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Usefulness of Phase Sensitive Inversion Recovery MRI Sequence in the Detection of Cortical Lesions in Multiple Sclerosis

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Abstract

Background: The presence of cerebral cortical lesions in multiple sclerosis has an important clinical impact on the prognosis of the disease and associated disability. However, the accurate detection of cortical lesions using conventional magnetic resonance imaging sequences remains challenging. The study aims to assess the value of phase-sensitive inversion recovery sequence in the detection of cortical lesions in multiple sclerosis patients and to evaluate their relation with clinical subtypes, duration, and clinical disability of the disease. **Patients and Methods:** Seventy cases, 51 females and 19 males, of multiple sclerosis, confirmed by McDonald criteria, were enrolled in this cross-sectional study and phase-sensitive inversion recovery images, axial and coronal sections, were obtained for each patient in every MRI session. Cortical lesions were subclassified into intracortical, leukocortical, and juxtacortical. Clinical disability was assessed using the extended disability status scale. The number of detected cortical lesions on phase-sensitive inversion recovery images was calculated and compared with that detected on conventional T2-weighted and fluid-attenuated inversion recovery images. **Results:** The number of cortical lesions detected on phase-sensitive inversion recovery was lesser compared to the T2-weighted sequence, a total of 1151 versus 1258 lesions respectively. The T2-weighted sequence was significantly better in the detection of leukocortical and juxtacortical. On the other hand, phase-sensitive inversion recovery was better than fluid-attenuated inversion recovery in detecting intracortical, while fluid-attenuated inversion recovery was better in detecting juxtacortical, and both sequences detected the same number of leukocortical lesions. The overall number of detected cortical lesions showed a statistically significant correlation only with the extended disability status scale and not with the clinical subtype or duration of multiple sclerosis.

Conclusion: phase-sensitive inversion recovery detected more intracortical lesions and fewer juxtacortical lesions than fluid-attenuated inversion recovery, cortical lesions were significantly correlated with the degree of clinical disability of multiple sclerosis.

Keywords: Brain, Cortical, Inversion Recovery, Magnetic Resonance Imaging, Multiple Sclerosis.

Article Information

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INTRUDUCTION

Multiple sclerosis (MS) is a global problem, with rising incidence both worldwide (1) as well as in Iraq (2). The symptoms of MS are tremendously diverse and depend on the severity and location of lesions within the CNS (3,4). MS is a clinical diagnosis but the McDonald criteria incorporating magnetic resonance imaging (MRI) have been established (5) while diagnostic criteria combining clinical, imaging, and laboratory evidence have evolved (6). MRI is of utmost importance in the

diagnosis of MS and is particularly helpful in excluding other pathologies or showing features suggesting alternative diagnoses (7,8). The T2-weighted (T2W) and fluid-attenuated inversion recovery (FLAIR) as well as contrast-enhanced T1-weighted (T1W) are most commonly and routinely utilized sequences in the imaging evaluation of MS (9, 10). The white matter (WM) lesions characteristic of MS do not represent the whole pathology of MS (11). There was radiological and pathological evidence of the presence of the so-called cortical lesions (CL) that were found to be closely associated with cognitive impairment independent of WM lesions (12,13). However, unlike WM lesions, not all these CLs can be depicted using conventional MRI sequences (12, 14).

Therefore, there was a need for a feasible imaging technique to detect CLs with reasonable accuracy. A double inversion recovery (DIR) sequence has been utilized for this mission (15) by suppressing both WM and cerebrospinal fluid signals, hence improving the conspicuity of demyelinating plaques (16, 17). However, the DIR sequence is generally susceptible to image artifacts and both false-negative and false-positive results with a low signal-to-noise ratio (18). Another T1-W MRI sequence, the phase sensitive inversion recovery (PSIR), has also been used for better detection of CLs (19), utilizing its advantages of the wider range of signal intensity resulting from the combination of both negative and positive longitudinal magnetization, with consequent higher contrast resolution with lesser acquisition time (1:30 minutes for whole brain) than DIR, FLAIR and routine T1-W FSE sequences (19, 20, 21). However, most of the conducted studies utilized high-strength MRI machines (3-7 Tesla), which are generally scarce in our region and not feasible like the conventional 1.5 Tesla devices.

Therefore, the current study was conducted to evaluate the accuracy of the PSIR sequence in detecting cerebral CLs in MS patients using a 1.5 T machine commonly utilized and readily available MRI machine for daily clinical practice in our neuroscience center and regional hospitals. The study also aimed to assess the relation of CLs with the subtypes, duration, and clinical disability of the disease.

