Original Article

Bibliometric analysis of myelin imaging studies of patients with multiple sclerosis (2000–2022)

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Background: Multiple sclerosis (MS) is a condition that can impact the central nervous system (CNS) and cause damage to the myelin, which is responsible for facilitating the normal transmission of electrical impulses along the nerves. We performed a bibliometric analysis of the scientific publications on myelin imaging in MS to reveal the development trends in this field and to evaluate research trends in myelin imaging in MS.

Methods: The Web of Science Core Collection was searched for articles related to myelin imaging in MS published between January 2000 and December 2022. CiteSpace, VOSviewer, and R language were used to evaluate and visualize contributions by and co-occurrence relationships among countries and institutions, authors, journals, citations, keywords, and so on.

Results: A total of 1,639 articles addressed the topic of myelin imaging in MS. The United States had the largest number of annual publications. The University of London was the institution with the highest number of publications (n=118) and citations (n=9,885). The top 3 productive authors were all from the University of British Columbia in Canada. An article published by Mackay *et al.* in 1994 had the most citations (n=272). *Neuroimage* [impact factor (IF) =7.40, Journal Citation Reports quartile 1 (Q1)] was the most productive journal in terms of the number of articles relating to myelin imaging in MS (n=149). In recent years, myelin water imaging, synthetic magnetic resonance imaging (SyMRI), inhomogeneous magnetization, positron emission tomography (PET) imaging, and aquaporin-4 (AQP4) have been researched hotspots of myelin imaging in MS.

Conclusions: With advancements in the pathophysiological research on myelin changes in MS, myelin imaging is playing an important role in the diagnosis and treatment of MS. In addition, the use of new sequences of myelin imaging to distinguish MS from other inflammatory demyelinating diseases is a future development trend in this field.

Keywords: Multiple sclerosis (MS); magnetic resonance imaging (MRI); myelin

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Introduction

Multiple sclerosis (MS) is an immune-mediated chronic, inflammatory, demyelinating disease of the central nervous system (CNS) with diverse clinical symptoms and disease outcomes (1). In addition to clinical manifestations and laboratory tests, neuroimaging is an important means of diagnosing MS, and magnetic resonance imaging (MRI) can support and replace clinical MS data. As early as 2001, imaging criteria were included in the MS McDonald criteria, making imaging results useful in the accurate diagnosis and early treatment of MS (2,3). Typical focal hyperintensity lesions on T2 and T2 fluid-attenuated inversion recovery (FLAIR) sequences of conventional MRI were once key features for diagnosing MS demyelinating lesions. MS can be monitored by observing the distribution and morphology of abnormal signals and signal changes and measuring clinical indicators. However, due to the diverse manifestations of MS, the utility of conventional MRI data in the assessment of the prognosis and evolution of MS is limited. Although conventional MRI has high diagnostic sensitivity for MS, it lacks specificity and cannot reasonably explain the wide heterogeneity of clinical outcomes (4,5). With improvements in MRI technology and the continuous generation of new MRI sequences as well as the continuous deepening of the understanding of the pathophysiological mechanism of MS, MRI can now be used to more accurately diagnose MS and assess MS progression and treatment efficacy in terms of demyelinating lesions and outcomes, myelin changes in normal-appearing white matter (NAWM) regions, and iron changes in demyelinating lesions (6,7). Clinically, there has been controversy regarding the treatment time and treatment plan for MS patients, and many pathophysiological mechanisms that can lead to disability and poor prognosis are often ignored. Therefore, more extensive development and utilization of advanced MRI technologies are critical to more accurately and quickly diagnose and treat MS and to provide personalized monitoring of changes in MS conditions (8).

Recent research focusing on the topic of myelin imaging in MS has continuously increased and applied more sophisticated methods (9-11). However, there has been no comprehensive and systematic assessment of the publications, countries and institutions, authors, journals, research directions, and prospects of this area of research.

Bibliometrics, as an emerging discipline, can be used to systematically analyze and study the characteristics of the published literature; in this approach, a variety of statistical and mathematical methods are used to quantitatively analyze all knowledge carriers, including different research components (such as authors, countries, institutions, references, etc.) and structural relationships (12,13). Bibliometrics can be used to realize the secondary visual analysis of research topics, clarify the foundation, frontiers, and developmental evolution of entire disciplines in research fields, analyze the timeline of research hotspots, predict future research directions, and enable scientists to understand the research domain (14).

Methods

Data retrieval strategy

The Web of Science Core Collection (WoS by Clarivate Analytics, WoSCC) database was searched for articles related to this topic published between 1 January 2000 and 31 December 2022. The search language was limited to “English”, the search article type was limited to “studies” or “reviews”, and Boolean search operators were used to limit the search formula to TS = (“myelin” OR “myelin sheath” OR “medullary sheath” OR “medullary sinus” OR “myelination”) AND TS = (“magnetic resonance imaging” OR “MR” OR “MRI”) AND TS = (“multiple sclerosis” OR “disseminated sclerosis” OR “MS”), focusing on the information in abstracts and keywords. Manual secondary screening was performed to exclude duplicates and articles missing author information, the publication year, a title, or an abstract.

Statistical and bibliometric analyses

The studies included after screening were exported in RefWorks format and saved in “.txt” format for bibliometric visualization analysis. The analyses were performed in VOSviewer (version 1.6.18; https://www.vosviewer.com/), CiteSpace V (version 6.16; https://citespace.podia.com/), Pajek (portable-XXL 5.16; http://mrvar.fdv.uni-lj.si/pajek/), and R studio’s bibliometrix package (version 2022.12.0+353; https://www.bibliometrix.org/home/). The parameters for CiteSpace V were set as time segments from 2000 to 2022 (each time segment was 1 year), and the node types included authors, research institutions, countries, keywords, and references. Microsoft Office Excel 2021 (Microsoft, Redmond, WA, USA) was used to conduct descriptive statistical analyses and to generate graphs and tables.

