2 JCR division except for PLOS One. Eight had an IF of more than ten. The results indicate that this research field is extremely important and a current hotspot. As rendered in Figure 5, 8 main citation paths are available in our dataset, with the domains most frequently covering the records (z = 6.669, 3.979, respectively) being: physics, materials, chemistry and molecular, biology, immunology. Following these 2 domains, the literature is mostly influenced by the fields of chemistry, materials, physics and molecular, biology, genetics. This indicates the multidisciplinary aspect of this field, since publications involving multiple domains contribute to the citation landscape of the domain.

Table 3 showed the top ten co-cited references, which mainly focused on 2 themes: firstly, the recent advances in the development of multifunctional nanoparticles and their biomedical applications to multimodal imaging and cancer therapy[20,27–29] and advances in OCT angiography in ocular diseases.[30] To automatically label clusters of cited references, we extracted candidate terms from the titles and abstracts of the citing articles. Labels extracted by logarithmic likelihood ratio tend to reflect a unique aspect of the cluster. Purple nodes represent early clustering labels that included biomedical nanomaterial (#4) and targeting alpha v beta (#9), while red nodes represent recent clustering labels, such as synergistic therapy (#1), recent advances (#3), and age-related macular degeneration (#6). In clusters #1 and 3, the literatures mainly focus on multimodal imaging-guided synergistic therapy using nanoparticles/agents in cancer[31–35] and advanced nanotechnology in the research field.[36–39] In cluster #6, the literature focuses on application of multimodal imaging in treating age-related macular degeneration,[40,41] and clinical applications of OCTA.[42,43]

4.2. Research hotspots and emerging topics

Keywords are indicators of emerging trends and new developments. Visualizing the timeline of references and keywords can present the evolution of new hotspots, and reference clusters and citation bursts can characterize the emerging topics in the discipline.[22,44–46] We aimed to objectively summarize the hotspots and emerging trend of multimodal molecular imaging research via the analysis of keyword co-occurrence (Table 4 and Fig. 9), keyword timeline view and burst (Figs. 9 and 10), reference cluster (Fig. 6), timeline view (Fig. 7), and burst (Fig. 8).

Multimodal imaging-guided synergistic therapy in fighting cancer is 1 main hotspot in the research field. As shown in Figures 6 and 7, synergistic therapy is one of the largest clusters and most active topic. From the burst references, Liu et al[29] pointed out that photothermal therapy or photoacoustic imaging has been intensively investigated for the treatment and diagnosis of cancer. Fan et al[47] summarized nanotechnology for multimodal synergistic cancer therapy and its remarkable super additive effects. Zhu et al[48] introduced near-infrared (NIR)-II imaging for cancer imaging and surgery. Furthermore, photoacoustic microscopy, natural history, nanoplatform, tumor microenvironment, bevacizumab, and pathogenesis all indicated synergistic cancer therapy is the current frontier in this research field (Figs. 9 and 10).

Advances in biomaterials in molecular imaging is another research hotspot. In reference timeline view, recent advances in nanotechnology is ongoing. Exogenous contrast agents, chemical dyes, and all kinds of nanostructures (carbon nanomaterials, gold nanomaterials, transition metal dichalcogenides, etc) are extensively studied recently.[49–51] As shown in Table 4, nanoparticles, contrast agents, and nanocrystals have high occurrence and total link strength.

Application of multimodal imaging in ophthalmology is the third research frontier. Spaide et al[52] presented the integration of OCTA in multimodal imaging in the evaluation of retinal vascular occlusive diseases, diabetic retinopathy, uveitis, inherited diseases, age-related macular degeneration, and disorders of the optic nerve. As shown in Figure 9 and 10, OCTA, age-related maculopathy, panuveitis, and retinitis pigmentosa are future research hotspots.

