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Applications of T1 Subtraction Imaging in Non – Vascular Magnetic Resonance Imaging

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ABSTRACT

Background: Subtraction imaging of T1 post contrast sequence is a useful imaging technique in assessing the enhancement patterns of intrinsically T1 hyperintense lesions. This helps in better characterization of lesions. This study shows the utility of T1 post contrast subtraction sequence in various pathologies. ***Aims:*** To study the applications of T1 subtraction imaging in nonvascular magnetic resonance imaging. ***Settings and Design:*** Prospective observational study, conducted in the Department of Radiodiagnosis, Kasturba Medical College, Manipal. The patients were subjected to MRI imaging on Philips Achieva 1.5 T MRI and GE Signa HDxT 1.5 Tesla MRI. ***Methods and Materials:*** Total number of 21 patients were included for the study based on strict inclusion and exclusion criteria. Patients harbouring T1 hyperintense lesions in various parts were included and were subjected to T1 subtraction imaging. ***Statistical analysis:*** The acquired data was analysed using the statistical package SPSS version 20. Cohen's Kappa measure of agreement was performed for each variable.***Results:*** Study included 7 cases of musculoskeletal system, 6 cases of brain, 6 of pelvis and 2 cases of liver. There was good agreement is assessing enhancement pattern between two observers. Inter-observer variability was seen in only 2 cases. Lesion characterization was found to be better in subtracted images.***Conclusion:***T1 post contrast subtracted imaging is useful technique to assess enhancement pattern in intrinsically T1 hyperintense lesions and should be used on a routine basis

Keywords: T1 subtraction imaging, T1 hyperintense lesion, MRI , post contrast imaging , Avascular necrosis of femur**.**

1.1. INTRODUCTION

Contrast magnetic resonance imaging (MRI) has enhanced the sensitivity of detection and characterization of the lesions. Difficulty in characterization of enhancement is noticed in lesions that are already hyperintense on pre-contrast T1W sequence such as lesions with hemorrhage or proteinaceous contents [1]. The T1 subtraction imaging facilitates in a way native high T1 signal will be removed and remaining signal on subtracted images will be solely due to the enhancement [2]. This research focuses on the utility of subtraction imaging in non-vascular MRI.

1.1. MATERIALS AND METHODS

This is a prospective observational study, conducted in the Department of Radiodiagnosis, Kasturba Medical College, Manipal. Informed consent was taken from the 21 cases included in the study. The study was approved by the institutional ethics committee (IEC). This study included those patients who were presented with lesions in different parts of the body (heterogeneous sample) which were hyperintense in pre-contrast T1W sequences. Patients with suspected avascular necrosis of the bone were also included. Cases were excluded when there were variations in technical specifications between the unenhanced and enhanced sequences (TR,TE,flip angle,slice thickness,matrix,zero interpolation factor), change in patient position or patient unable to maintain a breath hold for sequences.

MR examinations of different parts of body were performed using 1.5 Tesla Philips MRI machine and GE Signa HDxT 1.5 Tesla MRI machine. Pre and post contrast sequences were acquired keeping all technical parameters similar. Pre-enhanced sequence was digitally subtracted from post contrast enhanced sequence using the image subtraction function available on our systems.

Visual assessment of the subtraction images was done by authors twice to assess enhancement and its shape and was compared with pre- and post-contrast sequences. Each author classified the post contrast T1 hyperintense lesion into enhancing, non-enhancing or indeterminate. After 2 weeks, the subtraction images of each case were visualized and the lesions were again classified into enhancing, non-enhancing or indeterminate. Variables such as enhancement seen on post contrast, enhancement seen on subtraction, shape of enhancement, enhancement seen only after subtraction, shape seen only after subtraction and impression as tumor or non-tumor were studied.

The acquired data was analysed using the statistical package SPSS version 20. Cohen's Kappa measure of agreement was performed for each variable for assessment of the agreement between the observers.

1.1. **RESULTS**

This study included 21 patients presenting with T1 hyperintense lesions in different parts of the body and in whom visual assessment of enhancement was difficult and was crucial for accurate diagnosis of these lesions. The study includes 7 (33.3 %) cases of musculoskeletal system, 6 (28.6%) cases of brain, 6 (28.6%) of pelvis and 2 (9.5%) cases of liver.

Table:1 shows inter-observer frequency distribution of use of T1 post contrast subtraction MRI in evaluation of enhancement.

