Original Article

Current status and trends in quantitative MRI study of intervertebral disc degeneration: a bibliometric and clinical study analysis

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Background: Quantitative magnetic resonance imaging (MRI) has the function of noninvasive quantitative evaluation, providing unique advantages in intervertebral disc degeneration (IDD) assessment. Although studies exploring the field for domestic and international scholars are increasingly being published, there is a lack of systematic scientific measurement and clinical analysis of the literature in this field.

Methods: Articles published from the respective database establishment to September 30, 2022, were obtained from the Web of Science core collection (WOSCC), PubMed database, and ClinicalTrials.gov. The scientometric software (VOSviewer 1.6.18, CiteSpace 6.1.R3, Scimago Graphica, and R software) were used for bibliometric and knowledge graph visualization analysis.

Results: We included 651 articles from the WOSCC database and 3 clinical studies from ClinicalTrials.gov for literature analysis. With the passage of time, the number of articles in this field gradually increased. The United States and China were the top 2 countries in terms of the number of publications and citations, and Chinese publications lacked international cooperation and exchange. The author with the most publications was Schleich C, while the author with the most citations was Borthakur A, who have both made important contributions to research in this field. The journal publishing the most relevant articles was *Spine*, and the journal with the most mean times cited per study was *Radiology*, both of which are the authoritative journals in this field. Keyword co-occurrence, clustering, timeline view, and emergent analysis revealed that recent studies in this field have focused on quantifying the biochemical components of the degenerated intervertebral disc (IVD). There were few available clinical studies. The more recent clinical studies mainly used molecular imaging technology to explore the relationship between different quantitative MRI sequence values and the IVD biomechanical environment and biochemical components content.

Conclusions: The study provided a knowledge map of quantitative MRI for IDD research in terms of countries, authors, journals, cited literature, and keywords through bibliometric analysis, and systematically sorted the current status, hotspots, and clinical research features in the field to provide a reference for future research.

Keywords: Intervertebral disc degeneration (IDD); quantitative magnetic resonance imaging; bibliometrics; visual analysis

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Introduction

Low back pain (LBP) is extremely common worldwide, with approximately 80% of people experiencing acute or chronic LBP at some point during their lives (1). Intervertebral disc degeneration (IDD) is considered the most important cause of LBP, which can lead to pathological changes such as disc herniation, spondylolisthesis, osteophyte hyperplasia, and spinal instability (2). Epidemiological studies have shown that LBP is a major cause of disability, which not only seriously affects quality of life, but also leverages a considerable economic burden on families and society (1). With changes to the metabolism of the intervertebral disc (IVD), an imbalance in the synthesis and catabolism of the extracellular matrix (ECM) occurs, which causes decreased water content of the nucleus pulposus, decreased elasticity of the annulus fibrosus, and increased calcification of the endplate, resulting in degenerative changes to the IVD, nerve root compression, and corresponding symptoms and signs (3). According to relevant studies, most people over 30 years old have signs of IDD, but this is not always accompanied by lumbago or other uncomfortable symptoms. However, with increasing age, the degree of degeneration gradually worsens (4,5). Therefore, the early diagnosis of degenerative disc disease (DDD) is important for the reconstruction and regeneration of degenerative IVD. Traditional magnetic resonance imaging (MRI) is a qualitative method for evaluating IDD by observing the IVD signal and morphological changes through sequences such as T2-weighted imaging (T2WI) and T1-weighted imaging (T1WI). However, these sequences can only detect intermediate and terminal IVD changes, and are insensitive to early IVD changes, which makes it difficult to accurately quantify the extent of IDD (6). A recent study showed the spine has extremely high individual variation in static and dynamic conditions, which makes the diagnosis and evaluation of spinal disease more difficult (7).

Quantitative MRI has the capability of non-invasive quantitative evaluation, which has unique advantages in IDD assessment. This technology is sensitive not only to the water content of the IVD but also to proton-matrix interactions, matrix organization, and water diffusion. Quantitative MRI includes diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI), T2 mapping, T2* mapping, q-space imagery (QSI), spin-lattice relaxation time constant in the rotating frame (T1ρ), magnetic resonance spectroscopy (MRS), and etc. (8). While several reviews have reported on the relevant literature exploring quantitative MRI both in China and internationally (9-11), there is a lack of systematic organization and analysis of the articles in this field. Bibliometrics can provide objective data for scientific publications, discipline development, and other purposes, which can help scholars identify the hotspots and trends in a given scientific field (12). Although bibliometric methods have been used in the field of disc degeneration, its diagnosis has received little attention (13,14).

VOSviewer, developed by Van Eck (15) from Leiden University in the Netherlands, and CiteSpace, developed by Chen (16) from Drexel University in the USA, are the bibliometrics software packages that have commonly been used in various research fields in recent years. Both play important roles in analyzing the current status of disciplinary research, detecting disciplinary frontiers, and selecting research directions. The purpose of this study was to perform a metrological analysis of the studies related to the application of quantitative MRI in IDD, to draw a visual knowledge map, to provide a comprehensive description of the research hotspots and frontiers in this field, and to analyze the characteristics of clinical trials. Through this, we aimed to clarify the development of the field with a view to providing reference for subsequent research.

Methods

Data sources and search strategies

We searched the Web of Science core collection (WOSCC) database from the establishment of the database to September 30, 2022. To focus on the research of quality articles, the publication type was limited to articles and reviews, and the language was restricted to English. The PubMed database was searched with the combination of subject terms and free terms, and Carrot2 software was used to perform topic clustering analysis for keyword verification. To avoid bias caused by database updates, all searches were completed on September 30, 2022, and imported into

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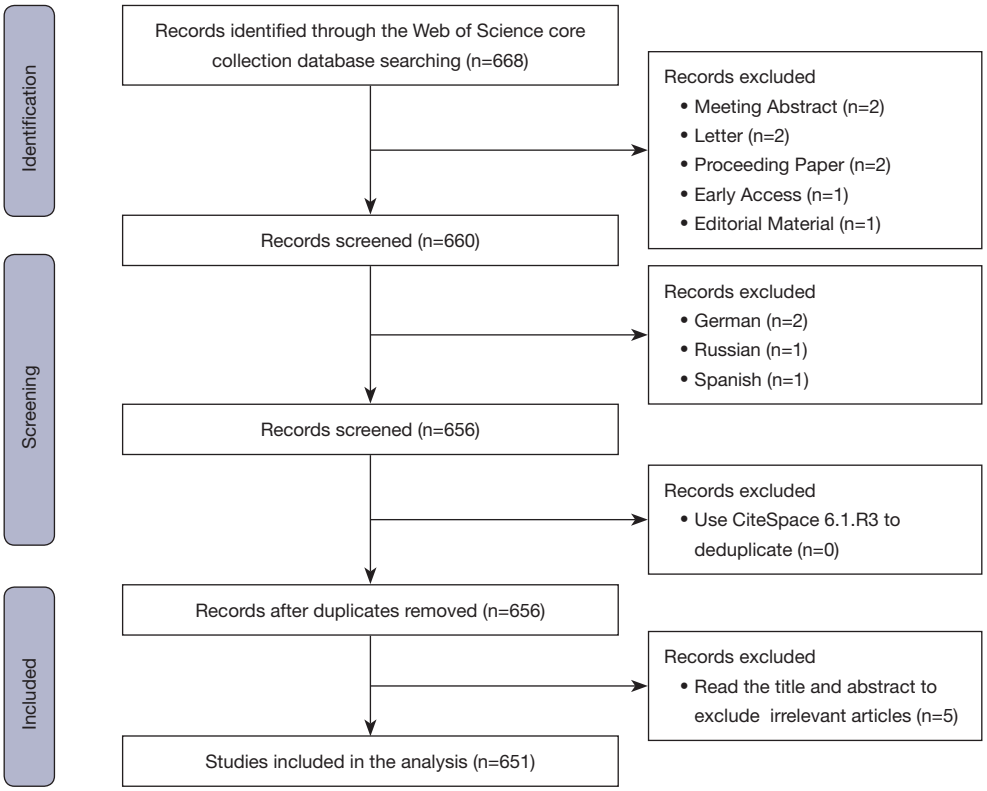

Figure 1 Flow chart of search strategy and document screening.

the bibliometric tools for analysis. Using the WOSCC database as an example, we used the following search terms: ("Intervertebral Disk Degeneration*") OR ("intervertebral disk*") OR ("intervertebral disc*") OR ("disc herniat*") OR ("disk herniat*") OR ("disc disease*") OR ("disk disease*") (Topic) AND ("Quantitative Magnetic Resonance Imaging*") OR ("quantitative MRI*") OR ("qMRI*") OR ("diffusion weighted imaging*") OR ("DWI*") OR ("diffusion tensor imaging*") OR ("DTI*") OR ("magnetic resonance spectroscopy*") OR ("T1ρ imaging*") OR ("T1rho*") OR ("T1 mapping*") OR ("T2 mapping*") OR ("apparent diffusion coefficient*") OR ("ADC mapping*") OR ("sodium MRI*") OR ("q-space imaging*") OR ("QSI*") OR ("chemical exchange saturation transfer*") OR ("CEST*") OR ("magnetic resonance spectroscopy*") OR ("MRS*") (Topic). S Chen and D Sun independently screened the articles, and N Wang was responsible for review. In case of disagreement, the 3 researchers discussed and reached a consensus. The document screening process is shown in *Figure 1*.

Data collection

In the WOSCC database, the search results were downloaded as in plain text file format with full record and cited references. After careful screening, the data were imported into Microsoft Excel 2016 and bibliometric software for further analysis.

