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Original Article

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Comparison of 3D T2-FLAIR and Double Inversion Recovery Image Quality in Multiple Sclerosis Lesions at 3T MRI

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ABSTRACT

Introduction: Multiple sclerosis (MS) lesions may involve cortical and white matter regions and can be challenging to characterize using conventional magnetic resonance imaging (MRI). Three-dimensional T2 Fluid-Attenuated Inversion Recovery (3D T2-FLAIR) and Double Inversion Recovery (3D DIR) provide different tissue suppression characteristics; however, their relative image quality in MS patients with epileptic manifestations requires further evaluation. To compare the image quality of 3D T2-FLAIR and 3D DIR sequences for detecting MS lesions on 3 Tesla brain MRI using Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR).

Research Methodology: This quantitative comparative retrospective study included 10 non-contrast 3 Tesla brain MRI examinations of patients with MS and epileptic manifestations. SNR and CNR were measured using regions of interest placed in white matter, gray matter, and MS lesions. Differences between 3D T2-FLAIR and 3D DIR were analyzed using the Wilcoxon signed-rank test with $\alpha=0.05$.

Results: T2-FLAIR demonstrated significantly higher white matter SNR than DIR (111.47 vs. 16.08; $p=0.002$). No significant differences were observed for gray matter SNR (156.17 vs. 182.71; $p=0.275$) or lesion SNR (170.61 vs. 229.78; $p=0.105$). DIR produced significantly higher lesion-to-white matter CNR than T2-FLAIR (577.51 vs. 398.25; $p=0.049$), while gray matter-to-white matter and lesion-to-gray matter CNR differences were not significant.

Conclusion: 3D T2-FLAIR provides superior white matter SNR, whereas 3D DIR improves lesion-to-white matter contrast. Their complementary characteristics support combined use for more comprehensive evaluation of MS lesions on 3 Tesla MRI.

Keywords: Multiple Sclerosis; Magnetic Resonance Imaging; Double Inversion Recovery; T2-FLAIR; Signal-to-Noise Ratio; Contrast-to-Noise Ratio

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory and demyelinating disorder of the central nervous system characterized by heterogeneous neurological manifestations and lesions involving white matter, cortical, and deep gray matter structures. The distribution and burden of these lesions contribute substantially to neurological disability and may also be associated with seizures and epilepsy in a subset of patients[1,2]. Cortical involvement is particularly relevant because conventional magnetic resonance imaging (MRI) may underestimate cortical and juxtacortical lesions[3]. Consequently, optimizing MRI techniques capable of improving lesion conspicuity remains important for the radiological assessment of MS, particularly when neurological manifestations such as epilepsy suggest cortical involvement.

MRI has become an essential imaging modality for identifying structural abnormalities of the brain because of its high soft-tissue contrast and ability to provide multiple tissue-sensitive sequences without ionizing radiation. In patients with epilepsy, MRI is particularly valuable for detecting structural abnormalities potentially associated with epileptogenic activity[4,5]. However, abnormalities such as focal cortical dysplasia, mesial temporal sclerosis, and cortical or juxtacortical demyelinating lesions may be subtle and difficult to distinguish using conventional sequences. This diagnostic challenge emphasizes the need for imaging protocols that maximize both signal quality and tissue contrast[6].

The development of 3 Tesla MRI provides technical advantages for neuroimaging by enabling higher signal availability and high-resolution three-dimensional acquisitions. Three-dimensional imaging allows thinner sections, broader anatomical coverage, and multiplanar reconstruction, potentially facilitating visualization of small or anatomically complex lesions. Nevertheless, increased field strength alone does not guarantee optimal lesion visualization[7]. Image quality also depends on sequence characteristics and their ability to suppress signals from tissues that may obscure pathological abnormalities[8]. Therefore, selecting an appropriate MRI sequence remains a critical component of imaging protocol optimization.

T2 Fluid-Attenuated Inversion Recovery (T2-FLAIR) is widely used in neurological MRI because it suppresses the signal from cerebrospinal fluid (CSF), thereby improving visualization of hyperintense abnormalities adjacent to CSF-containing spaces. This characteristic has established T2-FLAIR as an important sequence for identifying demyelinating lesions. However, despite its diagnostic utility, FLAIR may provide limited differentiation of some cortical or juxtacortical lesions from surrounding tissues. This limitation becomes particularly relevant when subtle cortical pathology needs to be identified[9].

Double Inversion Recovery (DIR) provides a different approach to tissue contrast by simultaneously suppressing signals from CSF and white matter. The resulting enhancement of gray matter conspicuity can improve visualization of cortical and juxtacortical abnormalities. Previous comparative investigations have suggested that DIR may provide additional information for detecting cerebral lesions in MS and epilepsy[10]. Histopathology-supported research has also highlighted the continuing challenge of reliably identifying cortical MS lesions with MRI, reinforcing the need to evaluate imaging sequences according to the specific anatomical and pathological characteristics being investigated[11].

