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Role of Different Magnetic Resonance Imaging Pulse Sequences in Assessment of Patients with Multiple Sclerosis

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Abstract

Magnetic resonance imaging (MRI) plays an important role in the diagnosis of multiple sclerosis and has been incorporated into the McDonald diagnostic criteria for MS. Additionally, MR has proven useful for studying the natural history of the disease and monitoring the effects of new treatments. Selective identification of lesions that contribute most to the patient's disability and clinical progression can be better achieved by using newer imaging techniques which are more sensitive in identifying abnormalities of the central nervous system related to MS and may facilitate prediction of neurologic impairment and evaluation of response to disease-modifying therapy in the future.

Keywords: Magnetic resonance imaging, Multiple sclerosis, McDonald diagnostic criteria.

1. Introduction

Multiple sclerosis (MS) is a chronic, persistent inflammatory–demyelinating disease of the central nervous system (CNS), more prevalent in women than men [3 - 4 times], between the ages of 20-50 years, characterized pathologically by areas of inflammation, demyelination, axonal loss, and gliosis scattered throughout the CNS with a predilection for the optic nerves, brainstem, spinal cord, and cerebellar and periventricular white matter, although cortical and subcortical gray matter damage is also prominent [1]. In addition to clinical presentation and examination of the cerebrospinal fluid, imaging, in particular magnetic resonance imaging (MRI), plays an important role in the diagnosis and disease monitoring of MS [2, 3].

The first important role for MRI in the diagnosis of MS allows for an early diagnosis of MS, The second important role for MRI in the diagnostic work-up of suspected MS patients is to rule out alternative diagnoses obvious on MRI, such as spinal stenosis and most brain tumors[4].

Multiple sclerosis is typically diagnosed based on the presenting signs and symptoms, in combination with supporting medical imaging and laboratory testing [5] It can be difficult to confirm, especially early on, since the signs and symptoms may be similar to those of other medical problems.[6] The McDonald criteria, which focus on clinical, laboratory, and radiologic evidence of lesions at different times and in different areas, is the most commonly used method of diagnosis, While the above criteria allow for a non-invasive diagnosis, some state that the only definitive proof is an autopsy or biopsy where lesions typical of MS are detected [7].

2. Diagnostic criteria of MS

Diagnostic criteria for multiple sclerosis (MS) include clinical and paraclinical laboratory assessments emphasizing the need to demonstrate dissemination of lesions in space (DIS) and time (DIT) and to exclude alternative diagnoses. Although the diagnosis can be made on clinical grounds alone, magnetic resonance imaging (MRI) of the central nervous system (CNS) can support, supplement, or even replace some clinical criteria, as most recently emphasized by the so-called McDonald Criteria of the International Panel on Diagnosis of MS. The McDonald Criteria have resulted in earlier diagnosis of MS with a high degree of both specificity and sensitivity, allowing for better counseling of patients and earlier treatment.[8] Fig (1, 2 and 3).

DIS Can Be Demonstrated by ≥1 T2 Lesion[a] in at Least 2 of 4 Areas of the CNS:
Periventricular
Juxtacortical
Infratentorial
Spinal cord[b]

Based on Swanton et al 2006, 2007.[22,27]
[a]Gadolinium enhancement of lesions is not required for DIS.
[b]If a subject has a brainstem or spinal cord syndrome, the symptomatic lesions are excluded from the Criteria and do not contribute to lesion count.
MRI = magnetic resonance imaging; DIS = lesion dissemination in space; CNS = central nervous system.

Fig (1) 2010 McDonald MRI Criteria for Demonstration of DIS

DIT Can Be Demonstrated by:
1. A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI
2. Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time

Based on Montalban et al 2010.[24]
MRI = magnetic resonance imaging; DIT = lesion dissemination in time.

