Is MRI diffusion-weighted imaging a reliable tool for the diagnosis and post therapeutic follow up of extremity soft#tissue neoplasms?

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Aims and objectives

Soft tissue sarcomas/tumors (STSs) are a diversified class of neoplasia that have diagnostic and therapeutic problems for clinical care (1).

DWI has been presumed to have the ability to discriminate between benign and malignant soft-tissue tumors because malignant tumors have more cellularity and therefore have more restricted diffusion than benign tumors (2).

The diagnosis of such masses remains a challenge for the clinician because malignant and benign tumors, as well as non-neoplastic masses following inflammation or trauma, have a similar presentation (3).

MRI is the modality of choice to evaluate soft tissue masses. In spite the presence of some MRI findings indicative for malignancy, such as infiltration of adjacent tissues, osseous destruction, and the size of the mass, there are no clear standards to discriminate benign masses from malignancies. Thus, the histopathologic workup is required for reliable characterization of soft tissue masses. DWI may reveal the microstructure of such masses and may, therefore, be helpful to distinguish (3).

DWI allows quantitative and qualitative analyses of tissue cellularity and cell membrane integrity and has been widely used for tumor detection and characterization and to monitor treatment response *(4).*

The aim of work is to evaluate the ability of Diffusion-Weighted MRI in the characterization of the extremity soft tissue tumors and determining whether benign or malignant and trying to define a threshold or cut off ADC values of benign & malignant tumors as well as using DWI in the post-therapeutic follow up of extremity soft tissue masses.

Images for this section:

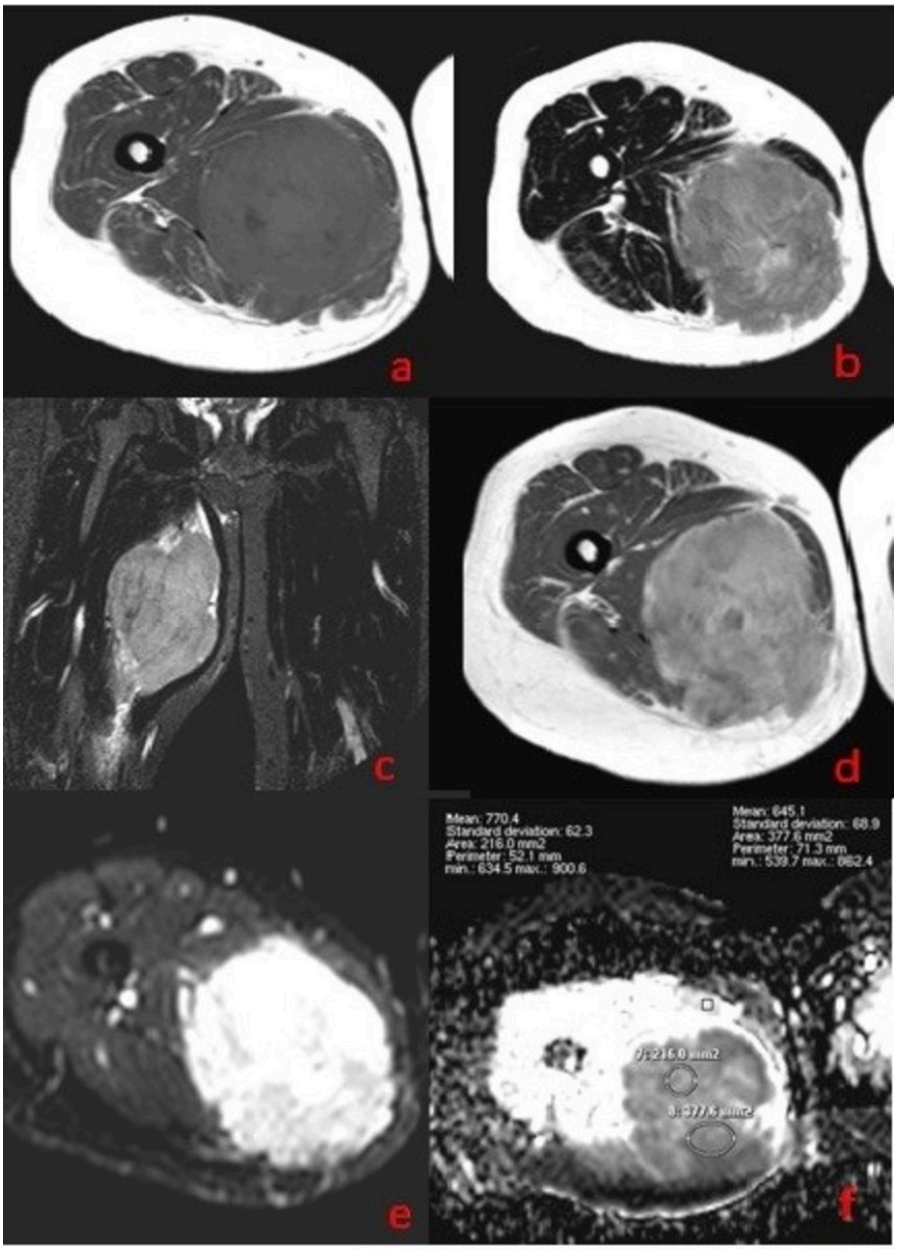

Fig. 1: Figure 1 Rhabdomyosarcoma in a 34 years old woman (a) Axial T1WI and (b) Axial T2WI & (c)Coronal STIR WIs showed a round fairly defined irregular outline mass at the mid-thigh eliciting heterogeneous low T1 and high T2/STIR signal with foci of low signal in T1 and high signal in T2 (break down). Postcontrast Axial T1 WIs (d) showing intense heterogeneous enhancement with areas of cystic breaking down. Corresponding DWI (e) & ADC maps (f) showed high signal in DWI & low signal on ADC (restricted diffusion) with a mean ADC value = 0.70 x10-3 mm2/sec.

Methods and materials

The study population included 90 patients presenting with extremity soft tissue masses for an initial assessment at the National Cancer Institute in Egypt. The study has been approved by the "Ethical Committee of Faculty of Medicine, Cairo University", in compliance with Helsinki Declaration. The patients' ages range from 1 to 75 years with the mean age of 36 years. We performed a prospective lesion-based analysis for 108 newly diagnosed soft tissue lesions. We also include post-therapeutic imaging follow up for 18 patients.

Magnetic resonance imaging:

The patients had their MRI done on high field system (1.5 Tesla) closed magnet unit (Phillips Achieva XR) using the optimal surface coil to cover the examined area for each patient.

Imaging protocol:

All patient underwent a full MRI exam including conventional MRI sequences, DWI and Post Gadolinium DTPA MR imaging was performed. The DWI was obtained with 3 b values including 0, 400, and 800 s/mm^2.

Conventional MR imaging evaluation:

The morphological features of each lesion were recorded including signal characteristics and pattern of enhancement. The provisional diagnosis was reported.

Diffusion-weighted imaging evaluation:

We reviewed the diffusion images with ADC values for final radiological characterization and detection of masses. The lesion was determined on DWI and ADC map by using the conventional MR images as a guide. Measurements were done via placing the region of interest (ROI) to include the largest area of the lesion. ADC of the minimum and mean values were obtained.

Statistical analysis:

Statistical analysis was performed using the statistical software (Med-calc). Numerical data were expressed as a mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage.

ROC analysis (Receiver Operator Characteristic) was done to select the best cutoff point for ADC value. The findings on MRI were analyzed and correlated with histopathological findings after needle biopsy or resection or with previous imaging and investigations when available. A P value less than 0.05 was considered as statistically significant.

