Original Article

Knowledge atlas of white matter microstructure: a bibliometric analysis

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Background: White matter microstructure is valued for being an indicator of neural network integrity, which plays an indispensable role in the execution of advanced brain functions. Although the number of publications has increased in the past 10 years, no comprehensive analysis has yet been conducted of this field. Therefore, this study aimed to identify the research hotspots and trends in research on white matter microstructure using a bibliometric analysis of the related literature published from 2013 to 2022.

Methods: VOSviewer and CiteSpace were used to objectively analyze the research articles concerning white matter microstructure, which were retrieved from the Web of Science Core Collection (WoSCC).

Results: A total of 5,806 publications were obtained, with the number of published articles increasing annually over the past decade. The United States, China, the United Kingdom, and Canada maintained the top positions worldwide and had strong cooperative relationships. The top institution and journal were Harvard Medical School and Neuroimage, respectively. Alexander Leemans, Marek Kubicki, and Martha E Shenton were the most productive authors. Thematic keywords mainly included "diffusion tensor imaging" (DTI), "white matter integrity", and "connectivity". The keyword analysis revealed that DTI has a critical role in detecting white matter microstructure integrity and that fractional anisotropy is the main parameter in the assessment process. Keyword burst detection identified four research hotspots: movement, distortion correction, voxelwise analysis, and fixel-based analysis.

Conclusions: This bibliometric analysis provided a systematic understanding of the research on white matter microstructure and identified the current frontiers. This may help clinicians and researchers comprehensively identify hotspots and trends in this field.

Keywords: Bibliometric analysis; white matter microstructure; CiteSpace; VOSviewer; hotspots

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Introduction

Researchers have increasingly realized that the connection between the white matter microstructure of the human brain and neural synchronization plays a critical role in execution of brain functions (1). The structural basis of white matter integrity is the networks of myelinated axons and the associated surrounding neurons which support the coordination and transmission of neural signals (2). In one study, the integrity of the white matter fiber bundles were reported to be already compromised prior to the observation of high signals on conventional magnetic resonance imaging (MRI) (3). However, the pathogenesis of white matter microstructure damage remains unclear and effective therapeutic strategies are unavailable. Studies conducted in the general population have shown that the degradation of white matter microstructure integrity is independently associated with an increased risk of stroke (4). In a study of a stroke survivor population, damaged peri-infarct white matter microstructure was found to mediate cognitive decline (5). The microstructural characteristics of white matter has drawn extensive attention and a large number of related papers have been published. Considering the absence of a comprehensive knowledge map of this field, this study aimed to provide insights into the current state of the area of white matter microstructure using reliable and informative bibliometric methods. The research hotpots within the past 10 years were identified, which may contribute to providing directions for future research.

Methods

Data source and retrieval strategy

Relevant publications were obtained from the Science Citation Index Expanded (SCI-E) bibliographic database of the Web of Science Core Collection (WoSCC) on February 16, 2023. Our study focused on investigating the microstructural integrity of the cerebral white matter preceding the appearance of hyperintensities, as it could be an imaging marker for both disease prediction and treatment. Meanwhile, we excluded the terms associated with white matter hyperintensities due to their potential impact on microstructure. Original articles and reviews accounted for the vast majority of publications and contained all the elements needed for bibliometric analysis. We selected the past decade as the temporal scope of this study, as it allows researchers to identify the latest research trends. The retrieval strategy is presented in *Table 1* and was as follows: TS = (white matter AND (microstructural integrit* OR integrit* OR microstructur*)) NOT TS = ([white matter AND (disease* OR lesion* OR hyperintensit*)] OR leukoaraiosis). Refined by language: (English) AND document: (Article or Review) AND timespan = (2013–2022). A total of 5,806 publications were obtained for subsequent analysis of the latest research trends.

