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Artificial Intelligence in Multiple Sclerosis Detection: Current Landscape and Future Trends

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***Abstract*—This study conducts a bibliometric analysis of Artificial Intelligence (AI) in Multiple Sclerosis (MS) detection, examining 1502 peer-reviewed publications from 1994 to 2024 using ScientoPy, VOSviewer and Biblioshiny to understand its rapid evolution, current landscape, and emerging trends. A significant surge in research activity has been observed since 2017, driven by breakthroughs in machine learning and neuroimaging. The United States, Germany, China, and Italy are the most active countries by author appearances, while the most productive individual institutions are located in Europe, particularly Italy, Spain, and the United Kingdom. Key research clusters focus on gait analysis, lesion segmentation, biomarker discovery, and advanced neuroimaging. The analysis highlights the growing application of convolutional neural networks (CNNs), support vector machines (SVMs), and generative models to enhance diagnostic precision, monitor disease progression, and predict symptom trajectories in MS. AI models have demonstrated diagnostic accuracies exceeding 95% in some cases, providing personalized prognostic insights and real-time clinical decision support, thereby serving as a valuable complement to conventional neuroimaging and clinical assessments. The study also indicates a paradigm shift towards multimodal data integration, regulatory-compliant model design, and clinically explainable AI systems, with an increasing emphasis on transparency, reproducibility, and standardized validation frameworks such as AutoML and federated learning. Furthermore, the integration of biomarkers like cerebrospinal fluid analysis and brain atrophy metrics into predictive models reflects a holistic approach to MS care.**

***Index Terms*—Artificial Intelligence, Bibliometrics, Citation analysis, Multiple Sclerosis**

I. INTRODUCTION

Multiple Sclerosis (MS) is a complex, chronic autoimmune disorder characterized by demyelination and neurodegeneration within the central nervous system (CNS). This progressive condition leads to significant changes in brain morphology and structure, primarily due to damage to the myelin sheath, and is a leading cause of disability among young adults [1]. Fig. 1 illustrates the topography of MS lesions found in affected patients. The disease presents diverse clinical manifestations, with relapsing-remitting MS (RRMS) being the most prevalent form, often transitioning to secondary progressive MS (SPMS) over time [2]. The heterogeneous nature of MS pathology and clinical presentation necessitates precise diagnostic and monitoring tools [3].

Magnetic Resonance Imaging (MRI) has been a cornerstone in the diagnosis and management of MS since the 1980s. It provides invaluable insights by visualizing demyelinating lesions, axonal loss, and inflammatory changes through various sequences such as T1- and T2-weighted imaging [4]. MRI is not only critical for initial diagnosis but also for assessing disease stage, predicting patient outcomes, and meticulously monitoring disease progression and the efficacy of therapeutic interventions [2]. The ability of MRI to capture the temporal evolution of lesions, whether they enhance, expand, remain stable, or decrease in size, is fundamental to MS care [4].

Despite the indispensable role of MRI, conventional manual interpretation of scans by neuroradiologists presents significant challenges. This process is inherently time-consuming, laborious, and susceptible to considerable variability between and within observers [1]. Such inconsistencies in lesion detection and measurement can lead to subtle yet critical disease changes being overlooked, potentially impacting timely treatment decisions and patient management. Furthermore, the increasing availability and sophistication of advanced imaging methods place a growing demand for clinical resources, expertise, and time, highlighting a pressing need for more efficient analytical approaches [5]. Recent advancements in Artificial Intelligence (AI) have further enhanced the utility of these imaging techniques, offering improved diagnostic accuracy, personalized treatment strategies, and predictive capabilities.

While several reviews have explored the broader application of artificial intelligence in medical imaging [7], [8], there remains a notable gap in comprehensive analyses focused specifically on its use in the detection of Multiple Sclerosis (MS). This study addresses that gap by presenting a detailed bibliometric analysis of AI-driven approaches in MS detection over the past two decades. The analysis identifies key research

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themes, influential contributors, technological trends, and the extent of clinical translation.

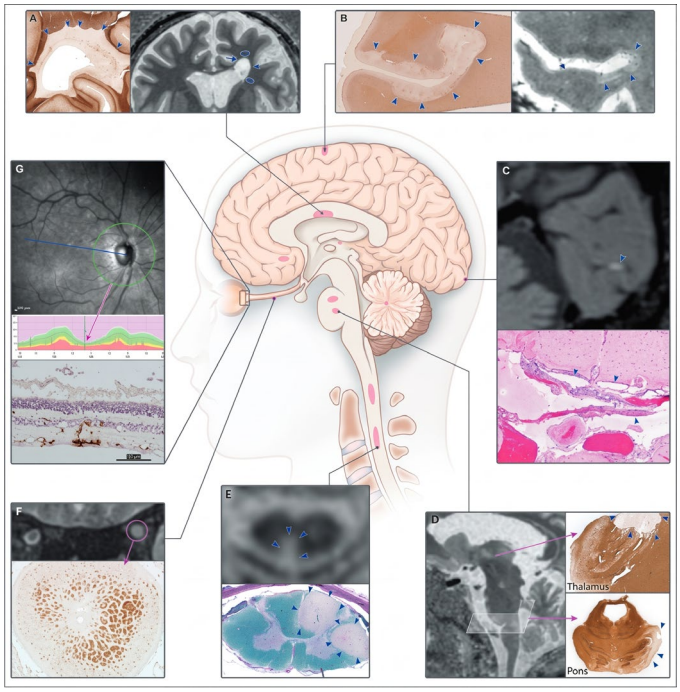


Fig. 1. Topography of Multiple Sclerosis (MS) Lesions [6].

By mapping this intellectual landscape, the study provides actionable insights that can guide future research priorities, address existing limitations, and accelerate the integration of AI into real-world MS diagnostic workflows. Specifically, this study aims to answer the following research questions:

RQ1: What has been the publication volume and growth trend in research on AI-based MS detection over time?

RQ2: Which countries, institutions, and subject areas have produced the most scientific publications on AI-based MS detection?

RQ3: What are the top journals, papers, and other publication sources that are contributing research on AI-based MS detection, and what is the most cited paper on this topic?

RQ4: Based on keyword occurrence analysis, what are the major research themes and topics being investigated in relation to AI-based MS detection?