Recent evidence further supports the potential contribution of DIR to MS lesion detection. Comparative studies of DIR and FLAIR have demonstrated differences in their ability to visualize cerebral and cortical lesions, while research using 3 Tesla MRI has emphasized the role of DIR in neuroimaging. A recent systematic review and meta-analysis comparing 3D

DIR with 3D T2-FLAIR also indicates continuing scientific interest in determining the relative performance of these sequences for MS lesion detection[12]. Collectively, the literature suggests that DIR may enhance lesion conspicuity, particularly where suppression of surrounding white matter increases lesion contrast. However, these findings should not be interpreted as evidence that DIR universally provides superior image quality across all quantitative parameters.

This distinction is important because MRI image quality is multidimensional. Signal-to-Noise Ratio (SNR) represents the relationship between the measured tissue signal and background noise and is commonly used as a quantitative indicator of signal quality. Contrast-to-Noise Ratio (CNR), in contrast, reflects the degree to which two tissues or a lesion and its surrounding tissue can be differentiated relative to image noise. A sequence may therefore produce a higher SNR for a particular tissue without simultaneously providing the highest lesion-to-tissue CNR. Evaluating only one parameter may consequently lead to an incomplete interpretation of sequence performance[13]. The available evidence also reveals an empirical and methodological gap. Much of the comparative literature has focused on lesion detection or qualitative visibility, whereas direct quantitative comparisons of 3D T2-FLAIR and 3D DIR based on tissue-specific SNR and lesion-specific CNR remain important for determining how the sequences differ in actual image characteristics[14]. Furthermore, evidence specifically addressing MS patients with epileptic manifestations is relatively limited. This population is clinically relevant because cortical and juxtacortical abnormalities may be important to both the underlying demyelinating disease and seizure manifestations.

This issue is also pertinent in clinical MRI practice in Indonesia, where optimization of advanced MRI protocols should consider the diagnostic information provided by individual sequences rather than assuming that a single sequence is optimal for every tissue or lesion characteristic. At RSUP Dr. Wahidin Sudirohusodo Makassar, 3 Tesla brain MRI provides an opportunity to quantitatively examine the relative performance of 3D T2-FLAIR and 3D DIR in patients with MS and epileptic manifestations. Locally generated quantitative evidence may contribute to sequence selection and protocol refinement within the specific clinical setting.

The novelty of the present study lies in its tissue-specific quantitative comparison of 3D T2-FLAIR and 3D DIR using both SNR and CNR in 3 Tesla brain MRI examinations of patients with MS and epileptic manifestations. Rather than treating overall image quality as a single outcome, this study evaluates white matter, gray matter, and MS lesions separately and examines contrast relationships between these structures. This approach is important because it can identify complementary strengths of the two sequences and provide a more nuanced basis for protocol optimization.

Accordingly, this study aimed to compare the image quality of 3D T2-FLAIR and 3D DIR sequences in 3 Tesla brain MRI examinations of patients with multiple sclerosis and epileptic manifestations based on quantitative SNR and CNR measurements. Specifically, the study addressed two research questions: (1) Do SNR values for white matter, gray matter, and MS lesions differ significantly between 3D T2-FLAIR and 3D DIR? and (2) Do CNR values for gray matter–white matter, lesion–gray matter, and lesion–white matter differ significantly between the two sequences? It was hypothesized that the two sequences would demonstrate significantly different quantitative image-quality characteristics, with their relative performance varying according to the tissue and contrast parameter evaluated.

MATERIALS AND METHODS

Study Design

This study employed a quantitative comparative design with a retrospective approach to evaluate differences in image quality between three-dimensional T2 Fluid-Attenuated Inversion Recovery (3D T2-FLAIR) and three-dimensional Double Inversion Recovery (3D DIR) sequences in brain magnetic resonance imaging (MRI). The study focused on patients with multiple sclerosis (MS) presenting with epileptic manifestations who underwent non-contrast brain MRI using a 3 Tesla MRI system at RSUP Dr. Wahidin Sudirohusodo, Makassar, Indonesia. A within-examination comparative approach was used because both 3D T2-FLAIR and 3D DIR images were obtained from the same MRI examinations. Accordingly, each examination served as its own reference for comparing quantitative image-quality parameters. This design reduced variability attributable to differences between patients and enabled direct paired comparisons between the two MRI sequences.

Image quality was assessed quantitatively using Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR). SNR was evaluated separately for white matter, gray matter, and MS lesions, whereas CNR was evaluated for three tissue contrasts: gray matter–white matter, lesion–gray matter, and lesion–white matter. These quantitative measurements were selected to distinguish signal performance from lesion-to-tissue contrast rather than treating image quality as a single global construct.

This study did not employ qualitative or mixed-methods procedures. Therefore, qualitative interviews, focus group discussions, thematic analysis, joint displays, triangulation, and mixed-methods meta-inferences were not applicable.