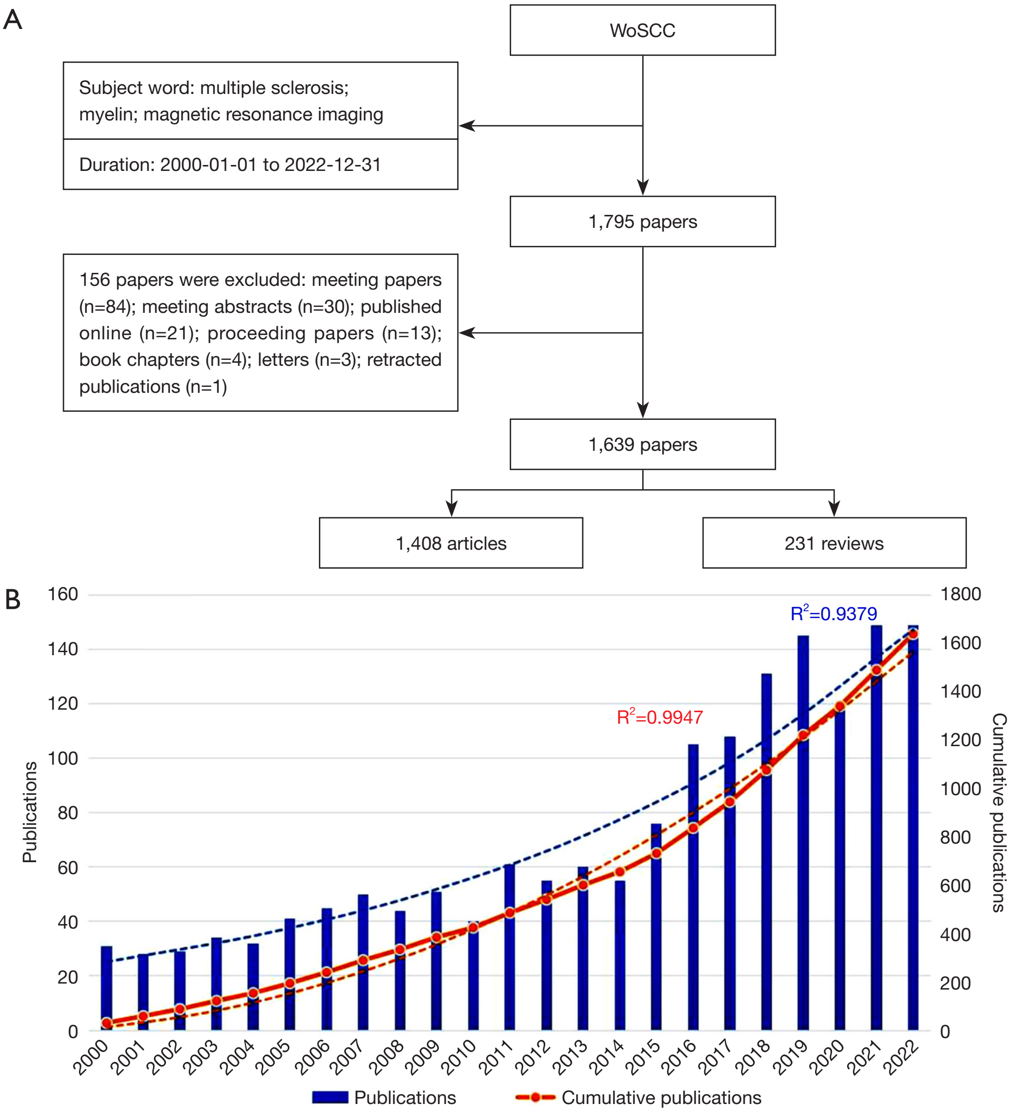

Figure 1 Analysis of the quantity of annual publications. (A) Flow chart of the literature screening process. (B) Publication growth trend of myelin imaging in multiple sclerosis from 2000 to 2022. WoSCC, Web of Science Core Collection.

Results

Research profile

A total of 1,639 articles related to MRI findings of MS demyelinating lesions from the WoSCC database, including 42,508 citing articles and 73,568 cited articles, were included in this analysis (*Figure 1A*). The H-index for all publications was 134.

Annual publications analysis

From 2000 to 2022, the number of annual publications increased (*Figure 1B*). The number of publications related to MRI studies of MS demyelinating lesions increased abruptly in 2016. Each year between 2016 and 2022, the number of annual publications exceeded 100; however, the number of annual publications dropped slightly in 2020, possibly because of the coronavirus disease of 2019 (COVID-19) pandemic. The total number of publications and the cumulative number of publications were fitted with quadratic function curves, with the goodness of fit R^2 values of 0.9379 and 0.9947, respectively, indicating that MRI of MS demyelinating lesions will become a future research focus.

Table 1 Top 10 most productive countries

Rank	Country	Documents	Total citation	Average article citations	H-index	Freq.
1	United States	466	26,243	56.30	48	0.284
2	United Kingdom	202	12,058	104.90	37	0.123
3	Canada	140	8,450	41.80	24	0.085
4	Germany	115	6,959	49.70	37	0.070
5	Netherlands	74	4,411	80.20	30	0.045
6	Austria	68	2,745	101.70	29	0.041
7	Italy	62	2,489	40.10	28	0.038
8	Japan	55	2,011	27.20	33	0.034
9	France	55	1,554	22.90	32	0.034
10	Switzerland	41	1,403	34.20	19	0.025

Freq., frequency.