Bibliometric analysis

In this study, we used Microsoft Excel 2016 software to count the general information of the documents including annual publications, country/region, journals, authors, frequency of citations, and etc. The journal impact factor (IF) and partition were determined using the data from the 2021 Journal Ranking by Clarivate Analytics Journal Citation Reports (JCR). We used VOSviewer 1.6.18 and Scimago Graphica for visual analysis, while CiteSpace 6.1.R3 was used to depict the dual-map overlay of journals. Keywords were used as nodes, and the clustering algorithm

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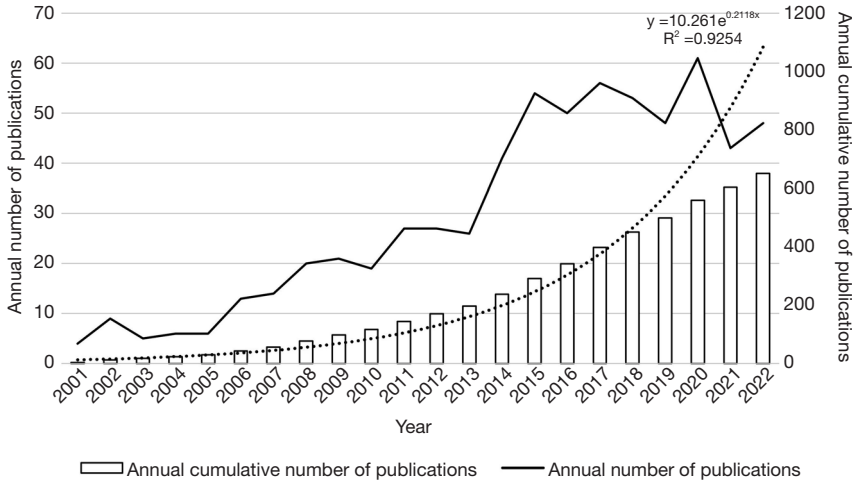

Figure 2 Annual number of publications and cumulative number of publications of quantitative MRI in IDD research collected by the WOSCC database from 2001 to 2022. MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration; WOSCC, Web of Science core collection.

chosen was the likelihood ratio (LLR) algorithm for keyword clustering, timeline view, and emergent analysis to clarify the research hotspots and trends within a certain time period. We merged similar keywords, such as "patients" and "patient" into "patients", and "intervertebral disk" and "disc herniation" into "intervertebral disc". In addition, the R package software "Biblimetrix" were used for the world map and the three fields plot.

Carrot2 was used to display PubMed's main topics tree map and pie chart.

We collected clinical trial research of quantitative MRI in IDD from ClinicalTrials.gov (https://www.clinicaltrials.gov/) to analyze and summarize the current clinical research characteristics in this field. The keywords searched were "degenerative disc disease" and "quantitative magnetic resonance imaging", and the status included studies that had been completed or were recruiting.

Results

Annual publications and trends

A total of 651 articles were included in this study. As can be seen from *Figure 2*, the annual number of publications showed a wave-like upward trend, and the annual cumulative number of publications continued to increase (the fitting curve function formula was as follows: $y=10.261e^{0.2118x}$; $R^2=0.9254$), indicating the related studies of quantitative MRI in IDD have attracted greater attention and may be a hotspot in current research.

Country/region analysis and international cooperation

Publications from 45 countries were collected, and their distribution is shown in *Figure 3A*. The United States was the country with the most publications (n=229, 25.22%), followed by China (n=158, 17.40%), and Germany (n=78, 8.59%) (*Table 1*). In terms of citations, the United States (n=7,550, 35.29%) far exceeded China (n=1,937, 9.05%), and Canada (n=1,723, 8.05%).

VOSviewer software was used to visualize and analyze the connections between countries/regions (*Figure 3*), with different nodes representing different countries, the size of the nodes or fonts reflecting the frequency, and different colors representing different clusters. There was close cooperation between countries in each cluster, with the strength of the links between nodes representing the strength of cooperation between countries. Countries in the WOSCC database (documents ≥5) were divided into 6 clusters. European countries led by Austria, Germany, Greece, Slovakia, Hungary, and Switzerland were grouped into cluster 1 and showed strong cooperation among them. Asian countries, led by China, were in cluster 2 and North American countries, led by the United States, were in cluster 4 (*Figure 3B*).

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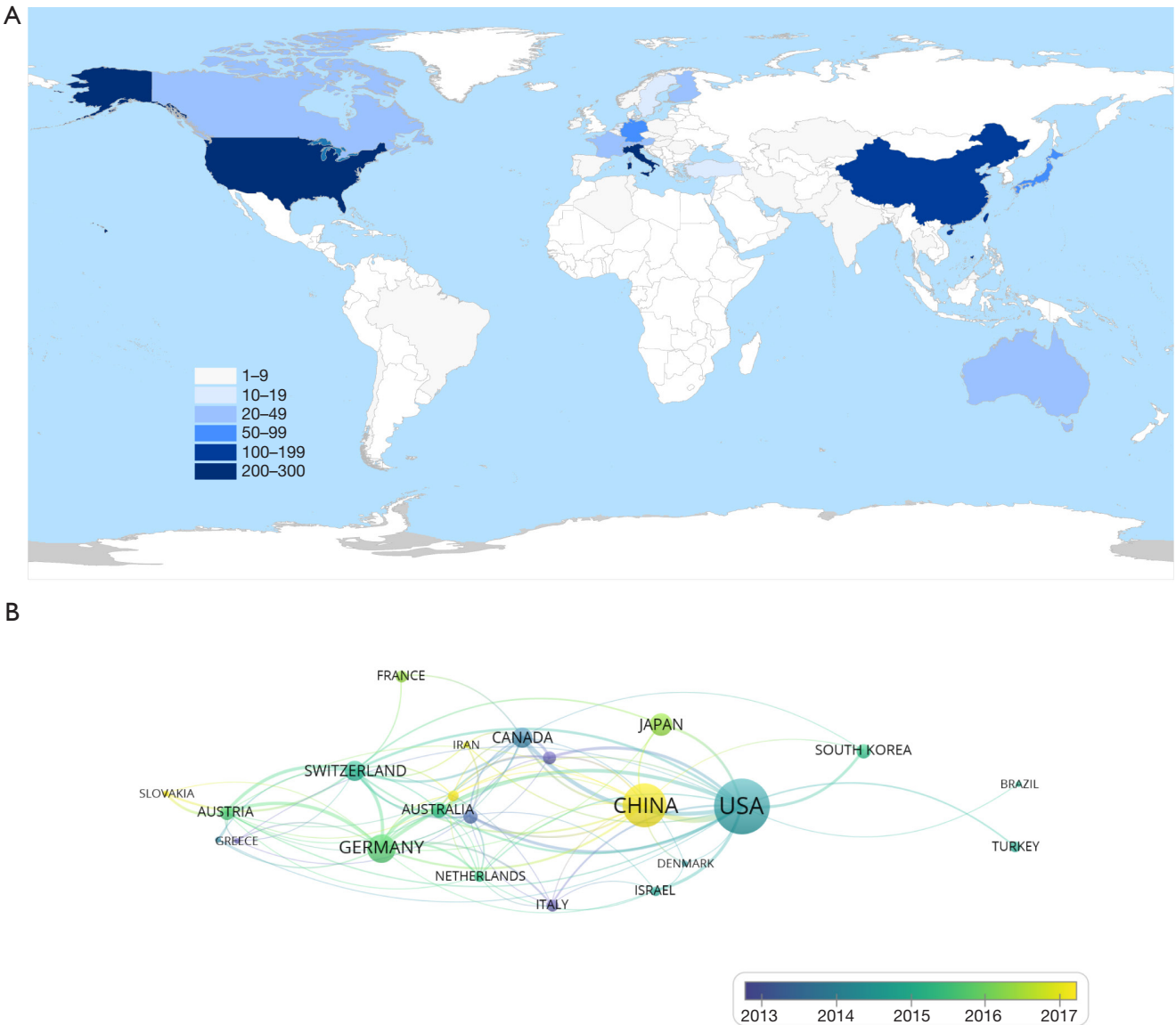

Figure 3 National/regional contribution of quantitative MRI and IDD-related research. (A) World map of the published literature in the WOSCC database. The darker the blue, the greater the number of publications. The China and United States boards on the world map are both dark blue, indicating the 2 countries had the largest number of documents. (B) Network map of publication volume of countries/regions in the WOSCC database. Different nodes represent different countries, the size of the nodes or fonts reflect the frequency, and different colors represent different clusters. There was close cooperation between countries in each cluster, and the strength of the links between nodes represents the strength of cooperation between countries. MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration; WOSCC, Web of Science core collection.

Author contribution and collaboration analysis

A total of 3,341 authors published relevant articles. The 3 most published authors were Schleich C (n=18, 1.99%) from Germany, Trattnig S (n=16, 1.77%) from Austria, and Mueller-Lutz A (n=15, 1.66%) from Germany. The top 10 authors published 13.36% of the literature in the field (*Table 2*), among whom the most cited author was Borthakur A, followed by Elliott DM and Navon G, indicating these authors were influential in the field.

