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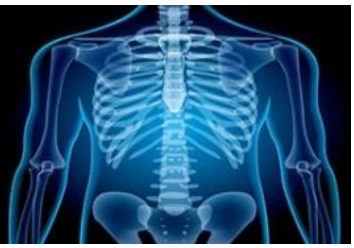

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Role of contrast-enhanced flair sequence in magnetic resonance imaging for evaluating intracranial pathologies

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Abstract
Background: Magnetic resolution imaging (MRI) has superior soft tissue contrast for characterization and diagnosing various intracranial lesions. Various MRI techniques are used for characterizing intracranial lesions. Post contrast T1 imaging is the traditional technique used for assessing lesion contrast enhancement. This study intends to assess the use of post contrast Fluid Attenuated Inversion Recovery (FLAIR) imaging for assessing lesion contrast enhancement.
Results: The participants were analyzed by age, gender, number of lesions observed for each participant, signal intensity pattern for all intracranial lesions on both post contrast sequences, comparison of degree of contrast enhancement of all intracranial lesions on both post contrast sequences, comparison between various intra-axial & extra-axial intracranial lesions on both post contrast sequences, comparison between various intracranial lesions based on their etiology on both post contrast sequences and comparison of each intracranial lesion on both post contrast sequences.
Conclusion: The study suggests that the overall degree of contrast enhancement is superior for contrast enhanced T1 sequences for the majority of the lesions, however complete lesion pathology cannot be assessed on this sequence alone. Although post contrast FLAIR sequence has shown greater degree of contrast enhancement in infectious meningitis, hemangioblastoma and toxoplasmosis, this was not statistically significant (p value >0.05) possibly owing to less sample size. Hence, further studies with more sample size should be assessed to establish the significance. Therefore, contrast enhanced FLAIR sequence is an important adjunct for imaging of the various intracranial pathologies and should be incorporated for evaluating various intracranial pathologies.

Keywords: brain neoplasms, ring enhancing lesions, pachymeningitis, toxoplasmosis, magnetic resonance imaging, contrast media

Introduction
Magnetic resonance imaging (MRI) is the mainstay of diagnosis for various intracranial lesions. It is important to identify and effectively diagnose various intracranial lesions for optimum clinical diagnosis and management of the patient. MRI provides a non-invasive method to provide high resolution images with superior tissue contrast for characterizing most lesions compared to other imaging methods due to its ability to combine anatomic imaging with the quantitative evaluation of tissue function at multiple scales such as macroscopic, microscopic, and molecular level with evolving additional advanced applications to characterize lesions.
Gadolinium-based intravenous contrast agents are widely used to accurately detect and characterize suspected intracranial lesions [1]. Most institutions commonly use contrast-enhanced T1WI sequence as the preferred method to assess intracranial lesions[2].
However, contrast-enhanced fluid-attenuated inversion recovery (FLAIR) can also be used to evaluate intracranial lesions [2]. FLAIR is an inversion recovery pulse sequence which essentially produces T2-weighted cerebrospinal fluid (CSF) nulled images. It is a special inversion recovery pulse with a long repetition time (TR) and echo time (TE) & an inversion time (TI) which nulls signals from the cerebrospinal fluid [2, 3].
Contrast agents accumulate in tissues and shortens both T1 and T2. But, shortening of T1 is primarily observed at therapeutic doses which is the phenomenon exploited to detect contrast enhancement of intracranial pathologies in contrast-enhanced T1WI[4]. Intracranial lesions which enhance on contrast-enhanced T1WI also enhance on contrast-enhanced FLAIR

imaging because contrast enhancement on FLAIR produces a mild T1 effect due to the long TI [2]. Post-contrast FLAIR images are useful in detecting meningeal pathologies and in various parenchymal pathologies, where sometimes intracranial pathologies are more conspicuous on contrast-enhanced FLAIR imaging as compared to contrast-enhanced T1WI [4].

This study intends to use contrast-enhanced FLAIR sequence as a diagnostic tool to evaluate intracranial pathologies and to understand its role for effective characterization of various intracranial pathologies.

Materials and Methods

A prospective study, 123 participants underwent MRI Brain with contrast to assess, characterize and diagnose various intracranial lesions. The study is conducted between October 2019 - July 2021 at the Department of Radiodiagnosis, JSS Hospital, and Mysuru.

Patients are selected according to inclusion criteria. The inclusion criteria include patients referred/admitted to our institution with clinical suspicion of intracranial pathologies and subjected to MR imaging. The exclusion criteria include contrast allergy, no contrast enhancement on both T1WI and FLAIR imaging, renal failure with estimated glomerular filtration rate (eGFR) <30mL/min/1.73m [2]. After obtaining relevant clinical history and consent from the patient, they are subjected to MR imaging using a 3.0 Tesla MRI Scanner (PHILIPS INGENIA 3.0 Tesla MRI Scanner). Images are acquired using standard scanning protocols. The scanning protocol includes 2D Sagittal T1, Coronal and axial T1, T2, Diffusion weighted imaging (DWI), Gradient Recalled Echo (GRE) and Fluid-attenuated inversion recovery (FLAIR) sequences. Post contrast axial and coronal T1 and post contrast axial FLAIR are acquired after administration of Gadodiamide (Contrast agent).

The MR imaging parameters for the FLAIR images are 4780–9000ms (TR), 93–124ms (TE), 1745– 2497ms (TI), 150° (flip angle) and 320–384 x 196–235 (matrix). The other parameters are as follows: section thickness of 5 mm with a 2 mm gap, field of view of 193 x 220 mm, number of excitations of 2; and the acquisition time of 2 minutes 33 seconds and 2 minutes 42 seconds, respectively. Axial CE-FLAIR imaging in all patients are performed immediately after the routine CE coronal and axial T1WI. Scanning of axial CE-T1WI and axial CE-FLAIR imaging are started at 2 minutes 40 seconds and 5 minutes after the injection of contrast material respectively.

Images are transferred to a dedicated workstation (Philips, Ingenuity workstation) for postprocessing using Philips FIBRETRAK (Philips Healthcare, Andover, Massachusetts, USA).

The participants are analyzed by age, gender, number of lesions observed for each participant, signal intensity pattern for all intracranial lesions on both post contrast sequences, comparison of degree of contrast enhancement of all intracranial lesions on both post contrast sequences, comparison between various intra-axial & extra-axial intracranial lesions on both post contrast sequences, comparison between various intracranial lesions based on their etiology on both post contrast sequences and comparison of each intracranial lesion on both post contrast sequences.

Calculation of the degree of contrast enhancement index (DCEI) is performed by placing region of interest (ROI) tool at site of lesion to measure signal intensity (SI) in pre- and post-contrast T1 and FLAIR images. Degree of contrast enhancement index is calculated as (DCEI): $I_D = I_b – I_a / I_a$. Where I_D is DCEI, I_a is the lesion signal intensity (SI) on pre-contrast images and I_b is the lesion SI on post-contrast images.

Data is entered in Microsoft Excel sheet and statistical analysis is done using IBM SPSS Statistics V25.0. Pearson, Wilcoxan and Spearman's Rho tests were used for comparison of the various parameters.

