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The importance of MRI in the diagnosis and monitoring of multiple sclerosis treatment

Mihaela Mihanović[1], **Tatjana Matijaš**[1]

[1] University of Split, Faculty of Health Sciences, Split, Croatia

Corresponding author: Tatjana Matijaš, email: tmatijas@ozs.unist.hr

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Abstract

Multiple sclerosis (MS) is a chronic, autoimmune disease of the central nervous system that affects a growing global population each year. Magnetic Resonance Imaging (MRI) is the most important imaging modality, providing optimal information for initial diagnosis and insight into disease activity and progression. The introductory part of this paper describes multiple sclerosis, its clinical forms, and common symptoms. MRI is detailed as the key imaging technique for MS due to its superior ability to visualize soft tissue structures, particularly the brain and spinal cord, where MS pathology occurs. The discussion provides an in-depth review of MS lesion presentation on MRI, highlighting the importance of specific imaging sequences for accurate lesion differentiation and classification. Artificial intelligence is presented as a promising advancement that could be increasingly used in the future as a tool for faster and more precise diagnosis. Finally, the critical role of the radiologic technologist in obtaining the highest quality images, essential for accurate and precise clinical interpretation, is emphasized.

Keywords: lesions; magnetic resonance imaging; multiple sclerosis; radiological technologist; sequences

Abbreviations and acronyms: AI (Artificial Intelligence), CIS (Clinically Isolated Syndrome), CNN (Convolutional Neural Networks), DIR (Double Inversion Recovery), GRE (Gradient Echo Sequence), MPRAGE (Magnetization-Prepared Rapid Acquisition of Gradient Echoes), MRI (Magnetic Resonance Imaging), MS (Multiple Sclerosis), MSSEG-2 (Multiple Sclerosis New Lesions Segmentation Challenge), PD (Proton Density), PPMS (Primary Progressive Multiple Sclerosis), PSIR (Phase-Sensitive Inversion Recovery), RIS (Radiologically Isolated Syndrome), RRMS (Relapsing-Remitting Multiple Sclerosis), SNR (Signal-To-Noise Ratio), SPMS (Secondary Progressive Multiple Sclerosis), T2-FLAIR (T2-Fluid-Attenuated Inversion Recovery)

Introduction

Autoimmune diseases occur when the immune system mistakenly attacks the body's own healthy cells, confusing them for harmful substances such as viruses or toxins. Between 80 and 150 such diseases are known, most of which are chronic and incurable. Treatment is generally focused on relieving symptoms and improving quality of life. The exact cause is not fully understood, but genetic factors, infections, and certain medications are believed to contribute to the development of the condition. People with a family history of autoimmune diseases are at higher risk, and certain viruses and bacteria may trigger the disease, especially in genetically predisposed individuals [1, 2].

Multiple Sclerosis

Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system. It is estimated that approximately 2.3 million people worldwide are affected by this condition, with most diagnoses occurring between the ages of 20 and 40. Women of Caucasian descent are more frequently affected by MS, and the disease exhibits significantly higher prevalence in Northern Hemisphere countries [3].

The central nervous system comprises the brain, spinal cord, and optic nerves. In MS, the immune system attacks myelin, the protective protein substance surrounding nerve fibers. Myelin plays a key role in the transmission of impulses between neurons and is responsible for the white appearance of the brain's white matter. In addition to damaging the myelin sheath, MS also causes injury to the cell bodies of neurons located in the brain's gray matter [4].

The exact cause of MS remains unknown, but it is thought to result from a combination of genetic and environmental factors. Some studies suggest that, in individuals with specific genetic predispositions, an external environmental factor may trigger the disease. Although MS is not directly inherited, having certain genes can increase the risk of developing it. One potential risk factor is vitamin D deficiency, as the body naturally produces this

vitamin through sunlight exposure. This connection explains why MS is more common in northern regions, where sunlight is less abundant. Smoking is another important risk factor; smokers have about a 50% higher chance of developing MS compared to non-smokers. Additionally, children exposed to second-hand smoke at home may be more likely to develop MS later in life or during childhood [5, 6].

Types of Multiple Sclerosis

MS is a heterogeneous disease that affects each person differently, as does the treatment process. Understanding the different forms of this disease is essential for choosing the most effective therapy to reduce symptoms and enhance daily life. There are five currently recognized types:

- **Clinically isolated syndrome (CIS)** – describes the first episode of neurological symptoms persisting for at least 24 hours. It is often the initial sign pointing to a potential MS diagnosis, but it remains unclear why some individuals with CIS develop MS while others do not [7].
- **Relapsing-remitting multiple sclerosis (RRMS)** – initial diagnosis for most people with MS. It features episodes of symptom worsening (relapses) that last from weeks to months, characterized by episodes of symptom worsening (relapses) followed by periods of partial or complete recovery (remissions) that can last for years [7].
- **Secondary progressive multiple sclerosis (SPMS)** – over time, most people with RRMS eventually transition to SPMS, characterized by a gradual worsening of symptoms without periods of remission [7].
- **Primary progressive multiple sclerosis (PPMS)** – affects a smaller number of patients and involves a gradual worsening of symptoms from the start, resulting in progressive disability [7].
- **Radiologically isolated syndrome (RIS)** – the rarest form of MS, characterized by the absence of classic symptoms but with abnormalities on magnetic resonance imaging that can be interpreted as MS. However, symptoms may develop later in life [4].

Symptoms of Multiple Sclerosis

Early signs of MS are often nonspecific, which can delay a timely diagnosis. Although symptoms vary from person to person, the most common initial signs include fatigue and numbness throughout the body. These symptoms result from nerve damage but are rarely immediately linked to MS due to their nonspecific nature. One of the more noticeable early symptoms is vision disturbance, known as optic neuritis, which involves inflammation of the optic nerve and can cause pain, blurred vision, or even permanent vision loss. Early signs may also include muscle weakness, painful spasms, balance problems, and dizziness. Symptoms can also appear psychologically. Mental fatigue, depressive mood, emotional instability, as well as cognitive challenges like memory issues, concentration problems, and reduced multitasking ability, are also typical early signs of the disease [4, 8].

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a non-invasive diagnostic technique that uses a strong and stable magnetic field to produce three-dimensional images of the body's internal structures. The system includes a powerful magnet, gradient coils along the X, Y, and Z axes, and specialized coils for transmitting and receiving RF signals, and a computer that processes the data. MRI is effective at imaging soft tissues such as the brain and spinal cord, making it critical for MS diagnosis. It works by aligning hydrogen protons in the body using a powerful magnetic field. Radiofrequency waves then cause these protons to become temporarily disoriented. When the waves are turned off, the protons return to their original positions, emitting energy that the coils detect. Different tissue types can be distinguished based on relaxation times and the amount of energy emitted, allowing for detailed visualization of internal structures [9-11].

Types of Magnets

MRI is a diagnostic imaging technique that has greatly improved over the years, allowing for high-quality images and more precise diagnosis of various diseases. Today's image quality is primarily due to technological advances in MRI systems, especially the development of magnets, which are a vital part of the MRI machine. There are several types of magnets used in MRI systems, including permanent magnets, iron-core magnets, resistive magnets, and superconducting magnets [9].