We employed VOSviewer software to cluster the authors

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Table 1 Top 10 countries/regions in the number of publications and citations for quantitative MRI in IDD

Rank	Documents		Citations	
	Country (n=45)	n (%)	Country (n=45)	n (%)
1	USA	229 (25.22)	USA	7,550 (35.29)
2	China	158 (17.40)	China	1,937 (9.05)
3	Germany	78 (8.59)	Canada	1,723 (8.05)
4	Japan	51 (5.62)	Switzerland	1,338 (6.25)
5	Canada	43 (4.74)	Germany	1,223 (5.72)
6	Switzerland	43 (4.74)	Japan	947 (4.43)
7	Australia	30 (3.30)	Finland	901 (4.21)
9	England	26 (2.86)	England	697 (3.26)
8	Austria	26 (2.86)	Israel	630 (2.94)
10	South Korea	26 (2.86)	Australia	603 (2.82)

MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

Table 2 Top 10 authors in number of publications and citations in quantitative MRI in IDD

Rank	Documents		Citations	
	Author (n=3,341)	n (%)	Author (n=3,341)	n (%)
1	Schleich C	18 (1.99)	Borthakur A	547 (2.68)
2	Trattnig S	16 (1.77)	Elliott DM	525 (2.57)
3	Mueller-Lutz A	15 (1.66)	Navon G	499 (2.45)
4	Antoch G	12 (1.32)	Battie MC	491 (2.41)
5	Borthakur A	11 (1.21)	Regatte RR	488 (2.39)
6	Elliott DM	10 (1.10)	Videman T	480 (2.35)
7	Stelzenede D	10 (1.10)	Fehlings MG	442 (2.17)
8	Wittsack HJ	10 (1.10)	Kaprio J	436 (2.14)
9	Lotz JC	10 (1.10)	Gill K	419 (2.05)
10	Battie MC	9 (0.99)	Levalahti E	390 (1.91)

MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

(*Figure 4*), with the nodes indicating authors and the lines between nodes representing the strength of cooperation between authors. The important authors were divided into 5 clusters (*Figure 4*), with Trattnig S, Stelzenede D, Welsch GH, and others representing cluster 1, who formed a network of close collaborations. Trattnig S had the highest total link strength of 77. Cluster 2 is represented by Schleich C and Mueller-Lutz A, and cluster 3 by Takahashi K, Ohtori S, and others. Collectively, these authors play an important role in the study of quantitative MRI for IDD.

Journal analysis

A total of 193 journals published relevant literature. The results showed that *Spine* (IF =3.24, Q1) and *European Spine Journal* (IF =2.72, Q2) were the journals with the most publications (*Table 3*). Although *Radiology* (IF =29.15, Q1) had a low volume of publications, ranking 12th, it was the journal with the most mean times cited per study. This suggests *Radiology* may be a more authoritative journal in the field.

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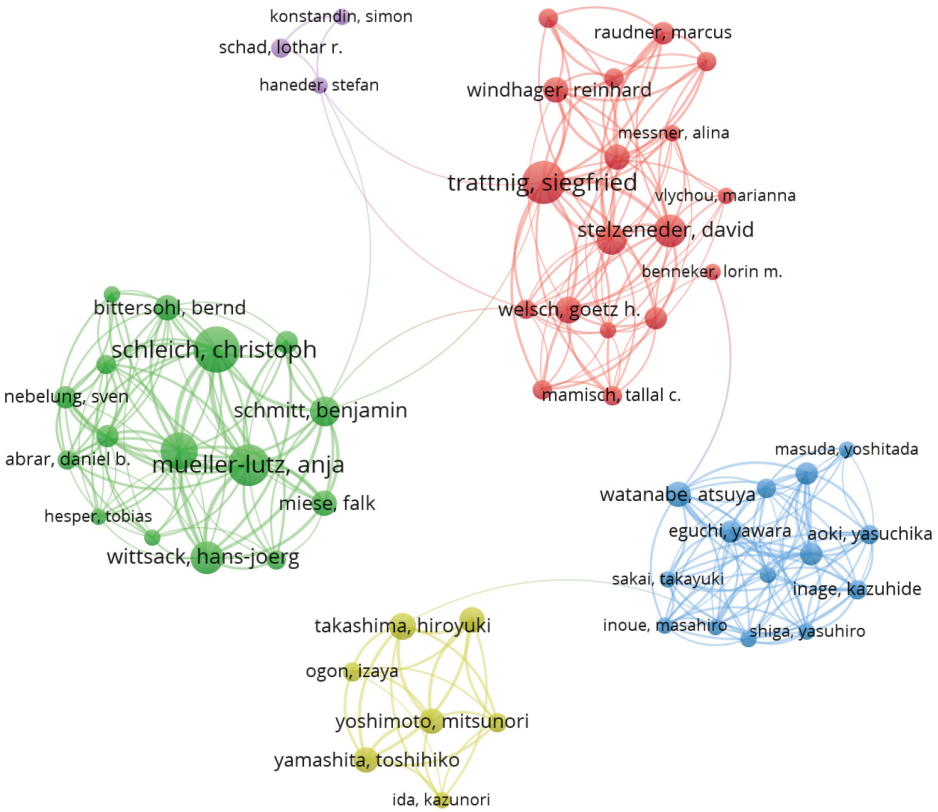

Figure 4 Network map of author contribution and collaboration in the WOSCC database. Different colors represent different clusters. The nodes indicate authors, with larger nodes indicating a larger number of documents. Lines between nodes represent the strength of cooperation between authors, with thicker lines indicating tighter cooperation. WOSCC, Web of Science core collection.

The network map of journal collaboration showed that *Spine* had the largest nodes in the network and the highest total link strength [421], followed by *European Spine Journal* [312], indicating their significant contribution in the field (*Figure 5A*).

The three fields plot displays the relationship between high-producing countries, journals, and authors. The results show high-producing countries often publish literature in journals with many documents and high impact, and these journals are strongly associated with the core authors (*Figure 5B*). In the dual-map overlay of journals in *Figure 6*, the left side of the curve represents the references cited in the study, while the right side of the curve indicates the cited reference source. The width of the curve trajectory is proportional to the z score scaled frequency of the references, with a thicker path indicating a higher frequency of the reference (17). We found 8 main citation paths, including 4 pink paths and 4 green paths. Among them, the pink citation path with the highest z score scaled frequency included literature in the field of "hydrology, sports, philosophy" which mainly cited the literature published in the field of "molecular, biology, genetics", while the widest green citation path included literature in the field of "medicine, medical, clinical" which heavily cited literature in "health, nursing, medicine".

Frequently cited articles

Masuda published the study titled "*A new rabbit model of mill, reproducible disc degeneration by an anulus need function: correlation between the degree of disc injury and radiological and historical appearances of disc degeneration*" in *Spine* in 2005, which was the most frequently cited article (total citations =450). The second most cited was Ling's 2008 article in *Proceedings of the National Academy of Sciences of the United States of America* with 422 citations, while Jarvik's study published in *Annals of Internal Medicine* in 2002 with 389 citations was the third most cited (*Table 4*). The

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Table 3 Top 20 journals in number of publications of quantitative MRI in IDD

Rank	Journal (n=193)	Documents (%)	Citations	Mean times cited per study[†]	IF	JCR partition
1	*Spine*	64 (9.83)	3,164	49.44	3.24	Q1
2	*European Spine Journal*	51 (7.83)	915	17.94	2.72	Q2
3	*Journal of Magnetic Resonance Imaging*	23 (3.53)	635	27.61	5.12	Q1
4	*Spine Journal*	20 (3.07)	589	29.45	4.30	Q1
5	*Bmc Musculoskeletal Disorders*	18 (2.76)	224	12.44	2.56	Q2
6	*Journal of Orthopaedic Research*	18 (2.76)	397	22.06	3.10	Q1
7	*Magnetic Resonance Imaging*	18 (2.76)	305	16.94	3.13	Q3
8	*Magnetic Resonance in Medicine*	15 (2.30)	324	21.60	3.74	Q1
9	*European Radiology*	14 (2.15)	401	28.64	7.03	Q1
10	*Plos One*	13 (2.00)	161	12.38	3.75	Q2
11	*NMR in Biomedicine*	12 (1.84)	321	26.75	4.48	Q1
12	*Radiology*	11 (1.69)	993	90.27	29.15	Q1
13	*American Journal of Neuroradiology*	10 (1.54)	182	18.20	4.97	Q2
14	*European Journal of Radiology*	10 (1.54)	126	12.60	4.53	Q2
15	*Scientific Reports*	10 (1.54)	31	3.10	5.00	Q1
16	*Skeletal Radiology*	10 (1.54)	264	26.40	2.13	Q3
17	*Acta Radiologica*	8 (1.23)	150	18.75	1.70	Q3
18	*Journal of Orthopaedic & Sports Physical Therapy*	8 (1.23)	156	19.50	6.28	Q1
19	*Diagnostics*	7 (1.08)	13	1.86	3.99	Q2
20	*Magnetic Resonance Materials in Physics Biology and Medicine*	7 (1.08)	78	11.14	2.53	Q3

[†], average number of citations per study in the journal. IF, impact factor (Journal Citation Reports 2021, released on September 30, 2022); JCR, Journal Ranking by Clarivate Analytics Journal Citation Reports; MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

normalized total citations can eliminate the interference of paper publishing time and type, standardize the number of citations, and thus measure the quality of articles (13). The study with the highest normalized total citations was "*Clinical applications of chemical exchange saturation transfer (CEST) MRI*" written by Jones in 2018. Although the article was published recently, it received many citations immediately after its publication.

The most frequently cited articles were visualized with VOSviewer software (*Figure 7*). The different nodes represent the cited articles, the node size represents the citation frequency of the article, and the node color represents the publication time of the article. Masuda (2005), Ling (2008), and Jarvik (2002) ranked top in terms of citation frequency. Among them, the node representing Masuda (2005) is the largest and most cited, and the blue color indicates its earlier publication (*Figure 7*).

Cocited articles

There were 14,142 references generated in 651 articles, and in terms of citations, 3 of the top 5 references were published in *Spine* (Table S1). Pfirrmann's article published in *Spine* in 2001, entitled "*Magnetic resonance classification of lumbar intervertebral disc degeneration*", had the most citations [250] and the highest total link strength [1,712] in the cocitation analysis, demonstrating this article was instructive in the field.

