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Quantitative Assessment of MRI Lesion Load in Cerebral Multiple Sclerosis: A Comparison of Conventional Sequences and Double Inversion Recovery

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Abstract

Background: It has been established to use FLAIR sequence in detection of MS lesions in central nervous system. In this study, we introduced a Double Inversion Recovery (DIR) pulse sequence at 1.5 T, which allows a sufficient attenuation of the CSF and the NAWM (Normal Appearing White Matter) of 34 patients with MS, and compared it to the conventional (T2, FLAIR) sequences. MS lesions were classified anatomically into supratentorial lesions and infratentorial lesions. The supratentorial lesions were further categorized into cortical, juxta-cortical and subcortical and deep white matter (DWM).

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.

Patients and Methods: This Cross Sectional Study was carried out in Radio-diagnosis Department Faculty of Medicine Ain Shams University during the period from January 2021 till August 2021. The study was approved by Ethical Committee of Faculty of Medicine, Ain Shams University. It included 34 known MS patient.

Results: A total of 34 patients were enrolled in this study. There were 26 (76.5%) female and 8 (23.5%) male patients, with age ranges from 19 to 43 years with a median of 31.5 years and a mean (± standard deviation) of 30.47 years (±6.7). Regarding the total lesion load, DIR was found to be significantly superior to the T2 sequence in 85.3% of cases and superior to FLAIR sequence in 82.4% of cases. Regarding cortical lesions, DIR was found to be significantly superior to T2 and FLAIR sequences in 97% and 93.9% of the cases with cortical affection respectively. Regarding juxta and subcortical lesions, DIR was found to be significantly superior to T2 and FLAIR sequences in 64.5% and 54.8% respectively in cases with juxta and subcortical affection. Regarding DWM lesions, DIR was found to be superior to T2 and FLAIR sequences in 47.1% and 35.3% of cases respectively and equal to T2 and FLAIR sequences in 17.6% of cases. Regarding the infratentorial lesions, DIR was found to be significantly superior to T2 and FLAIR sequences in 65.2% of cases with infratentorial affection.

Conclusion: We found DIR brain imaging had the highest sensitivity in the detection of cortical, juxtacortical and infratentorial lesions compared with FLAIR and T2 sequences. DIR showed better delineation between the WM, GM, and the MS lesions due to its high image contrast measurements. DIR sequence should be included in the routine MR protocols of MS patients especially to answer the question about cortical and infratentorial lesions for better prognostic values to the patients.

Key Words: *Multiple sclerosis – Central nervous system – Double inversion recovery – Fluid-attenuated inversion recovery.*

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Introduction

MULTIPLE sclerosis (MS) is the most common chronic inflammatory demyelinating disease of the central nervous system (CNS), that is characterized by focal demyelinating plaques and diffuse neurodegeneration, resulting in both physical and neurocognitive disability **[1]**.

Although MS has been known as a white matter disease, MS lesions occur in all CNS parenchymal areas, including cerebral cortex and deep grey matter.

Approximately two million people worldwide are affected by this disorder, and it is the most common non-traumatic neurological disability affecting young adults **[2]**.

Multiple Sclerosis (MS) is diagnosed according to the McDonald criteria which are clinical, radiographic and laboratory criteria. They were originally introduced in 2001 and revised multiple times, most recently in 2017. The McDonald Criteria have resulted in earlier diagnosis of MS with a high degree of both specificity and sensitivity, allowing for better counseling of patients and earlier treatment **[3]**.

Magnetic resonance imaging (MRI) has played a very important role in elucidating the pathophysiology, diagnosis and treatment of MS. According to the McDonald criteria for MS, the diagnosis requires objective evidence of lesions disseminated in time and space. As a consequence there is an important role for MRI in the diagnosis of MS, since MRI can show multiple lesions (dissemination in space), some of which can be clinically occult, and MRI can show new lesions on follow-up scans (dissemination in time) [1].