PATIENTS AND METHODS

This cross-sectional diagnostic study was conducted on 70 MS patients at Middle Euphrates Neuroscience Center, AL-Sadir Medical City in Najaf Province – Iraq, during a period of one year from January 2021 to January 2022 .According to the inclusion and exclusion criteria, patients with a confirmed diagnosis of MS using McDonald criteria (2017) (6) of both genders and their age above 10 years were included. However, patients with the presence of any of the following were excluded: MRI contraindications, past medical history of neurological, major medical or neuropsychiatric illnesses; failure to complete the MRI exam, or

missing of one or several sequences; significant artifact and refusal to participate in the study.

The study was approved by the Institutional Review Board and informed oral agreement was taken from all patients for acceptance to participate in the study.

Clinical data including age, gender, medical history, type and duration of MS, drugs used by the patients, and expanded disability status scale (EDSS) were obtained from the registry and history.

Due to the imaging protocol and analysis, all examinations were conducted using a 1.5 T MRI machine (Achieve Philips, Netherlands, 2011). The PSIR sequence was performed for each patient as part of routine MRI sequences. The routine examination also included conventional T1-W, T2W-TSE, and FLAIR. A board-certified specialist radiologist, with more than 13 years of experience in neuroradiology, interpreted the T2-W-TSE, FLAIR, and PSIR images. CLs were subclassified into three locations: intracortical (IC), when they are confined to the GM; leukocortical (LC), when lesions involve both grey and white matters of the cortex; and juxtacortical (JC) when lesions involve the subcortical U-fibers (figure 1) (21). The total number of CLs in each cerebral region was assessed separately on the T2-W-TSE, FLAIR, and PSIR sequences respectively.

STATISTICAL ANALYSIS

The statistical analysis of the data was carried out by using SPSS-27 (IBM Inc., Chicago, IL, USA for Windows ®); the data were presented in frequency, percentage, mean, and standard deviation. The significance of difference was tested by using the students-t-test for two independent means, Paired-t-test for paired observations, two dependent means, or ANOVA test for more than two independent means. P-values less than (0.05) were considered statistically significant.

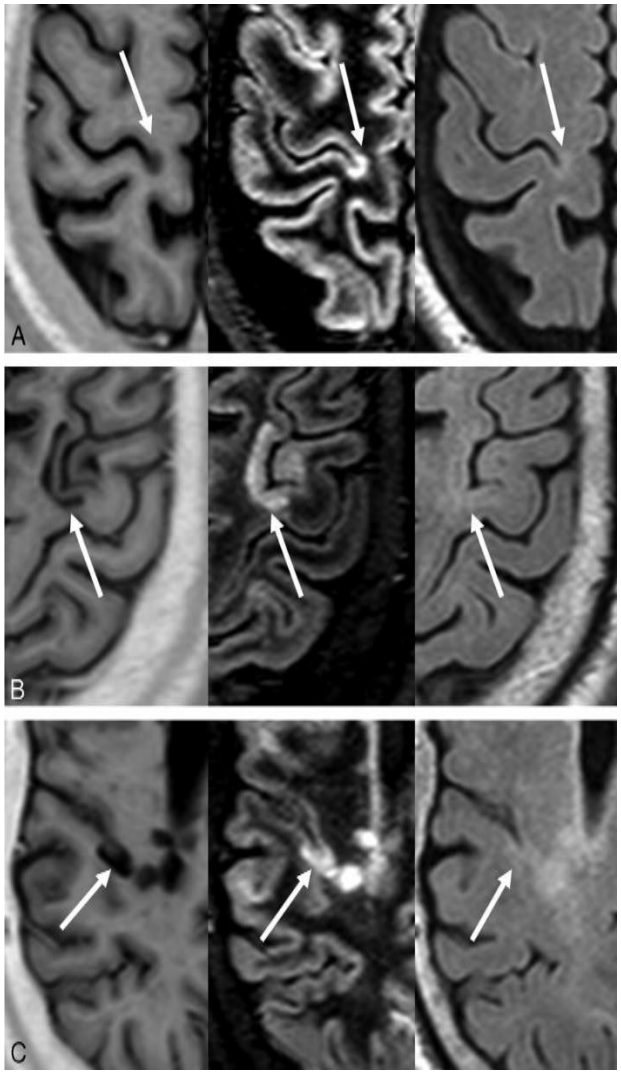

Figure 1. Classification of cortical lesions according to the location into intracortical (A), leukocortical (mixed) (B), and juxtacortical (C) (Adapted from Nelson F et al (19) with permission from American Society of Neuroradiology) .

