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Research Article

Advanced magnetic resonance imaging (MRI) technique (double inversion recovery sequence) in the diagnosis of multiple sclerosis (MS) grey matter lesions

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Abstract

Background: Background: MS (multiple sclerosis) is an inflammatory demyelinating disease of the central nervous system. In spite of description of the grey matter involvement in MS, the conventional MRI sequences don't have the ability of detection of MS cortical lesions. Aim of Study: To assess the diagnostic value of DIR sequence in the detection of MS lesions by comparing DIR with FLAIR and T2-weighted pulse sequences in the brain. **Methods**: This Cross Sectional Study was carried out in Radio-diagnosis Department, Faculty of Medicine Minia University. 30 MS patients aged (20 to 50) years were included. MR imaging was performed to all patients (T1WI, T2WI, FLAIR, DIR, DWI and ADC sequences are performed in axial planes in addition to sagittal planes for FLAIR and DIR). **Results:** A total of 30 patients were enrolled in this study, females 26 (86.7%) predominated males 4 (13.3%). The median number of cortical and juxtacortical lesions ± IQR detected by DIR sequence (3.00 ± 3.00) and (2.00 ± 2.00) respectively was significantly higher than that detected by FLAIR sequence (1.00± 2.00) and (1.00± 1.00) respectively and T2 sequence (0.00 ±1.00) and (1.00± 2.00) respectively, with (P-value<0.0001 & <0.0001) respectively. DIR identified significantly more infratentorial lesions in comparison to FLAIR (P-value <0.039), but detected lower number of lesions when compared to T2 sequence, but the difference was below the statistical importance (p-value<0.275). **Conclusion:** DIR brain imaging sequence had the highest sensitivity in the detection of cortical and juxtacortical lesions compared with FLAIR and T2 sequences.

Keywords: multiple sclerosis, double inversion recovery (DIR), fluid-attenuated inversion recovery (FLAIR), T2 weighted image (T2WI)

Introduction

MS is the most common chronic inflammatory demyelinating disease of the central nervous system. It is the 2^{ed} most common cause of non-traumatic disability in young adults after trauma which is the most common cause. It is characterized by multiple inflammatory demyelinating foci called MS plaques and its clinical presentation depends on its location **(1)**.

MRI allows diagnosis and monitoring of MS within the specific diagnostic criteria. MRI imaging for MS diagnosis is performed using a multisequence protocol including FLAIR (fluid-attenuated inversion recovery, T2WI (T2 weighted image), pre contrast and postcontrast T1-weighted images **(2)**.

Different pulse sequences have different sensitivity for detection of MS lesions; FLAIR has the highest sensitivity for detection of lesions close to CSF such as peri ventricular and juxtacortical lesions, T2 has the highest sensitivity for detection of infra tentorial lesions. Yet, there is no pulse sequence has the ability to provide high sensitivity for detection

of supra and infra tentorial MS lesions at different anatomical locations [3].

In spite of description of the grey matter involvement in MS, the conventional MRI sequences don't have the ability of detection of MS cortical lesions as these lesions are typically small, have poor contrast with the surrounding normal appearing grey matter and partial volume effects from the CSF [3].

Later on, at the last few years a new MRI pulse sequence called DIR (double inversion recovery) was developed and introduced in MS diagnosis for cortical lesions. It uses two inversion times to suppress the signal from white matter and from the CSF simultaneously and so, allows better delineation of the cortical grey matter lesions [4].

DIR is used to improve the sensitivity of MRI in detection of such cortical lesions. The increased contrast between the lesions and the surrounding normal appearing GM resulting in an improved distinction between juxtacortical and mixed WM-GM lesions. Cortical lesions appear hyperintense in DIR compared to the adjacent normal appearing grey matter [5].

DIR revealed that cortical lesions are significantly more numerous and frequent at later stages of MS but also can be detected in early stages of the disease. Cortical lesions are related to the clinical disability as changes that occur in the cerebral cortex are found to be associated with progression of disability in MS patients [6].

Aim of the study:

To assess the diagnostic value of DIR sequence in the detection of MS lesions with certain emphasis on cortical grey matter lesions, by comparing DIR with FLAIR and T2-weighted pulse sequences in the brain.

Methods

The study was conducted in the department of diagnostic Radiology, faculty of Medicine, Minia university hospital and after being ethically approved by ethical committee of faculty of medicine. All patients gave their consent to participate in the study.

