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Overview of Roles of MRI in the Diagnosis and Evaluation of Multiple Sclerosis

[1]Ibrahim Abdulrhman Hamed Alazwari, [2]Mohammed Hassan Almalki,
[3]Waleed Abdullah Alzahrani, [4]Yasser Yahya Alzahrani, [5]Ftayes Saeed Kadasah,
[6]Abdulhadi Salem Towairqi

Abstract: **The aim of this review study was to overview the role of MRI in the diagnosis and severity evaluation of multiple sclerosis (MS). We conducted a narrative search using electronic databases; Medline, PubMed, Embase, and Scopus from their inception dates up to end of 2016. Studies that reporting roles of MRI in detection and evaluation of multiple sclerosis were included in this review. Keywords used for the PubMed search included the medical terms as following: "multiple sclerosis" along with "magnetic resonance imaging". Restriction to English language and human subjected published articles was applied during our search. In the diagnostic procedure of patients with believed multiple sclerosis, use of post-contrast series provides essential details for differential medical diagnosis. MRI stays a valuable tool for recognition of children and adults with numerous sclerosis, both at the time of an incident attack when applied serially to verify the chronic nature of this disease. Advanced imaging strategies provide info about local CNS participation with greater level of sensitivity than standard MRI and might contribute to diagnostic uniqueness. Whether MRI features constant with multiple sclerosis in the absence of medical involvement can confirm several sclerosis medical diagnosis stays an area of argument that requires further study and deliberation, specifically in view of proof that some such individuals have international and focal loss of tissue stability however are not eligible for multiple-sclerosis-directed therapies at present.**

Keywords: **Multiple Sclerosis (MS), MRI, Medical Involvement.**

1. INTRODUCTION

Multiple sclerosis (MS), a chronic inflammatory, demyelinating disease of the central nervous system (CNS) that is typically thought about to be autoimmune in nature. White matter tracts are affected, consisting of those of the cerebral hemispheres, infratentorium, and spine. MS lesions, called plaques, may form in CNS white matter in any location; thus, scientific discussions may vary. Continuing lesion development in MS frequently leads to physical disability and, sometimes, to cognitive decline [(1)]. Magnetic resonance imaging (MRI) has actually played an expanding and unique role in the medical diagnosis and management of numerous sclerosis (MS), since the beginning of its application by Young et al. in this field [(2,3)]. Actually the initial examination of a patient believed of MS begins with MRI due to its charming level of sensitivity to depict focal white matter irregularities and medically silent sores. In spite of their constraints to show scattered damage to the white matter, neuroaxonal degeneration and irreversible demyelination, traditional T2-weighted and contrast enhanced T1-weighted images are currently the basic assessment techniques to verify or decline the scientific diagnosis [(4)]. MRI is also utilized as a prognostic tool at the first presentation in patients with medically separated syndrome (CIS) [(5,6)]. Typical sores are typically little, round or oval in shape and may occur in any part of the main nerve system where myelin exists. These sores are more regular in periventricular location, but infratentorial and juxtacortical regions are other common sites of involvement (**Figure 1**). MS is a white matter disease 5 - 10% of the sores may involve the gray matter (GM) consisting of cerebral cortex and basal ganglia [(7)]. GM lesions are typically little with intermediate high signal strength and a less sever degree of inflammation, which might trigger the obscure look of GM sores on MR imaging compared to that of white matter sores [(8)].