Enhancement	***Observer 1*** N=21	***Observer 2*** N = 21
Indeterminate on post contrast but seen only after T1 subtraction	8 (38.09%)	6(28.5%)
Indeterminate on post contrast and also not seen on T1 subtraction sequence	4 (19.04%)	4(19.04%)
Seen on both post contrast and on T1 subtraction sequence. Shape characterization only on T1 subtraction sequence	3(14.28%)	3(14.28%)
Seen on both post contrast and on T1 subtraction sequence. But better characterization of the margins and better delineation of the lesions	6(28.57%)	8(38.09%)

The two observers found 100% agreement in assessment of enhancement on T1 subtraction sequence.

There was disagreement among the two observers in 2 cases out of 21 when evaluating presence and shape of contrast enhancement of the lesions. First observer found T1 subtraction images to be more useful for assessment of the same. 2nd observer found both T1 post contrast and post contrast subtracted images to be useful for similar assessment of the lesions. However, this discrepancy of inter observer variability was observed only in 2 cases. The enhancement shapes were characterized as linear(benign) and nodular (pathological) patterns on subtraction T1 post contrast sequence. Both observers agreed in 100 % of cases for the shape of enhancement – Amongst the lesions, linear in one (4.8 %) case and nodular in fourteen (66.7 %) cases was observed. Rest of the cases showed no enhancement.

Among three post-operative brain tumor cases, one case showed linear enhancement consistent with blood -brain barrier disruption or gliosis, which is suggestive of absence of residual tumor. In the rest of the two cases, nodular enhancement was appreciated, thereby suggesting the presence of residual tumor **(IMAGE 1).**

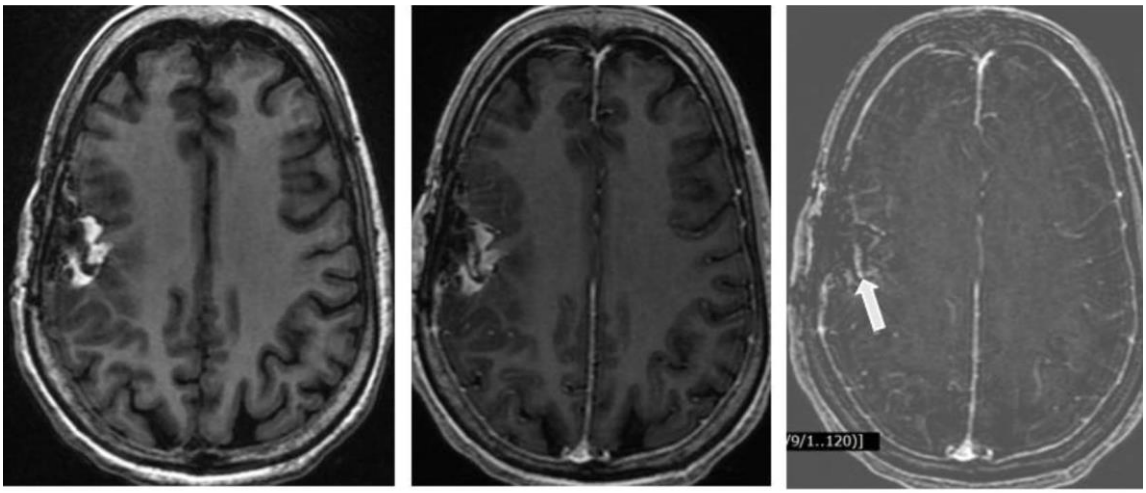


IMAGE:1 Post-Operative follow up MRI of right fronto-temporal low-grade glioma in 65 years old shows A) Unenhanced T1-weighted image shows right postsurgical changes with hyper intense area consistent with subacute hemorrhage. B) Contrast-enhanced T1 -weighted image of same slice shows mild enhancement along the posteromedial aspect of lesion, however that is difficult to distinguish from adjacent hemorrhage. C) Subtraction of A from B clearly shows posteromedial nodular enhancement (arrow) consistent with residual tumor. Rest of the areas shows signal void with linear peripheral enhancement – s/o post-operative changes.