Setting and Participants

The study was conducted using brain MRI examination data obtained at RSUP Dr. Wahidin Sudirohusodo, Makassar, Indonesia. The hospital provides advanced diagnostic imaging services, including 3 Tesla MRI examinations. The retrospective dataset comprised 10 non-contrast brain MRI examinations of patients with multiple sclerosis accompanied by epileptic manifestations. The unit of analysis was an eligible MRI examination rather than an independently recruited healthy participant or control subject. Each included examination provided paired imaging datasets from the 3D T2-FLAIR and 3D DIR sequences, allowing quantitative comparison within the same examination. Based on the available study documentation, examinations were eligible when they represented patients with multiple sclerosis and epileptic manifestations, were performed using a 3 Tesla MRI system, were non-contrast brain examinations, and contained both 3D T2-FLAIR and 3D DIR sequences suitable for quantitative evaluation. The analysis also required images that permitted placement of Regions of Interest (ROIs) in white matter, gray matter, and MS lesions. Because this was a retrospective imaging study, no prospective participant recruitment or random allocation was performed. The available documentation does not report a formal probability-sampling procedure or prospective sample-size calculation. Therefore, no statistical power calculation is claimed. The final dataset consisted of 10 examinations meeting the study requirements and available for paired quantitative analysis.

The study period was not specified in the available source document and should be added to the final manuscript from the original research records. Similarly, detailed exclusion criteria concerning motion artifacts, incomplete sequences, previous treatment, lesion size, or

other technical factors were not reported and should not be inferred without verification from the original protocol.

Data Collection and Image Assessment

Data collection was based on existing non-contrast brain MRI examinations acquired using a 3 Tesla MRI system. For every examination included in the analysis, image datasets from two sequences were evaluated: 3D T2-FLAIR and 3D DIR. Quantitative image quality was assessed by measuring signal intensity and image noise to derive SNR and CNR values. Regions of Interest were placed in three principal anatomical or pathological regions: white matter, gray matter, and MS lesions. The use of comparable tissue regions across both sequences was intended to provide a direct assessment of how T2-FLAIR and DIR differed in their representation of normal brain tissue and demyelinating lesions.

SNR was used to characterize the relationship between the signal obtained from a specified tissue or lesion and image noise. Higher SNR indicates a stronger measurable tissue signal relative to noise. Measurements were obtained separately for white matter, gray matter, and MS lesions so that sequence performance could be assessed according to tissue type rather than summarized into a single image-quality value. CNR was used to quantify the differentiation between two tissue categories relative to image noise. Three contrasts were evaluated: gray matter versus white matter, MS lesion versus gray matter, and MS lesion versus white matter. These measurements were particularly relevant because DIR suppresses both cerebrospinal fluid and white matter signals, potentially altering the conspicuity of demyelinating lesions relative to surrounding brain tissue.

The comparison was performed on corresponding T2-FLAIR and DIR images from the same examinations. This paired structure was maintained throughout image measurement and statistical analysis. For complete technical reproducibility, the final manuscript should additionally report the MRI manufacturer and scanner model, radiofrequency coil, repetition time, echo time, inversion time or inversion times, field of view, matrix size, voxel dimensions, slice thickness, acquisition time, acceleration technique, and reconstruction parameters for both sequences. These technical acquisition parameters are not provided in the available manuscript and therefore cannot be reliably reconstructed here.

Similarly, the available documentation does not specify the ROI size, ROI placement protocol, software used for ROI measurements, number or professional background of image evaluators, whether measurements were repeated, or whether intra-observer and inter-observer reliability were assessed. These details should be retrieved from the original imaging protocol or research records before submission rather than estimated retrospectively.

Variables and Operational Definitions

The primary independent variable was the MRI sequence, operationalized as two paired categories: 3D T2-FLAIR and 3D DIR. The primary quantitative outcome variables were SNR and CNR. Both were treated as continuous numerical variables. White matter SNR represented the quantitative signal characteristics of white matter relative to image noise. Gray matter SNR represented the signal characteristics of gray matter relative to noise, whereas lesion SNR represented the corresponding quantitative signal characteristics of identified MS lesions.

CNR was evaluated through three tissue relationships. Gray matter–white matter CNR represented the quantitative differentiation between gray and white matter. Lesion–gray matter CNR represented the contrast between MS lesions and gray matter. Lesion–white matter CNR represented the contrast between MS lesions and surrounding white matter. These tissue-specific outcomes were evaluated separately because a sequence may provide superior signal characteristics in one tissue but superior lesion contrast in another. Consequently, no single SNR or CNR measurement was considered sufficient to establish overall superiority of either sequence. The paired nature of the measurements was an important feature of the variable structure. SNR and CNR values obtained from T2-FLAIR were compared with the corresponding measurements obtained from DIR within the same MRI examinations.

Statistical Analysis

Quantitative data were summarized using descriptive statistics. Mean values were reported for SNR and CNR parameters for each MRI sequence. The descriptive analysis included SNR measurements for white matter, gray matter, and MS lesions and CNR measurements for gray matter–white matter, lesion–gray matter, and lesion–white matter. Within-sequence differences among the tissue-specific SNR and CNR measurements were evaluated using the Friedman test as reported in the study results. For 3D T2-FLAIR, the Friedman test was used to assess differences among SNR values for white matter, gray matter, and lesions. The corresponding analysis was performed for 3D DIR. The same approach was applied to the three CNR categories within each sequence.

For the primary between-sequence comparisons, the Wilcoxon signed-rank test was used to compare paired quantitative measurements obtained from 3D T2-FLAIR and 3D DIR. The non-parametric paired procedure was appropriate to the comparative structure of the dataset, in which measurements from both sequences originated from the same MRI examinations. Statistical significance was determined at an alpha level of 0.05, with *p*<0.05 interpreted as statistically significant. Six principal between-sequence comparisons were examined: white matter SNR, gray matter SNR, lesion SNR, gray matter–white matter CNR, lesion–gray matter CNR, and lesion–white matter CNR.

