

## Research Article

## Detection of Multiple Sclerosis Lesions in Supra- and Infra-Tentorial Anatomical Regions by Double Inversion Recovery, Flair, and T2 MRI Sequences: A Comparative Study in Iraqi Patients

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## Abstract

**Background:** In young adults, multiple sclerosis is a prevalent chronic inflammatory demyelinating condition. It is characterized by white matter affection, but many individuals also have significant gray matter involvement. A double-inversion recovery pulse (DIR) pattern was recently proposed to improve the visibility of multiple sclerosis lesions. **Objective:** To find out how well a DIR sequence, FLAIR, and T2-weighted pulse sequences can find MS lesions in the supratentorial and infratentorial regions. **Methods:** A total of 37 patients with established diagnoses of multiple sclerosis were included in this cross-sectional study. Brain MRI was done using double inversion recovery, T2, and FLAIR sequences. The number of lesions was counted and compared in the three sequences. **Results:** The DIR sequence detected more infratentorial lesions when compared to the T2 and FLAIR sequences. In the supratentorial region, DIR detected more lesions than T2 and FLAIR. **Conclusion:** The DIR sequence is highly superior to both the T2 and FLAIR sequences in depicting the lesions, regardless of their anatomical distribution. Moreover, the DIR sequence detected more multiple sclerosis lesions in the infratentorial region than the traditional T2W and FLAIR sequences.

**Keywords:** Double inversion recovery sequence, FLAIR sequence, Multiple sclerosis, T2 weighted image.

الكشف عن آفات التصلب المتعدد في المناطق التشريحية فوق وتحت الوترية عن طريق استعادة الانعكاس المزدوج، والتوهج، وتسلسل التصوير بالرنين المغناطيسي T2: دراسة مقارنة في المرضى العراقيين

## الخلاصة

**الخلفية:** عند البالغين الشباب، يعد التصلب المتعدد حالة التهابية مزمنة سائدة ومزيلة للميالين. ويتميز بتأثير المادة البيضاء، ولكن العديد من الأفراد لديهم أيضًا مشاركة كبيرة في المادة الرمادية. تم مؤخرًا اقتراح نمط نبض استرداد الانعكاس المزدوج (DIR) لتحسين رؤية آفات التصلب المتعدد. **الهدف:** مقارنة الفائدة التشخيصية لتسلسل DIR في الكشف عن آفات مرض التصلب العصبي المتعدد في المناطق فوق الخيمة وتحت الخيمة مع تسلسل النضج الموزون FLAIR وT2. **الطرق:** تم تضمين 37 مريضًا مع تشخيص ثابت لمرض التصلب المتعدد في هذه الدراسة المستعرضة. تم إجراء التصوير بالرنين المغناطيسي للدماغ باستخدام الاسترداد المزدوج للانعكاس، وتسلسلات T2 وFLAIR. تم حساب عدد الآفات ومقارنتها في التسلسلات الثلاثة. **النتائج:** اكتشف تسلسل DIR المزيد من الآفات تحت الخيمة بالمقارنة مع تسلسل T2 وتسلسل FLAIR. في المنطقة فوق الخيمة اكتشف DIR آفات أكثر من T2 و FLAIR. **الاستنتاج:** تسلسل DIR يتفوق بشكل كبير على كل من تسلسل T2 وFLAIR في تصوير الآفات بغض النظر عن التوزيع التشريحي. علاوة على ذلك، اكتشف تسلسل DIR المزيد من آفات التصلب المتعدد في المنطقة تحت الخيمة مقارنة بتسلسلات FLAIR وT2 التقليدية.

