ORIGINAL RESEARCH

Utility of diffusion weighted imaging and apparent diffusion coefficient values in differentiating benign and malignant soft tissue tumors: A scientific article

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ABSTRACT

Objective: This study aimed to characterize benign and malignant soft tissue tumors on MRI via diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) values.

Materials and Methods: The investigation conducted was an observational study with cross-sectional design. The study population consisted of 30 Indian patients who presented at a tertiary care center in South India to the Department of Radiodiagnosis between November 2019 to May 2021. Study subjects were selected based on strict inclusion and exclusion criteria. They were then put through a detailed clinical assessment followed by imaging via MRI, performed using a 1.5 Tesla MRI scanner. Imaging and interpretation were performed by a team of radiologists who were unaware of the patient demographics, presentation and suggested clinical differential diagnoses. A detailed protocol utilizing various imaging techniques in multiple planes was employed. Apparent diffusion coefficient values were calculated automatically by an inbuilt software. Further methods involved drawing a fixed region of interest (ROI) over the tumor showing diffusion restriction. Preliminary imaging diagnoses were confirmed by histopathology.

Results: Study data revealed a significant difference in the mean apparent diffusion coefficient values of benign and malignant soft tissue tumors. Additional information derived included frequency of certain tumor subtypes among patients and demographic characteristics relating to certain tumors.

Conclusion: Results from this study support the prevailing idea that diffusion weighted imaging and apparent diffusion coefficient values are valuable supplemental tools to diagnose and manage soft tissue tumors.

Key words: Soft tissue tumors, diffusion weighted imaging, apparent diffusion coefficient

INTRODUCTION

Soft tissue tumors are often encountered by radiologists in their daily clinical practice. Imaging plays a critical role in the diagnosis and management of benign and malignant soft tissue tumors.

DWI is a technique capable of detecting the diffusion of proton-containing molecules in tissue or fluid by utilizing the use of additional gradient pulses [1]. Structural geometry of the environment influences diffusional processes, particularly in samples where the boundary lengths affecting diffusion are so compact that it does not permit adequate resolution with conventional MRI [2]. Previously, DWI has been used successfully to differentiate benign and malignant central nervous system tumors [3].

ADC is a measure of the magnitude of diffusion of water molecules within a tissue. Evidence indicates that a combination of minimum ADC and ADC difference values significantly elevate the diagnostic performance of breast DWI of various masses [4]. Presently, DWI is increasingly used to discriminate between malignant and benign soft tissue tumors and identify post-operative residue and recurrence [5].

Characterization of soft tissue tumors based on clinical history, location of the lesionand signal characteristics on various MRI sequences can

a) Determine the diagnosis for a subset of determinate lesions that have defining clinical and radiologic features
b) Narrow the differential diagnosis for lesions that demonstrate indeterminate characteristics, to select patients who warrant a biopsy to rule out malignancy thereby delivering high value care by limiting unnecessary biopsies[6].

Differentiating between malignant and benign tumors includes comprehensive assessment via clinical history, imaging, and subsequent biopsy. Diagnostic imaging is critical for generalists and specialists alike to identify and characterize soft tissue tumors. DWI and ADC values have emerged as evaluative tools for the characterization of certain tumors. DWI utilizes the random motion of water molecules which allows for calculation of the impedance of these molecules via the ADC to gain insight into the status of the cell membrane and tissue cellularity [7]. Study data revealed the advantages of DWI and ADC values to characterize soft tissue tumors.

MATERIALS AND METHODS

A cross-sectional study was conducted from November 2019 to May 2021 at a tertiary care center in South India. The study population comprised of patients presenting to the Department of Radiodiagnosis. Patients were selected successively in series. Strict inclusion and exclusion criteria were applied to select a total study sample of 30 patients with clinically suspected soft tissue tumors for further evaluation with MR imaging.

Inclusion criteria selected patients with a soft tissue tumor found clinically who required imaging to clarify the nature of the entity.

Patients with general contraindications to MRI, inflammatory and infective lesions, lymph nodal masses, vascular malformations, post-traumatic hematomaand those who could not be followed up till histopathology or were lost to follow-up were excluded from the study.

After a detailed history and clinical examination, MR imaging was performed using a 1.5 Tesla MRI scanner (Siemens MagnetomAvanto, Erlangen, Germany).Imaging and interpretation were performed by a team of radiologists with experience in diagnosing soft tissue tumors blinded to patient demographics, presentation, and clinical differential diagnoses.

The following MRI examination protocol was applied in different planes when necessary:

- T1-WI (TR/TE = 500-700/12-20; FOV, 200-300 mm) in axial, coronal ± sagittal.
- T2-WI (TR/TE = 4000-6000/76-90; FOV, 150-250 mm) in axial and coronal.
- Short tau inversion recovery (STIR) sequence (TR/TE = 4000-5000/39-40, FOV, 200-300mm) in axial and coronal.
- T1-fat suppression (TR/TE = 700-800/12-15; FOV, 200-300mm) in coronal.
- Post gadolinium T1-fat suppression (TR/TE = 700-800/12-15; FOV, 200-300mm) in axial, coronal and sagittal. Post gadolinium study was done only if needed.
- Gradient echo (GRE) (TR/TE = 5000-5100/20-30; FOV, 200-300mm).
- DWI (TR/TE = 4500-5000/75-85 with different b-values viz. b 50, b 400, b 800).
- ADC values were calculated automatically by the inbuilt software and displayed as a parametric map. A fixed ROI measuring approximately 50mm^2 in area was drawn over a homogeneous part of the tumor showing diffusion restriction. In smaller lesions, an appropriate ROI was drawn to measure ADC values.