The FLAIR sequence is a sequence that suppresses the signal of cerebrospinal fluid (CSF) with a reverse cycle (inversion recovery) pulse and a high time Echo (TE values increase) T2-weight. This sequence increases the contrast of supratentorial lesions, in particular lesions that arise in juxtaposition to the CSF but is less sensitive in the posterior fossa [4].

A T2WI relies upon the transverse relaxation (also known as "spin-spin" relaxation) of the net magnetization vector (NMV). T2 weighting tends to require long TE and TR times. T2-weighted conventional spin-echo or turbo spin-echo (T2 TSE) sequences are known to be more sensitive in the detection of infratentorial lesions but have difficulties detecting juxtacortical lesions. DIR sequence produces two different inversion pulses, which attenuates the CSF together with the whole white matter, thus providing a remarkable delineation between gray and white matter. MS plaques located in the grey matter are more easily delineated using DIR [5].

Aim of the work:

The aim of our work is to assess the diagnostic value of a DIR sequence in the detection of MS lesions by comparing DIR with FLAIR and T2-weighted pulse sequences in the brain.

Patients and Methods

Type of study: Cross Sectional Study.

Study setting: The study was conducted at Radiology Department at Ain-Shams University Hospitals.

Study period: From January 2021 till August 2021.

Study population: 34 known MS patients.

Inclusion criteria: Patients already diagnosed to have multiple sclerosis according to the 2017 revised McDonald criteria. Both sexes were included. Adults only (From 18 to 75 year old).

Exclusion criteria: Patients known to have contraindications for MRI, e.g. an implanted magnetic device, pacemakers or claustrophobia. Patients with bad general condition needing life support. Patients less than 18 years old.

Sampling method: Convenience sampling.

Sample size: Assuming a correlation coefficient of 0.6 between the three techniques, a sample of 34 patients was included to reveal such correlation if true, at 0.01 alpha error and 0.90 power of the test.

Ethical considerations: The study was conducted after approval of the Research Ethical Committee of Faculty of Medicine, Ain Shams University. An informed consents were obtained from all eligible patients The privacy of participants and confidentiality of data was guaranteed during the various phases of the study.

Study tools and procedures: The study was done in MRI Unit at Ain Shams University Hospitals on Philips Machine Ingenia 1.5 Tesla. Clinical history and imaging findings of the included patients were obtained from the picture archiving and communications system (PACS) of the Radiology Department, Ain Shams University Hospitals from January 2021 till August 2021. All patients underwent MRI of the brain using head coil (quadrature detection, Transmit/Receive coil solution). The imaging sequences and their acquisition parameters are listed below:

Axial T1WI (TR=581, TE=15), Sagittal T1WI (TR=142, TE=2.2), Axial FLAIR (TR=11000, TE=130), Sagittal FLAIR (TR=10000, TE=140), Axial T2WI (TR=4846, TE=110), Coronal T2WI (TR=4811, TE=120) , Axial DWI and ADC maps (TR=3935, TE=114), 3D_Brain_VIEW_DIR (TR=5500, TE=317).

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.

Axial T2, FLAIR and DIR hyperintense demyelinating lesions have been assessed as total lesion load per patient and site of lesions and their number in each site as follows: Cortical, Juxta-Cortical and subcortical, Deep white matter and Infratentorial.

Statistical analysis:

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package

for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data. Frequency and percentage of 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.

- *p*-value: Level of significance.
- $p>0.05$: Non significant (NS).
- $p<0.05$: Significant (S).

Results

A total of 34 patients were enrolled in this study.

There were 26 (76.5%) female and 8 (23.5%) male patients, with age ranges from 19 to 43 years with a median of 31.5 years and a mean (± standard deviation) of 30.47 years (±6.7).

Table (1): Demographic data for the study group.