Two patients with intraparenchymal T1 hyperintense brain lesions with indeterminate post contrast enhancement showed no enhancement in one case and linear enhancement in another case on subtracted images, suggestive of intraparenchymal hemorrhage **(IMAGE 2).**

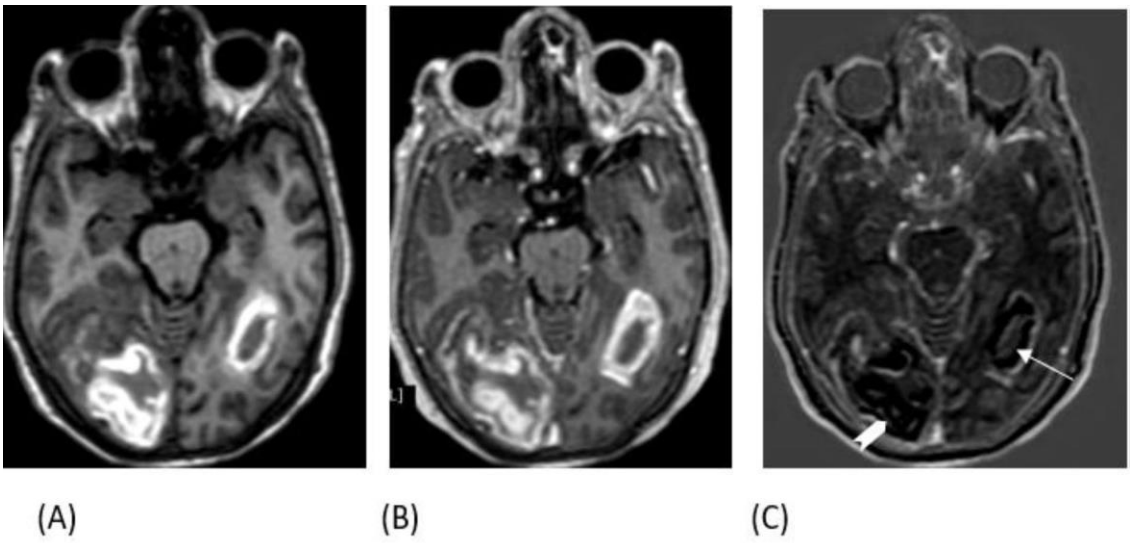
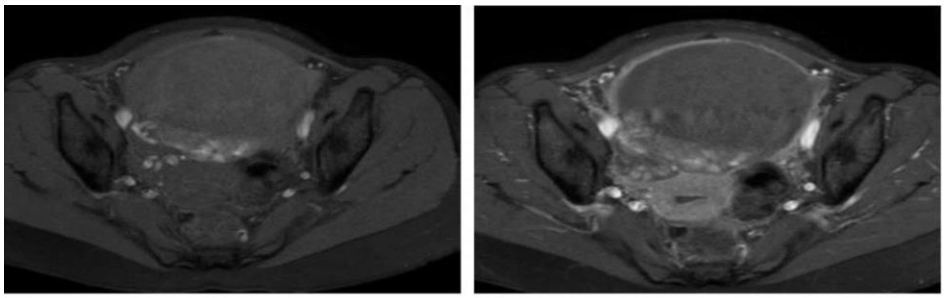
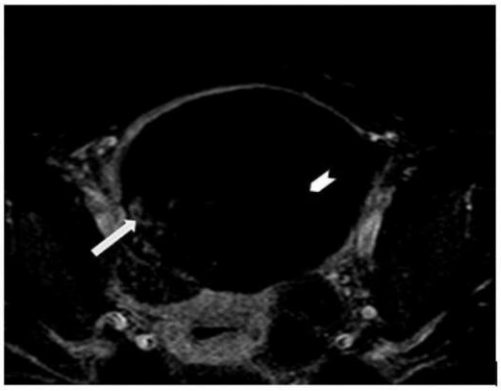


IMAGE:2 70 years old with headache. A) Pre contrast T1WI shows T1 hyper intense lesions in bilateral occipital lobes. B) Post contrast T1WI images shows high signal intensity. It is difficult to ascertain whether this is due to enhancement or hemorrhage. C) Subtracted image shows linear peripheral enhancement (arrow) with central signal void (arrowhead) – s/o hemorrhage.

Three patients presented with T1 hyperintense adnexal lesions (two ovarian and one hydrosalpinx). The first ovarian lesion showed no enhancement, thus suggesting chocolate cyst; the next one showed areas of nodular enhancement within the lesion, suggestive of ovarian malignancy **(IMAGE 3**) and the last case with T1 precontract hyperintense dilated tube showed absence of enhancement suggesting hydrosalpinx with proteinaceous /hemorrhagic component **(IMAGE 4).**



(A) (B)



(C)

IMAGE:3 30-year female with pelvic pain. Pre and post contrast enhanced T1W MRI images (A and B) of pelvis shows a large adnexal lesion exhibiting hyperintense signal in both pre and post contrast images. Assessment of enhancement cannot be done with confidence. Subtraction image (C) show definite areas of nodular enhancement (arrow) along the periphery of lesion while rest of the lesion shows complete signal void (arrowhead), suggesting the possibility of malignant etiology.