Country and institution analysis

Analyses of the number of publications on related topics in each country can, to a certain extent, reflect the importance and impact of a country on research topics. *Table 1* lists the top 10 countries with the most related annual publications from 2000 to 2022. There were four countries of corresponding authors with more than 100 publications per year. The United States (466 publications, 28.4%) had the largest number of annual publications, followed by United Kingdom (202 articles, 12.3%), Canada (140 articles, 8.5%), and the Germany (115 articles, 7.0%). As seen in *Table 1*, the number of cited articles from American publications was 26,243, twice that (n=12,058) from British publications. Moreover, the H-index for related publications in the United States was as high as 48, indicating that the United States has substantial influence in this field. In addition, although the cumulative number of publications in Austria was only 68, the average number of publication citations was 101.70, ranking second among all countries, indicating that Austria has great research potential. Articles in which the first author and the corresponding author were from different countries were considered to indicate cooperative relationships. The VOS clustering technique enabled visualization of countries and intercountry collaboration analysis *(Figure 2A)*. The cooperation between the United States and Canada was the closest, followed by that between the United States and the United Kingdom, which are all developed countries. As shown in *Figure 2B*, the University of British Columbia was the most active research institution, collaborating with 107 institutions, followed by the University College London, with 59 recorded collaborations. In addition, the University of London was the institution with the highest total number (n=118) of publications (number of citations, 7,413; H-index, 48), followed by the University of British Columbia and the Udice French Research University. Additionally, in terms of citation frequency, the University of London topped the list with 9,885 citations, followed by the University College London (*Table 2*). Overall, institutions in the United Kingdom were indicated to be the most reliable for MRI studies of myelin changes in MS.

Author analysis

David Li had 61 publications and was the author with the most publications in this field, followed by Alex Mackay (57 publications) and Cornelia Laule (56 publications). They began to publish their research in 2007 (*Table 3*), and they were all experts from the same institution. In addition, 9 of the top 10 authors were from Canada, including 8 from a team at the University of British Columbia. The relationship between the number and time of publications by the same authors was analyzed (*Figure 3*). The results showed that the past 5 years were the peak output period for publications in this field, suggesting that this field is becoming a research focus.

Journal analysis

The bibliometrix package in R was used to explore and identify high-quality and productive journals for MRI

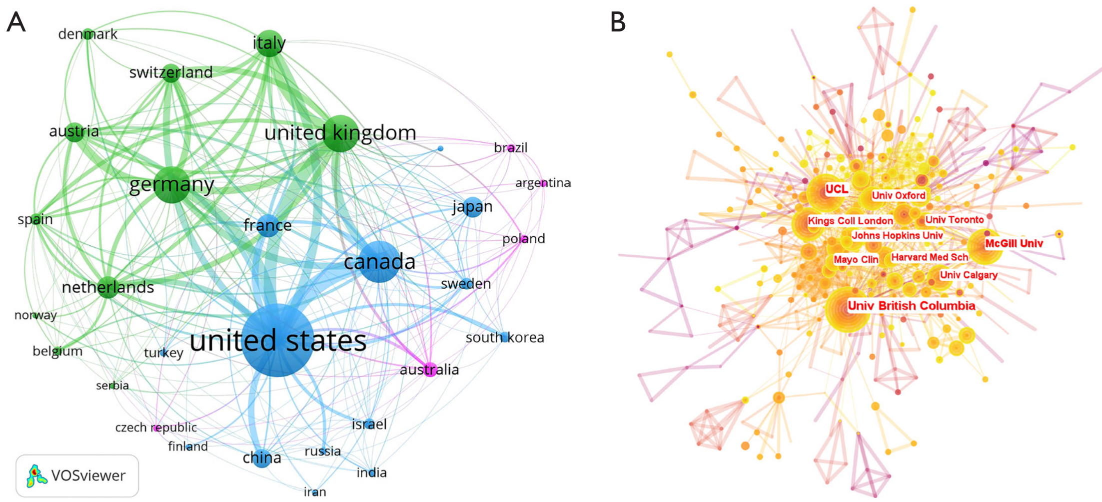

Figure 2 The co-occurrence analysis profile of the countries and institutions. (A) The visualization of countries and intercountry collaboration analysis. (B) A network visualization map of collaboration among institutions.

Table 2 Top 10 most productive institutions

Rank	Institution	Country	Documents	Total citation	Cited frequency	H-index
1	University of London	United Kingdom	118	7,413	9,885	48
2	University of British Columbia	Canada	115	3,278	5,481	37
3	Udice French Research Universities	France	79	2,417	2,688	24
4	University College London	United Kingdom	76	5,565	7,040	37
5	University of Columbia System	United States	72	2,613	2,918	30
6	Harvard University	United States	71	3,569	4,097	29
7	National Institutes of Health (NIH) USA	United States	61	3,169	3,768	28
8	McGill University	Canada	60	3,100	4,133	33
9	Vrije University Amsterdam	Netherlands	59	5,146	6,275	32
10	Centre National de la Recherche Scientifique (CNRS)	France	46	1,639	1,822	19

Table 3 Top10 most productive authors

Rank	Author	Institutional/country	Documents	Total citation	Cited frequency	Centrality	H-index
1	Li, David K. B.	University of British Columbia/Canada	61	1,446	2,761	0.08	28
2	Mackay, Alex L.	University of British Columbia/Canada	57	1,787	3,474	0.00	31
3	Laule, Cornelia	University of British Columbia/Canada	56	1,300	2,601	0.01	26
4	Vavasour, Irene M.	University of British Columbia/Canada	49	1,403	2,280	0.00	22
5	Kolind, Shannon H.	University of British Columbia/Canada	37	801	1,117	0.01	18
6	Arnold, Douglas L.	McGill University/Canada	36	1,289	1,562	0.04	23
7	Traboulsee, Anthony L.	University of British Columbia/Canada	33	561	679	0.00	15
8	Barkhof, Frederik	Vrije University Amsterdam/the UK	32	2,981	3,468	0.09	23
9	Rauschar, Alexander	University of British Columbia/Canada	29	581	809	0.01	16
10	Moore, GRW	University of British Columbia/Canada	26	1,135	1,901	0.00	19