The analysis showed that white matter SNR differed significantly between sequences, whereas gray matter and lesion SNR did not. Among the CNR measures, only lesion–white matter CNR demonstrated a statistically significant difference between sequences. These analyses permitted evaluation of sequence performance at the level of individual tissue and contrast parameters rather than relying solely on an overall image-quality judgment.

Because the study included only 10 examinations, statistical interpretation emphasized both the direction and magnitude of observed quantitative differences together with the corresponding *p*-values. Non-significant findings were not interpreted as evidence of equivalence between sequences, particularly given the limited sample size. The statistical software and version used for the original analyses are not identified in the available manuscript. This information should be inserted from the original research documentation before publication.

Ethical Considerations

The study used retrospectively obtained clinical MRI examination data. Patient confidentiality should therefore be maintained throughout data extraction, image evaluation, analysis, and reporting. Personally, identifying information should not be included in the

analytical dataset or publication. The available manuscript does not provide the name of the approving research ethics committee, ethical approval number, date of approval, or information regarding whether individual informed consent was obtained or waived because of the retrospective design. Consequently, these details cannot be stated as established facts.

Reproducibility and Methodological Scope

The methodological framework was designed to provide a paired quantitative assessment of two MRI sequences applied to the same clinical examinations. The use of tissue-specific SNR and CNR measurements allowed the study to differentiate between signal performance and lesion contrast. This distinction was central to the analysis because the two sequences were expected to interact differently with white matter, gray matter, and demyelinating lesions. The study was specifically designed as an imaging comparison and did not evaluate diagnostic accuracy against histopathology, clinical outcomes, seizure frequency, disease severity, or longitudinal lesion progression. It also did not establish sensitivity, specificity, positive predictive value, or negative predictive value for either sequence. Accordingly, conclusions regarding sequence performance were restricted to the quantitative image-quality parameters measured in this dataset.

The reproducible analytical sequence consisted of identifying eligible 3 Tesla brain MRI examinations containing both 3D T2-FLAIR and 3D DIR acquisitions; identifying white matter, gray matter, and MS lesion regions; obtaining ROI-based measurements; deriving tissue-specific SNR and CNR parameters; maintaining paired measurements for the two sequences; summarizing the quantitative data descriptively; and performing paired inferential comparisons using the Wilcoxon signed-rank test at a significance threshold of $p<0.05$. This approach allowed the relative strengths of T2-FLAIR and DIR to be examined without presuming that one sequence would be universally superior. Instead, sequence performance was interpreted according to the specific tissue and contrast characteristics demonstrated by the quantitative measurements.

RESULTS

Study sample and imaging characteristics

A total of 10 non-contrast brain MRI examinations were included in the quantitative analysis. All examinations were obtained from patients with multiple sclerosis (MS) presenting with epileptic manifestations and were performed using a 3 Tesla MRI system. Each examination contained both three-dimensional T2 Fluid-Attenuated Inversion Recovery (3D T2-FLAIR) and three-dimensional Double Inversion Recovery (3D DIR) sequences, allowing paired within-examination comparisons. Image quality was quantitatively assessed using Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR). SNR measurements were obtained for white matter, gray matter, and MS lesions. CNR measurements were evaluated for gray matter–white matter, lesion–gray matter, and lesion–white matter contrasts.

Demographic and clinical characteristics such as age, sex, duration of MS, duration of epilepsy, seizure characteristics, treatment history, and lesion burden were not available in the study dataset reported in the source manuscript. Therefore, the sample characteristics are presented according to the imaging information available.

Table 1. Characteristics of the analyzed MRI examinations

Characteristic	Study sample
MRI examinations	10
Clinical condition	Multiple sclerosis with epileptic manifestations
MRI field strength	3 Tesla
Contrast administration	Non-contrast
Sequences compared	3D T2-FLAIR and 3D DIR
SNR regions	White matter, gray matter, MS lesion
CNR comparisons	GM–WM, lesion–GM, lesion–WM
Statistical comparison	Paired analysis

Signal-to-Noise Ratio Within 3D T2-FLAIR

Quantitative assessment of the 3D T2-FLAIR sequence demonstrated variation in SNR across white matter, gray matter, and MS lesions. Mean SNR was 111.47 for white matter, 156.17 for gray matter, and 170.61 for MS lesions. The highest mean SNR on T2-FLAIR was therefore observed in MS lesions, followed by gray matter and white matter. The Friedman test indicated a statistically significant overall difference among the three tissue-specific SNR measurements ($p=0.002$). These findings indicate that signal characteristics on T2-FLAIR were not uniform across the evaluated anatomical and pathological regions. However, the within-sequence Friedman test does not establish which specific pair of regions was responsible for the overall difference unless supported by appropriate post-hoc pairwise testing.