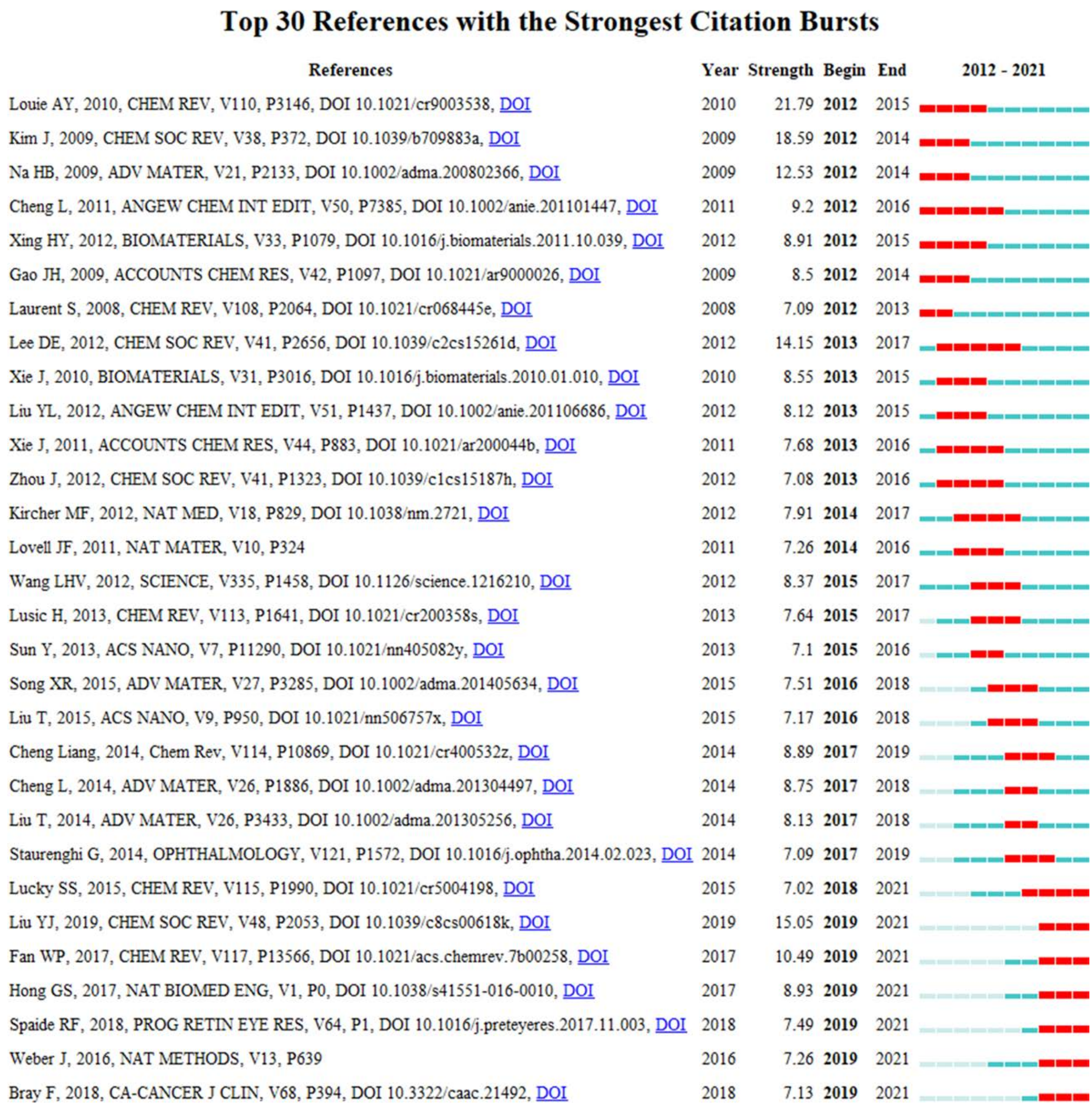

Figure 7. Visual analysis of references bursts. The intensity value reflects the cited frequency. Red bar indicates the citation frequency, while green bars indicate fewer citations.

