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Diagnostic Accuracy of Contrast-Enhanced Fluid-Attenuated Inversion Recovery (Flair) Images in Various Intracranial Pathologies.

Akshay Patel[1]*, Anil Rathva[2], Deepak Bhimani[3], Dharmesh Baria[4].

[1]*Postgraduate Resident (R3), Department of Radiodiagnosis, Parul Sevashram Hospital, Parul Institute of Medical Sciences and Research, Vadodara, Gujarat, India.*

[2]*Professor and Head, Department of Radiodiagnosis, Parul Sevashram Hospital, Parul Institute of Medical Sciences and Research, Vadodara, Gujarat, India.*

[3]*Associate Professor, Department of Radiodiagnosis, Parul Sevashram Hospital, Parul Institute of Medical Sciences and Research, Vadodara, Gujarat, India.*

[4]*Associate Professor, Department of Radiodiagnosis, Parul Sevashram Hospital, Parul Institute of Medical Sciences and Research, Vadodara, Gujarat, India.*

Correspondence:
Dr. Akshay Patel.
Department of Radiodiagnosis Parul Sevashram Hospital Parul Institute of Medical Sciences and Research Vadodara, Gujarat, India.

Email:
akshaynpatel780@gmail.com

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Abstract

Background: Intracranial pathologies including meningitis, leptomeningeal carcinomatosis, primary and secondary brain tumours, and inflammatory disorders require prompt and accurate neuroimaging diagnosis. Conventional contrast-enhanced T1-weighted imaging (CE-T1WI) is the standard post-contrast sequence; however, subtle leptomeningeal and sulcal abnormalities may be obscured by normal vascular enhancement. Contrast-enhanced fluid-attenuated inversion recovery (CE-FLAIR) suppresses cerebrospinal fluid and vascular signals, potentially improving lesion conspicuity. This prospective observational analytical study was conducted in the Department of Radiodiagnosis, Parul Sevashram Hospital, over one year. Ninety-two consecutive patients with suspected or confirmed intracranial pathology who underwent contrast-enhanced MRI brain with both CE-T1WI and CE-FLAIR sequences were enrolled. Enhancement detection, lesion conspicuity, and diagnostic accuracy were compared between sequences. The mean age was 48.02 ± 21.20 years with a male-to-female ratio of 1:0.80. Pathologies included primary tumours (35.87%), infective/inflammatory conditions (32.61%), metastases (23.91%), and miscellaneous lesions (7.61%). CE-FLAIR demonstrated superior lesion conspicuity in 54 cases (58.70%), while CE-T1WI was superior in 17 cases (18.48%), with equivalent conspicuity in 21 cases (22.83%) ($p<0.001$). CE-FLAIR superiority was most pronounced in infective/inflammatory pathologies (86.67%). Overall weighted sensitivity was 87.5% for CE-FLAIR versus 81.2% for CE-T1WI, with diagnostic accuracies of 87.7% and 83.6%, respectively. CE-FLAIR demonstrated significantly superior diagnostic performance for detecting abnormal enhancement in intracranial pathologies, particularly for meningeal and leptomeningeal diseases. CE-FLAIR should be incorporated as an essential adjunct sequence in contrast-enhanced brain MRI protocols.

Keywords: Contrast-enhanced FLAIR; magnetic resonance imaging; intracranial pathologies; diagnostic accuracy; meningitis.

INTRODUCTION

Neurological disorders represent one of the most pressing challenges in global public health. According to the World Health Organization and Global Burden of Disease estimates, more than 3 billion people worldwide are currently living with some form of neurological condition.[1] The burden falls most heavily on low- and middle-income countries, where delayed diagnosis, restricted access to advanced neuroimaging, and inadequate specialist services contribute to avoidable mortality and long-term neurological sequelae.[1]

Within this clinical spectrum, intracranial pathologies including meningitis, leptomeningeal carcinomatosis, primary and secondary central nervous system tumours, and inflammatory and demyelinating disorders demand rapid, accurate, and non-invasive diagnostic evaluation. Meningitis remains one of the most urgent neurological emergencies, with approximately 2.5 million cases reported annually globally.[2,3] Bacterial meningitis carries significant mortality, while survivors frequently suffer irreversible complications including sensorineural hearing loss, cognitive impairment, and seizures.[2] The burden of primary and secondary intracranial tumours demands highly precise neuroimaging for initial diagnosis and post-surgical surveillance.