II. Literature Review

The early diagnosis of MS is challenging due to its heterogeneous clinical presentation and the similarity of its symptoms to other neurological disorders. Traditional diagnostic methods rely heavily on clinical evaluation, MRI, and cerebrospinal fluid analysis. MRI is particularly valuable as it provides detailed images of the brain and spinal cord, allowing for the visualization of MS lesions. However, the interpretation of MRI scans can be subjective and time-consuming, leading to potential misdiagnosis or delayed diagnosis.

AI-based methods, particularly machine learning (ML) and deep learning (DL), have emerged as powerful tools for improving the accuracy and efficiency of MS diagnosis. These techniques can analyse complex patterns in MRI data, identify subtle abnormalities, and differentiate MS from other conditions. For instance, convolutional neural networks (CNNs) have been successfully applied to MRI scans to detect MS lesions with high sensitivity and specificity [9], [10]. Additionally, AI models can integrate multimodal data, such as clinical, genetic, and imaging information, to enhance diagnostic precision [11], [12].

Recent studies have demonstrated the potential of AI in achieving remarkable accuracy in MS diagnosis. For example, a study employing a combination of feature extraction techniques and classifiers such as Random Forest and Support Vector Machines (SVM) achieved an accuracy of 97.97% in distinguishing MS patients from healthy controls [10]. Another study utilizing ResNet features and SVM classifiers reported an accuracy of 88.10% and an F1 score of 90.53% [13]. These results highlight the potential of AI-based methods to revolutionize MS diagnosis by reducing diagnostic delays and improving accuracy.

A. Monitoring Disease Progression

Monitoring MS progression is essential for assessing disease activity, evaluating treatment response, and predicting future disability. Traditional methods for monitoring MS progression include regular MRI scans, clinical assessments, and the Expanded Disability Status Scale (EDSS). While these methods provide valuable insights, they have limitations. For example, MRI lesions often show only moderate correlation with clinical outcomes, a phenomenon known as the clinico-radiological paradox [14].

AI-based approaches have shown promise in overcoming these limitations by analysing complex MRI data to identify subtle changes that may not be apparent through visual inspection. Machine learning models, such as XGBoost and Random Forest, have been used to predict disease progression and disability outcomes, such as EDSS scores, with high accuracy [14], [15]. These models can identify influential MRI features, such as lesion load, brain atrophy, and tissue microstructural changes, which are strongly associated with disease progression [12], [15].

Moreover, AI techniques have been applied to predict specific aspects of MS progression, such as the conversion of clinically isolated syndrome (CIS) to MS, cognitive outcomes, and motor disability [14]. For instance, a study employing explainable AI models, such as SHAP analysis, demonstrated the ability to predict MS trajectories using baseline MRI parameters, outperforming traditional multiple linear regression methods [15]. These advancements underscore the potential of AI in providing personalized prognostic information, enabling tailored treatment strategies.

B. Predicting Symptoms and Disease Trajectories

Predicting MS symptoms and disease trajectories is crucial for improving patient outcomes and optimizing treatment plans. Traditional methods for predicting MS progression rely on clinical assessments and MRI findings, but these methods often

lack the precision needed for individualized care. AI-based approaches, particularly those integrating MRI and clinical data, have shown significant promise in this regard.

Deep learning models, such as CNNs and U-Net, have been successfully applied to MRI scans to predict disease progression and symptom development [16], [17]. These models can identify subtle changes in brain structure and tissue composition that are associated with specific clinical outcomes. For example, a study employing CNNs to analyse MRI scans demonstrated the ability to predict cognitive outcomes and disability progression with high accuracy [14].

Furthermore, AI models have been used to simulate disease progression and predict future MRI patterns. For instance, a study employing StyleGAN models to simulate MS progression on MRI scans demonstrated the ability to predict brain volume loss and lesion extent, providing valuable insights into disease trajectories [18]. These predictive capabilities have the potential to enable early intervention and personalized treatment strategies, improving patient outcomes.

C. AI-Based vs Traditional Diagnostic Approaches

The integration of AI-based methods into MS diagnosis and monitoring has introduced several advantages over traditional approaches. AI models can analyse large datasets, identify complex patterns, and provide objective interpretations, reducing the subjectivity associated with traditional methods. Additionally, AI-based approaches can integrate multimodal data, such as imaging, clinical, and genetic information, to provide a more comprehensive understanding of the disease [11], [12].

However, traditional methods still play a critical role in MS diagnosis and monitoring. Clinical assessments and MRI scans remain the gold standard for diagnosing MS, and AI-based methods should be viewed as complementary tools rather than replacements for traditional approaches. The combination of AI and traditional methods has the potential to enhance diagnostic accuracy, improve monitoring, and enable personalized treatment strategies.

III. METHODOLOGY

The study's objective is to meticulously chart the research landscape surrounding the application of Artificial Intelligence in Multiple Sclerosis detection. The title is deliberately formulated to reflect the dual focus on the historical evolution of the field and its forward-looking potential, aiming to uncover the key technological and conceptual shifts that are shaping its trajectory.

This investigation employs a bibliometric analysis, a robust quantitative method for evaluating the scholarly output of a specific research domain. By statistically analysing bibliographic data, this method reveals publication trends, influential contributors, and intellectual structures. Both SCOPUS and Web of Science (WOS) databases were chosen for this analysis due to its extensive coverage of peer-reviewed literature in medicine, computer science, and engineering, ensuring a reliable foundation for mapping the research landscape. Using RStudio, both databases are merged, and duplicates are removed for analysis.

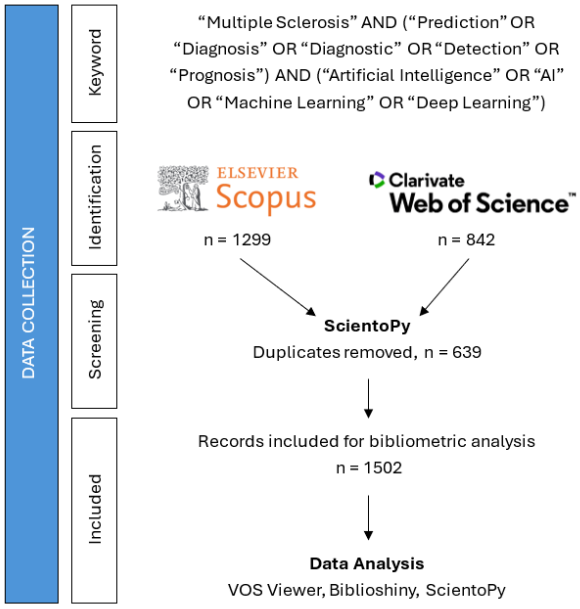


Fig. 2. Flow diagram of data extraction and analysis.

