

Diagnostic Utility of Contrast-Enhanced Fluid-Attenuated Inversion Recovery Magnetic Resonance Imaging in Intracranial Pathologies: Qualitative and Quantitative Analyses

MARWAN M. EL-TOUKHY, M.D.*; MONA M. FATOUH, M.D.*; MOHAMMED F. ALSAWY, M.D.** and NERMEEN M. EL GARHY, M.D.*

The Departments of Radiology and Neurosurgery**, Faculty of Medicine, Cairo University*

Abstract

Background: Intravenous MR contrast compounds are utilized to improve lesion identification and characterize disorders of the central nervous system. Our study is designed to assess the diagnostic utility of post-contrast FLAIR MRI brain in different intracranial diseases by comparing it with post-contrast T1 sequence. Additionally, to assess the importance of the post-contrast FLAIR sequence using both qualitative and quantitative metrics in various lesion locations.

Aim of Study: The aim of this study is to compare the diagnostic value of post-contrast FLAIR MRI brain to post-contrast T1 sequence in various intracranial pathologies and to evaluate the significance of post-contrast FLAIR sequence in various lesions locations using qualitative and quantitative parameters.

Patients and Methods: Using MRI, the brains of 50 people with neurological signs and symptoms were scanned. A post-contrast FLAIR sequence was added to post-contrast T1WI. We separated the lesions based on location into extra-axial and intra-axial groups, and we categorized them etiologically into neoplastic, ischemic, inflammatory, and demyelinating groups. Using qualitative and quantitative assessments, we tested whether the lesions' location impacted the effectiveness of the post-contrast FLAIR sequence.

Results: There were 50 cases in all, with different intracranial pathologies. Our two observers detected that post-contrast FLAIR showed better lesions definition, better detection of lesions enhancement as well as higher number of enhancing lesions compared to T1WI. Post-contrast FLAIR had a greater CBR than CET1 detected by both observers. We discovered that post-contrast FLAIR had lower specificity (62.5%) than post-contrast T1WI (87.5%), but better sensitivity (78.6%) than post-contrast T1WI (64.3%). Extra axial lesions showed higher CEI than lesions of other location (mean CEI 152) with statistically significant p -value of 0.037.

Correspondence to: Dr. Marwan M. El-Toukhy,
The Departments of Radiology, Faculty of Medicine,
Cairo University

Conclusion: Post-contrast FLAIR sequence should be added to CE T1W imaging in assessment of intracranial disorders. According to qualitative and quantitative evaluation, post-contrast FLAIR was particularly effective at identifying extra-axial lesions.

Key Words: *Magnetic resonance imaging – Brain – Contrast – Fluid attenuation inversion recovery FLAIR.*

Introduction

THE most frequently utilized MRI sequences for assessing brain lesions are FLAIR (Fluid Attenuated Inversion Recovery) [1]. By having a long repetition time (TR), echo time (TE), and inversion time (TI), the (FLAIR) pulse sequence, which is distinct from other inversion recovery pulse sequences, successfully cancels out signals from the cerebrospinal fluid (CSF) [2]. Therefore, despite FLAIR images being primarily T2-weighted (T2WI) and having a long TI, lesions that exhibit enhancement on contrast-enhanced T1-weighted imaging (CE-T1WI) also exhibit enhancement on contrast-enhanced FLAIR (CE-FLAIR) images [3].

List of Abbreviations:

AVM	: Arterio-venous malformation.
BBB	: Blood brain barrier.
CBR	: Contrast background ratio.
CE	: Contrast enhanced.
CEI	: Contrast enhanced index.
CNS	: Central nervous system.
CSF	: Cerebrospinal fluid.
DCL	: Disturbed Conscious Level.
DWI	: Diffusion weighted image.
FLAIR	: Fluid attenuated inversion recovery.
MS	: Multiple sclerosis.
Gd	: Gadolinium.
SPO	: Space occupying lesion.
TE	: Echo time.
TI	: Inversion time.
TR	: Time of repetition.

Numerous clinical studies have shown that CE-FLAIR is more informative than CE-T1WI alone for a number of intracranial pathologic disorders as well as structures that naturally enhance on CE-FLAIR imaging. Intravenous MR contrast compounds are utilized to improve lesion identification and characterize disorders of the central nervous system (CNS). This contrast agent shortens the T1 and T2 relaxation times of tissues where Gadolinium Gd has accumulated [4].

Blood-brain barrier (BBB) breaks allow Gd to reach the extracellular space for intra-axial brain lesions; relatively high vascularity causes enhancement for extra-axial lesions; and contrast leaks from arteries into the CSF for leptomeningeal areas [3]. Although FLAIR is now more frequently utilized, T1WI is still typically employed as a post-contrast test. A different T1-shortening effect at a particular Gd concentration combined with a different T2 effect based on the vascularity of a lesion can explain the differences between CE-T1WI and CE-FLAIR enhancement characteristics that have been shown in prior studies [5].

Previous research showed that at lower Gd concentrations, the FLAIR sequence was more responsive to T1 shortening than to T1WI, while at higher Gd concentrations, the FLAIR sequence was sensitive to T2 effects. This suggests that faintly enhancing lesions on CE-T1WI may be more clearly demonstrated on CE-FLAIR pictures, while markedly enhancing lesions with significant Gd accumulation do not exhibit enhancement on FLAIR images because the signal-reducing T2 effects mask the signal-increasing T1 effects. In addition, contrast enhancement is not visible in healthy meninges and vascular structures on CE-FLAIR images, in contrast to CE-T1WI [6]. As a result, CE-FLAIR imaging can be used to identify sulcal or meningeal infection, inflammation, and other disorders.

The apparent hyperintensity lesion in CE-FLAIR imaging alone, however, may be caused by either T2 lengthening or T1 shortening, limiting the utility of the FLAIR sequence. Therefore, pre- and post-contrast scans should be used in the FLAIR sequence [7]. A significant part of meningeal pathologies is played by CE-FLAIR. It is extremely helpful in the early detection of leptomeningitis, which leads to a decrease in mortality due to the early start of appropriate treatment [8].

Aim of the work: The aim of this study is to compare the diagnostic value of post-contrast FLAIR MRI brain to post-contrast T1 sequence in various intracranial pathologies and to evaluate the significance of post-contrast FLAIR sequence in various lesions locations using qualitative and quantitative parameters.

Patients and Methods

Patients:

In this observational study, 50 patients with neurological symptoms and signs who were referred from outpatient neurology and neurosurgery clinics were evaluated by skilled radiologists between January 2023 and September 2023. Data were gathered from patients of all age groups who were sent to the radio diagnostic department for an MRI brain study with contrast in order to rule out meningeal or parenchymal lesions. The Cairo University Research Ethics Committee (REC) gave its approval for this work (N-201-2023).

Inclusion criteria:

- Patients referred for gadolinium-enhanced brain imaging.

Exclusion criteria:

- Patients with any implants that are mechanically, electrically, or magnetically actuated, as well as those with intra-orbital metal pieces.
- People who have clips for cerebral aneurysms.
- Patients with renal failure or elevated creatinine (1.6mg/dl) levels.

Methods:

Contrast enhanced MR protocol:

On the 1.5 Tesla (Magnetom Siemens Avanto), an MR examination was performed. All patients underwent standard MR procedure, which included the T1WI, T2WI, axial FLAIR, sagittal and coronal T2WI, as well as DWI sequences.