Results

The total range of the patients included in the study were between 8 days up to 86 years old. The majority of the patients included in the study were adults more than twenty years old with a total number of 106 patients out of 123 patients observed in this group. Whereas, the patients of age twenty years or less with a total count of only 17 out of 123 patients. The majority of the patients were in the 2nd to 4th decades of life making up 34% of the total cohort. The mean age was 42 years. The median age was 45 years. The standard deviation was 21 years with 25th percentile being 28 years old and 75th percentile being 60 years old. Based on gender, 65 patients were male (52.8% of the total cohort) and 58 patients were female (47.2% of the total cohort).

The number of lesions observed for each case on post contrast T1 is more than post contrast FLAIR as the maximum number of lesions observed are 132 and 70 lesions respectively [Table 1 and figure 1]. The minimum number of lesions observed for each case on post contrast T1 and post contrast FLAIR is 1 lesion. This suggests that for all of the various intracranial pathologies observed in this study, each of the intracranial pathology is identified on both sequences. The mean number of lesions observed for each case on post contrast T1 and post contrast FLAIR sequences are similar being approximately 3 lesions. The standard deviation for each case on post contrast T1 is 15 lesions. Whereas, the standard deviation for each case on post contrast FLAIR being 9 lesions. The 25th and 75th percentiles for each case on both post contrast T1 and post contrast FLAIR sequences being 1 lesion. The Pearson correlation for post contrast T1 and post contrast FLAIR sequences showed a p value of 0.01 and correlation coefficient of 0.972 suggesting a strong linear positive correlation between the number of lesions observed for each case between post contrast T1 and post contrast FLAIR sequences [Figure 2]. Thereby, suggesting that as the number of observed lesions increase on post contrast T1 then the number of observed lesions also increase on post contrast FLAIR sequences. However, the absolute number of lesions observed for each case being more conspicuous on post contrast T1 sequence as compared to post contrast FLAIR sequence.

The signal intensity pattern is similar on both sequences with only 1 lesion appearing hyperintense on post contrast T1 sequence and the corresponding lesion appearing heterointense on post contrast FLAIR sequence. The Wilcoxan test performed shows a p value of 0.18, hence suggesting that there is no significant difference of signal intensity pattern of the lesions on comparison between post contrast T1 and post contrast FLAIR sequences.

The mean, standard deviation and range for degree of contrast enhancement is greater on post contrast T1 than post contrast FLAIR sequence for intracranial pathologies in

this study with the Wilcoxan test depicting a significant p value of <0.0001 [Table 2 and figures 3 & 4]. Therefore, for all intracranial pathologies in general, the degree of contrast enhancement on post contrast T1 sequence is generally more markedly greater than the degree of contrast enhancement on post contrast FLAIR sequence. The Spearman's Rho correlation for degree of contrast enhancement for various intracranial pathologies in this study shows a significant p value at 0.01 level and correlation coefficient of 0.473 suggesting that there is a non-linear fair positive correlation between post contrast T1 and post contrast FLAIR sequences [Table 3 and figure 5]. Hence, as the degree of contrast enhancement increases on post contrast T1 sequence then the degree of contrast enhancement would also increase on post contrast FLAIR sequence albeit being a weak correlation and the rate of increase being a non-linear relationship.

Intra-axial and extra-axial intracranial pathologies were observed on post contrast T1 and post contrast FLAIR sequences. The total number of extra-axial intracranial lesions observed are 72 out of 138 lesions comprising 52.2% of the total number of intracranial lesions. The total number of intra-axial intracranial lesions observed are 66 out of 138 lesions comprising 47.8% of the total number of intracranial lesions. The highest degree of contrast enhancement is significant for post contrast T1 sequence (as compared to post contrast FLAIR sequence) for both intra-axial and extra-axial intracranial lesions as the p value is <0.0001 for both [Table 4].

According to the final radiological diagnosis, lesions are categorised based on their aetiology. The most common etiology of intracranial lesions observed in the study was neoplastic comprising a total of 90 out of 138 intracranial lesions forming 65.2% of all intracranial pathologies. The second most common aetiology of intracranial lesions observed in the study was infectious comprising a total of 46 out of 138 intracranial lesions forming 33.3% of all intracranial pathologies. The least common intracranial lesions observed were demyelination and postoperative lesions with a total of 1 lesion each out of 138 intracranial lesions forming 0.7% each of all intracranial pathologies. Of all the intracranial pathologies, only neoplasms showed a significant degree of contrast enhancement on post contrast T1 sequence (as compared to post contrast FLAIR sequence) with a p value of <0.0001 [Table 5]. The degree of contrast enhancement on both sequences for infectious intracranial pathologies was not significant as p value is 0.3. The degree of contrast enhancement for demyelination and post-operative lesions could not be analyzed due to inadequate sample size with only 1 lesion each [Table 5].

A total of 33 intracranial pathologies were observed in the study [Table 6]. The most common intracranial pathology was meningitis with a total of 26 cases comprising 18.8% of all the intracranial pathologies. The second most common intracranial pathology was meningioma with a total of 22 cases comprising 15.9% of all the intracranial pathologies. The rest of the intracranial pathologies comprised less than 10% each of all intracranial pathologies. Of all the intracranial pathologies, the Wilcoxan test was applied to 13 intracranial pathologies to ascertain the p value [Table 7]. The rest of the twenty intracranial pathologies could not be assessed due to the low sample size of less than 3 lesions for each intracranial pathology. Of the 13 intracranial pathologies assessed using Wilcoxan test, only 3 intracranial pathologies have shown a higher degree of contrast enhancement on post contrast FLAIR sequence (as compared to post contrast T1 sequence). The three intracranial pathologies which have shown a higher degree of contrast enhancement on post contrast FLAIR sequence (as compared to post contrast T1 sequence) are meningitis, hemangioblastoma and toxoplasmosis. However, none of the three intracranial pathologies have shown a significant p value of <0.05. Of the 13 intracranial pathologies assessed using Wilcoxan test, 10 intracranial pathologies have shown a higher degree of contrast enhancement on post contrast T1 sequence (as compared to post contrast FLAIR sequence). The ten intracranial pathologies which have shown a higher degree of contrast enhancement on post contrast T1 sequence (as compared to post contrast FLAIR sequence) are meningioma, schwannoma, cerebral metastasis, cerebral abscess, oligodendroglioma, low grade glioma, GBM, high grade glioma, astrocytoma and meningeal metastasis. Of the ten intracranial pathologies showing a greater degree of contrast enhancement on post contrast T1 sequence, five intracranial pathologies have shown a significant p value of <0.05. They are meningioma (<0.0001), schwannoma (0.003), cerebral metastasis (0.005), low grade glioma (0.043) and GBM (0.043).