Magnetic resonance imaging (MRI) has established itself as the principal non-invasive modality for evaluating intracranial disease, owing to its superior soft-tissue contrast and sensitivity to blood-brain barrier disruption. Conventional contrast-enhanced T1-weighted imaging (CE-T1WI) has traditionally served as the standard post-contrast sequence; gadolinium-based contrast agents shorten T1 relaxation time, producing conspicuous signal enhancement in regions of abnormal vascular permeability.[4,5]However, despite its widespread utility, CE-T1WI possesses inherent limitations. The intrinsic hyperintense signal generated by normal slow-flowing vascular structures, prominent enhancement of dural venous sinuses, and hyperintensity of orbital and subcutaneous fat can collectively obscure minute, early-stage leptomeningeal or subarachnoid lesions.[6]

The fluid-attenuated inversion recovery (FLAIR) sequence was developed to address limitations associated with conventional imaging. FLAIR is a specialized inversion recovery pulse sequence that suppresses free cerebrospinal fluid (CSF) signal while maintaining sensitivity to pathological tissue changes.[7] Contrast-enhanced FLAIR (CE-FLAIR) combines these properties with gadolinium administration, offering potential advantages for detecting subtle meningeal enhancement. The FLAIR sequence is significantly more sensitive to ultra-low concentrations of gadolinium than conventional T1WI.[8]

Contemporary studies report very high sensitivity for CE-FLAIR-based sequences in detecting leptomeningeal metastasis, often exceeding that of conventional 2D CE-T1WI.9,12 CE-FLAIR has demonstrated outstanding sensitivity (96%) for detecting abnormal meningeal enhancement compared to CE-T1WI (68%).[9]

Despite growing evidence, CE-FLAIR remains inconsistently incorporated into routine MRI protocols because of concerns regarding scan time, workflow efficiency, and institutional practice variation. Therefore, the present study was undertaken to systematically evaluate the diagnostic accuracy of CE-FLAIR across heterogeneous intracranial pathologies and to compare its performance with conventional CE-T1WI.

Aim

To evaluate the diagnostic utility of contrast-enhanced fluid-attenuated inversion recovery magnetic resonance imaging in detecting and characterizing abnormal enhancement in patients with intracranial pathologies, and to compare its diagnostic contribution with conventional contrast-enhanced T1-weighted imaging.

MATERIALS AND METHODS

Study Design and Setting

This prospective, hospital-based, observational analytical study was conducted in the Department of Radiodiagnosis, Parul Sevashram Hospital, Parul Institute of Medical Sciences and Research, Limda, Vadodara, Gujarat, India. The study was conducted for one year from the date of approval by the Institutional Ethics Committee.

Ethical Considerations

The study was carried out with approval from the Institutional Ethics Committee (IEC Reference Number: ECR/702/Inst/GJ/2015/RR-21/8407. All participants or their legally accepted representatives provided written informed consent prior to enrolment and imaging. Patients were educated about the purpose of the study, the imaging procedure, use of contrast agents, associated risks, and their right to withdraw without affecting their treatment. Patient confidentiality was maintained throughout the study, with personal data anonymised during entry and analysis. Imaging data were used solely for academic and research purposes.

Sample Size

The expected patient load was estimated at approximately six eligible cases per month. Over the planned 12-month enrolment period, the finite study population was estimated to be 72 patients. The initial sample size was calculated using the standard formula for estimating a proportion (Z=1.96 for 95% confidence interval, P=0.50, margin of error=0.10), yielding approximately 96. After finite population correction, the minimum adjusted sample size was 41 patients. Ninety-two eligible patients were consecutively recruited during the study period.

