Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH

Open Access

Comparison between the diagnostic utility of three-dimensional fluid attenuated inversion recovery (3D FLAIR) and three dimensional double inversion recovery (3D DIR) magnetic resonance sequences in the assessment of overall load of multiple sclerosis lesions in the brain

Nehal S. Saad[1], Azza A. Gad[1], Mahmoud M. Elzoghby[1] and Heba R. Ibrahim[1*]

Abstract

Background Multiple sclerosis (MS) is a complex CNS demyelinating disease. Assessment of MS plaques in specific anatomic locations in the brain was challenging to detect by conventional MRI sequences. So, this study aimed to compare the diagnostic accuracy of 3D FLAIR (Fluid attenuation inversion recovery), or 3D DIR (Double inversion recovery) sequences to conventional 2D FLAIR and T2 sequences in detecting MS plaques in different anatomic sites, as well as counting the total lesion burden.

Methods A comparative cross-sectional study enrolled 30 MS patients on the basis of McDonald's criteria 2017. All participants underwent a brain MRI study including 3D FLAIR or 3D DIR sequences, conventional 2D FLAIR, and T2 sequences.

Results No statistically significant difference between the 3D DIR and 3D FLAIR in total lesion (plaque) burden results; however, when each is compared to the conventional ones, both are superior. 3D FLAIR detected the most significant number of plaques in the periventricular region, followed by 2D FLAIR and T2W sequences, with 3D DIR being the least accurate in this region. Meanwhile, 3D DIR was the most precise and can detect a statistically significant number of cortical plaques compared to the 3D FLAIR and the conventional sequences. No statistically significant results on which sequence is best in regard to infratentorial plaque detection.

Conclusion 3D FLAIR and 3D DIR were superior to 2D FLAIR and T2 sequences in detecting overall lesion burden in MS. Moreover, the 3D DIR sequence was the most precise in the detection of the cortical plaques.

Keywords Brain MRI, 3D DIR, 3D FLAIR, Multiple sclerosis

*Correspondence:
Heba R. Ibrahim
h.refaat83@yahoo.com; h.refaat@med.suez.edu.eg
[1] Department of Diagnostic Radiology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Background

Multiple sclerosis (MS) is a complex demyelinating CNS disease of autoimmune nature that causes demyelination of neural axons and subsequent variable grades of axonal loss. It is considered one of the most common causes

of non-traumatic disability and decreased quality of life among young and middle-aged adults. MS is a relatively common disease affecting approximately 2.8 million people worldwide with women being more commonly affected with a female-to-male ratio of 2:1 [1–3].

Although MS has been classically described as a white matter disease, recently significant gray matter involvement has been proven to be part of the disease as well. Accordingly, cortical lesions were added to the most updated version of McDonald's Criteria 2017 [4]. White matter affection is usually seen as juxtacortical, periventricular, and infratentorial demyelinating lesions, while gray matter affection is seen in the brain cortex [5–7].

Diagnosis and follow-up of MS by brain magnetic resonance imaging has been included in McDonald's criteria since 2001 [8]. MS has a predilection for certain CNS sites with the ultimate method for white and gray matter lesions detection by MRI has been a subject of investigation. Due to technical insufficiencies conventional MRI sequences such as; T2 weighted, two-dimensional fluid-attenuated inversion recovery (2D FLAIR), T1 weighted pre and post-gadolinium can sometimes be inadequate, especially detection of MS lesions in certain locations such as; cortical, juxta cortical and infratentorial [3, 9–12].

Thus, technical advances have been made to conventional brain MRI sequences aiming to increase their sensitivity in MS lesion detection in certain anatomic locations. 3D Double Inversion Recovery (DIR) and 3D FLAIR were newly introduced MRI sequences. The diagnostic accuracy of these pulse sequences depends on the anatomic location of the lesion. No single pulse sequence was able to provide high sensitivity in detecting all MS lesions [13–16].

3D-FLAIR provides a more homogenous cerebrospinal fluid (CSF) suppression, better image resolution, is less affected by artifacts, and allows multi-planar reformatting compared to 2D FLAIR [17]. 3D DIR is a special pulse sequence that uses two inversion pulses suppressing the signal from both CSF and white matter of the brain, which increases the contrast of cortical lesions and is useful to detect MS at the earliest stages [18].

So, our study aim was to compare the diagnostic accuracy of 3D FLAIR (Fluid attenuation inversion recovery), or 3D DIR (Double inversion recovery) sequences to conventional 2D FLAIR and T2 sequences in detecting MS lesions in different anatomic sites, as well as counting the total lesion burden.

Methods

An ethically approved comparative analytical study by the local institutional ethics committee, signed consent was obtained from all participant patients in this study.

Study population

Thirty patients were enrolled in this comparative analytical study. These patients were diagnosed with multiple sclerosis on the basis of Mac Criteria (22 females and 8 males, with a mean age of 37.40 ± 14.85 years). This study was done during the period from September 2022 to August 2023.

Inclusion criteria included: a) Patients older than 18 years old, who were clinically diagnosed with MS on the basis of McDonald's criteria 2017 [4].

The *exclusion criteria* included a) Patients with any vascular, neoplastic, metabolic, or any other immunological CNS diseases, and b) Patients with MRI contraindications such as non-MRI compatible pacemakers, or MRI claustrophobia.

Clinical evaluation and brain magnetic resonance imaging were performed for all studied patients as the following.

Demographic data and history taking

The study included the patient's age, gender, and the clinical type of MS (relapsing–remitting- primary progressive, secondary progressive, or clinically isolated).

Brain magnetic resonance imaging

A) Patient preparation and position: The patients were instructed to remove all metallic objects. Explanation of the procedure to the patient for reassurance. Patients were informed about the value of being motionless during the scan time.

b) Brain magnetic resonance scan: A 1.5 Tesla MR scanner (Philips Medical Systems, Achieva 1.5 T A-series) was used to perform brain MRI for our studied patients. Interpretations of images were done by two different independent radiologists with > 10 years, and another one with 3 years of experience in neuroradiology, who were not aware of the patient's information.

Conventional brain magnetic resonance imaging

Conventional MRI sequences included axial and sagittal T2WI images with the following scan parameters (Repetition time (TR) of 4000 ms, echo time (TE) of 98 ms, a field of view (FOV) of 230 mm, matrix of 256 × 256, and a cut of 5 mm thickness, with a scan time of one minute and 28 s). Axial, and sagittal Fluid attenuated inversion recovery (FLAIR) was also performed with the following scan parameters (TR of 6000 ms, TE of 120 ms, FOV of 230 mm, a matrix of 256 × 256, and a cut of 5 mm thickness), the scan time of 4 min and 30 s for axial and sagittal planes.

Additional sequences

Additional sequences were added in terms of three-Dimensional Fluid attenuated inversion recovery (3D FLAIR), and three-Dimensional Double inversion recovery (3D DIR) Image acquisitions, as the following:

The 3D FLAIR sequence image acquisition in axial planes, with reformatted sagittal and coronal. The scan parameters included (TR of 4800 ms, TE of 351 ms, a FOV of 256×256, a matrix of 192×192 mm, and a cut of 1.5 mm thickness). The scan time was 5 min and 22 s.

The 3D DIR sequence image acquisition in sagittal planes, with reformatted axial and coronal. The scan parameters included (TR of 5500 ms, TE of 301 ms, a FOV of 256×256, a matrix of 192×192 mm, and a cut of 1.5 mm thickness). The scan time: 6 min and 70 s.