Analytical methods and analysis tools

Full records of the downloaded publications with cited references were exported as plain text files for data processing and analysis. The impact factor (IF) was retrieved from the 2021 version of Journal Citation Reports (JCR), reflecting the influence of journals. Microsoft Excel was used to display the trends of published through a drawing of the line graph. Ethical approval was not required for this study. VOSviewer and CiteSpace run on Java software were used to analyze and visualize the architectures and hotspots of the selected articles. CiteSpace, which was developed by Professor Chen Chaomei of Drexel University, can be used to draw cooperation network maps and help researchers more easily apprehend the latest research trends (6). Specifically, we used CiteSpace to visualize the cooperation network of authors who have contributed to this field and detected the burst strength of the keywords. VOSviewer, which was developed by Eck and Waltman, has powerful cluster network analysis and cocitation analysis functions (7). VOSviewer was used to visualize the cooperation network analysis of institutions, countries, and regions. Moreover, the software was used to conduct a co-occurrence cluster analysis of keywords.

Results

Analysis of annual global publication output and trends

We identified 5,806 original articles and reviews concerning white matter microstructure published from 2013 to 2022. As shown in *Figure 1*, the annual number of publications increased over the decade, and this pattern of grown fit a linear growth model. To some extent, this indicates that the field of white matter microstructure has consistently expanded over time.

Analysis of country cooperation

The 5,806 publications were distributed across 78 countries and regions. The international cooperation in the field

Table 1 Query and search strategy

Set	Search query
#1	TS = (white matter AND (microstructural integrit* OR integrit* OR microstructur*))
#2	TS = (leukoaraiosis OR [white matter AND (hyperintensit* OR lesion* OR disease*)])
#3	#1 NOT #2

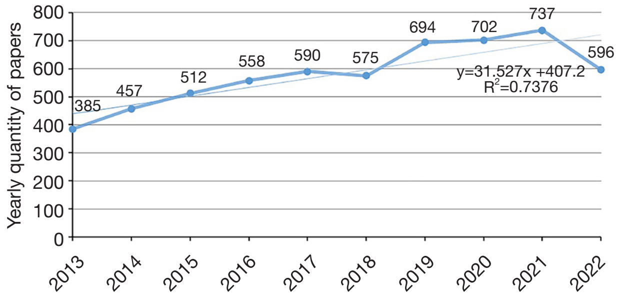

Figure 1 Quantitative distribution of publications on white matter microstructure.

is visualized in *Figure 2*. Each node represents a country, the size of nodes represents the number of publications, and the lines among the nodes represent the cooperation intensity. The top 10 countries in terms of number of publications are listed in *Table 2*. The leading country with the most publications was the United States (n=2,688, 46.3%), followed by China (n=803, 13.8%), the United Kingdom (n=652, 11.2%), and Canada (n=585, 10.1%). The countries with high centrality were the United Kingdom, Canada, and France, and these countries played important roles and maintained close cooperation in white matter

