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Original Article

Radiology Section

Utility of 3D Double Inversion Recovery Sequence in Paediatric Epilepsy and its Comparison to 3D Fluid Attenuation Inversion Recovery Sequence and T1 Inversion Recovery Sequence: A Cross-sectional Study

AMARNATH CHELLADURAI[1], CHIRTRARASAN PARAMAN[2], SIVAKUMAR KANNAPPAN[3], PRIYA MUTHAIYAN[4], GUHAN RAMASAMY VELAPPAN[5], PRADEEBHA THIYAGARAJAN[6]

ABSTRACT

Introduction: Epilepsy is a disease with predisposition to generate epileptic seizures, associated with neurobiological, cognitive, psychological, and social consequences. Nearly 30% of children undergoing medical treatment for epilepsy become refractive to the treatment. For those children, the ability to find the epileptogenic area is higher with Magnetic Resonance Imaging (MRI) of the brain. The traditional 2D spin-echo sequences used in epilepsy protocol for adults cannot be used alone in paediatric structural neuroimaging. Additional sequences are needed to identify epileptogenic areas due to differences in myelination. Here, present study compared the role of three volumetric sequences 3D-Fluid Attenuated Inversion Recovery (FLAIR) , 3D-T1 weighted Inversion Recovery (T1-IR) and 3D-Double Inversion Recovery (DIR) for paediatric epilepsy, as a part of structural neuroimaging.

Aim: To assess the utility of 3D-DIR in paediatric epilepsy disorders and localisation of epileptogenic foci in brain, congenital malformations of brain and to compare its findings with, 3D-FLAIR and 3D-T1-IR.

Materials and Methods: The present study was a cross-sectional study of 51 children diagnosed with paediatric epilepsy, who were evaluated with MRI brain at Stanley Medical College, Chennai, Tamil Nadu, India, between April 2020 to April 2021 with three sequences, 3D-DIR, 3D-T1-IR and 3D-FLAIR. Lesions of atleast 3 mm in diameter were identified as foci of high signal intensity and counted in each of the three sequences separately and classified according to their location. Then, average signal intensities of the lesions were calculated manually on each of sequences using Region of Interest (ROI) analysis which had a mean size of 3 mm^2. Then the Signal-to-Noise Ratio (SNR), Contrast to-Noise Ratio (CNR), Contrast Ratio (CR), and Asymmetry Signal Ratio (ASR) were calculated.

Results: Evaluation was done on 51 paediatric epilepsy patients and showed the total number of lesions detected (208 lesions) and measured contrast parameters (CR, CNR and ASR) which were found to be significantly higher in 3D-DIR, showed higher detection of the intracortical and white matter lesions than 3D-FLAIR and 3D-T1-IR. SNR was higher in 3D-FLAIR.

Conclusion: Present study concluded that the greatest value of the DIR sequence has a higher ability in detecting epileptogenic foci and congenital malformations of the lesions in comparison with FLAIR and T1-IR.

Keywords: Magnetic resonance imaging, Seizures, Signal intensity

INTRODUCTION

Epilepsy is a disease characterised by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition. Seizures and epilepsy are not the same. Seizure is an event, and epilepsy involves recurrent unprovoked seizures [1]. An epileptic seizure is a transient occurrence of signs and symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is one of the most common severe neurological disorders prevalent in childhood, and more than 50% of seizures have their onset in childhood. The prevalence rate for epilepsy was 6.24/1000 among the Indian paediatric population [2].

The ILAE Task Force (International League Against Epilepsy) has consolidated the aetiologies into six categories, based on which management can be made appropriately. These categories are: 1. structural; 2. genetic; 3. infectious; 4. metabolic; 5. immune; and 6. unknown. More than one of the categories can often be applied to one patient. Neuroimaging may be less effective in generalised epilepsy syndromes like juvenile absence epilepsy and juvenile myoclonic epilepsy, as well as focal epilepsy syndromes like benign rolandic epilepsy, benign occipital epilepsy, and panayiotopoulos syndrome [3]. Nearly 30% of children undergoing medical treatment for epilepsy become refractive to the treatment [4]. For those children, the ability to find the epileptogenic area is higher with Magnetic Resonance Imaging (MRI) of the brain. The traditional 2D spin-echo sequences used in epilepsy protocol for adults cannot be used alone in paediatric structural neuroimaging. Additional sequences are needed to identify epileptogenic areas due to differences in myelination. Present study compared the role of three volumetric sequences 3D-FLAIR, 3D-T1 weighted IR and 3D-DIR for paediatric epilepsy as part of structural neuroimaging. All three sequences are volumetric and acquired with inversion pulses, which selectively nulls the signal received from either tissue or fluid. Volumetric inversion sequences have a longer scan time than traditional spin-echo sequences. T1-IR has better contrast intensity between gray matter and white matter.