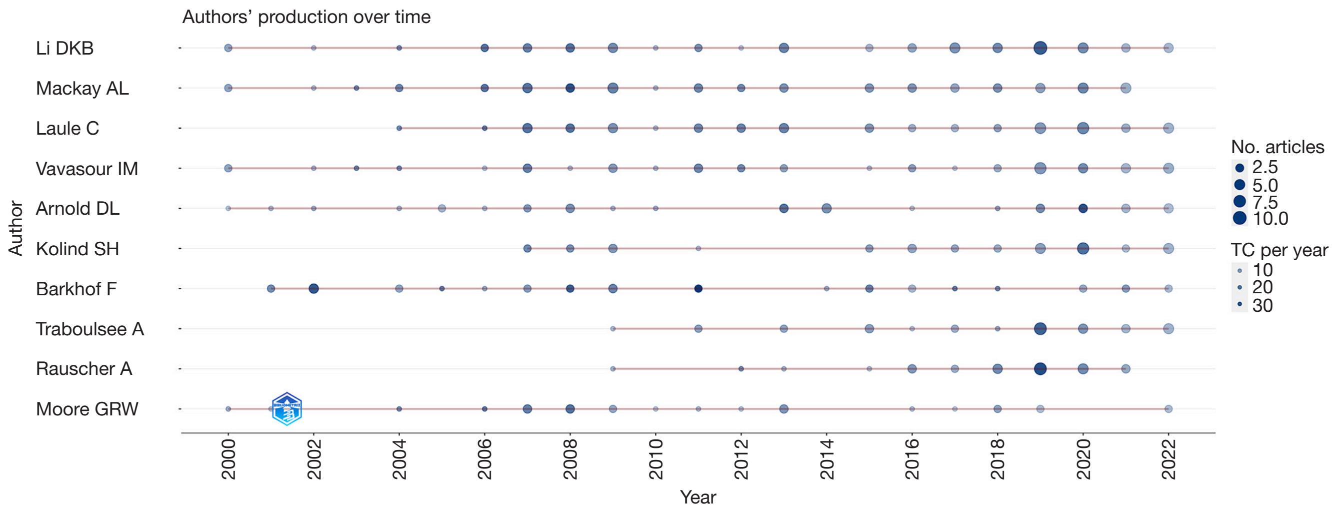

Figure 3 Top 10 authors from 2000 to 2022. TC, total citation.

Table 4 Top10 most productive journals

Rank	Journals	Documents	IF, JCR [2022]	H-index	All cited journals	Total citation
1	*Neuroimage*	149	7.40, Q1	55	*Neuroimage*	6,357
2	*Magnetic Resonance in Medicine*	95	3.73, Q3	38	*Neurology*	5,318
3	*Multiple Sclerosis Journal*	69	5,86, Q2	29	*Magnetic Resonance in Medicine*	4,726
4	*Neuroimage-Clinical*	43	4.89, Q2	15	*Annals of Neurology*	3,605
5	*Multiple Sclerosis and Related Disorders*	42	4.81, Q3	11	*Brain*	3,370
6	*American Journal of Neuroradiology*	42	4.97, Q3	23	*Multiple Sclerosis Journal*	2,729
7	*NMR in Biomedicine*	39	4.48, Q3	19	*American Journal of Neuroradiology*	1,909
8	*Brain*	37	15.25, Q1	29	*Journal of Neurology Neurosurgery and Psychiatry*	1,519
9	*Journal of Magnetic Resonance Imaging*	37	5.12, Q2	20	*Journal of Magnetic Resonance Imaging*	1,461
10	*Journal of Neurology*	33	6.68, Q2	19	*Journal of Neurology*	1,430

IF, impact factor; JCR, Journal Citation Reports; Q, quartile.

publications on myelin changes in MS journals. *Table 4* lists the top 10 journals that published the greatest number of related articles, of which *Neuroimage* [impact factor (IF) =7.40, Q1] ranked first (149 articles), followed by *Magnetic Resonance in Medicine* (95 articles, IF =3.73, Q3) and *Multiple Sclerosis Journal* (69 articles, IF =5.86, Q2). Furthermore, the number of publications in authoritative journals in the field has gradually increased; 1,639 articles have 40,467 citing articles, and five journals had more than 3,000 citations, with four being Journal Citation Reports (JCR) quartile 1 (Q1) journals with very high professional influence. *Neuroimage* (IF =7.40, Q1) had the largest number of citing articles (n=6,357).

CiteSpace software was used to complete a dual-map analysis based on global scientific journals, revealing a scientific hybrid model of global journal maps in this field. The left panel (*Figure 4A*) shows the citing articles, and the right panel (*Figure 4B*) shows the cited articles. *Figure*