Fig. 2 illustrates the flow of data collection. The data collection process involved a systematic keyword search strategy targeting articles published between 1994 and 2024 from two major scholarly databases, SCOPUS and Web of Science (WOS). The search query was constructed using Boolean operators: ("Multiple Sclerosis") AND ("Diagnosis" OR "Prediction") AND ("Deep Learning" OR "Machine-learning"). This strategy was designed to retrieve literature on both general machine learning and the more specific Artificial Intelligence approaches. After omitting 231 based on their document types, 2141 papers remained. Of these papers, 39.3% of the papers are from WOS while the other 60.7% are from SCOPUS. The initial results were rigorously screened for duplicates, resulting in a removal of additional 639 duplicate papers. A refined dataset of 1502 peer-reviewed publications are obtained comprising of 837 papers (55.7%) from WOS and 665 papers (44.3%) from SCOPUS.

The refined dataset was analysed using ScientoPy, VOSviewer, and Biblioshiny to conduct a multi-faceted bibliometric assessment. Performance analysis was used to track publication trends and identify the most influential documents and journals, establishing the field's growth and foundational works. To map the intellectual and social structures, we conducted a bibliographic coupling analysis of countries and institutions to visualize collaborative networks, alongside bibliographic coupling to reveal core research fronts. However, due to limitations on using multiple databases for VOSviewer, the analysis is done separately for SCOPUS and WOS databases.

Finally, a temporal co-occurrence analysis of keywords was performed to distinguish between established concepts and emerging research hotspots, thereby charting the field's thematic evolution and future trajectories.

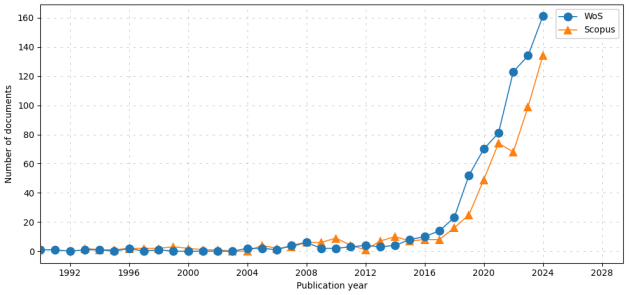


Fig. 3. Trends of publications from each database from the year 1994 to 2024.

IV. Results and Discussion

A. What has been the publication volume and growth trend in research on AI-based MS detection over time?

Fig. 3 illustrates the publication and citation trends in the field of Artificial Intelligence (AI) for Multiple Sclerosis (MS) detection from 1994 to 2024. For much of the period between 1994 and 2016, research output in this area remained relatively low, with the annual number of publications rarely exceeding two, and total citations remaining negligible. A slight increase in publications was observed around 2009 and 2012, but these instances were minor fluctuations.

A significant surge in research activity began in 2017, with annual publications consistently increasing, reaching over 10 publications in 2018 and continuing to rise sharply. The most remarkable growth occurred from 2019 onwards, where the number of publications jumped from around 10-15 to over 30 in 2020, and then dramatically to over 50 in 2021 and 2022. The peak in publications appears to be in 2023, with over 60 articles.

Correspondingly, total citations began to show a notable increase around 2017, mirroring the rise in publications. However, the most substantial growth in citations occurred from 2021 to 2023. In 2021, total citations surpassed 1000, escalating rapidly to over 2000 in 2022, and reaching their peak in 2023, approaching 3000 citations. This strong correlation between the increase in publications and citations from 2017 onwards indicates a burgeoning interest and impact of AI applications in Multiple Sclerosis detection within the scientific community.

B. Which countries, institutions, and subject areas have produced the most scientific publications on AI-based MS detection?

Fig. 4 shows a chart that details the top ten most active affiliations, offering critical insights into the institutional landscape driving research in MS detection using AI. The distribution of publications underscores key centres of excellence and highlights the collaborative dynamics within this rapidly evolving field.

Sapienza University of Rome emerges as the leading contributor, with 43 articles, demonstrating a significant output in AI-driven MS detection research. This positions the institution as a pivotal hub of innovation and expertise. Closely following are Hospital Universitari Vall d'Hebron with 40 articles and University College London with 38 articles. The comparable productivity of these top three institutions indicates a concentrated and highly active research front, suggesting robust research programs and substantial investment in this specialized area. Such prominent contributions from these institutions are likely fostering significant advancements in diagnostic methodologies for MS.

Further analysis reveals a blend of academic institutions and hospital-based research centres among the most prolific affiliations. University of Girona (30 articles), Miguel Servet University Hospital (27 articles), and Vita-Salute San Raffaele University (26 articles) also show substantial engagement. The inclusion of both university-based research groups and hospital-affiliated units, such as Hospital Universitari Vall d'Hebron and Miguel Servet University Hospital, highlights the interdisciplinary nature of this research field. It suggests a strong nexus between theoretical AI development and its practical clinical application in patient care and diagnostics. This integration is crucial for translating AI advancements into tangible improvements in MS detection.

Geographically, the top affiliations demonstrate a broad international presence, including institutions from Europe (e.g., Italy, Spain, UK, Germany), North America (University of British Columbia), and the Middle East (Imam Abdulrahman Bin Faisal University). This global distribution indicates that research in AI for MS detection is a worldwide endeavour, benefiting from diverse perspectives and collaborative networks across continents.

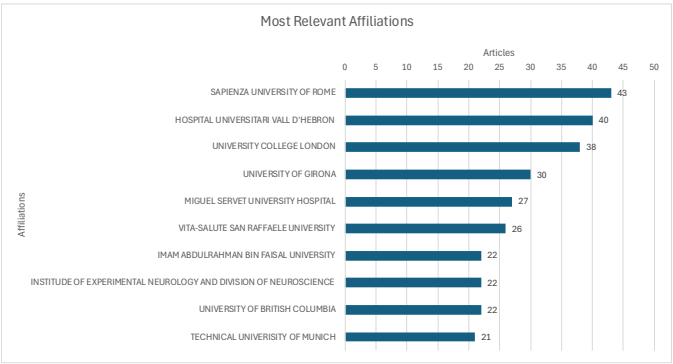


Fig. 4. Top 10 Most Relevant Affiliations by publications.