Tables

Table 1: Total number of lesions on T1PC and CE-flair

	T1PC		CE-FLAIR	
Number of lesions	**Count**	**Column N %**	**Count**	**Column N %**
1.0	98	79.7%	98	79.7%
2.0	12	9.8%	12	9.8%
3.0	3	2.4%	3	2.4%
4.0	2	1.6%	2	1.6%
5.0	1	0.8%	1	0.8%
6.0	3	2.4%	3	2.4%
9.0	1	0.8%	1	0.8%
17.0	1	0.8%	1	0.8%
63	0	0	1	0.8%
78	0	0	1	0.8%
105.0	1	0.8%	0	0
132.0	1	0.8%	0	0

Table 2: Highest degree of contrast enhancement for all the intracranial pathologies on post contrast T1 and post contrast FLAIR sequences

Highest Degree of contrast enhancement	Mean	SD	Median	Q1	Q3
T1PC	1.37	1.60	0.99	0.40	1.71
CEFLAIR	0.65	1.16	0.41	0.21	0.78

P<0.0001 (Wilcoxan test)

Table 3: Spearman's Rho correlation for degree of contrast enhancement in post contrast T1 and post contrast FLAIR sequences for all intracranial pathologies in this study

Correlations			
		Highest Degree of contrast enhancement T1PC	**Highest Degree of contrast enhancement CEFLAIR**
Spearman's Rho	Correlation Coefficient	1.000	.473**
	Sig. (2-tailed)	.	.000
	N	138	138

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4: Degree of contrast enhancement in T1PC and CE-FLAIR for intra-axial and extra-axial intracranial pathologies

		n	**Median**	**Q1**	**Q3**	**p**
Extra Axial	Highest Degree of contrast enhancement T1PC	72	1.16	0.61	1.98	<0.0001
	Highest Degree of contrast enhancement CEFLAIR	72	0.61	0.35	1.01	
Intra Axial	Highest Degree of contrast enhancement T1PC	66	0.63	0.20	1.38	<0.0001
	Highest Degree of contrast enhancement CEFLAIR	66	0.25	0.10	0.48	

Table 5: Degree of contrast enhancement in T1PC and CE-FLAIR for various intracranial pathologies based on etiology

Cause		**n**	**Median**	**Q1**	**Q3**	**p**
Infectious	Highest Degree of contrast enhancement T1PC	46	0.54	0.22	1.38	0.3
	Highest Degree of contrast enhancement CEFLAIR	46	0.48	0.14	1.04	
Neoplasms	Highest Degree of contrast enhancement T1PC	90	1.14	0.50	1.82	<0.0001
	Highest Degree of contrast enhancement CEFLAIR	90	0.37	0.21	0.66	
Demyelination	Highest Degree of contrast enhancement T1PC	1	1.91	1.91	1.91	
	Highest Degree of contrast enhancement CEFLAIR	1	0.32	0.32	0.32	
Postoperative	Highest Degree of contrast enhancement T1PC	1	1.05	1.05	1.05	
	Highest Degree of contrast enhancement CEFLAIR	1	4.73	4.73	4.73	

Table 6: Various intracranial pathologies

Diagnosis	**Count**	**Column N %**
Meningitis	26	18.8%
Meningioma	22	15.9%
Schwannoma	12	8.7%
Cerebral metastasis	10	7.2%
Cerebral abscess	9	6.5%
Oligodendroglioma	5	3.6%
Low grade glioma	5	3.6%
GBM	5	3.6%
High grade glioma	4	2.9%
Toxoplasmosis	3	2.2%
Meningeal metastasis	3	2.2%
Hemangioblastoma	3	2.2%
Astrocytoma	3	2.2%
Pituitary Macroadenoma	2	1.4%
Neurocytoma	2	1.4%
NCC	2	1.4%
Ependymoma	2	1.4%
Encephalitis	2	1.4%
Craniopharyngioma	2	1.4%
Cerebritis	2	1.4%
Cavernous hemangioma	2	1.4%
Tuberculoma	1	0.7%
Subdural empyema	1	0.7%
Sturge Weber syndrome	1	0.7%
Pleomorphic Xanthoastrocytoma	1	0.7%
Pineocytoma	1	0.7%
Pineoblastoma	1	0.7%
Paraganglioma	1	0.7%
Meduloblastoma	1	0.7%
Dural enhancement - Post-operative.	1	0.7%
Demyelination	1	0.7%
Cavernous sinus hemangioma	1	0.7%
? Fungal/ tubercular abscess	1	0.7%
Total	138	100.0%

Table 7: Degree of contrast enhancement for various intracranial pathologies

Diagnosis		Count	Median	Q1	Q3	P value
Meningitis	Highest Degree of contrast enhancement T1PC	26	0.58	0.36	1.82	0.26
	Highest Degree of contrast enhancement CEFLAIR	26	0.93	0.48	1.53	
Meningioma	Highest Degree of contrast enhancement T1PC	22	1.31	0.90	1.71	<0.0001
	Highest Degree of contrast enhancement CEFLAIR	22	0.32	0.25	0.53	
Schwannoma	Highest Degree of contrast enhancement T1PC	12	2.08	1.56	2.97	0.003
	Highest Degree of contrast enhancement CEFLAIR	12	0.79	0.61	1.10	
Metastasis	Highest Degree of contrast enhancement T1PC	10	0.78	0.32	1.42	0.005
	Highest Degree of contrast enhancement CEFLAIR	10	0.32	0.09	0.42	
Intracerebral abscess	Highest Degree of contrast enhancement T1PC	9	0.16	0.04	0.51	0.4
	Highest Degree of contrast enhancement CEFLAIR	9	0.11	0.06	0.14	
Oligodendroglioma	Highest Degree of contrast enhancement T1PC	5	0.43	0.17	0.47	0.22
	Highest Degree of contrast enhancement CEFLAIR	5	0.07	0.03	0.21	
Low grade glioma	Highest Degree of contrast enhancement T1PC	5	0.76	0.24	0.98	0.043
	Highest Degree of contrast enhancement CEFLAIR	5	0.12	0.04	0.13	
GBM	Highest Degree of contrast enhancement T1PC	5	1.49	1.15	1.90	0.043
	Highest Degree of contrast enhancement CEFLAIR	5	0.61	0.37	0.62	
High grade glioma	Highest Degree of contrast enhancement T1PC	4	1.00	0.63	1.05	0.14
	Highest Degree of contrast enhancement CEFLAIR	4	0.35	0.28	0.51	
Diagnosis		**Count**	**Median**	**Q1**	**Q3**	**P value**
Astrocytoma	Highest Degree of contrast enhancement T1PC	3	1.82	0.17	1.90	0.3
	Highest Degree of contrast enhancement CEFLAIR	3	0.21	0.21	0.93	
Toxoplasmosis	Highest Degree of contrast enhancement T1PC	3	0.24	0.18	1.38	0.28
	Highest Degree of contrast enhancement CEFLAIR	3	0.33	0.02	0.48	
Hemangioblastoma	Highest Degree of contrast enhancement T1PC	3	0.44	0.05	1.85	0.9
	Highest Degree of contrast enhancement CEFLAIR	3	0.73	0.37	1.18	
Meningeal metastasis	Highest Degree of contrast enhancement T1PC	3	1.05	0.89	1.24	0.1
	Highest Degree of contrast enhancement CEFLAIR	3	0.49	0.49	0.66	

Discussion

Gadolinium contrast agents are the mainstay for contrast enhancement in MRI imaging. The contrast enhancement for pathological lesions in the brain follow two main types of mechanisms i.e. the intravascular and interstitial mechanisms[5]. Hence, the enhancement depends on the alterations in the blood-brain barrier and/or relative increase in blood volume or blood flow owing to various pathological processes [5].