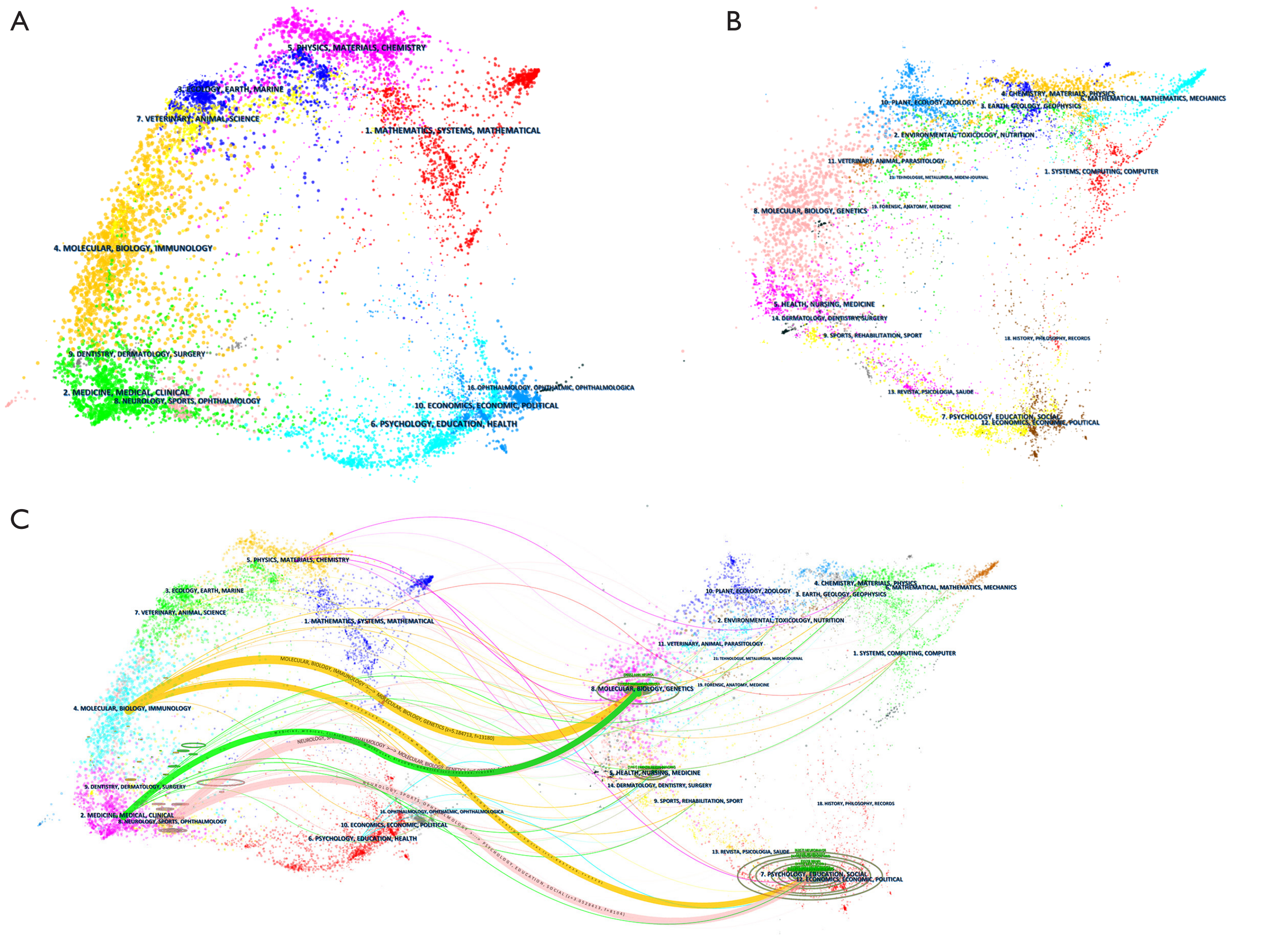

Figure 4 Journal overlay map. Citing journals overlay (A), cited journals overlay (B), and dual map overlay (C) of journals with colored paths indicating citation relationships.

4C shows that after Z score correction, there are five main information streams, namely, molecular/biology/genetics and psychology/education/social, which are the main theoretical and technical bases of the research, with few interdisciplinary studies and the strongest correlations, and molecular/biology/immunology, medicine/medical/clinical and neurology/sports/ophthalmology, in which citing articles were mainly clustered. The following research focus in this field will be pressed in neurology/sports/ophthalmology.

Reference analysis

Table 5 lists 15 articles with more than 100 citations among the 1,639 articles. Among them, Mackay's "*In vivo* visualization of myelin water in brain by magnetic resonance", published in 1994, ranked first, with 272 citations. CiteSpace software allows the analysis of co-cited references. In this study, the log-likelihood ratio (LLR) algorithm revealed a total of 13 clusters from the titles of citing articles (*Figure 5A*). The modularity Q and the weighted mean silhouette S were 0.8025 and 0.9412, respectively, indicating good clustering quality. Based on the co-cited references through the timeline view (*Figure 5B*), #1 myelin oligodendrocyte glycoprotein, #3 myelin water fraction, #9 gray matter alteration, and #11 expanding lesion were the research hotspots in recent years.

Keyword analysis

Burst keyword analysis

Burst keywords refer to those that frequently appear in a short period (15). *Figure 6A* shows the 20 keywords with

Table 5 The top 15 most cited articles (more than 100 citations) on MRI of myelin in MS

Rank	Title	First author	Year	Source	Total citation
1	*In vivo* visualization of myelin water in brain by magnetic resonance	Mackay A	1994	*Magnet Reson Med*	272
2	Myelin water imaging in multiple sclerosis: quantitative correlations with histopathology	Laule C	2006	*Mult Scler*	216
3	Magnetization transfer ratio and myelin in postmortem multiple sclerosis brain	Schmierer K	2004	*Ann Neurol*	184
4	Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS)	Kurtzke JF	1983	*Neurology*	163
5	Myelin water imaging of multiple sclerosis at 7 T: correlations with histopathology	Laule C	2008	*Neuroimage*	163
6	Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria	Polman CH	2011	*Ann Neurol*	160
7	*In vivo* measurement of T2 distributions and water contents in normal human brain	Whittall KP	1997	*Magn Reson Med*	157
8	Water content and myelin water fraction in multiple sclerosis. A T2 relaxation study	Laule C	2004	*J Neurol*	156
9	Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria	Thompson AJ	2018	*Lancet Neurol*	135
10	International consensus diagnostic criteria for neuromyelitis optica spectrum disorders	Wingerchuk DM	2015	*Neurology*	128
11	Axonal transection in the lesions of multiple sclerosis	Trapp BD	1998	*N Engl J Med*	126
12	Gleaning multicomponent T1 and T2 information from steady-state imaging data	Deoni SCL	2008	*Magn Reson Med*	114
13	Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis	Mcdonald WI	2001	*Ann Neurol*	111
14	Heterogeneity of multiple sclerosis lesions: implications for the pathogenesis of demyelination	Lucchinetti C	2000	*Ann Neurol*	106
15	Quantitative interpretation of NMR relaxation data	Whittall KP	1989	*J Magn Reson*	105

MRI, magnetic resonance imaging; MS, multiple sclerosis.

the most burst citations, including myelin water imaging, quantitative MRI, and neuromyelitis optica spectrum disorder, with extremely high frequency in recent years, suggesting that myelin quantification is popular in MS research and that the differential diagnosis of MS from other demyelinating diseases has become a popular research topic.