Thirty MS patients with age between 20 and 50 years were included and referred from department of neurology. Patients diagnosed with multiple sclerosis (MS) according to revised McDonald criteria 2017, both sexes were included.

Patients with absolute contraindications to MRI as an implanted magnetic device, cardiac pacemaker or claustrophobic patients, patients with associated other neurological disease with MS were excluded from the study.

The patients are subjected to:

Full history taking and neurological examination were done to all MS patients**.**

All patients underwent MR imaging of the brain using 1.5 tesla MRI, using a standard head coil for the brain. Patients in a supine position. T1WI, T2WI, FLAIR, DIR, DWI and ADC sequences are performed in axial planes in addition to sagittal planes for FLAIR and DIR with a slice thickness about 1.3 mm.

Image interpretation*:* all images were analyzed by two neuroradiologists. Detailed brain analysis was performed on axial T2-weighted images along with FLAIR and DIR sequences. Assessment of the distribution of MS plaques in different sites of the brain among 30 MS patients (including periventricular, deep white matter, cortical, juxtacortical and infratentorial regions as well as deep grey matter region of the brain) and their number in each site.

Statistical analysis:

Analysis of the data was done by personal computer using SPSS (Statistical program for social science) version 19. The data of all software patients were fed into an IBM personal computer. Median and Inter-quartile range (IQR) are used for non-parametric numerical data. Frequency and percentage are used for non-numerical data. Mann Whitney Test (U test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups and Kruskal-Wallis H Test for two groups or more. The difference was expressed as probability of value (P value). The difference was considered significant if $P < 0.05$.

Results:

The study involved 30 MS patients (86.7% were females and 13.3% were males), with age ranged from (20-50) years with median ± IQR was (25.00± 25.00) years as shown in table 1.

Relapsing Remitting Multiple sclerosis (RRMS) was the most common disease course among the studied patients (86.7%), while clinically isolated syndrome (CIS) was reported in (13.3 %) as shown in figure 1.

Regarding clinical presentation: visual disorder was the most common presenting symptom (26.7%), 23.30% had tingling and numbness, 16.70% had ataxia, 13.30% had monoparesis, 10% had hemiparesis, 6.70% had headache and vertigo and 3.30% had paraparesis as shown in table 2.

The periventricular and deep white matter (DWM) lesions were detected in all studied patients at DIR, FLAIR and T2 sequences, followed by infratentorial lesions in (93.3%, 66.7% and 80% of patients respectively) and juxtacortical lesions in (86,7%, 83.3% and 63.3% of patients respectively), as shown in table 3.

The percentage of cases with cortical and deep grey matter affection detected in DIR sequence among the studied MS patients was (76.7% and 66.7%) respectively and in FLAIR sequence in (40% and 33.3%) respectively, as shown table 3.

Regarding the cortical lesions, the median number of cortical lesions ± IQR detected by DIR sequence (3.00 ± 3.00) was significantly higher than that detected by FLAIR sequence (1.00± 2.00) and T2 sequence (0.00 ±1.00), with a statistically significant difference (P-value< 0.001 and 0.0001 respectively) as shown in table 4 & figure 2.

Regarding the juxta cortical lesions, median number of juxta cortical lesions ± IQR in DIR sequence (2.00 ±2.00) was significantly higher than that of FLAIR sequence (1.00±1.00) and that of T2 sequence (1.00 ±2.00), with statistically significant difference (P-value <0.032), as shown in table 5.

Regarding the infratentorial lesions, the median number ± IQR detected by DIR sequence (2.00 ±2.00) was significantly higher than that of FLAIR sequence (1.00±3.00) with statistically significant difference (P-value <0.039), as shown in table 5.

Regarding peri ventricular lesions, median number of peri ventricular lesions ± IQR in FLAIR sequence (5.00±3.00) was significantly higher than that of DIR sequence (4.00 ±5.00) and that of T2 sequence (2.00 ±3.00), with statistically significant difference (P-value = <0.0001).

As Regards DWM lesions, we found that T2 sequence detected the highest number of lesions, with median± IQR (13.00 ± 14.00) superior to FLAIR sequence (9.00 ± 12.00) and DIR sequence (7.00 ± 8.00), with (P-value < .,20 and 0.018) respectively.

Median number of corpus callosum lesions ± IQR detected by sagittal FLAIR (2.00 ± 2.00) was higher than that detected by DIR sequence (1.00 ± 3.00) but with no statistically significant difference ((P-value <0.185), as shown in figure 2.