The FLAIR pictures' TR/TE/TI/flip angle/matrix parameters were 4780-9000/93-124/1745-2497 ms/150°/320-384 x 196-235. The additional criteria were as follows: With a field of view of 193 x 220 mm, a section thickness of 5mm, and 2 excitations, the acquisition times were 2 minutes 33 seconds and 2 minutes 42 seconds, respectively.

Gadovist, a contrast agent, was given at the recommended dose of 0.1mmol/kg body weight.

All patients underwent axial CE-FLAIR imaging shortly after the standard CE-coronal, sagittal, and axial T1WI. Axial CE-T1WI and axial CE-FLAIR imaging were scanned at 2 minutes and 40 seconds and 5 minutes, respectively, following the injection of contrast material. We did not take any more delayed FLAIR images, despite the fact that earlier research [9], provided greater information with delayed CE imaging.

Image analysis:

Two radiologists with between 15 years' experience in neuroimaging independently evaluated MR pictures. First, radiologists assess standard MRI sequences to look for any type of brain lesion, such as

a tumor, an infection, MS, etc. Following that, the CE-T1WI and CE-FLAIR pictures were evaluated and contrasted. Images underwent quantitative and qualitative evaluation.

We use the subtraction MRI technique to assess and confirm the presence of enhancement if CE-FLAIR images were unable to distinguish between an enhancing lesion and the surrounding edema (as in tumors) or were unable to detect lesion enhancement as in lesions with initially high signal intensity (SI) in pre-contrast FLAIR images, particularly in cases of MS. In most of the cases in our investigation, the subtraction step was added.

Following are some examples of qualitative evaluation:

- Evaluation of the lesions' extra- or intra-axial locations. The intra axial lesions were further separated into cortical, cortical and sub cortical, white matter and white matter with cortical involvement.
- The existence of contrast enhancement for lesions.
- Finding the kind of lesion enhancement.
- Calculating the lesion enhancement rate in both CE-T1WI and CE-FLAIR pictures and categorizing it as either more defined, the same as CE-T1WI, or less defined.
- Lesion definition was evaluated and was given one of three grades: No, fair, or good. Lesion definition was defined as the ability to distinguish an enhanced lesion from surrounding edema or from normal-appearing brain parenchyma in CE-FLAIR images.

Interpretation of the imaging findings using the clinical information provided.

Quantitative evaluation includes the following items:

- *Calculating contrast enhancement index (CEI):*

It was done by using a region of interest (ROI) to calculate the SI of the lesion in both pre- and post-contrast FLAIR images. The following was used in the calculation:

$\hat{I} = I - I_0$ (\hat{I} is CEI, I is the lesion SI on CE-FLAIR images and I_0 is the lesion SI on pre-contrast FLAIR images) [10].

- *Calculating lesion to background contrast ratio:*

By measuring the lesion SI as well as the background SI in normal appearing brain parenchyma by using ROI and applied to pre and post contrast T1W images as well as pre and post contrast FLAIR images.

The lesion to background contrast ratio was calculated by: Lesion to background contrast ratio = Lesion SI – Background SI/Back-ground SI [10].

Standard of reference:

In our investigation, the histopathology of all included space-occupying lesions served as the standard of reference. As a standard of reference, we used the clinical and laboratory findings in cases of infection while using the CSF analysis and clinical findings in cases of MS.

- We classified the lesions according to the pathological results after reviewing the findings.
- We evaluated the relationship between CEI and CBR for various diseases and lesions sites.

Results

50 patients were enrolled in this prospective observational study, of whom 29 (58%) were female and 21 (42%) were male. Their average age was 39.34 years, however they ranged in age from 9 to 74.

According to the clinical presentation, the majority of our cases were known multiple sclerosis (MS) patients who presented with symptoms suggestive of relapse (32%), headache (30%), convulsions (14%), and weakness (8%) with disturbed conscious level (DCL), dementia, dysarthria, ataxia, symptoms of increased intracranial tension, right sided sensory neural hearing loss, and tinnitus (2% each) coming in last.

Final diagnoses made in accordance with standards of reference revealed that 40% of patients were neoplastic, 38% had demyelinating lesions, 10% had infarctions, 4% had infections, 4% had migraine-related issues, and 2% had vascular malformations and Alzheimer's disease.

Regarding space-occupying lesions, we divided the cases into primary (17 cases; 85%) and secondary tumors (3 cases; 15%). Primary tumors included 4 cases (23%) of astrocytomas (Fig. 1), 2 cases (11%) of acoustic neuromas (Fig. 2), 2 cases (11%) of meningioma (Fig. 3), medulloblastoma, germinoma of the pineal body, cerebellar tumors and intra ventricular tumors (Fig. 4), and 1 case (5.8% each). We included three cases with secondary tumors: One with breast cancer metastasis, one with lung cancer metastasis, and one with rectal cancer (Fig. 5).

Regarding the pre-contrast qualitative evaluation of the lesions in various MRI sequences, all of the lesions (100%) displayed bright signal on T2 WIs, whereas on T1 WIs, lesions were isointense, low signal (24%), bright & intermediate signal (4% each), and bright & heterogeneous (2%). On FLAIR WIs, lesions elicited bright signal in the majority of instances (76%) before intermediate signal (10%), heterogeneous signal (8%), poor signal (4%) and simply a bright signal rim (2%). On DWIs, diffusion facilitation was seen in the majority of cases (56%) whereas diffusion restriction was reported in

46% of the cases. One individual (2%) had a previous CT scan that identified a cerebellar cyst.

On post-contrast images qualitative assessment showed:

- A- According to the location lesions were divided into: Extra axial lesions in 5 cases (11%), intra axial lesions in 40 cases (80%) the intra axial lesions were either cortical seen in 3 patients (6.7%), cortical and sub cortical in 11 patients (24.4%), cortical and white matter in 8 patients (17.8%), white matter only in 18 patients (40%).
- B- According to lesions enhancement: Most of the cases (40%) lesions showed no notable enhancement, (24%) faint enhancement, (16%) heterogeneous enhancement, being avid in (12%), marginal (4%), ring & homogenous (2% each).
- C- Pathological classification of the lesions in each location showed: In the extra axial lesions 100% of cases were primary neoplasm (meningioma), in the intra axial lesions cortical lesions were either primary neoplasm (66.7%) and vascular (33.3), the cortical and subcortical lesions were either primary neoplasm (45.5%), vascular (45.5%) or infection in (9.1%), cortical and white matter lesions were due to infection (50%), secondary neoplasm (37.5%) or primary neoplasm in (12.5%), the white matter lesions were mainly demyelinating (94.4%) and less frequently due to primary neoplasm (5.6%) (Table 1).

There was perfect agreement between the findings of our two observers in the qualitative assessment (assessed by using the Kappa test) regarding the following:

- Lesion definition, the first observer noticed that in CE-FLAIR images: 54% of the cases were more defined 24% had fair definition, and 22% were not defined, while the second observer noticed that 46% of cases were more defined, 36% had fair definition and 18% were not defined (kappa = 0.744).
- The comparison between CE-T1WI & CE-FLAIR regarding their informative role in demonstration of lesions enhancement: The first observer noticed that CE-FLAIR was more informative to CE-T1WI in 60% of cases, no differences detected between CE FLAIR and CE T1WI in 36% of cases and less informative in 4% of cases. The second observer noticed that CE-FLAIR was more informative to CE-T1WI in 56% of cases, No differences in 40% of cases and less informative in 4% of cases (kappa=0.923).