The data collected was analyzed for arriving at an imaging diagnosis which was then confirmed by histopathological examination. The data was evaluated using descriptive statistics by calculating mean ADC values by individual histopathological tumor type and combinatorial values for all tumors under broader classifications of benign and malignant tumors. Data was analyzed by independent sample t test and an alpha value of 0.05 was considered to determine statistical significance for this study.

RESULTS

The study population ranged from 21 to 70 years of age. Of them 19 were males and 11 were female patients. Most of the patients presented in their 6th decade of life (26.67%), followed by the4th decade (23.3%). The mean age at presentation was 47.2 years with a standard deviation of 15.60 years.

A total of 6 different subtypes of benign and malignant tumors were identified in the data from the study population. 19 benign and 11 malignant tumors were found and further characterized [Tables 1, 2]. Benign tumors were predominant in the younger age group with 70% of them seen in those less than 50 years of age. Most of the malignant tumors were found in the elderly with 73% occurring in those over 50 years. A male predominance was noted in the incidence of malignant tumors connoted by a male: female ratio of 2.6:1.3.

The mean ADC values of all the benign and malignant tumors included in this study were 1.27x10^{-3} mm^2/s

and 0.84x10^{-3} mm^2/s respectively with the cut-off value between them being 1.087 x 10^{-3}mm^2/s. The corresponding sensitivity, specificity, and accuracy of 72.22%, 90.9%, and 76.67% to deliver a noninvasive diagnosis were gleaned respectively. A statistically significant difference was observed between the mean ADC values of benign and malignant soft tissue tumors (p<0.05) [Table 3].

Many of the tumors identified in the study population were in the subcutaneous plane. Specifically, 16 of the tumors could be ascribed to the subcutaneous plane. Other frequently identified planes of discovery were the intermuscular and intramuscular planes [Figure 3].

Table 1: Mean ADC values in benign soft tissue tumors

Pathology	Number of cases	Mean ADC value (x10^{-3} mm^2/s)
Lipoma	6	0.42 +/- 0.07
Spindle cell neoplasm	5	1.78 +/- 0.59
Neurofibroma	4	1.59 +/- 0.39
Fibromatosis	2	1.34 +/- 0.05
Fibrohistiocytic tumor	1	1.74
Schwannoma	1	1.10
Total	19	

Table 2:Mean ADC values in malignant soft tissue tumors

Pathology	Number of cases	Mean ADC values (10^{-3} mm^2/s)
UPS	4	0.88 +/- 0.04
Dermatofibrosarcoma protuberance (DFSP)	2	0.85 +/- 0.03
Rhabdomyosarcoma	2	0.83 +/- 0.07
Liposarcoma	1	0.49
MPNST	1	1.10
Synovial sarcoma	1	0.84
Total	11	

Table 3: Mean of all ADC values according to benign and malignant soft tissue tumors

Pathology	Mean ADC value (x10^{-3} mm^2/s)
Benign	1.271
Malignant	0.845

Table 4:Distribution of tumors based on plane

Plane	Total
Subcutaneous	16
Intermuscular	4
Intramuscular	6
Trans-spatial	1
Intra-parotid	1
Retroperitoneum	2
Total	30