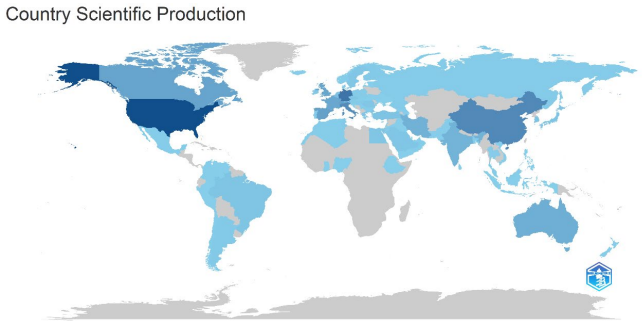


Fig. 5. Distribution of scientific production by country.

TABLE I
MOST ACTIVE COUNTRIES BY AUTHOR APPEARANCES

Rank	Country	Author appearances	Share of top 10 (%)
1	United States	1061	22.6
2	Germany	717	15.3
3	China	547	11.6
4	Italy	520	11.1
5	Spain	344	7.3
6	Switzerland	336	7.2
7	Canada	326	6.9
8	United Kingdom	310	6.6
9	France	296	6.3
10	Australia	242	5.2

Analysis of country-level research output shows the United States of America as the top contributor, with 1061 author appearances, or 22.6% of the appearances recorded for the ten most productive countries, indicating its emergence as a major contributor to Artificial Intelligence for use in the medical field. These counts follow the country scientific production measure of Biblioshiny, which records the affiliation country of every author on every paper. A paper with several authors is therefore counted once for each of them, so the totals in Table I exceed the 1502 papers analysed and measure research participation rather than the number of papers. Table I also reveals that Germany follows with 717 appearances, which can be attributed to its focus on developing cutting-edge technological capabilities. China ranks third with 547 appearances, reflecting its status as a leader in digital health innovations. Other productive countries include Italy with 520 appearances and Spain with 344, followed closely by Switzerland and Canada with 336 and 326, respectively. Overall, the European region dominates the list, with Germany, the United Kingdom, Spain, and Italy together accounting for about 40% of the top-ten total. This suggests that research activity in using Artificial Intelligence for Multiple Sclerosis detection is more concentrated in regions where higher standards of socio-economic and healthcare are present. However, the United States leads among single countries, as shown in Table I and in the country map in Fig. 5. In contrast, Fig. 4 shows that the most active individual institutions are situated in Europe, and none of the ten most active institutions is in the United States.

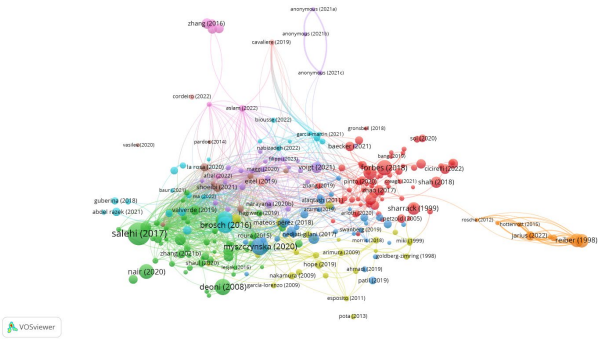


Fig. 6. Network map of Bibliographic Coupling for AI-based MS Diagnosis from SCOPUS Database.

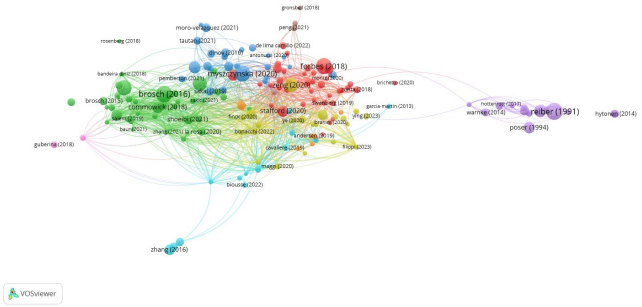


Fig. 7. Network map of Bibliographic Coupling for AI-based MS Diagnosis from WOS Database.

C. What are the top journals, papers, and other publication sources that are contributing research on AI-based MS detection, and what is the most cited paper on this topic?

Fig. 6 illustrates the network map of documents relating to MS diagnosis using AI from SCOPUS database. To avoid redundant clusters to form a minimum threshold of citation needs to be chosen. Consequently, too high a threshold may lead to important documents to be remove from the network map. Therefore, a threshold of at least 25 citations is chosen. By applying bibliographic coupling analysis using VOSviewer on the exported SCOPUS database, seven (7) distinct clusters are revealed, each representing a cohesive thematic direction within the literature.

1) Cluster 1 (red): Machine Learning for Gait Analysis and Disease Prediction in Multiple Sclerosis

This cluster represents a prominent research direction, showcasing the burgeoning application of machine learning and deep learning methodologies to assess gait dynamics and other clinical parameters in the context of Multiple Sclerosis. The research aims to leverage objective measures obtained from instrumented walkways and smartphone data to develop robust and interpretable models for early diagnosis and disease progression prediction. Key contributions include studies on predicting MS from gait dynamics, identifying MS subtypes using unsupervised machine learning and MRI, and developing explainable models for pre-emptive diagnosis. Representative works in this area include Barnett [19] on AI-based MRI monitoring, Kaur [20], [21] on predicting MS from gait dynamics, and Eshaghi [22] on identifying MS subtypes.

2) Cluster 2 (green): Deep Learning for MRI-based Lesion Segmentation and Imaging in Multiple Sclerosis

A core theme within the field, this cluster highlights the critical role of deep learning and convolutional neural networks (CNNs) in automating the segmentation and comprehensive analysis of lesions and various brain structures from MRI scans of MS patients. Research efforts in this domain are primarily directed towards enhancing the accuracy, efficiency, and generalizability of these advanced imaging techniques, which are crucial for precise diagnosis and monitoring of MS. Notable contributions involve the simultaneous segmentation of lesions and brain structures, as seen in McKinley [23], and the application of deep learning for automated segmentation of gadolinium-enhancing lesions, as investigated by Gaj [24].

3) Cluster 3 (blue): Advanced MRI Techniques and Deep Learning for MS Diagnosis and Progression

This cluster delves into the sophisticated integration of advanced MRI techniques, including ultra-high-field MRI, with deep learning algorithms. The primary objective is to improve the detection, characterization, and prognostication of disease progression in MS, with a particular emphasis on the subtle and often elusive cortical and white matter lesions. Works such as Storelli [25] explore deep learning for predicting disease progression, while La Rosa et al. [26], [27] focus on cortical lesion detection and the significance of central vein sign and paramagnetic rim lesions.