Image analysis

MS lesion was identified as a hyper-intense focus with a size of > 3 mm on a T2WI weighted sequence. Comparison between T2WI, 2D FLAIR, 3D FLAIR, and 3D DIR was done by counting the detected lesions in each sequence in different anatomical locations and then calculating the total lesion burden. The anatomical locations were as the following: (a) Cortical/juxta cortical lesions: Cortical lesions lie entirely within the cortex, while juxta cortical ones abut the cortex without intervening with normal white matter, (b) Periventricular lesions: Lesions that lay in direct contact with the lateral ventricle without intervening white matter, (c) Infratentorial lesions which were defined as T2 hyperintense lesion in the brainstem, cerebellar peduncles or cerebellum.

Statistical analysis

The data was entered into the computer and analyzed with the IBM SPSS software program version 20.0. IBM Corporation, Armonk, New York Numbers and percentages were used to describe qualitative data. The Shapiro–Wilk test was done to ensure that the distribution was normal. Range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) were used to characterize quantitative data. The significance of the acquired results was determined at a 5% level. The Friedman test was used to compare more than two periods or stages of quantitative data that had an abnormal distribution. For pairwise comparisons, the Post Hoc Test (Dunn's) is utilized.

Results

Demographic and clinical data

Thirty patients were examined (22 females and 8 males), and most of them were in the age group of 20–40 years. The majority of the participants were female patients (73%), while only a quarter of the participants were males. Most participants were young adults, where 40% of them were between 20 and 30 years of age, 30% were between 31 and 40 years of age, and only 13% of the participants were > 50 years of age, as shown in (Table 1).

Three clinical forms of MS were represented in our study which included relapsing–remitting MS, secondary progressive MS, and clinically isolated syndrome. Most patients had relapsing–remitting MS, the second most common clinical type in our study was secondary progressive MS, and 3% of patients had clinically isolated syndrome. There were no patients who had the primary progressive type of MS.

Imaging data

The number of MS plaques in each location and the total number of MS plaques (lesions) were calculated separately in each sequence in all studied patients. The study evoked that each sequence displayed different numbers of detected MS plaques per location. These locations included the cortical/juxta-cortical, periventricular, and infratentorial regions (Figs. 1, 2, 3, 4, 5, 6 and 7), as the following:

Cortical/juxta-cortical plaques

Cortical/juxta cortical plaques were counted in each sequence in all patients. A statistically significant difference between the detected number of cortical plaques in 3D DIR, and the other sequences (T2, 3D FLAIR, and 2D FLAIR) was observed. However, there was no statistically significant difference between the number of cortical plaques detected by 3D FLAIR to those detected by 2D FLAIR.

Regarding the plaques in the cortical/juxta-cortical region, 3D DIR showed the highest number of detected

Table 1 Distribution of the studied cases according to demographic data (n = 30)

Demographic data	No	%
Sex		
Male	8	26.7
Female	22	73.3
Age (years)		
20–30	12	40.0
31–40	9	30.0
41–50	5	16.7
> 50	4	13.3
Min. – Max	19.0–76.0	
Mean ± SD	37.40 ± 14.85	
Median (IQR)	33.0 (29.0–45.0)	

IQR: Inter quartile range, SD: Standard deviation

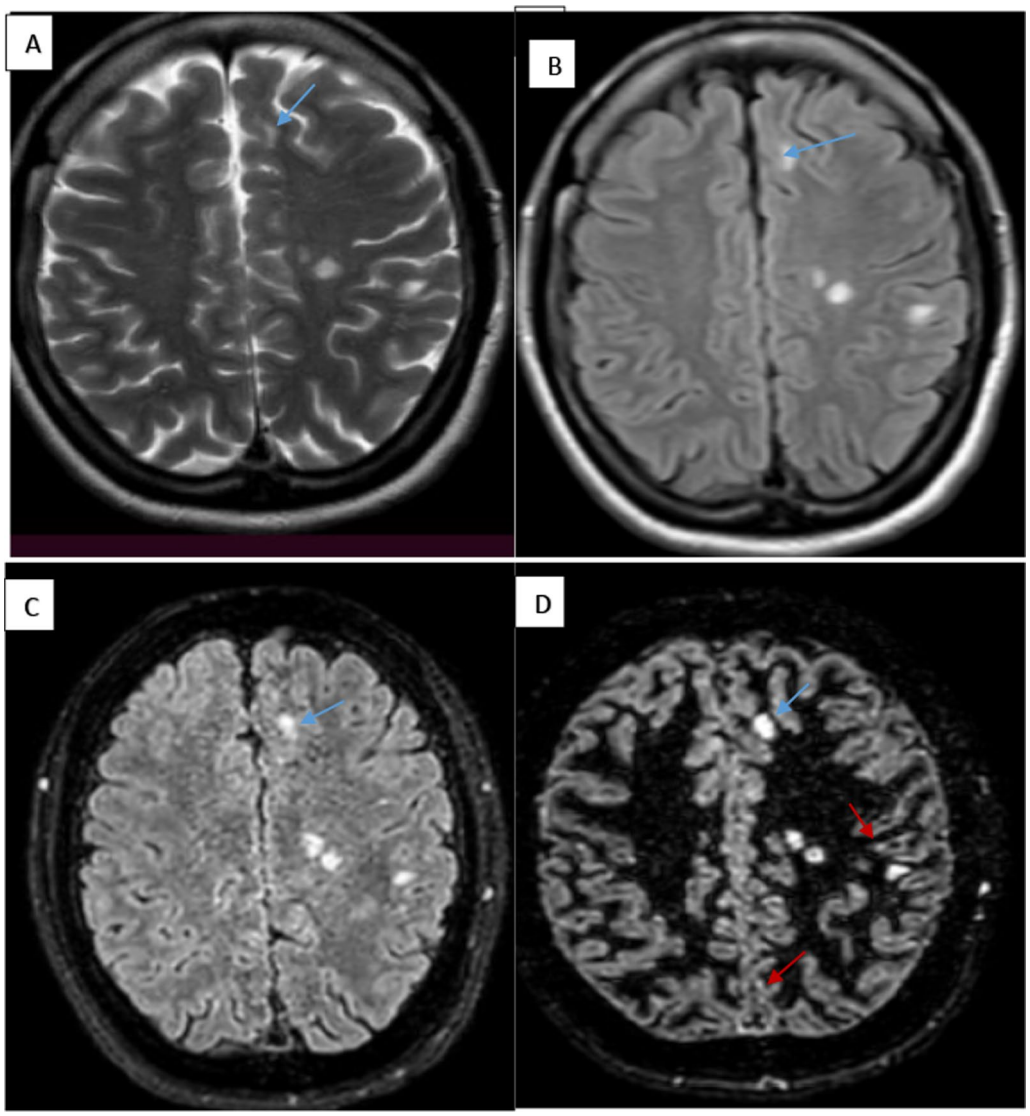

Fig. 1 Brain MRI images of a 35-years old female with relapsing–remitting multiple sclerosis (RRMS) for 5 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D FLAIR, (**d**): axial 3D DIR. The blue arrows refer to a juxta cortical lesion seen in all the sequences, with poor characterization in the conventional sequences (**a**, **b**) and perfect characterization in (**d**) at the 3D DIR sequence. The red arrows demonstrate 3 mm cortical lesions which are present only in the 3D DIR sequence

plaques (lesions) with the highest mean value of (32.33 ± 25.84), meanwhile, the T2W sequence showed the lowest mean value. Comparisons between the different sequences were shown in (Table 2), and (Fig. 8a).

Periventricular plaques

Periventricular plaques were counted in each studied sequence and comparisons were made as displayed in (Table 3), and (Fig. 8b).

A statistically significant difference was recorded between the periventricular plaque (lesion) count detected by 3D FLAIR to those detected by any of the other three sequences as seen by P values (P1, P2, P3, P4, and P5). Regarding the periventricular region, the 3D FLAIR sequence showed the highest number of detected plaques with a mean of (24.20 ± 23.05).

Infratentorial plaques

Infratentorial plaques were counted in each sequence in all studied patients. The P value for comparing the infratentorial plaque (lesion) count in each sequence 3D DIR, 3D FLAIR, 2D FLAIR, and T2 showed no statistically significant difference between them regarding their ability to detect plaques in the infratentorial region.