Images for this section:

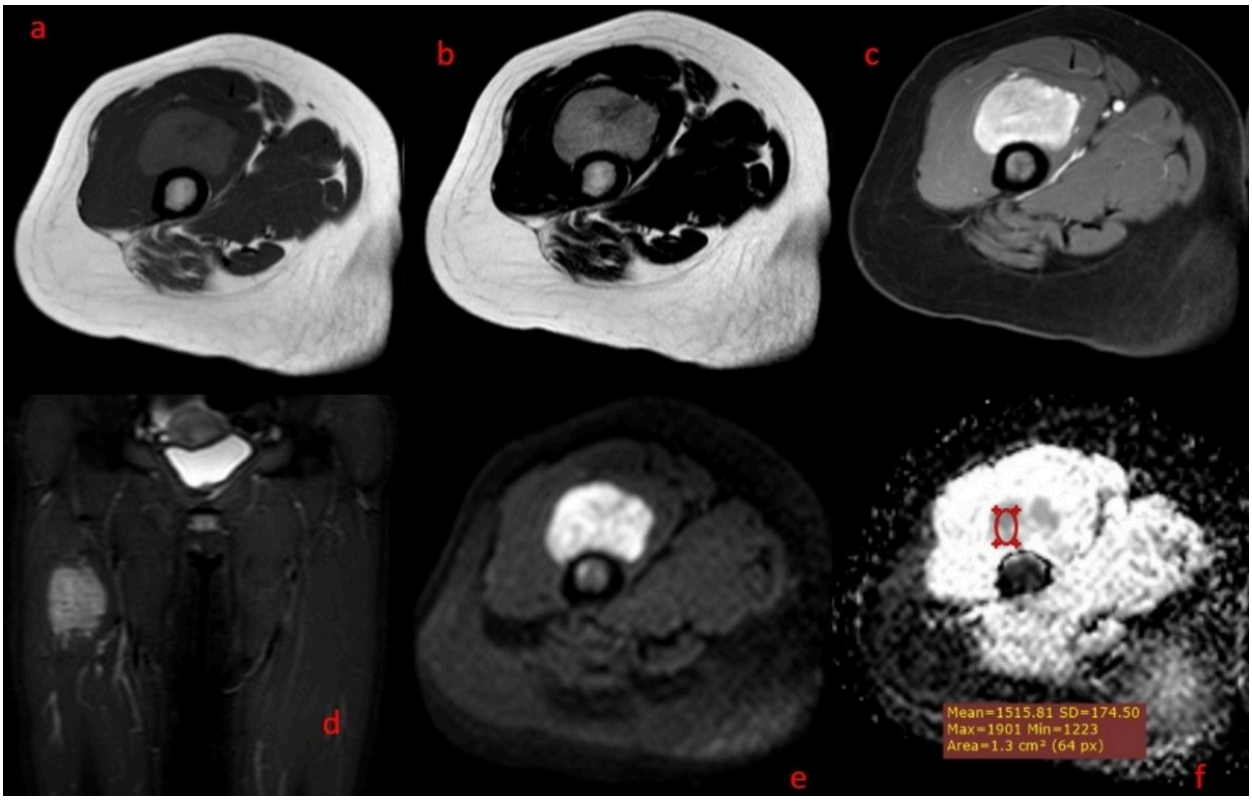

Fig. 2: Figure 2, Paraganglioma in a 20 years old woman (a) Axial T1WI and (b) Axial T2WI & (c) Post contrast Axial THRIVE WI (d) Coronal STIR WIs showed a well-defined soft tissue mass is seen involving the anterior thigh compartment at a deep peri-osseous location eliciting isointense to low signal on T1& heterogeneous isointense and high T2/STIR signal. with intense homogeneous enhancement in post-contrast images. Corresponding DWI (e) & ADC maps (f) showed high signal in DWI & low ADC signal with a mean ADC value = 1.55 x10-3 mm2/sec.