Sampling Technique

A consecutive sampling technique was employed. All patients undergoing contrast-enhanced MRI brain for suspected or established intracranial pathology during the study period were screened for eligibility.

Eligibility Criteria

Inclusion Criteria: Patients of any eligible age and sex with suspected or established intracranial pathology who underwent MRI brain with gadolinium-based contrast administration, including post-contrast T1-weighted and post-contrast FLAIR sequences.

Exclusion Criteria: 1. Known renal failure or impaired renal function precluding safe administration of gadolinium-based contrast agent 2. Claustrophobia preventing completion of MRI examination 3. Any contraindication to MRI, including non-MRI-compatible metallic implants, pacemakers, cochlear implants, intracranial aneurysm clips of uncertain compatibility, or other unsafe ferromagnetic devices 4. Known history of hypersensitivity or allergy to gadolinium-based contrast agents 5. Incomplete MRI examination or technically inadequate image quality preventing reliable interpretation

MRI Technique and Imaging Protocol

All MRI examinations were performed using a 1.5 Tesla MRI scanner (GE Healthcare, Chicago, Illinois, USA) according to the institutional brain MRI protocol for contrast-enhanced intracranial evaluation. The routine MRI protocol included: T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery imaging, diffusion-weighted imaging, apparent diffusion coefficient mapping, susceptibility-weighted imaging, post-contrast T1-weighted imaging, and post-contrast FLAIR imaging.

Gadolinium-based contrast was administered intravenously according to standard institutional practice after confirming eligibility for contrast administration. Post-contrast T1-weighted imaging and post-contrast FLAIR imaging were acquired after contrast injection. The sequence order and timing were kept as consistent as practically feasible within routine clinical workflow.

Image Interpretation and Assessment Parameters

CE-FLAIR and CE-T1WI images were systematically evaluated for the following parameters: 1. Presence or absence of abnormal enhancement 2. Anatomical location of enhancement 3. Pattern of enhancement (linear, nodular, leptomeningeal, pachymeningeal, ring, solid, rim-like, ependymal, cranial nerve, or mixed) 4. Lesion conspicuity on CE-FLAIR compared with CE-T1WI 5. Visibility of meningeal or sulcal enhancement 6. Differentiation between pathological enhancement and vascular enhancement 7. Additional diagnostic contribution of CE-FLAIR over CE-T1WI

For comparison, enhancement on CE-FLAIR was categorized as superior to, equivalent to, or inferior to CE-T1WI, depending on lesion conspicuity and diagnostic clarity.

Reference Standard

Final diagnostic impression was made with the combination of MRI findings, clinical information, laboratory tests, CSF findings, follow-up imaging, operative findings, histopathologic findings, and/or final clinical diagnosis, wherever available.

Statistical Analysis

Data were entered into a structured database and checked for completeness and consistency before analysis. Statistical analysis was performed using SPSS version 30.0. Continuous variables were expressed as mean ± standard deviation when normally distributed and as median with interquartile range when non-normally distributed. Categorical variables were summarized as frequencies and percentages.

Comparisons of age between different pathology categories were made using one-way analysis of variance (ANOVA). Categorical variables were compared using chi-square test or Fisher's exact test as appropriate. For paired categorical comparisons between CE-FLAIR and CE-T1WI, McNemar's test was applied. Diagnostic performance indices including sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. A p-value of <0.05 was considered statistically significant.

RESULTS

Study Population

During the study period, 92 patients were consecutively enrolled. Complete MRI brain evaluation was conducted in all patients using the institutional brain MRI protocol.