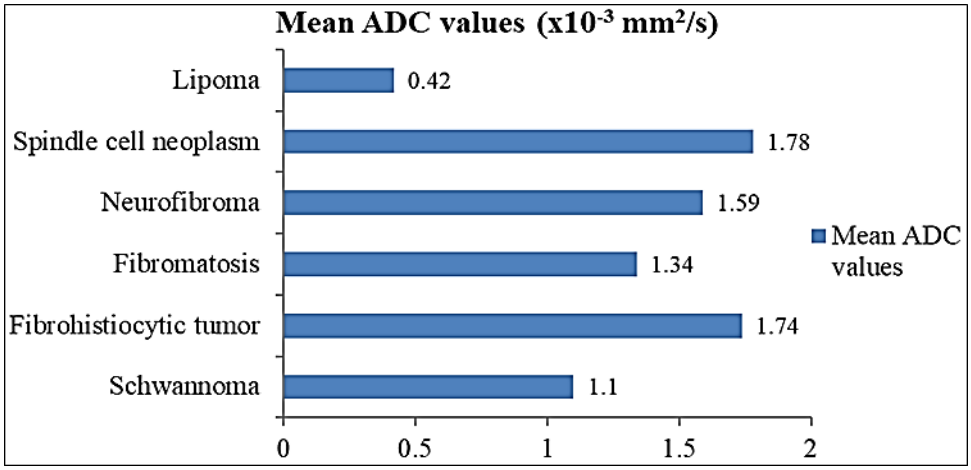

Fig 1: A bar graph depicting the mean ADC values of benign soft tissue tumors

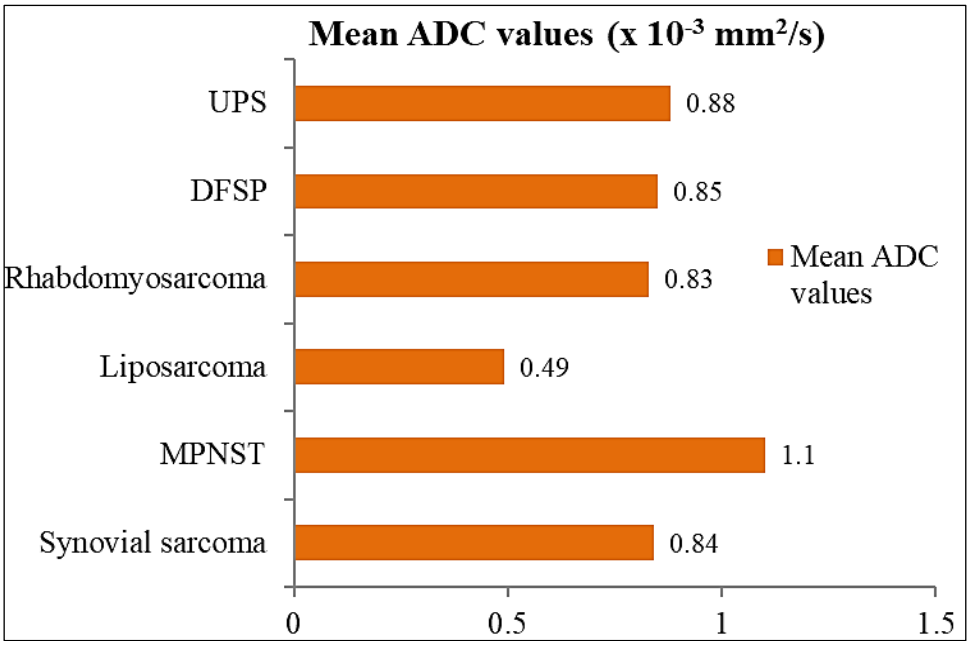

Fig 2: A bar graph depicting the mean ADC values of malignant soft tissue tumors

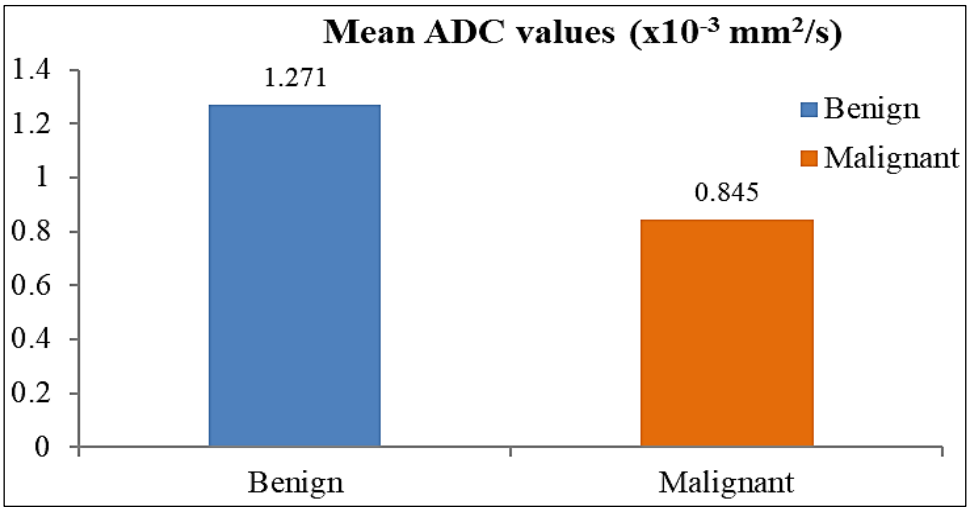

Fig 3: A comparison of the mean ADC values for benign and malignant soft tissue tumors. The mean ADC value of benign tumors was higher than the mean ADC value of malignant tumors, with a statistically significant difference between the two (p<0.05)