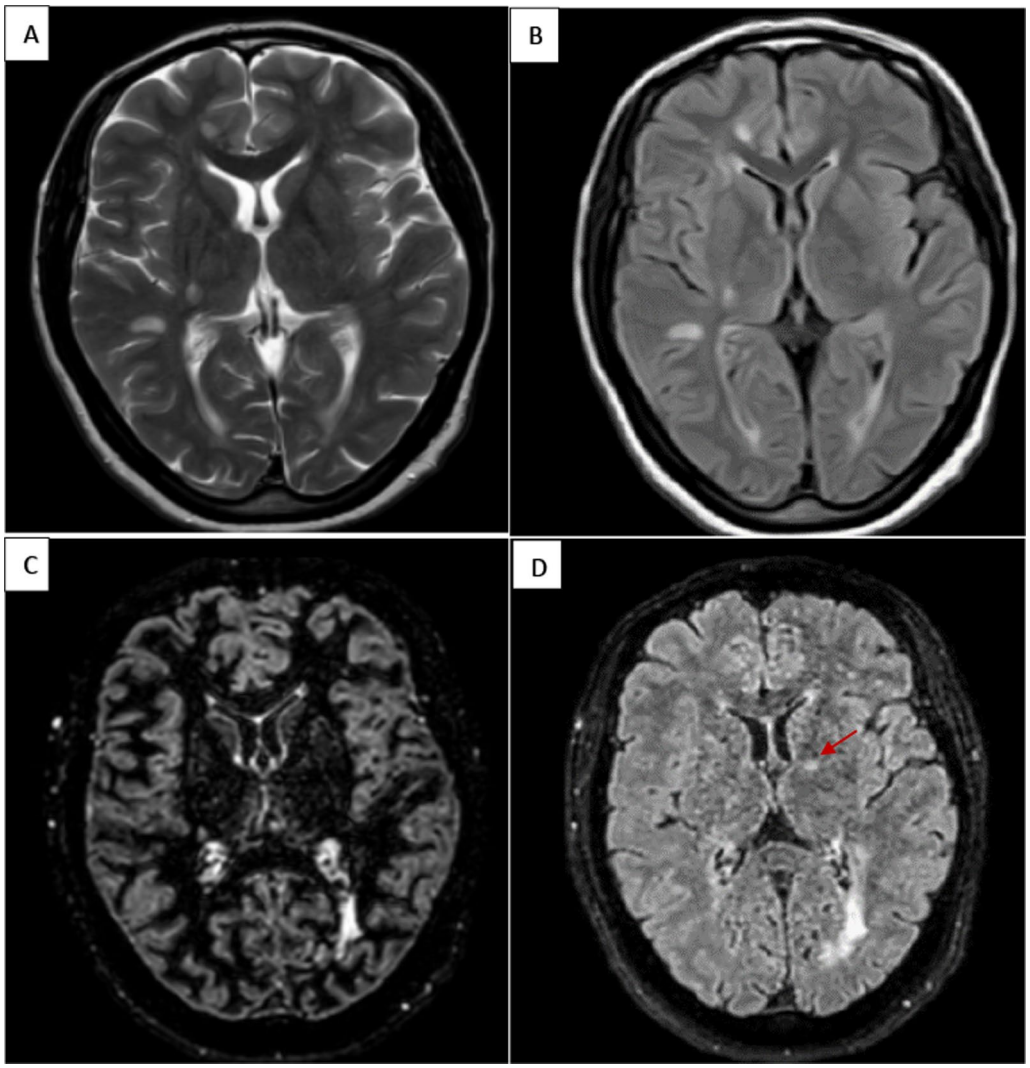

Fig. 2 Brain MRI images of a 46-years old female with relapsing–remitting multiple sclerosis (RRMS) for 10 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D FLAIR, (**d**): axial 3D DIR. The red arrow represents a periventricular lesion that is only visible in the 3D FLAIR sequence

The four sequences had similar mean values with no statistically significant difference in their ability to detect infratentorial plaques, as shown in (Table 4), and (Fig. 8c).

Total plaque (lesion) burden

The total plaque (lesion) count in each sequence was calculated and compared with the other sequences as seen in (Table 5), and (Fig. 8d). There was no statistically significant difference between 3D DIR, and 3D FLAIR sequences regarding the total plaque (lesion) burden count. However, there was a statistically significant difference between the total plaque (lesion) count detected by the 3D FLAIR to that detected by T2, and 2D FLAIR sequences. Regarding the 3D DIR sequence, there was also a statistically significant difference between its total plaque (lesion) count to that of T2, as well as, 2D FLAIR sequences.

Regarding the total plaque (lesion) load, there was no statistically significant difference between the new sequences, the 3D DIR and 3D FLAIR; however, if we compared any of them to the conventional sequences, they showed a statistically significant difference.

Discussion

Many studies have linked the abundance of both cortical and infratentorial lesions to MS progression and patient disability. Conventional MRI sequences often encounter difficulty depicting lesions in these specific brain sites. Due to their importance, cortical lesions, in particular, were added to McDonald's criteria in 2017 [4].