4) Cluster 4 (yellow): Predictive Modelling and Lesion Quantification in Multiple Sclerosis using Machine Learning

Focused on quantitative analysis and predictive analytics, this cluster centres on the application of machine learning and CNNs for accurate lesion volume quantification, early diagnosis, and the anticipation of lesion evolution in MS. This research frequently involves the synergistic integration of diverse imaging modalities, such as MRI and Optical Coherence Tomography (OCT), to achieve more insights. De Oliveira [28] illustrates lesion volume quantification using CNNs, and López-Dorado [29] investigates early MS diagnosis using swept-source OCT and CNNs.

5) Cluster 5 (purple): AI and Machine Learning for Comprehensive MS Diagnosis and Biomarker Discovery

This cluster represents a broader, more holistic approach to leveraging Artificial Intelligence (AI) and machine learning in Multiple Sclerosis research. It encompasses the multifaceted challenges and opportunities associated with diagnostic processes, the strategic utility of optical coherence tomography (OCT), and the sophisticated analysis of biomarkers using cutting-edge techniques such as Surface Plasmon Resonance Imaging (SPRI). Aslam [30] provides an overview of diagnostic challenges and opportunities, while Malinick [31] explores biomarker analysis with SPRI and machine learning.

6) Cluster 6 (turquoise): Deep Learning for Neural Tissue Segmentation and Data Augmentation in MS Imaging

A highly specialized cluster, this area of research specifically investigates the deployment of deep learning for precise neural tissue segmentation in MRI scans of MS patients. Furthermore, it explores innovative methods for data augmentation, notably employing generative adversarial neural networks (GANs), to enhance the analysis of brain structural connectivity in MS, addressing the common challenge of limited datasets. Barile [32] demonstrates data augmentation with GANs for brain structural connectivity, and Narayana [33] examines the effect of training set size on deep-learning-based neural tissue segmentation.

7) Cluster 7 (orange): Convolutional Neural Networks for MRI-based MS Identification

This compact yet significant cluster is dedicated to the development and application of convolutional neural networks (CNNs) specifically for the identification of Multiple Sclerosis using brain FLAIR MRI scans. The research in this cluster is foundational for creating automated and highly accurate diagnostic tools, with Yılmaz Acar [34] presenting a pivotal CNN model for this purpose.

Overall, the bibliographic coupling analysis reveals a dynamic research landscape in Multiple Sclerosis, heavily influenced by the rapid advancements in artificial intelligence and machine learning. These clusters collectively underscore a concerted effort to enhance early diagnosis, predict disease progression, and quantify pathological changes, primarily through the innovative application of imaging and computational techniques.

Fig. 7 illustrates the network map of documents relating to MS diagnosis using AI from WOS database. By using the same threshold from the previous database, the bibliographic coupling analysis yielded ten distinct clusters, each representing a thematic research stream in the application of artificial intelligence (AI) to Multiple Sclerosis (MS) diagnosis, prognosis, and treatment monitoring. These clusters offer a panoramic view of how the integration of AI in MS research has evolved across technical, clinical, and translational dimensions.

Cluster 1 predominantly centres around predictive modelling and disability progression forecasting in MS. Representative studies, such as De Brouwer et al. [35] and Montolio et al. [36], utilized machine learning models trained on longitudinal and multimodal datasets, including MRI, optical coherence tomography (OCT), and clinical scales, to enhance early prediction of disease trajectory. These efforts reflect the growing interest in digital phenotyping and personalized disease management, where AI is harnessed to tailor prognoses and inform timely interventions.

Cluster 2 comprises works that focus on deep learning applications for automated MS lesion detection using MRI. Notable studies like Shoeibi et al. [37] and Afzal et al. [38] provide comprehensive reviews and technical implementations of convolutional neural networks (CNNs) for segmentation tasks. This cluster highlights the rapid progress in AI-based neuroimaging, with a strong emphasis on enhancing lesion detection sensitivity and reducing inter-observer variability in radiological assessments. The inclusion of image synthesis and data augmentation techniques further reinforces this cluster's commitment to overcoming data scarcity in MS research.

Cluster 3 reveals a broader scope where AI is applied to neurodegenerative diseases beyond MS, such as Alzheimer's and ALS. Pioneering reviews by Myszczynska et al. [39] and Raghavendra et al. [40] demonstrate how cross-disease modeling, structural neuroimaging, and transfer learning have informed innovations in MS-focused AI frameworks. This thematic area bridges interdisciplinary approaches and positions MS research within the wider AI-in-neurology paradigm.

Cluster 4 explores the use of deep learning for enhanced disease classification, particularly through novel imaging modalities and radiomics. Works by Bonacchi et al. [41] and Storelli et al. [25] illustrate how conventional and synthetic MR imaging can be integrated with advanced neural architectures to improve disease differentiation, including identifying MS mimics and subtypes. These studies emphasize technical rigor and translational readiness, reflecting a convergence between

clinical neurology and applied AI.

Cluster 5 is defined by a biological and immunological lens, focusing on the use of genetic, proteomic, and fluid biomarkers for MS characterization. Representative documents include Warnke et al. [42] and Jokubaitis et al. [43], which explored cerebrospinal fluid (CSF) indices and genetic predictors of MS severity. The incorporation of machine learning in these studies underscores the shift toward integrating omics data with imaging and clinical profiles for holistic MS assessment.

Cluster 6 stands out for its emphasis on hybrid AI approaches using diverse imaging techniques such as OCT and susceptibility-weighted imaging (SWI). Aslam et al. [30] and Nabizadeh et al. [8] present systematic reviews of DL and ML applications that address diagnostic challenges across imaging modalities. The adoption of unsupervised and semi-supervised learning in this space reflects a pragmatic response to limited annotated datasets and the heterogeneity of MS presentations.

Cluster 7 further delves into molecular-level investigations, where AI is applied to identify biochemical markers such as cytokines and metabolites linked to disease onset and progression. Studies like Fagone et al. [44] and Gautam et al. [45] contribute to the development of integrative biomarkers that could inform individualized treatment protocols and early diagnosis.

Cluster 8 presents a personalized medicine perspective, focusing on individualized treatment predictions and stratified care. Peng et al. [46] and Rocca et al. [47] illustrate how AI frameworks can stratify patients based on their likelihood to respond to specific therapies or develop aggressive disease courses. This reflects a pivotal shift from reactive to proactive MS care enabled by precision algorithms.

Cluster 9 represents a frontier in radiological innovation, featuring research such as Kaka et al. [48] that advocates for AI's integration into neuroradiological workflows. These contributions explore real-world challenges in deploying AI in clinical radiology and emphasize usability, interpretability, and clinical validation.