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## INTRODUCTION

Multiple sclerosis (MS) is one of the most prevalent chronic inflammatory demyelinating diseases of the central nervous system and is considered a common cause of neurological disability in young and middle-aged patients, resulting in both physical and neurocognitive disability [1,2]. It is characterized by central nervous system (CNS) inflammation and demyelination, along with varying degrees of axonal and neuronal damage [3]. The tentorium is a dural reflection that divides the cranial cavity into two sections: supratentorial and infratentorial. The supratentorial compartment contains the cerebral hemispheres, as well as the thalamus and the basal ganglia. The brain stem and cerebellum are housed in the infratentorial region, also known as the posterior fossa [4]. Pathologically, multiple sclerosis is characterized by the formation of focal regions of demyelination, often scattered around perivenular areas, as well as reactive gliosis, axonal injury, and neuronal degeneration [5]. While the condition primarily affects the periventricular areas, callosal-septal interface, cerebellum, brainstem, and basal ganglia, The McDonald criteria diagnose multiple sclerosis (MS) by requiring objective evidence of lesions dispersed in time and space, either clinically or radiologically, as well as the elimination of other conditions that may mimic MS based on their clinical and laboratory profiles [6]. In certain instances, the 2017 revisions of the McDonald criteria on multiple sclerosis diagnosis [8] reinforced the significance of brain and spinal cord MRI exams [7,8]. The diagnostic, prognostic, and monitoring value of MRI in individuals with multiple sclerosis is well established [9]. The role of MRI in the diagnosis of MS is substantial; MRI protocols are divided into two separate categories: "conventional" and "advanced." The conventional protocols include T1-weighted pre- and post-gadolinium contrast and T2-weighted and fluid-attenuated inversion recovery (FLAIR) pulse sequences at 1.5T magnetic field strengths in the spinal cord and brain. T2-weighted and FLAIR sequences are the most commonly utilized for brain MRI. T2-weighted sequences seem to be the most sensitive for detecting lesions in the brainstem and cerebellum, but FLAIR is more sensitive for detecting periventricular and cortical/juxtacortical lesions [10]. The application of the DIR sequence in the diagnosis of neurological diseases such as infectious, vascular, and neoplastic problems has been the subject of numerous studies [11]. A research project by Hamed *et al.* (2019) and was conducted to assess the diagnostic effectiveness of a double inversion recovery (DIR) sequence in identifying MS lesions in the brain and infratentorial structures [12]. The present study aimed to evaluate the diagnostic utility of the DIR sequence in detecting MS lesions in supratentorial and infratentorial regions with FLAIR and T2-weighted pulse sequences.

## METHODS

### Study designs and ethical considerations

A prospective study was conducted during the period from November 2022 to May 2023, which included 37 patients (17 males and 20 females) who underwent brain MRIs of known MS disease cases in different genders and age groups (they had already received a multiple sclerosis diagnosis in accordance with the 2017 revised McDonald Criteria). All patients were referred from the Neurology Department/outpatient clinic for multiple sclerosis to the MRI unit of the radiology department at Al Shaheed Ghazi Al Hariri Hospital, Medical City. The local ethical committee of the College of Medicine, University of Baghdad, approved the study. All patients were informed to obtain their consent before inclusion, and their information was used anonymously in this study. The data were collected and interpreted by two qualified radiologists.

### Inclusion criteria

Adults with definitive diagnosis of MS coming for regular follow up or have acute exacerbation of symptoms.

### Exclusion criteria

Multiple sclerosis patients who also have a concurrent neurological disease, patients with no MRI detectable CNS lesions due to remission, and patients with any neoplastic, vascular, or immunological CNS illnesses in the current or past medical history were excluded.

### Outcome measurements

A 1.5 T MR imaging scanner (Philips Achieva Nova, dual 16-channel, Netherlands) was used to perform brain MRI, in which all patients underwent supine scans using a conventional circularly polarized head coil. We performed T2W, FLAIR, and DIR sequences in axial sections. The parameters are summarized in Table 1.

**Table 1:** parameters of MRI sequence

Parameter	DIR	FLAIR	T2W
TR (ms)	14000	6000	1000
TE (ms)	25	120	110
TI (ms)	3400/325**	2000	
Slice thickness (mm)	3	3	3
FOV (mm)	300	300	300
Matrix size	350	350	350
Voxel size	0.7, 0.8, 4	0.7, 0.8, 4	0.7, 0.8, 4
NSA	2	2	2
Time (min)	5:22	2:06	1:22

\* TR: repetition time, TE: echo time, TI: inversion time, FOV: field of view, NSA: number of signal averaging. \*\* TII (3400 ms) is the time interval between the initial 180° inversion pulse and the 90° excitation pulse. The second 180° inversion pulse and the 90° excitation pulse are separated by the short inversion time TII (325 ms).

The number of high-signal-intensity lesions in the brain that were at least 3 mm in size were tallied in

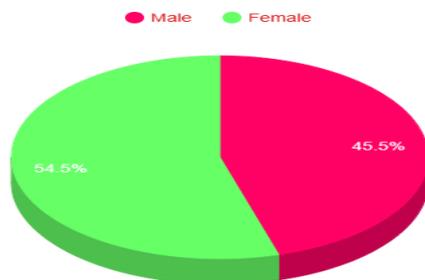
each of the three pulse sequences; hyperintense lesions were only counted once when they appeared on multiple contiguous slices. Their location was documented and classified into supratentorial and infratentorial lesions.