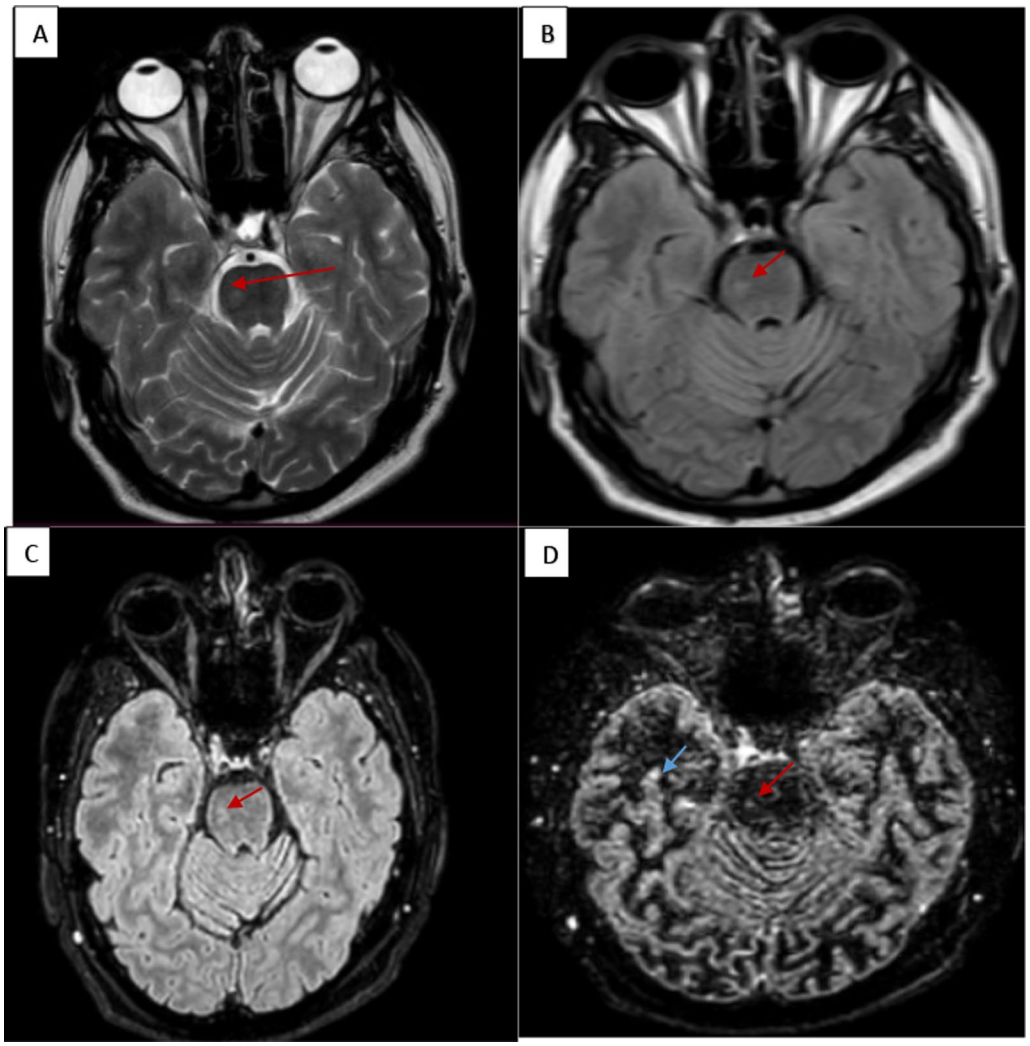

Fig. 3 Brain MRI images of a 32-years old male with a history of relapsing–remitting multiple sclerosis (RRMS) for 5 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D FLAIR, (**d**): axial 3D DIR. The red arrow demonstrates an infratentorial lesion that is present in all sequences with poor characterization at 3D DIR however is still present. The blue arrow shows a cortical lesion seen in the 3D DIR sequence only (**d**) and is not seen in all other sequences

Additionally, Patients with higher plaque/lesion load were found to progress to secondary progressive MS faster and had a poorer prognosis; therefore, assessing lesion load is essential in monitoring MS [12].

Thus, technical advances have been made to conventional MRI sequences to increase their sensitivity in detecting lesions in these particular sites and assessing the total lesion burden. Subsequently, new sequences like Double Inversion Recovery (DIR) and Three-dimensional (3D) FLAIR were introduced [1, 12].

In this study, we aimed to assess the ability of new MRI sequences, such as 3D DIR and 3D FLAIR, to detect plaques/lesions in these challenging locations, assess the overall brain lesion load, and compare the findings to those of the conventional sequences.

We studied thirty patients, twenty-two of them were females corresponding to a ratio of (73.3%) and eight were males, with a ratio of (26.5%). These percentages were consistent with the description of MS as a female-predominant disease whose percentage among males is nearly 25%, as stated by many studies, including Coyle et al. [19], and Walton et al. [1].

The participants' ages ranged from 19 to 76 years, with a mean of 37.40 ± 14.85. Most participants (74%) were between 19 and 45 years old, consistent with most

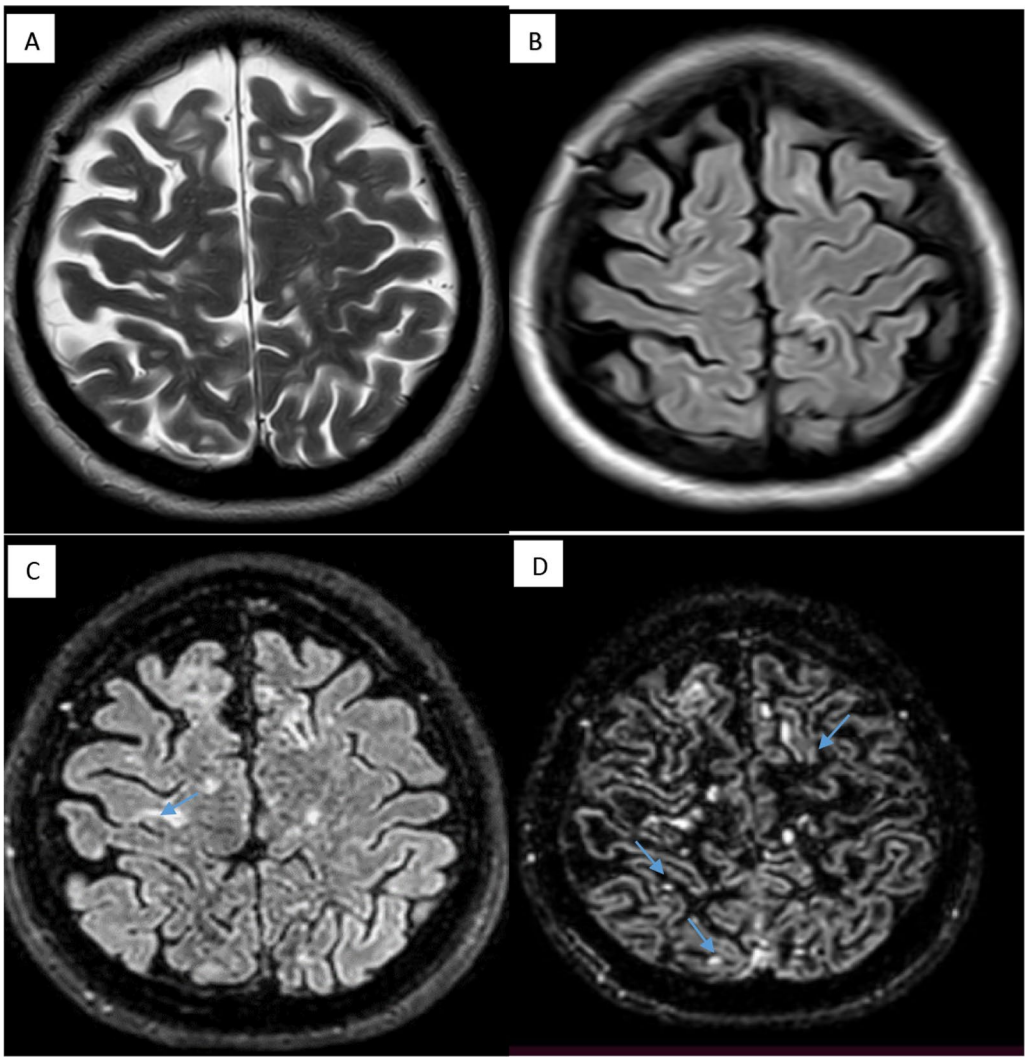

Fig. 4 Brain MRI images of a 31-years old female with relapsing–remitting multiple sclerosis (RRMS) for 5 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D FLAIR, (d): axial 3D DIR. The blue arrows show the cortical lesions only seen in 3D sequences and not seen in other sequences. It is also noted even the cortical lesion seen in all the other sequences shows better characterization in 3DIR (**d**), the 3D FLAIR (**c**) comes second while the conventional sequences (**a**, **b**) show fewer lesions with poor characterization

epidemiological studies stating that MS is a disease of young and middle-aged adults [1].

Regarding MS clinical types, out of the thirty patients, twenty-two had the relapsing–remitting form (RRMS), which equals a ratio of (73.3%). This was similar to the results of Abdelrahman et al. [14], who examined eighty-two patients, fifty-nine of which had RRMS with a percentage of 72%. Both percentages were close to the one reported by a systematic review done by McKay et al. [20], who showed that RRMS is the most common clinical type found in 85% of MS patients.

For the other clinical types in our study, 23.3% of the participants had the secondary progressive form, which was higher than the percentage found in other similar studies examining MS lesions by DIR sequence like Abdelrahman et al. [14] in which 6% only of their participants had secondary progressive MS (SPMS).

To assess each MRI sequence in its ability to detect the burden of MS plaques (lesions) at the different anatomic locations, we counted the number of MS plaques in each location and the total number of MS plaques separately in each sequence in all patients and the results differed per each location.