Fig (2) 2010 McDonald MRI Criteria for Demonstration of DIT

Clinical Presentation	Additional Data Needed for MS Diagnosis
≥2 attacks[a]; objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack[b]	None[c]
≥2 attacks[a]; objective clinical evidence of 1 lesion	Dissemination in space, demonstrated by: ≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord)[d]; or Await a further clinical attack[a] implicating a different CNS site
1 attack[a]; objective clinical evidence of ≥2 lesions	Dissemination in time, demonstrated by: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack[a]
1 attack[a]; objective clinical evidence of 1 lesion (clinically isolated syndrome)	Dissemination in space and time, demonstrated by: For DIS: ≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord)[d]; or Await a second clinical attack[a] implicating a different CNS site; and For DIT: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack[a]
Insidious neurological progression suggestive of MS (PPMS)	1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria[d]: 1. Evidence for DIS in the brain based on ≥1 T2 lesions in the MS-characteristic (periventricular, juxtacortical, or infratentorial) regions 2. Evidence for DIS in the spinal cord based on ≥2 T2 lesions in the cord 3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index)

Fig (3) The 2010 McDonald Criteria for diagnosis of MS

The 2010 revisions to the McDonald Criteria will in some instances allow a more rapid diagnosis of MS, with equivalent or improved specificity and/or sensitivity compared with past Criteria and will in many instances clarify and simplify the diagnostic process with fewer required MRI examinations. A proportion of patients with nonspecific symptoms(eg, fatigue, weakness, or dizziness) and nonspecific MRI findings are referred to secondary and tertiary MS centers in the developed world for a second opinion and do not in fact have MS. These revised McDonald Criteria for MS diagnosis should therefore be applied only when patients have experienced a typical clinically isolated syndrome (or progressive paraparesis / cerebellar / cognitive syndrome in the case of suspected PPMS) [8].

3. MR imaging of Multiple sclerosis

3.1 Conventional MRI

Conventional MRI assessment of lesions on non-contrast T1-weighted and T2-weighted images, and on gadolinium-enhanced T1-weighted images, provides an important tool to monitor the disease course [9].

Compared with other techniques, non-enhanced T1-weighted MRI is far less sensitive in detecting MS lesions. the acute MS lesions are often isointense to the normal white matter but can be hypointense or localized leukomalacia if chronic tissue injury or severe inflammatory edema occurs (so-called black holes) [10] Fig (4).

post gadolinium T1-weighted study is most helpful for detecting acute, active MS lesions associated with BBB disruption. [11] There are 2 patterns of enhancement: uniform enhancement, reflecting the onset of a new lesion, and ringlike enhancement, indicating reactivation of an older lesion. Nonenhancing lesions are the result of earlier episodes of disease[12], Fig (5).

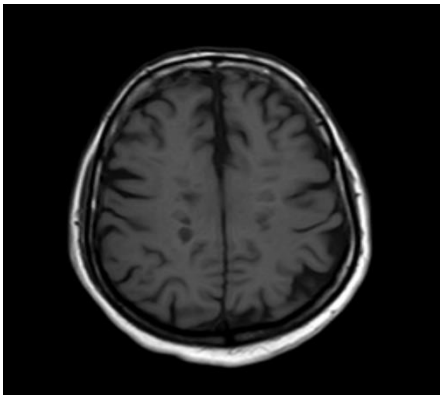

Fig (4) chronic stage in MS T1WI

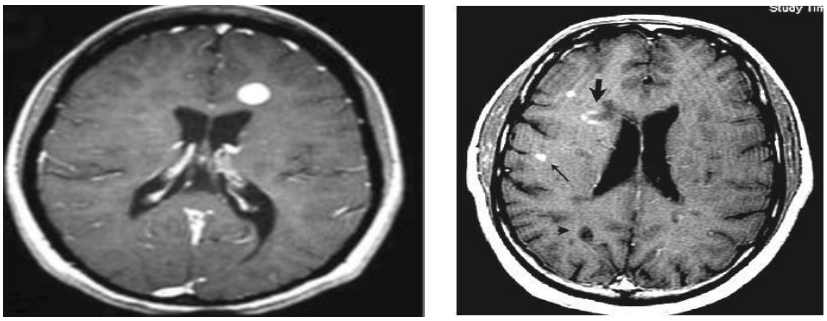

Fig (5) patterns of enhancement.

T2-weighted MR imaging is considered the most sensitive diagnostic test for demonstrating disease dissemination, but with moderate specificity. Acute-phase plaques appear as rounded areas of high-signal intensity on T2 sequences [12] MS lesions often appear on T2 MRI images as ovoid-shaped periventricular white matter lesions oriented perpendicular to the ventricular surface (Dawson's fingers) [13] Fig (6).

