Comparative between Double Inversion Recovery and Fluid-Attenuated Inversion Recovery Sequences for Detection of Brain Multiple Sclerosis

Abstract

Multiple sclerosis (MS) is the most common chronic inflammatory demyelinating disease of the central nervous system (CNS). MS diagnosis and disease monitoring are mostly based on Magnetic Resonance Imaging (MRI). This study aims to compare a double inversion recovery MRI sequence with a fluid-attenuated inversion recovery sequence in Multiple Sclerosis (MS) in the brain. A study was conducted on 75 patients whose aged between 10 and 70 years who were having MS in the brain to compare a double inversion recovery DIR sequence with a fluid-attenuated inversion recovery FLAIR sequence at King Salman Specialist Hospital. in this study the age group (30-49) and female patient represented the highest percentage (69%) and (60%) respectively, A correlation between DIR and FLAIR in terms of the number of MS lesions and mean $\pm$SD was found. DIR detected a higher total number of MS lesions in 75 patients tested (a total of 1886 MS lesions were detected in DIR compared to 1723 MS lesions in FLAIR). FLAIR imaging showed higher rates of periventricular lesions (a total of 508 lesions, the Mean $\pm$SD was 9.5$\pm$ 9.5) than DIR imaging (a total of 423 lesions, the Mean $\pm$ SD was 9.0$\pm$ 9.0), statistically significant (p = 0.007). The DIR sequence detected a higher total number of MS lesions than the FLAIR sequence, while the FLAIR sequence is better at detecting periventricular lesions. There was no statistically significant relationship between the patient's age groups and the number of lesions in DIR and FLAIR P-value > 0.05.

Keywords: *Magnetic resonance imaging, Double inversion recovery, Fluid-attenuated inversion recovery, Multiple sclerosis*

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Introduction

Multiple sclerosis is the utmost common chronic inflammatory demyelinating disease of the central nervous system (CNS), affecting mainly the white matter but also parts of the gray matter.[1] The diagnosis of MS and the observation of the disease are essentially based on magnetic resonance imaging (MRI), which lets an early diagnosis of MS be based on diagnostic criteria.[1, 2] According to recent studies, the degree of cortical damage is closely linked to the advancement of the patient's disease progress, the depth of cognitive impairment, and the degree of physical handicap.[3] T2- weighted, fluid-attenuated inversion recovery (FLAIR), before and after contrast T1- weighted sequences are used in multi-sequence MR imaging for the diagnosis of MS.[4] According to the anatomic site of the inflammatory brain lesions, the pulse sequences have varying sensitivity in detecting them.[2] FLAIR imaging has the maximum sensitivity for lesions near the cerebrospinal fluid (CSF), similar to the juxtacortical and periventricular white matter, but fewer profound lesions in the infratentorial region. T2-weighted sequences are extra profound for detecting posterior fossa lesions but are more difficult to detect paracortical lesions.[5, 6] In a more recent imaging technique, known as double inversion recovery (DIR), two inversion pulses are combined to provide adequate attenuation of both cerebrospinal fluid (CSF) and normal-appearing white matter (NAWM).[6] There have been several studies that examined the use of the DIR sequence in the diagnosis of CNS diseases, including vascular, infectious, and neoplastic conditions.[7] A study conducted by Hamed, *et al*., 2019 Our research's objective was to evaluate the diagnostic efficacy of a double inversion recovery (DIR) sequence in the detection of MS lesions in the brain and spinal cord. DIR's accuracy in counting the number of white matter lesions is unaffected by the higher rate of cortical lesion detection. A superior morphological characterization and delineation of white matter lesions were

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also obtained by DIR, with clear distinctions between juxtacortical and mixed white matter-gray matter lesions.[8] In a study conducted by Abdelaziz M. Elnekeidy *et al.*, 2014, the DIR MR Sequence was compared with T2 and FLAIR sequences for the detection of cortical and white matter lesions in MS. Compared to T2W and FLAIR sequences, DIR can detect more MS lesions in any anatomical location compared to the imaging workup for MS. A high image contrast allowed DIR to easily distinguish white matter, gray matter, and MS lesions.[9]

Materials and Methods

A retrospective cross-section study was performed on 72 patients all of them have multiple sclerosis (MS) referred from the Neurology clinic to the Radiology Department at king Salman and King Khalid hospitals in Hail city, Saudi Arabia during the period from January 2021 to February 2022, all the patients were diagnosed by MRI scan and their age range (20-70) years old.