Finally, *Cluster 10* encompasses outlier studies and emerging topics, including data preprocessing methodologies, federated learning, and digital twin modeling. While less cohesive, this cluster signals the emergence of new methodological frontiers and research that has yet to gain dense bibliographic connections but holds future potential for disruption.

Table II summarizes the 10 most important documents published related to MS detection using AI. The list is sorted based on the Total Link Strength (TLS) to measure the document's significant contribution to AI-based MS detection from both databases.

TABLE II
TOP 10 SIGNIFICANT DOCUMENTS BY LINK STRENGTH

No.	Document	Author	Citations	TLS	Ref
1	Uncovering convolutional neural network decisions for diagnosing multiple sclerosis on conventional MRI using layer-wise relevance propagation	Eitel et al. (2019)	117	157	[49]
2	Automatic segmentation of the spinal cord and intramedullary multiple sclerosis lesions with convolutional neural networks	Gros et al. (2019)	200	154	[50]
3	ALL-Net: Anatomical information lesion-wise loss function integrated into neural network for multiple sclerosis lesion segmentation	Zhang et al. (2021)	31	153	[51]
4	Automated volumetric assessment with artificial neural networks might enable a more accurate assessment of disease burden in patients with multiple sclerosis	Brugnara et al. (2020)	22	147	[52]
5	Review of Deep Learning Approaches for the Segmentation of Multiple Sclerosis Lesions on Brain MRI	Zeng et al. (2020)	77	135	[1]
6	Multi-branch convolutional neural network for multiple sclerosis lesion segmentation	Aslani et al. (2019)	131	133	[53]
7	Cortical lesions, central vein sign, and paramagnetic rim lesions in multiple sclerosis: Emerging machine learning techniques and future avenues	La Rosa et al. (2022)	31	122	[27]
8	Multiple sclerosis cortical and WM lesion segmentation at 3T MRI: a deep learning method based on FLAIR and MP2RAGE	La Rosa et al. (2020)	92	122	[54]
9	Fully automated longitudinal segmentation of new or enlarged multiple sclerosis lesions using 3D convolutional neural networks	Krüger et al. (2020)	53	121	[55]
10	Improving automated multiple sclerosis lesion segmentation with a cascaded 3D convolutional neural network approach	Valverde et al. (2017)	303	118	[56]

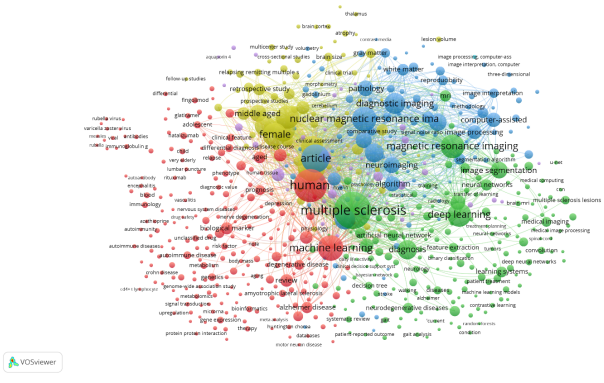


Fig. 8. Network Map of co-occurrence analysis for AI-Based MS Detection from SCOPUS and WOS databases.

D. Based on keyword occurrence analysis, what are the major research themes and topics being investigated in relation to AI-based MS detection?

Fig. 8 shows the network map of co-occurrences between documents related to AI-based MS detection from SCOPUS and WOS. By using a threshold minimum of 10 keyword occurrences, the co-occurrence analysis using VOSviewer revealed five distinct thematic clusters, each representing a critical trajectory in the evolving landscape of artificial intelligence (AI) applications in Multiple Sclerosis (MS) diagnosis and monitoring. These clusters not only consolidate current knowledge but also signal emerging future directions that are likely to define the next phase of translational and computational MS research.

The first cluster revolves around advanced neuroimaging and radiomic innovation. Keywords such as *magnetic resonance imaging*, *lesion volume*, *optical coherence tomography*, and *segmentation* underscore a future shift towards multimodal, high-resolution, and contrast-agent-free imaging techniques. The growing emphasis on automated lesion detection and quantification through AI-based radiomics suggests a move toward clinically explainable imaging pipelines. Future studies are expected to leverage synthetic imaging, cross-modality learning (e.g., OCT + MRI fusion), and saliency mapping to enhance diagnostic precision, particularly in early and subclinical MS stages.

The second cluster highlights the intersection of clinical-demographic modelling and disease phenotyping. Co-occurring terms like *disease progression*, *cognition*, *fatigue*, *EDSS*, and *relapsing-remitting MS* point toward an increasing focus on personalized prediction models. These models aim to capture heterogeneous clinical presentations and disease trajectories. Future research will likely explore longitudinal deep learning architectures capable of forecasting relapses, cognitive decline, and functional disability based on baseline phenotypic, demographic, and neuroimaging data. Stratified models that account for age, sex, and disease subtype are also poised to become instrumental in precision medicine for MS.

The third cluster, comprising terms such as *machine learning*, *deep learning*, *support vector machine*, *convolutional neural network*, and *classification*, reflects the methodological core of AI-based MS diagnostics. The prevalence of supervised learning approaches and feature engineering highlights the technical maturity of this domain. However, the future lies in developing interpretable, lightweight, and regulatory-compliant ML frameworks. AutoML, neural architecture search (NAS), and federated learning will drive the next wave of research, enabling scalable, privacy-preserving diagnostic tools. Moreover, the integration of explainability modules is expected to bridge the gap between algorithmic predictions and clinical trust.

The fourth cluster emphasizes biomarker integration and pathophysiological modelling. Keywords such as *cerebrospinal fluid*, *functional connectivity*, *brain atrophy*, and *biological markers* suggest a promising trend toward multimodal biomarkers that transcend imaging alone. The convergence of molecular, structural, and functional data opens pathways for developing robust predictive models of disease onset, progression, and treatment response. Future research will likely incorporate *omics* data (e.g., genomics, proteomics) alongside neuroimaging to build multidimensional diagnostic signatures, facilitating early intervention strategies and individualized therapeutic planning.

Finally, the fifth cluster points to a rising meta-scientific and methodological rigor in MS-AI research. The presence of terms like *systematic review*, *reproducibility*, *comparative study*, and *priority journal* reflects a scholarly movement toward standardization and evidence synthesis. As AI models grow in complexity, the need for reproducible, transparent, and standardized workflows becomes paramount. Future studies will benefit from adopting frameworks such as TRIPOD-ML, CONSORT-AI, and open benchmark datasets to ensure comparability and generalizability of findings across institutions and populations.

