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Multiple Sclerosis Diagnosis Methods Using Machine Learning and Imaging Techniques

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ABSTRACT

Multiple Sclerosis (MS) disease is immune disorder that destroys myelin in the nervous system and causes many complications including motor and sensory disorders. Nowadays, medical images including Magnetic Resonance Imaging (MRI) and Optical Coherence Tomography (OCT) are recognized as the basic tools in the diagnosis of MS disease. Due to the large amount of image data in this method, the use of machine learning methods, especially Neural Networks (NNs) plays an important role in image processing. This paper presents a comprehensive overview of different methods, which utilize NNs to MS diagnosis. This review presents the classical of NNs and Convolutional NNs (CNNs), which are used in the MS diagnosis. In addition, challenges, and recent developments in this field are presented, which provides directions for future researches in this field.

1. Introduction

Multiple Sclerosis (MS) is one of the inflammatory diseases of the nervous system that affects the many people life. The disease begins with an attack on myelin, which is the fatty layer that acts as an insulator and wraps around most nerves in the spinal cord and brain [1]. When this lining is damaged, it can lead to numerous problems including motor, sensory, balance and even cognitive problems. Early MS symptoms can be so subtle that they are easily confused with other neurological conditions, making a diagnosis difficult. This feature can cause a delay in diagnosis and a faster progression of the disease [2]. To make a more accurate diagnosis, Magnetic Resonance Imaging (MRI) is a prominent method, due to this method is able to identify and display the damaged caused by MS in the brain tissue, but interpreting these images requires a lot of skill and experience. So, it can be a challenging issue [3].

Nowadays, it is possible to analyze and diagnose MRI more accurately using Machine Learning (ML) and especially Deep Learning (DL). These technologies are able to discover complex and hidden patterns in big data. Using these technologies can provide faster and more accurate

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diagnoses [4]. With the help of this technology, it is possible to reduce the dependence on human experience and knowledge. In addition, it not only can achieve higher diagnostic accuracy, but also can speed up the diagnostic process and improve patient care standards. This type of approach can revolutionize the future of treatment and care for patients with MS [5].

In the field of MS diagnosis, several methods using DL have been proposed. Many of these methods rely on Convolutional Neural Networks (CNNs). These networks, which are powerful tools in the field of DL, are mainly used in image processing and pattern recognition. They consist of different layers, each of these layers identifies certain features in the images. For example, early layers may recognize surface features such as edges or colors, while deeper layers understand more complex patterns. In the field of medicine, and especially in the diagnosis of MS, the CNNs play an important role [6, 7].

In this review paper, the role and importance of NNs in the diagnosis of MS from MRI images is investigated. We review different methods, which are utilized NNs, challenges and recent advances in this field, and provide open research issue. This paper will be of added value to scientists, researchers, and medical and engineering professionals interested in the diagnosis and management of MS.

The organization of this paper is as follows. Section 2 introduce the backgrounds. Section 3 presents the research methodology. Section 4 presents comparison and open research issue. Conclusion is presented in section 5.

2. Background

2.1. Multiple sclerosis disease

The MS is a debilitating disease of the spinal cord and brain. This autoimmune disease is caused by the attack of the body's immune system on nerve fibers, which can destroy its protective sheath. As a result, nerve messages are not transmitted properly. So, body functions are disturbed [8]. The degree of nerve damage and the affected nerves determine the range of signs and symptoms associated with multiple sclerosis. The MS has no known treatment. On the other hand, some therapies can alter the disease's course, manage symptoms, and hasten recovery following attacks [9]. Relapsing episodes are common in MS patients. Days to weeks may pass between the onset of new symptoms or relapses in affected individuals. During these relapses, the symptoms usually or somewhat go better. A period of the disease's remission, which can extend for months or even years, is what leads to this return. The signs and symptoms of MS may momentarily intensify with a minor increase in body temperature, although this does not indicate a relapse [10].

2.2. Magnetic resonance imaging

The MRI is a non-invasive technology, which utilizes radio waves and magnetic fields to create highly detailed images of internal organs and tissues inside the body. They use this technology to diagnose and identify diseases and control treatment [11]. This type of imaging is based on a complex technology that stimulates the spin of water protons in living tissues and detects changes in them. The MRI uses very strong magnets that generate a magnetic field that forces protons in the body to align with this field [12].

Nowadays, a radio frequency current passes through the patient's body, and the protons are stimulated and rotate and get out of balance and create resistance in the direction of the magnetic field. Physicians can distinguish between different tissues based on these magnetic differences. When the radio frequency field is turned off, the MRI sensors can detect the released energy resulting from the reorientation of the protons with the magnetic field [13]. The environment and the chemical nature of the molecules affect both the amount of energy released by the protons and the time it takes for them to realign [14].