Demographic Characteristics

The mean age of participants was 48.02 ± 21.20 years, with ages ranging from 1 month to 85 years. The median age was 52.50 years (IQR: 30.00–61.25 years). The age group with the highest proportion of patients was 46–60 years (29.35%),

followed by 61–75 years (20.65%). Males accounted for 55.43% (n=51) and females 44.57% (n=41), with a male-to-female ratio of 1:0.80 (Table 1).

Table 1: Demographic Characteristics of Study Population (N=92)

Variable	Frequency	Percentage (%)
Age (years)		
0–15	6	6.52
16–30	18	19.57
31–45	13	14.13
46–60	27	29.35
61–75	19	20.65
76–90	9	9.78
Mean ± SD	48.02 ± 21.20 years	
Median (IQR)	52.50 (30.00–61.25) years	
Range	0.08–85.00 years	
Gender		
Male	51	55.43
Female	41	44.57
Male:Female Ratio	1:0.80	

Distribution of Intracranial Pathologies

The pathology spectrum was heterogeneous and representative of intracranial diseases encountered in a tertiary care setting. Primary tumours constituted the largest category (35.87%, n=33), followed by infective/inflammatory pathologies (32.61%, n=30), metastatic lesions (23.91%, n=22), and other miscellaneous conditions (7.61%, n=7) (Table 2).

Table 2: Distribution of Intracranial Pathologies by Major Category (N=92)

Pathology Category	Frequency	Percentage (%)
Primary Tumours	33	35.87
Infective/Inflammatory	30	32.61
Metastasis	22	23.91
Others/Miscellaneous	7	7.61
TOTAL	**92**	**100.00**

Parenchymal metastasis was the most common single diagnosis (21.74%), followed by meningioma (13.04%), tuberculoma/TB meningitis (11.96%), pituitary adenoma (8.70%), and glioma (8.70%).

Statistical analysis revealed significant differences in age distribution across pathology categories ($p<0.001$). Patients with metastatic disease were significantly older (mean age 61.50 ± 10.26 years) compared to those with infective/inflammatory conditions (mean age 34.64 ± 19.46 years). No statistically significant association was observed between gender and pathology category ($p=0.659$).

Overall Enhancement Comparison: CE-FLAIR versus CE-T1WI

In the overall assessment of lesion conspicuity, CE-FLAIR demonstrated superior enhancement detection in 54 cases (58.70%), while CE-T1WI was superior in only 17 cases (18.48%). Enhancement was considered equivalent on both sequences in 21 cases (22.83%). The binomial test comparing discordant pairs yielded a highly significant p-value (<0.001), confirming that CE-FLAIR provides significantly superior lesion conspicuity overall (Table 3).

Table 3: Overall Comparison of Lesion Conspicuity: CE-FLAIR vs CE-T1WI (N=92)

Enhancement Comparison	Frequency	Percentage (%)
CE-FLAIR Superior	54	58.70
Equivalent	21	22.83
CE-T1WI Superior	17	18.48
TOTAL	**92**	**100.00**

Statistical Analysis: Binomial Test (McNemar-like): $p<0.001$

Enhancement Comparison by Pathology Category

There was a highly significant association between pathology category and imaging sequence superiority ($p<0.001$). CE-FLAIR demonstrated marked superiority in infective/inflammatory pathologies (86.67%) and other/miscellaneous conditions (85.71%), while CE-T1WI was superior in nearly half of metastatic cases (45.5%). In primary tumours, CE-FLAIR was superior in 42.4%, equivalent in 36.4%, and CE-T1WI was superior in 21.2% of cases.

Among infective/inflammatory pathologies (n=30), CE-FLAIR showed superior conspicuity in 26 cases (86.67%), with equivalent conspicuity in 4 cases (13.33%). CE-T1WI was not superior in any infective/inflammatory case.

Diagnostic Accuracy Analysis

In the category of infective/inflammatory pathologies, CE-FLAIR showed the highest sensitivity (95.0%), significantly higher than CE-T1WI (68.0%). The overall diagnostic accuracy for CE-FLAIR in this category was 91.5% compared to 76.5% for CE-T1WI.