Contraindications for MRI

Although MRI does not expose patients to harmful ionizing radiation, certain contraindications should be considered before the procedure. Because of the strong magnetic field, MRI is not suitable for people with metal implants like pacemakers, as it could cause serious complications. A common contraindication is claustrophobia; the enclosed space of the MRI scanner can trigger discomfort and anxiety in some individuals. To address this, open MRI systems have been developed to offer a more comfortable experience. Additionally, the loud noise generated by the machine can cause further discomfort, which is why patients are usually given headphones to help reduce the sound. Concerning pregnancy, MRI is not an absolute contraindication; however, it is generally advised to avoid imaging during the first trimester when fetal organs are developing [11].

Aim of the paper

This paper aims to describe and showcase the presentation of multiple sclerosis lesions on MRI, highlighting the importance of using various imaging sequences for accurate diagnosis and monitoring. It also emphasizes advanced diagnostic features and emerging techniques, such as artificial intelligence, and underscores the vital role of the radiologic technologist in achieving high-quality MRI studies.

Discussion

MRI as a diagnostic method has greatly improved over time. It is essential for diagnosing, predicting, and assessing disease activity in MS. Patients with MS regularly undergo MRI scans to monitor the disease continuously and identify if any progression has occurred since the previous imaging.

Diagnosis of multiple sclerosis using MRI

The McDonald criteria for diagnosing MS include clinical, laboratory, and radiological findings and are used to confirm a definitive diagnosis. First introduced in 2001 and most recently updated in 2017, these criteria allow for earlier diagnosis of MS, especially in patients with CIS, and have shown high sensitivity and accuracy in predicting a second clinical attack. They also help incorporate MRI findings into clinical practice and support more effective treatment plans. Due to the risk of misdiagnosis, the criteria should only be used after carefully ruling out other possible diagnoses [12, 13].

Lesion assessment on MRI in multiple sclerosis

MRI has greatly advanced and simplified diagnosing multiple sclerosis. However, misinterpreting MRI results and incorrectly applying diagnostic criteria can lead to wrong diagnoses. Other conditions may meet MRI criteria for MS, especially when biomarkers are inconclusive. Improved MRI technology allows for more accurate detection of characteristic MS lesions, which often appear as focal hyperintense areas on T2-weighted, T2-FLAIR, and proton density (PD) sequences. These lesions typically appear in both cerebral hemispheres but can be asymmetric in early disease stages. The most common areas of white matter affected include the periventricular, juxtacortical, infratentorial regions, and the spinal cord [14].

Periventricular lesions are T2 hyperintense white matter changes located next to the lateral ventricles, including those within the corpus callosum. They are often spread along deep medullary veins, appear ovoid on axial images, and are called Dawson's fingers. The most sensitive sequence for detecting these lesions is the T2-FLAIR sequence (preferably 3D), as it effectively differentiates lesions from enlarged perivascular spaces. Additional sequences, such as T2-weighted, PD-weighted, and MPRAGE, can help confirm periventricular lesions and distinguish them from age-related changes, especially in the frontal and occipital horns of the ventricles. It is important to recognize that similar-appearing lesions can occur in other neurological conditions; however, these usually do not border directly on the ventricles, are not oriented perpendicularly to them, and are typically not found within the corpus callosum, features that help differentiate true periventricular MS lesions [15-18].

Periventricular lesions in MS can be typical, atypical, or those that do not meet the diagnostic criteria for MS (Figure 1). The green flags in the figure indicate typical periventricular lesions for MS (A), as well as lesions oriented perpendicular to the corpus callosum, known as Dawson's fingers (B). The red flags represent atypical lesions, such as white matter lesions involving both the periventricular region and deep gray matter, which may suggest small vessel ischemic disease (C), or diffuse lesions affecting both white and deep gray matter, which are typical for systemic lupus erythematosus (G) [14].

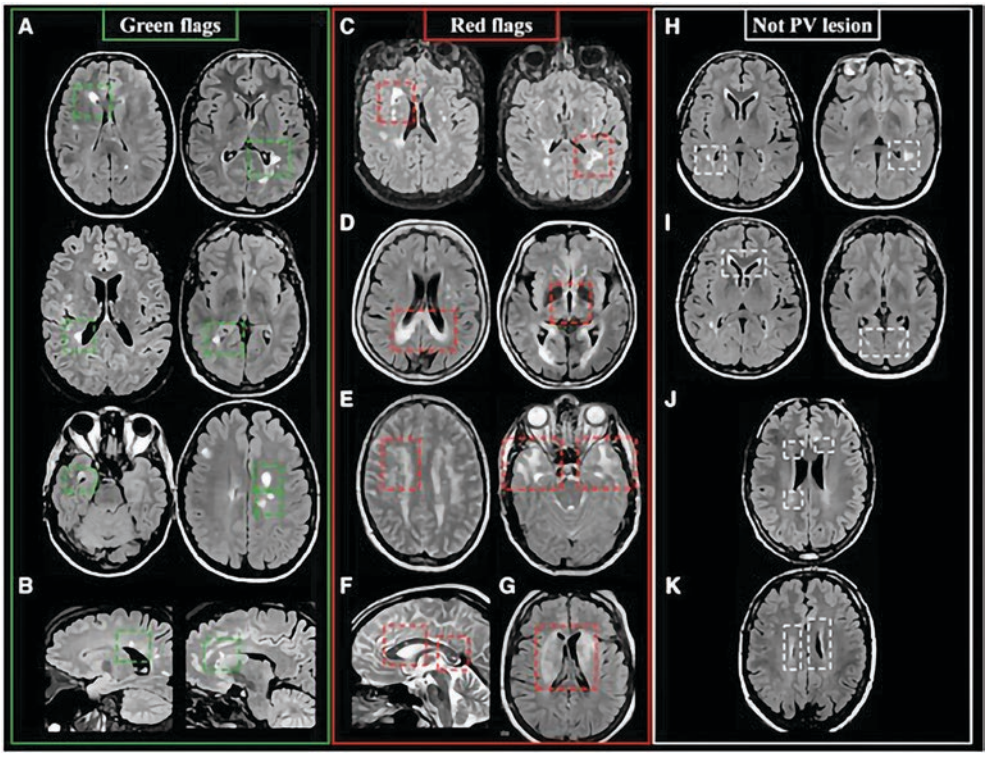

Figure 1. Periventricular lesions in MS
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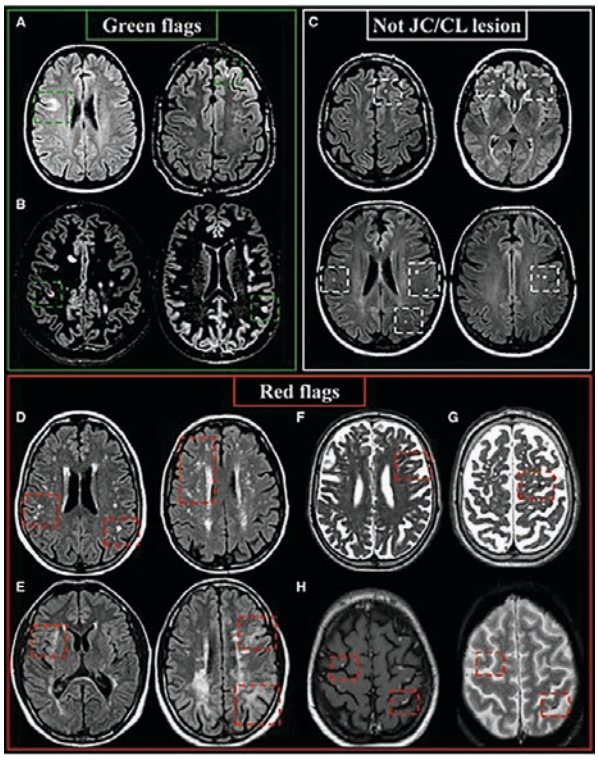