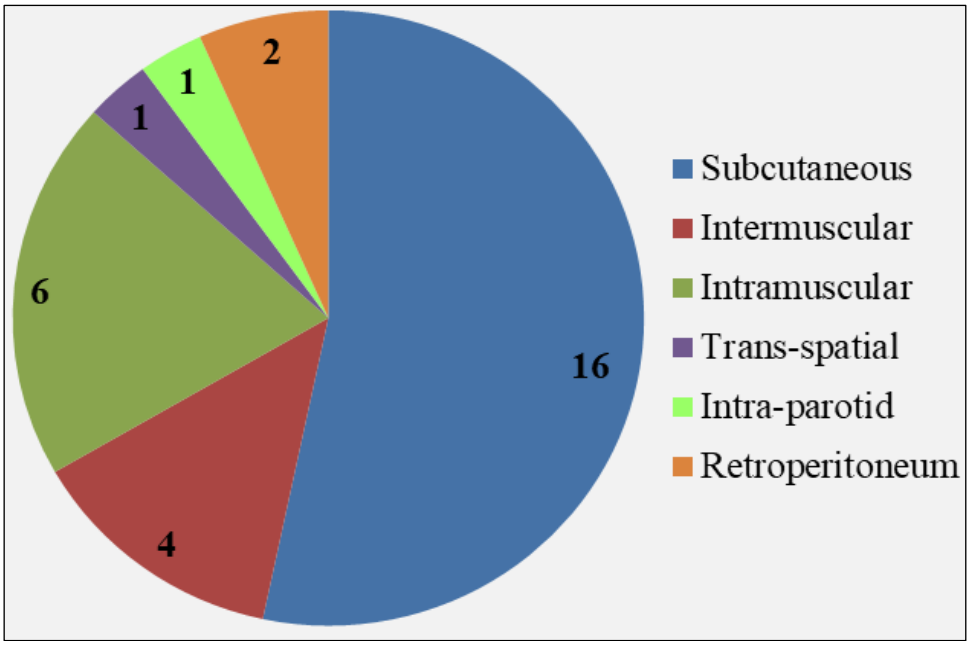

Fig 4: This diagram depicts the distribution of tumors in different anatomical planes based on the location of their discovery

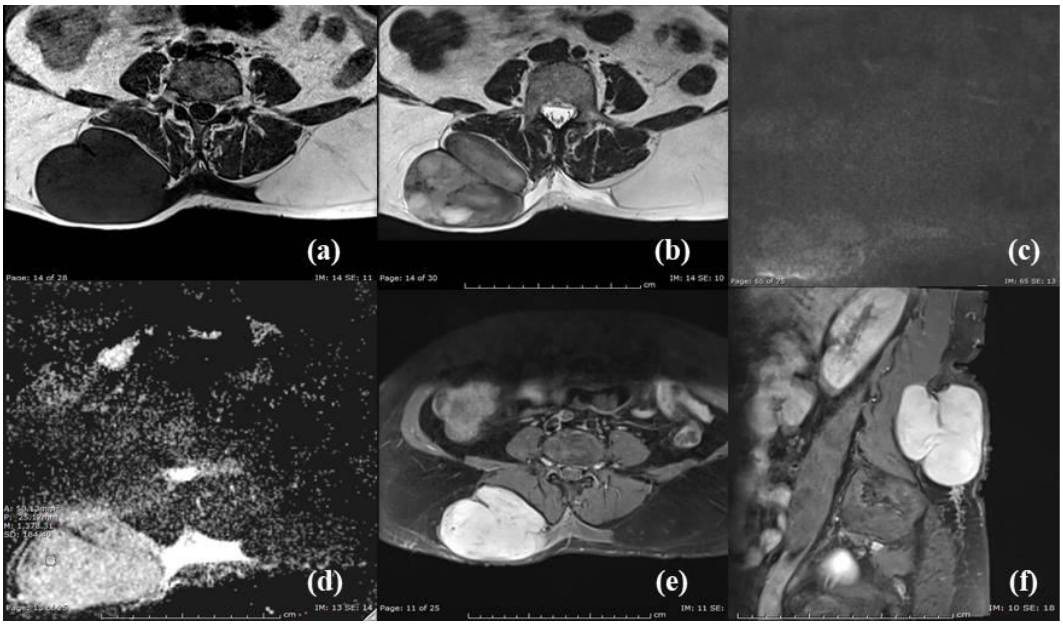

Fig 5 (a-f): Fibromatosis

A55 year old female presented with a painless swelling in lower back in right side.AxialT1 and T2 weightedMR images (a,b) without fat suppression show a well-defined lobulated T1W hypointense and T2W intermediate signal intensity lesion, with small area of hyperintensity in the subcutaneous plane of lower back on right side. The lesion is causing mild indentation over the right paraspinal muscles. However, intervening fat plane is well maintained. The lesion shows mild restriction on DWI (c), with an average ADC value of 1.37 x 10^{-3} mm^2/s (d). Axial and sagittalPost-Gd T1-FS images (e,f) show homogeneous enhancement, without any areas of necrosis within.