Results

The study included 108 newly diagnosed soft tissue lesions. Their histologic diagnoses were as follows:

Fibromatosis (n=42),dermatofibrosarcoma protuberans (n=4), NF (n=3), lipoma (n=9) , hemangioma (n=5) schwannoma(n=1), paraganglioma (n=1), GCT tendon sheath(n=1)/ synovial sarcoma (n=6)/ rhabdomyosarcoma (n=7), myxoliposarcoma (n=6), undifferentiated sarcoma (n=7)/ malignant melanoma (n=2), squamous cell carcinoma (n=3)/ mucor fungoides (n=1), leiyomyosarcoma (n=1), high grade sarcoma (n=3), myxofibrosarcoma (n=1), low grade sarcoma (n=2), malignant nerve sheath tumor (n=1), liposarcoma (n=1), MFH (n=1).

Our study results demonstrated that benign soft tissue masses had a mean ADC value 1.18$\pm$ 1.0191 x 10^{-3} mm^2/s; with the lowest recorded value was 0.1 x 10^{-3} mm^2/s in lipoma & the highest ADC value was 3.6 x 10^{-3} mm^2/s in hemangiomas. These benign soft tissue masses showed a mean minimum ADC value 0.9 $\pm$0.84 mm^2/s; with the lowest value 0.05 & the highest minimum ADC value for benign tumors was 2.9 x 10^{-3} mm^2/s.

For malignant soft-tissue masses, the mean ADC value was 1.3$\pm$ 0.7 x 10^{-3} mm^2/s with its lowest value 0.5 & highest value 3.4 meanwhile minimum ADC values was 0.85$\pm$0.84 x 10^{-3} mm^2/s with the lowest value 0.3 & the highest value 3.1.).

Myxomatous malignant masses had an ADC value of 2.6$\pm$ 0.55 x 10^{-3} mm^2/s while non-myxomatous malignant masses had an ADC value 1.1$\pm$0.8 x 10^{-3} mm^2/s.

Regarding fibromatosis patient the newly diagnosed cases demonstrated a mean ADC value 1.31+ 0.245 x 10-3 mm2/sec & minimum ADC value 0.71+ 0.4 x 10-3 mm2/sec.

Detailed analysis of ADC (mm^2/sec) values is shown in the **table (1)**, including the average ADC$\pm$ SD in newly diagnosed benign, malignant and fibromatosis lesions included in our study.

Final clinical diagnosis	**Mean ADC**	**Std. deviation**	**Min ADC**	**Std. deviation**
Malignant masses	**1.309**	**0.723**	**0.825**	**0.66**
Benign masses	**1.18**	**1.0191**	**0.9**	**0.84**

Myxoid malignant masses	**2.6**	**0.69**	**1.9**	**0.8**
Nonmyxoid malignant masses	**1.1**	**0.35**	**0.64**	**0.31**
Fibromatosis	**1.31**	**0.245**	**0.71**	**0.4**

Table (1), ADC (mm^2/sec) values in showing different pathological entities included in our study.

Attempted propagation of ADC cut off value between benign & non benign (including malignant & locally aggressive masses) was 0.6 x 10-3 mm2/sec with a sensitivity 98.3% & specificity 50% (P=0.5123).

Also attempted propagation of statistical difference between malignant soft tissue masses (mean ADC 1.309+0.723x10-3 mm2/s) & fibromatosis masses (mean ADC value 1.31 +0.245 x 10-3 mm2/s) using a comparative (T-test) showing a difference -0.0051, standard error =0.17 & poor significance level 0.9757 **(table 2).**

Diagnosis	**Mean ADC**	**Std. deviation**
Malignant masses	**1.309**	**0.723**
Fibromatosis	**1.31**	**0.245**
(T-test) Difference -0.0051 ,standard error=0.17,signifacnce level=0.9757		

Table 2 shows comparative T-test for comparison of ADC values of fibromatosis & malignant masses.