Figure 2. Cortical and Juxtacortical Lesions in MS
Source: https://tinyurl.com/2at32r7y

Juxtacortical lesions are T2 hyperintense white matter changes that are directly adjacent to the cortex but do not involve normal white matter. The optimal sequence for detecting them is 3D T2-FLAIR. These lesions can affect all cerebral lobes, including the cerebellum. Special MRI sequences such as DIR, PSIR, and MPRAGE help in more accurate localization of these lesions. Imaging cortical lesions is challenging due to technical and pathological factors, which is why guidelines exist for their identification. In the DIR sequence, lesions are defined as hyperintense areas larger than three pixels (≥1.0 mm²) compared to healthy gray matter. PSIR and MPRAGE sequences reveal lesions as hypointense relative to the surrounding cortex, affecting part or all of the cortex. Intracortical lesions are confined entirely to the cortex and are divided into several types. Type I lesions, also called leukocortical lesions, involve both the cortex and juxtacortical white matter. Type II lesions are small perivenular lesions within the cortex, without involvement of white matter or the pial surface. Type III lesions are the most common and are characterized by demyelination extending inward from the pial surface. The last type, Type IV lesions, involve the full thickness of the cortex but do not extend into the white matter [19-25].

As with periventricular lesions, the features of cortical and juxtacortical lesions in MS can be typical, atypical, or ones that should not be included (Figure 2). The green flags indicate juxtacortical (A) and cortical (B) lesions that are typical for MS, while the red flags point to atypical lesions, such as hypointensity on T2-weighted sequences suggesting hemosiderin deposition from hemorrhage (G), among others [14].

Infratentorial lesions are defined as T2 hyperintense areas located in the brainstem, cerebellar peduncles, and cerebellum. They are most commonly found near the surface but can also be situated more centrally, where they often have an ovoid shape. In the pontine region, lesions are frequently located near the cisterns, the floor of the fourth ventricle, the surface of the pons, or the entry point of the trigeminal nerve. These lesions can affect any part of the infratentorial white matter and are very often seen in the middle and superior cerebellar peduncles [14].

Regarding the characteristics of infratentorial lesions, they can be either typical or atypical (Figure 3). Green

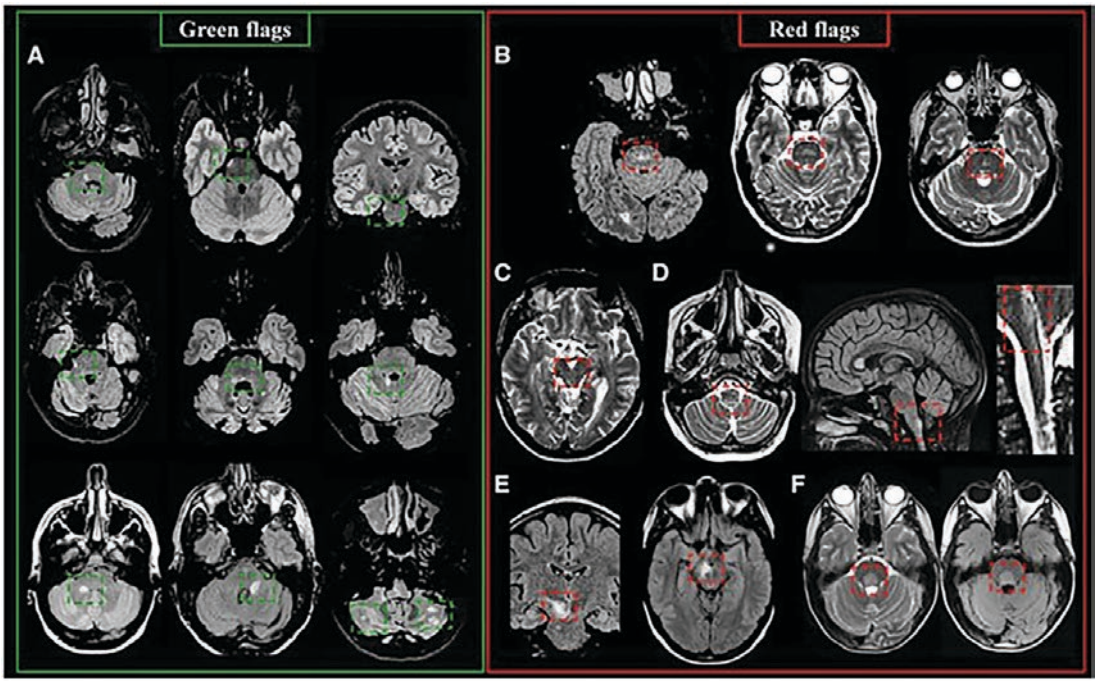

Figure 3. Characteristics of Infratentorial Lesions in MS
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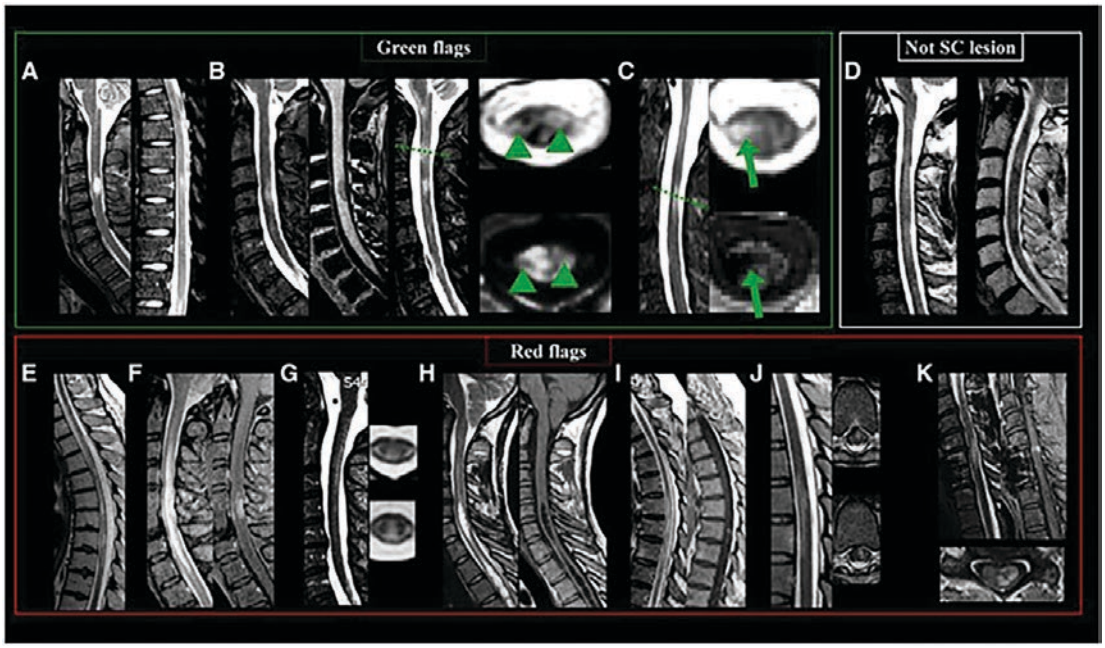

Figure 4. Characteristics of Spinal Cord Lesions in MS
Source: https://tinyurl.com/27ngmoro

flags indicate classic examples of infratentorial lesions in MS (A), while red flags represent atypical examples, such as symmetric central pontine lesions, which may be linked to small vessel disease (B) [14].