Our study results of 3D DIR being significantly superior in the cortical region matched with many studies, including Abdelrahman et al. [14], Higazi et al. [15], and Elkholy et al. [21]. For example, Higazi et al. [15] concluded that DIR was 1.5 to 5 more sensitive than conventional

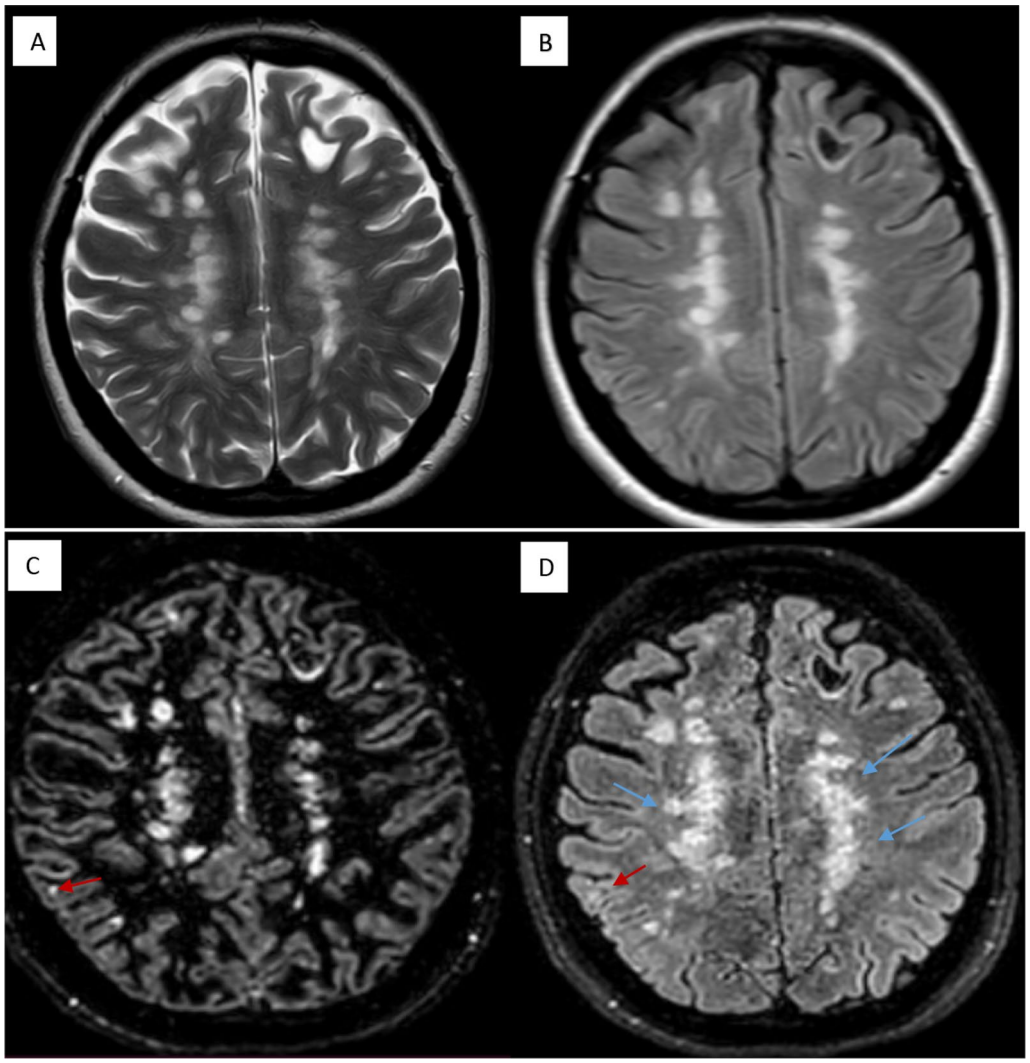

Fig. 5 Brain MRI images of a 31-years old female with secondary progressive multiple sclerosis (SPMS) for 6 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D DIR, (**d**): axial 3D FLAIR. The blue arrows: 3D FLAIR (**d**) shows the highest number of periventricular lesions while 3D DIR (**c**) shows the least number of lesions with poorer characterization. The red arrow: shows a cortical lesion that is clearly visible in the 3D DIR sequence (**c**), poorly characterized in the 3D FLAIR (**d**) sequence, and is not seen in the conventional sequences

MRI in detecting gray matter lesions. Similarly, Elkholy et al. [21], and Abdelrahman et al. [14] compared 3D DIR to FLAIR and found DIR more accurate in detecting intracortical lesions with a p-value of < 0.001.

The high ability of DIR to detect cortical lesions is likely due to the suppressed signal of both CSF and white matter, allowing much better contrast between gray and white matter with consequent superior delineation of the gray matter and its cortical subtypes. In contrast, the FLAIR sequence cannot precisely show the border between the cortex and subcortical white matter [15].

Additionally, our study showed no statistically significant difference when comparing 3D and 2D FLAIR in their ability to detect cortical lesions with a P-value of 0.147. This finding disagrees with the findings of Zamzam et al. [22], and Tawfik et al. [23], who both found that the 3D-FLAIR sequence significantly detected more cortical and overall lesions compared to the standard used 2D-FLAIR and T2 sequences with significant P values.

At the periventricular region, 3D FLAIR showed the highest number of lesions with a mean value of 24.20 ± 23.05 compared to the other three sequences. For instance, when we compared 3D FLAIR with 2D FLAIR, the mean value of 2D FLAIR was lower, 18.37 ± 17.75, and there was a statistically significant difference between the two, which was consistent with the findings of Zamzam et al. [22]. The 3D DIR sequence, however; scored the least mean value of 8.47 ± 10.26. these results