Regarding post-chemo-radiotherapy for soft tissue sarcoma patients:-

Follow up MR examinations were available for 9 patients with soft tissue sarcoma who received chemo+/-radiotherapy showing regression in size with the corresponding increase of mean ADC values **(table 3).**

	Mean ADC	**Standard deviation**
Pre therapy	**1.8222**	**0.8758**
Post therapy	**2.1**	**0.8689**
Mean difference using a paired sample t-test is 0.2778 with a standard deviation of 0.097 (P=<0.0001)		

Regarding post-chemo-radiotherapy for fibromatosis patients:-

Follow up MR examinations were available for 9 patients with fibromatosis (12 lesions) who received chemo+/-radiotherapy. Eight lesions showed a favorable response with an overall reduction or stabilization of tumor size accompanied by a decrease in their T2 signal intensity and an increase in the percentage of the low signal bands/areas within the tumor **(Table 4)**.

	Mean ADC	Standard deviation	Minimum ADC Value	Standard deviation
Favourable response to treatment	**1.4**	**0.19**	**0.79**	**0.43**
Poor response to treatment.	**1.5**	**0.3**	**0.8**	**0.25**

Table 4 show ADC values of fibromatosis patients with a favorable & poor response.

Lesions that showed a favorable response to chemo- or radiotherapy exhibited lower ADC values than those showing a progressive disease course. This difference was even more evident in the minimum than the mean ADC values.

Images for this section:

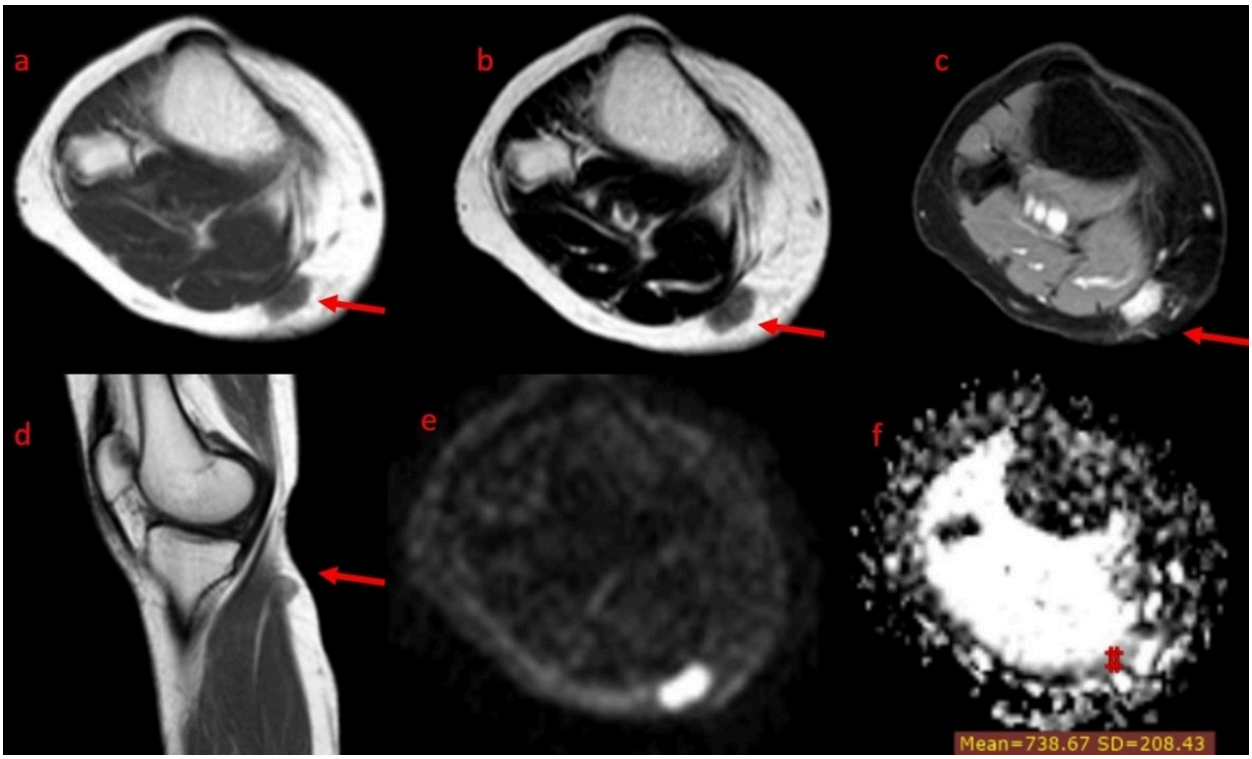

Fig. 3: Figure 3, Unclassified soft tissue sarcoma in a 30 years old woman (a) Axial T1WI (b) Axial T2WI & (c) post-contrast axial Thrive WI & (d) postcontrast sagittal T1 WIs showing well-defined superficial soft tissue nodule seen involving the posteromedial aspect of the upper leg at a subcutaneous location inseparable from the fascia of the medial head of gastrocnemius muscle. It elicits isointense signal to muscle on T1 WI, isointense to a high signal on T2 WIs with intense homogeneous enhancement on post-contrast series. Corresponding DWI (e) & ADC map (f) showed high signal in DWI & iso to low signal on ADC map with a mean ADC value = 0.74 x10-3 mm2/sec.