The visualization of cocitation analysis was plotted via VOSviewer software, and for better visualization, only

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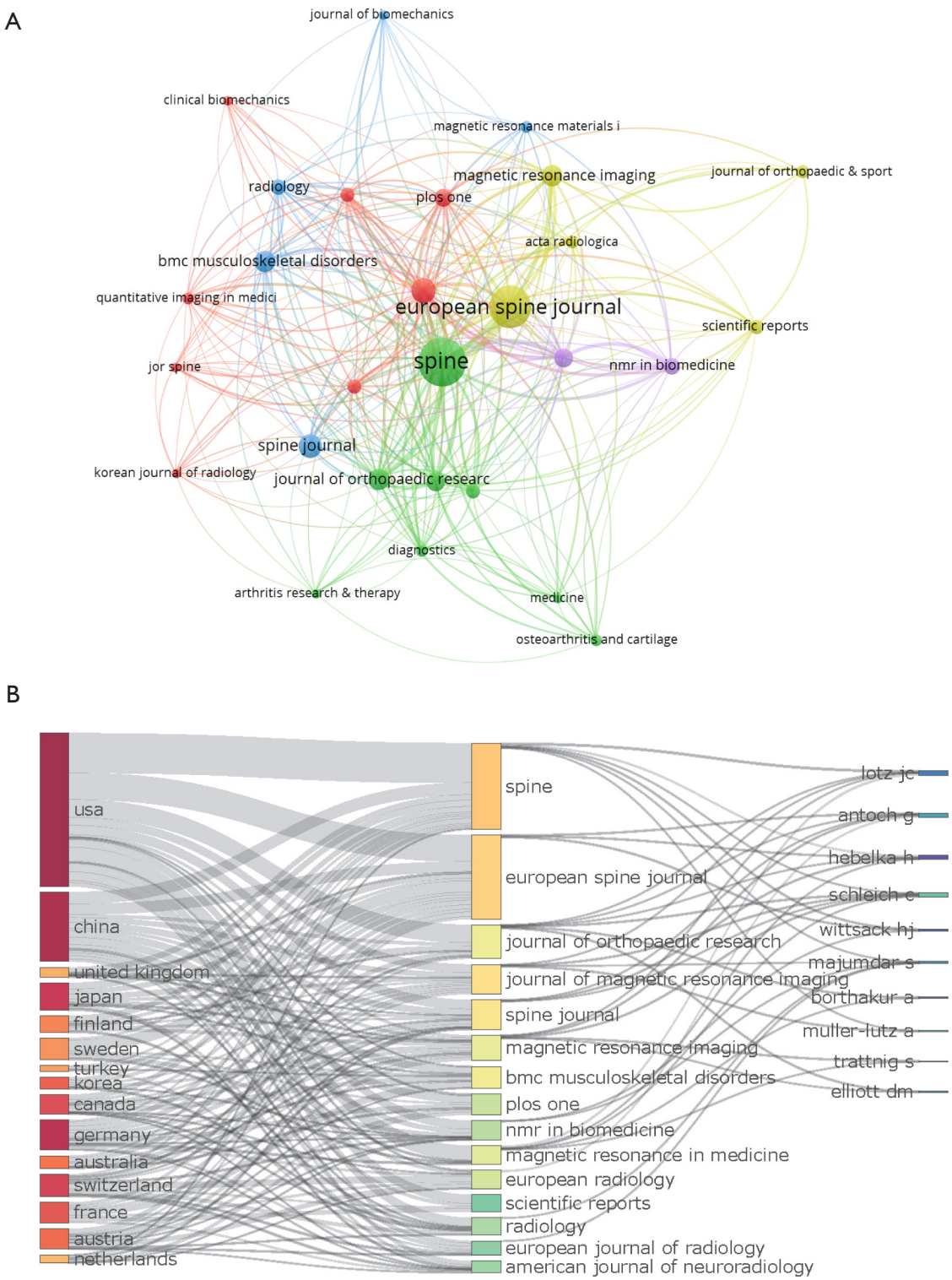

Figure 5 Journal characteristics of quantitative MRI and IDD-related research. (A) The journal network graph in the WOSCC database. The node represents the journal, and the larger the node, the more publications in the journal. (B) The three fields plot. The left column represents countries, the middle column represents journals, and the right column represents authors. MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration; WOSCC, Web of Science core collection.

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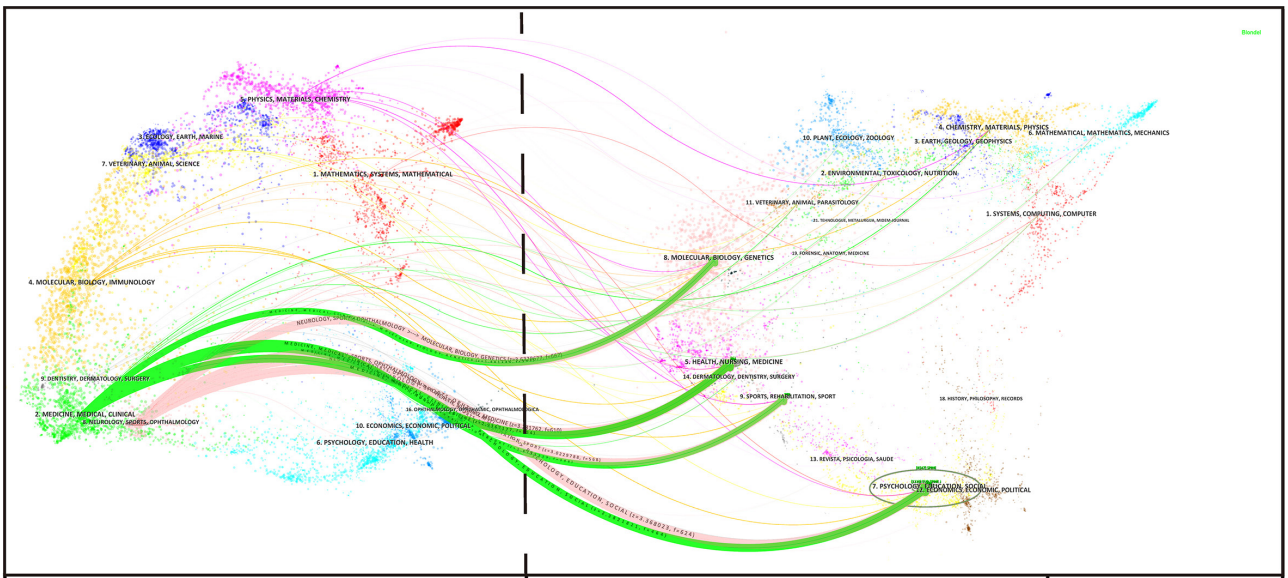

Citing domain	Cited domain	Z-score-scaled frequency
Medicine, medical, clinical	Molecular, biology, genetics	1.661
Medicine, medical, clinical	Health, nursing, medicine	2.934
Medicine, medical, clinical	Sports, rehabilitation, sport	1.976
Medicine, medical, clinical	Phychology, education, social	2.382
Neurology, sports, ophthalmology	Molecular, biology, genetics	3.633
Neurology, sports, ophthalmology	Health, nursing, medicine	3.282
Neurology, sports, ophthalmology	Sports, rehabilitation, sport	3.023
Neurology, sports, ophthalmology	Phychology, education, social	3.368

Figure 6 Dual-map overlay of journals in the WOSCC database. The dual-map overlay of the journals shows four pink primary citation paths and four green primary citation paths. WOSCC, Web of Science core collection.

Table 4 Top 20 most frequently cited articles related to quantitative MRI in IDD

Rank	Title	Journal	Author (year)	Total citations	Normalized total citations
1	A novel rabbit model of mild, reproducible disc degeneration by an anulus needle puncture: correlation between the degree of disc injury and radiological and histological appearances of disc degeneration	*Spine*	Masuda K (2005)	450	3.35
2	Assessment of glycosaminoglycan concentration *in vivo* by chemical exchange-dependent saturation transfer (gagCEST)	*Proceedings of the National Academy of Sciences of the United States of America*	Ling W (2008)	422	6.05
3	Diagnostic evaluation of low back pain with emphasis on imaging	*Annals of Internal Medicine*	Jarvik JG (2002)	389	5.14
4	2009 ISSLS prize winner: Does discography cause accelerated progression of degeneration changes in the lumbar disc: a ten-year matched cohort study	*Spine*	Carragee EJ (2009)	300	6.06

Table 4 (*continued*)

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Table 4 (*continued*)

