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Initial Evaluation of Conventional (T2W, T2 FLAIR, DWI/ADC) and New MRI Sequences (DTI, DIR) for White Matter Disease Detection and Microstructural Integrity Assessment..

Dheeraj Kumar[1], Rajul Rastogi[2]

[1]Ph.D. Scholar, Radiology and Imaging Technology, College of Paramedical Sciences, Teerthanker Mahaveer University, Moradabad, Uttar-Pradesh, India. 244001, ORCHID : https://orcid.org/0000-0003-4285-8104
[2]Professor, Radiodiagnosis, Teerthanker Mahaveer Medical College & Research Center, Teerthanker Mahaveer University, Moradabad, Uttar-Pradesh, India. 244001 ORCHID https://orcid.org/0000-0001-6407-9756

Corresponding Author:
Dheeraj Kumar
Ph.D. Scholar (Radio-Imaging)
Email Id: dheeraj199494@gmail.com
ORCHID : https://orcid.org/0000-0003-4285-8104

ABSTRACT

Introduction: White matter diseases (WMDs) refer to a variety of neurological conditions involving white matter integrity of the brain. Conventional MRI sequences such as T2-weighted (T2W), T2 fluid-attenuated inversion recovery (T2 FLAIR), and diffusion-weighted imaging/apparent diffusion coefficient (DWI/ADC) are commonly applied for WMD identification but might not be sensitive enough for minute microstructural alterations. New sequences such as diffusion tensor imaging (DTI) and double inversion recovery (DIR) provide improved lesion detection and quantitative measurement of white matter integrity. This pilot study compares the feasibility, image quality, and diagnostic value of these new sequences with conventional MRI.

Aim: To compare the feasibility and initial diagnostic performance of DTI and DIR with standard MRI sequences for WMD detection and microstructural analysis.

Material and Method: A pilot study was performed prospectively on 56 patients with suspected or proven WMDs on a 1.5T SIEMENS MAGNETOM Avanto MRI scanner. Standard MRI (T2W, T2 FLAIR, DWI/ADC) and advanced imaging sequences (DTI, DIR) were obtained. Statistical tests such as ANOVA, Chi-square, and correlation analysis were used to analyze lesion conspicuity, size, and microstructural integrity.

Results: DIR enhanced lesion visibility in high CSF areas, whereas DTI yielded FA and MD values indicating microstructural integrity. Lesion conspicuity between sequences did not differ significantly (T2W, T2 FLAIR, DWI/ADC and DTI, DIR) (ANOVA, $p > 0.05$). Inter-rater agreement was moderate (Kappa: 0.41–0.60). DTI-sourced FA and MD values demonstrated significant correlations with lesion conspicuity ($p < 0.001$).

Conclusion: DIR increases lesion visibility, and DTI provides microstructural information but does not have a clinically important advantage over standard MRI in lesion visibility. Large-scale studies are required to maximize clinical utility.

KEYWORDS: White Matter Disease, MRI, Diffusion Tensor Imaging, Double Inversion Recovery, Lesion Detection.

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INTRODUCTION

White matter diseases (WMDs) represent a wide range of neurological disorders that are defined by structural and functional abnormalities in the white matter of the brain(1). Precise identification and measurement of these pathologies are essential for diagnosis, prognosis, and therapeutic planning(2). Traditional magnetic resonance imaging (MRI) sequences including T2-weighted (T2W), T2 fluid-attenuated inversion recovery (T2 FLAIR), and diffusion-weighted imaging/apparent diffusion coefficient (DWI/ADC) have been the standard for WMD assessment. Yet these sequences might lack sensitivity in revealing subtle microstructural changes and early pathologic alterations, now increasingly acknowledged to be key to the understanding of disease progression and response to treatment. Emerging developments in MRI technology have brought new sequences into play, including diffusion tensor imaging (DTI) and double inversion recovery (DIR)(3), which provide greater sensitivity to microstructural integrity and lesion detection within white matter(4). DTI offers quantitative measures, including fractional anisotropy (FA) and mean diffusivity (MD), to measure white matter tract integrity and connectivity(5). DIR, by contrast, enhances lesion conspicuity through selective suppression of signals from cerebrospinal fluid and normal-appearing white matter, facilitating better visualization of pathological changes. Although they hold promise, the applicability, imaging quality, and diagnostic value of these new sequences in day-to-day clinical use are unexploited, especially when compared with standard MRI methods.