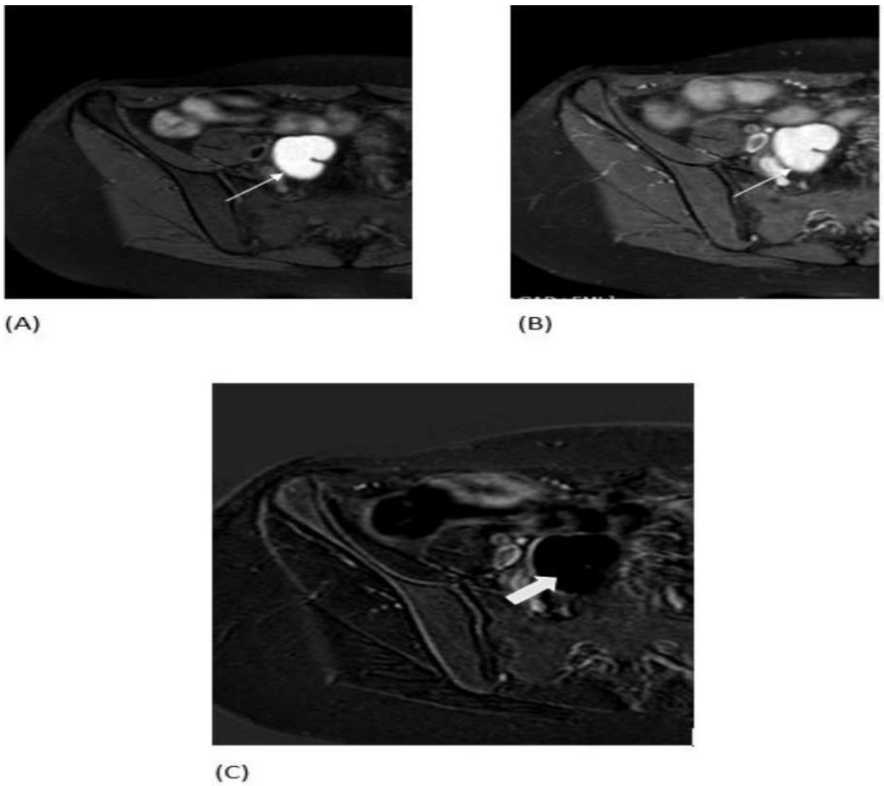


IMAGE:4 46-year female with pelvic pain shows tubular lesion (arrows) exhibiting hyperintense signal on pre (A) and post contrast (B) images with indeterminate enhancement in post contrast . Subtraction imaging (C) shows absence of enhancement within the lesion (bold arrow), suggesting the possibility of cystic lesion with hemorrhagic and proteinaceous component within.

Two patients on chemoradiotherapy, MRI was done to see the response of tumor (femur osteosarcoma and giant cell tumor with enhancing component), enhancing nodular margins were better observed on subtracted images, thus helped in better evaluation of residual or recurrent tumor **(IMAGE 5).**