**Statistical analysis**

Raw data were tabulated using Microsoft Excel 2016, which were later imported via the IBM Statistical Package for Social Sciences version 26 (IBM-SPSS v.26) to conduct descriptive statistics, normality testing (Shapiro-Wilk test), and inferential hypothesis tests, including the Spearman's rank-order correlation, paired (Wilcoxon signed-rank test) and unpaired testing (Mann-Whitney U test), and the analysis of variance (ANOVA) with post-hoc pairwise comparisons. We used the Bonferroni correction to reduce type I errors resulting from multiple comparisons. An alpha ( $\alpha$ ) value of 0.05 was considered the cut-off margin for statistical significance, corresponding to a 95% confidence interval (95%). We analyzed multiple brain lesions using different pulse sequences, including DIR, 2D-FLAIR, and T2. We represented the relative comparison of the number of MS brain lesions observed on DIR versus 2D-FLAIR and T2 imaging as a percentage indicating the gain or loss in the number of detected brain lesions.

**RESULTS**

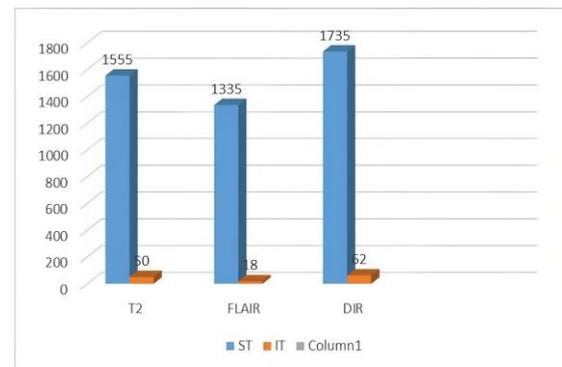
We included a total of 37 patients with an established diagnosis of MS in this study. The patients included 20 (54.05%) females and 17 (45.95%) males (Figure 1). The age ranges from 17 to 64 years. Different MRI sequences detected a total of 1605 lesions on T2W, 1353 lesions on FLAIR, and 1797 lesions on DIR. The DIR sequence was highly significant and superior to both the T2 and FLAIR sequences ( $p < 0.001$ ) in depicting the lesions regardless of their anatomical distribution (Table 2, Figure 2 and Figure 3).



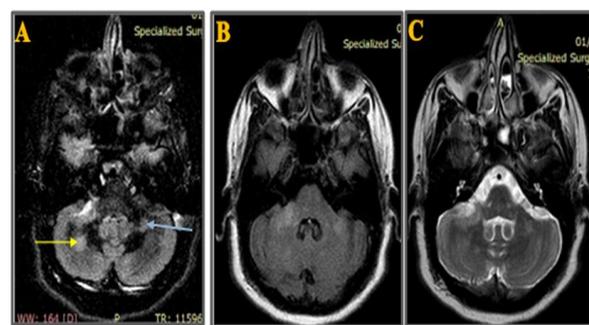
**Figure 1:** Gender prevalence in sampled multiple sclerosis patients

**Table 2:** The total lesions detected in the three MRI sequences (T2, FLAIR and DIR) regardless its anatomical distribution.

Parameters	Number of lesions	mean±SD	p-value
DIR total detected lesion	1797	48.57±35.1	0.000
T2 total detected lesion	1605	43.38±31.5	0.000
FLAIR total detected lesion	1353	36.57±21.6	0.000



**Figure 2:** Analysis of the total number of supratentorial and infratentorial lesions detected on DIR, T2 and FLAIR sequences. ST: supratentorial, IT: infratentorial.



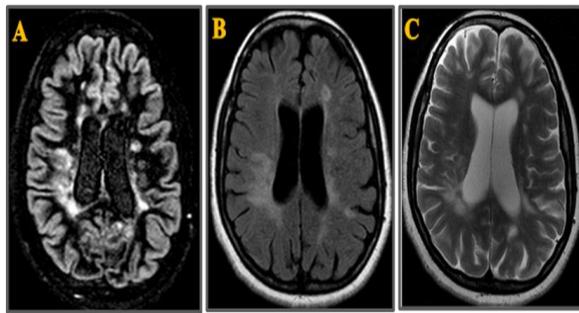
**Figure 3:** Infratentorial lesions in axial brain MRI of a 22 years old female with relapsing remitting MS. There is a lesion in the right cerebellar hemisphere (yellow arrow) that is more clearly seen at DIR (A), than T2 (C), the lesion is poorly seen at FLAIR (B). Another smaller lesion (blue arrow) is seen in the left cerebellar hemisphere at DIR(A)but not in T2(C) or FLAIR.