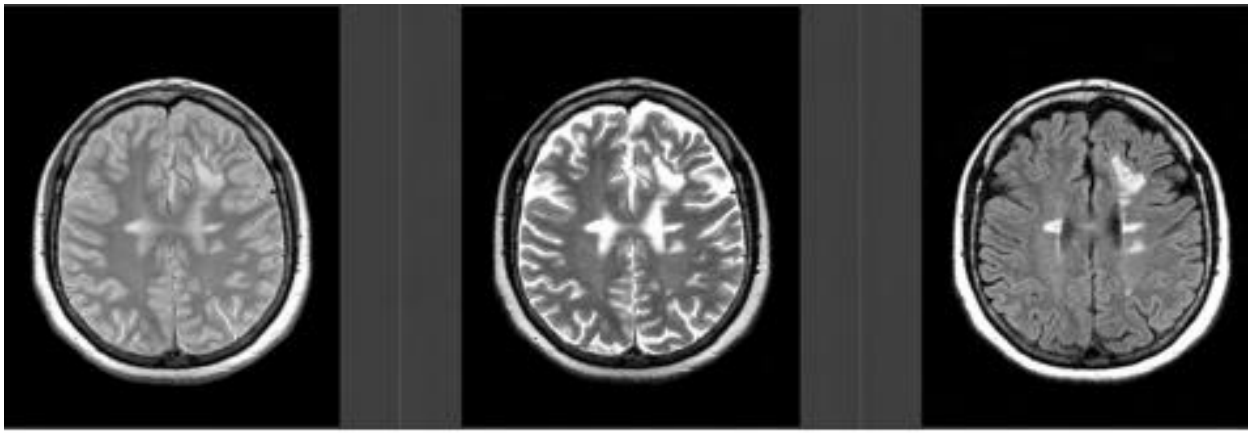

Figure 1: fluid attenuated inversion recovery (FLAIR) images illustrating the clinico-radiological paradox of multiple sclerosis, of relapsing remitting multiple sclerosis (RRMS) patient.

The aim of this review study was to overview the role of MRI in the diagnosis and severity evaluation of multiple sclerosis (MS).

2. METHODOLOGY

We conducted a narrative search using electronic databases; Medline, PubMed, Embase, and Scopus from their inception dates up to end of 2016. Studies that reporting roles of MRI in detection and evaluation of multiple sclerosis were included in this review. Keywords used for the PubMed search included the medical terms as following: "multiple sclerosis" along with "magnetic resonance imaging". Restriction to English language and human subjected published articles was applied during our search.

3. RESULTS

- **Diagnosis procedures of MS:**

MRI was officially included in the diagnostic work-up of patients presenting with a clinically separated syndrome suggestive of numerous sclerosis in 2001 by a worldwide panel of specialists [8]. Diagnosis of several sclerosis relies on proof of disease dissemination in space and time and exclusion of other disorders that can simulate multiple sclerosis by their scientific and laboratory profile. MRI can support and substitute clinical info for multiple sclerosis diagnosis, allowing an early and precise medical diagnosis and, as such, early treatment. MRI requirements for multiple sclerosis are based on the existence of focal lesions in the white matter of the CNS, which are thought about common for this disorder in terms of distribution, development, morphology, and signal abnormalities on standard MRI sequences (eg, T2-weighted and T2-weighted fluid-attenuated inversion healing (FLAIR) scans, and pre-contrast and post-contrast T1-weighted scans) [9,10,11]. In 2005 modified McDonald criteria1 have a simpler technique to dissemination in time, and more recently, an additional simplification has actually been proposed in regards to dissemination in time and area [12,13]. These more current criteria have actually been found to be slightly more sensitive than the initial 2001 McDonald criteria3 and the 2005 modified criteria,1 while keeping high specificity [12,13]. Hence, these requirements may enable a trustworthy diagnosis of MS to be made during the year after start of a typical clinically isolated syndrome suggestive of MS. The primary advantage of the newest requirements is that they do not need using contrast representatives, therefore saving both time and cost [12]. The downside is the minor loss of differential diagnostic info, and consequently they need to be used with care in older patients. The difficulties to be addressed consist of the provision of much better evidence for figuring out the accurate function of sores seen on conventional MRI of the spinal cord and assessment of the value of these diagnostic criteria in potential research studies in non-specialist centres. More contributions from MRI might come from the capability to determine the degree of tissue damage, including scattered modifications in the normal-appearing white matter, and the potential for the higher level of sensitivity of higher field systems to more subtle problems [14].