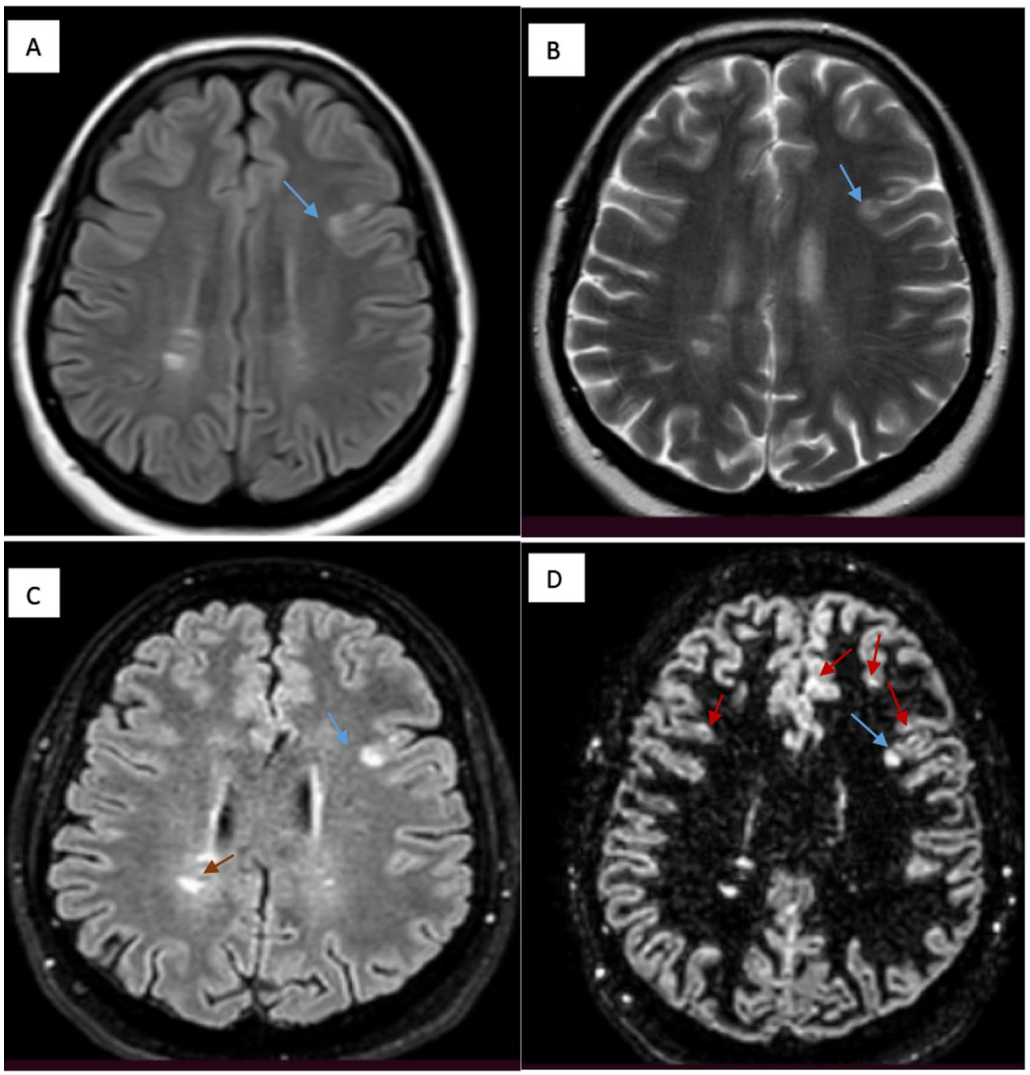

Fig. 6 Brain MRI images of a 40-years old female with relapsing–remitting multiple sclerosis (RRMS) for 8 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D FLAIR, (**d**): axial 3D DIR. The blue arrows: demonstrate a juxta cortical lesion which is visible in all sequences but is more pronounced in the 3D FLAIR and 3D DIR sequences. The red arrows: demonstrate small 3 mm cortical lesions which are present on the 3D DIR sequence only. The brown arrow: shows a periventricular lesion that is clearly visible on the 3D FLAIR sequence only

were consistent with Elhussein et al. [24], who found that FLAIR detected more periventricular lesions than DIR with a total of 583 lesions depicted by FLAIR compared to 423 only with DIR.

Our results of the FLAIR sequence being more superior in the periventricular region disagreed with Elkohly et al. [21] who stated that there was no statistical difference between DIR and FLAIR in detecting periventricular plaques.

In our study, FLAIR sequences, either 2D or 3D, showed more periventricular and overall plaque (lesion) count than the T2W sequence, consistent with the findings of Almutairi et al. [25] who compared the lesion load among DIR, FLAIR, and T2W sequences and their results showed that FLAIR sequences depict more plaques (lesions) than T2W sequence.

In regards the Infra tentorial plaques, there was no statistically significant difference between 3D FLAIR and 3D DIR which is unlike Elkholy et al. [21], and Abidi et al. [16] showed different results stating that DIR detected more plaques (lesions) in the infratentorial region than FLAIR and T2W.

Lastly, regarding the total lesion burden, which is the summation of the plaques (lesions) in all of the previously mentioned locations (cortical, periventricular, and infratentorial), there was no statistically

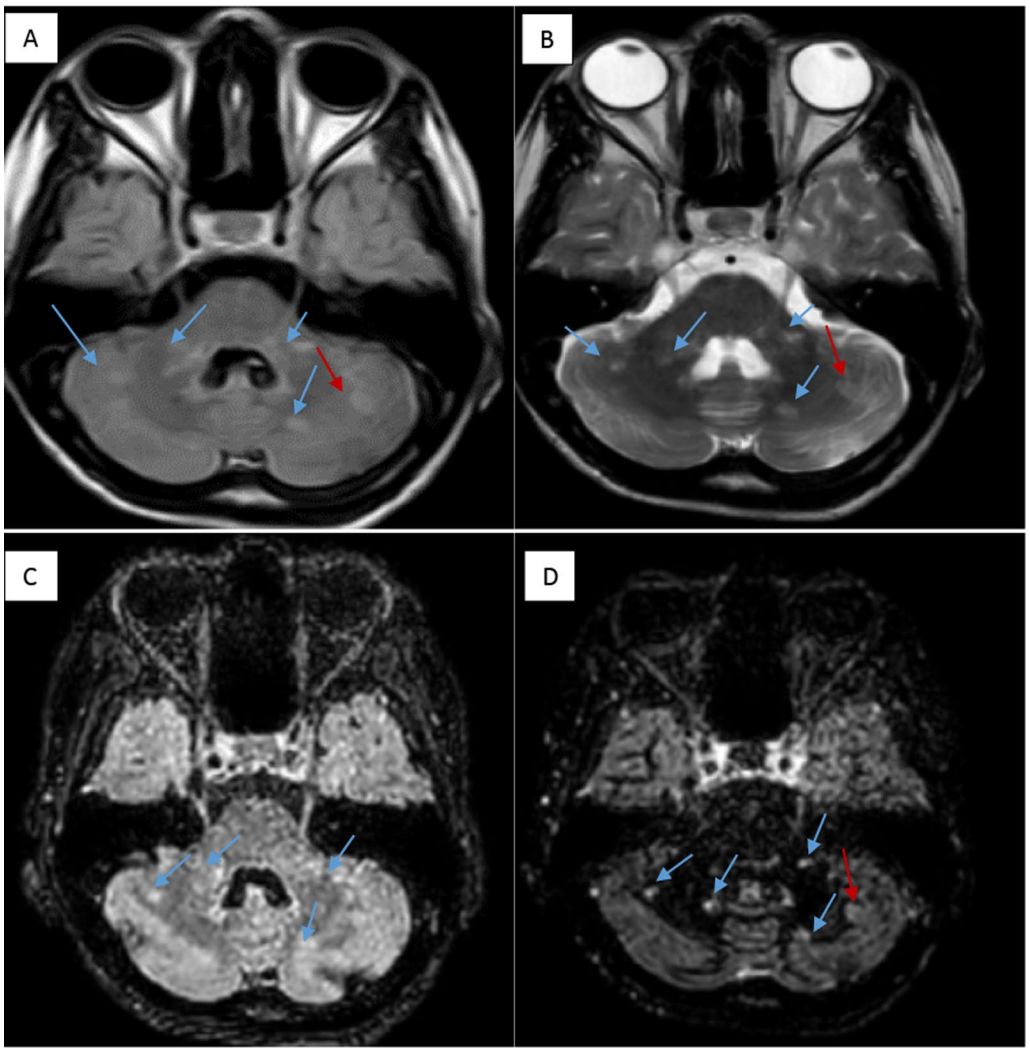

Fig. 7 Brain MRI images of a 33-years old female with relapsing–remitting multiple sclerosis (RRMS) for 3 years; (**a**): axial T2W, (**b**): axial 2D FLAIR, (**c**): axial 3D FLAIR, (**d**): axial 3D DIR. The blue arrows point to four cerebellar lesions that are present in all sequences however they are more obvious in the conventional sequences (**a**, **b**). the red arrows point to a lesion present in 2D FLAIR, T2W, and 3D DIR, however is not seen clearly in the 3D FLAIR sequence

Table 2 Comparison between the different MRI sequences in their ability to detect cortical plaques (n = 30)

Cortical/Juxta cortical plaques	T2	2D FLAIR	3D FLAIR	3D DIR	Fr	*p*
Min. – Max	0.0–65.0	0.0–60.0	0.0–56.0	4.0–130.0	71.263*	< 0.001*
Mean ± SD	7.40 ± 12.0	11.20 ± 13.98	14.30 ± 14.44	32.33 ± 25.84		
Median	4.0	7.0	10.50	25.50		
IQR	1.0–10.0	3.0–12.0	3.0–16.0	15.0–45.0		
Sig. bet. Periods	$p_1 = 0.016$*, $p_2 < 0.001$*, $p_3 = 0.147$, $p_4 < 0.001$*, $p_5 < 0.001$*					

IQR: Inter quartile range, SD: Standard deviation

Fr: Friedman test, Sig. bet. Periods were done using the Post Hoc Test (Dunn's)

p: *p*-value for comparing the different studied parameters, p_1: *p*-value for comparing T2 and 3D FLAIR, p_2: *p*-value for comparing T2 and 3D DIR, p_3: *p*-value for comparing 2D FLAIR and 3D FLAIR, p_4: *p*-value for comparing 2D FLAIR and 3D DIR, p_5: *p*-value for comparing 3D FLAIR and 3D DIR