There was positive correlation between the duration of the disease and the number of cortical lesions detected at DIR sequence (r= 0.396); increased duration of the disease is associated with increased number of cortical lesions detected at DIR sequence, that was statistically significant (P-value <0.030), as shown in figure 4.

The sensitivity, specificity, positive and negative predictive values (PPV, NPV) and accuracy of DIR sequence in the detection of cortical grey matter lesions were 97.1%, 100%, 100%, 50% and 97.15% respectively. The sensitivity, specificity, positive and negative predictive values as well as accuracy of FLAIR sequence were 100%, 50%, 97.1%, 100% and 97.14% respectively. AUC (area under the curve) for cortical lesions in DIR sequence was 0.875, relatively higher than that of FLAIR sequence 0.861. So, DIR has better diagnostic performance for detection of cortical grey matter lesions. As shown in table 6 and figure 5&6.

Table1: Socio-demographic data among the studied 30 MS patient:

Variable	Total (n =30)
Age (years)	
Median ± IQR	25.00± 25.00
Minimum	20.00
Maximum	50.00
Gender	
Male	4(13.3%)
Female	26(86.7%)

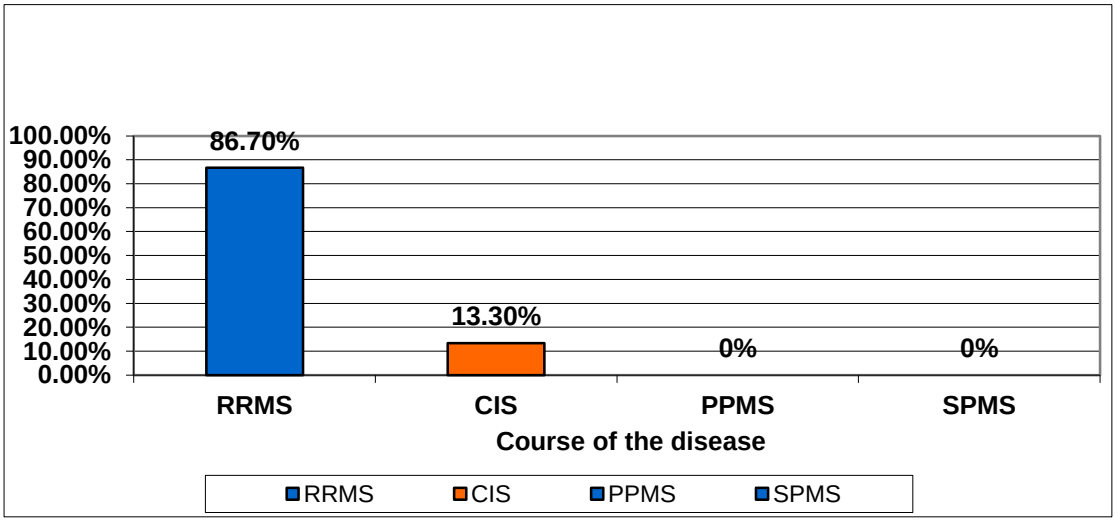


Figure 1: Clinical types of multiple sclerosis among the studied cases.

- *RRMS (relapsing remitting multiple sclerosis)*
- *CIS (clinically isolated syndrome)*
- *PPMS (primary progressive multiple sclerosis)*
- *SPMS (secondary progressive multiple sclerosis)*

Table 2: Clinical data among the studied cases:

Presenting symptoms	N (%) **(Total = 30)**
Visual disorder	8(26.7%)
Tingling and numbness	7(23.3%)
Ataxia	5(16.7%)
Monoparesis	4(13.3%)
Hemiparesis	3(10.0%)
Headache & vertigo	2(6.7%)
paraparesis	1(3.3%)

Table 3: Rate of detection of different brain lesions among MS patients in DIR, FLAIR and T2 sequences (No= 30)