3D-FLAIR is T2 based sequence that suppresses the signal from the Cerebrospinal Fluid (CSF). Sone D et al., showed that both left and right-sided temporal lobe epilepsy patients showed significant DIR signal increase in the ipsilateral anterior temporal lobe. Still, FLAIR showed no statistical significance, which could indicate that DIR is more effective than FLAIR in detecting anterior temporal lobe white

matter abnormal signal lesions [5]. 3D-DIR is an MRI pulse sequence that suppresses signals from white matter and CSF; thereby, better delineation of gray matter is possible, which could be attributed to the T1 relaxation times difference among gray matter, white matter and CSF. However, the available literature on this area is sparse.

Hence, the present study aimed to assess the ability of 3D-DIR sequence to identify the epileptogenic foci and congenital malformations in paediatric seizure patients.

MATERIALS AND METHODS

The present study was a cross-sectional study conducted in the Department of Radiodiagnosis at Government Stanley Medical College, Chennai, Tamil Nadu, India. The study was conducted between April 2020 to April 2021. Informed written consent was taken from parents of all the patients enrolled in the study as per the guidance of the ethical committee (DHR Registration number: EC/NEW/INST/2020/461).

Inclusion criteria: The study population included paediatric population less than 13 years of age with epilepsy who have come to department for imaging studies. Children who were clinically diagnosed as paediatric epilepsy and admitted for treatment of paediatric epilepsy without definite cause and had epileptogenic lesions were included in the study.

Exclusion criteria: Patients with contraindications to MRI such as internal cardiac pacemaker, implantable cardiac defibrillator, cochlear and ocular implant, MR incompatible metallic implant, aneurysm and haemostatic clips; claustrophobic patients, previous history of surgery. Those whose guardian have not given consent were excluded from the study.

Sample size calculation: The study group consisted of 51 children diagnosed with paediatric epilepsy as sample size (based on Wong-Kisiel LC et al., conducted a study to DIR MRI in identifying focal cortical dysplasia for paediatric epilepsy in which sensitivity was found to be 88% among paediatric epileptic patients [6].

Image Acquisition

The 3D-DIR, 3D-FLAIR, 3D-T1-IR sequences are coronal 3D acquisition of the whole head utilising body transmit and local signal reception with the dedicated 16-channel head coil. All imaging was performed on a 1.5-T clinical whole-body system (Siemens Amira, Siemens Medical Solutions, Erlangen, Germany). The DIR sequences acquired as a modification to a 3D-T2 weighted acquisition (sampling perfection with application optimised contrasts using different flip angle evolution) permitting for flexibility in k-space sampling strategy, echo trains and flip angle evolution schemes, as well as two separate inversion times in a DIR operation block. The sequences are acquired with parameters as given in [Table/Fig-1].

Parameters	3D-DIR	3D-FLAIR	3D-T1-IR
Repetition time (ms)	7500	12000	3550
Echo time (ms)	308	140	15
Inversion time (ms)	3000/450	2850	400
Slice thickness (mm)	1.5	4	3
Field of view (mm)	190	200	180
Matrix	256	256	256
Band width (Hz/Pixel)	698	592	698
Echo spacing (ms)	3.2	3.72	3.84
Echo train length (ms)	784	755	837
Voxel size (mm)	1.5×1.5×1.5	1×1×1	1×1×1
Parallel acceleration	GRAPPA	GRAPPA	GRAPPA
Parallel acceleration factor (iPAT)	2	2	2
Acquiring time (mins)	5.47	5.42	5.58

[Table/Fig-1]: MRI sequence parameters used in the study.
GRAPPA: GeneRalized autocalibrating partially parallel acquisitions; iPAT: Integrated parallel acquisition techniques

Image Interpretation

Lesions of atleast 3 mm in diameter were identified as foci of high signal intensity and counted in each of the three sequences separately and classified according to their location into infratentorial lesions, periventricular white matter lesions, deep white matter lesions, juxtacortical white matter lesions and intracortical lesions [7]. Then, average signal intensities of the lesions were calculated manually on the coronal DIR, FLAIR, and T1-IR images using the ROI analysis which had a mean size of 3 mm^2. The contralateral side of each lesion was further divided for comparison, and the average intensity was measured. The SNR,CNR,CR and ASR were then calculated. The signal intensities were also determined in Normal Appearing Gray Matter (NAGM) and Normal Appearing White Matter (NAWM) to calculate the Gray Matter and White Matter differentiation (GM/WM).

