ORIGINAL RESEARCH PAPER

Radiology

COMPARISON OF POST-CONTRAST 3D-T1-SPACE, 3D-T2-FLAIR AND 3D-T1-MPRAGE MR SEQUENCES IN THE EVALUATION OF MENINGEAL AND BRAIN PARENCHYMAL PATHOLOGIES

KEY WORDS: PC 3D-T1-SPACE,PC 3D-T2-FLAIR,PC 3D-T1-MPRAGE

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ABSTRACT

Background and purpose: The purpose of this study was to assess the value added by contrast-enhanced three-dimensional (3D) -T2 fluid-attenuated inversion recovery sequence (FLAIR) and 3D-T1 sampling perfection with application optimized contrast using different flip-angle evolutions(SPACE) sequences to conventional post-contrast 3D-T1 magnetisation prepared rapid gradient-echo (MPRAGE) images in the evaluation of meningeal and brain parenchymal diseases.

Materials and methods: A total of 60 patients with magnetic resonance imaging (MRI) findings suggestive of infectious / inflammatory / metastatic parenchymal and/or meningeal abnormalities, were selected from patients who underwent MRI brain with intravenous (IV) contrast from March 2019 to Nov 2019.All the patients had their diagnosis confirmed by histopathological or microbiological studies, as deemed appropriate. Two radiologists independently assessed the presence of additional information on post-contrast (PC) 3D-T2-FLAIR and 3D-T1-SPACE images and compared them with PC 3D-T1-MPRAGE images.

Results: Both reviewers found that post contrast 3 D-T1-SPACE provided more additional information than post contrast 3D-T1-MPRAGE in the evaluation of brain parenchymal and supratentorial meningeal abnormalities.PC 3D-T2-FLAIR is an excellent tool in the evaluation of intratentorial leptomeningeal abnormalities and identifying the scolex in patients with neurocysticercosis (NCC), presenting with ring enhancing lesions.

INTRODUCTION:

Post-contrast (PC) Magnetic Resonance (MR) brain imaging plays an important role in the study of various infectious ,inflammatory and neoplastic brain pathology. Contrast enhancement in the central nervous system is the result of combination of two processes, namely intravascular or vascular enhancement and extravascular or interstitial enhancement.Contrast leakage into cerebrospinal fluid (CSF) may occur in areas of meningeal inflammation, reflecting the increase in permeability of meningeal vasculature ,secondary to breakdown of blood-brain or blood-CSF barrier.

The most commonly used post Gadolinium based contrast agent (GBCA) sequence is 3D-T1- MPRAGE. Though it provides good grey-white matter differentiation , concomitant enhancement of cortical vessels may prove problematic when assessing meningeal enhancement. Splendiani et al have shown that PC 3D-T1-MPRAGE sequence has low sensitivity (50%) in detecting infectious meningitis.[2] Several other studies have shown that small lesions and meningeal abnormalities may be missed on PC 3D-T1-MPRAGE sequence. Mugler et al suggested that since lesions enhanced less on PC 3D-T1-MPRAGE compared to spin echo sequences , there is a possibility of missing lesions on PC 3D-T1-MPRAGE sequences.[3]

Two sequences that appear as promising alternatives to PC 3D-T1-MPRAGE include PC 3D-T1- SPACE and PC 3D-T2-FLAIR. SPACE is a 3D fast spin-echo sequence that is not affected by intralesional calcium deposits.This may prove useful in the assessment of disease activity in the case of granulomatous lesions.Kato et al reported more conspicuity and increased detectability of brain metastasis using PC 3D-T1-SPACE.[4]

Another sequence that does not find a place routinely in the post contrast imaging protocol is the 3D- T2-FLAIR sequence. Fukoaka et al have shown that PC 3D-T2-FLAIR provides more information on leptomeningeal enhancement than PC T1-w images.[5] In vitro phantom studies by Mamourian et al , have shown that gadolinium effects were evident on FLAIR images at a concentration four times lower than those on T1-weighted images.[6] Hence we sought to evaluate whether PC 3D-T1-SPACE and PC 3D-T2-FLAIR were viable alternatives to PC 3D-T1-MPRAGE.

AIMS AND OBJECTIVES:

To compare and evaluate the diagnostic efficacy of post-contrast 3D-T1-SPACE, 3D-T2-FLAIR and 3D-T1-MPRAGE with respect to

1. Meningeal enhancement.
2. Parenchymal lesions.
3. Identification of scolex

And to find out which among the three sequences best demonstrates , each abnormal enhancement pattern.