2.3. Neural network

The NNs are modern computing architecture for the ML to predict the output responses of complex systems. Inspired by the human brain, the NNs consist of interconnected processing units (neurons) that work together to process information and learn [15]. The core concept of this idea involves designing a new information processing system. This system is made up of many interconnected units called neurons, which collaborate to solve problems. These neurons communicate with each other using electrical signals, similar to how synapses work in the human brain. If one neuron is damaged, the other neurons can adapt and function without it [16].

The NNs can learn from experience. For instance, if a neuron is repeatedly exposed to a painful stimulus, it can learn to avoid that stimulus [17]. This learning process is adaptive, meaning the network adjusts its internal connections (synapses) based on examples to produce the correct output when presented with new information [18]. The fundamental idea behind artificial neural networks is to imitate how the human brain processes information, offering an alternative to traditional computing methods [19].

2.4. Medical image processing

Medical image processing involves analyzing 3D images of the human body, often from CT or MRI scans. It's used for diagnosing diseases, planning surgeries, and conducting medical research. Doctors, engineers, and medical professionals use it to study the anatomy of individual patients or groups. A major benefit of medical image processing is the ability to deeply examine internal organs without invasive procedures. Creating 3D models of the body can improve patient outcomes, lead to better medical devices and drug delivery systems, and enable more accurate diagnoses. In recent years, it has become an essential tool in medical advancements [20].

Advancements in medical image processing and software have allowed for precise digital reconstruction of anatomical structures, including bones and soft tissues, at various scales [21]. This enables the measurement, statistical analysis, and simulation of realistic anatomical geometry, providing a better understanding of how medical devices interact with patients. Medical image processing starts with raw data from CT or MRI scans, which is then reconstructed into a suitable format for specific software. This data often takes the form of a 3D map of grayscale density, composed of a grid of small volumetric cells. The grayscale density in CT scans is based on X-ray absorption, while in MRI scans, it's determined by the signals emitted by protons in response to strong magnetic fields [22].

3. Research methodology

This review paper explores how AI can improve MS diagnosis, disease monitoring, patient care, screening, and clinical decision-making using image techniques. It examines recent advancements, challenges, future possibilities, and ethical concerns related to AI-based MS diagnosis techniques. The paper collects, categorizes, summarizes, and analyzes existing studies in this field.

Farabi-Maleki et al. [23] have utilized the AI to manage the MS using retinal images. The AI-based approaches have yielded considerable capabilities to classify distinct MS subtypes based on retinal characteristics, help to identify the disease and guide appropriate treatment strategies. In addition, these algorithms are reduced the efficiency and accuracy of the Optical Coherence Tomography (OCT) image segmentation, simplified diagnostic processes, and human error.

Haj Messaoud et al. [24] have automatically segmented the MS lesions based on the CNNs. ***Figure*** 1 displays the workflow of the presented segmentation method in [24].