	Axial DIR N (%)	**Axial FLAIR N (%)**	**Axial T2 N (%)**
Patients with Cortical lesions			
yes	23 (76.7%)	20 (66.7%)	13 (43.3%)
no	7 (23.3 %)	10 (33.3%)	17 (56.6%)
Patients with Deep grey matter lesions			
yes	12 (40%)	10 (33.3%)	12 (40%)
no	18 (60%)	20 (66.7%)	18 (60%)
Patients with peri ventricular lesions			
yes	30 (100%)	30 (100%)	30 (100%)
no	0 (0%)	0 (0%)	0 (0%)
Patients with deep white matter lesions			
yes	30 (100%)	30 (100%)	30 (100%)
no	0 (0%)	0 (0%)	0 (0%)
Patients with juxta cortical lesions			
yes	26 (86.7%)	25 (83.3%)	19 (63.3%)
no	4 (13.3%)	5 (16.7%)	11 (36.7%)
Patients with infra tentorial lesions			
yes	28 (93.3%)	20 (66.7%)	24 (80%)
no	2 (6.7%)	10 (33.3%)	6 920%)

Table 4: Agreement between DIR, T2 and FLAIR results as regarding the cortical lesions among studied cases (No= 30)

Variable	**DIR**	**FLAIR**	**T2**	**Total p-value**	**DIR vs FLAIR**	**DIR vs T2**	**FLAIR vs T2**
cortical lesions							
Median ± IQR	3.00± 3.00	1.0± 2.00	0.00±1.00	<0.0001*	0.001*	<0.0001*	0.018*

- *Data displayed as Median, interquartile rang (IQR)*
- *Kruskal Wallis Test test for quantitative data between the groups,*
- *Man Whitney test for quantitative data between two groups*

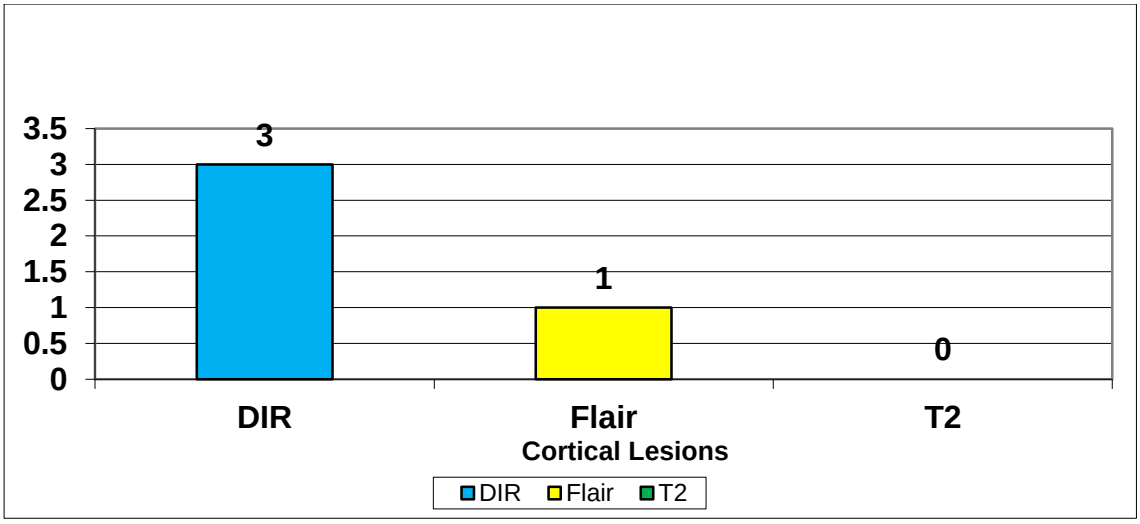


Figure 2: Median of DIR, FLAIR and T2 results as regarding cortical lesions among studied cases.

Table 5: Agreement between DIR, T2 and FLAIR sequences results as regarding number of lesions detected among the studied cases (No = 30)

Variable	DIR	FLAIR	T2	Total p-value	DIR vs FLAIR	DIR vs T2	FLAIR vs T2
juxta cortical lesions	2.0 ±2.0	1.00±1.00	1.00 ±2.0	0.032*	0.064	0.024*	0.667
DWM lesions	7.0 ±8.0	9.00±12.00	13.0±14.0	0.083	0.267	0.018*	0.203
Peri ventricular lesions	4.0 ±5.00	5.0±3.00	2.00 ±3.0	<0.0001*	0.125	<0.0001*	<0.0001*
DGM lesions	0.0 ±1.00	0.0 ±1.00	0.00 ±1.0	0.972	0.698	0.698	1.000
Infratentorial Lesions	2.0±2.00	1.00±3.0	2.00 ±3.0	0.119	0.039*	0.275	0.320