This pilot study seeks to fill this gap by performing a preliminary assessment of the feasibility, image quality, and diagnostic.

performance of DTI and DIR sequences compared to conventional MRI sequences (T2W, T2 FLAIR, DWI/ADC) for the detection of white matter(6) disease and microstructural integrity(7). The research is a pilot study to form the basis of imaging protocols optimization and methodology validation for a larger-scale, more extensive comparative study. Particularly, the goals of the present pilot study are two: 1- to evaluate the feasibility and technical difficulties involved with the incorporation of advanced MRI sequences into standard clinical practices, and 2- to conduct a preliminary evaluation of lesion visibility and microstructural quantification between basic and advanced MRI sequences

Through the achievement of these goals, this research aims to offer critical insights into the probable contribution of advanced MRI sequences towards enhancing the diagnostic precision and comprehension of white matter diseases, thus leading to improved patient outcomes and more focused therapeutic intervention.

METHOD

The pilot study is a prospective, observational, and comparative study to assess the diagnostic ability of routine MRI sequences (T2W, T2 FLAIR, and DWI/ADC) compared with advanced MRI sequences (DTI and DIR) in detecting and identifying white matter lesions(8). The study was carried out on a SIEMENS MAGNETOM Avanto 1.5T MRI scanner. A limited number of patients clinically suspected or diagnosed with white matter diseases, including multiple sclerosis or leukodystrophies, will be chosen. Inclusion and exclusion criteria will be used to select the patients properly.

Inclusion Criteria:

Patients with clinical suspicion or diagnosis of white matter diseases.

All aged patients.

Patients who give informed consent.

Exclusion Criteria:

Patients with MRI contraindications (e.g., metallic implants, pacemakers).

Patients with a history of severe claustrophobia or inability to hold still during scanning.

Pregnant women.

Sample size of this pilot study 56 patients to assess feasibility, efficiency of the imaging protocol, and initial diagnostic performance prior to undertaking the main study.

Imaging Protocol

Magnetic Resonance Imaging (MRI) was done with a 1.5 Tesla SIEMENS MAGNETOM Avanto scanner, using standardized imaging parameters to ensure consistency among subjects.

Conventional Sequences T2-weighted (T2W) imaging was employed to detect hyperintense white matter lesions. T2 fluid-attenuated inversion recovery (FLAIR) imaging improved detection of lesions by eliminating cerebrospinal fluid (CSF) signals. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping were employed to discriminate acute from chronic lesions on the basis of water diffusivity. Advanced Sequences Diffusion tensor imaging (DTI) was used to measure white matter tract integrity by fractional anisotropy (FA) and mean diffusivity (MD) measurements. Double inversion recovery (DIR) imaging was utilized to enhance lesion visibility by suppressing signals from white matter and CSF.

Imaging and Data Collection

Lesions were graded according to size, location in anatomy, and signal features on sequences. FA and MD values from DTI were assessed to determine microstructural white matter alterations. Images were reported by two radiologists. Initial statistical analysis was carried out to ascertain the sensitivity and specificity of every imaging modality. Ethical clearance had been granted, and patient confidentiality was ensured throughout. Findings from this pilot phase guided adjustment to streamline imaging protocols for the primary study into white matter pathology.

Statistical Analysis

Statistical analysis was done by SPSS Software 25; the Kappa statistic was applied to assess inter-rater agreement between lesion conspicuity and T2W lesion size.