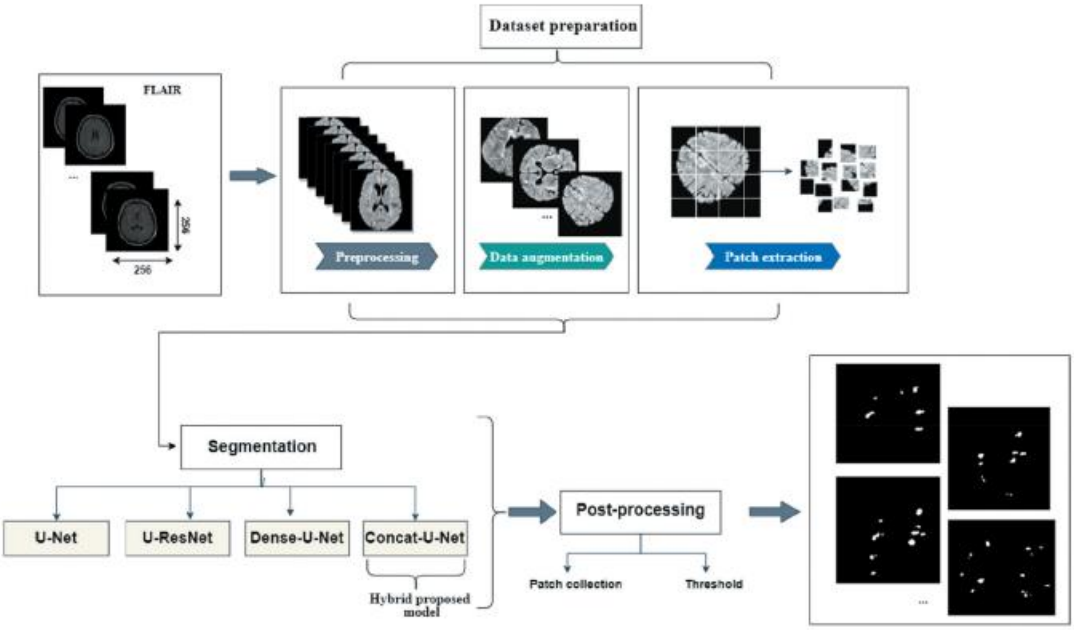

Figure 1. The utilized segmentation method in [24].

The main challenge in this method is to propose a model, which utilizes the CNN models including ResNet, U-Net, and DenseNet. The proposed models in [24] are simulated using Python. In [24], the private data set, the best dice sensitivity, PR curve, and accuracy are 80%, 77%, 98%, and 78%, respectively.

Ortiz et al. [25] have proposed an MS diagnosis method using OCT. This study evaluates retinal thickness in healthy individuals and MS patients using OCT images. The ROC curve is analyzed in different retinal areas to compare average thickness between eyes and identify differences. The study found that the ganglion cell layer, medial plexiform layer, and inner retinal layers show the most significant changes in MS patients.

A two-layer CNN is used to evaluate the diagnostic accuracy of retinal thickness and interocular difference. Using mean ganglion cell layer thickness and interocular difference in the inner plexiform layer as input, the CNN achieved an accuracy of 87%, sensitivity of 82%, and specificity of 92% in automatically detecting MS. ***Figure 2*** shows a cross-section of the retina, captured using spectral OCT. The left side of the image indicates the location of the cross-section, which extends between the optic nerve and the macula of the eye.

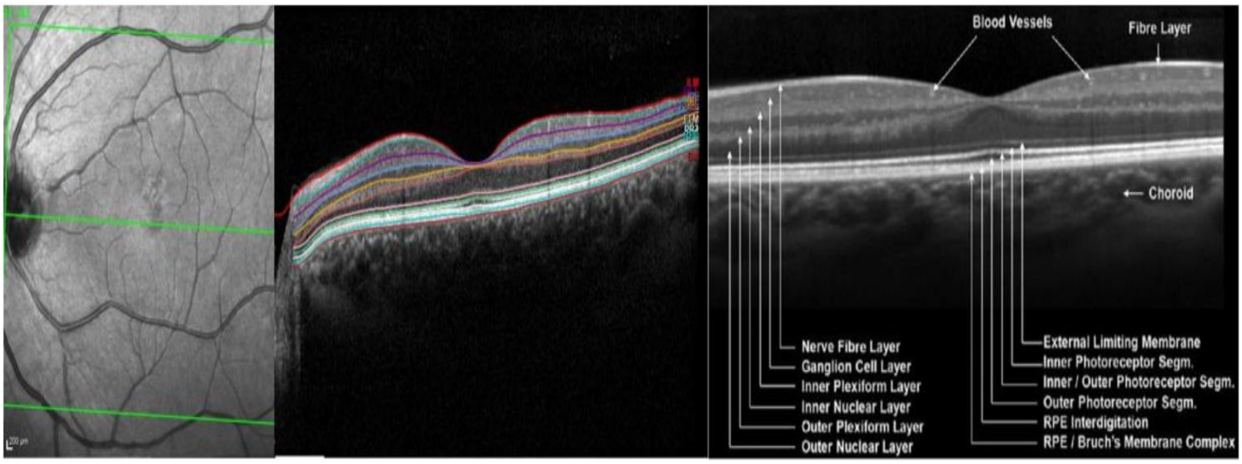

Figure 2. cross-section of the retina, captured using spectral optical coherence tomography in [25].

Nabizadeh et al. [26] have presented a comprehensive review of studies using AI to diagnose MS in 2023. They search four databases and included studies that used DL or other AI methods. The researchers analyze the precision, sensitivity, specificity, accuracy, and AUC of these studies using a random effects model. After reviewing 41 studies with a total of 5,989 participants, they found that the overall accuracy of AI models in diagnosing MS is 94%. The pooled sensitivity and specificity are both high at 92% and 93%, respectively. The authors conclude that AI models can significantly improve the performance of the MS diagnosis.