The contrast enhancement on post contrast T1 and FLAIR sequences can be used to assess various intracranial pathologies. The administration of IV gadolinium contrast agent produces T1 shortening effect which is responsible for the enhancement on post contrast images at clinical doses of gadolinium contrast [2, 6]. The enhancement on post contrast FLAIR sequence can be either due to T2 lengthening or T1 shortening, hence to evaluate the T1 shortening effect both pre-contrast and post-contrast FLAIR images should be obtained [2, 7].

The purpose of this study was to evaluate the various intracranial pathologies on post contrast T1 and post contrast FLAIR sequences and to identify their enhancement on both sequences to ascertain the lesion detection and characterization.

A total of 138 lesions were evaluated in 123 patients and 33 intracranial pathologies were identified. The majority of patients were adults above 20 years old with only few patients less than 20 years old. Hence, this study is more significant for the adult population and their corresponding pathologies than the paediatric population. The gender distribution was almost similar.

The current study showed that absolute number of lesions were detected more in post contrast T1 than post contrast FLAIR sequence. The mean number of lesions detected being similar on both sequences. There was a strong positive linear correlation between the numbers of intracranial pathologies detected on both sequences suggesting that lesions detected on post contrast T1 sequence should also be detected on post contrast FLAIR sequence. The study by Bhargava *et al.* [8] showed that lesions which did not enhance on post contrast T1 sequence have also not enhanced on post contrast FLAIR sequence. However, the absolute number of lesions are detected more in post contrast T1 as opposed to post contrast FLAIR sequence. The likely explanation for this can be due to better anatomical detail on post contrast T1 and due to perilesional edema. Edema appears hyperintense on T2 & FLAIR and hypointense on T1 sequences. Hence, as enhancement appears hyperintense on both sequences, the enhancing lesions associated with edema should be better delineated and identified on conventional post contrast T1 sequence rather than post contrast FLAIR sequence. All the lesions have also shown a similar contrast enhancement pattern on post contrast images with no significant statistical difference between them.

The degree of contrast enhancement for an intracranial pathology in general showed greater enhancement on post contrast T1 rather than post contrast FLAIR sequence with a significant statistical difference. However, the degree of contrast enhancement for any given lesion is complex and varies depending on the concentration of gadolinium, the location of the lesion, disruption of the blood-brain barrier, the blood volume & blood flow for the specific lesion and various other factors. Various studies have demonstrated that post contrast FLAIR sequences show better degree of contrast enhancement and are more sensitive in lower concentrations of gadolinium for the same lesion i.e. four times lower concentration than post contrast T1 sequences [2, 7, 9, 10]. The study by Bhargava *et al*. [8] suggested that solid and cystic components of the lesions were better assessed on

post contrast FLAIR than post contrast T1 sequences. Furthermore, other studies suggested that the degree of contrast enhancement for post contrast T1-FLAIR sequence was superior to post contrast T1 sequence alone for enhancing hyperintense lesions and non-enhancing cystic components within the lesion [11, 12]. Hence, it is important to understand that various mechanisms exist for contrast enhancement for any given lesion and the contrast enhancement for each specific lesion should be studied comprehensively taking into account the various factors and imaging protocols for that specific lesion. This study also shows that there is only a fair non-linear correlation which exists between the degrees of contrast enhancement for various intracranial pathologies on both sequences. Thereby, suggesting that the contrast enhancement mechanism is complex and is dependent on various factors as discussed above.

The current study also suggests that the degree of contrast enhancement is more conspicuous 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. Although, various studies [2, 6, 7, 10, 11, 13-18] have shown the contrary whereby suggesting that those lesions which are extra-axial and those lesions which are abutting the CSF to be more conspicuous on contrast enhanced FLAIR sequences (as compared to contrast enhanced T1 sequence). The study by Bhargava *et al*. [8] is inconclusive for extra-axial lesions in both sequences. However, as there are a wide variety of extra-axial tumors, it is important to consider the individual lesion for the degree of contrast enhancement rather than all the extra-axial intracranial pathologies as a whole.

The various intracranial pathologies have also been stratified into their etiology such as infectious, neoplasms, demyelination and post-operative. However, the demyelinative and post-operative lesions could not be assessed due to the low sample size. Of the infectious and neoplastic lesions, the degree of contrast enhancement is more conspicuous on post contrast T1 sequence (as opposed to post contrast FLAIR sequence) for neoplastic lesions and the difference being statistically significant. Whereas, the degree of contrast enhancement for infectious lesions are inconclusive between post contrast T1 and post contrast FLAIR sequences.

Of all the 138 lesions observed in 123 individuals, 33 intracranial pathologies were identified. However, only 13 intracranial pathologies were assessed for their degree of contrast enhancement as there was inadequate sample size for the rest of the intracranial pathologies.

The results demonstrated that 3 lesions showed more conspicuous contrast enhancement on post contrast FLAIR sequence than post contrast T1 sequence. They are infectious meningitis [figure 6], hemangioblastoma and toxoplasmosis. However, the 3 lesions did not show a statistically significant difference between both sequences. Hence, further evaluation with more sample size should be conducted to establish if there is a significant difference in contrast enhancement for post contrast FLAIR sequence than post contrast T1 sequence. Furthermore, significant literature exists including Lee *et al*. [2], Mahale *et al*. [11], Kamr *et al*. [13], Fukoka *et al*. [14, 15], Ahmad *et al*. [16], Parmar *et al*. [7] and Splendiani *et al*. [10] suggesting that contrast enhanced FLAIR sequence is superior to contrast enhanced T1 for infectious meningitis.

The case report by Chen *et al*. [19] shows that for hemangioblastoma contrast enhanced FLAIR sequence is superior to contrast enhanced T1 sequence as the cyst wall of the lesion is responsible for the significant enhancement on the former sequence with no enhancement on the latter sequence. However, the case report showed that this increased enhancement on FLAIR was secondary to a lower concentration of gadolinium in the cyst wall. However, on dynamic contrast enhancement there was signal loss from the cyst wall. Thereby, suggesting that lower contrast of gadolinium demonstrates more conspicuous contrast enhancement on contrast enhanced FLAIR sequence than contrast enhanced T1 for intracranial pathologies as previously discussed.

Ten intracranial pathologies showed more conspicuous contrast enhancement on post contrast T1 sequence than post contrast FLAIR sequence. They are meningioma [figure 7], schwannoma [figure 8], cerebral metastasis [figure 9], cerebral abscess [figure 10], oligodendroglioma, low grade glioma [figure 11], GBM [figure 12], high grade glioma, astrocytoma and meningeal metastasis. Of these 10 intracranial pathologies, only 5 intracranial pathologies showed a statistically significant difference between both sequences namely meningioma, schwannoma, cerebral metastasis, low grade glioma and GBM. Hence, further evaluation with more sample size should be conducted to establish if there is a significant difference in contrast enhancement on post contrast T1 sequence than post contrast FLAIR sequence for rest of the 5 intracranial pathologies.