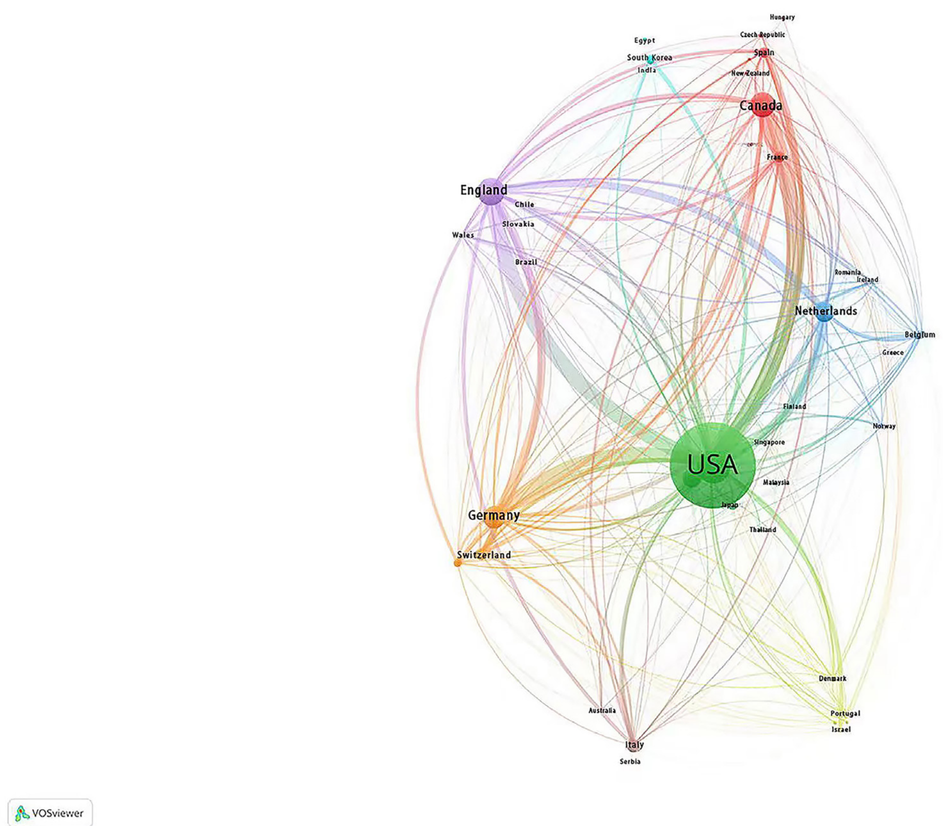

Figure 2 Cooperation network analysis of countries and regions created via VOSviewer software.

microstructure studies.

Analysis of journal cocitation

The top 10 most prolific journals in the field of white matter microstructure are listed in *Table 3*, and this information can offer insight for new researchers when evaluating related submissions. All of these journals ranked at the Q1 or Q2 levels. The journal *NeuroImage* had the highest number of citations (5,054 citations), followed by *Human Brain Mapping* (3,603 citations), *PLOS One* (3,349 citations), *Journal of Neuroscience* (3,262 citations), and *Brain* (2,807 citations), which are the mainstream journals in the field.

Table 2 Top 10 most productive countries

Rank	Count	Centrality	Country
1	2,688	0.1	USA
2	803	0.15	China
3	652	0.29	United Kingdom
4	585	0.24	Canada
5	515	0.1	Germany
6	430	0	Netherlands
7	398	0.15	Australia
8	268	0.05	Italy
9	223	0	Switzerland
10	208	0.25	France

Analysis of institutional cooperation

The network map in *Figure 3* provides information on the institutional collaboration in the field of white matter microstructure. There are a total of 830 institutions and 11,708 links in this map. The larger nodes represent institutions with a higher output, and the thickness of the links represent the closeness of collaboration between the connected institutions. The color of the nodes marks a different cluster of the institutions. The top 10 most prolific institutions are listed in *Table 4*. Harvard Medical School had the highest number of publications (n=236), followed by King's College London (n=173), the University of Toronto (n=166), and University College London (n=158).

Analysis of cocited references

The top cocited references with high frequency and high centrality are listed in *Table 5*. Jesper L. R. Andersson published the most frequently cited article in *Neuroimage* with 296 citations, which was followed by the article by Derek K. Jones (280 citations) and that by Anderson M. Winkler (142 citations). These highly cited articles represent landmarks in this field of research.

Analysis of author production and cooperation

The evaluation criteria of authors included the number and centrality of their publications and the cocitation relationships among them. The most productive authors

Table 3 Top 10 most cocited journals

Rank	Total number of citations	Centrality	Journal	Impact factor (2022)	Quartile in category (2022)
1	5,054	1.14	*NeuroImage*	5.7	Q1
2	3,603	0.23	*Human Brain Mapping*	4.8	Q1
3	3,349	0	*PLOS One*	3.7	Q1
4	3,262	0.44	*Journal of Neuroscience*	5.3	Q1
5	2,807	0.05	*Brain*	14.5	Q1
6	2,752	0.1	*Proceedings of the National Academy of Sciences of the United States of America*	11.1	Q1
7	2,657	0.05	*Cerebral Cortex*	3.7	Q2
8	2,231	0.66	*Biological Psychiatry*	10.6	Q1
9	2,191	0.28	*Magnetic Resonance in Medicine*	3.3	Q2
10	1,888	0	*American Journal of Neuroradiology*	3.5	Q2