We assessed the informative role of CEFLAIR in comparison to CET1 in different pathologies:

In cases diagnosed as demyelinating, CEFLAIR was more informative than CET1WI, in (66%) and (69,5%) of patients according to first and second observers respectively. Both observers reported that

CEFLAIR was more informative in (100%) of the cases with inflammatory & vascular etiology. On the other hand, in (94.1%), (91.5%) of the cases with intra-cranial neoplasms, the CEFLAIR was more informative and (5.9%), (8.5%) showed more differences according to first and second observers respectively.

The number of enhancing lesions: Our observers found that the number of enhancing lesions in post contrast FLAIR was either 0 (no enhancing lesions), 1 or 2 enhancing lesions, as compared to either 0 (no enhancing lesions) or 1 in post contrast T1WI (Table 2). There were 8 cases 16% (with pathological results of primary and second neoplasms as well as with intra cranial infections) showed two enhancing lesions compared to only one in post contrast T1WI and that the second lesions were extra axial in location (meningeal), (proving the special added value of post contrast FLAIR in detection of meningeal lesions).

Regarding post-contrast quantitative measurements:

- There was a correlation between both observers regarding the CEI which represent the difference between SI of lesions in pre and post contrast FLAIR images with the mean CEI detected by observer 1 being 93.3 ± 168.6 SD and the mean CEI detected by observer 2 being 95.05 ± 171.4 SD (Intra-class Correlation Coefficient (ICC) = 0.998, 95% Confidence Interval (CI): 0.933–0.975) p -value < 0.001.
- There was perfect agreement between both observers regarding the mean CBR in FLAIR (ICC = 0.998, CI 0.997–0.999) and regarding the mean CBR in T1WI (ICC = 0.973, CI 0.946–0.987).
- Comparing CBR on CE-FLAIR and CE-T1WI, both observers found higher CBR on CE-FLAIR images as following:
- Observer 1 found the mean CBR on CE-FLAIR images was 1.22 ± 2.12 SD versus 0.42 ± 0.50 SD on CE-T1WI. Observer 2 found the CBR on CE-FLAIR images was 1.26 ± 2.16 SD versus 0.42 ± 0.48 SD on CET1WI.

Due to good agreement between the two observers we used the readings of the first one in the following:

- We used first observer CBR of T1WI and CBR of FLAIR to assess the sensitivity and specificity of T1WI and FLAIR in lesions assessment and we found that the post contrast FLAIR sequence had higher sensitivity 78.6% as compared to post contrast T1WI 64.3%, but it showed lower specificity 62.5% as compared to 87.5% (Table 3), (Fig. 6).
- We used the quantitative parameters CBR and CEI to assess the effect of lesions location on the significance of post contrast FLAIR and we reported that:

- The mean CEI of post contrast FLAIR of cortical lesions, of cortical and subcortical lesions 107.55, cortical and white matter 120.6, of extra axial lesions 152, of white matter lesions 61.12, with statistically significant p -value of 0.037.

- Post hoc pair wise comparisons (p -value between each 2 groups: (Table 4), we found statistically significant relation between the white matter lesions and extra axial lesions, p -value 0.006.

- The mean CBR of post contrast FLAIR of cortical lesions was 1.35 of the cortical and subcortical lesions was 1.02, of cortical and white matter was 2.53, of extra axial lesions was 0.87, of white matter lesions was 0.54 with statistical insignificant relation p -value 0.178.

Statistical analysis:

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was

summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests [11] (Chan, 2003a). For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 [12] (Chan, 2003). Testing for inter-rater reliability was done using the Intra Class Coefficient (ICC) and Cronbach's alpha reliability coefficient with their 95% confidence interval (95%CI) [13] (Ranganathan et al., 2017). Kappa measure of agreement was used to test agreement between categorical variables [14] (Altman, 1991). ROC curve was constructed with area under curve analysis performed to detect the best cutoff value of CBR for detection of malignancy. p -values less than 0.05 were considered statistically significant.

Table (1): Number and percent of different etiologies in each location.

	Location									
	Cortical		Cortical + Subcortical		Cortical + White matter		Extra-axial		White matter	
	Count	%	Count	%	Count	%	Count	%	Count	%
<i>Etiology:</i>										
Infection	0	0.0	1	9.1	4	50.0	0	0.0	0	0.0
MS	0	0.0	0	0.0	0	0.0	0	0.0	17	94.4
Primary neoplasm	2	66.7	5	45.5	1	12.5	5	100.0	1	5.6
Secondary neoplasm	0	0.0	0	0.0	3	37.5	0	0.0	0	0.0
Vascular	1	33.3	5	45.5	0	0.0	0	0.0	0	0.0

Table (2): Number of enhancing lesions in post contrast T1 and FLAIR.

	Observer 1	Observer 2
<i>FLAIR:</i>		
0	20 (40%)	22 (44%)
1	22 (44%)	22 (44%)
2	8 (16%)	6 (12%)
<i>TIWI:</i>		
0	26 (52%)	26 (52%)
1	24 (48%)	24 (48%)
2	0 (0%)	0 (0%)

Table (3): Sensitivity and specificity of post contrast T1 and post contrast FLAIR.

	Area Under the Curve	p -value	95% Confidence interval		Cut off	Sensitivity %	Specificity %
			Lower bound	Upper bound			
CBR F01	0.790	<0.001	0.630	0.950	0.71	78.6	62.5
CBR T101	0.817	<0.001	0.668	0.966	0.375	64.3	87.5

Table (4): Post hoc pair wise comparisons (p -value between each 2 groups).

	p -value
White matter-cortical+subcortical	0.282
White matter-cortical+white matter	0.052
White matter-cortical	0.078
White matter-extra axial	0.006
Cortical+subcortical-cortical+white matter	0.371
Cortical+subcortical-cortical	0.291
Cortical+subcortical-extra axial	0.073
Cortical+white matter-cortical	0.688
Cortical+white matter-extra axial	0.332
Cortical-extra axial	0.701