Of the 5 intracranial pathologies showing a significant statistical difference on both sequences, 2 are extra-axial (meningioma and schwannoma) and 3 being intra-axial (cerebral metastasis, low grade glioma and GBM).

Despite meningiomas showing higher degree of contrast enhancement on post contrast T1 sequence, post contrast FLAIR sequence is also useful for evaluation of meningiomas as they have dual vascular supply [2]. The central portion of the lesion predominantly enhances more conspicuously on post contrast T1 due to the significant vascularity (supplied by meningeal arteries) and high concentration of gadolinium incurring signal loss on T2-FLAIR sequence [2]. Whereas, the periphery of the lesion corresponds to the vascular capsule (pial arteries) which has a lower concentration of gadolinium, therefore the border of the lesion which abuts the CSF is conspicuous on post contrast FLAIR sequences [2]. However, the dual vascular nature of the meningioma is not clearly demonstrated on smaller tumors (<2cm) [2]. Schwannomas also show more conspicuous enhancement on post contrast T1 than post contrast FLAIR sequence. However, post contrast FLAIR sequence is useful as the extra-axial lesion is better delineated and also the dural tail of the lesion is more conspicuous on post contrast T2-FLAIR sequence [11].

Cerebral metastasis and GBM both showed more conspicuous enhancement on post contrast T1 sequence. However, delayed post contrast FLAIR sequence can be used to differentiate between the two pathologies when imaging diagnosis on post contrast T1 sequence is inconclusive, where a greater degree of perilesional edema is present in case of metastatic disease [20]. Furthermore, better anatomical delineation of the lesion can be visualised on post contrast T1 FLAIR sequence (as compared to post contrast T1 sequence alone) due to improved contrast

between gray & white matter and between gray matter & lesion especially in intensely enhancing lesions [11]. Whereas, post contrast T2 FLAIR sequence would show better delineation between the CSF and the lesion [11].

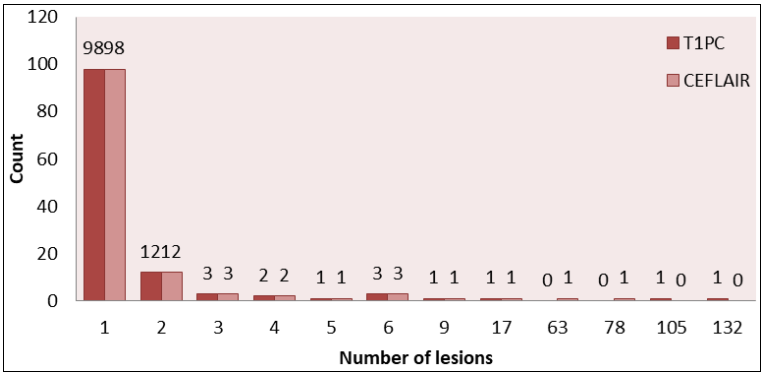


Fig 1: Total number of lesions on T1PC and CE-FLAIR

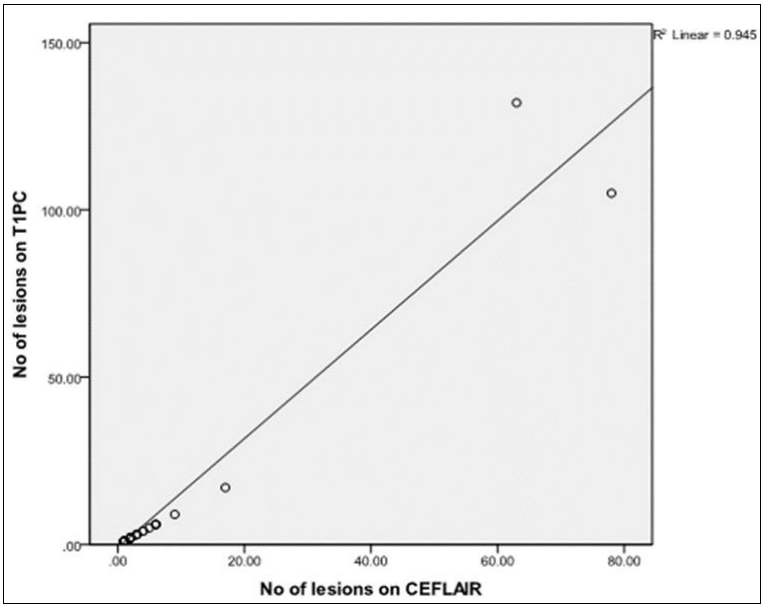


Fig 2: Pearson correlation for total number of lesions on T1PC and CE-FLAIR

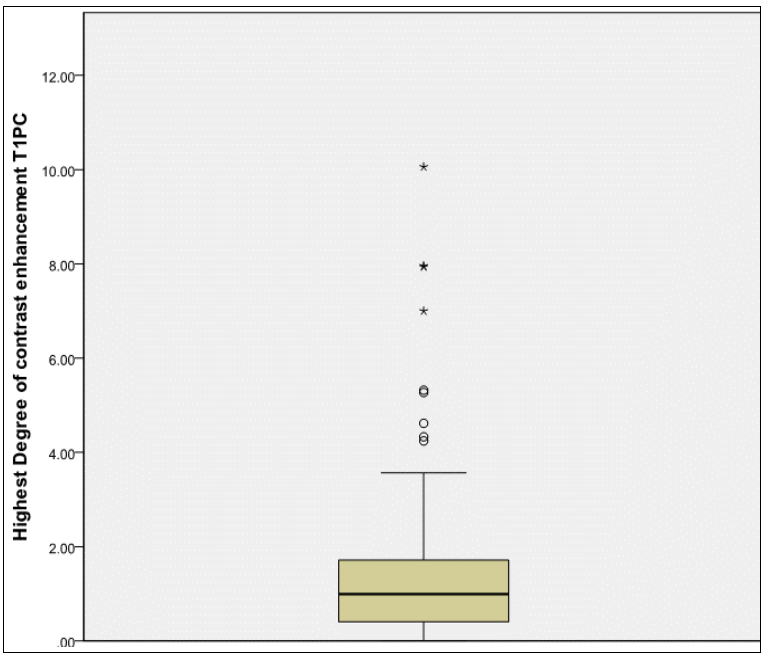


Fig 3: Box and Whisker plot depicting graphical representation of highest degree of contrast enhancement for all the intracranial pathologies on post contrast T1 sequence