4.3. Strength and limitations

This study uses a bibliometric method to analyze the current research landscape surrounding multimodal imaging techniques. We screened and analyzed over 4000 articles and reviews to elucidate trends, hotspots, and possible future topics of interest for this field. We were able to generate comprehensive visual representations of the existing knowledge base and progress of this topic. We believe that our study makes a significant contribution to the literature because it is the first analysis of its kind to the best of our knowledge and will help researchers better understand the dynamic changes in this research and pinpoint future topics of interest. This study has some inherent limitations. First, we only extracted articles from the Web of Science database. PubMed, Google Scholar, ProQuest, PsycINFO, and other databases were not included.[53] Second, the language was restricted to English, and linguistic bias may exist. Third, this study used articles published from 2012 to 2021. With recent efforts of researchers and continuous updating of the literature, the findings of this study may be different from current results.[54]

5. Conclusion

This study provides a visual analysis of the trends and frontiers of multimodal molecular imaging technology. With the help of CiteSpace and VOSviewer, we have a deeper understanding of the research landscape, frontier hotspots, and future trends of multimodal molecular imaging technology from the last decade. The leading countries of publication are the USA and China, and increasing numbers of articles published in international journals have a significant impact. Synergistic therapy in cancer, advanced nanotechnology, and applications in ophthalmology will be the highlights in future research. This study can provide important clues for researchers to understand the structure and dynamic patterns of the study field.

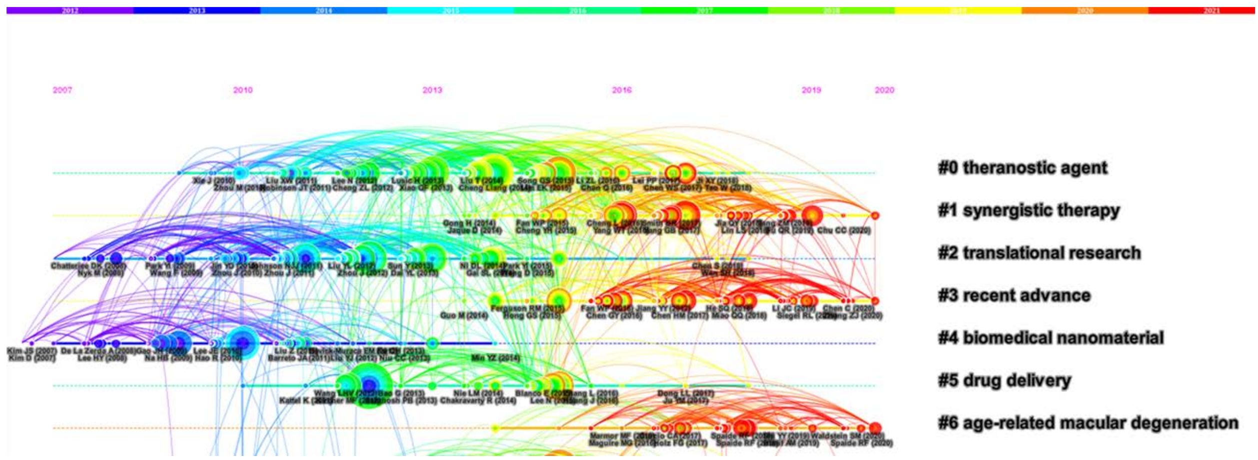

Figure 8. Timeline view of co-cited references. Each horizontal line represents a cluster; the smaller the number, the larger the cluster, and #0 is the largest cluster. The node size reflects the co-cited frequencies, and the links indicate the co-cited relationships; the color of node and line represent different years.