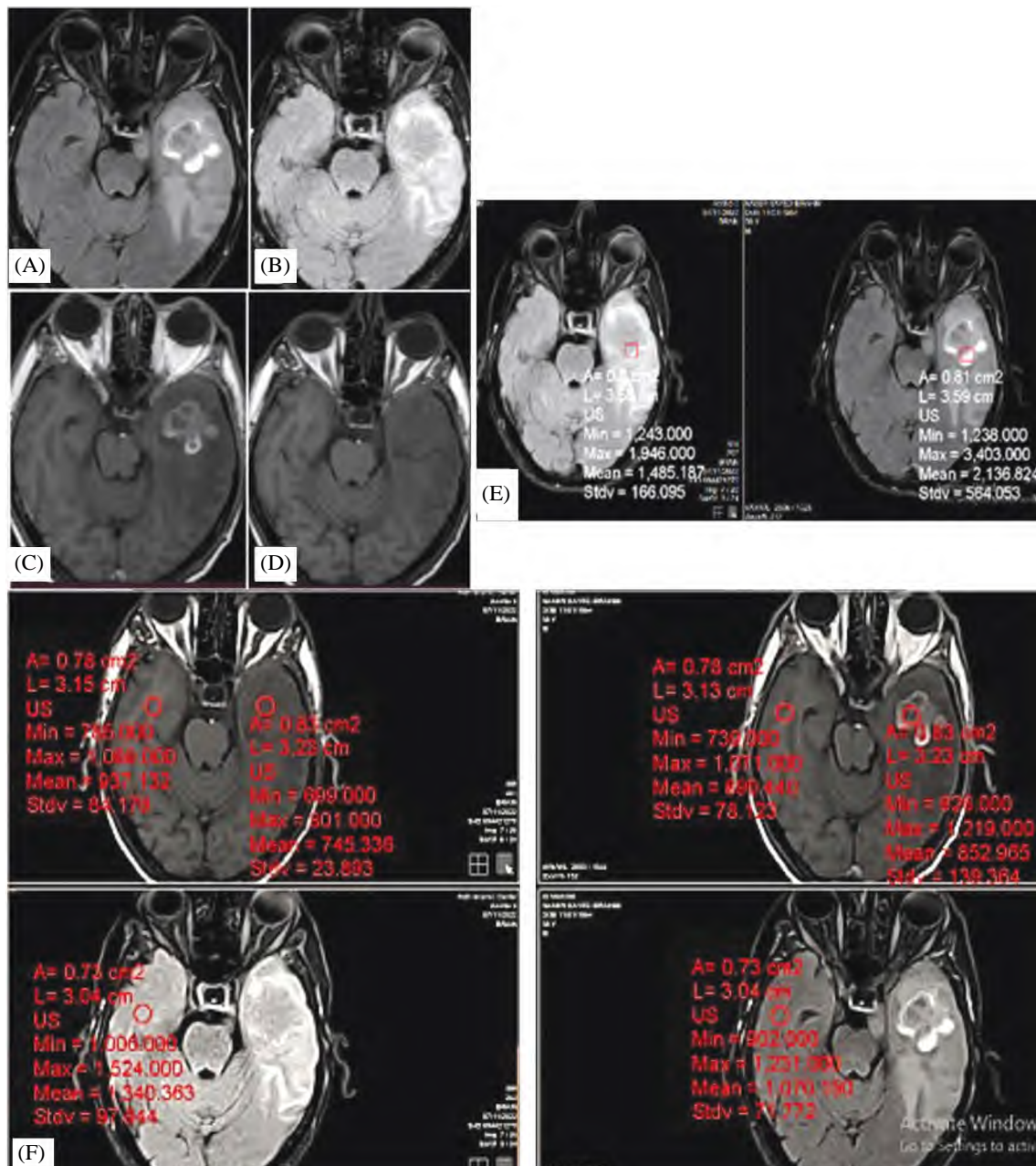


Fig. (1): 58 years old male patient, with right sided weakness & convulsions, suspecting SOL. A) Axial FLAIR image showing left temporal cortical and subcortical soft tissue lesion of iso intense center and peripheral rim of bright signal intensity surrounded by vasogenic edema. B) Axial FAIR post contrast image showing heterogeneous mainly peripheral enhancement. C) Axial T1WI showing iso-intense signal of the lesion. D) Axial T1WI post contrast showing heterogeneous enhancement of the lesion. The lesional enhancement is more intense in post contrast FLAIR. (e) ROI for CEI. (f) ROI for CBR.

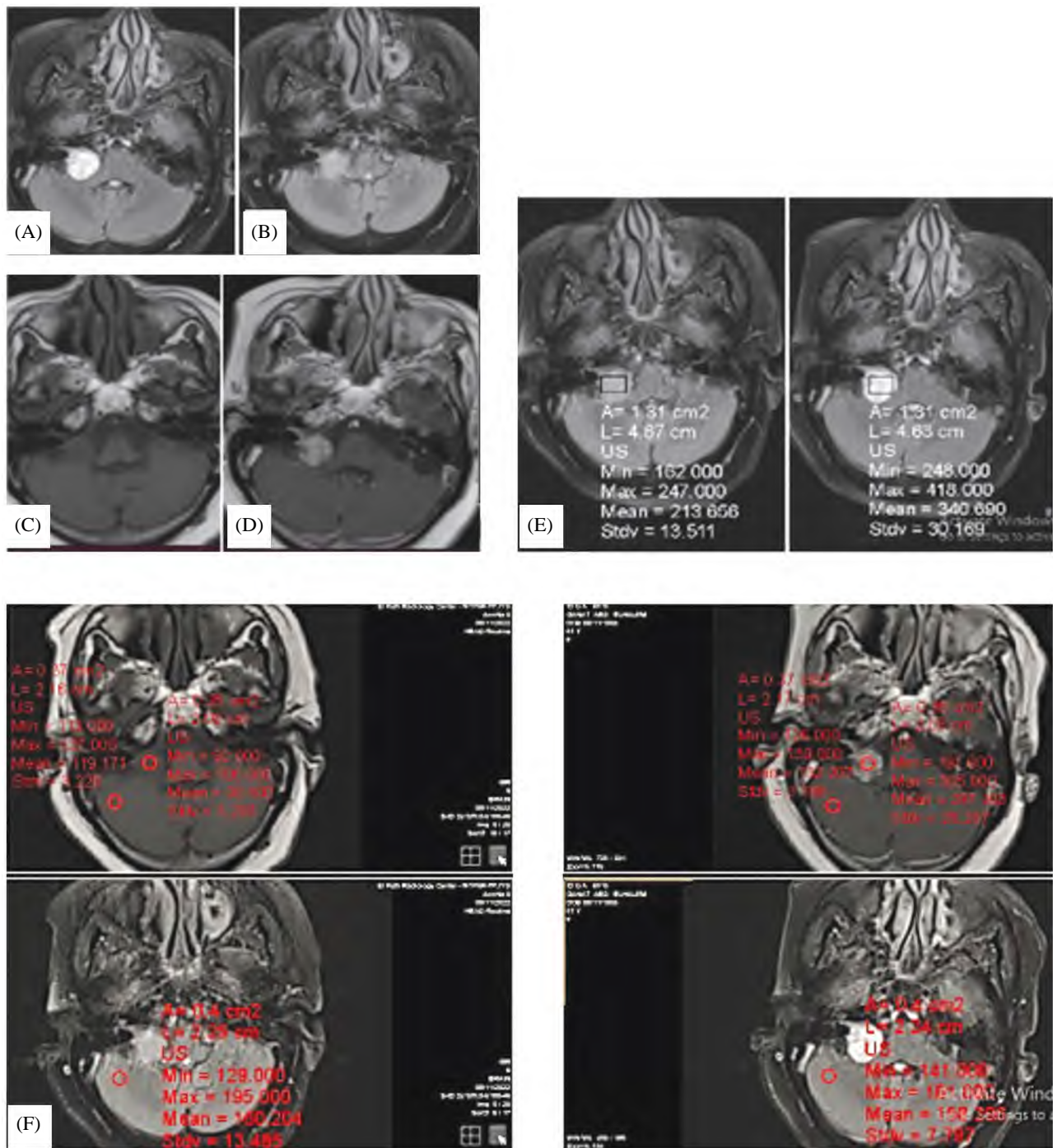


Fig. (2): 67 years old female patient, with right sided sensory neural hearing loss. A) Axial FLAIR image showing an extra axial soft tissue lesion implicating the right cerebello-medullary angle cistern an extending into the right internal auditory canal eliciting slightly bright signal intensity suggestive of acoustic neuroma. B) Axial FAIR post contrast image showing intense enhancement of the lesion. C) and D) Axial T1WI pre and post contrast showing intense enhancement of the lesion. The post contrast enhancement is more evident in post contrast FLAIR image (B) as compared to post contrast T1WI (D). (e) ROI for CEI (f) ROI for CBR.