Rank	Title	Journal	Author (year)	Total citations	Normalized total citations
5	Lumbar degenerative disk disease	*Radiology*	Modic MT (2007)	264	2.8
6	Acute cervical traumatic spinal cord injury: MR imaging findings correlated with neurologic outcome—prospective study with 100 consecutive patients	*Radiology*	Miyanji F (2007)	244	2.58
7	A slowly progressive and reproducible animal model of intervertebral disc degeneration characterized by MRI, X-Ray, and histology	*Spine*	Sobajima S (2005)	243	1.81
8	Generalized deep-tissue hyperalgesia in patients with chronic low-back pain	*European Journal of Pain*	O'neill S (2007)	216	2.29
9	Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: quantification with MR spectroscopy	*Radiology*	Mengiardi B (2006)	179	2.64
10	Heritability of low back pain and the role of disc degeneration	*Pain*	Battie MC (2007)	174	1.84
11	Factors associated with lumbar intervertebral disc degeneration in the elderly	*The Spine Journal*	Hangai M (2008)	172	2.47
12	Gellan gum-based hydrogels for intervertebral disc tissue-engineering applications	*Journal of Tissue Engineering and Regenerative Medicine*	Silva-correia J (2011)	166	4.58
13	Assessment of human disc degeneration and proteoglycan content using T1ρ-weighted magnetic resonance imaging	*Spine*	Johannessen W (2006)	157	2.32
14	Clinical applications of chemical exchange saturation transfer (CEST) MRI	*Journal of Magnetic Resonance Imaging*	Jones KM (2018)	141	9.83
15	Genetic and environmental effects on disc degeneration by phenotype and spinal level: a multivariate twin study	*Spine*	Battie MC (2008)	124	1.78
16	Fat infiltration of paraspinal muscles is associated with low back pain, disability, and structural abnormalities in community-based adults	*The Spine Journal*	Teichtahl AJ (2015)	123	5.91
17	T2 relaxation times of intervertebral disc tissue correlated with water content and proteoglycan content	*Spine*	Marinelli NL (2009)	120	2.42
18	Classification of intervertebral disk degeneration with axial T2 mapping	*American Journal of Roentgenology*	Watanabe A (2007)	111	1.18
19	Etiology of long-term failures of lumbar spine surgery	*Pain Medicine*	Waguespack A (2002)	105	1.39
20	ISSLS prize winner: prevalence, determinants, and association of Schmorl nodes of the lumbar spine with disc degeneration: a population-based study of 2449 individuals	*Spine*	Mok FPS (2010)	100	3.18

MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

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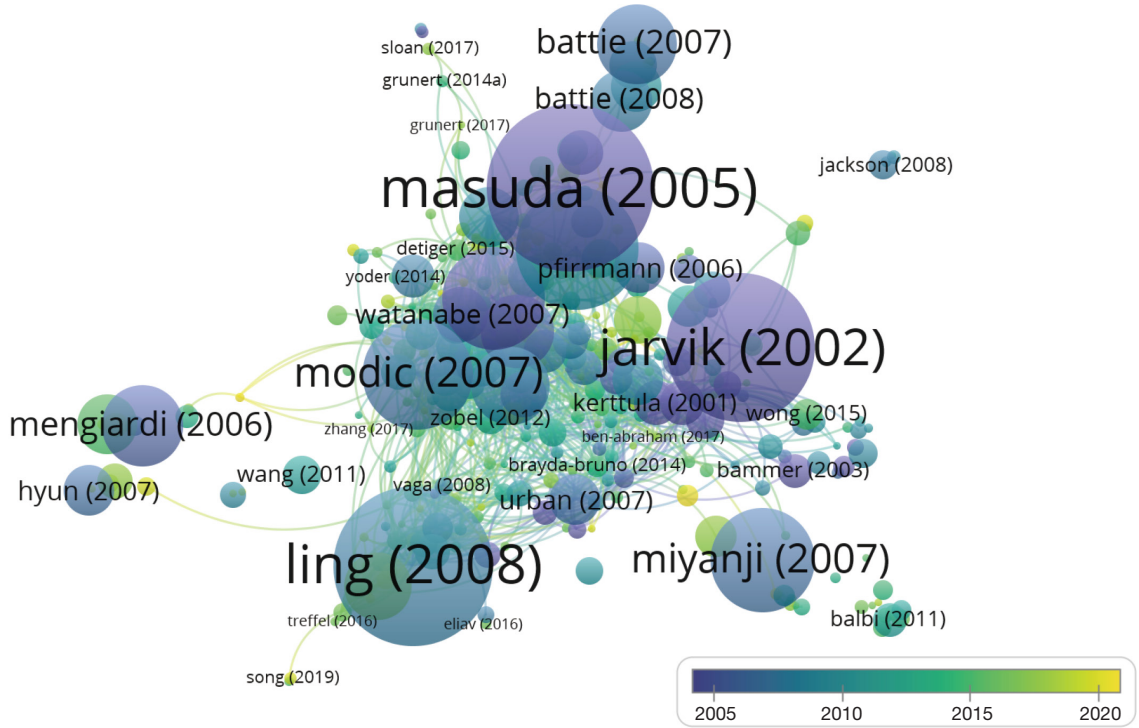

Figure 7 Visual network map of cited articles in the field. The different nodes represent the cited articles, the node size represents the citation frequency of the article, and the node color represents the publication time of the article.

references with citations ≥20 are shown in the plot. Each node represents a document, and the node size represents the frequency of citations. A total of 4 clusters of cocitation articles were formed (*Figure 8*). Pfirrmann (2001), with the most co-citations, was clustered to cluster 1, Johannessen (2006) and Adams (2006) to cluster 3, and Watanabe (2007) and Bumenkrantz (2010) to cluster 2.

Analysis of keywords

We performed frequency analysis of keywords with Microsoft Excel 2016 (*Table 5*). The highest-frequency keywords in this research field were "intervertebral disc" (occurrences =198), followed by "degeneration" (occurrences =193), "mri" (occurrences =193), "low-back-pain" (occurrences =156), and "magnetic resonance imaging" (occurrences =128) (*Figure 9A*). Carrot2 provided direct access to the PubMed database for topics clustering of search results, which was helpful for us to verify the results of the WOSCC database (18). The results show the topic "Disc degeneration, magnetic resonance imaging, quantitative" appeared most frequently, followed by "patients" and "evaluation" (*Figure 9B-9D*).

VOSviewer software was used to map the keyword co-occurrence network (*Figure 10A*). The visual graph divided the keywords into 6 clusters, with 120 keywords co-occurring more than 10 times. We saved the visual graph in VOSviewer in Game Maker Language (GML) format and imported it into Scimago Graphica software to determine the co-occurrence of the high-frequency keywords. The result is displayed in the form of a circular graph (*Figure 10B*).

Based on the keyword co-occurrence network, CiteSpace software was used to perform cluster analysis of the literature keywords, showing clusters as ID #0-9 (*Figure 11A*, Table S2). The keywords cluster's Q value =0.7491>0.3 and S value =0.8337>0.5, indicating the results were significant and reliable (14). The results showed ID #0 involved the construction of animal models of IDD, cluster ID #5 involved the diagnosis and treatment of sciatica, and the remaining clusters were related to different sequences of quantitative MRI to quantify the biochemical components of IVD.

Timeline view analysis was performed based on the keyword co-occurrence network (*Figure 11B*). In

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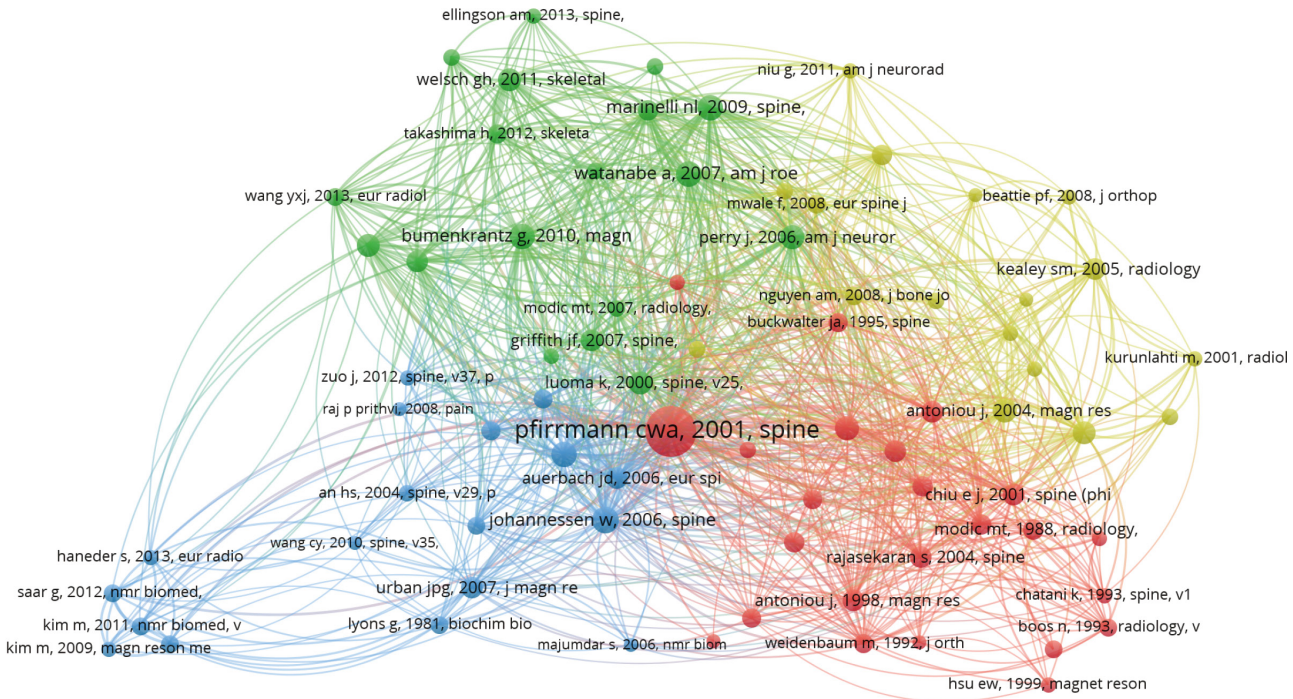

Figure 8 Visual network map of cocitation articles in the field. The nodes represent references, and larger nodes indicate more citations. Different colors represent different clusters.