*Statistically significant at $p \leq 0.05$

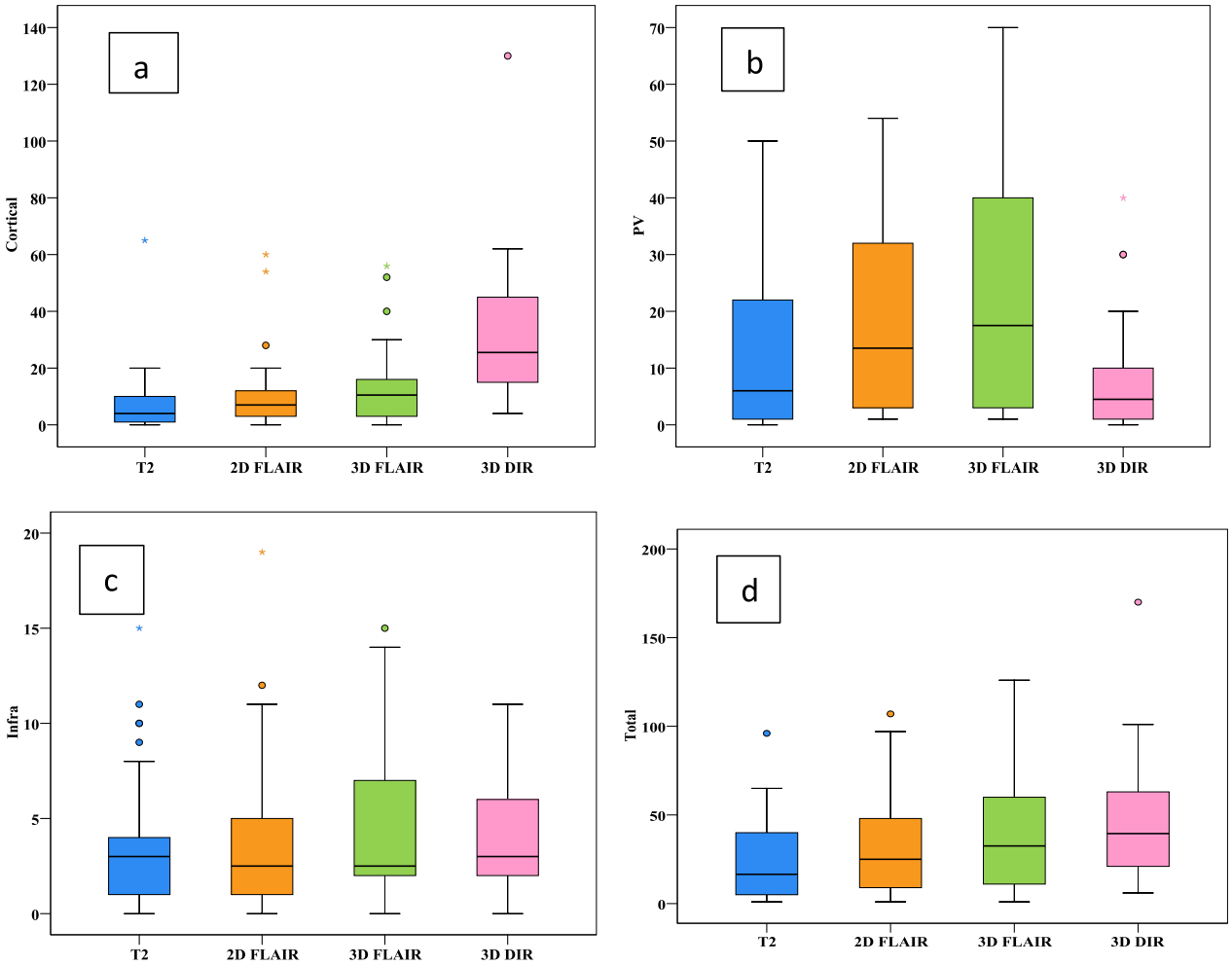

Fig. 8 Comparison between T2WI, 2D FLAIR, 3D FLAIR, and 3D DIR sequences in their ability to detect multiple sclerosis brain lesions in various anatomical locations; **a**) cortical/juxta cortical lesions. **b**) periventricular lesions. **c**) infratentorial lesions. **d**) total lesion burden

Table 3 Comparison between the number of periventricular plaques detected by each sequence (n = 30)

Periventricular plaques	T2	2D FLAIR	3D FLAIR	3D DIR	Fr	*p*
Min. – Max	0.0–50.0	1.0–54.0	1.0–70.0	0.0–40.0	72.131*	< 0.001*
Mean ± SD	13.60 ± 14.88	18.37 ± 17.75	24.20 ± 23.05	8.47 ± 10.26		
Median	6.0	13.50	17.50	4.50		
IQR	1.0–22.0	3.0–32.0	3.0–40.0	1.0–10.0		
Sig. bet. periods	$p_1 = 0.002$*, $p_2 < 0.001$*, $p_3 = 0.021$*, $p_4 < 0.001$*, $p_5 < 0.001$*					

IQR: Inter quartile range, SD: Standard deviation

Fr: Friedman test, Sig. bet. Periods were done using the Post Hoc Test (Dunn's)

p: *p*-value for comparing the different studied parameters, p_1: *p*-value for comparing T2 and 3D FLAIR, p_2: *p*-value for comparing T2 and 3D DIR, p_3: *p*-value for comparing 2D FLAIR and 3D FLAIR, p_4: *p*-value for comparing 2D FLAIR and 3D DIR, p_5: *p*-value for comparing 3D FLAIR and 3D DIR

*Statistically significant at $p \leq 0.05$

Table 4 Comparison between the different sequences in detecting the infratentorial plaques (n = 30)

Infra tentorial plaques	T2	2D FLAIR	3D FLAIR	3D DIR	Fr	*P*
Min. – Max	0.0–15.0	0.0–19.0	0.0–15.0	0.0–11.0	0.740	0.864
Mean ± SD	3.67 ± 3.88	3.97 ± 4.28	4.0 ± 3.74	3.87 ± 3.03		
Median	3.0	2.50	2.50	3.0		
IQR	1.0–4.0	1.0–5.0	2.0–7.0	2.0–6.0		

IQR: Inter quartile range, SD: Standard deviation, Fr: Friedman test

Table 5 Comparison between four (T2, 2D FLAIR, 3D FLAIR, and 3D DIR) sequences in their ability to determine the total plaque (lesion) burden in the brain (n = 30)

Total plaque (lesion) burden	T2	2D FLAIR	3D FLAIR	3D DIR	Fr	*p*
Min. – Max	1.0–96.0	1.0–107.0	1.0–126.0	6.0–170.0	55.920*	< 0.001*
Mean ± SD	24.67 ± 24.33	33.53 ± 29.84	42.50 ± 34.78	44.67 ± 35.49		
Median	16.50	25.0	32.50	39.50		
IQR	5.0–40.0	9.0–48.0	11.0–60.0	21.0–63.0		
Sig. bet. periods	$p_1 < 0.001^*$, $p_2 < 0.001^*$, $p_3 = 0.011^*$, $p_4 < 0.001^*$, $p_5 = 0.250$					

IQR: Inter quartile range, SD: Standard deviation

Fr: Friedman test, Sig. bet. Periods were done using the Post Hoc Test (Dunn's)

p: *p*-value for comparing the different studied parameters, p_1: *p*-value for comparing T2 and 3D FLAIR, p_2: p-value for comparing T2 and 3D DIR, p_3: *p*-value for comparing 2D FLAIR and 3D FLAIR, p_4: *p*-value for comparing 2D FLAIR and 3D DIR, p_5: *p*-value for comparing 3D FLAIR and 3D DIR

* Statistically significant at $p \leq 0.05$

significant difference between the 3D FLAIR and 3D DIR sequences, however; the site in which each is best differs. Namely, most of the plaques detected by the 3D DIR were in the cortical region. Meanwhile, 3D FLAIR, which was not as highly accurate in the cortical area, showed superior results to all sequences regarding plaque detection in the periventricular region.