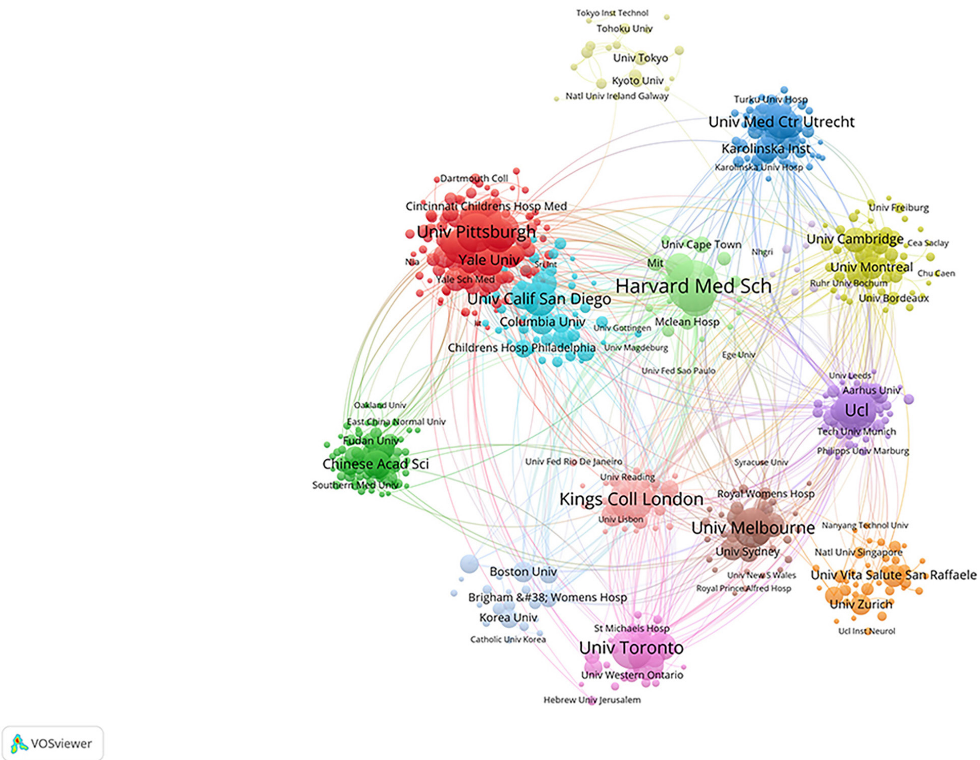

Figure 3 Institution collaboration network created via VOSviewer software.

Table 4 Top 10 most productive institutions

Rank	Count	Centrality	Institution
1	236	0.07	Harvard Medical School
2	173	0.35	King's College London
3	166	0.29	University of Toronto
4	158	0.04	University College London
5	149	0.02	University of Pittsburgh
6	139	0.69	University of Melbourne
7	135	0.02	Stanford University
8	117	0	University of California at San Diego
9	116	0.06	University of Oxford
10	116	0.25	University of California at Los Angeles

are listed in *Table 6*, and their collaborative relationship are visualized in *Figure 4*. Our analysis found the representative authors to be Alexander Leemans, Marek Kubicki, Martha E. Shenton, Ofer Pasternak, and Peter V. Kochunov. Alexander Leemans, Marek Kubicki, and Martha E. Shenton emerged as leaders in the field who collaborated as research partners in sharing knowledge, thoughts, and perceptions that ultimately enhanced their research productivity and quality.