Table 5 Top 15 keywords/topics in the WOSCC and PubMed database

Rank	WOSCC		PubMed	
	Keyword	Occurrences	Topic	Documents
1	Intervertebral disc	198	Disc degeneration, magnetic resonance imaging, quantitative	830
2	Degeneration	193	Patients	413
3	MRI	193	Evaluation	367
4	Low-back-pain	156	Measured	365
5	Magnetic resonance imaging	128	Years, age	270
6	Spine	118	Nucleus pulposus	266
7	Nucleus pulposus	105	Magnetic resonance imaging MRI	212
8	Intervertebral disc degeneration	93	MR imaging	201
9	Lumbar spine	76	Low back pain	186
10	Classification	71	ADC values, apparent diffusion coefficient ADC	177
11	Disc degeneration	65	Annulus fibrosus	155
12	In-vivo	65	Intervertebral disc IVD	155
13	Articular-cartilage	61	Lumbar intervertebral disc	135
14	Cartilage	57	Nucleus Pulposus NP	120
15	Diffusion	52	Fractional anisotropy FA, diffusion tensor imaging DTI	89

ADC, apparent diffusion coefficient; FA, fractional anisotropy; IVD, intervertebral disc; NP, nucleus pulposus; DTI, diffusion tensor imaging; WOSCC, Web of Science core collection; MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

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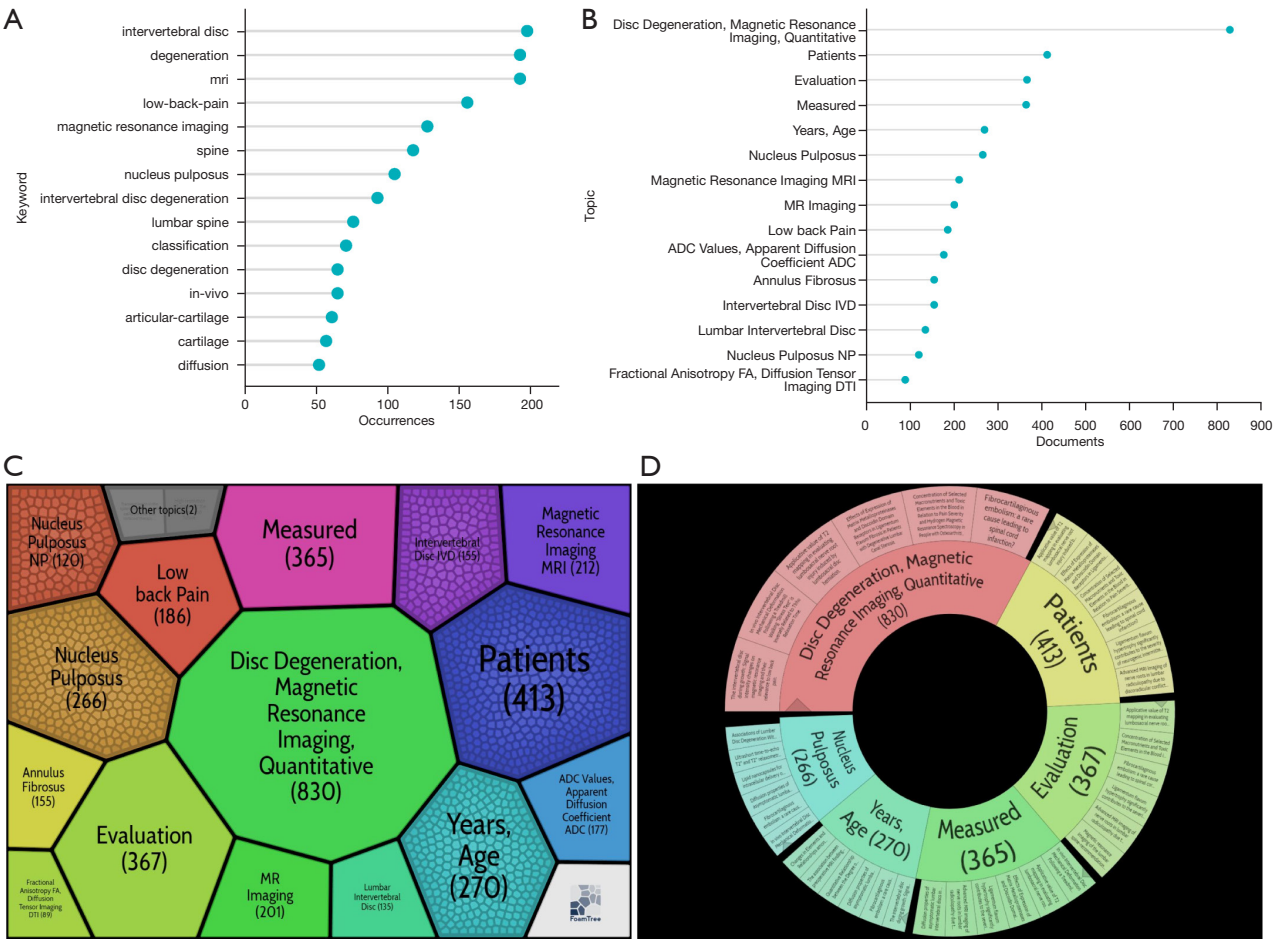

Figure 9 Frequency statistics of keywords and main topics. (A) Lollipop chart of the top 15 keywords in the WOSCC database. (B) Lollipop chart of the top 15 topics in the PubMed database. (C) Main topics tree map. (D) Main topics pie chart. WOSCC, Web of Science core collection.

Figure 11B, the X-axis of the timeline view is the year of occurrence of the keywords in the clusters, while the Y-axis was the clustering of each keyword, which can further show the occurrence, end, and time trend of each cluster and reflect the importance of a certain cluster and the time span of its distribution (17). As shown in *Figure 11B*, the time span of cluster "#4 (cerebrospinal fluid)" and "#8 (chemical exchange storage transfer)" cover the entire X-axis. The main component of quantitative MRI for IDD in recent years has been the quantification of the biochemical components of IVD, and particularly, the use of DTI to assess the function of the IVD.

CiteSpace software can detect emergent keywords with high frequency change rate and fast growth rate, which reflects the research frontiers in a given field to a certain extent (19). We obtained 14 emergent words from the keyword analysis (*Figure 11C*) emerging from 2001 to 2011 being "intervertebral disk", "bone marrow", "disk herniation", "collagen", "quantitative MR", "articular cartilage", and "pain", and those emerging from 2011 to 2014 being "cartilage" and "mechanical property". "Proteoglycan (PG) content", "diffusion tensor imaging", "tractography", "lumbar intervertebral disc", and "T2" were the keywords emerging from 2014 to 2020. This suggests that in recent years, researchers have been paying more attention to the relationship between the biochemical components of the IVD and DTI, tractography, and T2.

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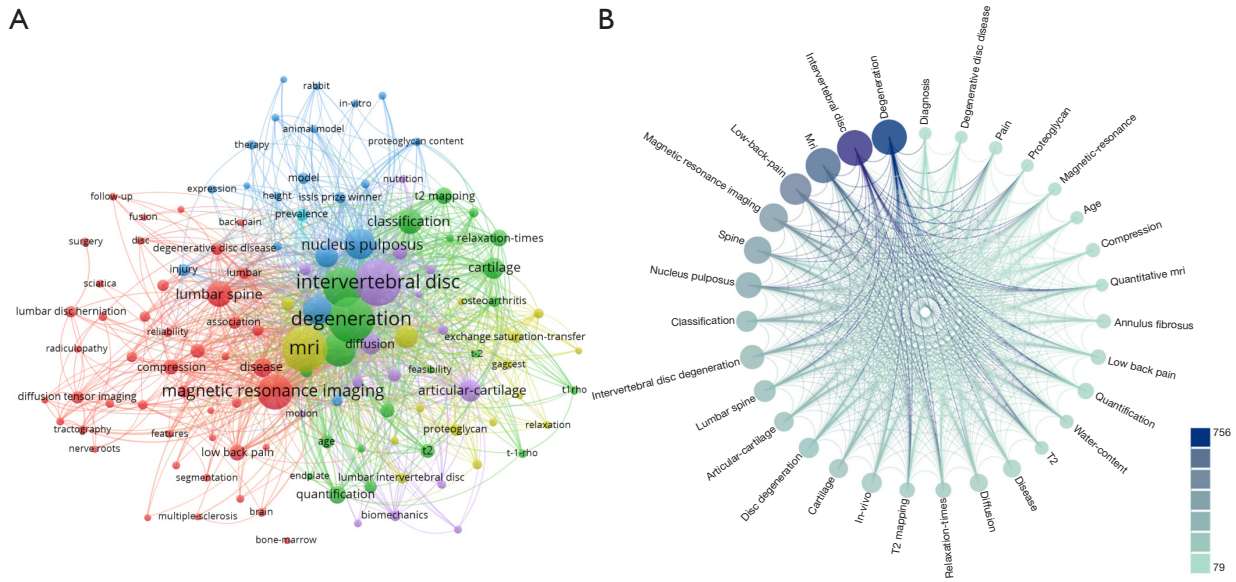

Figure 10 Keyword clustering of quantitative MRI and IDD-related research. (A) Keyword co-occurrence network graph in the WOSCC database. Different colors represent different clusters. The keywords are divided into 6 clusters. (B) Circular graph of high-frequency keywords in the WOSCC database. The higher the keyword co-occurrence frequency is, the larger the node while the higher the total link strength is, the darker the node blue. The stronger the connection between the keywords is, the darker the blue color of the line. MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration; WOSCC, Web of Science core collection.

Clinical research analysis

To further explore interests in current clinical research, we summarized and analyzed relevant clinical studies that had been completed or were recruiting at the time of our study. A total of 15 studies were retrieved according to the subject terms and only 3 clinical studies were obtained after careful reading of the title and content screening (Table S3). These were mainly interventional and observational studies, with 2 recruiting and 1 being completed in 2013.