The data was collected from patient's medical records by data collection sheet using Picture Archive and Communication System (PACS), from the radiology department, which includes (Age, gender, DIIR appearance, and FLAIR appearance)

Inclusion criteria
Patients with identified or supposed multiple sclerosis MS and both sex groups are included

Exclusion criteria
Contraindicated cases to MRI study as pacemaker placement and claustrophobic patients, patients with acute exacerbation of MS, and patients with another differential diagnosis of MS with vascular, malignant, infectious, and other immunological CNS diseases

Image acquisition
After the patients signed the consent form, they removed all the metal and wear the hospital gown, all patients had an MRI scan, 1.5 Tesla superconducting magnet (Siemens, Germany) in a supine position with head first, and place the head coil over the head and tide with a strap to avoid motion artifact, use knee support under the leg for patient comfort.

The MRI sequences done for the patients including (Axial T1WI, axial T2WI, axial FLAIR, sagittal T1WI, coronal T2WI, diffusion weighted imaging, sagittal and axial 3D FLAIR and sagittal and axial 3D DIR).

Data analysis
Statistical analysis was performed via SPSS (Statistical Package for Social Sciences) and Excel software, and the results were presented in the tables and graphs and comparisons between quantitative variables were done

Ethical consideration
Written informed consent was gotten from all patients. This study was approved by Hail University and Hail Health Cluster.

Results and Discussion

In this study the patient age ranged between 10 and 70 years old, the greatest affected age group was (30-49) years old by percentage 52 (69%), while the least affected group was (50 - 69) years old by percentage 2 (3%), as shown in **Table 1**.

Table 1. Showed age distribution (years) N= 75			
Age group (years)	Frequency	Percent	Mean ±SD
(10-29)	21	28%	
(30-49)	52	69%	
(50-69)	2	3.0%	34.8±10.3
Total	**75**	**100.0**	

Regarding gender, the study sample was 30 males and 45 females with percentages of 40.0%, and 60.0% respectively, which means the most affected patients were female, as shown in the **Table 1**.

Correlation between DIR and FLAIR concerning the number of lesions
Table 2 and **Figure 1** showed that the total number of MS lesions noticed by DIR was higher (a total of 1886 MS lesions were detected in DIR compared to 1723 MS lesions in FLAIR), and the difference was statistically significant (p < 0,05). The DIR detected a higher whole number of MS lesions in the paracortical regions (525 MS lesions were detected in the DIR versus 464 MS lesions in the FLAIR), and fewer MS lesions were detected in the lesions of the craniocervical junction (39 MS lesions in total in DIR versus 19 MS lesions in FLAIR). Additionally, FLAIR imaging showed a higher incidence of periventricular lesions (a508 lesions in total), compared to DIR imaging (423 lesions in total).

Table 2. Showed a Correlation between DIR and FLAIR concerning the number of lesions, and Mean ±SD N=75					
Number of lesions	DIR		FLAIR		P-value
Regions of lesions	No	Mean ±SD	No	Mean ±SD	
Periventricular lesions	463	9.0 ±9.0	508	9.5 ±9.5	>0.0007
Deep white matter lesions	523	5.5 ±2.5	522	4.5 ±2.5	0.002

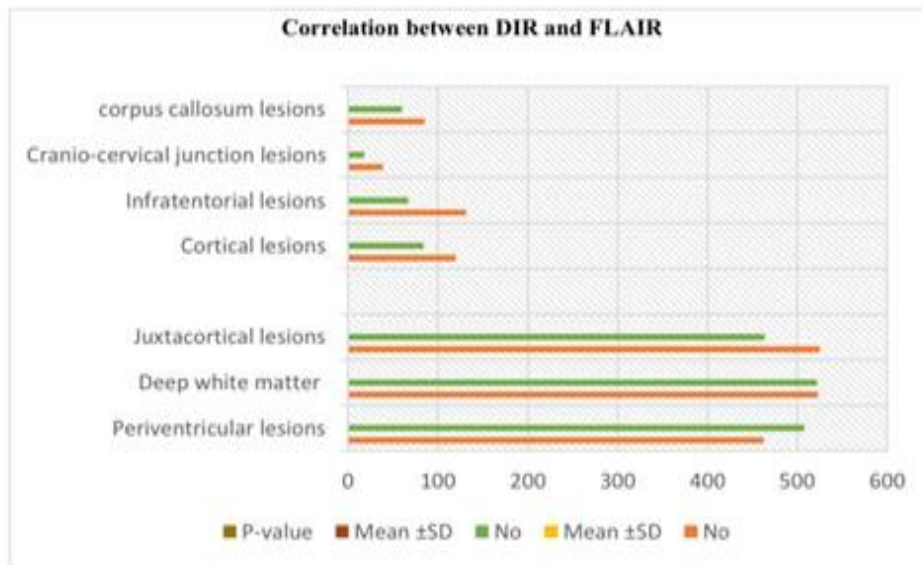|					
Juxtacortical lesions	525	7.5 ±5.5	464	7.0 ±6.0	>0.0001
Cortical lesions	120	2.0 ±2.0	84	1.5 ±1.5	0.004
Infratentorial lesions	131	2.0 ±1.0	67	1.5 ±0.5	>0.0007
Cranio-cervical junction lesions	39	9.0 ±9.0	18	0.2 ±0.01	>0.0007
corpus callosum lesions	85	9.0 ±9.0	60	0.8 ±1.06	>0.001