$SNR=SI1/SD_{no}$

$CNR=(SI1-SI2)/SD_{no}$

$CR=(SI1-SI2)/SI2$

$AI=(SI1-SI2)/(SI1+SI2)$

GM/WM differentiation=S-NAGM/S-NAWM

Here, SI1 is the signal intensity of lesion, SI2 is the signal intensity of NAGM/gray matter correspondingly on the contralateral side, SD_{no} is the Standard deviation of the noise acquired, S-NAGM is signal intensity of normal appearing gray matter, and S-NAWM is signal intensity of the normal appearing white matter [8].

STATISTICAL ANALYSIS

The collected data was analysed with International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 23.0. (Armonk, NY: IBM Corp). Descriptive statistics frequency analysis and percentage analysis were used for number of lesions identified. Furthermore, to find the significant difference between the bivariate samples in paired groups, the Wilcoxon's Signed-rank test was used. In all the above statistical tools, the p-value <0.05 was considered a significant level.

RESULTS

The number of lesions identified in 3D-DIR, 3D-T1-IR and 3D-FLAIR are summarised in [Table/Fig-2]. Relative ratio was also calculated for mean lesion load as given in [Table/Fig-3]. 3D-DIR sequences significantly detected more mean lesion load compared to 3D-FLAIR and 3D-T1-IR. In the multivariate analysis for repeated measures of SNR, CNR, CR, ASR and GM-WM differentiation, the Friedman test and the Repeated measures of ANOVA was used with Bonferroni correction to control the type I error on multiple comparisons and results were summarised in [Table/Fig-4]. Decreased SNR in the DIR technique compared to 3D-FLAIR, as well as inhomogeneity of the magnetic field in the limbic lobe cortex and diminished inhomogeneity in the central sulcus cortex, as seen in [Table/Fig-5]. Quantitative assessment of the detected lesions with help of CNR, CR, and ASR was done on all three sequences. CNR, CR and ASR were higher in 3D-DIR than 3D-T1-IR and 3D-FLAIR. This reflects the higher capability of the 3D-DIR sequence in lesion detectability over the 3D-FLAIR and 3D-DIR sequences as seen in [Table/Fig-6,7].

Region under analysis	3D-FLAIR	3D-T1-IR	3D-DIR
Number of intracortical lesions	51	63	83
Number of infratentorial lesions	14	14	17
Number of periventricular lesions	12	9	18
Number of juxtacortical lesions	44	51	66
Number of deep white matter lesions	15	21	24
Total number of lesions detected	136	158	208

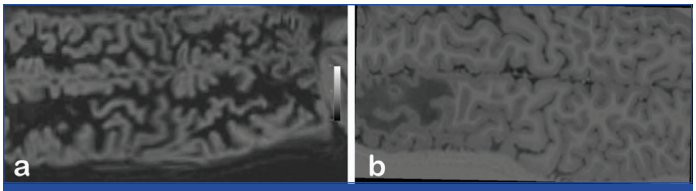
[Table/Fig-2]: Number of lesions recognised in each sequence.

Mean lesion load measurement (mean±SD)				Relative ratio			p-value (Wilcoxon's Signed-rank test)		
Region	3D-FLAIR	3D-T1-IR	3D-DIR	DIR over FLAIR	DIR over T1-IR	T1-IR over FLAIR	DIR over FLAIR	DIR over T1-IR	T1-IR over FLAIR
Intracortical lesions	1±0.82	1.235±0.97	1.62±1.48	162.7	131.7	123.5	0.003	0.0004	0.011
Infratentorial lesions	0.274±0.75	0.274±0.75	0.333±0.765	121.4	121.4	100.0	0.003	0.0004	0.011
Periventricular lesions	0.235±0.586	0.176±0.623	0.353±0.913	150.0	200.0	75.0	0.380	0.083	0.014
Juxtacortical lesions	0.863±1.06	1±1.549	1.29±1.9	150.0	129.4	115.9	0.186	0.007	0.007
Deep white matter lesions	0.294±0.729	0.412±1.004	0.471±1.172	160.0	114.3	140.0	0.014	0.024	0.083
Average valuesdetected in study	2.67±1.70	3.1±2.5	4±3.9	153	132	162	0.0005	0.0005	0.0005