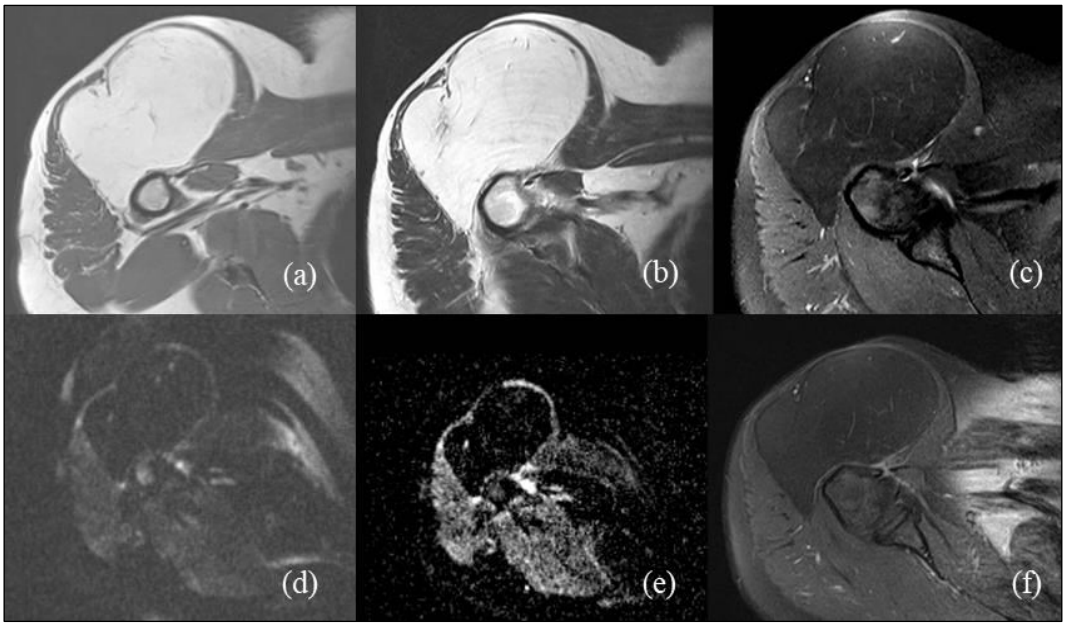

Fig 6 (a-f): Intramuscular Lipoma

A 45 year old female with a painless swelling in the right shoulder. (a,b) AxialT1 and T2 weightedMR images without fat suppression show a well-defined T1Wand T2W hyperintense lesion in the intramuscular plane of the right shoulder involving the deltoid muscle.(c) The fat signal is suppressed on T2-weighted fat-saturated image with few hyperintense intervening septa. (d)DWI shows hypo-intensity within the lesion. (e)However corresponding ADC map shows very low ADC value (0.32 x 10^{-3}mm^2/s). (f) Axial Post-Gd T1-FS image shows no significant enhancement in the lesion

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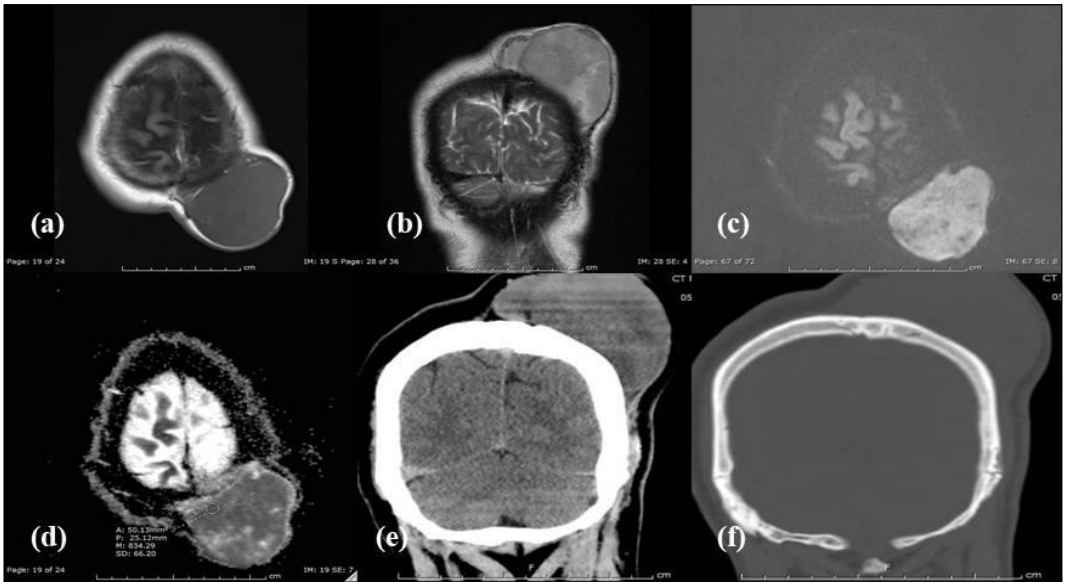

Fig 7 (a-f): Dermatofibrosarcoma Protruberans

A 37 year old male presented with progressively enlarging swelling over the left parietal region of scalp. Axial T1 and coronal T2 weighted MR images (a,b) without fat suppression show a well-defined T1W hypointense and T2W hyperintense lesion in the subcutaneous plane of left parietal region of scalp. The lesion shows restriction on DWI (c), with an average ADC value of 0.83 x 10^{-3} mm^2/s (d). Coronal reformatted CT images in soft tissue and bone window (e,f) show a soft tissue attenuating lesion in the left parietal region of scalp and the underlying bone appears to be normal.