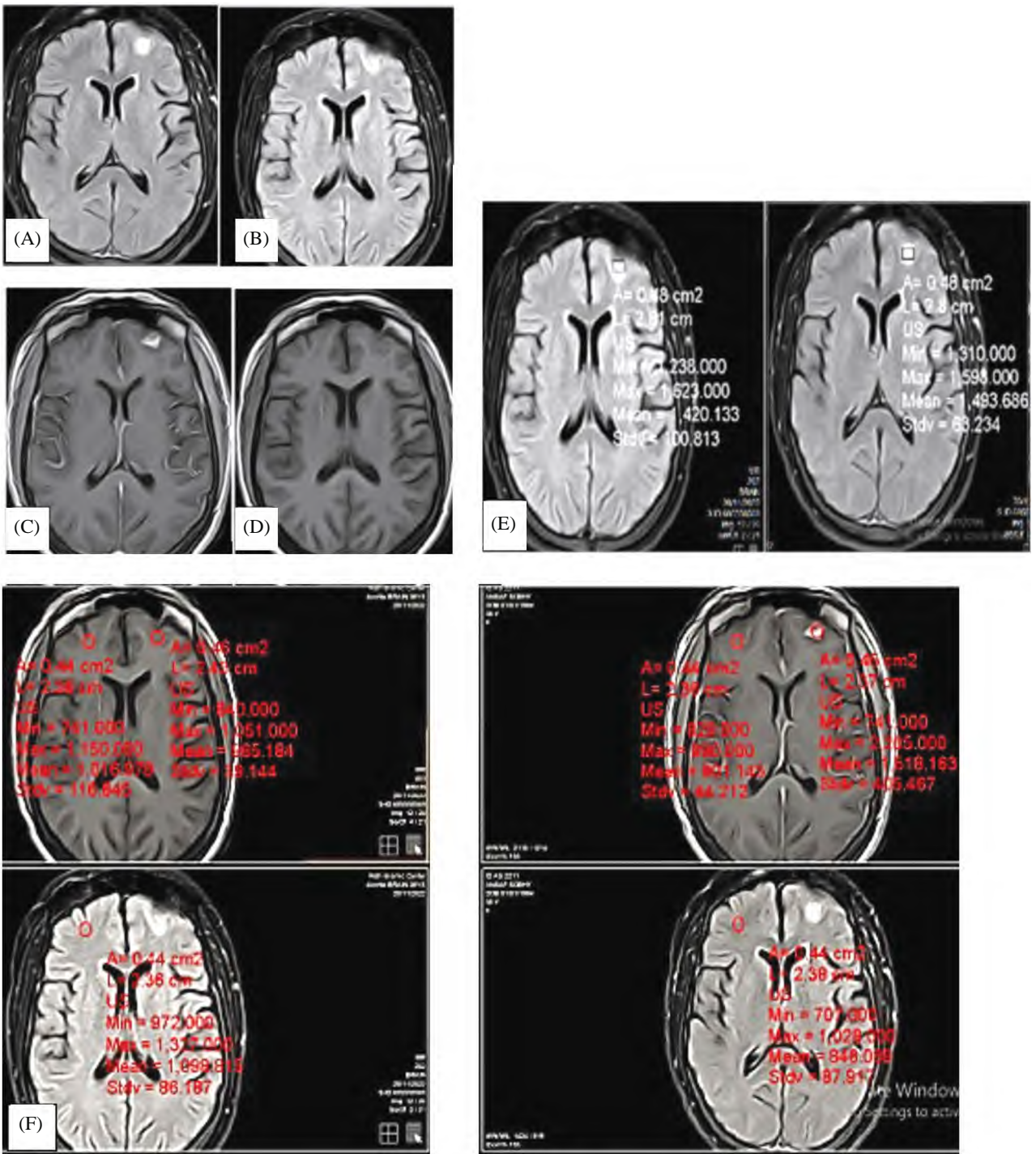


Fig. (3): 38 years old female patient, coming for follow up following gamma-knife session for small left frontal meningioma. A) Axial FLAIR image showing an extra axial small soft tissue lesion at the left frontal region. B) Axial FAIR post contrast image showing a well-defined intensely enhancing lesion. C) axial T1WI showing small extra axial left frontal lesion of iso-intense signal. D) axial T1WI post contrast showing small enhancing lesion. The lesion and its pattern of enhancement is more evident in post contrast FLAIR image (B) as compared to post contrast T1WI (D). (e) ROI for CEI. (f) ROI for CBR.