MATERIALS AND METHODS:

The study was carried out at Barnard Institute of Radiology, Madras Medical College, Chennai. Our department protocol was formulated to include all three 3D post-contrast sequences(T1-SPACE, T2-FLAIR, T1 MPRAGE) in all patients referred for MRI Brain studies with IV contrast. It was decided to subject data thus obtained for retrospective analysis.

Inclusion criteria:

Patients who underwent MRI brain with IV contrast from March 2019 to Nov 2019, with MR findings suggestive of infectious / inflammatory / metastatic parenchymal and/or meningeal abnormalities.

Exclusion criteria:

Patients in whom final diagnosis could not be correlated with microbiological / biochemical / pathological investigations.

Patients with solitary parenchymal lesion suggestive of primary neoplasm were excluded from the study.

Patients with extra-axial neoplasms were also excluded from the study.

MR protocol:
All the studies were done in 3 Tesla MRI SIEMENS SKYRA – Erlangen Germany. All the patients underwent non-contrast MRI brain followed by post-contrast MR Brain imaging.

Even though the acquisition time of 3D sequences is long, the 3D sequences provide 3D volume data with isotropic information, thus allowing thinner sections in any imaging plane; this eliminates partial volume effects in the case of smaller lesions. Randomisation of the order of the post-contrast sequences was done, to avoid bias resulting from time dependent decrease in blood Gadolinium concentration, with increasing time after injection.

Table 1:MR Sequence Parameters

PARAMETERS	3D-T1-SPACE	3D-T2-FLAIR	3D-T1-MPRAGE
Repetition time (TR)	700 ms	5000 ms	1800 ms
Time to echo(TE)	11.0 ms	388 ms	2.32 ms
Inversion time	-	2000 ms	900 ms
Imaging time	5 min 07s	4 min 47s	3 min 34s
Field of view	250 x 250 mm	250 x 250 mm	240 x 240 mm
Thickness	0.9 mm thick sections	0.9 mm thick sections	0.9 mm thick sections

Image evaluation: Images were evaluated separately by two radiologists , each with 5 to 6 yrs experience .The presence of additional information on either PC 3D-T2-FLAIR or PC 3D-T1-SPACE was compared separately with PC 3D-T1-MPRAGE images.

The additional information was evaluated using the following 4 point scoring system for meningeal abnormalities.
0 - no additional information
1 - more conspicuous meningeal enhancement .
2 - meningeal enhancement that can be discriminated from meningeal vasculature.

The following scoring system was used for the parenchymal lesions.
0 - no additional information
1 - increased conspicuity of existing lesions
2 - visualisation of new lesions.

Table 2: Distribution of final diagnosis

Tuberculosis	25%
Metastases	13.33%
Neurocysticercosis	10%
Bacterial meningitis	23.33%
Viral meningitis	10%
Demyelination	6.66%
Neurosarcoid	3.33%
Brain abscess	8.33%
Hypertrophic Pachymeningitis	2%

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean +/- SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Willcoxon Signed rank test has been used to find the significance of median score in two groups

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric testing for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Statistical Analysis: There was substantial agreement between the scores given by the two readers (kappa=0.75). Hence only the grades given by one reader (reader 2) were used to compare PC 3D-T1-MPRAGE imaging against the two other post contrast imaging techniques (3D-T1-SPACE and 3D-T2-FLAIR) by using the Wilcoxon signed rank test.

RESULTS:
Compared with PC 3D-T1-MPRAGE results, we found that lesion conspicuity of parenchymal lesions (1 to 3 cms in size) was more on PC 3D-T1-SPACE images (p value<0.01). However there was no significant difference among the three sequences, in the detection of parenchymal lesions , lesser than 3 cms in size. The above observation needs careful consideration, given that the nodular lesions in leptomeningeal carcinomatosis range from 2 to 5 mm in size. The assigned scores with regard to the supratentorial meningeal abnormalities were also significantly higher on the PC 3D-T1-SPACE than on the PC 3D-T1-MPRAGE images.

However, with regards to infratentorial meningeal enhancement, PC 3D-T2-FLAIR provided superior lesion conspicuity compared to either PC 3D-T1-MPRAGE or PC 3D-T1-SPACE.