Co-occurrence analysis (and cluster analysis) of keywords

Co-occurrence analysis is a method used to generate a co-occurrence network graph composed of nodes and connections formed by keywords as nodes (16). In this study, 2,618 author keywords were extracted from 1,639 articles. Each keyword that appeared at least five times was screened twice, and 206 author keywords were included in the co-occurrence analysis. As shown in the results of the graphic network visualization depicted in *Figure 6B*, the keywords (except for myelin, multiple sclerosis, and magnetic) were classified into four clusters. Cluster 1 (red) focused on the analysis of changes in myelin content using new MRI technologies, including myelin water imaging, and so on. Cluster 2 (green) included the etiology and MRI of the spectrum of diseases associated with MS demyelination, such as neuromyelitis optica and myelin oligodendrocyte

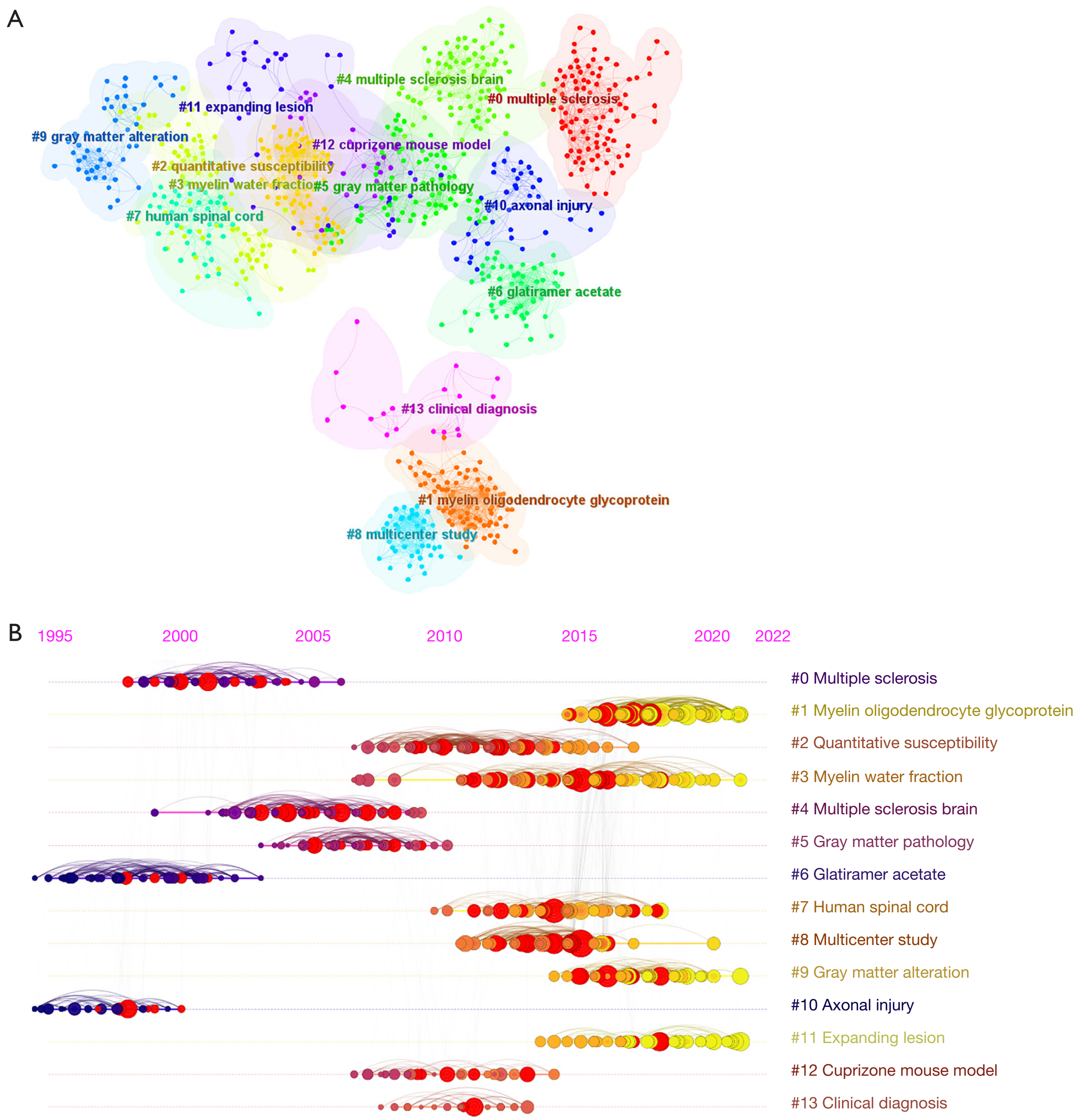

Figure 5 Co-cited reference analysis. (A) Clustering network analysis of references; (B) the timeline view of publications related to MS myelin imaging with relevant clusters. MS, multiple sclerosis.

glycoprotein. Cluster 3 (yellow) represented magnetic resonance (MR) studies of myelin signal performance in different stages of MS, including demyelination and remyelination. Cluster 4 (blue) included studies of the signal characteristics and significance of myelin in different MRI sequences in MS patients. The results of the dual-map visualization of the keyword analysis (*Figure 6C*) were consistent with the results of the previous analysis, and keywords such as myelin water imaging, synthetic MRI (SyMRI), inhomogeneous magnetization, positron emission tomography (PET) imaging, aquaporin-4 (AQP4), and neuromyelitis optica spectrum were highlighted, suggesting