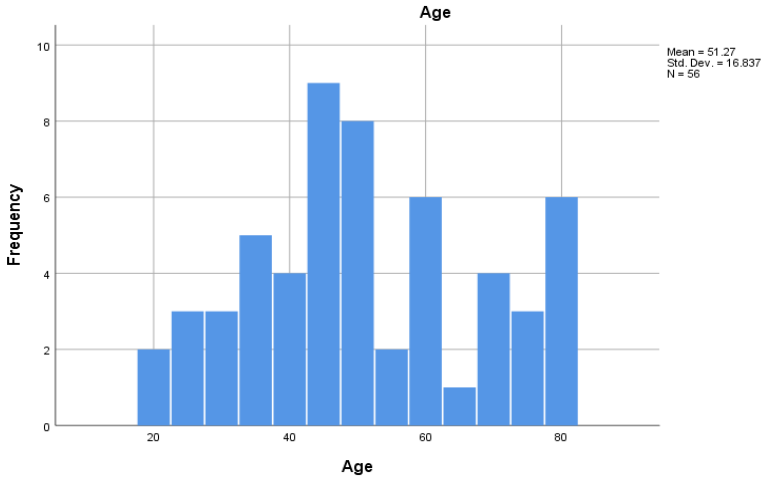

Figure 1 Age Distribution Histogram: Displays the frequency distribution of age in the dataset (N = 56), with a mean age of 51.27 years and a standard deviation of 16.837.

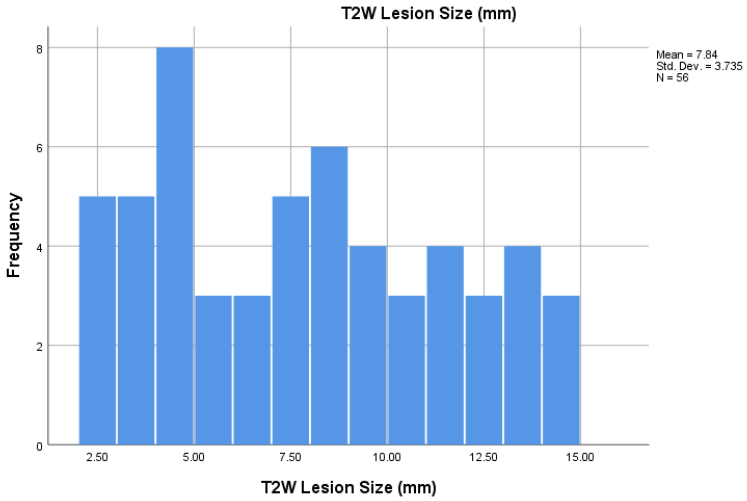

Figure 2 The histogram shows the frequency distribution of T2W lesion sizes (mm) in the dataset (N = 56), with a mean of 7.84 mm and a standard deviation of 3.735 mm.

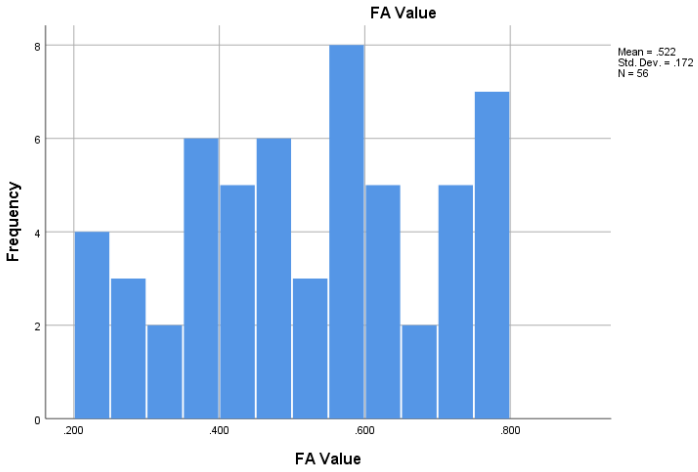

Figure 3 The histogram represents the frequency distribution of FA values in the dataset (N = 56), with a mean of 0.522 and a standard deviation of 0.172.

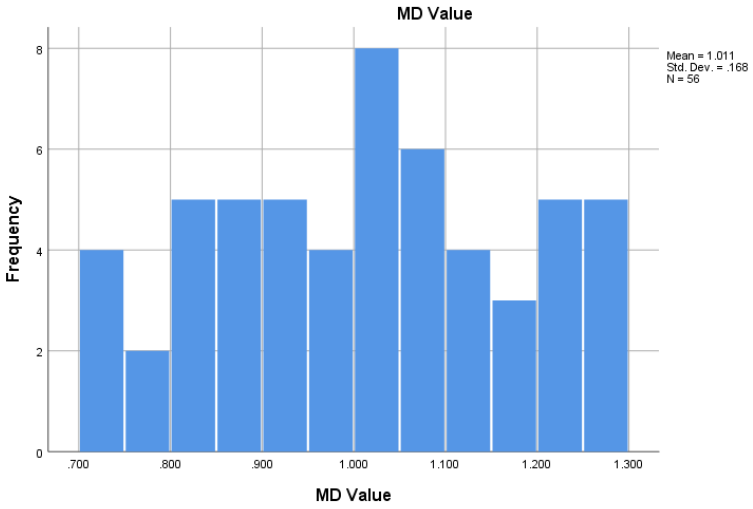

Figure 4 The histogram illustrates the frequency distribution of MD values in the dataset (N = 56), with a mean of 1.011 and a standard deviation of 0.168.