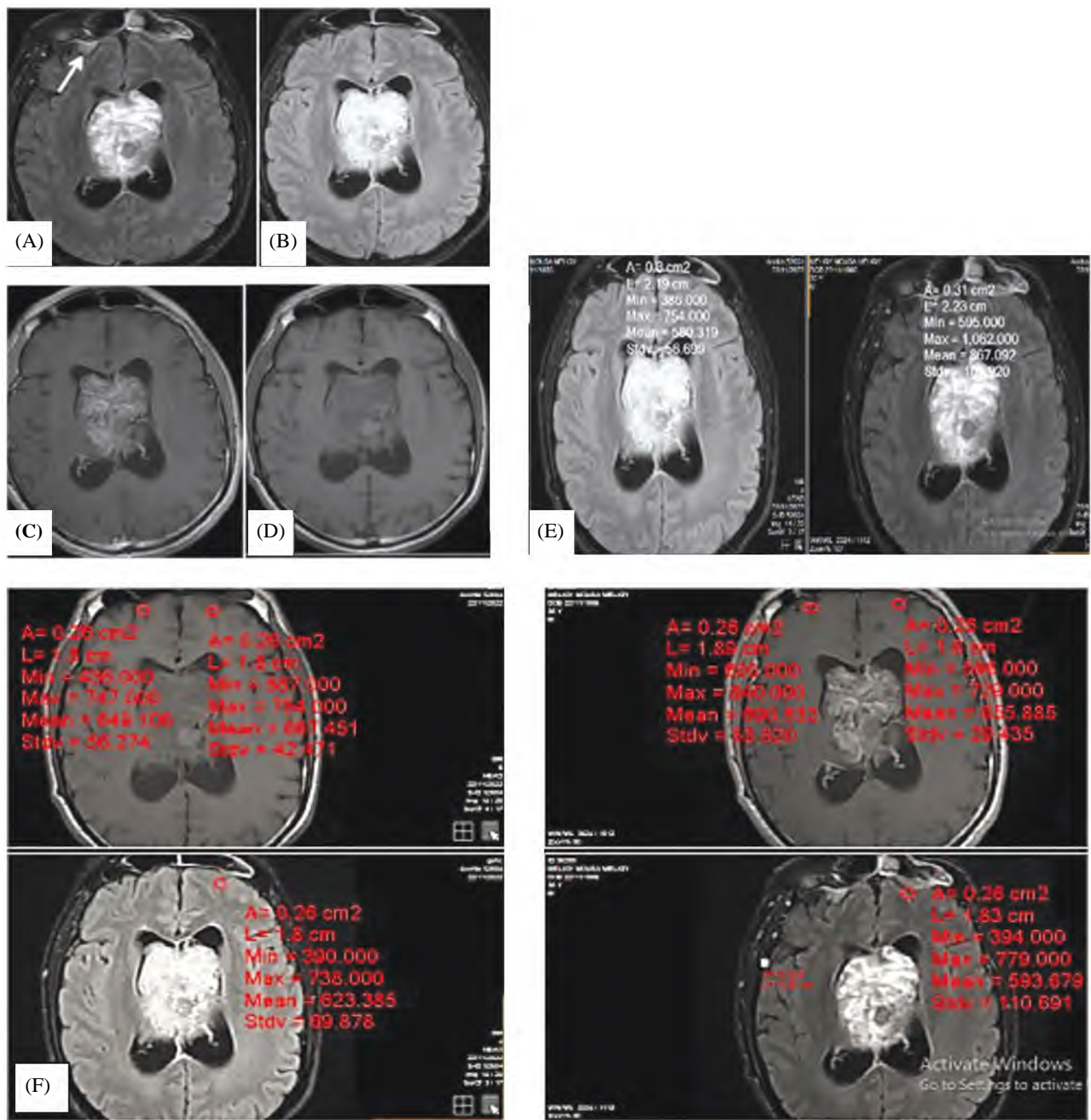


Fig. (4): 36 years old male patient giving history of intra-cranial neoplasm, shunt was inserted to relieve hydrocephalic changes. A) Axial FLAIR image showing an intra ventricular soft tissue lesion of heterogeneous bright signal intensity. B) Axial FAIR post contrast image showing still noted heterogeneous bright signal intensity of the lesion, significant contrast enhancement could not be detected but an ill-defined right frontal extra axial area of enhancement is noted denoting CSF seedling that is not apparent in pre contrast image. C) Axial T1WI showing intra ventricular lesion of heterogeneous iso-intense signal. D) Axial T1WI post contrast showing heterogeneous enhancement of the lesion, the right frontal extra axial enhancing area of CSF seedling seen in post contrast FLAIR could not be detected. (e) ROI for CEI. (f)ROI for CBR.

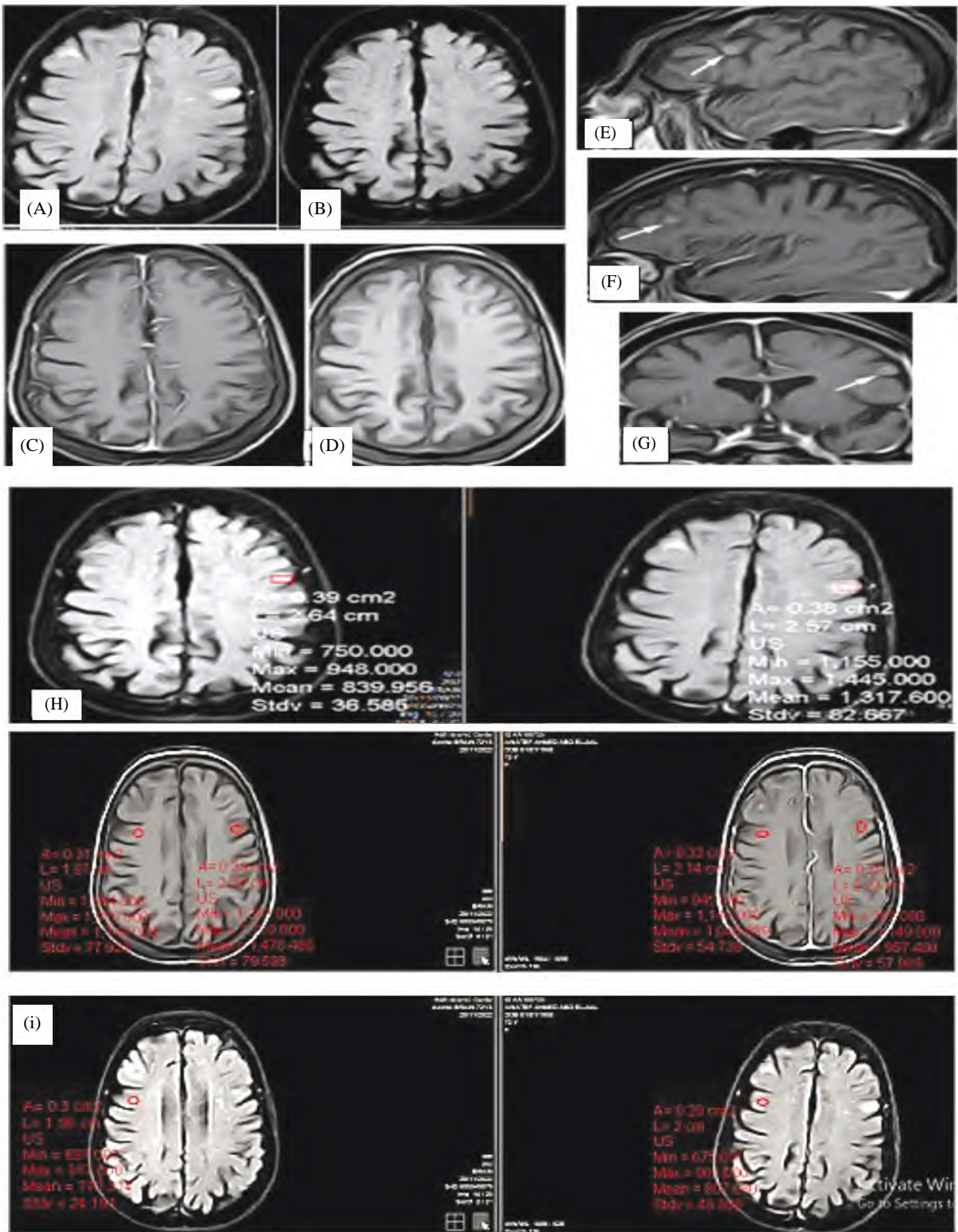


Fig. (5): 72 years old female patient, complaining of severe headache& dizziness. A) Axial FLAIR image showing left frontal faint cortical area of bright signal intensity. B) Axial FAIR post contrast image showing bilateral frontal cortical areas of enhancement. C) Axial T1WI showing no significant abnormalities. D) Axial post contrast T1WI showing no significant enhancement. E) & F) Sagittal post-contrast T1 WIs showing bilateral frontal small marginally enhancing lesions & G) Coronal post-contrast T1 WIs showing the left frontal marginally enhancing lesion. The lesions and their enhancement are only apparent in pre and post contrast FLAIR images. (e) ROI for CEI. (i) ROI for CBR.

Discussion

Gadolinium is the most often used intravenous contrast agent for brain imaging. The detection and characterization of various lesions are improved as a result [15]. Small groups in our practice are aware of the role of post-contrast T2-FLAIR sequence in certain cases, despite the fact that it is well recognized that T1 post-contrast has a significant significance in the identification of space-occupying lesions in the brain. As a result, there isn't many research examining how post-contrast T2 FLAIR pictures are used in various intracranial lesions [16].

Our study was designed to compare post-contrast FLAIR MRI brain to post-contrast T1 sequence to determine the diagnostic value of post-contrast FLAIR MRI brain in various intracranial pathologies. Additionally, to evaluate the significance of post-contrast FLAIR sequence in various lesions locations using qualitative and quantitative parameters.

According to our first and second observers, respectively, post contrast FLAIR was more informative in detecting lesions enhancement as compared to T1WI in 60% and 56% of cases ($\kappa=0.923$). These findings are consistent with those of Athar et al., who showed stronger enhancement in post-contrast T2 FLAIR (57.6%) [17]. Our findings concurred with those of Rastogi et al. [16], who discovered that in 63.2 percent of the cases they examined, post-contrast FLAIR images displayed superior enhancement. This is also consistent with the findings of Mahale et al. [18], who showed that in (72%) of the examined cases, CE-FLAIR was more effective at detecting lesions than CE-T1WI.