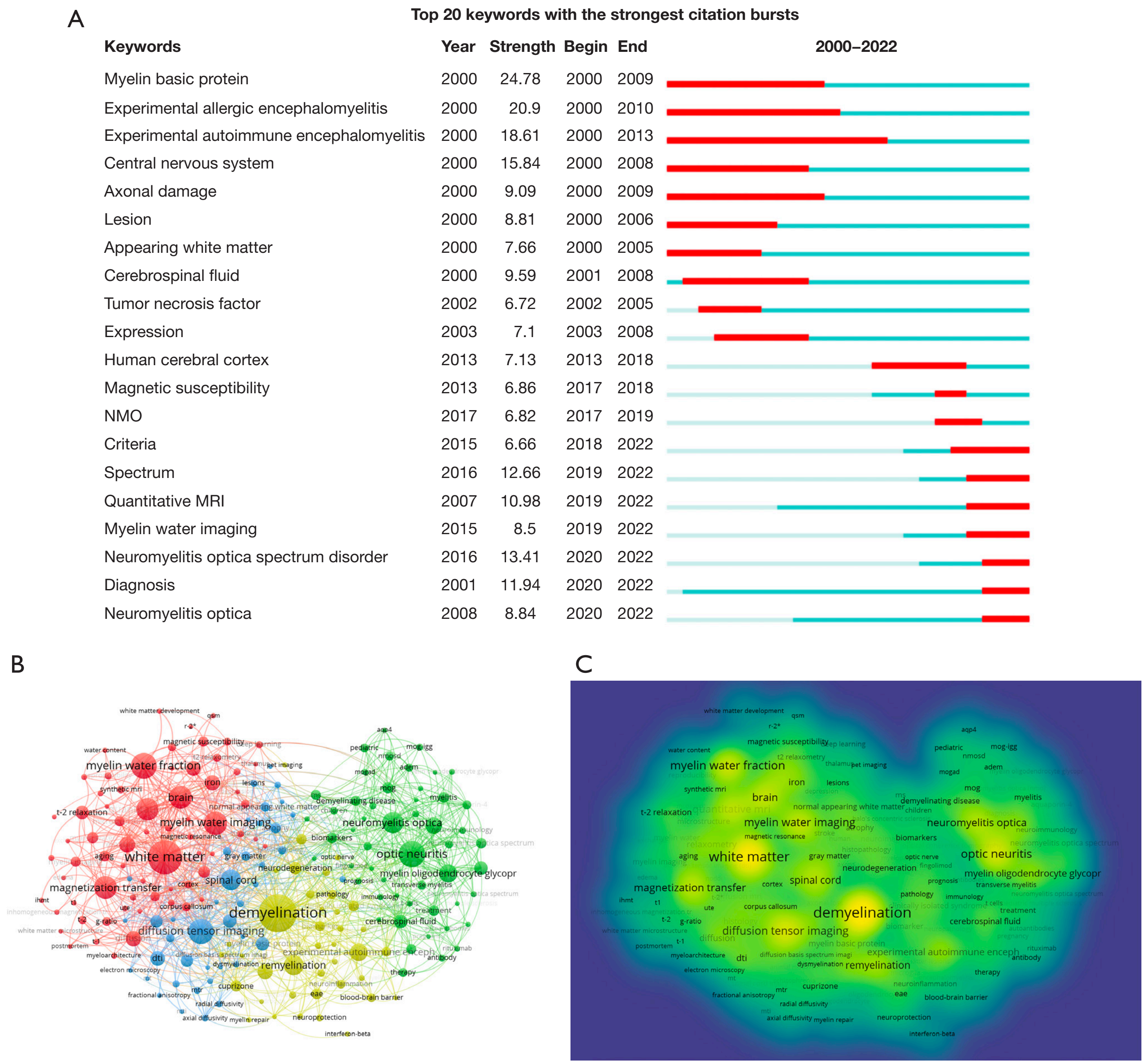

Figure 6 Co-occurrence network analysis of keywords pertaining to myelin imaging in MS. (A) Explosion period (blue sections) and intensity (red sections) of the top 20 keywords for burst detection. (B) The keywords were divided into four clusters with different colors, with the node size indicating the frequency of occurrence. (C) Visualization of the keyword cooccurrence network by average year of publication. Keywords in yellow appear later than those in blue. NMO, neuromyelitis optica; MRI, magnetic resonance imaging; MS, multiple sclerosis.

that these topics were research hotspots in recent years.

Discussion

MRI has continuously been an important tool for the diagnosis of MS. MRI was included in the international MS McDonald standard in 2001. Conventional MRI uses T2-weighted FLAIR, T2-weighted sequences, and other sequences to observe typical focal hyperintensities in white matter areas and uses them as the basis for diagnosis (17). However, several studies have demonstrated that the number, size, and signal evolution of abnormal

T2 hyperintense foci in white matter areas are poorly correlated with the prognosis of MS patients; hence, disease progression cannot be predicted by evaluating the diversity of white matter lesions (WMLs), myelin changes in the NAWM, or gray matter and cortical lesions (18,19). Therefore, in the past 20 years, the relationship between the precise and quantitative diagnosis of MS through new MR technologies and the pathophysiology of MS has attracted the attention of scientists, who have made remarkable progress.

Based on the articles retrieved from the WoSCC database, 1,639 papers and reviews on MRI research pertaining to MS demyelinating lesions were published from 2000 to 2022. Bibliometrics was used to conduct cluster analysis, keyword analysis, regional and institutional distribution analysis, and so on, to understand and determine related topics' research status and development trends. From 2011 to 2015, the number of annual publications exceeded 50; beginning in 2016, the number of annual publications exceeded 100. Although the number of publications in 2020 decreased slightly, the overall research output showed an upward trend. The research focus has switched from the observation of demyelinating lesions in abnormal-appearing white matter areas using conventional MRI to the relationship that changes in myelin content in NAWM areas and normal-appearing gray matter areas on T2-weighted and T2 FLAIR sequences have with disease progression, treatment prognosis, and clinical outcomes. The continuous development of quantitative MRI technology in recent years and the continuous integration of a better understanding of disease mechanisms provide more clinical decision support for MS patients (20,21). The clinical maturity of quantitative MRI and whether it has a targeted clinical application need to be further explored.

Research on myelin imaging in MS is distributed in many countries worldwide, and cooperation between countries is relatively frequent, with countries forming close cooperation networks. The top 10 countries in terms of the number of publications on related topics were all developed countries; the United States, as the country with the highest number of publications, is in a leading position in MR research on MS demyelinating lesions. This finding is consistent with the higher incidence of MS in residential areas of Caucasians of Northern European descent and in high-income countries (22). The United States has furthered its cooperation with many countries, mainly the United Kingdom and Canada, to publish higher-quality articles in this research field, and research progress has yielded good reference value. Furthermore, among the top 10 most productive institutions related to this field, 3 are in the United States, 2 are in the United Kingdom, and 2 are in Canada. This finding confirmed the importance of exchange and cooperation. The University of London, the United Kingdom, ranked first among all institutions in terms of publication volume, citations, and H-index, indicating the importance of the institution's research achievements in this field.