Spinal cord lesions in MS can be multiple and are usually short in the cranio-caudal direction. On T2-weighted sequences, they appear hyperintense and are most often found in the cervical region, although they can occur throughout the spinal cord, including the thoracic and lumbar segments. Since they can be mistaken for artifacts, lesions must be visible on at least two different sequences or in two imaging planes to confirm their true presence. The most commonly used sequences are T2 combined with STIR and PD. Lesions may be focal or diffuse (with poorly defined margins), but only focal lesions with clear borders support the diagnosis of MS. On sagittal images, they often look cigar-shaped, while on axial images they tend to have a wedge-like appearance. They usually involve up to two vertebral segments and less than half the cross-sectional area of the spinal cord. On axial views, lesions most often affect the periphery, though they can also extend into the anterior white matter and central gray matter. When using high-field MRI scanners, lesions appear hypointense on T1-weighted sequences, especial-

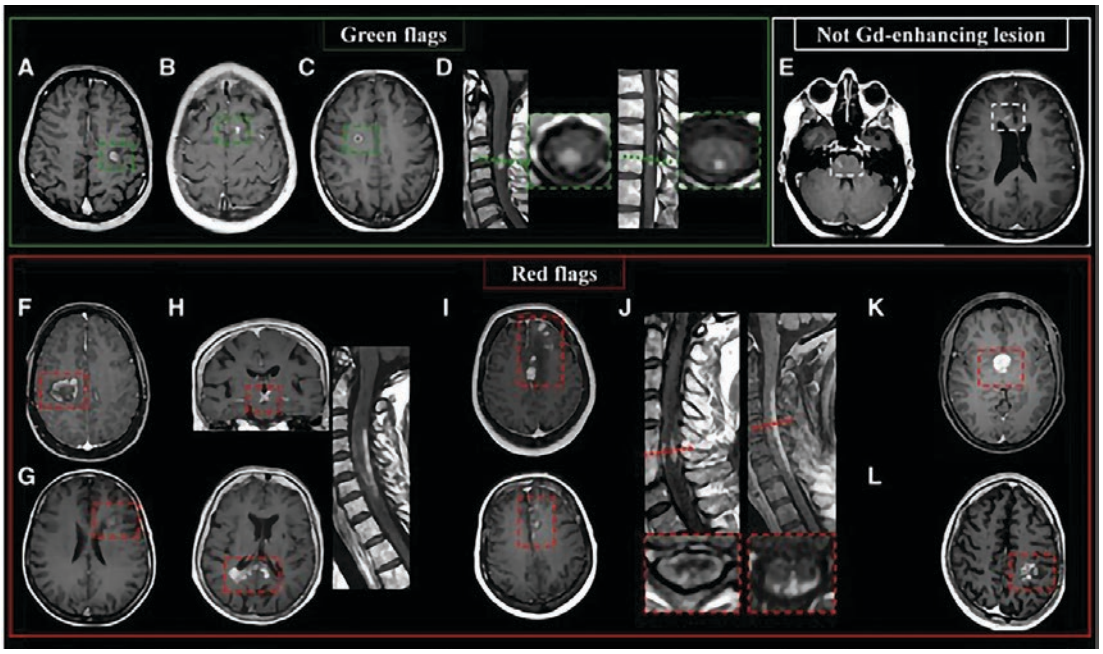

Figure 5. Characteristics of Gadolinium – Enhancing MS Lesions
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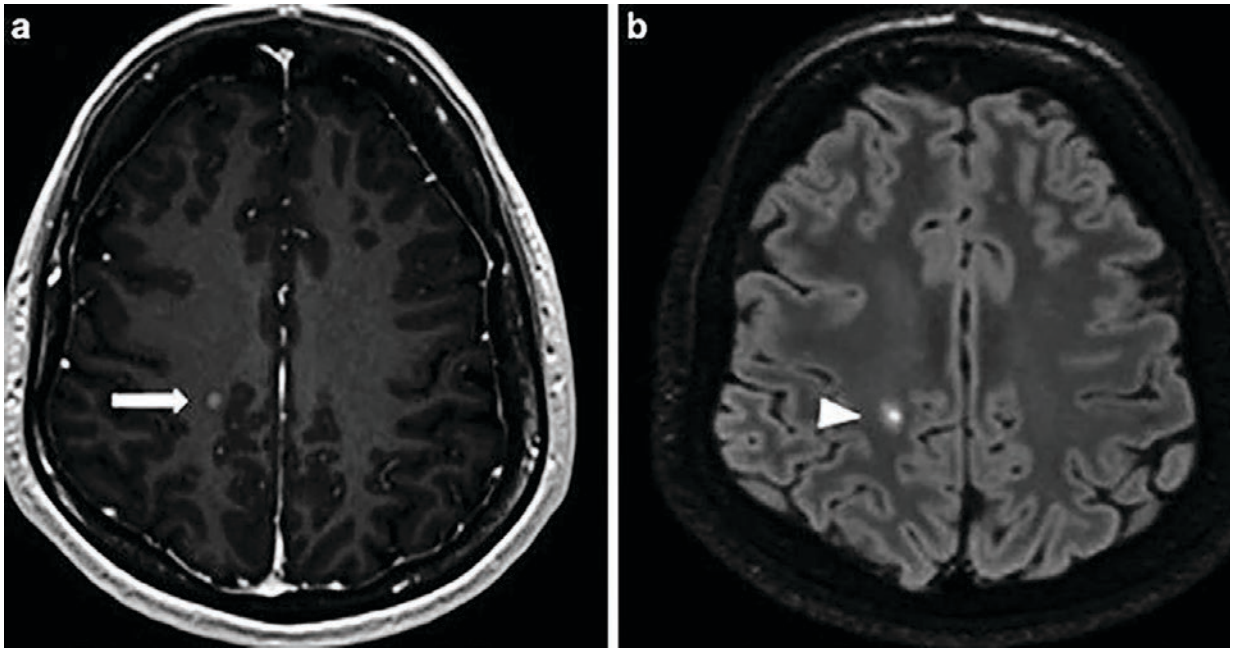

Figure 6. Gadolinium – Enhanced Active Lesion in Juxtacortical White Matter in PPMS
Source: https://tinyurl.com/27fohalh

ly with MPRAGE and PSIR. Unlike other lesions, spinal cord lesions are not typically seen in other neurological conditions such as migraine or cerebrovascular disease [26-30].

The features of spinal cord lesions can be typical, atypical, or those that should not be classified as true MS lesions, such as the diffuse lesions previously mentioned that lack clearly defined borders (D) (Figure 4). Green flags show examples of classic MS spinal cord lesions found in the cervical and thoracic regions (A, B, C). Red flags point out atypical lesions, like a hyperintense lesion spanning two spinal segments, which may suggest subacute ischemic myelopathy (J), among other possibilities [14].