Discussion

Bibliometric analysis of the state of research of quantitative MRI in IDD

We conducted a scientific metrological analysis of the literature on the application of quantitative MRI technology to IDD research in the WOSCC database and comprehensively evaluated the current situation, hotspots, and trends in this field. According to the annual publications and annual cumulative publications, the related research of quantitative MRI in IDD has attracted increasing attention. The results of the country/region contribution analysis showed the United States had the highest number of publications and the highest number of citations. The results of the country/region cooperation analysis showed that the United States also played an important role in this field by maintaining close cooperation with many other countries. In contrast, as the second largest country in terms of the number of publications, China played a weak role in the cooperation network and was isolated from other countries. Therefore, China should establish a stronger international cooperation network and strengthen mutual cooperation abroad. Analyzing the contributions of authors, the core authors in the field were Schleich C, Trattnig S, Mueller-Lutz A, and Borthakur A, most of whom come from the fields of medical imaging and biomedicine. However, there were fewer highly productive and well-known scholars in China, again suggesting greater communication with international scholars should be sought. The journal analysis results showed that *Spine* and *European Spine Journal* were the most influential journals in the field, and Radiology was the journal with the most mean times cited per study, which suggests it was a more authoritative journal. These high-producing journals were strongly associated with the core authors. Thus, clinicians should strengthen cooperation with these authoritative journals and core authors, which will be more conducive to

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A

CiteSpace, v. 6.1.R3 (64-bit) Basic
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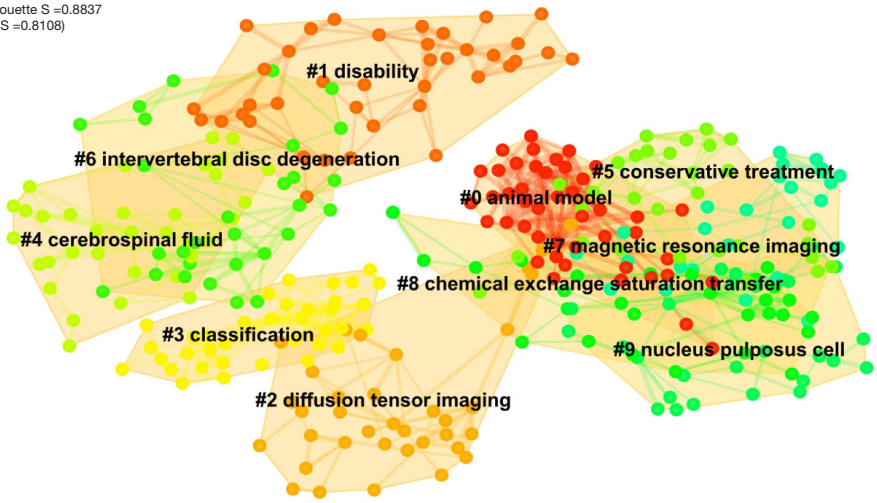
WoS: C:\Users\cs\citespace\Examples\Template\data\input
Timespan: 2001–2022 (Slice Length =1)
Selection Criteria: g-index (k =25), LRF =3.0, L/N =10, LBY =5, e =1.0
Network: N =532, E =1,173 (Density =0.0083)
Largest CC: 509 (95%)
Nodes Labeled: 1.0%,
Pruning: Pathfinder
Modularity Q =0.7491
Weighted Mean Silhouette S =0.8837
Harmonic Mean (Q, S =0.8108)



B

CiteSpace, v. 6.1.R3 (64-bit) Basic
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WoS: C:\Users\cs\citespace\Examples\Template\data\input
Timespan: 2001–2022 (Slice Length =1)
Selection Criteria: g-index (k =25), LRF =3.0, L/N =10, LBY =5, e =1.0
Network: N =532, E =1,173 (Density =0.0083)
Largest CC: 509 (95%)
Nodes Labeled: 1.0%,
Pruning: Pathfinder
Modularity Q =0.7491
Weighted Mean Silhouette S =0.8837
Harmonic Mean (Q, S =0.8108)

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C

Top 14 Keywords with the strongest citation bursts

Keywords	Year	Strength	Begin	End	2001–2022
Intervertebral disk	2001	4.67	2001	2007	
Bone marrow	2001	3.99	2002	2011	
Disk herniation	2001	3.22	2002	2010	
Collagen	2001	3.45	2004	2010	
Quantitative mr	2001	3.14	2004	2006	
Articular cartilage	2001	3.5	2005	2011	
Pain	2001	3.15	2009	2010	
Cartilage	2001	3.95	2011	2013	
Mechanical property	2001	4.08	2012	2014	
Proteoglycan content	2001	3.3	2014	2017	
Diffusion tensor imaging	2001	3.23	2014	2018	
Tractography	2001	3.2	2015	2016	
Lumbar intervertebral disc	2001	6.31	2018	2019	
T2	2001	3.48	2019	2020	

Figure 11 Keyword analysis of quantitative MRI and IDD-related research. (A) Visual map of keyword clustering analysis in this field. (B) Visual map of keyword timeline view analysis in this field. (C) Top 14 keywords with the strongest citation bursts in the WOSCC database. Red represents at high degree of keyword emergence during this period, while green represents a low degree of emergence. MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration; WOSCC, Web of Science core collection.

the early assessment of IDD and standardized diagnosis and treatment.

Analysis of the cited literature on quantitative MRI in IDD

The citation frequency of a document represents the degree of influence it carries in a given field of research. The higher the citation frequency of a document is, the higher its recognition degree in the academic circle and the more important the influence. In the analysis of author contribution, while Borthakur A had the highest citation frequency, there were no publications by this author in the literature of high citation analysis. We speculate this may be because the author's research has taken place over a long-time span and has not yet formed a representative study, leading to the low citation frequency of his articles. The first research in this field was published by Dietrich in 2001 in *Magnetic Resolution Materials in Physics Biology and Medicine*, and entitled "*Diffusion-weighted imaging of the spine using radial k-space trajectories*". This study developed a diffusion-weighted spin-echo sequence with k-space radial trajectories to measure the apparent diffusion coefficient (ADC) of the spine. The application of diffusion-weighted gradients in different directions allowed for the measurement of diffusion anisotropy and helped further quantify the degree of IVD degeneration (20). The 3 most cited articles were published in *Spine*, *Proceedings of the National Academy of Sciences of the United States of America*, and *Annals of Internal Medicine*, which reflects the complexity and diversity of the IDD mechanism. Masuda (21) examined the classical ring acupuncture method and the new acupuncture method with different sizes of needles (16G, 18G, and 21G) to cause damage to the IVD, with different MRI sequences then being used to assess the degree of IVD degeneration. This was the most cited experimental study. Another highly cited study was published by Ling *et al.* in 2008 (22). They found that through the use of chemical exchange saturation transfer (CEST) MRI technology, the glycosaminoglycan (GAG) concentration in the body could be directly measured, with high sensitivity, high saturation efficiency, specificity, and other advantages, which was of great significance for the evaluation of IDD. Jarvik published the first systematic review in this field in *Annals of Internal Medicine*, reviewing the accuracy of history information and imaging in the diagnosis of LBP in 150 previous studies and concluded MRI was the specific test with the highest sensitivity to effectively screen patients who have comorbidities (23). At present, glycosaminoglycan CEST (gagCEST) MRI is being applied to the clinical diagnosis and treatment evaluation of tumors, stroke, knee arthritis, IDD, and other diseases, and has aroused widespread interest in the academic community (24). A review published by Jones in 2018, which had the highest normalized total citations in this study, similarly highlighted the role of gagCEST MRI in measuring the biochemical composition of the IVD, suggesting it has a broad prospect in quantifying IDD (25).

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A collection of cocited articles constitutes the knowledge base in a given field. When 2 or more articles are cited by 1 or more articles at the same time, these 2 or more articles constitute a cocitation relationship (26). Pfirrmann's article published in *Spine* in 2001 had the most co-citations and the greatest total link strength. This article pioneered the development of a classification method for IDD based on conventional T2WI, which at the time was the most widely used visual classification system in clinical practice (27). Although the Pfirrmann grades provided a semiquantitative assessment of IDD, which was beneficial for morphological assessment, MRI relaxation time (T1ρ, T2 values) measurements could provide a quantitative assessment of IVD components. This view was confirmed by Bumenkrantz's article published in *Magnetic Resonance in Medicine* in 2010, which also holds high total link strength. These authors demonstrated that MRI relaxation time was negatively correlated with IDD classification, and T1ρ values decreased with the progression of degeneration and correlated with the Pfirrmann grades, as well as with clinical outcomes such as the Oswestry Disability Index (ODI) score and SF-36 health survey scale (28). Johannessen evaluated the PG content in the ECM of human degenerative IVD by using T1ρ MRI and found T1ρ values were strongly linearly correlated with the amount of PG and the water content of the nucleus pulposus (29). In conclusion, these studies suggest that quantitative MRI may become an important method for the assessment of IDD.

Analysis of research hotspots, trends, and current status of quantitative MRI in IDD

Keywords encapsulate the core theme of the article, and represent the concentration and refinement of its content (30). As shown by the keyword co-occurrence and clustering and timeline view analysis, recent studies on quantitative MRI of IDD have focused on quantifying the biochemical components of degenerated discs. The emerging keyword analysis showed that the current research keywords were "proteoglycan content", "diffusion tensor imaging", "tractography", "lumbar intervertebral disc", and "T2", which was consistent with the trend reflected in the keyword timeline view. Based on keyword analysis, we systematically reviewed the key hotspot technologies and the research status of quantitative MRI, as described below:

With abnormal changes in the content of biochemical components of the IVD (such as the decrease of PG, type II collagen, and other matrix macromolecules), the properties of IVD materials can change, resulting in biomechanical imbalance and degenerative changes in the discs (31,32). This strongly suggests changes in the biochemical content of the IVD are the initiating factor of IDD. T2 represents the transverse relaxation time in MRI, and T2WI is the most used MRI examination method for the diagnosis of DDD. T2 relaxation time depends on the integrity of water, PG content, and collagen composition, but patients with early-stage IDD have no obvious imaging manifestations, and it is difficult to make accurate diagnosis using T2WI alone. Compared with normal T2 sequences, quantitative MRI techniques such as DTI, T2 mapping, T1ρ, and gagCEST can accurately and quantitatively evaluate the imaging manifestations and extent of IDD.