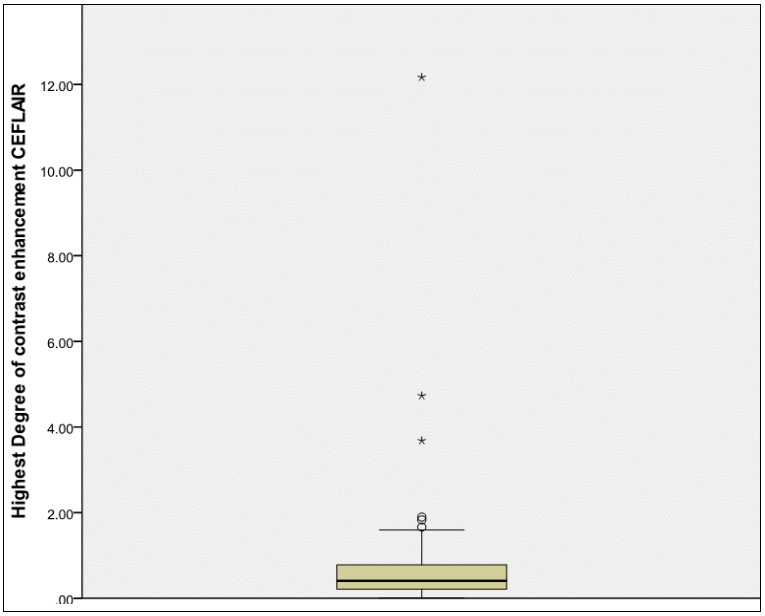


Fig 4: Box and Whisker plot depicting graphical representation of highest degree of contrast enhancement for all the intracranial pathologies on post contrast FLAIR sequence

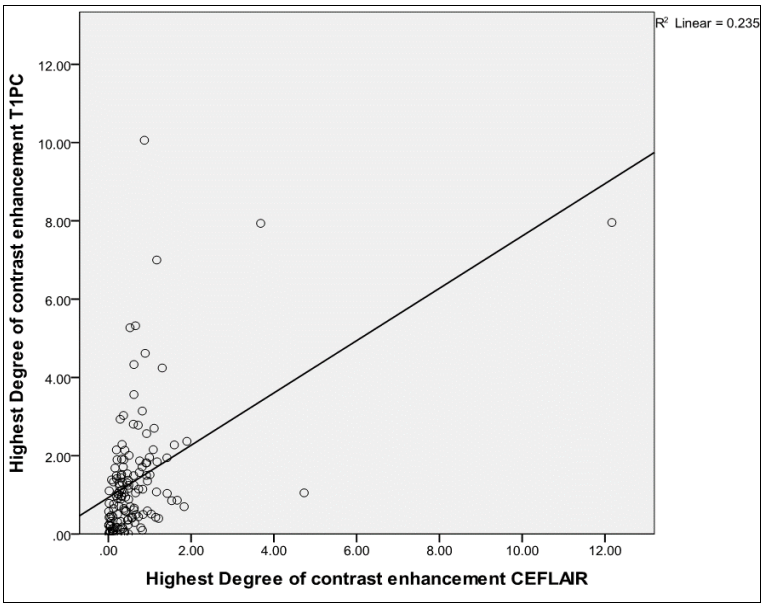
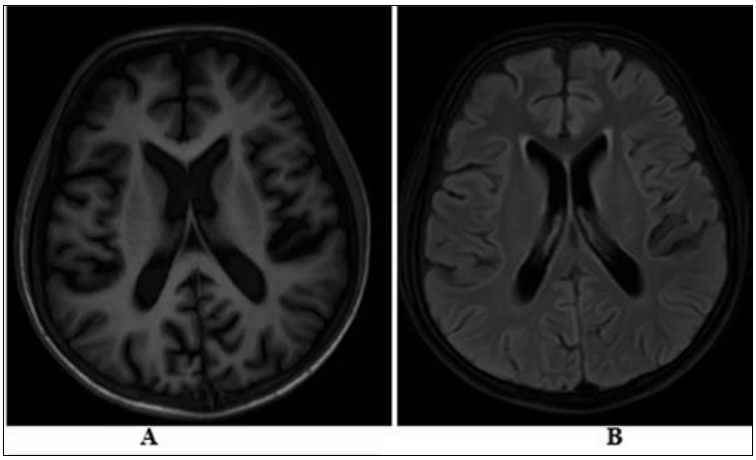


Fig 5: Spearman's Rho correlation for degree of contrast enhancement in post contrast T1 and post contrast FLAIR sequences for all intracranial pathologies in this study



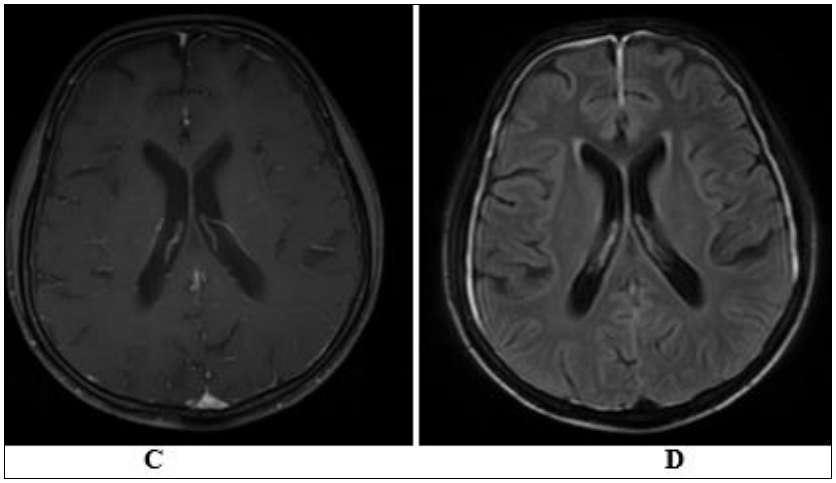


Fig 6: Cryptococcal meningitis in a 21 year old male patient who is a known case of retroviral disease presented with history of headache since 1 week showing pachymeningeal type of enhancement with PC-FLAIR showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	7.958
PC-FLAIR	12.167