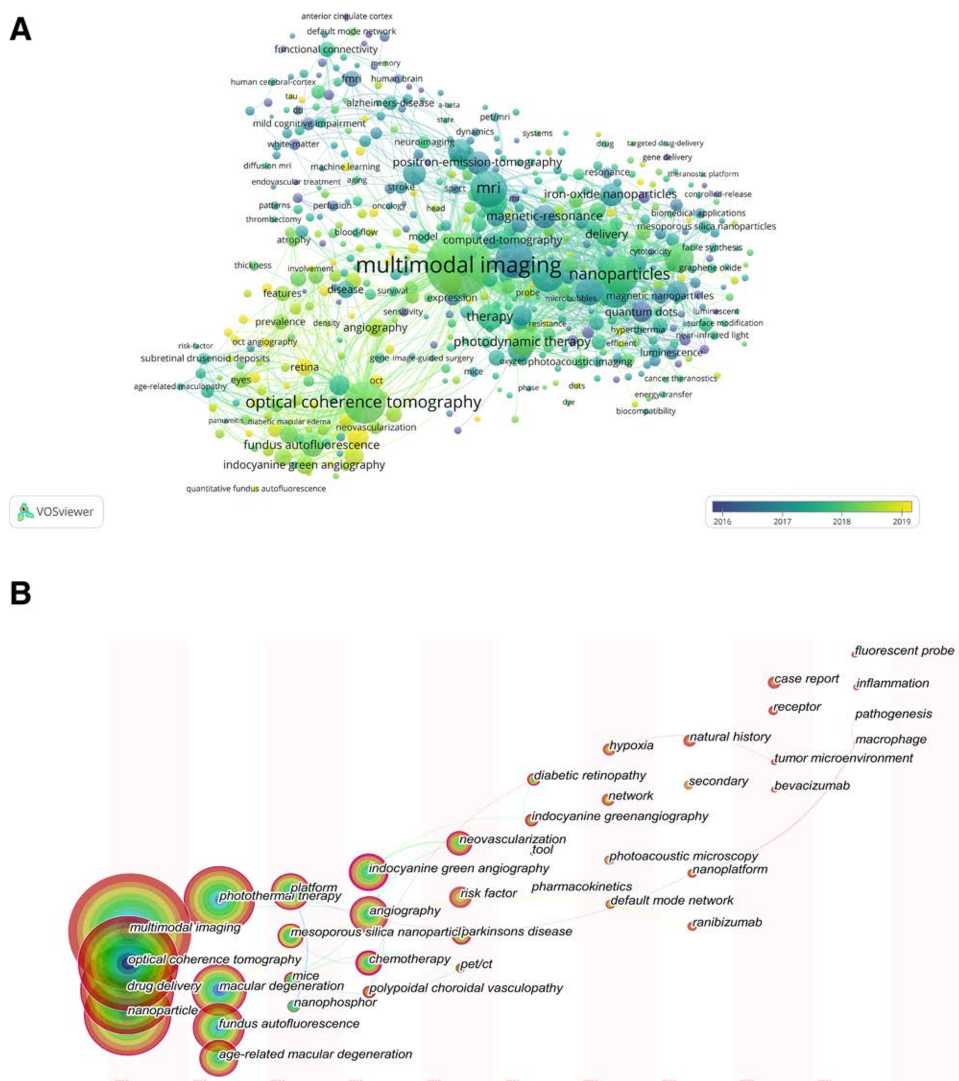

Figure 9. The co-occurrence network (A) and timeline view of keywords related to multimodal molecular imaging (B).

Table 4

Top 20 keywords.

Rank	Keywords	Occurrences	Total link strength	Rank	Keywords	Occurrences	Total link strength
1	Multimodal imaging	996	5329	11	Magnetic resonance imaging	200	1248
2	Nanoparticles	373	2383	12	Therapy	193	1159
3	In vivo	362	2312	13	Fluorescence	171	1112
4	Optical coherence tomography	458	2188	14	Magnetic-resonance	156	1068
5	Mri	349	2145	15	Iron-oxide nanoparticle	148	1050
6	Drug-delivery	254	1839	16	Pet	149	939
7	Photothermal therapy	232	1777	17	Nanocrystals	126	932
8	Cancer	278	1694	18	Delivery	142	929
9	Contrast agents	206	1464	19	Gold nanoparticles	123	919
10	Photodynamic therapy	200	1352	20	Positron-emission-tomography	150	889