Table 5 Top 10 most cocited references

Rank	Title	First author	Journal	Year	Total citations
1	An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging	Jesper L. R. Andersson	*NeuroImage*	2016	296
2	White matter integrity, fiber count, and other fallacies: The do's and don'ts of diffusion MRI	Derek K. Jones	*NeuroImage*	2013	280
3	Permutation inference for the general linear model	Anderson M. Winkler	*NeuroImage*	2014	142
4	FSL	Mark Jenkinson	*NeuroImage*	2012	136
5	MRtrix3: A fast, flexible and open software framework for medical image processing and visualisation	J-Donald Tournier	*NeuroImage*	2019	124
6	Diffusion tensor imaging of white matter tract evolution over the lifespan	C. Lebel	*NeuroImage*	2012	115
7	Denoising of diffusion MRI using random matrix theory	Jelle Veraart	*NeuroImage*	2016	107
8	NODDI: Practical in vivo neurite orientation dispersion and density imaging of the human brain	Hui Zhang	*NeuroImage*	2012	106
9	Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference	Stephen M. Smith	*NeuroImage*	2009	106
10	The cingulum bundle: Anatomy, function, and dysfunction	Emma J. Bubb	*Neuroscience and Biobehavioral Reviews*	2018	100

Table 6 Top 10 most productive authors

Rank	Quantity	Centrality	Author	Institutional affiliations
1	44	0.18	Alexander Leemans	University Medical Center Utrecht
2	44	0.10	Marek Kubicki	Harvard Medical School
3	44	0.09	Martha E. Shenton	Harvard Medical School
4	37	0.06	Ofer Pasternak	Harvard Medical School
5	35	0.03	Peter V. Kochunov	University of Maryland School
6	34	0.04	Catherine Lebel	University of Calgary
7	32	0.10	Derek K. Jones	Cardiff University
8	32	0.04	Daniel C. Alexander	University College London
9	32	0.02	Francesco Benedetti	University Vita-Salute San Raffaele
10	29	0.17	Paul M. Thompson	University of Southern California

Analysis of keyword co-occurrence

Keywords reflect an article's core content and ideas. *Figure 5* displays the 449 keywords that met the frequency over 25 thresholds; in this figure, six clusters are distinguished by color: "diffusion tensor imaging" (DTI) (in blue), "white matter integrity" (purple), "connectivity" (green), "fractional anisotropy" (yellow), "corpus callosum" (bluish green), and "spatial statistics" (red). The keyword analysis revealed that DTI plays a critical role in detecting white matter microstructure integrity and that fractional anisotropy is the main parameter in the assessment process.