	Mean / N	SD / %	Median (IQR)	Range
Age	30.47	6.70%	31.5 (25-35)	(19-43)
Sex:				
Male	8	23.5%		
Female	26	76.5%		

The lesions were classified anatomically into supratentorial lesions and infratentorial lesions. The supratentorial lesions were further categorized into cortical, juxta-cortical and subcortical and Deep white matter (DWM).

Total lesion load:

Regarding the total lesion load, DIR was found to be significantly superior to the T2 sequence in 85.3% of cases (p-value=0.019) and superior to FLAIR sequence in 82.4% of cases (p-value= 0.249).

Table (2): Total lesion load for the study group.

	Mean / N	SD / %	Median (IQR)	Range
Total lesion load affection	34	100.0%		
T2	18.62	12.45	17 (8-28)	(2-54)
FLAIR	25.15	21.15	19.5 (14-30)	(2-97)
DIR	28.29	20.36	24.5 (16-34)	(6-114)
DIR Vs. T2	29	85.3%		
DIR Vs. FLAIR	28	82.4%		

Cortical lesions:

The percentage of cases with cortical affection was 97.1 %.

Regarding cortical lesions, DIR was found to be significantly superior to T2 and FLAIR sequences in 97% and 93.9% of the cases with cortical affection respectively (p-value <0.001).

Table (3): Cortical affection for the study group.

	Mean/N	SD/%	Median (IQR)	Range
Cortical affection:				
No	1	2.9%		
Yes	33	97.1%		
T2	0.79	2.00	0 (0-1)	(0-9)
FLAIR	1.03	2.32	0 (0-1)	(0-12)
DIR	3.50	3.31	2.5 (1-5)	(0-17)
DIR Vs. T2	32	97.0%		
DIR Vs. FLAIR	31	93.9%		

Juxta-cortical and Sub-cortical lesions:

The percentage of cases with juxta and subcortical affection was 91.2%.

Regarding juxta and subcortical lesions, DIR was found to be significantly superior to T2 and FLAIR sequences in 64.5% (p-value=0.001) and 54.8% (p-value=0.023) respectively in cases with juxta and subcortical affection.

Table (4): Juxta and subcortical affection for study group.

	Mean/N	SD/%	Median (IQR)	Range
Juxta and subcortical affection:				
No	3	8.8%		
Yes	31	91.2%		
T2	1.85	2.22	1 (1-2)	(0-11)
FLAIR	2.24	2.4	2 (1-3)	(0-12)
DIR	3.59	3.21	3 (2-4)	(0-15)
DIR Vs. T2	20	64.5%		
DIR Vs. FLAIR	17	54.8%		

Deep white Matter lesions (DWM):

Regarding DWM lesions, DIR was found to be superior to T2 and FLAIR sequences in 47.1 % and 35.3% of cases respectively and equal to T2 and FLAIR sequences in 17.6% of cases.

Table (5): DWM affection for study group.

	Mean/N	SD/%	Median (IQR)	Range
DWM affection	34	100.0%		
T2	13.79	9.26	13 (6-20)	(1-33)
FLAIR	20.71	18.06	17 (10-25)	(1-90)
DIR	16.15	13.28	14.5 (7-22)	(1-60)
DIR Vs. T2	16	47.1%		
DIR Vs. FLAIR	12	35.3%		

Infratentorial lesions:

The percentage of cases with infratentorial affection was 67.6%.

Regarding the infratentorial lesions, DIR was found to be significantly superior to T2 and FLAIR sequences in 65.2% of cases with infratentorial affection with p-values=0.045 and 0.015 respectively.