In summary, the co-occurrence landscape reveals a field transitioning from isolated algorithm development toward holistic, explainable, and clinically integrated solutions. By aligning future work with these emerging themes, researchers can contribute to more trustworthy, generalizable, and impactful AI-driven tools for Multiple Sclerosis care.

V. Emerging Trends And Future Research Directions

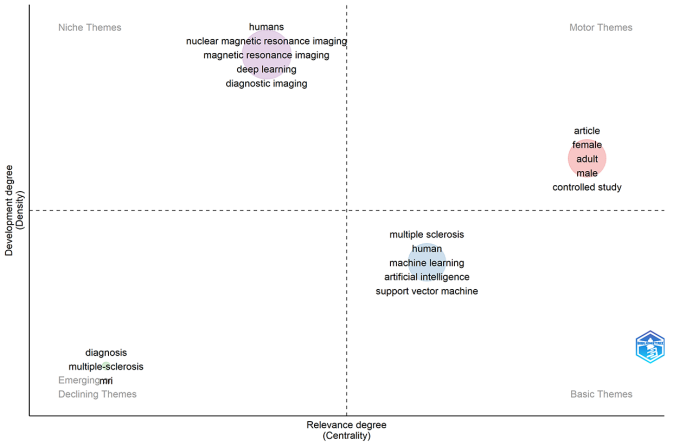
Fig. 9 shows the thematic map derived from bibliometric analysis using Biblioshiny reveals four distinct clusters that illustrate the conceptual structure of research on AI in MS detection. The axes represent centrality (relevance degree) and density (development degree), thereby positioning themes according to their importance and maturity within the field.

In the Motor Themes quadrant, the cluster comprising "article," "female," "adult," "male," and "controlled study" indicates highly central and well-developed concepts. These terms reflect the methodological and demographic focus in AI-based MS research, particularly the reliance on structured clinical studies and population-based investigations. This cluster demonstrates that research is anchored in standardized experimental designs, ensuring reproducibility and generalizability.

The Niche Themes quadrant is characterized by terms such as "humans," "nuclear magnetic resonance imaging," "magnetic resonance imaging," "deep learning," and "diagnostic imaging." These themes represent highly specialized and mature topics that are less connected to other clusters but remain crucial in advancing MS detection. Their positioning suggests that cutting-edge AI techniques, particularly deep learning applied to MRI data, are being explored in depth by select research groups. These investigations, while advanced, have not yet been fully integrated into broader mainstream clinical practice.

In the Basic Themes quadrant, concepts such as "multiple sclerosis," "human," "machine learning," "artificial intelligence," and "support vector machine" appear. These represent fundamental building blocks of the field, indicating both high relevance and moderate development. This suggests that core AI techniques and MS-specific applications are well-established as foundational areas of research. However, their

moderate density indicates opportunities for deeper methodological refinement and stronger integration with clinical outcomes.



Cluster	CallonCentrality	CallonDensity	RankCentrality	RankDensity	ClusterFrequency
All	All	All	All	All	All
article	0.158	1.452	4	3	1740
multiple sclerosis	0.115	0.793	3	2	1742
diagnosis	0.011	0.692	1	1	561
humans	0.090	2.285	2	4	2693

Fig. 9. Thematic map of bibliometric analysis.

The Emerging or Declining Themes quadrant is represented by terms such as "diagnosis," "multiple sclerosis," and "MRI." Their peripheral location with low density and centrality suggests that while diagnostic applications remain crucial, research explicitly emphasizing "diagnosis" as a keyword is either at an early stage of thematic development or being subsumed under more sophisticated frameworks, such as AI-driven imaging and predictive modelling. This may indicate a shift in focus from general diagnostic studies toward more technologically enhanced approaches.

The thematic evolution indicates that the field is moving from broad diagnostic considerations toward the integration of advanced AI techniques, particularly deep learning applied to MRI. The presence of support vector machines and machine learning in the Basic Themes quadrant highlights the longstanding reliance on traditional AI methods, while the emergence of deep learning in the Niche Themes quadrant reflects a methodological transition toward more powerful, data-intensive approaches. Future research is likely to consolidate these advancements by translating niche, high-density innovations such as deep learning and diagnostic imaging into central clinical applications. Furthermore, the prominence of demographic-related themes within the Motor quadrant suggests a growing emphasis on personalized AI-driven diagnostic models that account for variability across patient populations.

Looking ahead, the trajectory points toward the fusion of AI methodologies with multimodal imaging, predictive analytics, and real-world clinical validation. Specifically, the integration of nuclear magnetic resonance imaging with deep learning approaches is poised to transition from a niche area into a core, mainstream research theme. Additionally, as AI models mature, emphasis will likely shift toward explainability, clinical trust, and large-scale validation studies to bridge the gap between computational advances and routine MS care.

V. Discussion and Limitations

This bibliometric analysis demonstrates a rapidly expanding research landscape at the intersection of artificial intelligence (AI) and Multiple Sclerosis (MS), particularly since 2017, accompanied by a proliferation of deep learning models for lesion segmentation, disease classification, and prognostic modelling. While the field has made considerable progress, reflected in increasingly sophisticated architectures, multimodal MRI integration, and an emerging interest in federated learning, our findings highlight substantial methodological limitations that continue to impede reproducibility, generalizability, and clinical translation. Addressing these challenges is critical for transforming AI-driven MS research from promising prototypes into reliable clinical tools.

A central challenge identified in this review is the limited reproducibility of AI models. Many studies provide insufficient details on preprocessing pipelines, data harmonization, and hyperparameter settings, making exact replication challenging or impossible. The scarcity of publicly available code, trained weights, and standardized scripts further restricts the ability of independent groups to verify reported performance. Inconsistent reporting practices, such as the omission of confidence intervals, calibration metrics, or comparisons with human experts, exacerbate this issue. Without transparent, rigorous reporting, the field risks accumulating a body of literature with impressive but unverifiable claims, undermining cumulative scientific progress.