Seok et al. [27] have developed a DL model to distinguish between MS and Neuromyelitis Optica Spectrum Disorder (NMOSD) using brain MRI data. Their model, based on a modified ResNet18 CNN, is trained on five 2D slices extracted from 3D FLAIR images, which is shown in ***Figure 3***. The model achieves an accuracy of 76.1%, sensitivity of 77.3%, and specificity of 74.8% in distinguishing between MS and NMOSD. Additionally, it has a positive predictive value of 76.9% and a negative predictive value of 78.6%, with an area under the curve of 0.85. This compact model can aid in the clinical diagnosis of MS and NMOSD.

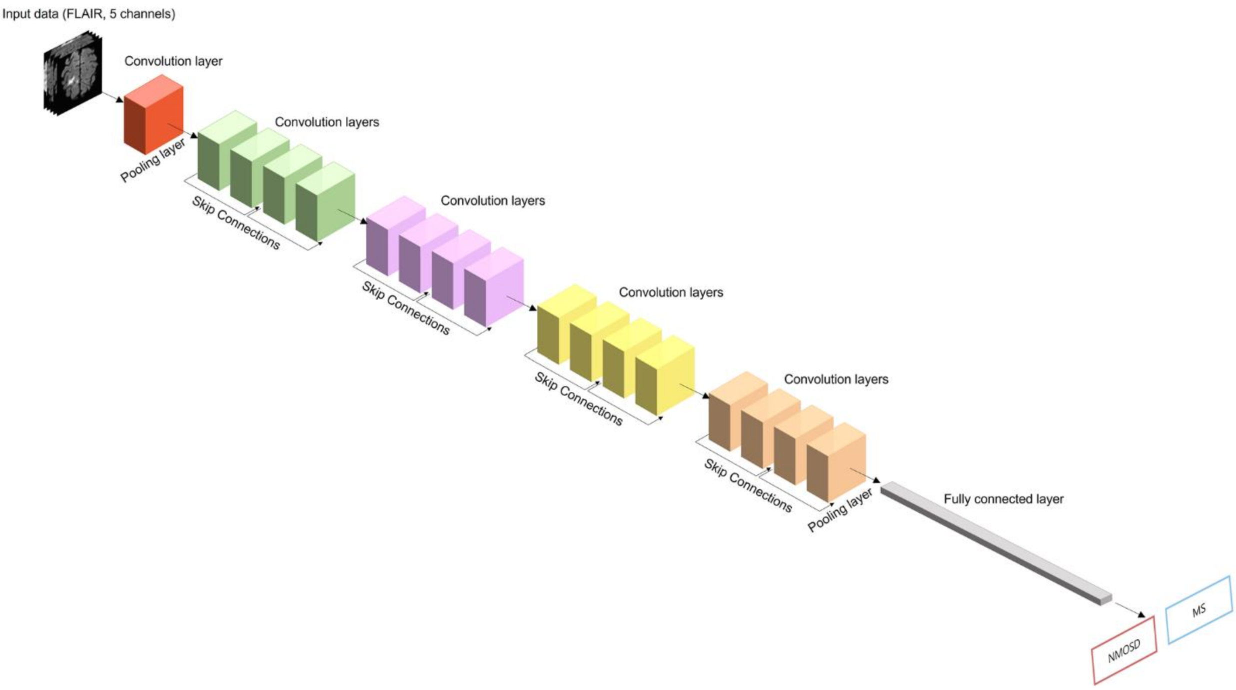

Figure 3. Utilized architecture in [27].

Filippi et al. [28] have reviewed the MS diagnosis using imaging techniques. The McDonald's 2017 criteria are highly accurate and sensitive in predicting a second clinical attack in patients with a typical isolated clinical syndrome, allowing for early MS diagnosis. These expanded criteria are evidence-based and can improve MS patient management. However, to avoid misdiagnosis, they should only be used by experienced doctors after careful evaluation of alternative diagnoses. Recent research has proposed new MRI markers to enhance MS diagnosis accuracy and reduce misdiagnosis. Central markers and chronically active lesions, like paramagnetic peripheral lesions, may improve diagnostic criteria, but further validation and standardization are needed before clinical implementation. Evaluating subarachnoid destruction and subject strengthening seems to have limited clinical significance in MS diagnosis. The AI tools may capture features of the MRI that are beyond human perception.

Montolio et al. [29] have proposed a DL approach to investigate the macular Retinal Ganglion Cell Layer (mRGCL) as a biomarker for MS diagnosis and early warning. They developed a computerized method to assist in diagnosis and prognosis by combining a cross-sectional study of MS patients and healthy controls with a longitudinal study of MS patients to predict disability progression. Using optical coherence tomography to measure mRGCL and deep neural networks as classifiers, the study achieved a 90.3% accuracy in MS diagnosis with 17 features. For predicting disability progression, the accuracy is 81.9% with a neural network containing two hidden layers and 400 cycles. The authors concluded that using DL techniques on clinical data and mRGCL thickness can effectively detect MS and predict its course. This approach offers a potential non-invasive, low-cost, and easy-to-implement solution.