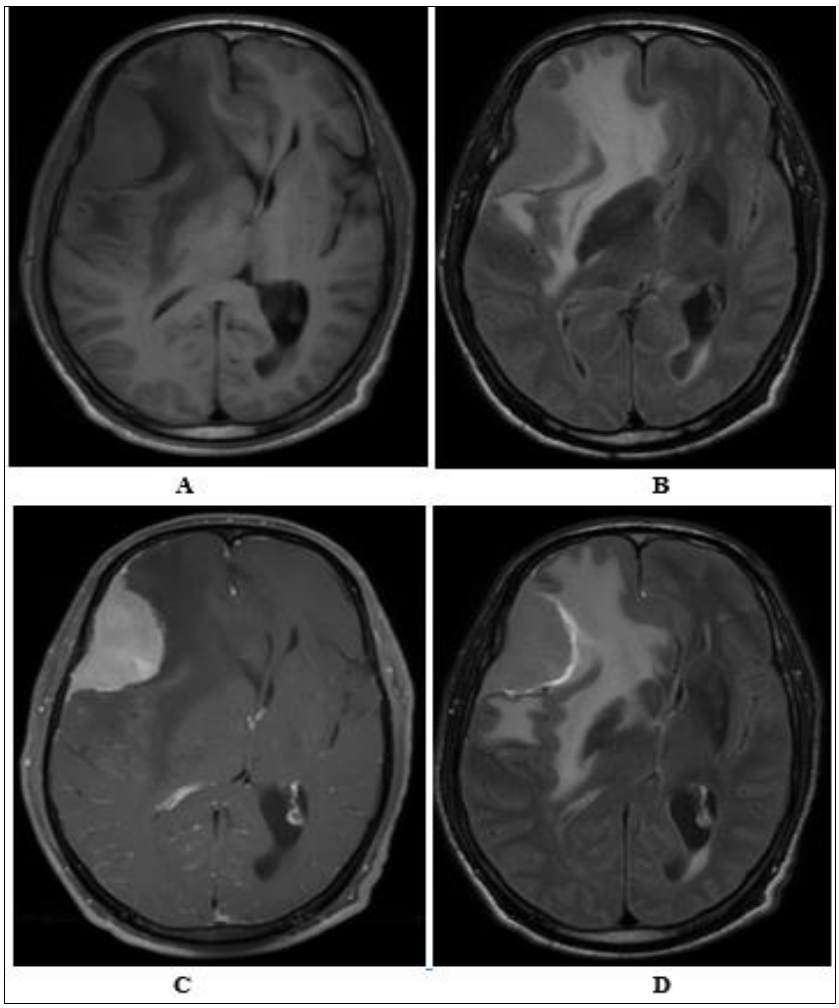


Fig 7: Right sphenoid wing meningioma in a 64 year old male patient presented with history of left hemiparesis since 2 months showing meningioma with dural tail/ dural flair sign and PC-T1 showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	1.490
PC-FLAIR	0.194

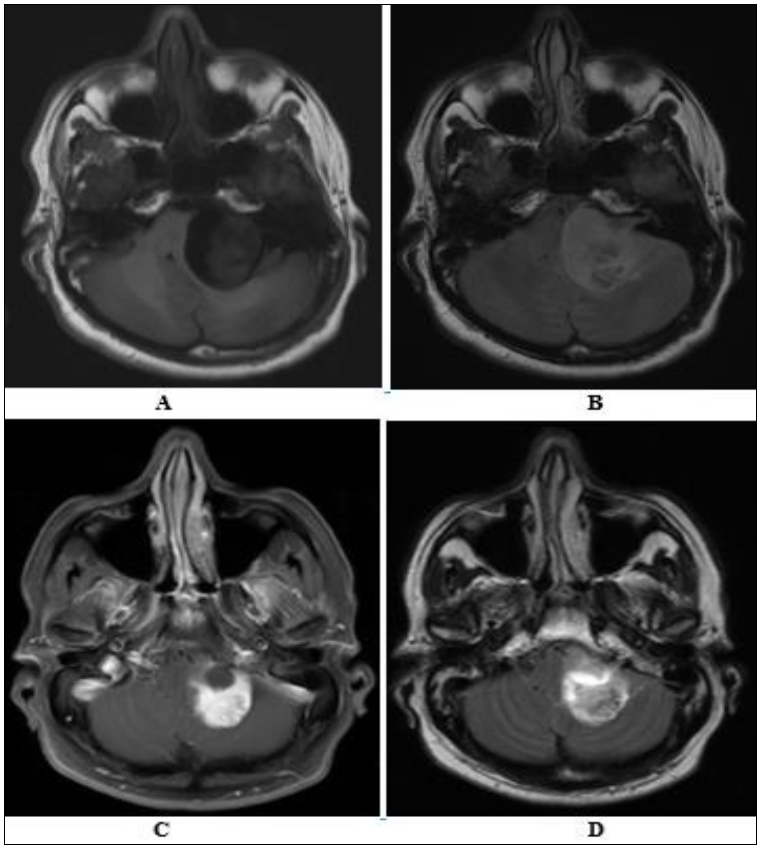


Fig 8: Left vestibular schwannoma in a 45 year old male patient presented with history of decreased left ear hearing, numbness of left upper face, swaying while walking and nystagmus showing extra-axial type of enhancement with dural tail/ dural flair sign and PC-T1 showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	10.059
PC-FLAIR	0.871

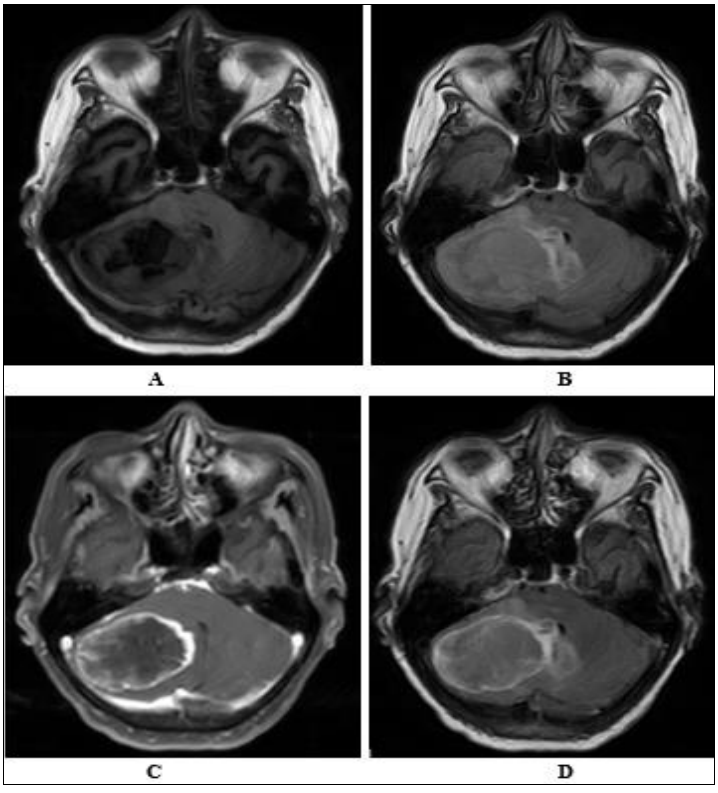


Fig 9: Metastasis in right cerebellar hemisphere in an 86 year old female patient who is a known case of Carcinoma breast presented with history of right hemiparesis showing ring enhancing type of enhancement with PC-T1 showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	2.289
PC-FLAIR	0.331