RESULTS

This study included a total of 70 MS patients, with a mean age was (31.1± 10.1) years, females (72.9%) more than males (27.1%), with a mean duration of MS of (4.1 ± 4) years. The most common treatment used was Betaferon, (29 41.4 %). Remitting relapsing (RR) type was the most common type of MS (71.4 %), followed by clinically isolated syndrome (CIS) (13 patients, 18.6 %), and the least was primary relapsing (PR), only one patient, 1.4%. Most of the patients (57, 81.5%) had a mild disease with EDSS of less than three (Table 1).

Table 1. General characteristics and MS variables of the study sample.

Variable		Number	%
Gender	Male	19	27.1
	Female	51	72.9
Age (years)	≤ 20	12	17.1
	21-30	24	34.3
	31-40	19	27.2
	> 40	15	21.4
Treatment	Betaferon	29	41.4
	Tysabri	17	24.3
	Rebif	14	20
	Gelenia	7	10
	Avonex	2	2.9
	Rituximab	1	1.4
Type of multiple sclerosis	Remitting relapsing	50	71.4
	clinically isolated syndrome	13	18.6
	Primary progressive	4	5.7
	Secondary progressive	2	2.9
	primary relapsing	1	1.4
Duration (years)	1_5	54	77.1
	6_10	10	14.3
	> 10	6	8.6
EDSS	< 3	57	81.5
	≥ 3	13	18.5

EDSS-Expanded disability status scale.

The total number of IC lesions, detected on T2-W sequence was more than on PSIR sequence, 123 versus 119 respectively, but without statistical difference (P=0.49). Regarding LC lesions, a total number of plaques were detected more on T2-W than PSIR sequences (292 versus 228 respectively) with statistically significant difference (p value 0.0001). Regarding JC lesions, more lesions were detected using the T2-W sequence than PSIR, 870 versus 804 respectively, with statistically significant difference, p value of 0.004. (Table 2).

Compared to FLAIR, a higher number of IC plaques were detected by using PSIR images, 50 versus 20 respectively, with a statistically significant difference (p-value 0.001), more JC lesions were seen on FLAIR than PSIR, 624 versus 580 respectively, with a statistically significant difference (p-value o0.003) while both FLAIR and PSIR sequences found a similar number of LC lesions, 147 for each. (Table 3).

Table 2: Number of cortical lesions detected on T2W and PSIR sequences.

Location	IC		LC		JC	
	T2-W	PSIR	T2-W	PSIR	T2-W	PSIR
Frontal lobe	63	55	119	95	399	378
Temporal lobe	6	5	37	27	58	38
Parietal lobe	49	53	93	78	248	245
Occipital lobe	5	6	43	28	165	143
Mean	1.76	1.70	4.17	3.26	12.43	11.49
Std. Deviation	3.241	2.634	3.538	3.855	8.050	9.002
Total	123	119	292	228	870	804
P Value	0.49		0.0001		0.004	

IC=intracortical; LC=leukocortical; JC=juxtacortical; T2-W=T2-weighted; PSIR=phase sensitive inversion recovery.

Table 3: Number of plaques detected on FLAIR and PSIR sequences.

Location	IC		LC		JC	
	FLAIR	PSIR	FLAIR	PSIR	FLAIR	PSIR
Frontal lobe	9	26	61	58	269	246
Temporal lobe	0	5	32	28	55	51
Parietal lobe	9	16	36	48	181	170
Occipital lobe	2	3	18	13	119	113
Mean	0.10	0.25	0.74	0.74	3.12	2.90
Std. Deviation	0.481	0.671	1.044	1.354	2.806	2.855
Total	20	50	147	147	624	580
P Value	0.001		0.277		0.003	

IC=intracortical; LC=leukocortical; JC=juxtacortical; FLAIR=fluid attenuated inversion recovery; PSIR=phase sensitive inversion recovery.

The total number of the detected CLs was statistically correlated with EDDS for all locations: IC, LC, and the JC lesions. However, it was most significant for IC lesions (p values of <0.001, 0.004 and 0.02 respectively) while no statistically significant correlation (p values > 0.05) was found with age, gender, duration of the disease, type of the treatment and type of MS (Table 3).

Table 3: Correlation between cortical lesions and study variables.