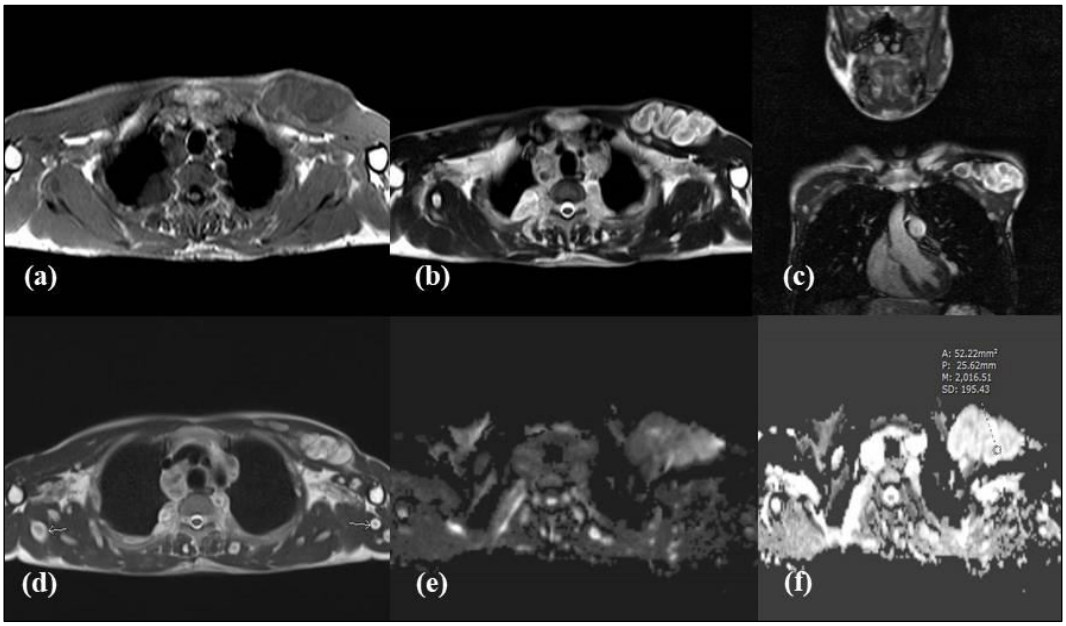

Fig 8 (a-f): Diagnosed case of Neurofibromatosis type 1

30 year old male diagnosed with neurofibromatosis type 1 presents with swelling in left pectoral region. Axial T1 and T2 weighted MR images (a,b) without fat suppression show a serpinginous T1W hypointense and T2W hyperintense lesion in the intramuscular plane involving the left pectoralis major muscle. Coronal and axial T2 weighted MR images (c,d) show that the lesions have a central area of low signal intensity surrounded by a T2 hyperintense rim (white arrows), suggestive of *"target sign"* of peripheral nerve sheath tumours. The lesion does not show significant restriction on DWI (e) and the corresponding ADC map (f) show high value (2.0 x 10^{-3} mm^2/s).

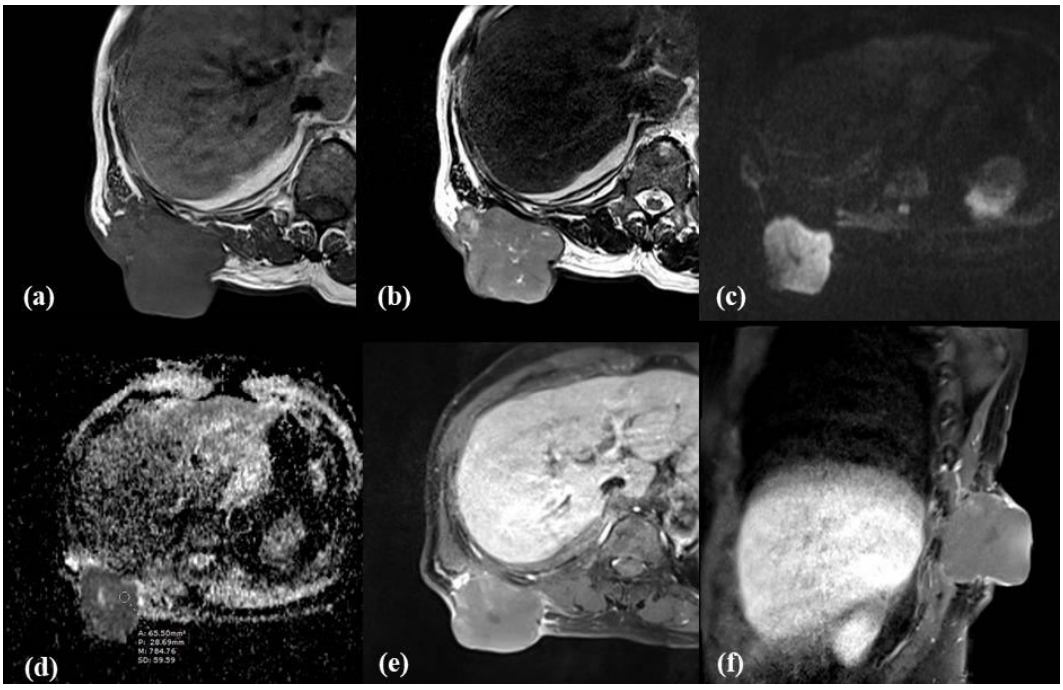

Fig 9 (a-f): Rhabdomyosarcoma

A 70 year old male with progressively enlarging mass in the right lower back. (a,b) Axial MR images show relatively well-defined lesion with exophtyic component which iso to slightly hyperintense to skeletal muscles on T1-weighted images and hyperintense on T2-weighted images. (c,d) The lesion shows restricted diffusion on DWI and low average ADC value of 0.78 x 10^{-3} mm^2/s. (e,f) Axial and sagittal post-Gd T1-FS images show mild internal enhancement of the lesion.