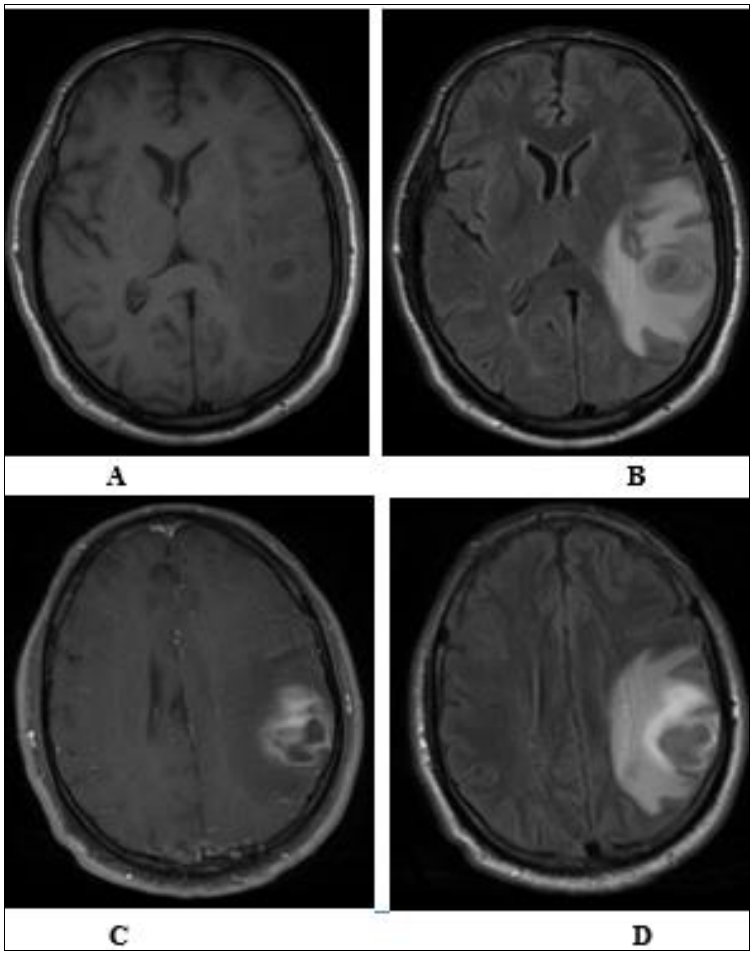


Fig 10: Left parietal lobe tubercular abscess in a 46 year old male patient who is a known case of pulmonary TB on irregular treatment showing ring enhancing type of enhancement with PC-T1 showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	0.509
PC-FLAIR	0.223

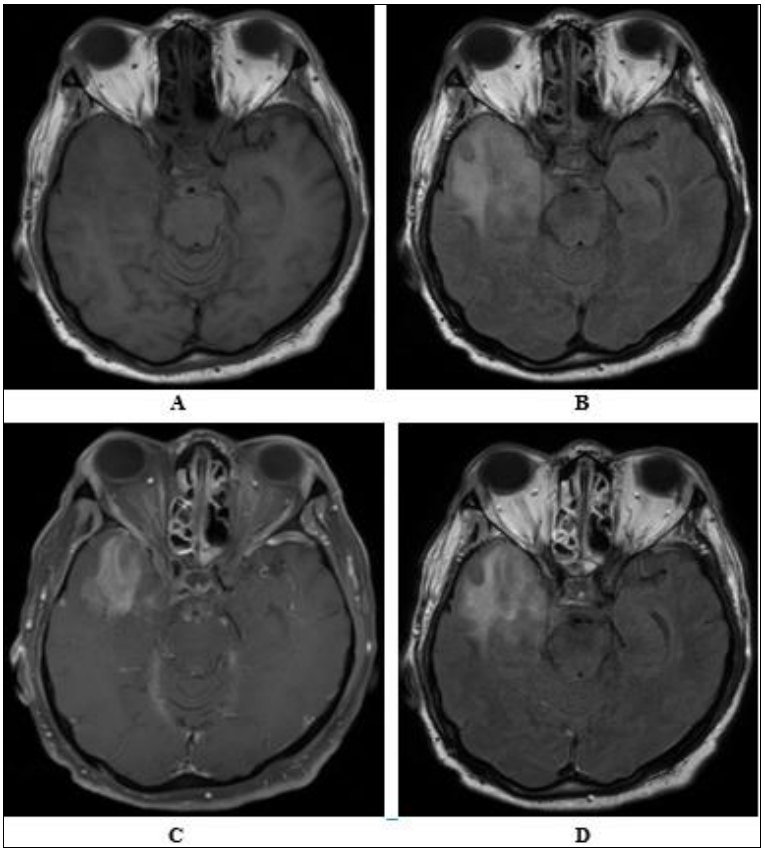


Fig 11: Right temporal lobe low grade glioma in a 73 year old male patient presented with history of altered sensorium and complex partial seizures showing subcortical type of enhancement with PC-T1 showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	0.764
PC-FLAIR	0.129

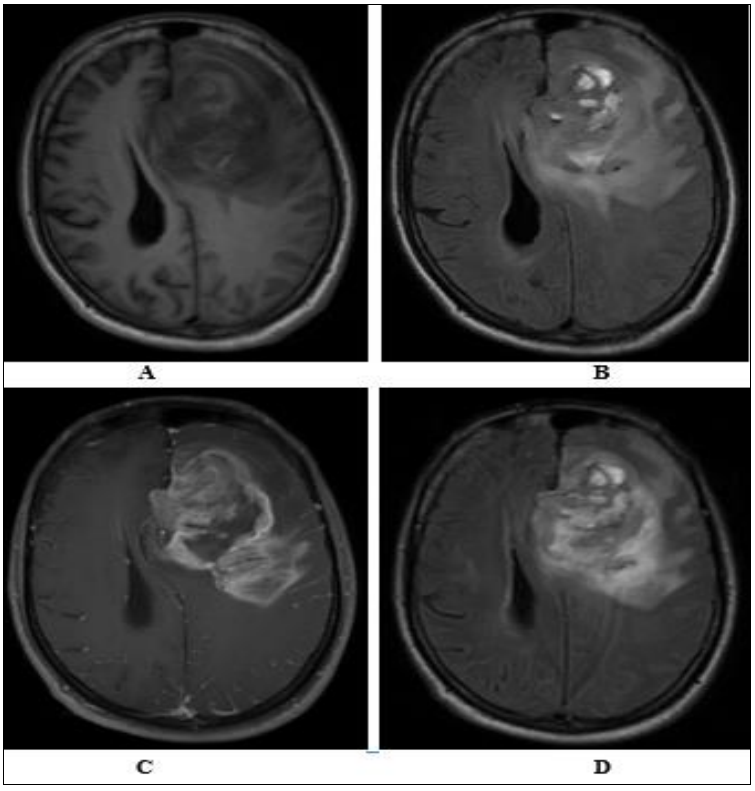


Fig 12: Left frontal lobe GBM in a 45 year male patient presented with history of slurring of speech and right sided weakness since 1 month showing subcortical type of enhancement with PC-T1 showing greater degree of enhancement. A: Pre contrast T1WI. B: Pre contrast FLAIR. C: Post contrast T1-FS. D: Post contrast FLAIR

Sequence	Degree of contrast enhancement
PC-T1WI	1.492
PC-FLAIR	0.612

Conclusion

The following conclusions were drawn from the study of 123 participants with various intracranial pathologies:

- Additional information for characterization and delineating various intracranial pathologies can be obtained by incorporating contrast enhanced FLAIR sequence especially if the lesion abuts the CSF.
- The degree of contrast enhancement varies depending on various factors and it is important to tailor the imaging sequences and imaging protocols required for characterizing specific intracranial pathologies.
- Despite the study showing that the overall degree of contrast enhancement to be superior for contrast enhanced T1 sequences for the majority of the lesions, complete lesion pathology cannot be assessed on this sequence alone. Hence, it is important to incorporate other novel contrast enhanced sequences (such as contrast enhanced FLAIR sequence) for adequate and accurate characterization of the lesion thereby improving diagnosis and treatment protocols.
- Therefore, contrast enhanced FLAIR sequence is an important adjunct for imaging of the various intracranial pathologies and should be incorporated for evaluating the same.

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