Gadolinium enhancement of lesions is important for assessing patients with suspected multiple sclerosis. These lesions are defined as areas at least 3 mm in size that appear clearly hyperintense on T1-weighted images taken at least five minutes after administering a gadolinium-based contrast agent. They are best seen on T1 spin-echo or GRE sequences. If no corresponding abnormalities are observed on T2 or T2-FLAIR sequences, the hyperintensities are often caused by flow artifacts from nearby blood vessels rather than true lesions [31].

Gadolinium-enhancing lesions can be typical, atypical, or those that should not be considered relevant for diag-

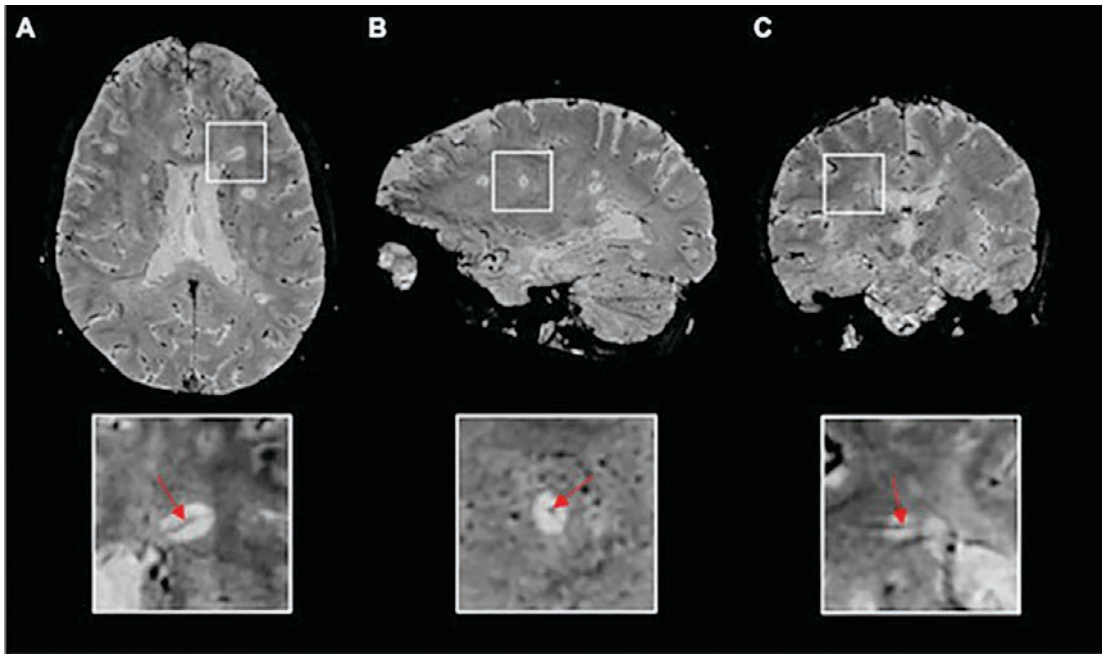

Figure 7. Central vein sign observed on a 3T MRI scan in axial, sagittal, and coronal planes in a patient with RRMS
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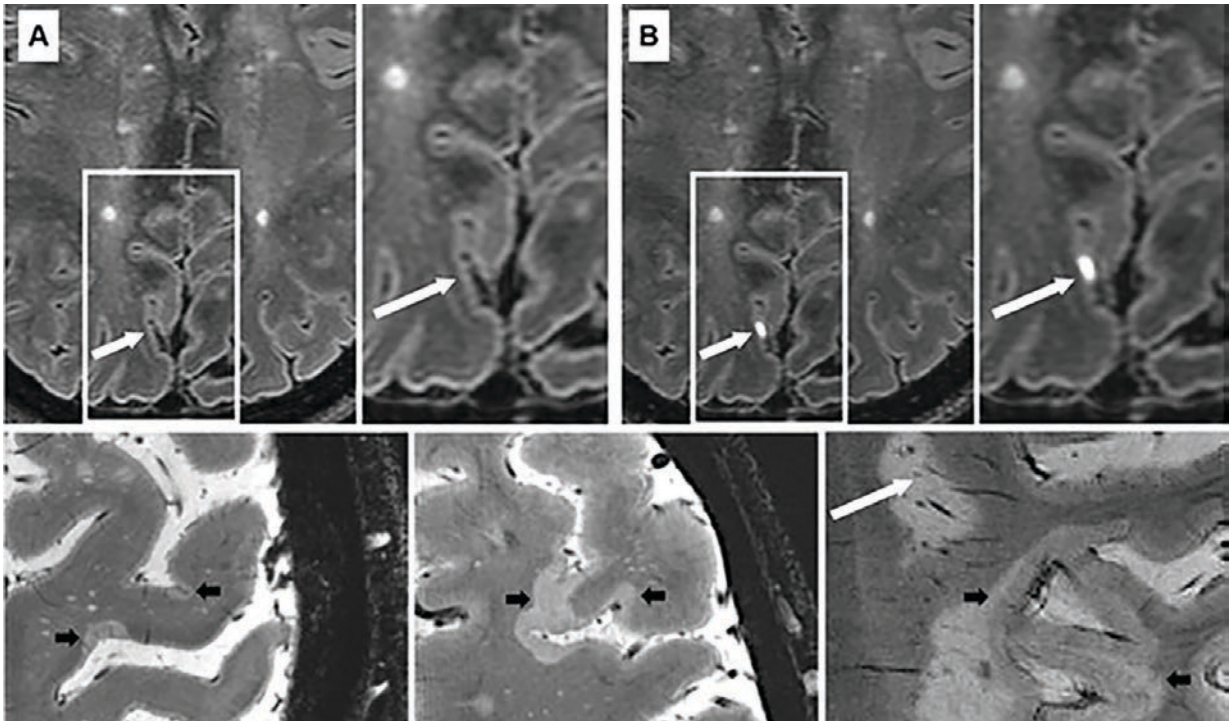

Figure 8. Leptomeningeal enhancement, cortical lesions, and subpial demyelination
Source: https://tinyurl.com/29zcn3ew

nostic criteria (E) (Figure 5). Green flags indicate typical lesions that, when enhanced with gadolinium, support the diagnosis of MS. Red flags represent examples of gadolinium-enhancing lesions that are not typical, such as a heterogeneous enhancing lesion suggestive of glioblastoma (L) [14].

Future diagnostic criteria in multiple sclerosis

Advancements in understanding the pathophysiology of multiple sclerosis are enabling the identification of more precise diagnostic features. These may enhance the speed and accuracy of diagnosis while reducing the risk of misdiagnosis. However, their implementation in clinical practice is still under investigation [13].

Since MS lesions most commonly develop around veins and venules, the central vein sign helps demonstrate this connection. For accurate detection, MRI scanners with a field strength of 7 T are preferred, although the sign can also be seen on 1.5 T and 3 T magnets. Visualization of veins is most effective with high-resolution 3D T2-GRE sequences, often combined with T2-FLAIR imaging. In lower field strength scanners (1.5 T), using gadolinium contrast can be beneficial. The central vein sign appears as a thin hypointense line or dot smaller than 2 mm, visible in at least two planes, with the vein running through the center of the lesion. Lesions larger than 3 mm or those with multiple veins are excluded. This sign is seen in about 80% of MS lesions but is harder to detect in infratentorial, spinal, and periventricular lesions due to the high density of veins in these regions [32, 33].