Figure 1. Showed a Correlation between DIR and FLAIR concerning the number of lesions, and Mean ±SD N=75

Correlation between DIR and FLAIR results & age groups

Table 3 showed there was no statistically significant correlation between the patient's age and the number of lesions in DIR and FLAIR (p < 0.05). A higher lesions number was detected in the age group (30-49) (a total of 1318 MS lesions were noticed in DIR compared to 1097 MS lesions in FLAIR), and the lower lesions were noticed in the age group (50-69) (a total of 70 MS lesions were noticed in DIR compared to 71 MS lesions in FLAIR)

Table 3. Showed the Correlation between DIR and FLAIR results & age of the patients N=75				
Age group (years)	**Number of lesions in DIR**	**P-value**	**Number of lesions in FLAIR**	**P-value**
(10-29)	607	0.529	498	0.485
(30-49)	1318	0.164	1097	0.286
(50-69)	70	0.649	71	0.864

The main objective of this study is to compare a double inversion recovery MRI sequence with a fluid-attenuated inversion recovery sequence in Multiple Sclerosis (MS) in the brain.

Regarding the age groups, in the present study, the most affected age group was (30-49) years old this result was consonant with Elkholy, S. F, *et al.* 2020, who said "Multiple sclerosis is a common cause of disability in young adults"

However, these results do not agree with Ligouri, M., *et al.* 2000, who reported; "patients older than 50 years tend to have a comparable disability, independently of the age at onset and this study demonstrates that an early age at onset cannot be considered a favorable prognostic factor".[10]

The present study reveals that females are more affected than males by a percentage of 60%. This result was compatible with Magyari, M. (2016), who said; "Females had a higher frequency of MS relapses than males because women's lifestyle has undergone tremendous changes in the last half-century".[11]

Regarding the correlation of detecting MS between DIR and FLAIR, the study shows; DIR detected a higher total number of MS lesions in 75 patients tested (a total of 1886 MS lesions were detected in DIR compared to 1723 MS lesions in FLAIR), this results confirmed by results reported by Elkholy, *et al.*, 2020, they said; " DIR showed a significantly higher total number of MS lesions in the 32 patients included in the

study (total of 1690 lesions were identified in DIR compared to 1469 lesions in FLAIR)".[12]

Also, these results were consonant with Abidi, Z., *et al.*, 2017, who showed "In the present study, 2658 lesions were identified with DIR imaging, while 2513 lesions with FLAIR and 2423 lesions were identified with T2W_TSE. A significantly higher total number of lesions were displayed on DIR images compared with FLAIR".[5]

In the present, study the deep white matter lesions had the same number in the FLAIR and DIR lesions 522 in FLAIR and 523 lesions in DIR, while in a study done by SUZAN, F. S., *et al.*, 2021, mentioned that; "Concerning DWM lesions, DIR was found to be superior to T2 and FLAIR sequences in 47.1 % and 35.3% of cases correspondingly and equal to T2 and FLAIR sequences in 17.6% of cases." [13]

In the present study FLAIR imaging showed greater rates of periventricular lesions a total of 508 lesions (9.5± 9.5), than DIR imaging a total of 423 lesions(9.0± 9.0), which disagreed with Elkholy *et al.*, who found "DIR sequence revealed a higher number of periventricular WM lesions (11.84 ± 8.07) compared to (11.31 ± 8.07) in FLAIR with a statistically significant difference p < 0.001".[12] Our results also disagreed to some extent with Abidi *et al.*, who found "the average lesions in DIR was 15.34 ± 11.34 compared to 15.18 ± 11.16 in FLAIR yet with an insignificant statistical difference".[5]