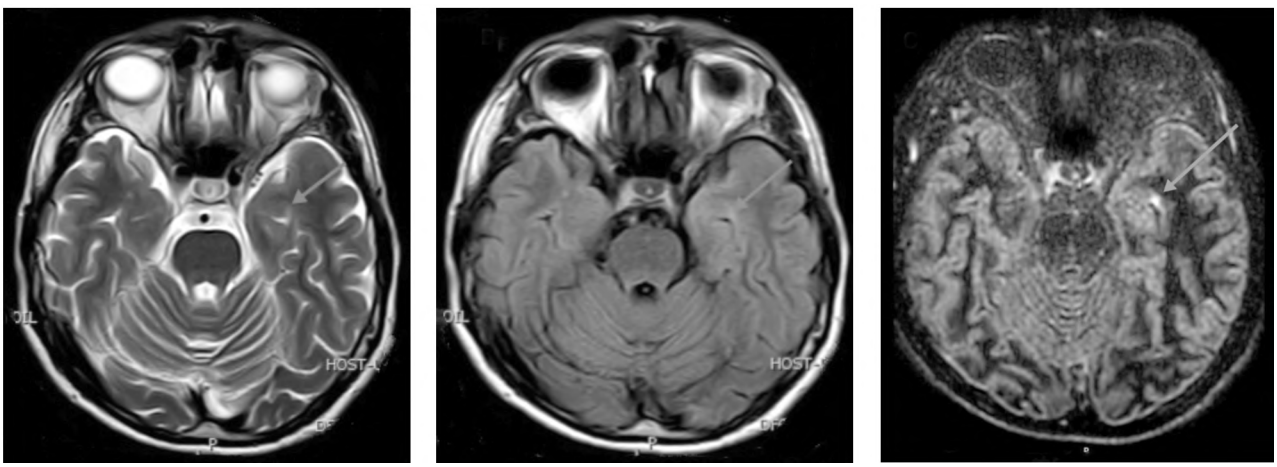
Table (6): Infratentorial affection for the study group.

	Mean/N	SD/%	Median (IQR)	Range
Infratentorial affection:				
No	11	32.4%		
Yes	23	67.6%		
T2	1.85	2.64	1 (0-2)	(0-9)
FLAIR	1.18	1.45	1 (0-2)	(0-6)
DIR	5.65	6.53	2.5 (0-10)	(0-22)
DIR Vs. T2	15	65.2%		
DIR Vs. FLAIR	15	65.2%		

Table (7): Comparison of number of lesions detected between DIR versus T2 and DIR versus FLAIR for study group.

	DIR	T2	Mann-Whitney test (p-Value)	FLAIR	Mann-Whitney test (p-Value)
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)		Mean ± SD Median (IQR)	
Cortical affection	3.5±3.31 2.5 (1-5)	0.79±2 0 (0-1)	<0.001*	1.03±2.32 0 (0-1)	<0.001*
Juxta and subcortical affection	3.59±3.21 3 (2-4)	1.85±2.22 1 (1-2)	0.001*	2.24±2.4 2 (1-3)	0.023*
DWM affection	16.15±13.28 14.5 (7-22)	13.79±9.26 13 (6-20)	0.645	20.71±18.06 17 (10-25)	0.294
Infratentorial affection	5.65±6.53 2.5 (0-10)	1.85±2.64 1 (0-2)	0.045*	1.18±1.45 1 (0-2)	0.015*
Total lesion load affection	24.5±20.36 24.5 (16-34)	18.62±12.45 17 (8-28)	0.019*	25.15±21.15 19.5 (14-30)	0.249

Fig. (1): 21 year old female patient, known MS, presented with vertigo and headache. (A, B and C) (blue arrows) representing T2, FLAIR and DIR sequences respectively, showing an insular cortical lesion appearing only in DIR.

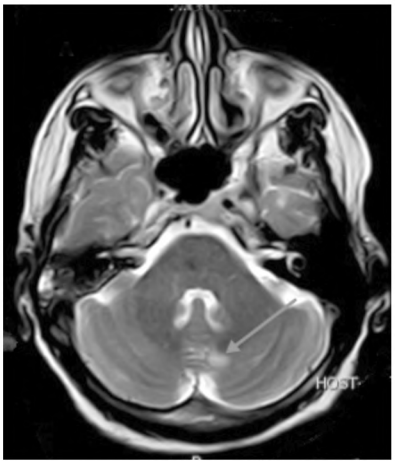


(A): Axial brain FLAIR sequence showing no detected demyelinating lesions.