- **Roles of MRI in detection and evaluation of MS:**

The diagnostic role of MRI in MS has to a particular degree overshadowed the fantastic capacity of MRI for disease and treatment monitoring of MS patients. In recent years, there has been considerable advancement in knowledge in this field

of research, particularly with regard to alternative MRI approaches and the concept of prediction of treatment efficacy and treatment safety monitoring. The capacity of MRI measures in monitoring and examining treatment efficacy is increasingly being recognized and valued. With approval of the new and more effective generation of MS therapeutics, the spectrum of MRI in treatment monitoring has ended up being more comprehensive, including the detection of opportunistic infections and paradoxical reactions (e.g., tumefactive demyelination). In addition, the development of immunomodulating drugs, which concentrate on alternative pharmacodynamic paths for preventing MS disease progression (e.g., remyelination), need brand-new imaging methods to keep track of disease activity [(15)]. Brain MRI need to be carried out at a minimum magnetic field strength of 1.5 T (T) while 3 T MRI reveals increased level of sensitivity to focal MS sore due to improved image resolution and signal-to-noise ratio, and therefore is advised [(16)]. Although it has actually been conclusively demonstrated that higher magnetic field strengths (e.g., 3 T) do reveal improved sensitivity for white matter (WM) and grey matter (GM) lesions in scientifically isolated syndrome (CIS) and MS patients as compared to basic field strengths (1.5 T), this does not have any consequences in terms of a possible earlier medical diagnosis of MS [(17)]. Standard MRI assessment of lesions on non-contrast T1-weighted and T2-weighted images, and on gadolinium-enhanced T1-weighted images, offers a crucial tool to monitor the disease course [(18)]. The restrictions of standard MRI consist of the weak associations with scientific status and the lack of sensitivity to other clinically appropriate findings, such as grey-matter disease and scattered damage throughout the white matter [(19,20)].

New methods have actually emerged in the locations of information management and post-processing. One approach includes the serial analysis of images to study vibrant pixel-wise signal modifications connected to sore development [(21)]. Through this technique, modifications in the progression pattern within specific sores may indicate an overarching shift of the patient's disease from more inflammatory to more degenerative pathological procedures, possibly heralding the introduction of atrophy and scientific disability [(21)]. Another related approach, referred to as subtraction imaging, displays modifications over time in between two scans in a single map [(22)]. This offers increased level of sensitivity to sore advancement compared with qualitative analysis (**Figure 2**). Lesion-based measures can be combined with innovative MRI measures of tissue stability, such as 1H-MRS, diffusion imaging, and magnetization transfer imaging, using voxel-wise likelihood maps and spatial circulation approaches.