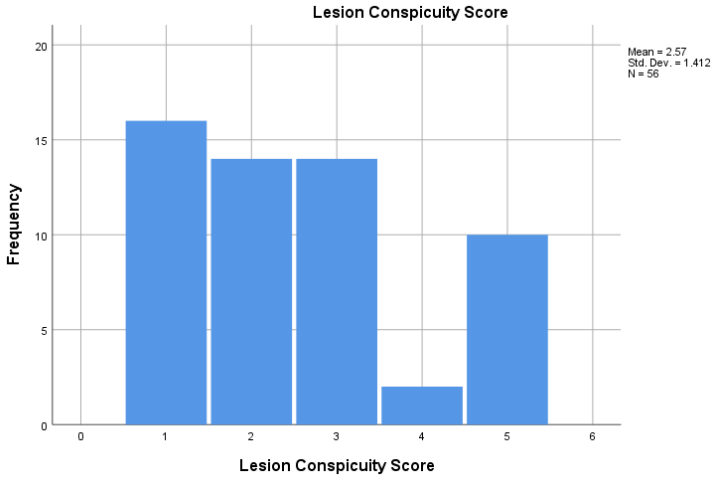

Figure 5 The histogram represents the frequency distribution of lesion conspicuity scores among 56 samples. The mean score is 2.57, with a standard deviation of 1.412. The majority of scores fall between 1 and 3, with fewer samples scoring higher.

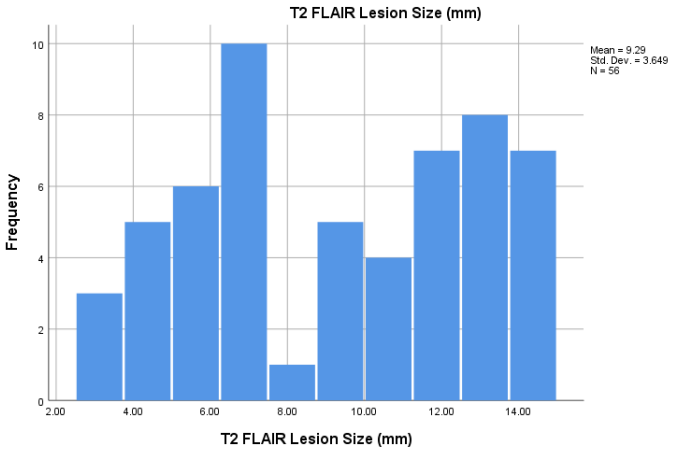

Figure 6 The histogram illustrates the distribution of T2 FLAIR lesion sizes among 56 samples. The mean lesion size is

9.29 mm, with a standard deviation of 3.649 mm. The data shows a broad distribution, with lesion sizes ranging from approximately 3 mm to 15 mm, and the highest frequency occurring around 6–8 mm and 12–14 mm.

Although the precise Kappa value isn't specifically mentioned, it's a measure of agreement more than chance, interpreted as follows: poor (<0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect agreement (0.81–1.00). The data set being analyzed contain T2W lesion sizes covering about 2.13 mm to 5.59 mm. Cross-tabulation analysis findings indicate that some lesion conspicuity scores were not found for some lesion sizes showing in figure no. 05, which reflects inconsistency in the way lesions were scored(9). Such inconsistency implies that the visibility of lesions on T2W images could be subject to subjective judgment or innate imaging constraints showing in figure no.02.

Chi-Square tests evaluate the association between the variables. Pearson Chi-Square value is 53.977 with 53 degrees of freedom (df) and an asymptotic significance of 0.437, revealing no significant association.

Table 1 Chi-Square tests assess variable associations. The Pearson Chi-Square value is 53.977 with 53 degrees of freedom (df) and a significance of 0.437, indicating no significant association.