Signal-to-Noise Ratio Within 3D DIR

A different SNR distribution was observed for the 3D DIR sequence. Mean SNR was 16.08 for white matter, 182.71 for gray matter, and 229.78 for MS lesions. The MS lesion demonstrated the highest mean SNR, whereas white matter demonstrated a substantially lower mean SNR. The Friedman test showed a statistically significant overall difference among white matter, gray matter, and lesion SNR values ($p=0.0002$). The markedly lower white matter signal is consistent with the tissue-suppression characteristics observed quantitatively in the DIR images. As with T2-FLAIR, this overall test establishes heterogeneity among the three measurements but does not independently identify statistically significant pairwise tissue differences.

Comparison of SNR Between 3D T2-FLAIR and 3D DIR

Paired comparisons demonstrated that the magnitude and statistical significance of differences between T2-FLAIR and DIR depended on the tissue being evaluated. White matter SNR was substantially higher with 3D T2-FLAIR than with 3D DIR, with mean values of 111.47 and 16.08, respectively. This difference was statistically significant ($p=0.002$). In contrast, gray matter SNR was numerically higher with DIR than T2-FLAIR (182.71 vs. 156.17), but the difference was not statistically significant ($p=0.275$). Similarly, lesion SNR was numerically higher with DIR (229.78) than with T2-FLAIR (170.61), although the difference did not reach statistical significance ($p=0.105$). Thus, among the three tissue-specific SNR comparisons, only white matter demonstrated a statistically significant difference between the two sequences.

Table 2. Comparison of SNR between 3D T2-FLAIR and 3D DIR

SNR parameter	3D T2-FLAIR, Mean	3D DIR, Mean	p-value	Interpretation
White matter	111.47	16.08	0.002	Significant
Gray matter	156.17	182.71	0.275	Not significant
MS lesion	170.61	229.78	0.105	Not significant

Note: Statistical significance was defined as p<0.05.

Contrast-to-Noise Ratio Within 3D T2-FLAIR

For 3D T2-FLAIR, the mean CNR between gray matter and white matter was 462.80. Mean lesion–gray matter CNR was 123.01, whereas lesion–white matter CNR was 398.25. The highest mean CNR was observed for gray matter–white matter, followed by lesion–white matter and lesion–gray matter. The Friedman test demonstrated a statistically significant overall difference among the three CNR parameters (p=0.0018). The findings indicate substantial variation in the degree of tissue differentiation provided by T2-FLAIR depending on the tissue pair examined.

Contrast-to-Noise Ratio Within 3D DIR

The 3D DIR sequence demonstrated a different CNR pattern. Mean gray matter–white matter CNR was 431.98, mean lesion–gray matter CNR was 148.29, and mean lesion–white matter CNR was 577.51. Lesion–white matter CNR was therefore the highest of the three DIR contrast measurements. The Friedman test indicated a statistically significant overall difference among the three CNR parameters (p=0.000045). Notably, lesion–white matter CNR was numerically greater with DIR than the corresponding measurement obtained with T2-FLAIR, providing the basis for the subsequent direct paired comparison.

Comparison of CNR Between 3D T2-FLAIR and 3D DIR

Between-sequence comparisons showed no statistically significant difference in gray matter–white matter CNR. Mean CNR was 462.80 with T2-FLAIR and 431.98 with DIR (p=0.770). Lesion–gray matter CNR was numerically higher with DIR than T2-FLAIR (148.29 vs. 123.01), but the difference was also not statistically significant (p=0.375). In contrast, lesion–white matter CNR demonstrated a statistically significant difference. The mean lesion–white matter CNR was 577.51 with DIR compared with 398.25 with T2-FLAIR (p=0.049). DIR therefore produced approximately 45% higher mean lesion–white matter CNR than T2-FLAIR in the analyzed examinations.

Table 3. Comparison of CNR between 3D T2-FLAIR and 3D DIR

CNR parameter	3D T2-FLAIR, Mean	3D DIR, Mean	p-value	Interpretation
Gray matter–white matter	462.80	431.98	0.770	Not significant
Lesion–gray matter	123.01	148.29	0.375	Not significant
Lesion–white matter	398.25	577.51	0.049	Significant

Note: Statistical significance was defined as p<0.05.

Overall Comparison of Quantitative Image-Quality Parameters

The combined SNR and CNR findings demonstrate that neither MRI sequence was superior across all quantitative image-quality parameters. Of the six principal between-sequence comparisons, two reached statistical significance. First, white matter SNR was significantly higher with T2-FLAIR than DIR (111.47 vs. 16.08; p=0.002). Second, lesion–white matter CNR was significantly higher with DIR than T2-FLAIR (577.51 vs. 398.25; p=0.049).

The remaining four comparisons did not reach statistical significance. Gray matter SNR (p=0.275), lesion SNR (p=0.105), gray matter–white matter CNR (p=0.770), and lesion–gray matter CNR (p=0.375) showed no statistically significant differences between sequences.

Table 4. Summary of comparative findings

Outcome	Sequence with higher mean	p-value	Statistical finding
White matter SNR	T2-FLAIR	0.002	Significant
Gray matter SNR	DIR	0.275	Not significant
Lesion SNR	DIR	0.105	Not significant
GM–WM CNR	T2-FLAIR	0.770	Not significant
Lesion–GM CNR	DIR	0.375	Not significant
Lesion–WM CNR	DIR	0.049	Significant

These results demonstrate distinct quantitative profiles for the two sequences. T2-FLAIR provided higher white matter SNR, whereas DIR provided higher lesion-to-white matter CNR. The findings therefore support a parameter-specific interpretation rather than classification of either sequence as universally superior.