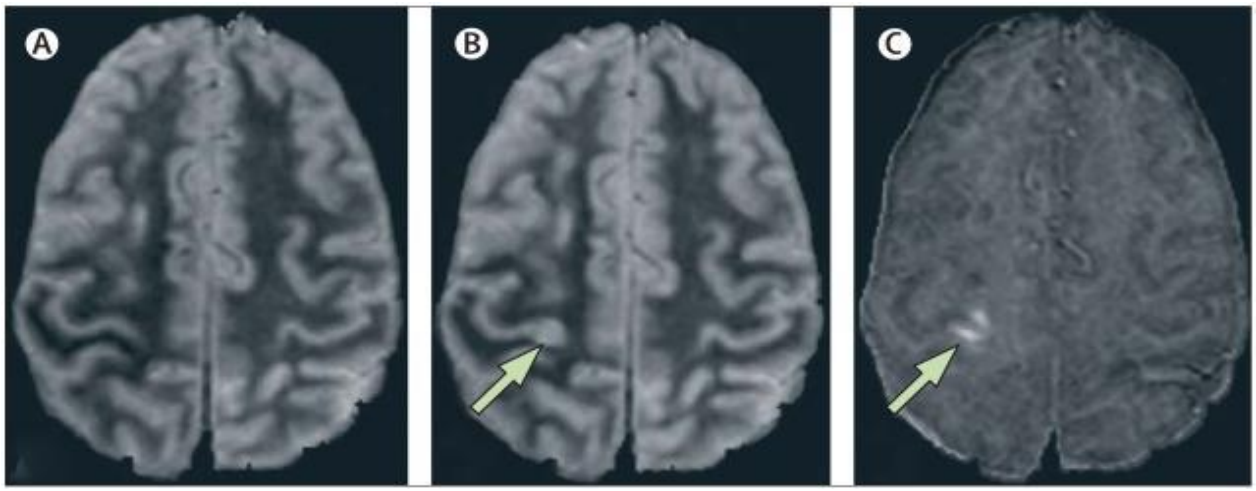

Figure 2: Lesion change in MS over time by use of a subtraction method involving image normalization, comparing the baseline (A) to follow-up scan (B), but is clearly visible on the subtraction image (C)

On traditional MRI scans, the enhancement of lesions by gadolinium injection indicates the build-up of the contrast representative in the interstitial area due to increased blood-- brain barrier permeability. Presently, there is a significant effort to discover biological markers of MS, especially cell subsets and particles that are necessary to the pathophysiology of MS. New MRI contrast representatives composed of iron particles, ultra-small particles of iron oxide, or super-paramagnetic iron particles of oxide have been utilized in patients with MS to track macrophages (**Figure 3**) [(23,24)]. Two MRI studies of patients with RRMS that utilized ultra-small particles of iron oxide and gadolinium have actually verified a mismatch of improvement, suggesting heterogeneity of the underlying pathology [(23,24)]. The complementary info supplied by tracking macrophages with iron particles might play a special part in the monitoring of the effectiveness of drugs targeting the cellular components of inflammation.

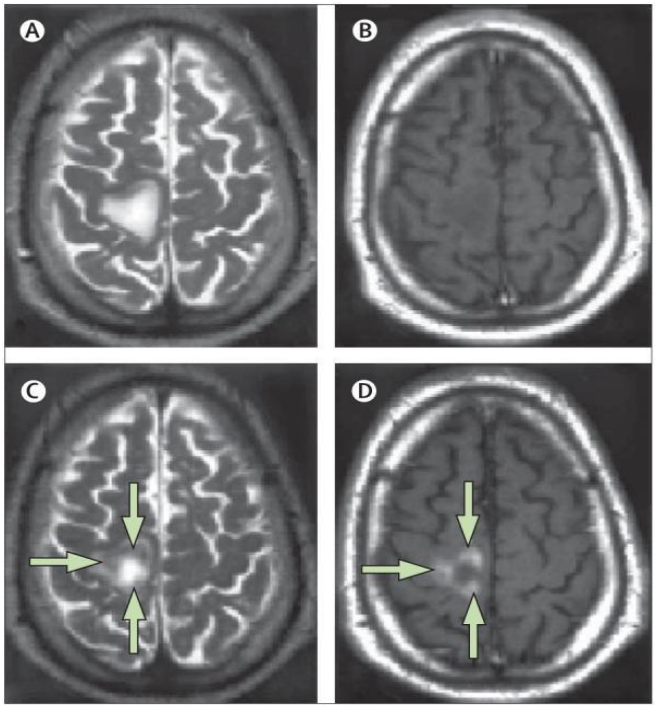

Figure 3: The lesion is hyperintense on the spin-echo T2-weighted image (A), but does not enhance with gadolinium on the T1-weighted image (B).

As a result of its high sensitivity to focal inflammatory demyelinating sores, MRI has a important but also challenging role in especially the early MS disease course. This issues in particular the establishment of an early (delicate), but likewise a particular, medical diagnosis based upon disease dissemination in space (DIS) and in time (DIT). MRI has the ability to find MS disease activity with focal sores in the brain and/or spinal cord while the patient may never have actually experienced any symptoms and therefore does not officially satisfy the McDonald criteria for MS (**Figure 4**). This has actually resulted in the idea of radiologically separated syndrome (RIS). RIS patients do reveal a higher risk for establishing a CIS suggestive of MS (patient-reported or objectively observed occasions common of an acute inflammatory demyelinating event in the CNS, historic or present, with duration of at least 24 h) and later on MS [(25)]. In order to correctly categorize those patients with incidental brain sores suggestive of MS pathology, current diagnostic criteria for RIS have actually been proposed. These criteria consist of the number, place, and shape of the brain lesions [(26)].