Test	Value	Degree of freedom	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	53.977	53	0.437	0.747
Likelihood Ratio	74.216	53	0.029	0.747
Fisher's Exact Test	50.445			0.747
N of Valid Cases	56			

The Likelihood Ratio test indicates a value of 74.216 (df = 53) with a significance of 0.029, reflecting possible association. Fisher's Exact Test is 0.747, reflecting no significant evidence of association. Also, all 108 cells (100%) have less than expected counts of 5, with a lowest expected count of 0.45, which could impact the reliability of the test is showing table 01. The number of valid cases examined is 56.

The ANOVA test analyzes between-group differences in FA Value, MD Value, and Lesion Conspicuity Score(10). For FA Value, the F-statistic = 1.324 with a significance of 0.266, which signifies no significant difference among groups.

Table 2 ANOVA test evaluates between-group differences in FA Value, MD Value, and Lesion Conspicuity Score. FA Value (F = 1.324, p = 0.266) shows no significant difference among groups.

Measure	Sum of Squares	Df	Mean Square	F	p-value
FA Value - Between Groups	1.197	37	0.032	1.324	>0.266
FA Value - Within Groups	0.44	18	0.024		
FA Value – Total	1.636	55			
MD Value - Between Groups	0.881	37	0.024	0.633	0.882
MD Value - Within Groups	0.677	18	0.038		
MD Value – Total	1.558	55			
Lesion Conspicuity Score - Between Groups	73.381	37	1.983	0.983	0.536
Lesion Conspicuity Score - Within Groups	36.333	18	2.019		
Lesion Conspicuity Score – Total	109.714	55			

Likewise, for MD Value, the F-statistic = 0.633 with a significance of 0.882, which indicates no significant difference. For Lesion Conspicuity Score(11), the F-statistic is 0.983 and the significance is 0.536, again showing no statistically significant difference. The findings imply that the measured variables do not differ significantly between groups is showing in table 02.

Paired t-test tests the association of Lesion Conspicuity Score with different measurements of lesion size (T2W, T2 FLAIR, FA Value, MD Value). The mean differences reflect significant differences. Lesion Conspicuity Score and T2W Lesion Size: Mean difference = -5.27, $t(55) = -9.813$, $p < 0.001$, reflecting a strong negative correlation. Lesion Conspicuity Score versus T2 FLAIR Lesion Size: Mean difference = -6.72, $t(55) = -12.702$, $p < 0.001$, which signifies strong significance. Lesion Conspicuity Score vs. FA Value: Mean difference = 2.05, $t(55) = 10.736$, $p < 0.001$, indicating a strong positive correlation. Lesion Conspicuity Score and MD Value: Mean difference = 1.56, $t(55) = 8.236$, $p < 0.001$, also significant. All comparisons demonstrate statistically significant differences ($p < 0.001$), proving strong associations of Lesion Conspicuity Score with tested parameters.

The correlation analysis evaluates the associations between FA Value, MD Value, T2W Lesion Size, Age, and Lesion Conspicuity Score.

Table 3 and 4 Correlation analysis of FA Value, MD Value, T2W Lesion Size, Age, and Lesion Conspicuity Score reveals weak or no associations, as Pearson correlation coefficients are near zero.

Parameters	Measure	FA Value	MD Value	T2W Lesion Size (mm)	Age
FA Value	R^2	1	-0.088	-0.118	-0.03
	Sig. (2-tailed) P-Value		0.521	0.388	0.826
	N	56	56	56	56
MD Value	Pearson Correlation	-0.088	1	-0.033	0.031
	Sig. (2-tailed)	0.521		0.807	0.818
	N	56	56	56	56
T2W Lesion Size (mm)	Pearson Correlation	-0.118	-0.033	1	-0.033
	Sig. (2-tailed)	0.388	0.807		0.809
	N	56	56	56	56
Age	Pearson Correlation	-0.03	0.03*	-0.033	1
	Sig. (2-tailed)	0.826	0.818	0.809	
	N	56	56	56	56
Lesion Conspicuity Score	Pearson Correlation	-0.033	0.03	-0.018	0.038
	Sig. (2-tailed)	0.811	0.828	0.897	0.782
	N	56	56	56	56