In cases of primary tumors, the sensitivity of CE-T1WI was slightly higher (90.0% vs 85.0%). Similarly, for parenchymal metastases, CE-T1WI showed slightly superior performance (88.0% sensitivity versus 82.0% for CE-FLAIR).

The overall weighted sensitivity of CE-FLAIR was 87.5% compared to 81.2% for CE-T1WI. The overall weighted specificity was 87.8% for CE-FLAIR and 86.1% for CE-T1WI. Overall weighted diagnostic accuracies were 87.7% for CE-FLAIR and 83.6% for CE-T1WI (Table 4).

Table 4: Diagnostic Accuracy of CE-FLAIR vs CE-T1WI by Pathology Category

Pathology Category	Sequence	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Infective/Inflammatory	CE-FLAIR	95.0	88.0	90.5	93.6	91.5
	CE-T1WI	68.0	85.0	81.0	73.9	76.5
Primary Tumours	CE-FLAIR	85.0	90.0	89.5	85.7	87.5
	CE-T1WI	90.0	88.0	88.2	89.8	89.0
Metastasis	CE-FLAIR	82.0	85.0	84.5	82.7	83.5
	CE-T1WI	88.0	85.0	85.4	87.8	86.5
Others	CE-FLAIR	85.0	85.0	85.0	85.0	85.0
	CE-T1WI	75.0	85.0	83.3	77.3	80.0
Overall Weighted	**CE-FLAIR**	**87.5**	**87.8**	**87.7**	**87.6**	**87.7**
	CE-T1WI	**81.2**	**86.1**	**85.4**	**82.1**	**83.6**

PPV = Positive Predictive Value; NPV = Negative Predictive Value

Normal Enhancement Patterns on CE-FLAIR

CE-FLAIR demonstrated effective suppression of normal vascular enhancement (cortical veins, dural sinuses), which significantly improved the conspicuity of subtle pathological enhancement in the subarachnoid space and along meningeal surfaces. Normal structures lacking a blood-brain barrier (pineal gland, pituitary stalk, choroid plexus) showed expected mild enhancement on CE-FLAIR.

DISCUSSION

The principal finding of this study is that CE-FLAIR provides significantly superior lesion conspicuity compared to CE-T1WI in the evaluation of intracranial pathologies, with overall superiority in 58.70% of cases. This superiority was most pronounced in infective/inflammatory conditions (86.67%), where CE-FLAIR demonstrated a sensitivity of 95.0% compared to 68.0% for CE-T1WI.

The heterogeneous pathology spectrum in this cohort, comprising primary tumors, infective/inflammatory lesions, metastatic disease, and miscellaneous conditions, reflects the clinical reality of tertiary-care neuroradiology practice. The relatively high proportion of tuberculosis-related CNS disease is particularly significant in the Indian context, where CNS tuberculosis remains an important differential diagnosis.[10]

The marked superiority of CE-FLAIR in detecting infective/inflammatory pathologies aligns with published literature. Vaswani et al. reported CE-FLAIR sensitivity of 96% for meningitis detection compared to 68% for CE-T1WI.[9] The

physical basis for this advantage lies in CE-FLAIR's ability to suppress normal CSF and vascular signals, thereby eliminating the "anatomical noise" that frequently obscures early meningitis or linear leptomeningeal metastasis on CE-T1WI.

In infectious meningitic disease, missing subtle enhancement has asymmetric clinical consequences because diagnostic delay may materially worsen neurologic outcome. Epidemiological data indicates that a delay of merely 4 to 6 hours in antibiotic administration following clinical presentation independently confers an 8.4-fold increased risk of mortality.24 Therefore, even moderate increases in sensitivity in this subgroup carry substantial clinical relevance.[9]

Conversely, CE-T1WI retained advantages in solid intra-axial tumors and parenchymal metastases. This observation is consistent with the known T2-shortening effects of concentrated gadolinium; densely enhancing solid tumours may show reduced FLAIR signal intensity due to T2 shortening.[8,9] For surgical or radiosurgical planning of parenchymal metastasis, lesion-bulk definition on CE-T1WI retains greater procedural importance.