Subpial demyelination is increasingly recognized as a potential diagnostic feature of MS. Cortical lesions, which can appear early in the disease, are a common substrate for MS development. MRI scanners with a field strength of 7 T have an advantage over those with lower strengths because they provide a higher signal-to-noise ratio (SNR) and submillimeter resolution, enabling better detection of cortical and subpial lesions. Twice as many cortical lesions are detected on 7 T scanners compared to 3 T scanners. Subpial lesions are a specific sign of MS and improve diagnostic accuracy; however, they are not exclusive to MS, as they can also occur in acute disseminated encephalomyelitis. Different stages of the disease require different MRI sequences, with T2-GRE, T2, DIR, FLAIR, and MPRAGE sequences most commonly used at 7 T. Proper interpretation of these findings requires extensive expertise and knowledge, which is why this diagnostic feature is not yet routinely used in clinical practice [14, 34-38].

Leptomeningeal enhancement can serve as an additional feature in diagnosing MS. Perivascular inflammatory infiltrates in the meninges are common across all forms of MS and may indicate meningeal inflammation that contributes to disease progression. Although meningeal inflammation is not clearly visible on post-contrast T1-weighted images, post-contrast FLAIR sequences are highly sensitive to small amounts of gadolinium in the cerebrospinal fluid and can effectively detect leptomeningeal enhancement, up to ten times more effectively than T1 sequences. However, leptomeningeal enhancement is not unique to MS, as it can also occur in other inflammatory neurological conditions [13, 39-41].

Use of artificial intelligence for diagnostic processing of multiple sclerosis

Artificial intelligence (AI) doesn't have a single, exclusive definition; it describes a computer or robot's ability to perform tasks based on human intelligence, such as reasoning, creativity, problem-solving, and more [42].

AI has significant potential to improve the diagnosis and monitoring of MS. The aim is to reduce incorrect or

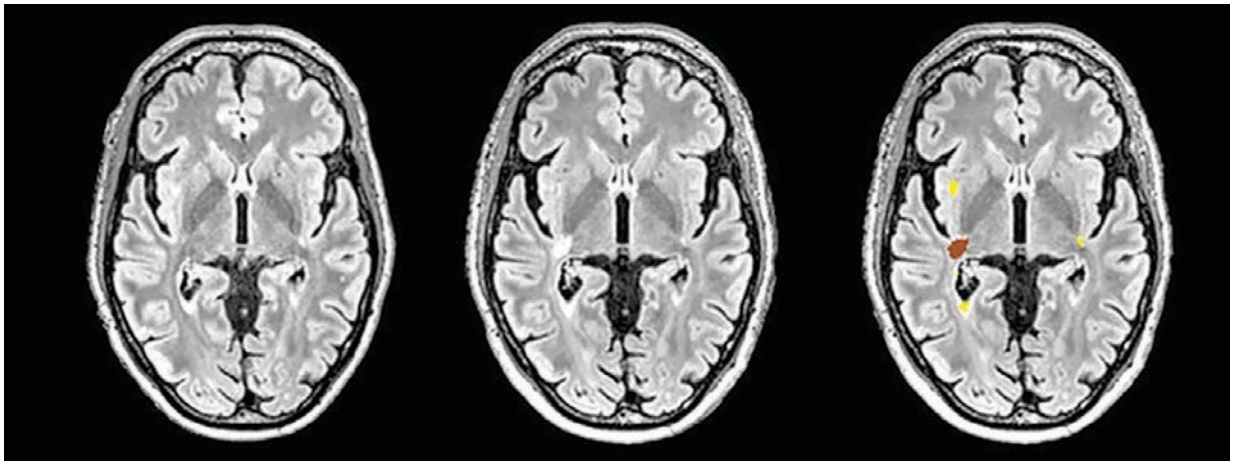

Figure 9. Detection of new MS lesions using the nnU-Net CNN on 3D-FLAIR sequences. Lesions identified at baseline are marked in yellow, while potential new lesions that may develop are marked in brown.
Source: https://tinyurl.com/25ua69h2

delayed diagnoses and to better distinguish MS from other conditions. Using machine learning, AI systems can analyse large datasets and recognize patterns that help differentiate MS types, identify prognostic markers, develop personalized treatments, and monitor disease progression more accurately. For these purposes, MRI data and other clinical information (such as patient speech analysis) are utilized. One important application is automated lesion segmentation on MRI, which plays a critical role in diagnosis and disease tracking. Initiatives like Open MS Data and the MSSEG-2 (Multiple Sclerosis New Lesions Segmentation Challenge) standardize methods for processing MRI data. Most teams employ convolutional neural networks (CNN), with nnU-Net v2 being notable for its accuracy in detecting and distinguishing between new and existing lesions [43-48].

Various studies evaluating machine learning models for diagnosing MS demonstrate good results when the comparison group includes healthy control subjects and patients with confirmed diagnoses. For more practical integration of machine learning models into clinical practice, it is essential to train and validate these models on patients in the early stages of the disease during diagnostic evaluation. Additionally, diagnostic accuracy should be optimized relative to other radiological mimics [43].

The role of the radiologic technologist in MRI

The radiologic technologist is a healthcare professional specializing in the use of diagnostic devices, whose expertise is crucial for obtaining high-quality images. The technologist's responsibilities encompass:

1. **Patient Preparation and Safety:** Reviewing the patient's medical records and history for contraindications (e.g., metal implants), explaining the procedure clearly to ease anxiety, and ensuring patient comfort and safety throughout the process.

2. **Equipment Operation and Optimization:** Operating the MRI equipment, carefully positioning the patient, and placing coils around the target area. The technologist is responsible for optimizing imaging sequences and parameters (e.g., SNR) to achieve the best possible image quality according to standard protocols and clinical needs.

3. **Procedure Execution:** Performing the scanning, often executing additional sequences for more precise diagnosis, and ensuring proper handling and administration of contrast agents in close collaboration with the radiology specialist.

4. **Continuous Education:** Maintaining ongoing education to stay updated on new advancements and rapidly changing technology, which is vital for effective professional development and the accurate application of complex protocols in MS imaging [49–51].

The technologist's skill directly enables the radiology specialist to make an accurate and timely diagnosis, minimizing potential errors.

Conclusion

MRI is the most important and widely used method for diagnosing MS as it allows for the detailed visualization of pathological changes in the brain and spinal cord. Given the varied clinical forms and symptoms of MS, choosing the right MRI sequences is essential for accurately depicting the disease. The radiologic technologist plays an indispensable role in this process; their comprehensive knowledge, technical proficiency, and commitment to ongoing professional development ensure that the high-quality images necessary for accurate interpretation and minimized diagnostic errors are consistently acquired. In the future, the integration of advanced criteria (like the central vein sign) and AI is expected to further speed up and enhance MS diagnosis, though their successful implementation in routine clinical practice will depend on continued research and specialized training.