Kaur et al. [30] have proposed a patch deep CNN method for segmentation of the MS brain lesions. This paper presents a deep CNN for extracting the MS brain lesions using MRI, which is shown in ***Figure 4***. To increase reliability, this framework uses separate convolutional paths for T1 and T2 sequences with different convolutional filters, The convolutional output is further passed through another set of convolutional filters to produce the final output. The performance of this framework is evaluated on the challenges of medical image computing and computer usage, which results in a low false positive rate of 0.5% and a high true positive rate of 74%. In addition, the results show that the accuracy of this method is 97%.

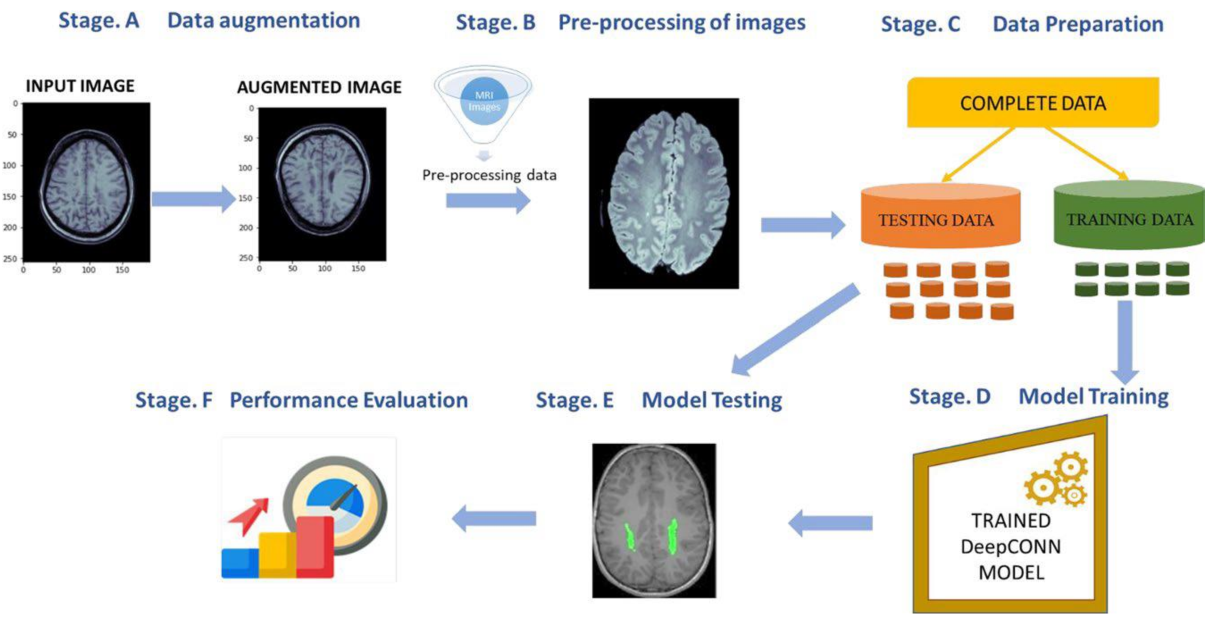

Figure 4. Utilizing Workflow in [30].

4. Comparison and open research issue

4.1. Comparison and discussion

In this section, the results of the related works are compared, analysis and discussed. In this analysis, some important points of each paper are stated:

• The paper by Farabi Maleki et al. [23] examines how artificial intelligence can be effective in the management of MS using retinal images. This paper has addressed the identification of new biomarkers for early detection and prediction of disease progression and presented the use of ML and DL algorithms for the analysis of OCT data.

• The paper by Haj Messaoud et al. [24] focuses on automatic segmentation of the MS lesions based on the CNN. This paper is devoted to the development of new CNN models for the automatic diagnosis of the MS brain lesions. It shows the improvement of the efficiency and accuracy of the diagnosis.

• The paper by Ortiz et al. [25] focuses on the diagnosis of the MS using optical coherence tomography. This paper discusses the identification of new biomarkers and the use of neural network structures for more accurate diagnosis of the MS.

• The paper by Nabizadeh et al. [26] is a systematic review and meta-analysis on the diagnostic performance of artificial intelligence in the MS. This paper demonstrates that AI models can improve diagnostic performance in the MS patients and improve current diagnostic approaches.