	Intracortical lesions	Leukocortical lesions	Juxtacortical lesions
	P value	P value	P value
Age	0.515	0.974	0.473
Gender	0.683	0.671	0.927
Duration	0.887	0.694	0.673
Treatment	0.171	0.269	0.141
Type of multiple sclerosis	0.634	0.633	0.810
*EDSS	<0.001	0.004	0.020

EDSS-Expanded disability status scale.

DISCUSSION

Cortical lesions in MS have an impact on neurological and cognitive functions; their diagnosis plays an important role in predicting the disease prognosis (22). However, CLs are difficult to visualize by conventional MRI sequences (23) and clinical implications and value for follow-up is not yet established (24, 25). PSIR provides a better grey matter/white matter contrast and differentiation than the T1-W sequence (18, 19, 22) and was applied in the evaluation of neoplastic space-occupying lesions whether extra-axial or intra-axial and in the detection of what is called "black hole" lesions (26, 27). The present study was conducted to compare the accuracy of PSIR sequence with conventional MRI sequences (T2-W and FLAIR) in the detection of CLs in MS patients using a 1.5 Tesla MRI scanner. PSIR images were more capable in the detection of IC lesions compared to the FLAIR images, which is consistent Hashemi et al's study which found a significantly higher number of IC and LC plaques by using the PSIR sequence compared to FLAIR sequence(18) Using 3 Tesla scanner MRI, studies have confirmed the same results with a higher number of CLs detected by PSIR sequence compared to FLAIR (16, 19, 20), with the advantage of improved classification of CLs subtypes(21)

The current study has shown no significant difference between PSIR sequence and T2-W in detecting IC lesions. However, other types of lesions like LC and JC were detected more on FLAIR and T-W images than PSIR sequences. This discrepancy between this study's results and other studies can be attributed to several factors: firstly; many lesions in the JC region are WM lesions rather than genuine cortical lesions which are easier to detect on FLAIR and T2W-TSE sequences similar to what was found by Wattjes et al study (28). Secondly, this discrepancy is related to the efficiency of MRI device used as significantly

higher numbers of CLs were detected using 3T MRI devices (29) and except for Hashemi et al (18), all previous studies were done by using the higher strength (3-7 Tesla) MRI devices. Despite the higher detectability of the CLs in T2-W sequence, this could be attributed to the fact that lesions detected on PSIR would be more reflective of the actual clinical situation because the hypointensity on T1-W images is thought to be more important than the hyperintensity seen on T2-W images during the follow-up of MS disease progression. Those T1-W hypointense lesions are potentially independent parameter of MS pathological process **(Error! Reference source not found.)** and correlated with the degree of pathological severity [30]. Moreover, the hyperintense lesions detected on T2-W images in MS may be overestimated due to the associated Wallerian degeneration [31, 32] in addition to the non-significant high T2-W signals incidentally found in healthy subjects [33] and various migraine and vascular headaches [34].

Studies have found an association between the presence of CLs and clinical disability [26, 35]. In the current study, the overall number of plaques seen was statistically correlated to the severity of the disease reflected by EDSS for all locations: IC, LC, and JC lesions, with the most significant correlation being with IC lesions. This supports the finding that IC plaques usually occur in the advanced stages of MS disease and their presence reflects the extent of clinical disability [36]. Furthermore, Rovaris et al found that the cognitive function of MS patients, reflected by EDSS is markedly influenced by the severity and extent of cortical and subcortical MS lesions. [37]

This study has some limitations. Most of the included MS patients in this study were of RRMS type, in which the probability of CL is thought to be lower compared to PPMS and SPMS [38]. The true maturity of JC lesions that were better detected on T2-W and FLAIR could be related to the WM and genuine cortical lesions. All images were evaluated by a single radiologist, hence the interobserver variation could not be assessed. The long-term relationship between the clinical course of the disease and the CL burden could not be evaluated.

CONCLUSIONS

The study has concluded that LC and JC lesions were detected more on T2-W than PSIR. There was no difference between T2-W and PSIR in the detecting IC lesions. LC was detected more on FLAIR than PSIR. There was no difference between FLAR and PSIR in the detection of LC lesions. IC lesions were detected more on PSIR than FLAIR. All subtypes of CL were statistically correlated with EDDS, most significantly for IC subtype. PSIR is as an adjuvant with T2-W and FLAIR sequences when a specific evaluation of IC location is required in regions where only the 1.5 Tesla strength MRI device is available. Future studies to investigate the value of PSIR in the progression of disease as well as in monitoring clinical response were recommended.

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