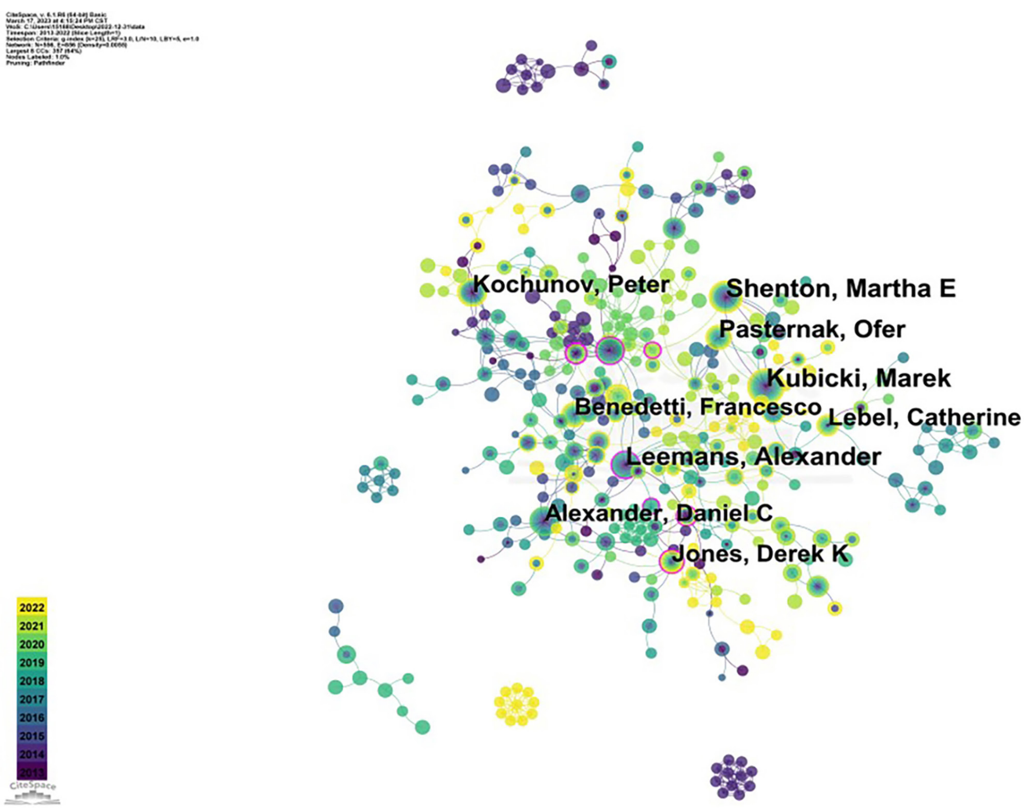

Figure 4 Author collaboration network created via CiteSpace software.

Hotspots and frontiers

A burst of keywords reflects the hotpots and emerging trends in a given field of research (8). The top 25 keywords with the strongest citation bursts from 2013 to 2022 are presented in *Figure 6*. Each line represents a keyword, with the beginning and ending of the citation burst. In addition, the red line represents a sudden increase in the citation of keywords in the corresponding year. By the end of 2022, "movement" had the greatest burst strength, followed by "distortion correction", "voxelwise analysis", and "fixel-based" analysis. In early 2013, voxel-based approaches had already been applied in white matter microstructure studies. In more recent years, the keywords with strong citation bursts were "diagnosis", "fiber density", "marijuana use", and "health".

Discussion

This study visualized and quantitatively analyzed the research articles on white matter microstructure from 2013 to 2022 by using bibliometric analysis methods, which provided an overview of this field. According to our study, the countries driving the research into white matter microstructure are mainly the United States, China, the United Kingdom, and Canada, with the United States being the center of cooperative networks. Moreover, international cooperation has enabled developing countries, such as China, to be involved in the knowledge creation process that is usually led by the developed countries (9). From the perspective of research institutions, Harvard Medical School, King's College London, the University of Toronto, and University College London had a significant impact in this field. The analysis of influential authors in the white matter microstructure field identified Alexander Leemans, a professor from University Medical Center Utrecht, as occupying the center position. He has researched the value and limitations of DTI fiber tractography in investigating white matter microstructure and has indicated that a reliable reconstruction of the brain microstructure with DTI to one of the major challenges (10,11). Marek Kubicki has explored the relationship between white matter microstructural changes and the onset of schizophrenia, and this knowledge