All data in this paper are part of the results of the undergraduate thesis "The importance of MRI in the diagnosis and monitoring of MS treatment " written at the Faculty of Health Sciences, University of Split [52]. ■

Važnost MR-a u dijagnostici i praćenju liječenja multiple skleroze

Sažetak

Multipla skleroza autoimuna je bolest središnjeg živčanog sustava koja iz godine u godinu pogađa sve više ljudi diljem svijeta. Najvažnija metoda oslikavanja koja pruža najbolju informaciju za dijagnozu i uvid u stanje ove bolesti je magnetska rezonancija. U uvodnom dijelu ovog rada opisana je multipla skleroza kao takva, njeni oblici i simptomi koji se, premda vrlo individualni, najčešće pojavljuju kod pacijenata. Također, opisana je magnetska rezonancija kao tehnika oslikavanja koja je danas ključna za prikaz multiple skleroze upravo zbog mogućnosti vizualiziranja mekotkivnih struktura, kao što su mozak i leđna moždina, u kojima se multipla skleroza pojavljuje. Rasprava daje uvid u prikaz lezija multiple skleroze na magnetskoj rezonanciji te opisuje važnost korištenja različitih sekvenci za razne vrste lezija kako bi se one mogle pravilno razlikovati i samim time definirati. Spominje se umjetna inteligencija kao iskorak u dijagnosticiranju multiple skleroze koji bi se mogao u budućnosti sve više primjenjivati kao alat za brže i preciznije postavljanje dijagnoze. Naposljetku, opisuje se važnost radiološkog tehnologa kao osobe koja je ključna za dobivanje što kvalitetnije slike kako bi ona mogla biti pravilno i precizno očitana.

Ključne riječi: lezije; magnetska rezonancija; multipla skleroza; radiološki tehnolog; sekvence

Literature

1. WebMD. Autoimmune diseases. [accessed 03.05.2025.]. Available at: https://www.webmd.com/a-to-z-guides/autoimmune-diseases
2. National Institute of Allergy and Infectious Diseases (NIAID). Autoimmune diseases. [accessed 03.05.2025.]. Available at: https://www.niaid.nih.gov/diseases-conditions/autoimmune-diseases
3. Haki M, Al-Biati HA, Al-Tameemi ZS, Ali IS, Al-Hussaniy HA. Review of multiple sclerosis: Epidemiology, etiology, pathophysiology, and treatment. Medicine (Baltimore). 2024 Feb 23;103(8)
4. National Institute of Neurological Disorders and Stroke (NINDS). Multiple sclerosis. [accessed 03.05.2025.]. Available at: https://www.ninds.nih.gov/health-information/disorders/multiple-sclerosis
5. National Multiple Sclerosis Society. What causes MS? [Internet]. New York: National MS Society. [accessed 08.05.2025]. Available at: https://www.nationalmssociety.org/understanding-ms/what-is-ms/what-causes-ms
6. Multiple Sclerosis International Federation. Causes of MS [Internet]. London: MSIF. [accessed 08.05.2025.]. Available at: https://tinyurl.com/yr8f2822
7. Multiple Sclerosis International Federation. Types of MS [Internet]. London: MSIF. [accessed 08.05.2025.]. Available at: https://www.msif.org/about-ms/types-of-ms/
8. MS Society UK. Early signs of MS [Internet]. London: MS Society. [accessed 10.05.2025.]. Available at: https://www.mssociety.org.uk/about-ms/signs-and-symptoms/early-signs-of-ms
9. Janković S, Mihanović F, Punda A, Radović D, Barić A, Hrepić D. Radiološki uređaji i oprema u radiologiji, radioterapiji i nuklearnoj medicini. Split: Sveučilište u Splitu; 2015.
10. Cleveland Clinic. Magnetic resonance imaging (MRI) [Internet]. Cleveland (OH): Cleveland Clinic. [accessed 10.05.2025.]. Available at: https://my.clevelandclinic.org/health/diagnostics/4876-magnetic-resonance-imaging-mri
11. National Institute of Biomedical Imaging and Bioengineering. Magnetic resonance imaging (MRI) [Internet]. Bethesda (MD): NIBIB. [accessed 10.05.2025.]. Available at: https://www.nibib.nih.gov/science-education/science-topics/magnetic-resonance-imaging-mri
12. Radiopaedia.org. McDonald diagnostic criteria for multiple sclerosis. [Internet]. Radiopaedia.org. [accessed 26.05.2025.]. Available at: https://radiopaedia.org/articles/mcdonald-diagnostic-criteria-for-multiple-sclerosis-4
13. Filippi M, Preziosa P, Arnold DL, Barkhof F, Harrison DM, Maggi P, Mainero C, Montalban X, Sechi E, Weinshenker BG, Rocca MA. Present and future of the diagnostic work-up of multiple sclerosis: the imaging perspective. J Neurol. 2023 Mar;270(3):1286-1299.
14. Filippi M, Preziosa P, Banwell BL, Barkhof F, Ciccarelli O, De Stefano N, Geurts JJG, Paul F, Reich DS, Toosy AT, Traboulsee A, Wattjes MP, Yousry TA, Gass A, Lubetzki C, Weinshenker BG, Rocca MA. Assessment of lesions on magnetic resonance imaging in multiple sclerosis: practical guidelines. Brain. 2019 Jul 1;142(7):1858-1875.
15. Filippi M, Rocca MA, Calabrese M, Sormani MP, Rinaldi F, Perini P, et al. Intracortical lesions: relevance for new MRI diagnostic criteria for multiple sclerosis. Neurology 2010; 75: 1988–94.
16. Wardlaw JM, Smith EE, Biessels GJ, Cordonnier C, Fazekas F, Frayne R, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol 2013; 12: 822–38.
17. Neema M, Guss ZD, Stankiewicz JM, Arora A, Healy BC, Bakshi R. Normal findings on brain fluid-attenuated inversion recovery MR images at 3T. AJNR Am J Neuroradiol 2009; 30: 911–6.
18. Solomon AJ, Naismith RT, Cross AH. Misdiagnosis of multiple sclerosis: Impact of the 2017 McDonald criteria on clinical practice. Neurology 2019; 92: 26–33.
19. Gramsch C, Nensa F, Kastrup O, Maderwald S, Deuschl C, Ringelstein A, et al. Diagnostic value of 3D fluid attenuated inversion recovery sequence in multiple sclerosis. Acta Radiol 2015; 56: 622–7.
20. Pareto D, Sastre-Garriga J, Auger C, Vives-Gilabert Y, Delgado J, Tintore M, et al. Juxtacortical Lesions and Cortical Thinning in Multiple Sclerosis. AJNR Am J Neuroradiol 2015; 36: 2270–6.
21. Nelson F, Poonawalla A, Hou P, Wolinsky JS, Narayana PA. 3D MPRAGE improves classification of cortical lesions in multiple sclerosis. Mult Scler 2008; 14: 1214–9.
22. Geurts JJ, Roosendaal SD, Calabrese M, Ciccarelli O, Agosta F, Chard DT, et al. Consensus recommendations for MS cortical lesion scoring using double inversion recovery MRI. Neurology 2011; 76: 418–24.
23. Bo L, Vedeler CA, Nyland HI, Trapp BD, Mork SJ. Subpial demyelination in the cerebral cortex of multiple sclerosis patients. J Neuropathol Exp Neurol 2003; 62: 723–32.
24. Sethi V, Yousry TA, Muhlert N, Ron M, Golay X, Wheeler-Kingshott C, et al. Improved detection of cortical MS lesions with phase-sensitive inversion recovery MRI. J Neurol Neurosurg Psychiatry 2012; 83: 877–82.
25. Sethi V, Muhlert N, Ron M, Golay X, Wheeler-Kingshott CA, Miller DH, et al. MS cortical lesions on DIR: not quite what they seem? PLoS One 2013; 8: e78879.
26. Ciccarelli O, Cohen JA, Reingold SC, Weinshenker BG; International Conference on Spinal Cord Involvement and Imaging in Multiple sclerosis. Spinal cord involvement in multiple sclerosis and neuromyelitis optica spectrum disorders. Lancet Neurol 2019; 18: 185–97.
27. Lycklama G, Thompson A, Filippi M, Miller D, Polman C, Fazekas F, et al. Spinal-cord MRI in multiple sclerosis. Lancet Neurol 2003; 2: 555–62.
28. Kearney H, Miszkiel KA, Yiannakas MC, Altmann DR, Ciccarelli O, Miller DH. Zahvaćenost sive tvari fokalnim