• The paper by Seok et al. [27] have developed a DL model to distinguish between the MS and neuromyelitis optica spectrum disorder using brain MRI data. This model is able to diagnose these two diseases with appropriate accuracy and sensitivity and can be used in differential diagnosis between them.

• The paper by Filippi et al. [28] have investigated how MRI can be effective in the diagnosis of the MS. This research deals with the development of the MRI criteria and their use for better management of patients with MS.

• The paper by Montolio et al. [29] have used a DL approach for diagnosis and prognosis in the MS. This research deals with the existence of biomarkers and their use in the MS diagnosis.

• The paper by Kaur et al. [30] have develop a CNN method for segmentation of the MS brain lesions. This method is able to accurately diagnose MS brain lesions. it can be useful in the diagnosis and follow-up of patients.

In summary, this research shows that the use of DL and artificial intelligence methods can be effective in the diagnosis and management of patients with the MS and distinguish these patients from other disorders that may have similar symptoms. ***Table 1*** summarizes the results of the related works.

Table 1. Comparison of completed works

Reference No	Publication year	Method type	correctness (percentage)	sensitivity (percentage)	accuracy (percentage)
[23]	2023	A review article on the integration of artificial intelligence with OCT in the field of MS	80	80	87
[24]	2023	Automatic segmentation of MS lesions of 2D images using DL approaches	76	75	83
[25]	2023	Identification of new biomarkers for early detection of MS using spectral domain optical coherence tomography and artificial intelligence.	81	69	84
[26]	2023	A systematic review and comprehensive meta-analysis on the role of artificial intelligence in the diagnosis of MS	80	79	81
[27]	2023	A deep learning model to distinguish between multiple sclerosis and neuromyelitis optica spectrum disorder using brain magnetic resonance imaging data.	82	75	92
[28]	2023	Examining the diagnosis of multiple sclerosis from the perspective of imaging	81	70	90
[29]	2023	A computerized approach to facilitate diagnosis and prognosis in MS	80	73	88
[30]	2024	A deep complex neural network for extracting multiple sclerosis brain lesions from magnetic resonance images	91	72	95

Based on our analysis that are summarized in ***Table 1***, the highest accuracy is 95%, which is related to [30] and the lowest accuracy is 81%, which is related to [26] on the other hand average accuracy in paper is 87.5. The highest sensitivity is 80%, which is related to [23] and the lowest sensitivity is 69%, which is related to [25]. The average sensitivity in paper is 74.125%. The highest correctness is 91%, which is related to [30] and the lowest correctness is 76%, which is related to [24]. The average correctness in paper is 81.375%. Reference [30] has the best performance with 95% accuracy, 72% sensitivity, and 91% accuracy. These results indicate that the use of deep complex neural network in extracting the MS brain lesions from the MRI can be a very effective approach. Reference [26] has the lowest accuracy, but it is still high accuracy, it shows that methods are also very important in the overall understanding of the role of machine learning in MS diagnosis. However, the sensitivity is on average lower than the accuracy, which could mean that the models face challenges in detecting positive MS cases. The use of machine learning methods in the diagnosis and management of the MS has shown promising results. To improve the sensitivity, more research can be done to provide better models and more data to train the models. It is very important to pay attention to the combination of precision, sensitivity and accuracy in evaluating the performance of models to ensure that the models are not only accurate but also able to correctly distinguish positive and negative cases.

4.2. Open research issue

Based on the results, we can divide the direction of research in the field of using machine learning for the diagnosis and management of the MS into several general categories:

- Advances in DL methods

- ✓ More complex models: using more complex neural networks, such as deep CNNs, which have produced very accurate results.
- ✓ Hybrid models: combining multiple ML and DL methods to improve detection accuracy, which can also increase sensitivity.

• Multipurpose integration of data
- ✓ Multi-dimensional images: Using multi-dimensional images such as 3D images for better and more accurate analysis of the MS lesions, which can contribute to the accuracy of models.
- ✓ Multiple data: combining different data including MRI, OCT and clinical information to improve the performance of models.

• Improved sensitivity
- ✓ Training models with more data: increasing the volume of training data, especially positive data, so that models can show better sensitivity to positive cases.
- ✓ Data augmentation methods: using data augmentation techniques to generate more samples from existing data and reduce the problem of data scarcity.

• Review and systematic analyses
- ✓ Comprehensive studies: Continue and increase the number of systematic review studies and meta-analysis to aggregate and compare different results, which can help identify the best methods and algorithms.
- ✓ Standardization of evaluations: creating specific standards for evaluating the performance of different models and comparing them in a consistent manner.

• Discovery of new biomarkers
- ✓ Advanced analytics: Using advanced analytical methods to discover new biomarkers that can help in the early diagnosis of MS.
- ✓ Integration of molecular and imaging methods: combining molecular data (e.g., genetics) with imaging data to provide more robust predictive models.