Both PC 3D-T1-MPRAGE and PC 3D-T1-SPACE failed to demonstrate scolices in 2 of the 6 cases of neurocysticercosis (NCC) (33%) ; PC 3D-T2-FLAIR was clearly better as it was able to demonstrate scolices in all the cases of NCC.(i.e.100% sensitive)

DISCUSSION:
Many meningeal and parenchymal brain abnormalities may be visible only following contrast administration. CSF analysis which is considered the gold standard for diagnosing leptomeningeal carcinomatosis , has only 50 % sensitivity in picking up malignant cells. Untreated metastasis to the central nervous system shortens survival time to less than 3 months. Early diagnosis of infectious meningitis is vital, since a delay of even 6 hrs in initiation of antibiotics, is associated with 8 fold increased risk of death.

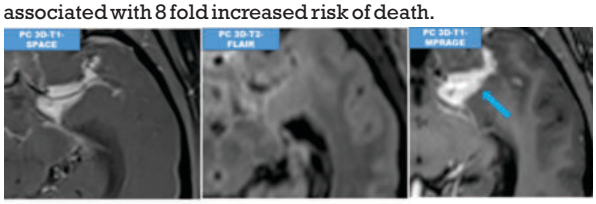

Figure 1. Tuberculous meningitis .Thickening and enhancement of meninges seen in left medial temporal lobe. The preserved flow void of left middle cerebral artery can be seen on the PC 3D-T1-SPACE.However left MCA cannot be seen distinctly, as the vessel also enhances in MPRAGE ( )

3D-T1-SPACE sequence is least affected by magnetic field inhomogeneities, and shows the absence of flow-related signal from vessels (Figure 1).The magnetization transfer (MT) effect in 3 D-T1- SPACE sequence leads to suppression of signal intensity from white matter of brain and better delineation of lesions; the trade-off here is the resulting poor grey matter - white matter differentiation (Figure 2) .3D-T1-SPACE is also sensitive to low gadolinium concentrations. With regards to improved conspicuity of parenchymal lesions ,PC 3D-T1-SPACE scored better than PC 3D-T2-FLAIR and PC 3D-T1-MPRAGE sequences. PC 3D-T1-SPACE was superior to PC 3D-TI-MPRAGE and PC 3D-T2-FLAIR in the detection of supratentorial leptomeningeal enhancement. This is consistent with the study by Gil et al.[7]

Even though PC 3D-T1-SPACE is the superior sequence, parenchymal lesions appeared more conspicuous on 3D-T2-FLAIR than on the 3D-T1- MPRAGE. This is in agreement with study by Ercan et al, who have found improved contrast between parenchymal metastasis and surrounding vasogenic edema on PC T2-FLAIR.[8]

However there was no significant difference between 3D-T2-FLAIR and 3D-T1-MPRAGE in the detection of parenchymal lesions. Ahn et al were able to show the supplementary value

of 3D-T2-FLAIR to PC 3D-T1-MPRAGE , only after doubling the dose of GBCA.[9]

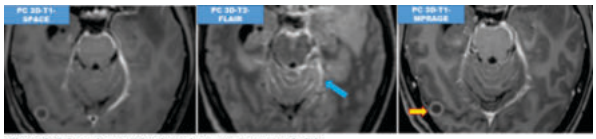

Figure 2. Tuberculoma with tuberculous meningoencephalitis
Ring enhancing lesion seen well on PC 3D-T1-MPRAGE and PC 3D-T1-SPACE ( )
Superior cerebellar folia enhancement seen on PC 3D-T2-FLAIR ( )
Also observe the reduced grey matter -white matter differentiation on PC 3D-T1-SPACE.

However , PC 3D-T2-FLAIR fared better in picking up infratentorial leptomeningeal enhancement.(Figure 2.)T2-FLAIR provide effective suppression of CSF signals from sulcal spaces.This may prove invaluable in the detection of leptomeningeal pathology devoid of mass effect, like leptomeningeal carcinomatosis. The better delineation of meningeal pathology, on PC T2 FLAIR images, is due to the synergistic effects of mild T1 shortening effects of Gadolinium and T2 prolongation effect of various brain pathology.[10]The effective suppression of CSF pulsation artefacts in the posterior fossa on PC 3D-T2-FLAIR sequences ,may also be a contributory factor.[11]

PC 3D-T2-FLAIR may also obviate the need for non-contrast FLAIR. If PC 3D-T2-FLAIR images are abnormal, then pre and post contrast T1-w images, will tell us whether the increased signal on PC 3D-T2-FLAIR is due to T1 shortening effects of Gad or due to T2 prolongation in brain pathology.