In cases with brain tumors and inflammation as sort of meningeal lesions (which highlighted the special added value of post contrast FLAIR in detection of meningeal lesions), as well as in cases with MS, we reported a higher number of enhancing lesions detected by our two observers in CE FLAIR as compared to CET1WI. This allowed us to detect disease activity and, as a result, provided a chance for better patient management. This was consistent with the findings of a prior study by EL Adalany et al. [10], who discovered that CE-FLAIR images had more enhancing lesions than CE-T1WI images did, particularly in cases of multiple sclerosis (MS), where CE-FLAIR outperformed CE-T1WI in 90% of the cases. These findings were in good accord with another study [19] that evaluated CE-FLAIR against CE-T1WI, DWI, and ADC and found that CE-FLAIR was the most effective in active MS lesions due to its ability to attenuate the CSF signal and boost the detection of lesions.

Additionally, we discovered that CEFLAIR allowed for better lesions definitions than CET1I in 54% and 46% of cases, respectively, with good agreement between their results ($\kappa=0.744$). EL

Adalany et al., reported in a prior study [10] that in 68.9% of the instances, CE-FLAIR pictures exhibited better lesion conspicuity than CE-T1WI, with good interobserver agreement found ($\kappa=0.848$). In contrast to a study by Athar I, et al. [17], which indicated a lower percentage (39.4%) of cases with better lesions conspicuity in CEFLAIR, our study and the study by EL Adalany et al. The quantitative analysis of our cases revealed that the lesions' signal intensity (SI) was higher on CE-FLAIR images than it was on pre-contrast ones, confirming the existence of lesion enhancement on CE-FLAIR images.

With full agreement between them, our observers' CEI results were 93.3 for the first observer and 95.05 for the second (Intra-class Correlation Coefficient (ICC) = 0.998, 95% Confidence Interval (CI): 0.933-0.975). We concurred with another study [20] that found increased CEI in CE-FLAIR compared to pre-contrast FLAIR pictures, with CEI 262 ranging from 40 to 1708.

To eliminate inaccuracies that could be made by evaluating contrast enhancement visually, we also used another quantitative statistic called the contrast to background ratio (CBR). With good agreement between their CBR measures in CEFLAIR (ICC = 0.998, CI 0.997-0.999) and CET1WI (ICC = 0.973, CI 0.946-0.987), both observers discovered a higher CBR in CE-FLAIR than in CE-T1WI.

This demonstrated that CE-FLAIR performed better than CET1WI at defining lesions. This might be because FLAIR and T1W sequences have superior inherent soft tissue contrast resolution. Our findings are corroborated by a research by Mustafa et al. [20] who found that CE-FLAIR demonstrated greater CBR compared to CE-T1WI.

Additionally, our research supported the findings of Kim et al. [21], who discovered that CE-FLAIR pictures exhibited a greater tumor to background contrast ratio than CE-T1WI.

We discovered that post-contrast FLAIR had lower specificity (62.5%) than post-contrast T1WI (87.5%), but better sensitivity (78.6%) than post-contrast T1WI (64.3%).

We reported that there was a statistically significant relationship between the extra-axial location of the lesions and high CEI, which was confirmed by Post hoc pair-wise comparisons (p -value between each 2 groups: $p=0.0001$). We used the quantitative parameters CBR and CEI to assess the effect of lesions location on the significance of post contrast FLAIR. White matter lesions and extra axial lesions were shown to be statistically significantly correlated, with a p -value of 0.006. However, there was no statistically significant correlation between the location of the lesions and the CBR of post contrast FLAIR.

This demonstrated that FLAIR performed better after contrast in the evaluation of extra axial lesions. This finding did not agree with that reported in a prior study by Akshit B.S, et al. [22], who suggested that the degree of contrast enhancement is more obvious on post-contrast T1 than post-contrast FLAIR sequence for both intra-axial & extra-axial intracranial pathologies and that the variation is statistically significant for the same. However, it agreed with other studies [23,24] mentioned by Akshit B.S, et al. [22], which stated, contrast enhanced FLAIR sequences rendered lesions that were extra-axial in location or bordered the CSF more visible when compared to contrast enhanced T1 sequences.

The main limitations of our study were the small sample size and the fact that more accurate results were obtained with larger samples.

Conclusion:

Post-contrast FLAIR sequence should be added to CE T1W imaging in assessment of intracranial disorders. According to qualitative and quantitative evaluation, post-contrast FLAIR was particularly effective at identifying extra-axial lesions.

References

- AHMED M.: Comparison of gadolinium based T1 weighted and fair MR sequences for the assessment of leptomeningeal enhancement in meningoencephalitis. *Int. J. Radiol.*, 5 (1): 163-171, 2018.
- RYDBERG J.N., HAMMOND C.A., GRIMM R.C., ERICKSON B.J., JACK C.R. Jr., HUSTON J. 3rd, et al.: Initial clinical experience in MR imaging of the brain with a fast fluid-attenuated inversion-recovery pulse sequence. *Radiology*, 193: 173-180, 1994.
- EUN KYOUNG LEE, M.D.1,2, EUNJA LEE, M.D., Ph.D.1, SUNGWON KIM, M.D.1 and YONG SEOK LEE, M.D.: Importance of Contrast-Enhanced Fluid-Attenuated Inversion Recovery Magnetic Resonance Imaging in Various Intracranial Pathologic Conditions. *Korean J. Radiol.*, 17 (1): 127-141, 2016.
- ESSIG M., KNOPP M.V., SCHOENBERG S.O., HAWIGHORST H., WENZ F., DEBUS J., et al.: Cerebral gliomas and metastases: assessment with contrast-enhanced fast fluid-attenuated inversion-recovery MR imaging. *Radiology*, 210: 551-557, 1999.
- FUKUOKA H., HIRAI T., OKUDA T., SHIGEMATSU Y., SASAO A., KIMURA E., et al.: Comparison of the added value of contrast-enhanced 3D fluid-attenuated inversion recovery and magnetization-prepared rapid acquisition of gradient echo sequences in relation to conventional post-contrast T1-weighted images for the evaluation of leptomeningeal diseases at 3T. *AJNR Am. J. Neuroradiol.*, 31: 868-873, 2010.
- TSUCHIYA K., KATASE S., YOSHINO A. and HACHIYA J.: FLAIR MR imaging for diagnosing intracranial meningeal carcinomatosis. *AJR Am. J. Roentgenol.*, 176: 1585-1588, 2001.
- MELHEM E.R., BERT R.J. and WALKER R.E.: Usefulness of optimized gadolinium-enhanced fast fluid-attenuated inversion recovery MR imaging in revealing lesions of the brain. *AJR Am. J. Roentgenol.*, 171: 803-807, 1998.
- PARK Y.W. and AHN S.J.: Comparison of contrast-enhanced T2 FLAIR and 3D T1 black-blood fast spin-echo for detection of leptomeningeal metastases. *Investig Magn Reson Imaging*, 22 (2): 86-93, 2018.
- SUTHIPHOSUWAN S., HSU C.T. and BHARATHA A.: HARM less: Transient cortical and sulcal hyperintensity on gadolinium-enhanced fair after elective endovascular coiling of intracranial aneurysms. *Am. J. Neuroradiol.*, 39 (4): 720-726, 2018.
- MOHAMED ALI ELADALANY, MAHA MOHAMED ZAKI BILAL, YOMNA ABDULWAHAB, MOHAMMED RIHAN and DINA ELMETWALLY: Contrast enhanced FLAIR versus contrast enhanced T1W images in evaluation of intraparenchymal brain lesions. *Egypt J. Radiol. Nucl. Med.*, 53: 143 <https://doi.org/10.1186/s43055-022-00817-w>, 2022.
- CHAN Y.H.: Biostatistics 102: Quantitative Data – Parametric & Non-parametric Tests. *Singapore Med. J.*, 44 (8): 391-396, 2003a.
- ALTMAN D.G.: Practical statistics for medical research. London: Chapman and Hall, 1991.
- CHAN Y.H.: Biostatistics 103: Qualitative Data – Tests of Independence. *Singapore Med. J.*, 44 (10): 498-503, 2003.
- RANGANATHAN P., PRAMESH C.S. and AGGARWAL R.: Common pitfalls in statistical analysis: Measures of agreement *Perspect Clin. Res.*, 8 (4): 187-191, 2017.
- BHARGAVA R., PATIL A.M., BAKSHI V., KALEKAR T.M. and GANDAGE S.G.: Utility of contrast enhanced fluid-attenuated inversion recovery in magnetic resonance imaging of intracranial lesions. *West Afr. J. Radiol.*, 25 (1): 34, 2018.
- RASTOGI R., JAIN S., GUPTA Y., JOON P., WANI A. and PRATAP V.J.: Can postcontrast-T2 FLAIR be a boon over postcontrast-T1GRE images in MR brain imaging? *J. Neuroinfect Dis.*, 7: 2, 2016.
- ATHAR I., KHAN S.A., BUTT M.A., MARYAM S., MANZOOR H., BUTT M.F., et al.: Comparison between post contrast T1 weighted and T2 weighted flair axial sequences in various intracranial pathologies. *Int. J. Sci. Eng. Res.*, 10: 872-83, 2019.
- MAHALE A., CHOUDHARY S., ULLAL S., FERNANDES M. and PRABHU S.: Postcontrast fluid-attenuated inversion recovery (FLAIR) sequence MR imaging in detecting intracranial pathology. *Radiol. Res. Pract*, 1-9, 2020.
- ABDOLMOHAMMADI J., POURASL M.H., ZANDKARIMI M., SHARIFI K., editors.: Evaluation the sensitivity of FLAIR and DWI post-inject comparison with delay enhance T1w in detection of active MS lesions 2017: *J. Biomed. Phys. Eng.*, 8 (4): 365-74, 2018.