Proton density (PD)–weighted MRI has an advantage over standard T2 imaging, because on PD series, MS lesions remain hyperintense, while the CSF signal is suppressed. Therefore, the lesions are easily identified.[14].

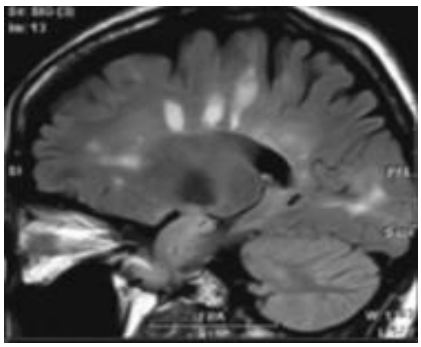

Fig (6) Dawson's fingers of MS T2WI

3.2 Newer MRI pulse sequences

FLAIR MRI is a heavily T2-weighted technique that dampens the ventricular (ie, free-water) CSF signal. Thus, the highest signals on the sequence are from certain brain parenchymal abnormalities, such as MS lesions, while the CSF appears black. FLAIR has been shown to be superior to PD-weighted sequences in the detection of MS lesions in the cerebral hemispheres. However, PD-weighted imaging remains the investigation of choice for infratentorial lesions [15].

Among the advanced techniques Diffusion weighted MRI, which is more specific to the underlying pathologic substrates of the disease and more sensitive to the full extent of ‘occult’ tissue damage in patients with MS. Diffusion measures the microscopic Brownian motion of water molecules.[16] water molecules move more easily parallel to tracts and are restricted in their

movement perpendicular to highly organized myelin fiber tracts [17].

Typically, MS plaques show increased mean diffusivity (MD) or ADC values and decreased fractional anisotropy (FA) when compared with the contralateral normal-appearing white matter. The ADC is especially high in contrast-enhancing lesions and T1-hypointense lesions.[18] The increased MD, increased ADC, and decreased FA is most likely nonspecific for the underlying pathology and reflects a variety of tissue changes, such as demyelination, gliosis, inflammation, axonal contraction, and axonal loss. A transient decrease in ADC values may occur in acute MS plaques, and likely reflect swelling of the myelin sheaths, reduced vascular supply leading to cytotoxic edema, or dense inflammatory cell infiltration [19].

4. Aim of the study

The aim of our study is to assess the role of different MRI pulse sequences in the diagnosis, evaluation and follow up of multiple sclerosis' patients.

5. Patients and methods

5.1 Patient selection

This study was conducted at the MRI unit – Radiology department– Al Ahrar teaching Hospital – Zagazig – Sharkia Governorate – Ministry of health. in the time frame from April 2014 till April 2016, included 30 clinically diagnosed MS patients who referred from Neurology Department and outpatient clinics. They were 20 females and 10 males. All patients have done magnetic resonance imaging including different pulse sequences and scanning planes, the study was conducted with institutional review based board (IRB) approval and informed consents were taken from all patients.

Patient inclusion criteria

1. Any age group and sex.
2. Patients with suspected multiple sclerosis or already diagnosed as MS under follow up, to perform MRI of the brain and/or spine.

Patient exclusion criteria

1. Absolute contraindications to MRI
2. Patients with different brain pathology (ies).
3. Patients unwilling to complete the study and Claustrophobic patients.

5.2 Technique

MRI was performed for all patients on (1.5 T) Phillips Achieva MRI machine. All patients were asked to get rid of any metallic subjects as well as they were asked about any contraindication to MRI examination (artificial heart valve, cardiac pacemaker, metallic stents or joint prosthesis except that made of titanium). The patients were informed about the duration of the examination, the position of the patient and the importance of being motionless. Patients were placed supine in a head coil to optimize the signal to noise ratio. A scout sagittal T1-weighted view was obtained to verify the precise position of the patient and to act as a localizer for subsequent slices, then multiple pulse sequences were used to obtain axial images followed by coronal and /or sagittal images.