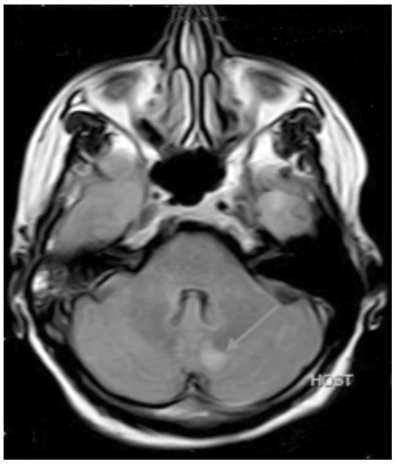
(B): Axial brain T2 sequence showing no detected demyelinating lesions

(C): Axial brain DIR reveals left cortical insular demyelinating lesion.

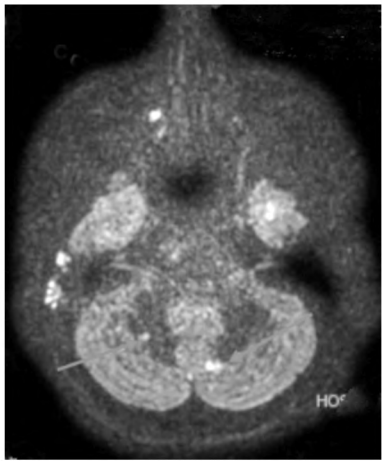
Fig. (2): 37 years old female patient, known MS, presented by blurring of vision. (A, B and C) are the axial brain MRI cuts of T2, FLAIR and DIR sequences respectively, showing a left cerebellar lesion (blue arrows) appearing in the three sequences with an extra lesion in the right middle cerebellar peduncle (red arrow) only appearing in DIR sequence.



(A): Axial brain T2 sequence showing left cerebellar lesion.



(B): Axial brain FLAIR sequence showing left cerebellar lesion.



(C): Axial brain DIR sequence showing left cerebellar and right middle peduncle lesions.

Discussion

Multiple sclerosis (MS) is the most common chronic inflammatory demyelinating disease of the central nervous system (CNS), that is characterized by focal demyelinating plaques and diffuse neurodegeneration, resulting in both physical and neurocognitive disability (Vural et al.) **[1]**.

MS has classically been described as a WM disorder; however, over the few past years, an increased attention has been pointed toward the involvement of GM in the pathophysiology of MS. Since abnormalities in cortical gray matter have been correlated with both physical and neuropsychological deficits in MS patients, it is essential to create a better assessment and a more accurate estimation of gray matter lesion load in vivo (Geurts et al.) **[4]**.

In this study, we introduced a DIR pulse sequence at 1.5 T, which allows a sufficient attenuation of the CSF and the NAWM (Normal Appearing White Matter) of 34 patients with MS, and compared it to the conventional (T2, FLAIR) sequences. MS lesions were classified anatomically into supratentorial lesions and infratentorial lesions. The supratentorial lesions were further categorized into cortical, juxta-cortical and subcortical and deep white matter (DWM).

Regarding the total lesion load, we found that DIR significantly detected more lesions compared to T2 (p-value=0.019) and was superior to FLAIR but the difference was below the statistical importance (p-value=0.249). This was equivalent to results done by Geurts et al. **[4]**; Elnekeidy et al. **[6]**; Hamed et al. **[7]** and Wattjes and Barkhof **[8]** found that DIR was significantly superior in comparison to both T2 and FLAIR sequences.