- *Data displayed as Median, interquartile rang (IQR)*
- *Kruskal Wallis Test for quantitative data between the groups*
- *Man Whitney test for quantitative data between the groups*
- *Significant level at P value < 0.05*
- *DWM (deep white matter)*
- *DGM (deep gray matter)*

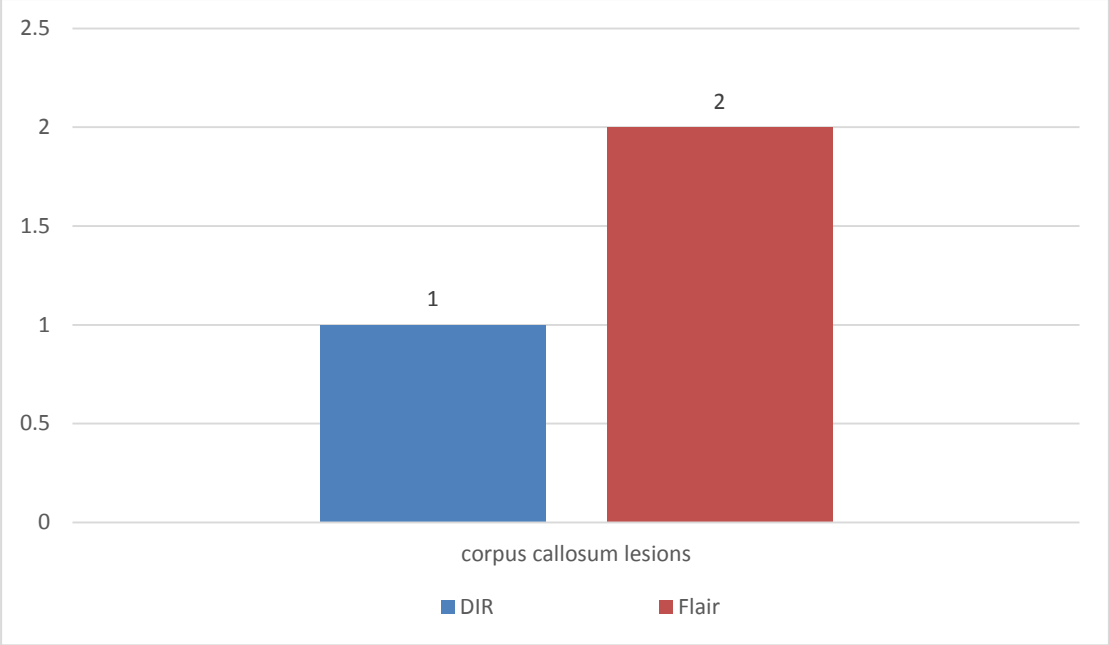
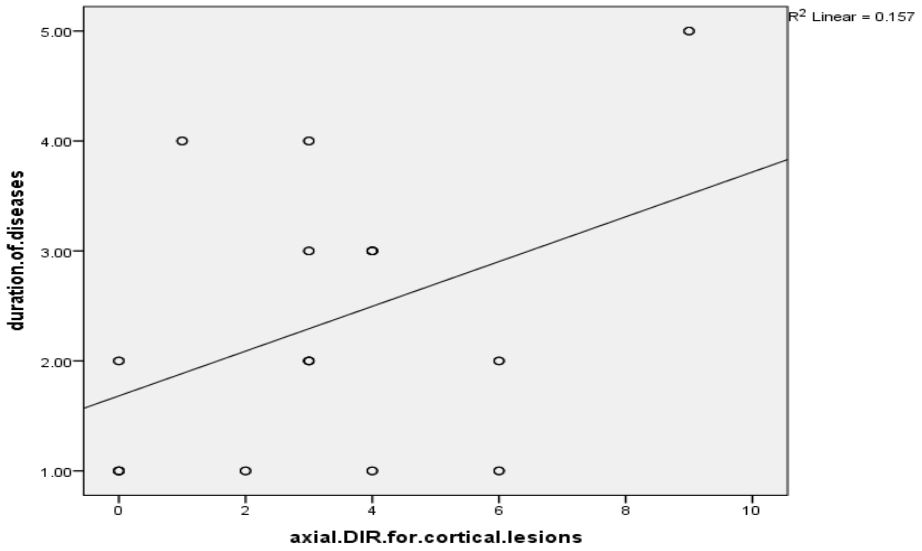


Figure 3: Median of DIR and FLAIR results as regarding corpus callosum lesions among studied cases.



N.B. r=0.3, p value= 0.03

Figure 4: Correlation between number of cortical lesions in DIR sequence and duration of the disease among the studied cases.