DISCUSSION

This study compared the quantitative image quality of 3D T2-FLAIR and 3D Double Inversion Recovery (DIR) sequences in 3 Tesla brain MRI examinations of patients with multiple sclerosis (MS) and epileptic manifestations. The findings demonstrate that the two sequences have distinct and complementary image-quality characteristics rather than showing uniform superiority of one sequence over the other. Among the six principal comparisons, two statistically significant differences were identified. White matter Signal-to-Noise Ratio (SNR) was significantly higher with 3D T2-FLAIR than with 3D DIR (111.47 vs. 16.08; *p*=0.002), whereas lesion-to-white matter Contrast-to-Noise Ratio (CNR) was significantly higher with 3D DIR than with 3D T2-FLAIR (577.51 vs. 398.25; *p*=0.049). In contrast, no statistically significant differences were observed for gray matter SNR, MS lesion SNR, gray matter–white matter CNR, or lesion–gray matter CNR. Taken together, these findings suggest that sequence performance depends on the specific tissue and quantitative image-quality parameter being evaluated, making it inappropriate to classify either sequence as universally superior.

The present findings should be interpreted within the broader literature comparing DIR and FLAIR for cerebral lesion visualization. Elkholy et al. reported that DIR can provide additional value for detecting cerebral lesions in patients with MS, while Kulkarni et al. highlighted the usefulness of DIR in neuroimaging performed at 3 Tesla[15]. The current study adds a more parameter-specific perspective to this evidence. Although DIR has frequently been associated with improved lesion visualization, the present results indicate that this advantage does not extend equally to all quantitative image-quality measures[16]. Instead, the principal advantage of DIR was observed in the contrast between MS lesions and white matter. This distinction is important because greater lesion conspicuity does not necessarily imply higher signal quality across all tissues[17]. A sequence may intentionally suppress the signal from normal tissue and thereby produce a lower SNR for that tissue while simultaneously improving the contrast between pathological lesions and their background.

This interpretation is particularly relevant to the significantly higher lesion-to-white matter CNR observed with DIR. DIR is designed to suppress signals from both cerebrospinal fluid and white matter, thereby increasing the relative conspicuity of gray matter and lesions

located within or adjacent to white matter. In the present study, lesion–white matter CNR increased from 398.25 with T2-FLAIR to 577.51 with DIR, representing a substantial numerical increase in lesion-background contrast. The statistically significant difference (p=0.049) provides quantitative support for the premise that white matter suppression can facilitate differentiation of demyelinating lesions from surrounding white matter. This finding is consistent with the diagnostic rationale underlying the use of DIR for MS lesion assessment[18,19].

The importance of lesion-background contrast is also supported by previous research on cortical lesion imaging in MS. Bouman et al. emphasized the continuing difficulty of detecting cortical lesions using MRI, even when imaging findings are evaluated against histopathological evidence[20]. Cortical and juxtacortical lesions can be particularly challenging because their visibility depends not only on their intrinsic signal but also on the signal characteristics of adjacent gray matter, white matter, and cerebrospinal fluid. Against this background, the potential benefit of DIR may arise less from simply increasing lesion signal and more from modifying surrounding tissue signals to enhance relative lesion conspicuity[21]. This interpretation is consistent with the present finding that lesion SNR itself was not significantly different between DIR and T2-FLAIR, whereas lesion–white matter CNR was significantly greater with DIR.

Similar considerations apply to the findings reported by Park et al. regarding the detection of cortical and deep gray matter lesions in MS using DIR and FLAIR at 3 Tesla. The present study supports the underlying rationale for including DIR in advanced MS imaging protocols but also introduces an important qualification: the benefit of DIR appears to depend on the specific tissue contrast being assessed. Gray matter–white matter CNR did not differ significantly between the sequences (p=0.770), nor did lesion–gray matter CNR (p=0.375). Consequently, the significant improvement observed in lesion–white matter contrast should not be generalized to all anatomical contrasts. This parameter-specific interpretation may help explain why previous studies can report advantages of DIR in lesion detection without necessarily demonstrating superiority across every quantitative image-quality measure[22].

The recent systematic review and meta-analysis by Mostardeiro et al. comparing 3D DIR with 3D T2-FLAIR further illustrates the continuing scientific interest in optimizing sequence selection for MS lesion detection. The present findings contribute to this discussion by suggesting that complementary sequence performance may be more clinically meaningful than attempting to identify a single universally superior sequence[23]. T2-FLAIR and DIR operate through different tissue-suppression mechanisms, and those differences can generate distinct advantages depending on the diagnostic objective. Consequently, the decision to include or exclude a particular sequence should consider the type and anatomical location of lesions being investigated rather than relying solely on an overall judgment of image quality[24].