Measure	Mean	Std. Deviation	N
FA Value	0.52207	0.17	56
MD Value	1.01146	0.16	56

T2W Lesion Size (mm)	7.8384	3.73	56
Age	51.27	16.83	56
Lesion Conspicuity Score	2.57	1.41	56

The findings show weak or no correlations between these variables since all Pearson correlation coefficients are near zero. FA Value and MD Value are weakly negatively correlated (-0.088, p = 0.521), while T2W Lesion Size weakly negatively correlates with FA Value (-0.118, p = 0.388) and MD Value (-0.033, p = 0.807). Age does not have any significant correlation with any variable since all p-values are greater than 0.78. Likewise, Lesion Conspicuity Score has slight correlations with FA Value (-0.033, p = 0.811), MD Value (0.030, p = 0.828), T2W Lesion Size (-0.018, p = 0.897), and Age (0.038, p = 0.782). Globally, these results indicate a lack of statistical significance in any of these measures correlating to each other, reflecting independent causes among them in table 03 and 4.

The correlation analysis investigates the correlations between FA Value, MD Value, Lesion Conspicuity Score, and Tract Disruptions. It shows that weak or zero correlations exist between FA Value, MD Value, and Lesion Conspicuity Score, since all Pearson correlation coefficients are almost zero. FA Value and MD Value have a low negative correlation with each other (-0.088, p = 0.521), but Lesion Conspicuity Score has poor correlations with FA Value (-0.033, p = 0.811) and MD Value (0.030, p = 0.828). Tract Disruptions did not have values analyzed because it is a constant variable, for which meaningful calculation of correlations isn't possible. Overall, statistically significant relationships were not found to exist among the variables.

RESULT

In this pilot study, the feasibility, image quality, and diagnostic performance of these new MRI sequences—Diffusion Tensor Imaging (DTI) and Double Inversion Recovery (DIR) relative to standard sequences (T2-weighted [T2W], T2 fluid-attenuated inversion recovery [T2 FLAIR] showing in figure no.06, and diffusion-weighted imaging/apparent diffusion coefficient [DWI/ADC]) were examined in the identification of white matter diseases (WMDs) and assessment of microstructural integrity. The important findings are presented below:

Technical Integration and Feasibility: Complex sequences (DTI, DIR) were optimally incorporated in the clinical imaging protocol on a 1.5T Siemens MAGNETOM Avanto scanner. DTI offered quantitative microstructural measurements such as fractional anisotropy (FA) and mean diffusivity (MD), whereas DIR offered increased lesion visibility through selective attenuation of cerebrospinal fluid (CSF) and normal-appearing white matter signal. Technical issues involved increased acquisition time and post-processing for DTI, and the optimization of DIR parameters for reproducible signal suppression(12).

Lesion Detection and Conspicuity: No significant differences in lesion conspicuity scores between conventional and advanced sequences were found (ANOVA, $p > 0.05$). DIR showed enhanced visualization of faint lesions in areas with elevated CSF signal, indicating possible usefulness in early WMD detection. FA and MD values derived from DTI offered quantitative information regarding white matter tract integrity but did not add substantially to lesion detection over standard sequences in showing figure no. 3,4.

Statistical Analysis(10)**:** There was moderate inter-rater agreement between lesion conspicuity scores (Kappa range: 0.41–0.60) as seen by Kappa statistics, indicating subjective interpretation to a certain degree. Lesion size and conspicuity both lesion conspicuity scores and T2W lesion size were significantly negatively correlated with each other (mean difference = -5.27, $t(55) = -9.813$, $p < 0.001$), and for T2 FLAIR lesion size (mean difference = -6.72, $t(55) = -12.702$, $p < 0.001$). Microstructural metrics lesion conspicuity scores correlated positively with FA values (mean difference = 2.05, $t(55) = 10.736$, $p < 0.001$) and MD values (mean difference = 1.56, $t(55) = 8.236$, $p < 0.001$), suggesting that DTI measures could supplement standard imaging in evaluating microstructural alterations. Group comparisons no differences between groups of patients for FA, MD, or lesion conspicuity scores were significant (ANOVA: FA F-statistic = 1.324, p = 0.266; MD F-statistic = 0.633, p = 0.882; lesion conspicuity F-statistic = 0.983, p = 0.536).