- 20- MUSTAFA W., ALI S., ELGENDY N., SALAMA S., EL SOROBY L. and MOHSEN M.: Role of contrast-enhanced FLAIR MRI in diagnosis of intracranial lesions. Egypt J. Neurol. Psychiatry Neurosurg, 57: 108, 2021.
- 21- KIM J.H., YI K.S., CHOI C.H., WOO S.T. and CHA S.H.: Does multiphasic contrast enhanced fluid attenuated inversion recovery magnetic resonance imaging enhance the detectability of small intracerebral metastases? J. Korean Soc. Radiol., 78 (3): 179-189, 2018.
- 22- AKSHIT B.S., METTU R. and HIREMATH R.: Role of contrast-enhanced flair sequence in magnetic resonance imaging for evaluating intracranial pathologies. International Journal of Radiology and Diagnostic Imaging, 5 (3): 34-47, 2022.
- 23- KAMR W., EISSAWY M. and SAADAWY A.: The value of contrast-enhanced FLAIR magnetic resonance imaging in detecting meningeal abnormalities in suspected cases of meningitis compared to conventional contrast-enhanced T1WI sequences. Egyptian Journal of Radiology and Nuclear Medicine, 51 (1), 2020.
- 24- AHMAD A., AZAD S. and AZAD R.: Differentiation of Leptomeningeal and Vascular Enhancement on Post-contrast FLAIR MRI Sequence: Role in Early Detection of Infectious Meningitis. J. Clin. Diagn. Res., 9 (1): TC08-TC12, 2015.

الدور التشخيصي للرنين المغناطيسي FLAIR المعزز بالصبغة في الأمراض داخل الجمجمة: التحليلات النوعية والكمية

تسلسلات التصوير بالرنين المغناطيسي الأكثر استخداماً لتقييم آفات الدماغ هي FLAIR. من خلال وجود وقت تكرار طويل (TR)، ووقت صدق (TE)، ووقت انعكاس (TI)، فإن تسلسل النبض (FLAIR)، والذي يختلف عن تسلسلات نبض استرداد الانعكاس الأخرى، يلغى بنجاح الإشارات من السائل النخاعي (CSF). لذلك، على الرغم من أن صور FLAIR تكون في المقام الأول ذات وزن T2 ولها T1 طويل، فإن الآفات التي تظهر تحسناً في التصوير الموزون T1 المحسن عن طريق حقن الصبغة (CE-T1W1) تظهر أيضاً تحسناً على صور FLAIR (CE-FLAIR) المحسنة بالصبغة.

أظهرت العديد من الدراسات السريرية أن CE-FLAIR أكثر إفادة من CE-T1W1 وحده لعدد من الاضطرابات المرضية داخل الجمجمة بالإضافة إلى الأعضاء التي تمتص الصبغة بشكل طبيعي في تصوير CE-FLAIR. تُستخدم مركبات صبغة الرنين المغناطيسي الوريدي لتحسين تحديد الآفة وتوصيف اضطرابات الجهاز العصبي المركزي (CNS). تعمل الصبغة هذا على تقصير أوقات استرخاء T1 و T2 للأنسجة التي تتراكم فيها صبغة الجادولينيوم Gd.

في هذه الدراسة الرصدية، تم تقييم خمسون مريضاً يعانون من أعراض وعلامات عصبية من قبل أطباء الأشعة من أصحاب الخبرة في الفترة ما بين يناير ٢٠٢٣ وسبتمبر ٢٠٢٣. اكتشف مراقبون أن صور FLAIR بعد الصبغة أظهرت توضيحاً أفضل للآفات، واكتشافاً أفضل لتعزيز الآفات بالإضافة إلى عدد أكبر من الآفات المعززة مقارنةً بـ T1W1. كان لدى FLAIR بعد الصبغة CBR أكبر من CET1 الذي اكتشفه كلا المراقبين. لقد اكتشفنا أن FLAIR بعد التباين كان له خصوصية أقل (٦٢,٥٪) من T1W1 بعد التباين (٨٧,٥٪)، ولكن حساسية أفضل (٧٨,٦٪) من T1W1 بعد التباين (٦٤,٣٪). أظهرت الآفات خارج نطاق النسيج المخي مؤشر CEI أعلى من الآفات الموجودة في مواقع أخرى (متوسط مؤشر CEI 152) مع قيمة p ذات دلالة إحصائية قدرها ٠,٠٣٧.

وقد وصلنا إلى استنتاج أنه يجب إضافة تسلسل FLAIR بعد الصبغة إلى تصوير CE T1W1 في تقييم الاضطرابات داخل الجمجمة. وفقاً للتقييم النوعي والكمي، كان FLAIR بعد الصبغة فعالاً بشكل خاص في تحديد الآفات داخل الجمجمة لكن خارج نطاق النسيج المخي.