Closely related to reproducibility is the pervasive reliance on small, single-centre datasets, which was evident across much of the literature surveyed. Deep learning models trained on limited cohorts often suffer from overfitting, learning site-specific or scanner-specific idiosyncrasies rather than robust disease-related features. These limitations frequently result in overly optimistic performance metrics, particularly when studies rely on internal cross-validation alone or inadvertently introduce data leakage (e.g., slice-level splits or reuse of follow-up scans across folds). The dominance of single-centre studies also restricts the diversity of patient demographics, scanner vendors, acquisition protocols, and disease phenotypes represented in training datasets. Such dataset homogeneity severely limits the clinical relevance of reported results and raises concerns regarding real-world deployability.

Another prominent challenge is poor generalizability across centres, scanners, and populations. Domain shift, arising from differences in MRI sequences, hardware, field strengths, or clinical workflows, remains a well-documented issue in neuroimaging AI research. Models that achieve high accuracy within a single institution frequently underperform when evaluated on external datasets. The scarcity of multisite external validation in the reviewed studies reinforces this concern. Without demonstrating reliability under diverse acquisition conditions, AI systems for MS diagnosis or monitoring cannot be safely integrated into clinical practice.

Additionally, the field continues to grapple with label noise

and annotation variability, particularly for lesion segmentation tasks. Manual lesion delineation is labour-intensive and inherently subjective, resulting in inter-rater variability that propagates uncertainty into supervised learning pipelines. Despite this, many studies do not report rater agreement or employ strategies to model label uncertainty, relying instead on single sets of annotations that may not adequately capture the complexity of MS pathology.

Although several studies attempt to mitigate data scarcity through augmentation techniques or synthetic data generation, these approaches carry their own risks. Synthetic images produced via generative models may introduce unrealistic anatomical patterns or subtle artefacts that a model can exploit, resulting in inflated performance on internal test sets but weaker generalization. Without rigorous validation on independent, real-world datasets, synthetic augmentation may inadvertently worsen generalizability rather than improve it.

Given these challenges, a shift toward more rigorous methodological standards is essential. First, reproducibility can be strengthened through comprehensive reporting of data splits, preprocessing steps, hyperparameters, and evaluation settings, following guidelines such as TRIPOD-ML and CONSORT-AI. Public sharing of code, model weights, and containerized environments should become standard practice whenever permitted by ethical constraints. Second, researchers should prioritize external validation, ideally through multisite collaborations or through simulated domain shifts (e.g., holding out entire scanners or centres for testing). Third, methodological robustness can be enhanced through domain-generalization strategies, harmonization tools such as ComBat, or scanner-aware normalization and adversarial learning approaches.

The growing interest in federated learning represents an especially promising direction, as it enables collaborative model development across institutions without exposing patient data. Such approaches can substantially increase dataset size and heterogeneity while preserving privacy, addressing many limitations inherent to single-centre research. Complementary to this, reporting inter-rater variability, incorporating probabilistic labels, and using label-quality estimation techniques can reduce the impact of annotation noise.

Ultimately, the future of AI-driven MS research depends on the field's ability to produce models that are not only accurate but also reproducible, robust, and clinically trustworthy. By embracing transparent reporting, rigorous validation, and collaborative data sharing frameworks, the community can overcome the methodological constraints identified in this review and accelerate the development of reliable AI systems for MS diagnosis, monitoring, and treatment planning.

VI. Conclusion

This study presents a bibliometric analysis of the application of Artificial Intelligence (AI) in Multiple Sclerosis (MS) detection, highlighting the rapid evolution, current landscape, and emerging trends within the field. Through an extensive examination of 1502 peer-reviewed publications from 1994 to 2024, the analysis reveals a pronounced surge in research activity beginning in 2017, driven by breakthroughs in machine learning and neuroimaging. By author appearances, the United States leads, followed by Germany, China, and Italy, whereas the most productive individual institutions are concentrated in Europe, particularly Italy, Spain, and the United Kingdom. Significant research clusters have developed around gait analysis, lesion segmentation, biomarker discovery, and advanced neuroimaging.

The thematic clustering and bibliographic coupling reveal a maturing research ecosystem where convolutional neural networks (CNNs), support vector machines (SVMs), and generative models are increasingly applied to enhance diagnostic precision, monitor disease progression, and predict symptom trajectories. Notably, AI models are not only demonstrating diagnostic accuracies exceeding 95% in some cases but also enabling personalized prognostic insights and real-time clinical decision support. These advancements underscore the transformative potential of AI as a complementary tool to conventional neuroimaging and clinical assessments.

Importantly, the co-occurrence analysis points to a paradigm shift toward multimodal data integration, regulatory-compliant model design, and clinically explainable AI systems. The rise of frameworks emphasizing transparency, reproducibility, and standardized validation, such as AutoML, federated learning, and guideline-driven model reporting, signals a readiness for clinical translation. Additionally, the growing incorporation of biomarkers, such as cerebrospinal fluid analysis and brain atrophy metrics, into predictive models reflects a holistic approach that transcends traditional imaging boundaries.

However, the review also identifies critical challenges, including the need for larger, harmonized datasets, standardization of validation protocols, and greater interpretability of AI algorithms to foster clinical trust and adoption. Future research should emphasize interdisciplinary collaboration between clinicians, data scientists, and regulatory bodies to bridge the translational gap and ensure that AI applications in MS diagnosis are robust, equitable, and generalizable across diverse patient populations.

Looking ahead, future research should prioritize the development of hybrid diagnostic frameworks that combine traditional imaging modalities with quantum-inspired neural networks (QINNs) and other emerging machine learning paradigms. These models have the potential to further improve diagnostic sensitivity and computational efficiency, particularly in analysing high-dimensional, longitudinal MRI datasets. Moreover, integrating omics data, such as genomics, proteomics, and metabolomics, with neuroimaging can offer a more holistic understanding of MS pathophysiology and enhance early prediction of disease subtypes and therapeutic response. Researchers should also explore the application of explainable AI (XAI) to foster transparency in clinical decision-making, as well as federated learning to enable secure, multicentre collaborations without compromising patient privacy. Finally, there is a pressing need for publicly accessible, annotated benchmark datasets and standardized evaluation protocols to facilitate reproducibility, benchmarking, and cross-

study comparison in AI-driven MS research.

In conclusion, AI is rapidly redefining the diagnostic and prognostic landscape of Multiple Sclerosis. By illuminating the intellectual structure, collaborative networks, and thematic trajectories of this domain, this study provides actionable insights that can inform future research agendas, facilitate strategic funding decisions, and accelerate the integration of AI-powered tools into routine MS clinical workflows. The findings not only chart the current state-of-the-art but also delineate a clear roadmap for the next generation of precision diagnostics in neuroimmunology.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of the paper.

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