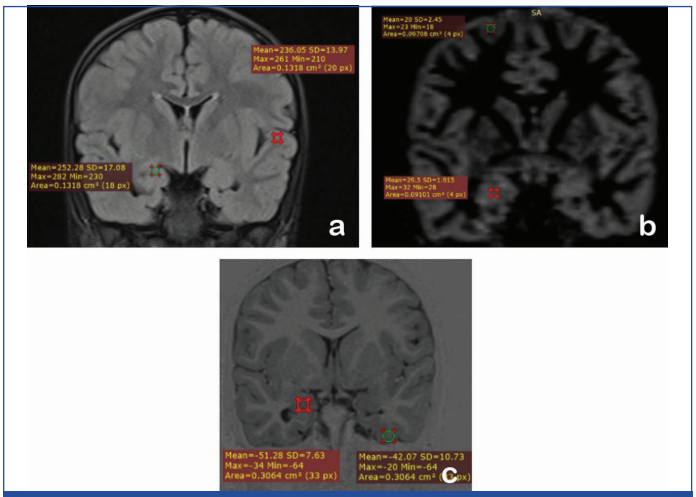
[Table/Fig-3]: Mean lesion load measurement based on number of lesions detected on each of the sequences and relative comparisons among the sequences with their p-value.

Parameters	Mean±SD			p-value		
	3D-FLAIR	3DT1-IR	3D-DIR	DIR over Flair	DIR over T1-IR	T1-IR over Flair
SNR	95±38	46±39	72±62	0.034	0.0005	0.0005
CNR	23±41	28±31	53±49	0.007	0.0005	0.0005
Contrast ratio	1.5±3.5	1.6±1.1	3.1±2	0.036	0.0005	1.000
Asymmentry signal ratio	0.15±0.38	0.37±0.3	0.55±0.16	0.0005	0.0005	0.16
GM-WM differentiation	1.67±2.58	1.9±0.98	2.34±1.14	0.016	0.09	0.97

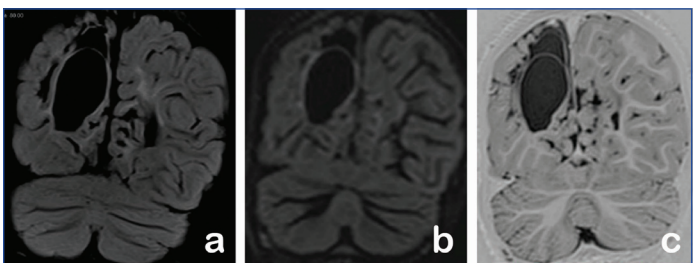
[Table/Fig-4]: Image contrast measurements in 3D-FLAIR, 3D-T1-IR and 3D-DIR with their p-values based on Friedman test and the repeated measures of ANOVA.



[Table/Fig-5]: Shows assessment of lesion using curved reformation on 3D-FLAIR (a) and 3D-DIR (b).



[Table/Fig-6]: Shows measurement of signal intensity in lesion (SI1) and normal appearing gray matter (SI2) on 3D-FLAIR (a), 3D-DIR (b) and 3-T1-IR (c).



[Table/Fig-7]: Shows assessment of hypoxic ischaemic encephalopathy on 3D-FLAIR (a), 3D-DIR (b) and 3D-T1-IR (c).