In this study, there was no statistically significant correlation between the patient's age and the number of lesions in DIR and FLAIR, this result is not equivalent to what Ligouri, M., *et al.* 2000 mentioned: "The results of the current study reveal that clinical debility in MS is influenced by the patient's age (p < 0.01) and not by the age at onset".[10]

Conclusion

The DIR sequence detected a higher total number of MS lesions than the FLAIR sequence, while the FLAIR sequence is better at detecting periventricular lesions. There was no statistically significant relationship between the patient's age groups and the number of lesions in DIR and FLAIR P-value > 0.05, thus, we recommend adding a DIR sequence in routine MR protocols for MS patients.

Ethics statement
This study was approved from Hail University and Hail Health Cluster and written informed consents were gotten from all patients.

References

1. Hassan TA, Elkholy SF, Mahmoud BE, ElSherbiny M. Multiple sclerosis and depressive manifestations: can diffusion tensor MR imaging help in the detection of microstructural white matter changes?. Egypt J Radiol Nucl Med. 2019;50(1):1-7.
2. Faizy TD, Thaler C, Ceyrowski T, Broocks G, Treffler N, Sedlacik J, et al. Reliability of cortical lesion detection on double inversion recovery MRI applying the MAGNIMS-Criteria in multiple sclerosis patients within a 16-months period. PLoS One. 2017;12(2):e0172923.
3. Filippi M, Rocca MA, Ciccarelli O, De Stefano N, Evangelou N, Kappos L, et al. MRI criteria for the diagnosis of multiple sclerosis: MAGNIMS consensus guidelines. Lancet Neurol. 2016;15(3):292-303.
4. Hemond CC, Bakshi R. Magnetic resonance imaging in multiple sclerosis. Cold Spring Harb Perspect Med. 2018;8(5):a028969.
5. Abidi Z, Faeghi F, Mardanshahi Z, Mortazavi H. Assessment of the diagnostic accuracy of double inversion recovery sequence compared with FLAIR and T2W_TSE in detection of cerebral multiple sclerosis lesions. Electron Physician. 2017 9(4):4162.
6. Favaretto A, Poggiali D, Lazzarotto A, Rolma G, Causin F, Gallo P. The parallel analysis of phase sensitive inversion recovery (PSIR) and double inversion recovery (DIR) images significantly improves the detection of cortical lesions in multiple sclerosis (MS) since clinical onset. PLoS One. 2015;10(5):e0127805.
7. Al-Mutairi A, Mahmud RB, Hassan HB. Double inversion recovery in evaluation of multiple sclerosis: a narrative review. Rev Latinoam Hipertens. 2019;14(3):325-7.
8. Hamed W, Fathi W, Mahmoud W, Elhawary G. Diagnostic accuracy of double inversion recovery in delineation of multiple sclerosis lesions and its clinical correlation with expanded disability scoring system. Egypt J Radiol Nucl Med. 2019;50(1):1-8.
9. Elnekeidy AM, Kamal MA, Elfatatry AM, Elskeikh ML. Added value of double inversion recovery magnetic resonance sequence in detection of cortical and white matter brain lesions in multiple sclerosis. Egypt J Radiol Nucl Med. 2014;45(4):1193-9.
10. Ligouri M, Marrosu MG, Pugliatti M, Giuliani F, De Robertis F, Cocco E, et al. Age at onset in multiple sclerosis. Neurol Sci. 2000;21(2):S825-9.
11. Magyari M. Gender differences in multiple sclerosis epidemiology and treatment response. Dan Med J. 2016;63(3).
12. Elkholy SF, Sabet MA, Mohammad ME, Asaad RE. Comparative study between double inversion recovery (DIR) and fluid-attenuated inversion recovery (FLAIR) MRI sequences for detection of cerebral lesions in multiple sclerosis. Egypt J Radiol Nucl Med. 2020;51(1):1-0.
13. Suzan FS, Ahmed F, Bassant T. Quantitative Assessment of MRI Lesion Load in Cerebral Multiple Sclerosis: A Comparison of Conventional Sequences and Double Inversion Recovery. Med J Cairo Univ. 2021;89(December):2835-41.