Table 6: ROC curve analysis for the prediction of cortical grey matter lesions using different MRI pulse sequences (DIR and Flair) among studied cases

characteristic	FLAIR	DIR
AUC	0.861	0.875
Sensitivity	100.0%	97.1%
Specificity	50.0%	100.0%
PPV	97.1%	100.0%
NPV	100.0%	50.0%
Accuracy	97.14%	97.15%

- *AUC (area under the curve)*
- *PPP (positive predictive value)*
- *NPP (negative predictive value)*

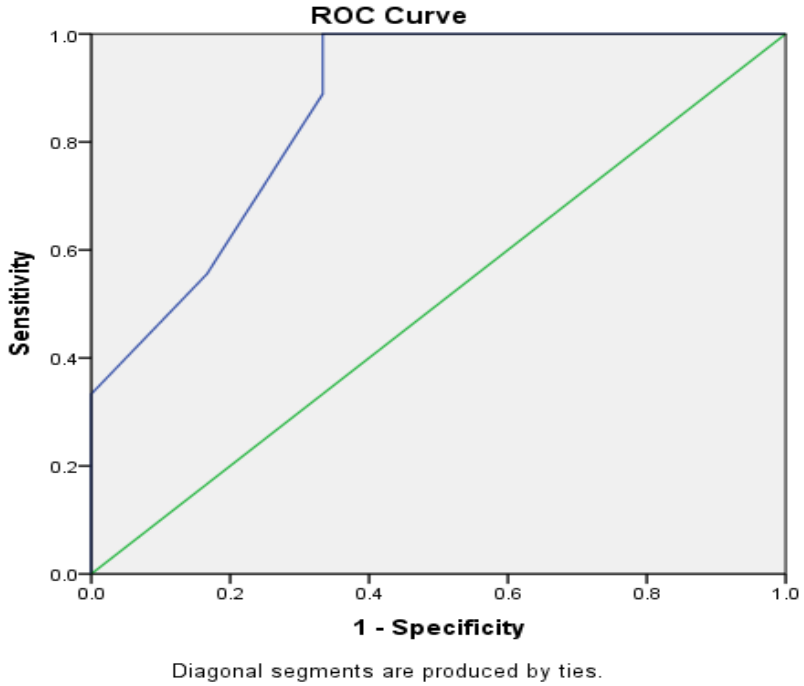


Figure 5: ROC curve analysis for the prediction of cortical grey matter lesions using FLAIR MRI pulse sequence among studied cases.

AUC (area under the curve) for cortical lesions in FLAIR sequence was 0.861

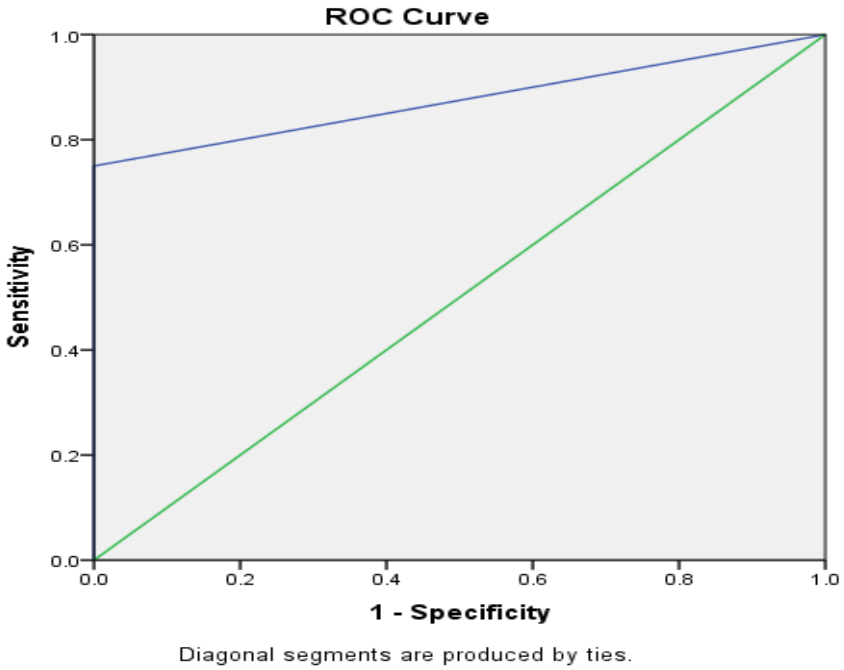


Figure 6: ROC curve analysis for the prediction of cortical grey matter lesions using DIR MRI pulse sequence among studied cases.
AUC (area under the curve) for cortical lesions in DIR sequence was 0.875.