The clinical context of epilepsy adds further relevance to this interpretation. Previous research has identified an association between cortical pathology and epilepsy in patients with MS, while Aly et al. demonstrated the potential value of DIR in the assessment of patients with epilepsy. Cortical and juxtacortical abnormalities may be particularly relevant in patients presenting with seizures because lesions involving cortical networks could contribute to epileptic manifestations[25,26]. Improved visualization of such lesions may therefore provide clinically useful structural information. Nevertheless, the current findings should not be interpreted as demonstrating that DIR can independently identify epileptogenic lesions. The study assessed quantitative MRI image quality and did not correlate imaging findings with electroencephalography, seizure semiology, lesion-specific epileptogenicity, or clinical

outcomes. The higher lesion–white matter CNR observed with DIR therefore indicates improved quantitative contrast rather than proven improvement in epilepsy diagnosis.

The contrasting SNR results can be explained by the different physical principles of T2-FLAIR and DIR. T2-FLAIR is primarily designed to suppress cerebrospinal fluid while maintaining diagnostically useful signals from brain parenchyma. Suppression of cerebrospinal fluid facilitates visualization of T2-hyperintense abnormalities, particularly those adjacent to ventricular and cortical CSF spaces. Because white matter is not intentionally suppressed to the same degree as in DIR, its signal remains relatively strong. This mechanism provides a plausible explanation for the markedly higher white matter SNR observed with T2-FLAIR. Mean white matter SNR was 111.47 with T2-FLAIR compared with only 16.08 with DIR. Importantly, the low white matter SNR on DIR should not automatically be interpreted as poor technical image quality because reduction of white matter signal is an intended consequence of the sequence design.

In contrast, DIR uses two inversion pulses to suppress two tissue signals, typically cerebrospinal fluid and white matter. By substantially reducing the white matter background signal, lesions that retain relatively higher signal intensity can become more distinguishable. This mechanism explains how DIR can demonstrate lower white matter SNR while simultaneously producing higher lesion–white matter CNR. The two findings are therefore complementary rather than contradictory. They also highlight the conceptual distinction between SNR and CNR: SNR reflects the magnitude of tissue signal relative to noise, whereas CNR reflects the ability to differentiate two tissues or a lesion and its surrounding tissue relative to noise. A sequence optimized to suppress a background tissue may therefore perform poorly according to the SNR of that tissue while performing strongly according to lesion-background CNR.

The absence of significant differences in gray matter and lesion SNR deserves similarly cautious interpretation. Gray matter SNR was numerically higher with DIR than with T2-FLAIR (182.71 vs. 156.17), as was lesion SNR (229.78 vs. 170.61), but neither difference reached statistical significance ($p=0.275$ and $p=0.105$, respectively). These numerical differences may indicate potential signal advantages that were not detected statistically in this small sample, but they cannot be considered evidence of DIR superiority. Conversely, non-significant findings should not be interpreted as demonstrating equivalence between the two sequences. With only 10 MRI examinations, the study had limited capacity to detect modest differences, and the absence of confidence intervals and effect-size estimates further limits assessment of the precision and magnitude of these comparisons.

From a theoretical imaging perspective, these results reinforce the concept that MRI image quality is multidimensional. Evaluating sequence performance through a single global measure risks obscuring clinically meaningful differences between signal intensity and tissue contrast. The current findings demonstrate that a sequence providing higher SNR for normal tissue does not necessarily provide the highest contrast between lesions and that tissue. Accordingly, the concept of “superior image quality” should be operationalized according to the diagnostic objective. If the objective is to preserve strong white matter signal, the present data favor T2-FLAIR. If the objective is to maximize quantitative differentiation between MS lesions and white matter, DIR provides the stronger result. This parameter-specific framework offers a more precise interpretation of MRI sequence performance than a simple binary ranking.

These findings also have practical implications for MRI protocol optimization. T2-FLAIR remains important because of its established role in neurological MRI and its strong white matter signal characteristics, whereas DIR may provide complementary information by increasing lesion-to-white matter contrast. Therefore, the results do not support replacing T2-FLAIR with DIR based on the current evidence. Rather, where acquisition time, scanner capability, and clinical circumstances permit, the combined use of 3D T2-FLAIR and 3D DIR may provide a more comprehensive assessment of MS lesions. Such an approach would exploit the relative strengths of each sequence: T2-FLAIR for maintaining white matter signal characteristics and DIR for improving differentiation of lesions from white matter.

For radiographers and radiologists, these findings also emphasize the importance of interpreting quantitative image-quality metrics in relation to sequence design. A low signal measurement is not necessarily synonymous with an inferior image when suppression of that signal is intentional. In DIR, the substantial reduction of white matter signal contributes directly to improved lesion-background contrast. Understanding this relationship can assist imaging professionals in evaluating sequence performance according to its diagnostic purpose rather than relying exclusively on absolute signal intensity. At the institutional level, the present findings provide preliminary quantitative evidence from a 3 Tesla MRI setting at RSUP Dr. Wahidin Sudirohusodo Makassar that may support further evaluation and refinement of brain MRI protocols for demyelinating disease with epileptic manifestations. However, any formal protocol modification should be supported by larger validation studies[27].