As regards the cortical lesions, we found that DIR detected significantly more cortical lesions when compared to T2 (p-value <0.001) and FLAIR (p-value <0.001). This was equivalent to studies done by Geurts et al. (2005) **[4]**; Elnekeidy et al. **[6]**; Hamed et al. **[7]**; Vural et al. **[1]**; Moraal et al. **[9]** and Wattjes and Barkhof **[8]**.

As Regards the juxta and subcortical lesions, we found DIR significantly detected more lesion compared to T2 (p-value=0.001). This was equivalent to studies done by Elnekeidy et al. **[6]** and Vural et al. **[1]** however, this result was in contrary with the result done by Geurts et al. **[4]** and Moraal et al. **[9]** which detected the highest number of lesions with T2.

Compared to FLAIR, DIR significantly detected more juxta and subcortical lesions (p-value=0.023) in our study. This was equivalent to Elnekeidy et al. **[6]** and Geurts et al. **[4]**; Yet, this result was in contrary with the result done by Wattjes and Barkhof **[8]**; Moraal et al. **[9]** which detected more lesions with FLAIR.

As Regards DWM lesions, we found that FLAIR detected the highest number of lesions followed by DIR and T2 came last. This was equivalent to the results done by Geurts et al. **[4]**.

Elnekeidy et al. **[6]** detected the highest DWM lesions by DIR. While Vural et al. **[1]** detected the highest DWM lesions by T2. Hamed et al. **[7]** found no significant difference of DWM lesions by FLAIR and DIR.

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=0.015). But, it was worthy of attention that DIR detected higher lesions even when compared with the T2 (p-value=0.045), which is considered the "gold standard" in the infratentorial region. This was consistent with the results done by Elnekeidy et al. **[6]**; Hamed et al. **[7]**; Geurts et al. **[4]** and Wattjes and Barkhof **[8]** but in contrary with results done by Moraal et al. **[9]** who found a similar number of lesions in the infratentorial region with DIR, FLAIR, and T2 images.

Conclusion:

We found DIR brain imaging had the highest sensitivity in the detection of cortical, juxtacortical and infratentorial lesions compared with FLAIR and T2 sequences. DIR showed better delineation between the WM, GM, and the MS lesions due to its high image contrast measurements. DIR sequence should be included in the routine MR protocols of MS patients especially to answer the question about cortical and infratentorial lesions for better prognostic values to the patients.

References

1- VURAL G., KEKLIKOG LU H.D., TEMEL S., DENIZ O. and ERCAN K.: Comparison of double inversion recovery and conventional magnetic resonance brain imaging in patients with multiple sclerosis and relations with disease disability. The Neuroradiology Journal, 26 2): 133-42, 2013.

2- MANOGARAN P., HANSON J.V., OLBERT E.D., et al.: Optical Coherence Tomography and Magnetic Resonance Imaging in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder. Int. J. Mol. Sci., 17 (11): 1894, 2016.

3- THOMPSON A.J., BANWELL B.L., BARKHOF F., et al.: Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. The Lancet Neurology, 17 (2): 162-73, 2017;.

4- GEURTS J.J., POUWELS P.J., UITDEHAAg B.M., et al.: Intracortical lesions in multiple sclerosis: Improved detection with 3D double inversion-recovery MR imaging. Radiology, 236: 254-260, 2005.

5- WATTJES M.P., LUTTERBEY G.G., GIESEKE J., TRÄBER F., KLOTZ L., SCHMIDT S. and SCHILD H.H.: Double inversion recovery brain imaging at 3T: Diagnostic value in the detection of multiple sclerosis lesions. American Journal of Neuroradiology, 28 (1): 54-9, 2007.

6- ELNEKEIDY A.M., KAMAL M.A., ELFATATRY A.M. and ELSKEIKH M.L.: Added value of double inversion recovery magnetic resonance sequence in detection of cortical and white matter brain lesions in multiple sclerosis. The Egyptian Journal of Radiology and Nuclear Medicine, 45 (4): 1193-1199, 2014.