All patients have done magnetic resonance imaging including different pulse sequences and scanning planes; Sagittal T1 WI as a localizer, Axial T1-weighted images, Axial and coronal T2-weighted images, Axial, sagittal and coronal Fluid-Attenuated Inversion-Recovery sequences (FLAIR), some patients had T1-weighted post contrast images. Few patients had MRI spine either dorsal or cervical; Sagittal T1WI, T2WI and Axial T1WI, T2WI.

FOV = 24-18 cm in axial images and 30-22 cm in coronal images, Matrix (frequency x phase) 192 X 160, Slice thickness = 6 mm with 2 mm interval... (In all sequences).

Some patients had DWI; the imaging sequence for DWI was a multi-section single shot spin echo EPI with diffusion sensitivities of b values =0 and 1000 s/mm2. The diffusion gradients were applied sequentially in three orthogonal directions (X, Y & Z directions). Sections of 5mm thickness, inter slice gap of 1mm, FOV 240mm and a matrix of 128x256 were used for all images. The total acquisition time was 80 sec.

Three types were obtained; orthogonal images, trace images and ADC maps. The ADC maps were calculated automatically by MRI software and included in the sequence.

5.3 Data analysis and Statistical data display

To obtain diagnostic values, we shall measure sensitivity, specificity, positive and negative predictive values of the analyzed data using commercially available PC-based software package (SPSS).

6. Results

The results recorded in table (1) shows that the study included 30 patients, 10 males and 20 females, where males represented 33.3% and females represented 66.7%.

Table (2) shows that from a total number of 30 multiple sclerosis cases , there were 2 patients among 10-19 Ys , 17 patients among 20-29 Ys , 9 patients among 30-39 Ys and 2 patients among 40-49 Ys.

The results achieved from table (3) shows that all patient has multiple lesions.

From 58 lesions, there were 30 lesions involving periventricular area , 11 lesions involving juxtacortical area , 10 lesions involving

infratentorial area and 7 lesions involving spinal cord which is documented in table (4).

Regarding to the size of the largest lesion; less than 10 mm in 6 studies, 10 mm to less than 20 mm in 20 studies, 20 mm to less than 30 mm in 5 studies and 30 mm and more in 2 studies; clearly described in table (5).

Table (6) shows that all cases show low signal in T1 and high T2, while 30 cases have FLAIR sequence; all show high signal in FLAIR, 24 cases have DWI sequence; Facilitated diffusion was found in 19 cases with only 5 show restricted diffusion, 4 cases show enhancement in the postcontrast series and 10 cases show no enhancement.

Facilitated diffusion was found in 19 cases with only 5 show restricted diffusion, while 4 cases show enhancement in the postcontrast series and 10 cases show no enhancement. Table (7).

Table (8) explains Validity of MRI in detection of lesions of clinically definite MS.

Table (1) Distribution of patients according to sex.

	Number	Percentage
Males	10	33.3%
Females	20	66.7%

Table (2) Patients age group affected with MS

	Number	Percentage
10-19 years	2	6.7%
20-29 years	17	56.6%
30-39 years	9	30%
40-49 years	2	6.7%

Table (3) Number of lesions [multiple or single]

	Number	Percentage
multiple	30	100 %
single	0	0 %

Table (4) Distribution of MS lesions

	Number	Percentage
periventricular	30	51.8%
juxtacortical	11	18.9%
infratentorial	10	17.2%
Spinal cord	7	12.1%

Table (5) The size of the largest lesion in each T2WI study.

	Number	Percentage
Less than 10 mm	6	18.1%
10-less than 20 mm	20	60.6%
20-less than 30 mm	5	15.2%
30 mm and more	2	6.1%

Table (6) Signal of lesion in different sequences of MS

	Low signal	High signal	sum
T1WI	33	0	33
T2WI	0	33	33
FLAIR	0	30	30
DWI	19	5	24
POSTCONTRAST	10	4	14

Table (7) Comparison between DWI and POSTCONTRAST T1WI sequences in detecting active lesions

	number	signal	% of Detection of activity
DWI	24	19 facilitated 5 restricted	20.8 %
postcontrast	14	10 not enhanced 4 enhanced	28.5 %

Table (8) Validity of MRI in detection of lesions of clinically definite MS.