Next, based on an analysis of productive authors in related fields, authors from the University of British Columbia in Canada were the most central. The team first proposed the concept of quantitative myelin imaging, laying the foundation for research in this field (23). A comprehensive analysis of the most productive and co-cited journals for myelin imaging in MS suggests that the articles published in *Neuroimage* (IF, 7.40; JCR, Q1) ranked first in this field, with more than 1,000 citations, indicating that studies on myelin imaging in MS published in the journal are high quality and have high reference value. Among the top 10 journals, only *Neuroimage* and *Brain* are JCR Q1 journals, suggesting that more in-depth and innovative research is needed in this field. Furthermore, studies published in medical or molecular/biology/genetics journals were often cited in clinical/medical/biology/immunology journals. Therefore, authors should search journals in these fields when preparing articles on this topic.

Highly cited articles are an important indicator of a research field, and this indicator is helpful for researchers to understand the main achievements in the field. In 1994, MacKay *et al.* found that myelin-related water has a shorter nuclear magnetic resonance (NMR) spin relaxation time (T2) than does water in other CNS tissues and, based on myelin water imaging, revealed the differences in the water environment of brain tissue unrecognized by conventional MRI (24); additionally, the team put forward the concept that T2 relaxation can be used to quantitatively measure myelination, laying a research foundation for the accurate monitoring of changes in myelin levels and for clinical interventions (25). Experts interested in this topic should read these articles first. Quantitative studies comparing myelin water imaging and histopathology were cited many times, confirming that multiecho T2-relaxation myelin water imaging can effectively marker myelin content in the CNS (26). MS often presents alternating relapses and remissions, accompanied by varying degrees of glial cell activation and proliferation, demyelination and remyelination, and a dynamic cascade of axonal loss (27), posing a challenge for myelin water imaging.

Diffusion-tensor imaging (DTI) can detect decreased microstructural integrity of lesional and NAWM in children with MS based on impaired water diffusivity, these changes in microstructure have been observed in NAWM. Research consistently indicates a decrease in fractional anisotropy and more diverse alterations in radial and axial diffusivity, suggesting the presence of axonal loss and demyelination, respectively (28,29).

Next, the magnetization transfer ratio (MTR) was first explored. Some studies have found that MTR can differentiate and quantitatively measure myelin and axon content by establishing a parametric model between histopathology and MR (9,30). On this basis, follow-up studies have found that a decrease in the MTR value is also related to the presence of focal cortical demyelination and white matter damage outside demyelinating lesions (31). A study reported that functional MRI (fMRI) can provide insights into the functional reorganization occurring in pediatric patients with MS (32). Proton magnetic resonance spectroscopy (^{1}H-MRS) has revealed that chronic MS lesions display decreased levels of N-acetylaspartate (NAA), indicating neuronal and axonal loss, and this reduction is particularly prominent in lesions that also appear hypointense on T1-weighted images. For ^{1}H-MRS, increased levels of creatine (Cr) and choline (Cho) were observed in lesions, suggesting ongoing gliosis and remyelination in isointense lesions on T1-weighted MR images, as well as membrane turnover involving demyelination and remyelination; in acute MS lesions, it demonstrated a range of abnormalities, including reduced NAA, increased Cho, and the presence of lipids (33-36).

Some direct myelin imaging sequence information should be mentioned. The 3-dimensional (3D) inversion recovery ultrashort echo time (IR-UTE) MRI can show more WMLs in MS patients than the T2-FLAIR sequence and is used for analyzing the WML quality in MS patients, but requires further optimization for the diagnosis of gray matter and infratentorial lesions (37). The signal intensity variations (SIVs) of MS lesions between IR-UTE and standard clinical sequences, such as magnetization prepared-rapid gradient echo (MPRAGE) imaging, correlate with patients' disabilities, which could be a novel biomarker for the prognosis of patients with MS (38).

Magnetic susceptibility MRI at ultrahigh magnetic field strength (7T) can show a low-intensity edge adjacent to white matter demyelinating lesions in MS but not in other CNS inflammatory vascular lesions or neuromyelitis optica, and later studies have confirmed that this is the manifestation of macrophage subsets and iron deposition by activated microglia at the edge of chronically active WMLs. The level, range, and rate of change in the MR images predict persistent inflammatory responses and tissue damage and can be used to observe and evaluate the effectiveness of anti-inflammatory treatments (39,40). In recent years, an increasing number of new MR techniques, such as quantitative susceptibility mapping (QSM), have been used to track acute myelin rupture in MS lesions by observing iron deposition (41). SyMRI can automatically generate the myelin volume fraction (MVF) to directly and quantitatively measure the MVF in voxels, with sensitivity to the loss of myelin in NAWM areas (42). These highly cited publications suggested that the correlation between MR manifestations and MS pathology *in vivo* and the identification of MS have always been research interests and challenges, and will remain research hotspots in this field in the future.

Keyword cluster analysis and burst intensity analysis can be used to explore research directions and research hotspots in this field. Notably, since 2019, in addition to popular research topics such as "quantitative MRI" and "myelin water imaging", "neuromyelitis optica spectrum", "spectrum", and "neuromyelitis optica" have appeared frequently in this field, suggesting that new research directions have emerged in recent years. Research on the quantitative analysis of MS myelin has mainly focused on the differential diagnosis of neuromyelitis optica, myelin-oligodendrocyte glycoprotein (MOG-IgG) antibody-associated diseases, and other antibody-mediated inflammatory diseases, yielding new discoveries and achieving research progress, which has improved the accuracy of diagnoses (43).

This study had certain limitations. The included studies were only from the WoS database, which avoided the disadvantage of lacking a citation analysis function in the PubMed database but created selection bias. In addition, only English articles were included; thus, articles published in other languages were not be included.

Conclusions

This study involved the first bibliometric analysis of 1,639 publications on myelin imaging in MS between 2000 and 2022, providing a comprehensive overview of the field and an assessment of future directions. The breakthrough of *in vivo* MRI of MS relies on the complex pathophysiological changes in MS itself, which is the biggest topic of interest among researchers in this field. In addition, the use of new MR technologies for myelin imaging to distinguish MS from other antibody-mediated inflammatory diseases represents the future development trend of this field. These findings provide researchers with reliable evidence and new insights.

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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-23-1157/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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