7- HAMED W., FATHI W., MAHMOUD W. and ELHAWARY G.: Diagnostic accuracy of double inversion recovery in delineation of multiple sclerosis lesions and its clinical correlation with expanded disability scoring system. Egyptian Journal of Radiology and Nuclear Medicine, 50 (1): 1-8, 2019.

8- WATTJES M.P. and BARKHOF F.: High field MRI in the diagnosis of multiple sclerosis: High field-high yield? Neuroradiology, 51: 279-292, 2009.

9- MORAAL B., ROOSENDAAL S.D., POUWELS P.J., VRENKEN H., VAN SCHIJNDEL R.A., MEIER D.S. and BARKHOF F.: Multi-contrast, isotropic, single-slab 3D MR imaging in multiple sclerosis. The Neuroradiology Journal, 22 (1 Suppl): 33-42, 2009.

التقييم الكمى لعدد الآفات بالرنين المغناطيسى فى التصلب المتعدد المخى : دراسة مقارنة بين التسلسلات التقليدية وتسلسل الانعاش الانعكاسى المزدوج

يعد التصلب المتعدد مرض إزالة الميالين الإلتهابى المزمن الأكثر شيوعاً للجهاز العصبى المركزى والذى يتميز ببقع من إزالة الميالين البؤرى وتنكس عصبى منتشر مؤدياً إلى عجز بدنى وعصبى معرفى.

وبالرغم من أن التصلب المتعدد كان يعرف بأنه اعتلال بالمادة البيضاء فإن إصابات التصلب المتعدد تحدث فى كل أجزاء نسيج الجهاز العصبى المركزى بما فيها القشرة المخية والمادة الرمادية العميقة.

وعلى وجه التقريب فإن اثنين مليون شخص على مستوى العالم مصابون بهذا الاعتلال وهو العجز العصبى غير الناتج عن الحوادث الأكثر شيوعاً فى التأثير على شباب البالغين.

وقد لعب الرنين المغناطيسى دوراً هاماً جداً فى توضيح آلية الاعتلال وتشخيص وعلاج التصلب المتعدد وطبقاً لمعايير ماكدونالد للتصلب المتعدد، يتطلب التشخيص دليلاً يمكن ادراكه على الاصابات المنتشرة فى الحيز والوقت.

وبالتبعية فإن للرنين المغناطيسى دور هام فى تشخيص التصلب المتعدد لأنه يمكنه توضيح الإصابات العديدة (الانتشار فى الحيز) والتى يمكن لبعضها أن تكون خفية بالفحص السريرى كما يمكنه تبيين الإصابات الجديدة فى فحوص المتابعة (الانتشار فى الوقت).

فى دراستنا، قمنا بمقارنة تسلسل الانعاش الانعكاسى المزدوج بالتسلسلات التقليدية T2 وتسلسل تثبيط المياة فيما يتعلق بقدرتها على اكتشاف الآفات المزيلة للميالين فى مناطق مختلفة من دماغ ٣٤ مريضاً معروفاً بالتصلب المتعدد.

فى الختام، وجدنا أن التصوير الدماغى تسلسل الانعاش الانعكاسى المزدوج كان له أعلى حساسية فى الكشف عن الآفات القشرية والمجاورة وتحت البطين مقارنة بتسلسل تثبيط المياة و T2 أظهر تسلسل الانعاش الانعكاسى ترسيماً أفضل بين المادة البيضاء والمادة الرمادية وآفات التصلب المتعدد بسبب قياسات تباين الصورة العالية. يجب تضمين تسلسل الانعاش الانعكاسى المزدوج فى بروتوكولات الرنين المغناطيسى الروتينية لمرضى التصلب المتعدد خاصة للاجابة على السؤال حول الآفات القشرية والداخلية من أجل قيم تنبؤية أفضل للمرضى.