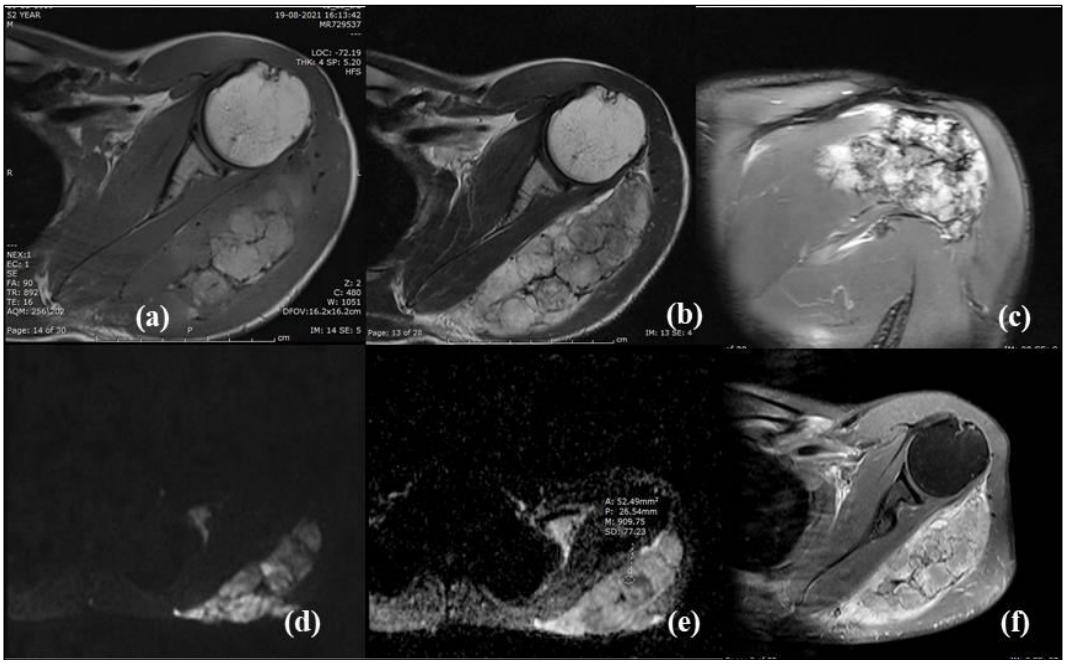

Fig 10 (a-f): Undifferentiated Pleomorphic Sarcoma

A 52 year old male with swelling in the left shoulder causing restriction of movements. (a,b) Axial T1 and T2 weighted MR images show a lobulated heterogeneous signal intensity lesion with hypointense internal septations in intermuscular plane of left shoulder. (c) Blooming artifact (white arrow) noted on Coronal T2*-weighted gradient-echo MR image. (d,e) DWI shows restricted diffusion in the lesion and low values on corresponding ADC map (0.91 x $10^{-3}$$mm^2$/s).

DISCUSSION

Soft tissue masses include a heterogeneous group of lesions, including those of benign and malignant neoplasms, inflammatory, traumatic, and vascular origins[6].Previously, the approach to evaluation of such lesions included histologic evaluation for determining the pathologic diagnosis of such lesions, and imaging tests for anatomic analysis and staging if required[6].However, with the advent of modern MRI techniques, the ability to diagnose soft tissue tumors utilizing diagnostic imaging has become increasingly possible[6].MRI is an indispensable imaging modality in the assessment of soft tissue tumors[6].Supplementingroutine MRI with DWI and ADC values adds great advantage to noninvasively differentiate between benign and malignant soft tissue tumors and meaningfully synthesize differential diagnoses for lesions with indeterminate characteristics.In many lesions, it is also capable of delivering a tissue-specific diagnosis. In this study, the distribution and imaging characteristics of 30 patients with soft tissue tumors were analyzed and described as follows.

In our study, most patients presented in the 6th decade of life with the mean age at presentation being 47.2 years. These findings are similar to the study conducted by Hassanien OA, *et al*., where the mean age was 42+/-18.5 years[8].Benign tumors were more common in the younger age group and most of the malignant tumors were identified in those over 50 years of age. 2 cases of dermatofibrosarcoma protuberance and 1 case of synovial sarcoma, which are neoplasms usually ascribed to older individuals, were discerned in patients below 50 years of age.