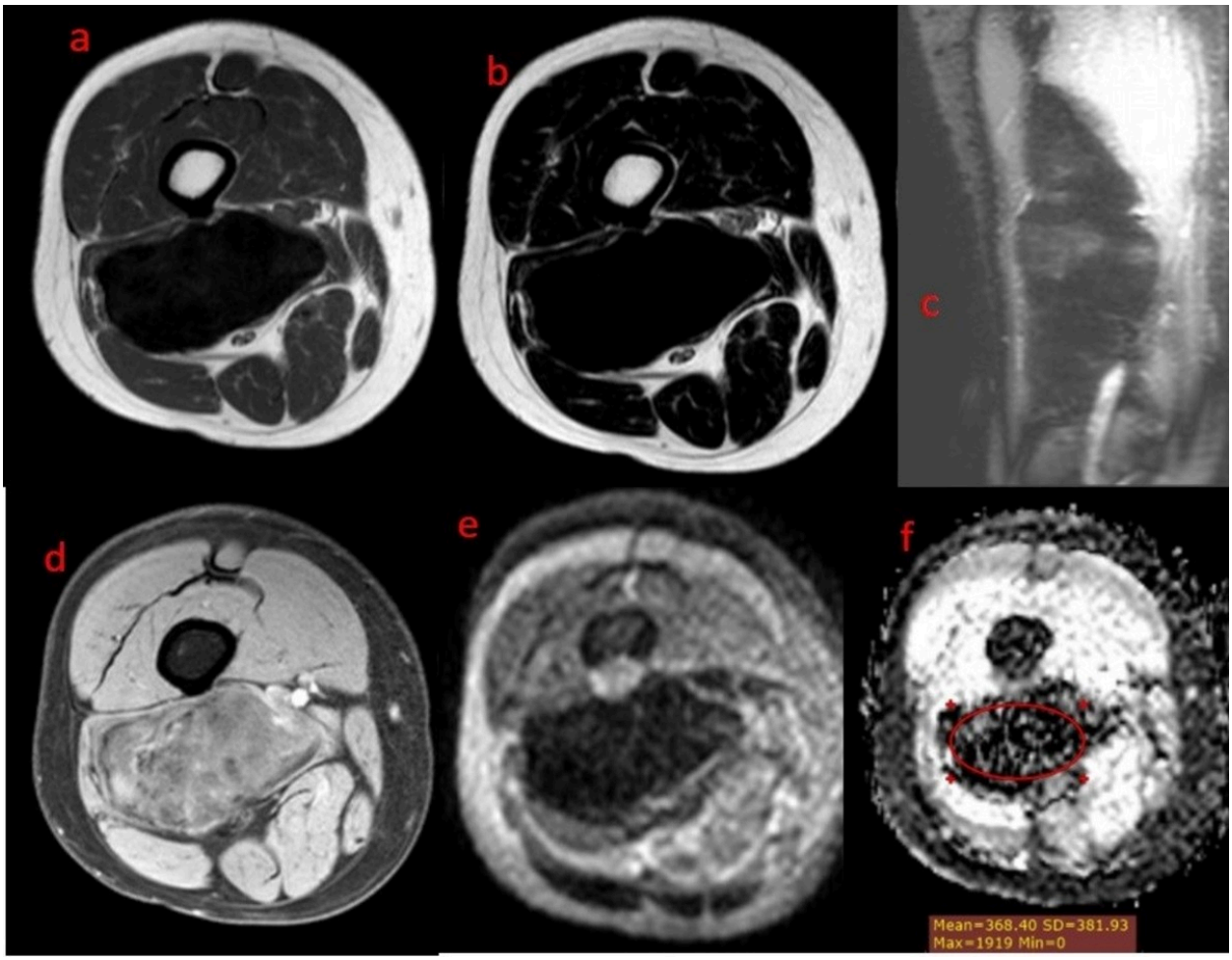

Fig. 4: Figure 4 Fibromatosis in a 35 years old man (a) axial T1WI (b) axial T2 WI & (c) coronal STIR WIs showing a well-circumscribed deep soft tissue mass in the posterior muscular compartment of the right thigh along the biceps femoris muscle abutting the lateral aspect of the lower femoral vessels eliciting marked hypointense signal on T1, T2 & STIR WIs. (d) Postcontrast axial THRIVE WIs showed mild heterogeneous enhancement. Corresponding DWI (e) & ADC map (f) showed low signal in DWI & ADC map with a mean ADC value = 0.37 x10-3 mm2/sec.

Conclusion

Regarding inital evaluation of soft tissue masses

A significant overlap between benign & malignant masses as benign & malignant ADC values were (mean ADC=1.2 x 10-3 mm2/sec & 1.31 x 10-3 mm2/sec ,respectively).

Mean ADC values for benign non myxoid tumors, myxoid malignant tumors & non myxoid malignant tumors were 1.2×10^{-3} mm^2/sec, 2.6×10^{-3} mm^2/sec & 1.1×10^{-3} mm^2/sec.

Newly diagnosed fibromatosis patients mean ADC values were 1.31 ± 0.25 × 10-3 mm2/ sec)

Regarding post-therapeutic follow up

Follow up soft tissue sacromas patients showed that lesions of a favourable theeapeutic response had increase of recorded ADC values about 0.28 x10-3 mm 2 /s between pre & post-therapy corresponding well to the decreased overall tumoral volume & enhancement pattern.

Follow up fibromatosis patients in our study showed that lesions of a favorable response to chemo- or radiotherapy exhibited lower ADC values than those showing a progressive disease course.

In conclusion, diffusion-weighted imaging with ADC mapping of extremity soft tissue tumors is so complicated that they alone may not be useful in differentiating between benign and malignant tumors. DWI with ADC mapping can be used as a tool for monitoring response to treatment.

Images for this section:

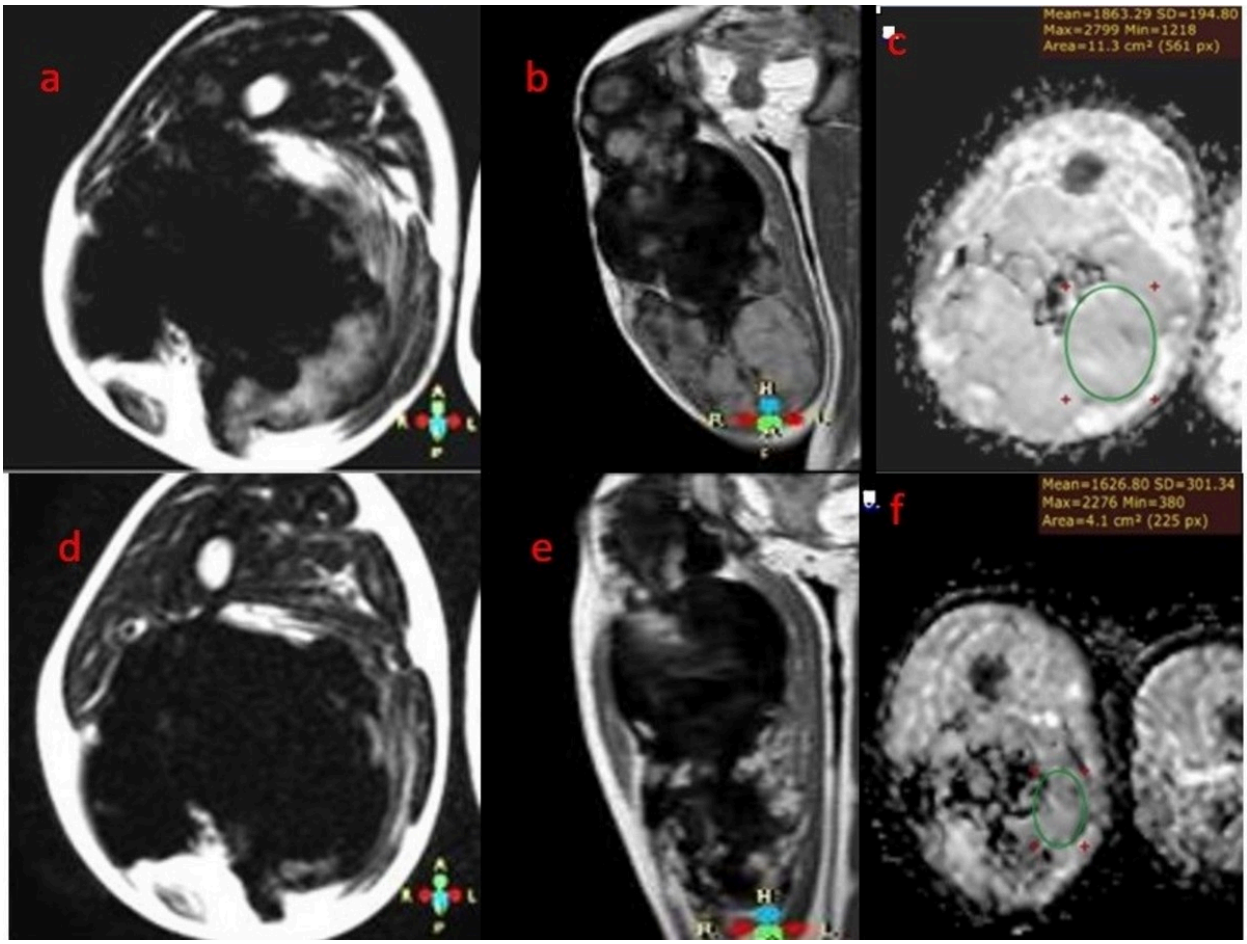

Fig. 5: Figure 5, 8 years old patient with fibromatosis on chemotherapy with pre-chemotherapy series (a) axial T2WI (b)post contrast coronal T1 WI & (c) ADC map & post chemotherapy series (d) axial T2WI (e)post contrast coronal T1 WI & (f) ADC map showing overall decrease of the high T2 WI signal with predominance of the low T2 signal ,marked decrease in the degree of post-contrast enhancement in the post-therapeutic images, as well as decrease of mean & minimum ADC values, previously reading 1.86 × 10-3 mm2/sec & 1.21 10-3 mm2/sec being 1.63 10-3 mm2/sec & 0.3810-3 mm2/sec in post-therapeutic series.

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