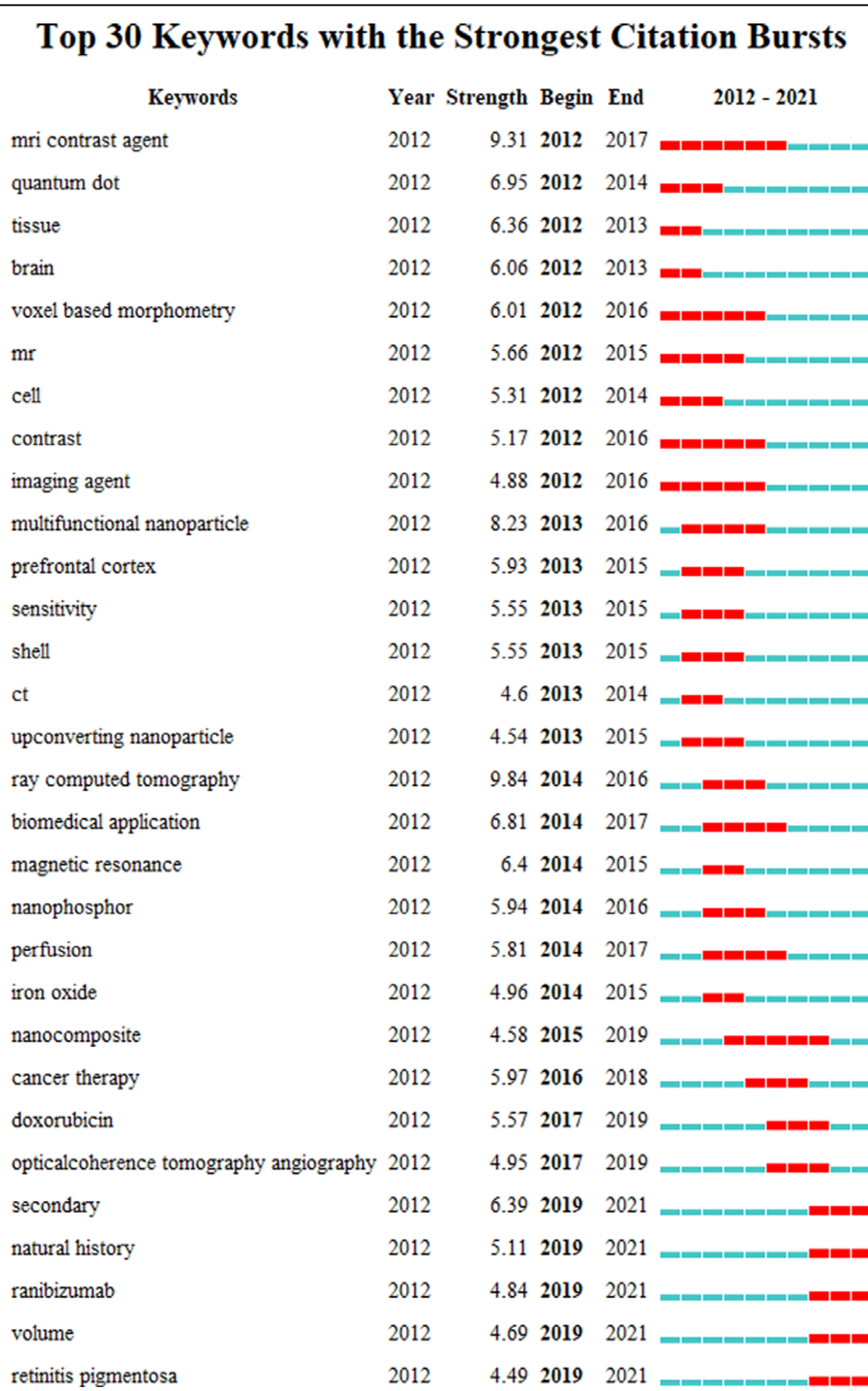

Figure 10. Top 30 keywords with citation burst (sorted by the beginning year of the burst).

Table 5

Top 10 authors and co-cited authors.

Rank	Authors	Count	Centrality	Co-cited author	Citations	Centrality
1	K Bailey Freund	81	0.06	Spaide RF	350	0.04
2	Giuseppe Querques	48	0.01	Cheng L	238	0.04
3	Francesco Bandello	45	0.02	Kim J	235	0.03
4	David Sarraf	36	0.02	Wang Y	220	0.01
5	Lawrence A Yannuzzi	30	0.01	Zhang Y	186	0
6	Zhuang Liu	29	0	Weissleder R	181	0.01
7	Christine A Curcio	26	0	Gass JDM	160	0.01
8	Eric H Souied	23	0.02	Chen Y	160	0.02
9	Liang Cheng	20	0	Liu Y	153	0.01
10	Alessandro Invernizzi	20	0.01	Zhou J	148	0.03

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Author contributions

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Data curation: Tianbing Wang.
Formal analysis: Tianbing Wang.
Methodology: Zhe Du.
Software: Zhe Du.
Visualization: Tianbing Wang.
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