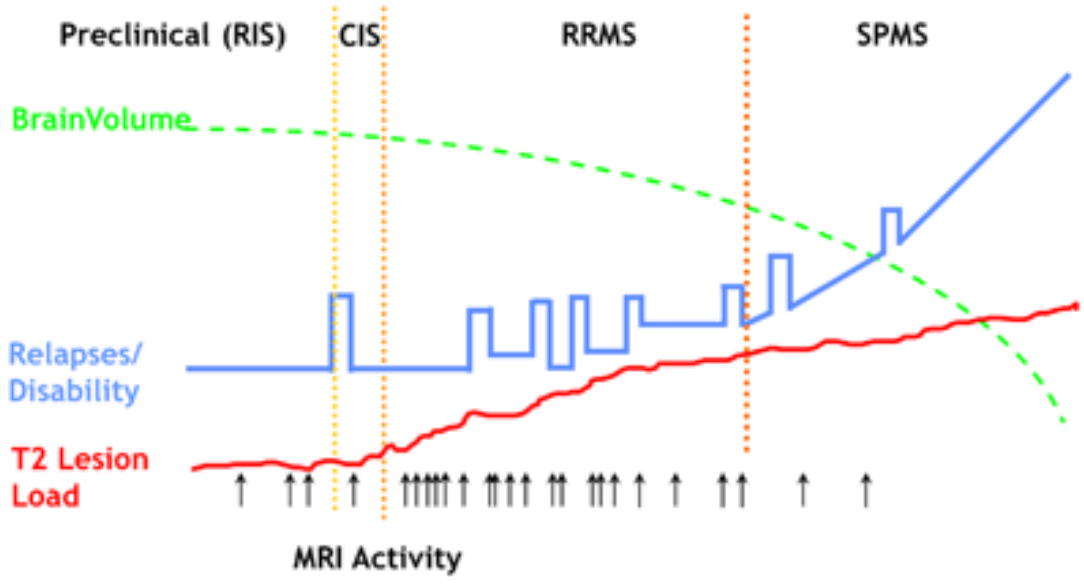

Figure 4: Magnetic resonance imaging (*MRI*) concept of multiple sclerosis in the context of disease course and clinical outcome measures. *RIS* radiologically isolated syndrome *CIS* clinically isolated syndrome.

MRI evaluation of MS Cortical lesions:

Results of pathology studies have shown comprehensive participation of the grey matter in numerous sclerosis [27,28]. Inning accordance with their location within the grey matter, various cortical lesion areas (subpial, purely intracortical, and leukocortical sores on the grey matter-- white matter border) have been identified [27]. Imaging cortical sores is challenging, specifically with conventional clinical MRI protocols. Different MRI methods have actually been proposed and are being compared for their sensitivity for cortical lesion detection, consisting of double inversion healing, [29] phase-sensitive inversion recovery, [30,31] and magnetization-prepared fast acquisition with gradient echo series (**Figure 5**). In spite of use of these strategies, results of correlative MRI pathology studies have actually shown that lots of cortical sores stay invisible on MRI, a minimum of with 1 · 5 T and 3 · 0 T MRI scanners [32,33]. With double inversion healing series, cortical sores have been determined in more than 30% of patients with a clinically separated syndrome [34]. In a friend of 80 patients with a clinically isolated syndrome, with 4-year follow-up, the accuracy of MRI diagnostic requirements for multiple sclerosis increased when the presence of a minimum of one intracortical lesion on standard scans was considered [34]. Cortical lesion evaluation may also aid with differential medical diagnosis in between numerous sclerosis and conditions that simulate numerous sclerosis, since cortical lesions have actually not been reported in patients with migraine with white matter T2 lesions32 or neuromyelitis optica [35]. Intracortical lesions are also uncommon in healthy controls (determined in one of 30 people who were scanned with phase-sensitive inversion recovery series) [30]. Even with these promising results, numerous unsolved problems stay concerning inclusion of cortical sore evaluation in the diagnostic work-up of patients with a medically isolated syndrome. MRI series used in research study settings for recognition of these lesions might not be readily available and quickly implementable on the majority of scientific scanners. Second, the acquisition criteria for these series still need to be standardised across scanning systems from various producers and for numerous field strengths. Third, arrangement amongst observers in assessment of these series is at finest moderate (total contract 19% for double inversion recovery), and guidelines for their evaluation are changing [30]. Fourth, different requirements and terms are used by different research study groups for the distinction between intracortical, leukocortical, combined white matter and grey matter, and juxtacortical sores [28,34].