Regarding the infratentorial (IT) region, DIR identifies significantly more lesions than T2 and FLAIR sequences ( $p < 0.001$  and  $p = 0.001$ , respectively). Furthermore, the supratentorial lesions detected by DIR were greater than those detected by T2 and FLAIR sequences, as demonstrated by ( $p = 0.019$  and  $p < 0.001$ , respectively), which is statistically significant (Table 3, Figure 2 and Figure 4).

**Table 3:** Total number of lesions detected in the supratentorial and infratentorial regions in the three sequences (DIR, T2 and FLAIR)

Parameters	n	mean±SD	p-value
DIR-infratentorial	62	1.68±1.75	0.019
T2- infratentorial	50	1.35±1.6	
FLAIR-infratentorial	18	0.49±0.8	<0.001
DIR-supratentorial	1735	10.92±9.8	<0.001
T2-supratentorial	1555	6.43±6.7	
FLAIR-supratentorial	1335	8.24±8.2	

Values are presented as mean±SD; n: number of lesions. DIR: double inversion recovery, FLAIR: fluid attenuation inversion recovery.



**Figure 4:** A 40 year's old female patient with RRMS. Axial brain MRI show more MS lesion load depicted on DIR (A) compared with FLAIR (B) and T2(C) images.

## DISCUSSION

T2W is a sensitive sequence in detecting infratentorial lesions, while FLAIR is extremely sensitive in depicting supratentorial brain lesions, especially in the periventricular white matter, due to CSF attenuation [13]. Combining two inversion pulses, the double inversion recovery sequence appropriately attenuates both CSF and WM. This resulted in a higher contrast ratio and greater distinction between gray and white matter, as well as a high sensitivity in identifying supratentorial brain lesions that was similar to FLAIR imaging, the gold standard in this field [14]. In this study, both conventional (T2, FLAIR) and DIR sequences were used to produce brain imaging sequences for MS patients. The total number of lesions found in DIR was much higher than in T2 and FLAIR sequences. The results of the studies by Elnekeidy *et al.* [15] and Abidi *et al.* [16] were also similar. In the infratentorial region, DIR detects more lesions than T2 and FLAIR. It detected a higher number of lesions, even more than T2W ( $P = 0.019$ ), which represents the gold standard for infra-tentorial lesions detection. These findings were similarly consistent with those reported by Elnekeidy *et al.* [15], Abidi *et al.* [16], Yousra *et al.* [17], Simon *et al.* [18], and Hamed *et al.* [12] studies, nonetheless, contrary to the findings of a study conducted by Ahmed and co-workers [19], who found a greater number of infratentorial lesions on T2 than on DIR, and they attributed this to more posterior fossa artifacts on DIR, which may lead to misinterpretation of some real lesions as artifacts. Fattouh *et al.* [14] and Almutairi *et al.* [20] were comparing MS lesion load in DIR, FLAIR and T2W sequences using 3T MR imaging scanners. They detected a greater number of infratentorials on the DIR. Performing the DIR sequence is a useful strategy that could influence the diagnosis and treatment decision at the onset of the disease, especially in patients with clinically isolated syndrome (CIS). The improved lesion identification at DIR would be extremely beneficial in suspected MS cases, allowing the diagnosis to be changed from “possible” to “definite” MS as it would complete the criteria of dissemination in space and time [14]. Furthermore, it can aid in the identification of patients at risk of developing aggressive MS. who will need more aggressive therapies like natalizumab [6]. In this

study, there were some DIR-related artifacts. In the extra-cortical areas, some bilateral high-signal ribbon-like artifacts were present due to the effect of cerebral cortical vessels. The observation of their anatomical location, variable appearance in continuous sections, and other MRI sequences, including T1W or FLAIR, can help to differentiate lesions from artifacts. CSF pulsation or the presence of venous sinuses and larger vessels might have caused other artifacts at the choroid plexus and posterior fossa. Despite the long acquisition time of DIR (5:22 minutes) relative to the shorter time of conventional sequences (2:06 minutes in FLAIR, 1:22 minutes in T2), the results in this study were very promising in detecting higher lesion loads on DIR in supratentorial and infratentorial locations.

## Study Limitations

Small sample study due to the exclusion criteria, by which many patients with remission have no detectable MRI lesion.

## Conclusion

The DIR sequence is highly superior to both the T2 and FLAIR sequences in depicting the lesions, regardless of their anatomical distribution. Moreover, the DIR sequence detected more multiple sclerosis lesions in the infratentorial region than the traditional T2W and FLAIR sequences. Including the DIR sequence in regular MRI investigations of MS patients can help resolve problems related to infratentorial lesions.

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## Conflict of interests

No conflict of interest was declared by the authors

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## Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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