	Percentage
Sensitivity	97 %
Specificity	90 %
PPV	55 %
NPV	85 %

7. Discussion

Multiple sclerosis is a chronic disease, affecting mainly central nervous system [brain and spinal cord] and rarely affecting the peripheral nervous system which is matching with [21] which reported that in MS the insulating covers of nerve cells in the brain and spinal cord are damaged.

MS is more prominent in periventricular area , corpus callosum, juxtcortical and spinal cord which differ to some extent from the results reported in [1] and [6] where MS lesions most commonly affect the white matter in the optic nerve, brain stem, basal ganglia, and spinal cord, or white matter tracts close to the lateral ventricles with more prominent in optic nerves.

Regarding the distribution of the patients according to sex, in our study the percentage of males was 33.3% and the percentage of females was 66.7% in a group of 30 patients which mean that MS is more prevalent in females than males by 2 time, in comparison to 3-4 times reported by [1].

The range of ages in our study was between 18 and 45 years with a mean of 27.8 ys, which was relatively similar to [1] patient group, whose between 20-50 years with a mean age of 29 years.

In our study MS is always seen as multiple lesions as reported by [22] as both acute and chronic cases has old and new lesions.

Regarding the symptoms the most affecting symptom in our study is physical problems such as muscle weakness, abnormal muscle spasms, or difficulty in moving; difficulties with coordination and balance (ataxia); problems in speech (dysarthria) or swallowing (dysphagia) which differ from results in [1] with most frequent symptom affected is visual problems such as nystagmus, optic neuritis, or diplopia.

Conventional MRI allows for determination of dissemination in space and time earlier than with clinical assessment alone. Furthermore, 2010 modifications to the McDonald criteria allow for even earlier MS diagnosis based on simplified MRI criteria for dissemination in space and time, with preserved sensitivity and specificity [13]. In our study conventional MRI has a high role in detection of MS lesions in clinically definite MS patients and provides an important tool to monitor the disease course as reported in.[9].

Compared with other techniques, no lesion shows high signal in T1WI matching with 14] non-enhanced T1-weighted MRI is far less sensitive in detecting MS lesions. Acute lesions usually are not depicted at all. Using T1-weighted MRI, we can gain a general appreciation of the global cerebral atrophy that occurs with advanced chronic MS. Global atrophy has been suggested to have the strongest imaging correlation with disability.

However in chronic patient, MS lesions may appear hypointense in T1WI as reported in [10] On T1-weighted imaging (T1WI), the acute MS lesions are often isointense to the normal white matter but can be hypointense or localized leukomalacia if chronic tissue injury or severe inflammatory edema occurs and usually persist for many years on T2WI. The accumulation of hypointense lesions (so-called black holes) may correlate with disease progression and disability.

T2WI is most sensitive but with moderate specificity which is the same as reported in [23] and matching with [4] who reported the same. The first important role for MRI in the diagnosis of MS allows for an early diagnosis of MS, The second important role for MRI in the diagnostic work-up of suspected MS patients is to rule out alternative diagnoses obvious on MRI, such as spinal stenosis and most brain tumors, magnetic resonance imaging (MRI) often shows more than ten new plaques [6]

In T1WI with contrast enhancement some lesion shows enhamncement which is considered as acute phase of MS which reported in [24] In the acute inflammatory phase, Leakage of Gd through the disrupted BBB is regarded as an indicator of the acute inflammatory activity initially involved in the pathogenesis of MS.

The role of conventional MRI less than newer imaging techniques as FLAIR and DWI which

have the abilities to detect more lesions in the same patient this is reported in [13] Newer imaging techniques are more sensitive in identifying abnormalities of the central nervous system related to MS and may facilitate prediction of neurologic impairment and evaluation of response to disease-modifying therapy in the future and also with what reported in [16]

FLAIR is potentially useful in the evaluation of patients with MS as reported in [15]. FLAIR increases the contrast between periventricular lesions and CSF, enhancing MS lesions detection.

DWI has important role in MS detection as reported in [16] DWI is more specific to the underlying pathologic substrates of the disease and more sensitive to the full extent of 'occult' tissue damage in patients with MS.

8. Conclusion

From this we can conclude that MRI [specially newer imaging technique] has dramatically improved our ability to detect lesions of clinically definite MS and early detection of the disease before symptoms appears.

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