lezijama vratne leđne moždine povezana je s progresivnom multiplom sklerozom. Mult Scler 2016; 22: 910–20.

29. Valsasina P, Aboulwafa M, Preziosa P, Messina R, Falini A, Comi G, et al. Cervical Cord T1-weighted hypointense lesions at MR imaging in multiple sclerosis: relationship to cord atrophy and disability. Radiology 2018; 288: 234–44.
30. Kearney H, Altmann DR, Samson RS, Yiannakas MC, Wheeler-Kingshott CA, Ciccarelli O, et al. Cervical cord lesion load is associated with disability independently from atrophy in MS. Neurology 2015; 84: 367–73.
31. Cakirer S, Karaarslan E, Arslan A. Spontaneously T1-hyperintense lesions of the brain on MRI: a pictorial review. Curr Probl Diagn Radiol 2003; 32: 194–217.
32. Sati P, Oh J, Constable RT, Evangelou N, Guttmann CR, Henry RG, et al. The central vein sign and its clinical evaluation for the diagnosis of multiple sclerosis: a consensus statement from the North American Imaging in Multiple Sclerosis Cooperative. Nat Rev Neurol 2016; 12: 714–22.
33. Kilsdonk ID, Wattjes MP, Lopez-Soriano A, Kuijer JP, de Jong MC, de Graaf WL, et al. Improved differentiation between MS and vascular brain lesions using FLAIR* at 7 Tesla. Eur Radiol 2014; 24: 841–9.
34. Kilsdonk ID, Jonkman LE, Klaver R, van Veluw SJ, Zwanenburg JJ, Kuijer JP, et al. Increased cortical grey matter lesion detection in multiple sclerosis with 7 T MRI: a post-mortem verification study. Brain. 2016;139(Pt 5):1472–1481.
35. Junker A, Wozniak J, Voigt D, Scheidt U, Antel J, Wegner C, et al. Extensive subpial cortical demyelination is specific to multiple sclerosis. Brain Pathol. 2020;30(3):641–652. doi: 10.1111/bpa.12813.
36. Jonkman LE, Klaver R, Fleysher L, Inglese M, Geurts JJ. Ultra-high-field MRI visualization of cortical multiple sclerosis lesions with T2 and T2*: a postmortem MRI and histopathology study. AJNR Am J Neuroradiol. 2015;36(11):2062–2067.
37. Fartaria MJ, Sati P, Todea A, Radue EW, Rahmanzadeh R, O'Brien K, et al. Automated detection and segmentation of multiple sclerosis lesions using ultra-high-field MP2RAGE. Invest Radiol. 2019;54(6):356–364.
38. La Rosa F, Beck ES, Maranzano J, Todea RA, van Gelderen P, de Zwart JA, et al. Multiple sclerosis cortical lesion detection with deep learning at ultra-high-field MRI. NMR Biomed. 2022;35(8):e4730.
39. Howell OW, Reeves CA, Nicholas R, Carassiti D, Radotra B, Gentleman SM, et al. Meningeal inflammation is widespread and linked to cortical pathology in multiple sclerosis. Brain. 2011;134(Pt 9):2755–2771.
40. Harrison DM, Wang KY, Fiol J, Naunton K, Royal W, 3rd, Hua J, et al. Leptomeningeal enhancement at 7T in multiple sclerosis: frequency, morphology, and relationship to cortical volume. J Neuroimaging. 2017;27(5):461–468.
41. Absinta M, Cortese IC, Vuolo L, Nair G, de Alwis MP, Ohayon J, et al. Leptomeningeal gadolinium enhancement across the spectrum of chronic neuroinflammatory diseases. Neurology. 2017;88(15):1439–1444.
42. Artificial intelligence. Definition, Examples, Types, Applications, Companies, & Facts [Internet]. Britannica. [accessed 11.06.2025.]. Available at: https://www.britannica.com/technology/artificial-intelligence/Methods-and-goals-in-AI
43. Amin M, Martínez-Heras E, Ontaneda D, Prados Carrasco F. Artificial Intelligence and Multiple Sclerosis. Curr Neurol Neurosci Rep. 2024 Aug;24(8):233-243.
44. Zhang Y-D, Pan C, Sun J, Tang C. Multiple sclerosis identification by convolutional neural network with dropout and parametric ReLU. J Comput Sci. 2018; 28:1–10.
45. Rozenstoks K, Novotny M, Horakova D, Rusz J. Automated assessment of oral diadochokinesis in multiple sclerosis using a neural network approach: Effect of different syllable repetition paradigms. IEEE Trans Neural Syst Rehabil Eng. 2019; 28:32–41.
46. Diaz-Hurtado M, et al. Recent advances in the longitudinal segmentation of multiple sclerosis lesions on magnetic resonance imaging: a review. Neuroradiology. 2022; 64:2103–17.
47. Isensee F, Jaeger PF, Kohl SAA, Petersen J, Maier-Hein KH. nnU-Net: a self-configuring method for deep learning-based biomedical image segmentation. Nat Methods 18, 203–211 (2021).
48. Maggi P, et al. CVSnet: a machine learning approach for automated central vein sign assessment in multiple sclerosis. NMR Biomed. 2020;33: e4283.
49. Mayo Clinic College of Medicine and Science. Magnetic Resonance Imaging (MRI) Technologist [Internet]. Rochester (MN): Mayo Clinic. [accessed 13.06.2025.]. Available at: https://college.mayo.edu/academics/explore-health-care-careers/careers-a-z/magnetic-resonance-imaging-mri-technologist/
50. Smith Chason College. Medical Imaging 101: What Does an MRI Tech Do? [Internet]. Los Angeles (CA): Smith Chason College. [accessed 13.06.2025.]. Available at: https://smithchason.edu/blog/medical-imaging-101-what-does-an-mri-tech-do/
51. CNI College. What Makes a Good MRI Technician? [Internet]. Los Angeles (CA): CNI College. [accessed 13.06.2025.]. Available at: https://cnicollege.edu/blog/careers/what-makes-good-mri-technician/
52. Mihanović M. Važnost MR-a u dijagnostici i praćenju liječenja mulitple skleroze (Undergraduate thesis). Split: Faculty of Health Sciences, University of Split; 2025 (accessed 1.9.2025.) Available at: https://repo.ozs.unist.hr/islandora/object/ozs%3A1910/datastream/PDF/view