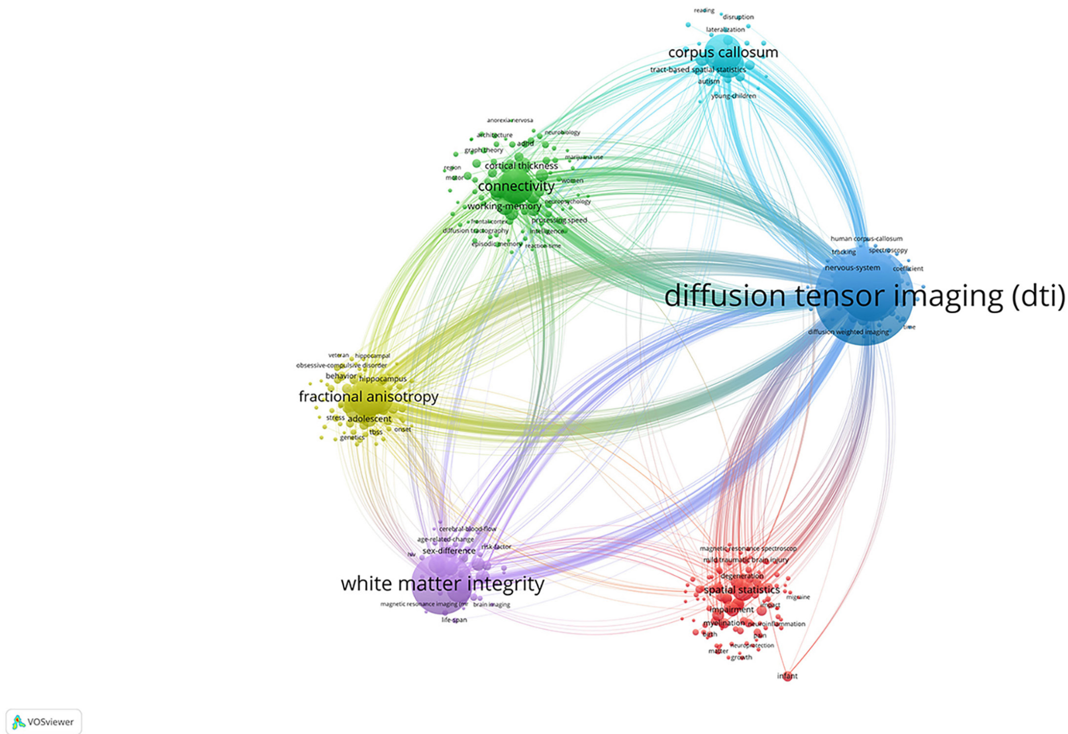

Figure 5 Keyword co-occurrence network created via VOSviewer software.

may promote the progress of new treatment strategies (12,13). Martha E Shenton used neuroimaging biomarkers to characterize brain microstructural abnormalities following traumatic brain injury, which may help elucidate pathophysiologic changes (14,15). In the analysis of cocited references, 9 of the top 10 most highly cited literatures were published in the medical imaging journal, *NeuroImage*. The most frequently cited article was that by Andersson JLR, which presented a technique for correcting distortions caused by eddy current and subject motion in diffusion imaging (16). The second and third ranked most cited articles pertained to the use of diffusion-weighted MRI and general linear model in imaging neuroscience, respectively (17,18). The authors of these articles investigated the structural integrity of human brain and defined improved practices in the area of imaging neuroscience. Furthermore, the analysis keyword co-occurrence revealed that the themes of DTI, white matter integrity, and connectivity dominate this field. The keyword hotspot analysis identified the hotspots and future trends in research. This indicated that the development of voxel-based analysis (VBA) was a landmark achievement in the field of whole brain white matter microstructure. At present, the important research approaches of DTI include region of interest (ROI), VBA, and tract-based special statistic (TBSS). VBA is part of an objective, unbiased, whole-brain imaging data analysis method, which is advantageous in examining the whole brain (19). The keywords with strong citation bursts in recent years were "diagnosis", "fiber density", "marijuana use", and "health". These are related to etiology, disease diagnosis, and prevention. It is worth noting that researchers have investigated the relationship between marijuana abuse and white matter microstructure. The adverse psychosocial outcomes caused by marijuana use have been partly attributed to aberrant brain integrity in pathways implicated in addiction and cannabinoid receptors (20,21). The word "health" suggests that increasing attention has been paid to the premorbid state in preparing for disease prevention. This indicates that the exploration of white matter microstructure has gradually deepened from the technical level to that of clinical application, thus promoting human health. Overall, the above findings may help researchers quickly grasp the potential research orientation and future trends in this field.

More importantly, the major contributing journals, authors, and keywords all suggested that neuroimaging,