• Clinical applications and decision making
- ✓ Decision support systems: development of clinical decision support systems that assist physicians in the diagnosis and treatment of the MS.
- ✓ Evaluation in the clinical environment: evaluation and testing of models in real clinical environments to measure performance and adapt to everyday medical needs.

Research on the use of AI for the diagnosis and management of the MS is moving towards the development of more complex and accurate models, the integration of multivariate data and the improvement of sensitivity. These trends can help to improve early diagnosis, more accurate diagnosis and better treatment of the MS patients.

5. Conclusion

This paper conducts a comprehensive examination of various diagnostic methods aimed at enhancing both the accuracy and speed of diagnosis, with a particular focus on the application of artificial neural networks technology. The findings of this review indicate that the implementation of artificial neural networks in the diagnosis of MS results in a substantial improvement in diagnostic accuracy and the differentiation of MS from other diseases and health conditions. Furthermore, these methodologies are presented as a robust tool to assist healthcare professionals in the prompt and precise diagnosis of MS, owing to their capacity to adapt to variations in imaging and the diverse complexities associated with the disease. These advancements have the potential to significantly improve patient care and accelerate the diagnosis and treatment of MS. This paper demonstrates that utilizing DL technologies substantially enhances MS diagnosis and management. By employing these sophisticated methods, we can markedly increase the accuracy of disease diagnosis, distinguishing between healthy and compromised brain regions. Given the intricate nature of MS and the imperative for rapid and accurate diagnosis, artificial neural networks have emerged as a formidable asset in this domain. These techniques possess the capability to adapt to image variations and recognize complex patterns, thereby enhancing the potential for early disease diagnosis and the initiation of effective treatment. In light of recent advancements in DL and neural networks, it is anticipated that these technologies will play a pivotal role in improving the quality of treatment and care for patients with MS. This paper not only serves to inspire future research in this area but also represents a significant milestone in the introduction of novel approaches to the diagnosis and management of the MS.

Guidelines that guarantee the validity, comprehensibility, and reliability of findings obtained from AI approaches are still required for their implementation in the clinical scenario. In the future, AI may help supplement human assessment to enhance diagnostic work and patient classification.

Reference

[1]. B. A. C. Cree, J. R. Oksenberg, and S. L. Hauser, "Multiple sclerosis: two decades of progress," *Lancet Neurol,* vol. 21, no. 3, pp. 211–214, 2022.

[2]. F. D. Lublin *et al,* "How patients with multiple sclerosis acquire disability," *Brain*, vol. 145, no. 9, pp. 3147–3161, 2022.

[3]. R. Rahmanzadeh *et al,* "A new advanced MRI biomarker for remyelinated lesions in multiple sclerosis," *Ann. Neurol,* vol. 92, no. 3, pp. 486–502, 2022.

[4]. A. Pal and Y. Rathi, "A review and experimental evaluation of deep learning methods for MRI reconstruction," *J. Mach. Learn. Biomed. imaging,* vol. 1, 2022.

[5]. G. Goh *et al,* "Multimodal neurons in artificial neural networks," *Distill,* vol. 6, no. 3, p. e30, 2021.

[6]. B. Souid, S. Yahia, T. Bouchrika, and O. Jemai, "Fusion of CNN and feature extraction methods for multiple sclerosis classification," in *Fifteenth International Conference on Machine Vision (ICMV 2022),* SPIE, 2023, pp. 353–360.

[7]. L. Coll *et al,* "Global and Regional Deep Learning Models for Multiple Sclerosis Stratification From MRI," *J. Magn. Reson. Imaging,* 2023.

[8]. G. Giovannoni, C. Hawkes, J. Lechner-Scott, M. Levy, E. Waubant, and J. Gold, "The COVID-19 pandemic and the use of MS disease-modifying therapies," *Mult. Scler. Relat. Disord,* vol. 39, 2020.

[9]. R. Magliozzi and A. H. Cross, "Can CSF biomarkers predict future MS disease activity and severity?," *Mult. Scler. J,* vol. 26, no. 5, pp. 582–590, 2020.

[10].M. P. Sormani *et al,* "Disease-modifying therapies and coronavirus disease 2019 severity in multiple sclerosis," *Ann. Neurol,* vol. 89, no. 4, pp. 780–789, 2021.

[11].R. Reda, A. Zanza, A. Mazzoni, A. Cicconetti, L. Testarelli, and D. Di Nardo, "An update of the possible applications of magnetic resonance imaging (MRI) in dentistry: a literature review," *J. imaging,* vol. 7, no. 5, p. 75, 2021.