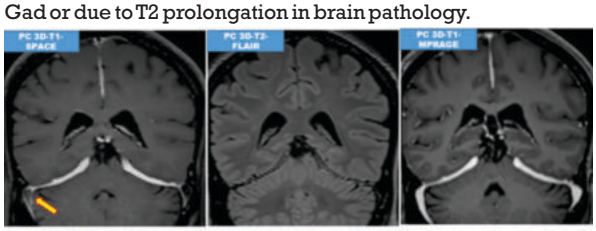

Figure 3. Hypertrophic pachymeningitis
PC 3D-T1-SPACE clearly shows preserved flow void in the right and left sigmoid sinuses.( )

In cases of parenchymal or meningeal lesions abutting dural venous sinuses ,3D T1 SPACE was able to show unambiguously dural sinus involvement /sparing, due to absence of flow related enhancement within the sinus.(Figure 3) Similarly superficial cortical vessels also appeared as flow voids on both PC 3D-T2-FLAIR and PC 3D-T1-SPACE images, thus aiding the detection of true leptomeningeal enhancement with greater degree of confidence.

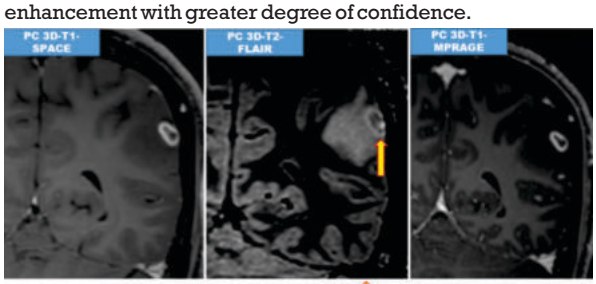

Figure 4 .Neurocysticercosis - eccentric scolex ( )better seen on PC 3D-T2-FLAIR

PC 3D-T2-FLAIR showed 100% sensitivity in picking up scolex in cases of NCC presenting as ring enhancing lesions.(Figure 4)This is not in keeping with previous study by Rastogi et al, where PC 3D-T1-MPRAGE was the superior sequence for picking up NCC.[12]However their study included only two cases of NCC.

These high resolution 3D sequences also did not show significant artefacts.This is in keeping with the observations by Komada et al, that the contrast to noise ratios (CNR) for lesion-GM and lesion-WM was higher on 3D-T1-SPACE than 3D-T1-MPRAGE.[13]

In some cases of CNS tuberculosis , PC 3D-T1-SPACE was able to demonstrate the tandem lesions ,which appeared merely as ring enhancing lesions on the PC 3D-T2-FLAIR and PC 3D-T1- MPRAGE sequences .(Figure 5).This may be due to the higher spatial resolution, afforded by the PC 3D-T1 - SPACE sequence.This better visualization of mural detail may prove invaluable in the identification of intracavitary projections in fungal granulomas and in the assessment of internal characteristics of intracranial neoplasms.

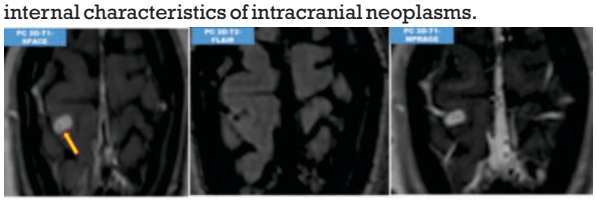

Figure 5. Tuberculoma -Tandem lesions better appreciated on 3D-T1-SPACE

Post contrast 3D FLAIR and PC 3DT1 SPACE images were free from enhancement in cortical veins, an important cause for spurious leptomeningeal enhancement in the 3DT1 MPRAGE sequences. In our experience, PC 3D-T2-FLAIR fared less well than either PC 3D-T1-MPRAGE or PC 3D-T1-SPACE ,in the detection of parenchymal lesions.

CONCLUSIONS:

- PC 3D-T1-SPACE and PC 3D-T2-FLAIR sequences added significantly more information to the now commonly used PC 3D-T1-MPRAGE sequence, with respect to leptomeningeal enhancement.
- PC 3D-T1-SPACE may obviate the need for PC 3D-T1-MPRAGE. If PC 3D-T1-SPACE images are normal, then it is unlikely that PC 3D-T1-MPRAGE will be abnormal.
- PC 3D-T2-FLAIR has the highest sensitivity in picking up scolex in cases of NCC.
- PC 3D-T2-FLAIR fared better in picking up infratentorial leptomeningeal enhancement.

We feel that PC 3D-T1-SPACE should be routinely incorporated into PC MR Brain imaging protocol, supplanting PC 3D-T1-MPRAGE.The radiologist may decide on including PC 3D-T2- FLAIR in select cases, depending on the clinical question at hand.

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