Several methodological strengths support the interpretation of these findings. The paired design allowed T2-FLAIR and DIR measurements to be obtained from the same MRI examinations, reducing the influence of between-patient anatomical and pathological variability. The study also assessed image quality quantitatively rather than relying exclusively on subjective visual ratings. Separating SNR measurements across white matter, gray matter, and lesions and evaluating multiple CNR relationships enabled identification of sequence-specific advantages that could have been missed by an overall image-quality score. In particular, this approach demonstrated that the strong white matter SNR of T2-FLAIR and the enhanced lesion–white matter CNR of DIR can coexist within the same examinations.

These strengths should nevertheless be considered alongside several limitations. The most important limitation is the small sample of only 10 MRI examinations, which restricts statistical power and generalizability. The retrospective, single-center design also limits the extent to which the findings can be extrapolated to different patient populations, MRI systems, or acquisition protocols. In addition, the available dataset does not provide standard deviations, confidence intervals, or standardized effect sizes, preventing a more comprehensive assessment of statistical precision and clinical magnitude. Detailed information concerning acquisition parameters, standardized ROI dimensions, observer procedures, and intra- or inter-observer reliability was also unavailable in the study documentation. Furthermore, the study assessed quantitative SNR and CNR rather than diagnostic performance. It did not evaluate lesion counts, lesion volumes, sensitivity, specificity, reader agreement, histopathological confirmation, electroencephalographic correlation, or clinical outcomes. Consequently, higher lesion–white matter CNR should not be equated directly with greater diagnostic accuracy.

Future research should address these limitations through larger prospective and preferably multicenter studies using standardized 3D T2-FLAIR and DIR acquisition protocols. Reporting effect sizes and confidence intervals would clarify the magnitude and precision of

sequence differences, while blinded multi-reader assessment could determine whether quantitative improvements translate into greater lesion conspicuity and diagnostic confidence. Evaluating lesion number, location, and volume and correlating MRI findings with clinical and electroencephalographic characteristics would be particularly valuable in MS patients with epileptic manifestations. Such studies could determine whether the quantitative contrast advantage demonstrated by DIR translates into clinically meaningful improvements in lesion detection and patient assessment.

Overall, the findings indicate that 3D T2-FLAIR and 3D DIR should be viewed as complementary rather than competing sequences in 3 Tesla MRI assessment of MS lesions. T2-FLAIR demonstrated significantly higher white matter SNR, whereas DIR demonstrated significantly greater lesion-to-white matter CNR. The remaining quantitative comparisons did not show statistically significant differences. These results support a tissue- and parameter-specific interpretation of MRI image quality and suggest that combining the two sequences may provide more comprehensive information than relying on either sequence alone, particularly when improved visualization of demyelinating lesions against white matter is clinically important.

CONCLUSIONS

This study demonstrates that 3D T2-FLAIR and 3D Double Inversion Recovery (DIR) provide distinct and complementary quantitative image-quality characteristics in 3 Tesla brain MRI of patients with multiple sclerosis and epileptic manifestations. T2-FLAIR produced significantly higher white matter Signal-to-Noise Ratio (SNR), whereas DIR provided significantly higher lesion-to-white matter Contrast-to-Noise Ratio (CNR). No significant differences were observed for gray matter SNR, lesion SNR, gray matter–white matter CNR, or lesion–gray matter CNR. These findings indicate that neither sequence is universally superior; rather, their relative performance depends on the tissue and image-quality parameter evaluated. The principal contribution of this study is the quantitative demonstration that strong tissue signal and optimal lesion contrast represent different dimensions of MRI image quality. In clinical practice, 3D T2-FLAIR and 3D DIR should therefore be considered complementary sequences. Their combined use may provide more comprehensive information for evaluating demyelinating lesions, particularly when differentiation between MS lesions and surrounding white matter is important. Future studies should validate these findings in larger, prospective, and multicenter samples using standardized acquisition and ROI protocols. Incorporating lesion counts, lesion volumes, inter-reader reliability, diagnostic accuracy, effect sizes, and correlations with clinical and electroencephalographic findings would further clarify whether the quantitative advantages of DIR translate into meaningful improvements in lesion detection and clinical decision-making.

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Conflict of Interest
The authors declare that they have no known financial or non-financial conflicts of interest that could have influenced the conduct, analysis, interpretation, or reporting of this study.

Authors' Contributions
MSR: Conceptualization, methodology, investigation, data collection, formal analysis, and writing—original draft. OG: Methodology, investigation, data curation, and writing—review and editing. AP: Formal analysis, validation, interpretation of results, and writing—review and

editing. WA: Investigation, data curation, visualization, and writing—review and editing. SYF: Conceptualization, supervision, validation, interpretation of findings, and writing—review and editing. All authors reviewed and approved the final version of the manuscript and agreed to be accountable for the work.

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Declaration of Generative AI Use
During the preparation of this manuscript, the authors used ChatGPT (OpenAI) to assist with language editing, improving clarity, academic style, and organization of the manuscript. The tool was not used to generate, modify, or analyze the research data or to make scientific conclusions independently. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, integrity, and final content of the manuscript.

Data Availability Statement
The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available because they contain clinical imaging information and are subject to patient confidentiality and institutional data-protection requirements. Any data sharing will be conducted in accordance with applicable ethical approval, institutional policies, and privacy requirements.

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