Contemporary neuroimaging literature supports the complementary rather than competitive nature of these sequences. Recent technical studies demonstrate excellent results for detecting parenchymal metastases with CE-T1WI, while multiparametric approaches incorporating CE-FLAIR show superior performance for meningeal and inflammatory disease.[11,12] The present findings support pathology-weighted sequence prioritization rather than indiscriminate sequence replacement.

The documentation of normal CE-FLAIR enhancement patterns (pineal gland, pituitary stalk, choroid plexus) and suppression of cortical veins and dural sinuses is clinically important for avoiding false-positive interpretation. This knowledge enhances the translational usability of CE-FLAIR for routine reporting.

Strengths and Limitations

The methodological strengths of this study include its prospective design, consecutive patient enrollment, broad and clinically realistic pathology spectrum, paired within-patient comparison, and thoughtful subgroup analyses. Sequence performance was interpreted not only globally but also by pathology category, lesion location, and enhancement pattern.

However, several limitations warrant acknowledgment. The overall sample size was moderate, and several disease subclasses were small; therefore, subgroup percentages may appear striking but remain statistically fragile. The study was single-center, limiting geographic and equipment-related generalizability. The present data were generated on a 1.5-T platform; applicability to 3-T systems or advanced post-processing environments should be inferred cautiously. Quantitative lesion-to-background contrast metrics, interobserver reliability statistics, and standardized blinded reader performance were not available.

Clinical Implications

The clinical implications favor consideration of CE-FLAIR as a routine adjunct sequence when inflammatory disease of the meninges, sulci, cisterns, leptomeninges, or superficial brain layers is clinically suspected. This includes patients with probable meningitis, tuberculous meningitis, encephalitic meningeal involvement, leptomeningeal carcinomatosis, and selected extra-axial tumours. CE-FLAIR should be considered not as an optional redundant add-on but as a sequence with well-defined high-yield indications. Combining CE-FLAIR and CE-T1WI provides more comprehensive enhancement characterization than either sequence alone.

CONCLUSION

This prospective study demonstrates that contrast-enhanced FLAIR MRI provides substantial diagnostic value in the evaluation of intracranial pathologies and serves as an important adjunct to conventional contrast-enhanced T1-weighted imaging. CE-FLAIR showed superior lesion conspicuity in 58.70% of cases, with overwhelming superiority in infective/inflammatory pathologies (86.67%). The overall weighted diagnostic accuracy for CE-FLAIR (87.7%) exceeded that of CE-T1WI (83.6%). CE-FLAIR excels in detecting meningeal, sulcal, cisternal, and leptomeningeal abnormalities, while CE-T1WI remains essential for solid parenchymal lesions with strong enhancement. The two sequences complement each other in their diagnostic value, and both together provide better characterization of intracranial enhancement than either sequence alone. CE-FLAIR should be incorporated as a standard adjunct sequence in contrast-enhanced brain MRI protocols, particularly in tertiary care centers where intracranial infections, inflammatory, neoplastic, and metastatic diseases are frequently encountered.

DECLARATIONS

Ethics Approval: This study was approved by the Institutional Ethics Committee, Parul Institute of Medical Sciences and **Research (Reference Number:** [ECR/702/Inst/GJ/2015/RR-21/8407]).

Informed Consent: Written informed consent was obtained from all participants or their legally accepted representatives prior to enrolment.

Conflict of Interest: The authors declare no conflicts of interest.

Author Contributions: - Akshay Patel: Conceptualization, methodology, data collection, data analysis, writing – original draft, writing – review and editing - Anil Rathva: Supervision, conceptualization, methodology, writing – review and editing - Deepak Bhimani: Supervision, methodology, writing – review and editing - Vaibhav Gadara: Data collection, writing – review and editing

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