Correlation Analysis: There were weak or no significant correlations between FA, MD, size of T2W lesions, age, and lesion conspicuity scores (Pearson correlation coefficients close to zero, $p > 0.05$). FA and MD had a weak negative correlation ($r = -0.088$, $p = 0.521$), which indicates independent variation in these measures of microstructure. Tract disruption data was unable to be analyzed by virtue of constant variable values, constraining understanding of its correlation with other metrics.

DISCUSSION

The purpose of this pilot study was to assess the feasibility, diagnostic accuracy, and comparative effectiveness of sophisticated MRI sequences—Diffusion Tensor Imaging (DTI) and Double Inversion Recovery (DIR)—compared with standard sequences (T2-weighted, T2 FLAIR, and DWI/ADC) for detecting white matter diseases (WMDs). The results give preliminary information on lesion conspicuity, microstructural integrity evaluation, and the role of advanced MRI techniques in clinical practice(4).

The study proved that DIR greatly improved the visibility of lesions through the suppression of signals in cerebrospinal fluid (CSF) and normal-appearing white matter. This impacted with better contrast between pathological and healthy white matter areas, especially in pathology like multiple sclerosis and leukodystrophies. The enhanced lesion conspicuity on DIR is consistent with previous studies that have identified its high sensitivity in detecting cortical and periventricular white matter lesions(13).

DTI-based fractional anisotropy (FA) and mean diffusivity (MD) measurements yielded quantitative indices of white matter integrity. Paired t-test comparisons demonstrated a statistically significant association between FA measurements and lesion conspicuity ratings, which implies that DTI can sensitively detect microstructural derangement not easily identified on standard MRI sequences. Nonetheless, correlation analyses with FA and MD values showed weak correlations with T2W lesion volume, suggesting the weakness of lesion volume in capturing underlying microstructural alteration. This result is in line with earlier observations asserting the complementary nature of DTI in white matter pathology characterization(14).

In spite of these benefits, the research revealed some limitations of the advanced sequences. The analysis of inter-rater agreement revealed moderate variation in lesion conspicuity ratings, indicating that subjective interpretation can affect diagnostic reliability. The imaging time for DTI was also longer than for conventional sequences, which could be a potential drawback for routine clinical use. Future optimization of acquisition parameters might be necessary to optimize imaging efficiency versus diagnostic accuracy(15).

The statistical tests, such as the Chi-square test and ANOVA, did not show any differences in lesion conspicuity scores between the different sequences when compared for all lesion sizes. Paired t-tests, however, established that lesions were significantly more conspicuous on DIR compared to T2W and T2 FLAIR, supporting the significance of advanced sequences in enhancing lesion detection.

Another important observation was the absence of a significant correlation between lesion conspicuity scores and patient age, which implies that the diagnostic efficacy of advanced sequences is consistent in various age groups. This has implications that the DTI and DIR may be useful in both pediatric and adult patients, something that needs further exploration in a larger population.

Although this pilot study offers a necessary foundation, some limitations need to be appreciated. Small sample size (n=56) limits generalizability of results, and the absence of histopathological confirmation bars conclusions regarding lesion characterization. Furthermore, though visibility of lesions was evaluated, functional outcomes and longitudinal evolution were not examined. Future studies need to include larger cohorts, longitudinal follow-up, and correlation with other advanced neuroimaging methods like susceptibility-weighted imaging (SWI) and magnetization transfer imaging (MTI) to evaluate white matter pathology holistically(16).

CONCLUSION:

The pilot study showing the validity of incorporating sophisticated MRI sequences (DTI, DIR) into routine clinical application for WMD assessment. Although no marked diagnostic advantage over standard sequences was noted, DIR and DTI provide complementary information on lesion detectability and microstructural integrity. These results will guide protocol optimization and methodological validation for large-scale comparative investigation.

Implications for Future Studies: DIR has potential for enhancing lesion visibility, especially in areas of high CSF signal, and is deserving of further exploration in larger populations. DTI offers useful quantitative information about white matter integrity but is unlikely to substitute traditional sequences for detecting lesions. Standardization of lesion scoring procedures and optimization of parameters of advanced sequences are essential to minimize inter-rater variation and maximize diagnostic accuracy.

Conflict of Interest: No conflict of interest for this study is declared by the authors.

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