[12].A. Tiwari, S. Srivastava, and M. Pant, "Brain tumor segmentation and classification from magnetic resonance images: Review of selected methods from 2014 to 2019," *Pattern Recognit. Lett,* vol. 131, pp. 244–260, 2020.

[13].N. Weiskopf, L. J. Edwards, G. Helms, S. Mohammadi, and E. Kirilina, "Quantitative magnetic resonance imaging of brain anatomy and in vivo histology," *Nat. Rev. Phys,* vol. 3, no. 8, pp. 570–588, 2021.

[14].C. Z. Cooley *et al,* "A portable scanner for magnetic resonance imaging of the brain," *Nat. Biomed. Eng,* vol. 5, no. 3, pp. 229–239, 2021.

[15].G. R. Yang and X.-J. Wang, "Artificial neural networks for neuroscientists: a primer," *Neuron,* vol. 107, no. 6, pp. 1048–1070, 2020.

[16].N. Talpur, S. J. Abdulkadir, H. Alhussian, M. H. Hasan, N. Aziz, and A. Bamhdi, "Deep Neuro-Fuzzy System application trends, challenges, and future perspectives: a systematic survey," *Artif. Intell. Rev,* vol. 56, no. 2, pp. 865–913, 2023, doi: 10.1007/s10462-022-10188-3.

[17].X. Liu, S. Tian, F. Tao, and W. Yu, "A review of artificial neural networks in the constitutive modeling of composite materials," *Compos. Part B Eng,* vol. 224, p. 109152, 2021.

[18].F.-L. Fan, J. Xiong, M. Li, and G. Wang, “On interpretability of artificial neural networks: A survey,” *IEEE Trans. Radiat. Plasma Med. Sci*, vol. 5, no. 6, pp. 741–760, 2021.

[19].S. Chung and L. F. Abbott, “Neural population geometry: An approach for understanding biological and artificial neural networks,” *Curr. Opin. Neurobiol,* vol. 70, pp. 137–144, 2021.

[20].J. L. Semmlow and B. Griffel, *Biosignal and medical image processing*. CRC press, 2021.

[21].X. Liu, L. Song, S. Liu, and Y. Zhang, “A review of deep-learning-based medical image segmentation methods,” *Sustainability,* vol. 13, no. 3, p. 1224, 2021.

[22].Y. Li, J. Zhao, Z. Lv, and J. Li, “Medical image fusion method by deep learning,” *Int. J. Cogn. Comput. Eng,* vol. 2, pp. 21–29, 2021.

[23].S. Farabi Maleki *et al,* “Artificial Intelligence for multiple sclerosis management using retinal images: pearl, peaks, and pitfalls,” in *Seminars in Ophthalmology*, Taylor & Francis, 2023, pp. 1–18.

[24].N. Haj Messaoud *et al,* “Automated segmentation of multiple sclerosis lesions based on convolutional neural networks,” *Comput. Methods Biomech. Biomed. Eng. Imaging Vis,* vol. 11, no. 4, pp. 1359–1377, 2023.

[25].M. Ortiz *et al,* “Diagnosis of multiple sclerosis using optical coherence tomography supported by artificial intelligence,” *Mult. Scler. Relat. Disord,* vol. 74, p. 104725, 2023.

[26].F. Nabizadeh, E. Ramezannezhad, A. Kargar, A. M. Sharafi, and A. Ghaderi, “Diagnostic performance of artificial intelligence in multiple sclerosis: a systematic review and meta-analysis,” *Neurol. Sci,* vol. 44, no. 2, pp. 499–517, 2023.

[27].J. M. Seok *et al,* “Differentiation between multiple sclerosis and neuromyelitis optica spectrum disorder using a deep learning model,” *Sci. Rep,* vol. 13, no. 1, p. 11625, 2023.

[28].M. Filippi *et al,* “Present and future of the diagnostic work-up of multiple sclerosis: the imaging perspective,” *J. Neurol,* vol. 270, no. 3, pp. 1286–1299, 2023.

[29].A. Montolío, J. Cegoñino, E. Garcia-Martin, and A. Pérez del Palomar, “The macular retinal ganglion cell layer as a biomarker for diagnosis and prognosis in multiple sclerosis: A deep learning approach,” *Acta Ophthalmol,* 2023.

[30].A. Kaur, L. Kaur, and A. Singh, “DeepCONN: patch-wise deep convolutional neural networks for the segmentation of multiple sclerosis brain lesions,” *Multimed. Tools Appl,* vol. 83, no. 8, pp. 24401–24433, 2024.