Discussion

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating and neurodegenerative disease of the central nervous system. Magnetic resonance imaging (MRI) has an important role in diagnosis of MS [(1)].

30 patients diagnosed with MS according to revised McDonald criteria 2017 were included and examined in this study. Regarding the demographic data, including the range of age of the studied cases which was from (20-50) years and the median age of all patients ± IQR was (25.00± 25.00) years. 86.7% were females and 13.3% were males, this was in agreement with Sarbu N, et al., (2016) who reported that MS is a disease of female predilection with female/male ratio 2:1[(7)].

The studied patients were categorized according to their clinical course (86.7% were RRMS type while only 13.3% were categorized as CIS type). This matches with the finding of Lublin FD, et al., (2014) and Frohman EM et al., (2005) as they demonstrated that RRMS is the most common disease course in MS [(8,9)].

The percentage of patients with cortical lesions detected in DIR sequence was higher than those with detected cortical lesions in FLAIR sequence (76.6% versus 66.7%) of cases. This was in agreement with the findings of Abidi Z, et al., (2017) who reported that rate of cortical lesions detection is higher in DIR than FLAIR sequence [(3)].

Rate of deep grey matter lesions detected in DIR sequence was higher than FLAIR (40% versus 33.3%) of cases. We were in agreement with Lucchinetti CF, et al., (2011) who reported that deep grey matter lesions are better delineated at DIR more than FLAIR sequence [(10)].

As regard the cortical lesions, we found that DIR sequence detected significantly more cortical lesions with median± IQR (3.00 ± 3.00), when compared to FLAIR and T2 sequences (1.00± 2.00) and (0.00±1.00) respectively, (P-value = <0.0001). This was in agreement with the studies done by Abidi Z, et al., (2017) and Lucchinetti CF, et al., (2011) who reported that cortical lesions detected in

DIR sequence was higher than those detected at the FLAIR and T2 sequence [3,10].

As regard the median number of juxta cortical lesions ± IQR detected in DIR sequence (2.00 ±2.00) was significantly higher than that detected by FLAIR sequence (1.00±1.00) and T2 sequence (1.00 ±2.00), with (P-value = 0.032), that was in consistent with the findings of Abidi Z, et al., (2017) [3] who reported that the number of juxta cortical lesions detected by DIR were higher than those detected by FLAIR&T2 sequences [3].This result was in contrary with the result done by Geurts et al., (2005) [5] which detected the highest number of lesions with T2.

Another important advantage of DIR in our study was its ability to detect infratentorial lesions. DIR identified significantly more lesions in comparison to FLAIR (p-value=0.039). But, it was worthy of attention that DIR detected higher lesions even when compared with the T2 sequence, but the difference was below the statistical importance (p-value=0.275), which is considered the "gold standard" in the infratentorial region. This was consistent with the results done by Elnekeidy et al. (2014) [6], Geurts et al. (2005) [5] and Wattjes and Barkhof (2007) [11], but in contrary with results done by Moraal et al., (2009) [12], who found a similar number of lesions in the infratentorial region with DIR, FLAIR, and T2 images.

As Regards DWM lesions, we found that T2 detected the highest number of lesions median± IQR (13.00 ± 14.00) followed by FLAIR and DIR came last. This was equivalent to Vural et al., (2013) [13], who reported the highest DWM lesions was detected by T2. While Tawfik, A.I, Kamar, W.H. (2020) [14], reported that number of deep white matter lesions detected in FLAIR was higher than other examined sequences.

There was positive correlation between the duration of the disease and the number of cortical lesions that detected at DIR sequence (r= 0.396); increased duration of the disease is associated with increased number of cortical lesions detected at DIR sequence, that was statistically significant (p value=0.030). This finding was in agreement with Roosendaal SD, et al., (2009) who reported that number of cortical lesions increase significantly over time [15].

Conclusion:

It was found that DIR brain imaging had the highest sensitivity in the detection of cortical, juxtacortical and infratentorial lesions compared with FLAIR and T2 sequences. DIR sequence should be included in the routine MR protocols of MS patients especially as it has better diagnostic performance for detection of cortical grey matter lesions

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