T2 mapping is sensitive to the detection of early IDD (33) and facilitates the visualization of the biochemical composition of IVD, translating the water content of nucleus pulposus, PG content, and collagen sequences into T2 values for quantitative assessment of metabolite concentrations in IVD tissues (34). Studies have shown T2 mapping values correlate with the Pfirrmann classification, which can be used as an imaging biomarker for quantitative evaluation of the IVD, allowing for the better assessment of its function (35). Compared with T2 relaxation time measurement, T1ρ has a wider dynamic range to evaluate IDD, which may be sensitive to early degenerative changes, such as those in PG content in the IVD (36,37). In recent years, the number of studies on the application of DTI to IDD have gradually increased (38-40). DTI is a noninvasive examination method for examining the tissue microstructure and can display and observe IVD lesions in a more 3-dimensional manner. Its quantitative parameters are mainly fractional anisotropy (FA) and ADC, which can quantify the diffusion rate and direction of water molecules, reflecting the microstructure and functional information of the IVD (41). It is worth mentioning that the FA value and ADC value of DTI can quantify the microstructural changes of compressed nerve roots in disc herniations. Recent studies have shown that a decrease in the FA value reflects the tissue injury, demyelination, and axonal injury of compressed nerve roots, while an increase of ADC value is associated with inflammatory response and tissue edema (40). The application prospects of gagCEST MRI have been corroborated in the frequently cited literature mentioned above. The gagCEST value, an important parameter in this imaging technique, is closely related to T2 relaxation time and GAG concentration (42). In addition, the contrast of gagCEST MRI decreases with age,

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and the gagCEST value is statistically significant between Pfirrmann grades I and II (43,44). In the future, quantitative MRI methods such as gagCEST MRI may be used for the early quantitative diagnosis of IDD by non-invasively assessing the level of GAG within the IVD.

However, most current quantitative MRI imaging technology studies are still based on the Pfirrmann grades as the reference standard, lacking objective pathological diagnostic criteria. Subsequent relevant studies of quantitative MRI in IDD should be actively improved, and new sequences should be added for comprehensive exploration.

Clinical research analysis of quantitative MRI in IDD

ClinicalTrials.gov, maintained by the National Library of Medicine (NLM) of the National Institutes of Health (NIH), is a database of private and publicly funded clinical studies conducted around the world (30). We searched for clinical studies registered on ClinicalTrials.gov and found only 3 were eligible, indicating a paucity of clinical studies of quantitative MRI techniques applied to IDD. At present, most clinical studies employ molecular imaging technology to quantify the concentration of gag in the IVD, and explore the relationship between different quantitative MRI sequences and the spinal biomechanical environment. In summary, physicians involved in the diagnosis and treatment of DDD should focus more on combining the relatively subjective clinical grade judgments with the objective indicators of quantitative MRI, and design higher quality clinical programs to investigate the clinical application value of different MRI sequences in spinal degenerative diseases.

Strengths and limitations

This study provided the first scientific bibliometric analysis of IDD-related research literature on quantitative MRI techniques in the WOSCC database, offering a new perspective for exploring the development of this research field. In addition, we used a variety of visualization tools to ensure the reliability of the data. However, the study has some limitations. We only analyzed English-language articles in the WOSCC database and were unable to include studies throughout 2022, which might have led to omission of some literature. Furthermore, the results of bibliometric analysis may differ from those of actual research activity, and some recently published high-quality literature may go unnoticed because of the low number of citations. In future research, we will consider including other types of documents, such as conference papers or preprints, that have shorter publication times to gain broader insight.

Conclusions

Using bibliometric analysis, this study demonstrated the knowledge map of countries, authors, journals, cited literature, and keywords in quantitative MRI in IDD-related research systematically and clarified the current status, hotspots, and trends of the research field. With the passage of time, the number of articles in this field has gradually increased. The United States and China were the top 2 countries in terms of the number of publications and citations, but the latter lacks international cooperation and exchange. The author with the most publications was Schleich C, and the author with the most citations was Borthakur A, with having made important contributions to research in this field. *Spine* was the journal with the most published literature on this topic, while the journal with the most mean times cited per study was *Radiology*. Both are authoritative journals in this field. Keyword co-occurrence, clustering, timeline view, and emergent analysis revealed recent studies in this field have mainly focused on quantifying the biochemical components of degenerated IVD. Few clinical studies were available. Recent clinical studies have mainly used molecular imaging technology to explore the relationship between different quantitative MRI sequence values and the IVD biomechanical environment and biochemical components content. In the future, it will be necessary to further strengthen research quality control and design by incorporating large-sample, multi-center clinical protocols to verify the application value of quantitative MRI for DDD.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE

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uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1219/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors were responsible for all aspects of the work to ensure that issues related to the accuracy or integrity of any part of the work were properly investigated and resolved. All data were retrieved through a public database. There were no medical institutions or patients involved, so ethical approval or informed consent did not apply.

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Supplementary

Table S1 Top 10 cocited articles of quantitative MRI for IDD in the WOSCC database

Rank	Author	Title	Journal	Year	Citations	Total link strength
1	Pfirrmann CWA	Magnetic resonance classification of lumbar intervertebral disc degeneration	*Spine*	2001	250	1712
2	Johannessen W	Assessment of human disc degeneration and proteoglycan content using T1rho-weighted magnetic resonance imaging	*Spine*	2006	68	751
3	Adams MA	What is intervertebral disc degeneration, and what causes it?	*Spine*	2006	63	547
4	Watanabe A	Classification of intervertebral disk degeneration with axial T2 mapping	*American Journal of Roentgenology*	2007	62	579
5	Bumenkrantz G	*In vivo* 3.0-tesla magnetic resonance T1rho and T2 relaxation mapping in subjects with intervertebral disc degeneration and clinical symptoms	*Magnetic Resonance in Medicine*	2010	60	663
6	Marinelli NL	T2 relaxation times of intervertebral disc tissue correlated with water content and proteoglycan content	*Spine*	2009	60	567
7	Antoniou J	The human lumbar intervertebral disc: evidence for changes in the biosynthesis and denaturation of the extracellular matrix with growth, maturation, ageing, and degeneration	*The Journal of Clinical Investigation*	1996	57	467
8	Perry J	The value of T2 relaxation times to characterize lumbar intervertebral disks: preliminary results	*American Journal of Neuroradiology*	2006	57	590
9	Antoniou J	Apparent diffusion coefficient of intervertebral discs related to matrix composition and integrity	*Magnetic Resonance Imaging*	2004	56	563
10	Kerttula L	Supraspinatus outlet view in the diagnosis of stages II and III impingement syndrome	*Acta Radiologica*	2001	53	560

WOSCC, Web of Science core collection; MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

Table S2 The keyword clustering of quantitative MRI in IDD

Cluster ID	Size	Sihouette	Year	Top terms
#0	46	0.832	2010	animal model; dgemric; rabbit; degeneration; annulus fibrosus
#1	39	0.821	2010	disability; cross sectional area; pathology; diffusion tensor MRI; magnetic resonance imaging
#2	36	0.867	2014	diffusion tensor imaging; fractional anisotropy; mean diffusivity; spinal cord;
#3	36	0.95	2006	classification; ankylosing spondylitis; manual therapy; nucleus pulposus; lumbar spinal stenosis
#4	34	0.892	2013	cerebrospinal fluid; disc herniation; cervical radiculopathy; cervical myelopathy; agreement
#5	30	0.832	2014	conservative treatment; surgery; 3.0 t; sciatica; epidural abscess
#6	29	0.893	2014	intervertebral disc degeneration; quantitative MRI; fatty infiltration; dual-tuned proton/sodium mr imaging; lumbar intervertebral disk degeneration
#7	28	0.891	2011	magnetic resonance imaging; t2 mapping; contrast media; gadolinium; vertebral body
#8	27	0.828	2011	chemical exchange saturation transfer; age related change; glycosaminoglycan; disc height index; field inhomogeneity correction
#9	26	0.888	2015	nucleus pulposus cell; intervertebral disc degeneration; subcutaneous fat; corticosteroid; adipose tissue

MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

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Table S3 Clinical studies in ClinicalTrials.gov

ClinicalTrials.gov identifier	Status	Title	Country	Study type	No. of patients	Conditions	Primary outcome measurement
NCT02815696	Recruiting	MRI analysis of glycosaminoglycan (GAG) modifications inside the intervertebral disk after distraction and posterior fusion	Belgium	Interventional	5	Lumbar spine instability	Gycosaminoglycan (GAG) concentration of the intervertebral disk
NCT04647279	Recruiting	New MRI sequences in spine and joint	China	Observational	300	Degeneration of spine and osteoarticular	New MRI sequences in the diagnosis of spine and joint
NCT01973257	Completed	Perfusion and diffusion mechanism of intervertebral disc-significance with age, degeneration, posture and stress loading	China	Interventional	50	Spinal cord injury, degenerative spinal disease.	Disc Perfusion

MRI, magnetic resonance imaging; IDD, intervertebral disc degeneration.

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