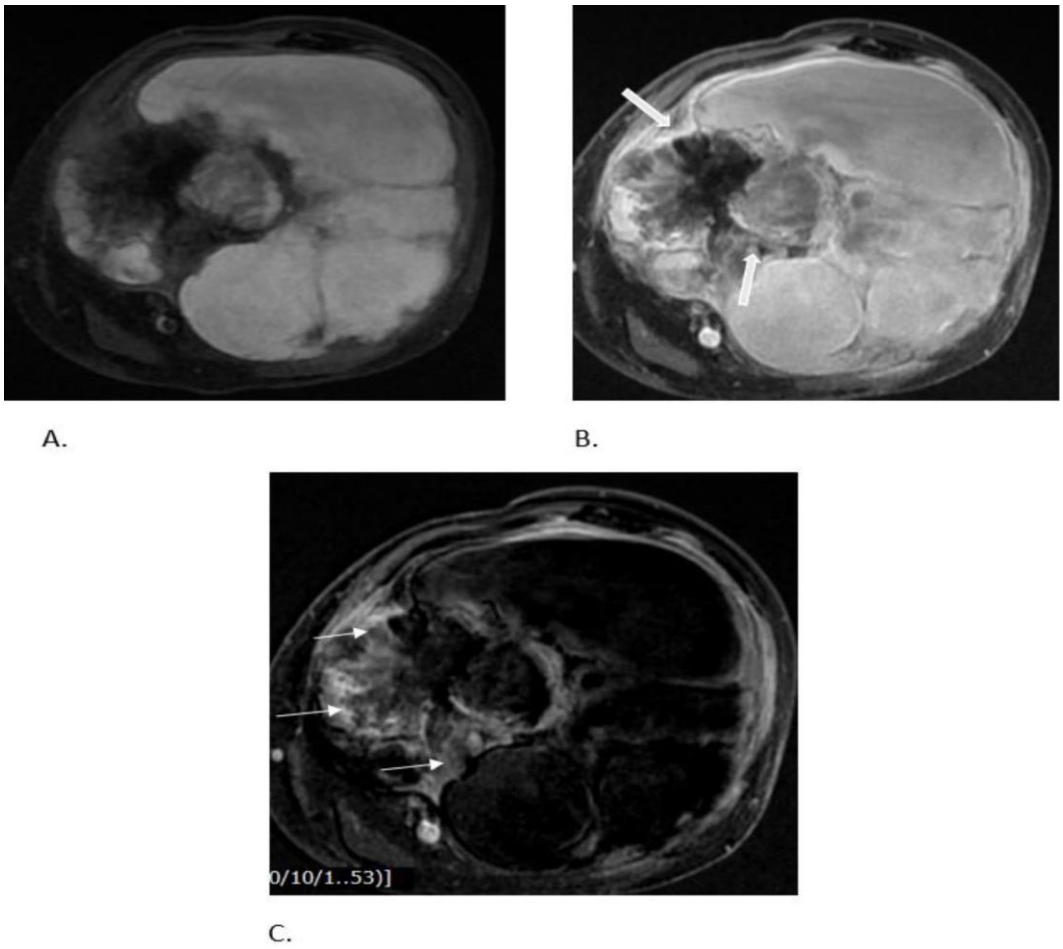


IMAGE: 5 17 years old with distal femur osteosarcoma on neoadjuvant chemotherapy on follow up MRI study. A) Axial T1 pre contrast SPGR image of femur lesion shows heterogenous mass with areas of high signal intensities within. B) Axial T1 SPGR contrast enhanced images shows that the lesion shows heterogenous enhancement on right side of the lesion (arrow), however enhancement of the hyperintense areas is indeterminate. C) Subtracted images shows nodular enhancement (arrows) representing the viable tumor margins better.

One patient who had presented with multiple focal hepatic lesions on background of cirrhosis showing T1 hyperintense signal. Subtracted images showed that only 1 lesion showed nodular enhancement suggestive of hepatocellular carcinoma or high-grade dysplastic nodule. However, the rest of the lesions showed no enhancement suggestive of regenerative or low-grade dysplastic nodules.

One patient with known diagnosis of HCC, being managed by Trans-arterial chemoembolization (TACE) on follow up showed positive nodular enhancement with better delineation of active tumor margins in subtracted images compared to routine post contrast T1 sequence – thus denoting residual or recurrent tumor.

Two cases with T1W hyperintense lesions in pelvis and inguinal region, showed indeterminate post contrast enhancement, however showed nodular enhancement on subtracted images, consistent with tumor. Biopsy was concordance with subtraction findings. Histopathological reports were suggestive of spindle cell neoplasm in the inguinal region and sarcomatous lesion in pelvis.
Two cases of Perthes disease with one avascular femoral head each were included in the study. It was observed that normal femoral heads were showing some enhancement suggestive of normal perfusion, on post contrast images as well as subtracted sequence. In avascular femoral heads– subtraction sequence depicted absence of enhancement suggestive of ischemia.

Two patients with soft tissue lesions having intrinsic T1 hyperintensities within showed nodular enhancement on subtracted images consistent with tumor.

One patient, known case of carcinoma stomach presented with T1 hyperintense vertebral lesions showing subtle post contrast enhancement, however, shows definite nodular enhancement on T1 subtraction – denoting metastatic lesions.

DISCUSSION

The purpose of this study was to explore the non-vascular applications of post contrast T1 subtraction imaging in detection of enhancement in lesions that pose challenges in evaluating enhancement due to the inherent high T1WI signal caused by hemorrhagic or proteinaceous components.

T1 Subtraction imaging is a technique whereby intrinsic T1 hyperintense signal is digitally subtracted from the identical sequence on post contrast imaging, maintaining the similar technical parameters as pre contrast T1 sequence. Any T1 hyperintense signal on the subtraction image would be solely due to enhancement, thus providing better identification of enhancing components within the lesions [3].