Although there was no statistically significant difference between the 3D FLAIR and 3D DIR sequences in total lesion burden, a significant difference was found when comparing any of these two with the conventional ones. For example, a P value of < 0.001 was found between the total number of plaques detected by 3D DIR to that of 2D FLAIR. Likewise, 3D FLAIR was found superior in detecting the total plaque (lesion) burden compared to the conventional MRI sequences with a mean value of 42.50 ± 34.78 and a statistically significant P value of 0. 011.

Tawfik et al. [23] found that there were significantly more plaques detected by the 3D-FLAIR, mainly in the supratentorial region (periventricular, deep WM, and juxta-cortical) than in T2 and 2D FLAIR sequences.

This study displays a few limitations in the form of a relatively small number of the studied sample, not all clinical types of multiple sclerosis were represented, and there were no patients with the primary progressive type of multiple sclerosis and a small number of patients with clinically isolated syndrome. So, more large-sized studies are needed to obtain more precise results, and standardization of results to help increase the external validity and generalization of results.

Conclusions

In conclusion, 3D FLAIR and 3D DIR were superior to 2D FLAIR and T2 sequences in detecting overall plaque (lesion) burden in MS. Moreover, the 3D DIR sequence was the most precise in the detection of the cortical plaques. So, adding these sequences can help with precise diagnosis and early management.

Abbreviations

3D DIR	Three-dimensional double inversion recovery
3D FLAIR	Three-dimensional fluid-attenuated inversion recovery
FLAIR	Fluid-attenuated inversion recovery
MS	Multiple sclerosis
PPMS	Primary progressive multiple sclerosis
RRMS	Relapsing–remitting multiple sclerosis
SPMS	Secondary progressive multiple sclerosis

Acknowledgements

Not-applicable

Author contributions

NS; Formulation of the study, preparation of methodology, data collection, and analysis of the data. AA; Formulation of the study, preparation of methodology, analysis of the data, and revision of the paper. MM; Formulation of the

study, preparation of methodology, data collection, analysis of the data, and writing the paper. HR; Formulation of the study, preparation of methodology, analysis of the data, and writing the paper. The authors have read and approved the manuscript.

Funding
The authors state that this work has not received any funding.

Availability of data and materials
The dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approved by the local institutional ethics committee; Faculty of Medicine, Suez Canal University Health Research Ethics Board. It follows The Code of Ethics of the World Medical Association (Declaration of Helsinki). Written informed consent was obtained from all patients and controls.

Consent for publication
Consent for publication was obtained from the patients and controls.

Competing interests
The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Received: 12 October 2023 Accepted: 1 August 2024
Published online: 12 August 2024

References

1. Walton C, King R, Rechtman L et al (2020) Rising prevalence of multiple sclerosis worldwide: insights from the Atlas of MS. Mult Scler J 26(14):1816–1821
2. Koch-Henriksen N, Magyari M (2021) Apparent changes in the epidemiology and severity of multiple sclerosis. Nat Rev Neurol 17(11):676–688
3. Morgan BP, Gommerman JL, Ramaglia V (2021) An "outside-in" and "inside-out" consideration of complement in the multiple sclerosis brain: lessons from development and neurodegenerative diseases. Front Cell Neurosci 14:600–656
4. Thompson AJ, Banwell BL, Barkhof F et al (2018) Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 17(2):162–173
5. Filippi M, Preziosa P, Banwell BL et al (2019) Assessment of lesions on magnetic resonance imaging in multiple sclerosis: practical guidelines. Brain 142(7):1858–1875
6. McGinley MP, Goldschmidt CH, Rae-Grant AD (2021) Diagnosis and treatment of multiple sclerosis: a review. JAMA 325(8):765–779
7. Lublin FD, Reingold SC, Cohen JA et al (2014) Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology 83(3):278–286
8. Polman CH, Reingold SC, Banwell B et al (2011) Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol 69(2):292–302
9. Nazareth TA, Rava AR, Polyakov JL et al (2018) Relapse prevalence, symptoms, and health care engagement: patient insights from the multiple sclerosis in America 2017 survey. Multiple Sclerosis Related Disord 26:219–234
10. Krieger SC, Cook K, De Nino S et al (2016) The topographical model of multiple sclerosis: a dynamic visualization of disease course. Neurol-Neuroimmunol Neuroinflammation. https://doi.org/10.1212/NXI.0000000000000279
11. Ömerhoca S, Akkaş SY, İçe NK (2018) Multiple sclerosis: diagnosis and differential diagnosis. Arch Neuropsychiatry 55(1):S1
12. Kaunzner UW, Gauthier SA (2017) MRI in the assessment and monitoring of multiple sclerosis: an update on best practice. Ther Adv Neurol Disord 10(6):247–261
13. Gramsch C, Nensa F, Kastrup O et al (2015) Diagnostic value of 3D fluid attenuated inversion recovery sequence in multiple sclerosis. Acta Radiol 56(5):622–627
14. Abdelrahman AS, Khater NH, Barakat MM (2022) Diagnostic utility of 3D DIR MRI in the estimation of MS lesions overall load with special emphasis on cortical subtypes. Egypt J Radiol Nucl Med 53(1):47
15. Higazi MM, Ghany HSAE, Fathy AW et al (2022) Diagnostic accuracy of double inversion recovery (DIR) in detection of cortical gray matter lesions in patients with MS. Egypt J Radiol Nucl Med 53:1–9
16. Abidi Z, Faeghi F, Mardanshahi Z et al (2017) Assessment of the diagnostic accuracy of double inversion recovery sequence compared with FLAIR and T2W_TSE in detection of cerebral multiple sclerosis lesions. Electron Phys 9(4):41–62
17. Polak P, Magnano C, Zivadinov R et al (2012) 3D FLAIRED: 3D fluid attenuated inversion recovery for enhanced detection of lesions in multiple sclerosis. Magn Reson Med 68(3):874–881
18. Kolber P, Montag S, Fleischer V et al (2015) Identification of cortical lesions using DIR and FLAIR in early stages of multiple sclerosis. J Neurol 262(6):1473–1482
19. Coyle PK (2021) What can we learn from sex differences in MS? J Personal Med 11(10):1006
20. McKay KA, Kwan V, Duggan T et al (2015) Risk factors associated with the onset of relapsing-remitting and primary progressive multiple sclerosis: a systematic review. BioMed Res Int. https://doi.org/10.1155/2015/817238
21. Elkholy SF, Sabet MA, Mohammad ME et al (2020) 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 51:1–10
22. Zamzam AEA, Aboukhadrah RS, Khali MM et al (2022) Diagnostic value of three-dimensional cube fluid attenuated inversion recovery imaging and its axial MIP reconstruction in multiple sclerosis. Egypt J Radiol Nucl Med 53(1):1–9
23. Tawfik AI, Kamr WH (2020) Diagnostic value of 3D-FLAIR magnetic resonance sequence in detection of white matter brain lesions in multiple sclerosis. Egypt J Radiol Nucl Med 51(1):1–9
24. Elhussein N, Alazmi N, Fadulemulla IA et al (2022) Comparison between double inversion recovery and fluid-attenuated inversion recovery sequences for detection of brain multiple sclerosis. Clin Cancer Investig 11(6):41–44
25. Almutairi AD, Abu HH, Suppiah S et al (2020) Lesion load assessment among multiple sclerosis patient using DIR, FLAIR, and T2WI sequences. Egypt J Radiol Nucl Med 51:209

Publisher's Note