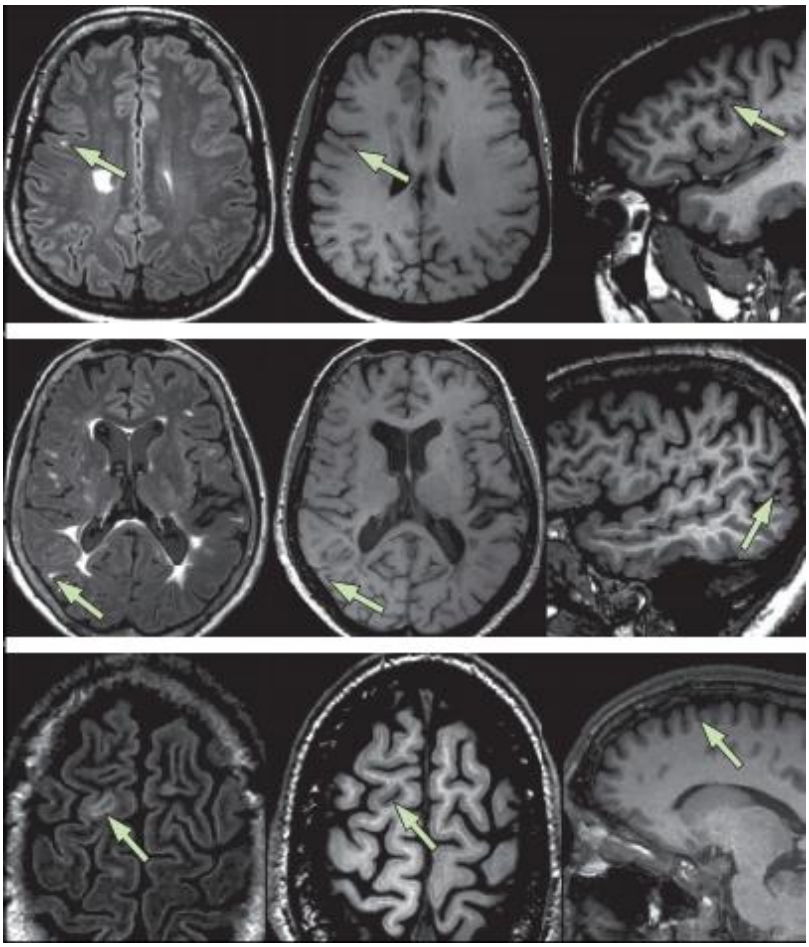

Figure 5: Cortical and juxtacortical lesion detection with MRI

4. CONCLUSION

In the diagnostic procedure of patients with believed multiple sclerosis, use of post-contrast series provides essential details for differential medical diagnosis. MRI stays a valuable tool for recognition of children and adults with numerous sclerosis, both at the time of an incident attack when applied serially to verify the chronic nature of this disease. Advanced imaging strategies provide info about local CNS participation with greater level of sensitivity than standard MRI and might contribute to diagnostic uniqueness. Whether MRI features constant with multiple sclerosis in the absence of medical involvement can confirm several sclerosis medical diagnosis stays an area of argument that requires further study and deliberation, specifically in view of proof that some such individuals have international and focal loss of tissue stability however are not eligible for multiple-sclerosis-directed therapies at present.

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