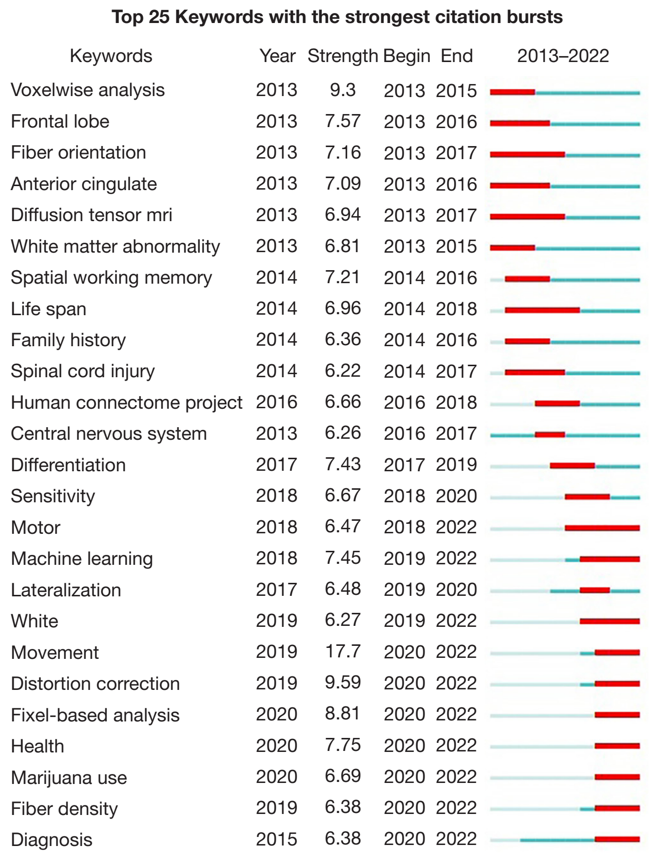

Figure 6 The top 25 keywords with the strongest citation bursts during 2013–2022 via CiteSpace software.

especially DTI, is an essential tool in assessing the integrity of white matter microstructure. White matter microstructural integrity can be noninvasively quantified with the special sequence of MRI and DTI, by measuring the extent of directional restriction and diffusivity of water molecules in the brain (22). DTI can track the movement of water molecules of white matter fiber bundles and then construct the structural network connections based on a fiber bundle skeleton. White matter microstructural integrity can be assessed using DTI-based parameters, such as fractional anisotropy and mean diffusivity. Moreover, the fiber tracking technique that builds the complex network of connections within the brain is a critical component of this field (10). Therefore, we can confirm that the neuroimaging techniques continue to be a research hotspot and that its data analysis methods and clinical applications will receive more attention. Future research is likely to focus on exploring white matter microstructure as an imaging marker for predicting and treating diseases. Researchers have discovered that cortical and subcortical microstructure is related to cognitive decline, making it a valuable predictor for monitoring disease severity (23). The degeneration of white matter fiber has been associated with cognitive impairment and poor prognosis in stroke survivors (5,24). Childhood maltreatment can alter the microstructure of white matter in healthy adults, which might increase their vulnerability to mental disorders such as anxiety and posttraumatic stress disorder (25,26). Poor sleep quality might lead to neural injury by damaging the white matter microstructure, and this knowledge may provide guidance for decision-making in precision medicine (27). In emerging fields, the glymphatic system is identified as a fluid-waste clearance pathway that promotes the circulation of cerebral spinal fluid in the central nervous system, ultimately clearing potentially toxic metabolites into lymphatic drainage vessels (28). DTI can quantify the diffusivity of individuals and therefore can be used to understand a patient's glymphatic systems (29). This may provide neurosurgeons with new prognostic and diagnostic tools for traumatic brain injury and neurovascular damage (28).

Additional studies have demonstrated that the dysregulation of the glymphatic system is involved in neuroinflammatory and traumatic disease processes (30,31), and the impaired balance of increased production coupled with decreased clearance of the interstitial fluid seems to contribute to the pathogenesis of Alzheimer disease (32). DTI can discern white matter with greater sensitivity than can standard MRI techniques in the brains of patients with Alzheimer disease (33,34). These studies and their findings may provide researchers with a direction for future research.

Conclusions

This is the first bibliometric study to systematically analyze the literature on white matter microstructure-related and has characterized the intellectual structure of the field and identified its hotspots, which will prove advantageous for cutting-edge research in this domain. However, some limitations to this study should be mentioned. First, the data in this bibliometric analysis were incomplete since we only retrieved and analyzed literature from the WoSCC. In addition, although the study analyzed a wide range of publications and provided a general map of the research field, a deep understanding of the landmark publications in this field is lacking, and more attention should be paid to researchers and institutions that have advanced research. Third, emerging trends and keyword co-occurrence are constantly changing over time, indicating that the subjects and directions of this field are also changing accordingly. It is necessary to continuously analyze and explore the relevant literature in order to maintain an up-to-date understanding of this field. In the end, it is strongly recommended that future studies expand their scope to include more journals with a greater range of coverage.

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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-23-1397/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.

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