19 males and 11 female patients were present in this study. The present study did not show significant gender differences in the incidence of benign tumors. However, a predominance was noted among males in the incidence of malignant tumors which included 1 case of synovial sarcoma, 1 case of dermatofibrosarcoma protuberance, and 1 case of liposarcoma [Table 1].

After MRI examination, the diagnosis was confirmed with histopathology via Trucut biopsy or fine needle aspiration cytology (FNAC). In 19 patients with benign tumors, lipoma was the most common pathological diagnosis found in 6 patients and uncommon identified benign tumors were fibrohistiocytic tumor and schwannoma [Table 1].

Spindle cell neoplasm showed the highest mean ADC value of 1.78x10^{-3} mm^2/s. Lipomas showed the lowest mean ADC value of 0.42x10^{-3} mm^2/s, which is comparable to the study done by Hassanien, OA. *et al*.[8]. This study found that benign tumors had mean ADC values above 1.10x10^{-3} mm^2/s, with the exception being lipoma [Table 1]. Nagata, S. *et al*., conducted a similar study on 88 patients with histopathologically proven tumors, where the mean ADC values of benign non-myxoid tumors were significantly higher than malignant non-myxoid tumors[9].

In 11 patients with malignant tumors, undifferentiated pleomorphic sarcoma was the most common

pathological diagnosis identified in 4 patients. All the malignant lesions had lower mean ADC values compared to benign lesions, with the lowest value of $0.49x10^{-3}$ mm^2/s seen in liposarcoma [Table 2]. In a similar study conducted by Jeon, JY. *et al*.,on 60 histologically proven superficial soft tissue tumors, a combination of conventional MRI and DWI, the calculated sensitivity, specificity, and accuracy for noninvasive diagnosis were 96%, 85.7%and 90% respectively[10]. The study also concluded that the group mean ADCs of malignant superficial soft tissue tumors were significantly lower than that of benign superficial soft tissue tumors with $p<0.001$[10]. Similarly, Hemat, EM. *et al*., conducted a cross-sectional study on 38 patients with histopathologically confirmed orbital masses and reported that malignant orbital masses had significantly lower ADC values than benign masses[11]. The cutoff ADC value to differentiate between benign and malignant orbital lesions was reported to be $0.93 \times 10^{-3} mm^2/s$. The sensitivity was 80%, the specificity was 83.3%and the accuracy was 82% for delivering a radiologic diagnosis[11].

We identified 2 cases of rhabdomyosarcoma in our study with a mean ADC value of $0.83+/-0.07x10^{-3}$ mm^2/s (mean+/- standard deviation) and 4 cases of undifferentiated pleomorphic sarcoma with a mean ADC value of $0.88+/- 0.04 \times 10^{-3}$ mm^2/s (mean+/- standard deviation). These values are comparable to the mean ADC value of malignant soft tissue tumors reported by Oka, K. *et al*., of $0.92+/-0.139 \times 10^{-3} mm^2/s$[12].

The mean ADC values of benign and malignant tumors evaluated in this study were $1.27x10^{-3}$ mm^2/s and $0.84x10^{-3}$ mm^2/s respectively with a cutoff value between them of $1.087x10^{-3} mm^2/s$ and the calculated sensitivity, specificity, and accuracy being 72.22%, 90.9%and 76.67% respectively for making a radiologic diagnosis. A statistically significant difference was observed between the mean ADC values of benign and malignant soft tissue tumors with $p<0.05$ [Table 3].

This study has four main limitations. We assessed 6 patients with histologically confirmed lipoma who demonstrated low signal intensity on DWI with the corresponding ADC maps showing very low values (mean ADC value = $0.42+/- 0.07x10^{-3}$ mm^2/s), similar to that of malignant soft tissue tumors. We considered this a false positive and a limitation to deliver a confirmatory radiologic diagnosis for this tumor type. These results were consistent with those derived by Dietrich, O.*et al*., and Einarsdottir, H. *et al*.[13,14]. The authors stated that benign soft tissue tumors such as lipomas may show some overlap with malignant growths pertaining to areas of diffusion restriction[13,14]. Another pitfall could be the presence of malignant features which may later develop in some parts of an initially benign lesion and hence may not be detected by DWI in the early stage of the neoplastic process. Next, most of the tumors identified in our study were in the subcutaneous plane [Figure 3]. Since DWI and ADC may be scribed differently depending on the tissue types and location of the tumor, studies that evaluate variability in values attributable to these factors could inform the utility of DWI for tumors found in other planes. Lastly, although the radiologists were blinded to patient presentation and clinical differential diagnoses and a strict inclusion and exclusion criteria was applied, considering the cross-sectional and observational nature of this study, there is a potential for occurrence of residual confounding.

CONCLUSION

MRI is an excellent and indispensable imaging modality in the assessment of soft tissue masses. Supplementing routine MR examination with DWI and ADC values is a great advantage as it allows for noninvasive differentiation of benign and malignant soft tissue tumors and provides the evidence to narrow down the differential diagnoses meaningfully for lesions with indeterminate characteristics. In many lesions, it has the capability of delivering a tissue-specific diagnosis and hence an opportunity to deliver high value care by minimizing unnecessary biopsies of benign lesions.

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