DISCUSSION

In the present study, about 51 paediatric epilepsy examination are done with MRI inversion recovery sequences. Around 37% were between 1-5 years and about 47% are between 6-10 years. The number of lesions is detected with each of the three sequences and made a comparison among them. On visual assessment, it was noted that the lesions were predominantly hyperintense on 3D-DIR and 3D-FLAIR, while those lesions are seen as hypointense on 3D-T1-IR. Also, most of the lesions are better visualised on 3D-DIR than 3D-FLAIR and 3D-T1-IR. 3D-DIR sequences detected more overall load of lesions compared to 3D-FLAIR and 3D-T1-IR, which was consistent with previous study result of Cotton F et al., [9]. DIR sequences also revealed statistically significant number of lesions in intracortical region and juxtacortical region than 3D-FLAIR and 3D-T1-IR as seen in [Table/Fig-3], which was consistent with previous study done by Moraal B et al., [10]. This can be emphasised that, the greater benefit of DIR sequence in the detection of intracortical lesions compared to the 3D-FLAIR and 3D-T1-IR sequences, in turn is explained by the better contrast between gray matter and white matter in background of good Cerebrospinal Fluid (CSF) suppression. Also, with 3D-DIR imaging, entire white matter and CSF signals are completely suppressed, leading to better delineation of the lesions. This high-image contrast measurement in the DIR sequence led to detection of higher number of lesions as compared to 3D-FLAIR and 3D-T1-IR. In some individuals, the interference of enhanced gray matter signals with the high signal of lesions may render lesions less visible on DIR; CSF nulling on DIR pictures is less uniform in some patients than on FLAIR images. CSF nulling, on the other hand, was suitable on DIR images. Flow artefacts have been detected in the posterior fossa, choroid plexus, periventricular white matter, and periaqueductal, brainstem tissue in previous research study by Turetschek K et al., [11], which could be caused by CSF pulsation or by sinuses and larger veins. In extracortical regions, certain other two-sided high-signal ribbon-like artefacts in the phase direction were frequently found, and their appearance changed in continuous sections.

The mean value of SNR obtained on 3D-DIR was not statistically higher, when compared to the SNR values obtained from 3D-FLAIR and 3D-T1-IR. The mean value of SNR obtained was significantly higher in 3D-FLAIR than the 3D-DIR and 3D-T1-IR. The above data can conclude that, the SNR value was higher in 3D-FLAIR than 3D-T1 IR and 3D-DIR. Low SNR in 3D-DIR can also be attributed to the increased CSF pulsation artefacts in 3D-DIR.

Lee JK et al., T1-IR provided better tissue contrast of lesions even with very shorter scan time. Also, the enhanced contrast and clarity of the gray matter and white matter interfaces seen on the T1-IR images helps in the evaluation of cortical dysplasias and migrational abnormalities, particularly as it applies to the screening of epilepsy patients [12]. Present study also confirms the observations of Lee JK et al., confirming the increased contrast intensity of T1 inversion recovery than FLAIR. The gray matter white matter difference among the sequences was found to have a higher mean value in 3D-DIR than the other two sequences, namely 3D-FLAIR and 3D-T1-IR. Elnekeidy AM et al., showed that DIR exhibited improved separation between the white matter, grey matter, and lesions due to high-image contrast [7]. No such significance could be established in present study. This can be attributed to the variation among the age

group examined in both studies. Also, 3D-T1-IR has more mean quantification of gray matter and whote matter ratio difference than 3D-FLAIR. DIR sequences also revealed statistically significant number of lesions in intracortical region and juxtacortical region than 3D-FLAIR and 3D-T1-IR , which was consistent with the previous study by Moraal B et al., [10].

Limitation(s)

First, present study included only 51 patients; this number could have resulted in minor differences between sequences, especially with different brain lesions. Secondly, authors did not assess their signal intensity on postcontrast lesions. Finally, authors did not assess the size of the lesions. Hence, more studies should be undertaken to evaluate the complete comparison among sequences.

CONCLUSION(S)

In present study, evaluation was done on 51 children diagnosed with epilepsy. The total number of lesions detected, CNR, CR and ASR was higher in 3D-DIR than 3D-FLAIR and 3D-T1-IR. Present study concluded that the most outstanding value of the DIR sequence was its higher ability in detecting multiple characteristics of the lesions in one sequence. Also, it should be clear that every MRI sequence has its importance, and the DIR isn't meant to replace any of them; rather, it's meant to supplement them for the patient's benefit.

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PARTICULARS OF CONTRIBUTORS:

1. Professor and Head, Department of Radiodiagnosis, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India.
2. Professor, Department of Radiodiagnosis, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India.
3. Assistant Professor, Department of Radiodiagnosis, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India.
4. Assistant Professor, Department of Radiodiagnosis, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India.
5. Junior Resident, Department of Radiodiagnosis, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India.
6. Senior Resident, Department of Radiodiagnosis, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Priya Muthaiyan,
Assistant Professor, Department of Radiodiagnosis, Government Stanley Medical College, Old Jail Raod, Old Washermanpet, Chennai, Tamil Nadu, India.
E-mail: dr3priya@yahoo.com

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