In our study we observed that subtraction imaging was helpful in evaluating brain lesions where it becomes quite difficult to distinguish the residual enhancing tumour from contiguous areas of gliosis or blood-brain barrier disruption in the setting of subacute haemorrhage .We observed that no or linear enhancement on subtraction, suggest the possibility of non-neoplastic etiology whereas nodular enhancement is more suggestive of neoplastic etiology, our findings are in concordance with the findings of the study done by Hanna et al [4] and Lee et al [5].

In cases of ovarian tumors / complex ovarian cysts with intermediate USG characteristics, MRI is usually performed to rule out malignancy [6,7]. We observed in our study that subtraction imaging was able to better assess the enhancement, allowing us to distinguish non-neoplastic cystic adnexal lesions [containing hemorrhagic / proteinaceous components] from the neoplastic lesions. Non - neoplastic lesions showed linear or no enhancement after subtraction while neoplastic lesions showed nodular enhancement.

Our findings are similar with the findings of the study done Abougabal et al [2], who had used subtraction imaging in evaluation of enhancement of biopsy proven neoplastic and non-neoplastic adnexal cystic lesions. He also concluded that in individuals who were diagnosed with chocolate cysts, subtraction images revealed no enhancement in the lesions. Mucinous cystadenoma lesions revealed enhancing thin internal septations, without any evidence of solid enhancing component, whereas the patients who were diagnosed with mucinous cystadenocarcinoma revealed enhancing solid component within the lesion.

It is not very uncommon to see regenerative and dysplastic nodules as well as HCC to exhibit high signal intensity on pre contrast T1WI, hence making the evaluation of degree of enhancement difficult. Our study included one patient with multiple T1 hyperintense hepatic lesions in cirrhotic background, subtracted images showed nodular enhancement in one lesion, suggesting the possibility of HCC. The rest of the lesions showed no enhancement suggesting the possibility of regenerative nodules.

On subtraction images, the conspicuity of the marginal or peritumoral rim enhancement is increased. This discovery aids in the identification of focal lesions with fibrotic pseudo capsules [8,9]. In the cirrhotic liver, the enhanced visibility of contrast enhancement of portal vein thrombus on subtraction helps differentiate malignant from bland portal vein thrombosis [10]. Percutaneous ablation is beneficial in the treating tumours, however not all the tumours are entirely cured with the initial session [11,12]. As a result, it is essential to do continuous imaging surveillance to identify the residual tumour as soon as possible for more ablation or alternative treatment options as required [13]. We observed that subtraction helped in detecting and differentiating linear enhancement due to hyperemia /granulation tissue from nodular enhancement that signifies residual tumor in post trans arterial chemoembolization (TACE) patients.

Our study has included two patients with [one with femur osteosarcoma and other with giant cell tumor with enhancing component] on chemoradiotherapy where MRI was done to see the response of tumor, subtracted images better delineated the margins of viable tumor by differentiating from hemorrhagic /necrotic component when compared to the post contrast images without subtraction.

Gadolinium-enhanced dynamic subtraction MR imaging has been demonstrated to be more sensitive in detecting early ischemia and correlating well with femoral head bone scintigraphy, as well as portraying the amount of necrosis and revascularization [14,15]. In our study, we observed that subtraction imaging depicts ischemia as an absence of enhancement, thereby helping in making a confident diagnosis of abnormal hip in the Perthes disease. It also helps in evaluation of contralateral hip to rule out early devascularization if present.

There were certain limitations in this study. Sample size was small and heterogenous with non-uniformity of cases included in the study. We were unable to recruit enough cases due to variable breathing during pre and post contrast images acquisition which led to misregistration artifacts on subtraction, hence such cases were excluded from the study. Subtraction image requires a subjective determination of lesion by a radiologist. When enhancement is subtle in some neoplasms there may be interobserver variability.

1.1. **CONCLUSION**

In conclusion, subtraction imaging which has been used for MR angiography since long time is a still underutilized but extremely useful tool in MRI applications, especially assessing intrinsic T1 hyperintense lesions as described in this study.

It helps in arriving a confident diagnosis by better evaluation of enhancement when visual assessment of the enhancement becomes difficult due to pre contrast T1 hyperintensities, like in lesions with haemorrhagic or proteinaceous contents. It can also be a problem-solving tool in assessing post operative and post ablation lesions. Further larger studies with respect to T1 subtraction imaging in different lesions will give more insights in this technique of imaging.

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