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ORIGINAL ARTICLE

Imaging Spectrum in Soft Tissue Sarcomas

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Abstract Imaging plays an important role in detection, diagnosis as well as pre and post operative management of patients with soft tissue sarcomas. Soft tissue sarcomas are generally a diagnostic dilemma needing the complimentary use of both radiology and pathology for their accurate diagnosis. In this review article, we have tried to highlight the important facts about the various imaging modalities available as well as the recent advances in the field of radiology.

Keywords Soft tissue sarcoma · Imaging · Ultrasound · CT · MRI · PET-CT

Soft tissue sarcomas (STS) pose a difficult diagnostic challenge for both the clinicians and pathologists. STS are rare cancers and their prognosis is dismal as they are generally detected at a later stage and recurrences are fairly common. About 10% of STS arise in the retroperitoneal tissues. Overall incidence of STS's has been increasing. While malignant soft tissue tumors are rare, benign tumors are not; it is estimated that there are 100 benign lesions for each sarcoma [1]. The advent of computer—assisted imaging has revolutionized the radiologic evaluation of a suspected soft tissue mass. The currently available imaging modalities offer numerous noninvasive methods to diagnose and stage suspected soft tissue sarcomas. This article highlights the general imaging approach to patients presenting with soft tissue masses. The purpose of this article is to give an overview emphasizing the fundamental principles inherent to tumor imaging and the specific applications of the newer imaging modalities.

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Initial Evaluation

As no single imaging modality is ideal for every tumor, hence a multimodality approach is warranted for. Initial diagnostic evaluation should begin with radiographs of the mass or region in question. Although radiographs are frequently unrewarding; they can provide invaluable information when positive. Radiographs may give information about skeletal deformity masquerading as a soft tissue mass or soft tissue mineralization that may be suggestive, and at times characteristic, of a specific diagnosis. Extrinsic bone erosion, cortical destruction or periosteal reaction is well revealed on plain radiographs (Fig. 1a & b). Plain radiographs can also reveal the presence and the pattern of soft tissue calcification and ossification, which can suggest a specific diagnosis that may be of help. For example formation of phleboliths is suggestive for hemangiomas, characteristic nodules located near large joints suggest synovial chondromatosis, calcifications starting at the periphery of a lesion are seen in myositis ossificans, and non specific poorly defined, amorphous calcifications are not infrequently found in synovial sarcomas [2–4].

Other soft tissue sarcomas that may be seen with accompanying calcifications include alveolar soft part sarcoma and epitheloid sarcoma [5–7]. Plain radiography can also provide an excellent method for assessment of

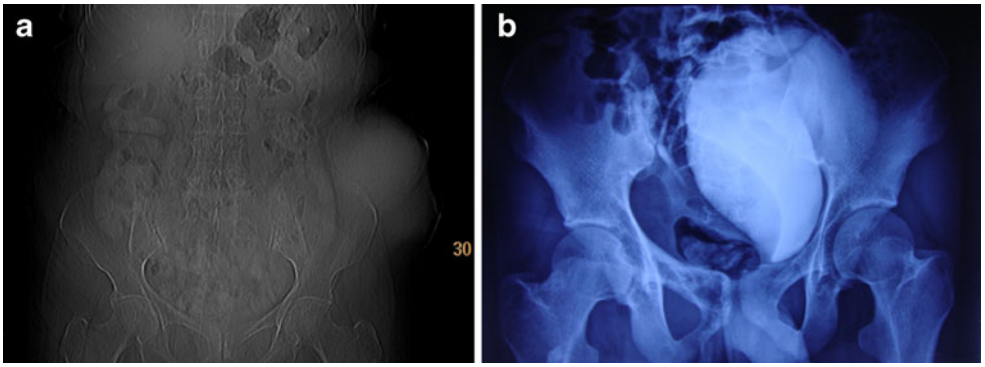

Fig. 1 **a** Plain radiograph in a case of known STS showing soft tissue mass overlying left iliac bone. **b** Radiography taken in excretory phase of intravenous urogram showing a right sided pelvic soft tissue mass causing bladder displacement and compression with pubic bone erosion

osseous involvement by a soft tissue tumor, such as remodeling, periosteal reaction or overt destruction.

Additional Imaging Modalities

While radiographs may be sufficient for diagnosis of specific benign tumors such as intramuscular cavernous hemangioma or myositis ossificans, additional imaging is often required in cases of STS. Further imaging may be needed for diagnosis in order to determine the true local extend of a lesion, to evaluate its relationship to adjacent structures and stage suspected malignancy. Additional available modalities include ultrasonography (US), computed tomography (CT), magnetic resonance imaging and positron emission tomography (PET).

Ultrasonography

Ultrasonography (US) is a readily available, noninvasive and relatively inexpensive technique and is generally used in the early evaluation of a soft tissue mass. It gives an initial evaluation of the size, location and consistency of soft tissue lesions, particularly when located in the abdomen or extremities. Differentiation between cystic and solid lesions is an important ability of US. It must be emphasized that the specificity of US in further characterizing a soft-tissue mass is low. Ultrasound criteria indicating a high suspicion of malignancy include increased size, irregular margins, heterogeneity and architectural distortion, whereas benign masses tend to be smaller, more homogeneous, well defined, superficially located and displacing rather than invading structures (Fig. 2a & b). Ultrasonography can also be used to guide percutaneous needle biopsy. If a malignant lesion is suspected, fine needle aspiration or preferably Tru-cut biopsy can be performed. For accurate histopathological examination, it is important to avoid necrotic or hemorrhagic areas. Using US, a high yield of solid, representative tissue can be achieved.

Adjunct to US are power and color doppler which are important aids in determining the amount and pattern of vascularity of a soft tissue masses. High-grade soft tissue sarcomas may demonstrate predominant peripheral flow, due to outgrowth of blood supply with concomitant central necrosis (Fig. 2c & d). In selected cases, color doppler ultrasonography may also be used to monitor the effects of locoregional (tumor perfusion) or systemic chemotherapy, which has been proved to be worthwhile in bone tumors with associated soft tissue extension. Increased or decreased changes in tumor (neo) vascularization and peripheral resistance reflect absence or presence of response [8, 9].

Ultrasonography may also be used to detect local tumor recurrence, particularly when MR imaging is unattainable due to metallic fixation devices used in reconstructive surgical procedures. Though presence of a hypoechoic soft-tissue mass highly suggests recurrent sarcoma, differentiation from seroma, hematoma, abscess and/or granulation tissue may be difficult, particularly in the early postoperative phase. In such cases color Doppler or additional MR imaging may be performed. Recent literature has shown three dimensional (3D)ultrasonography to be a valuable adjunct to conventional ultrasonography providing previously unattainable scan planes and three-dimensional views. This new technique also gives spatially oriented and standardized views thereby reducing operator dependence, making follow up studies easier. 3D data processing gives an accurate anatomical display and is valuable in carrying out interventional procedures by using multiplanar views. With the advent of 3D ultrasound the acceptance of clinicians for the use of sonography may increase.

Computed Tomography

The most effective modality for the detailed evaluation of osseous architecture is computerized tomography. Introduction of multidetector scanners and high-quality multiplanar reformatted images has revolutionized the image quality (Figs. 3, 4). More volume coverage is possible due to faster gantry rotation speed. Superior reformatted images and three dimensional reconstructions depict the malignant pathology exquisitely. Motion artifact is reduced due to

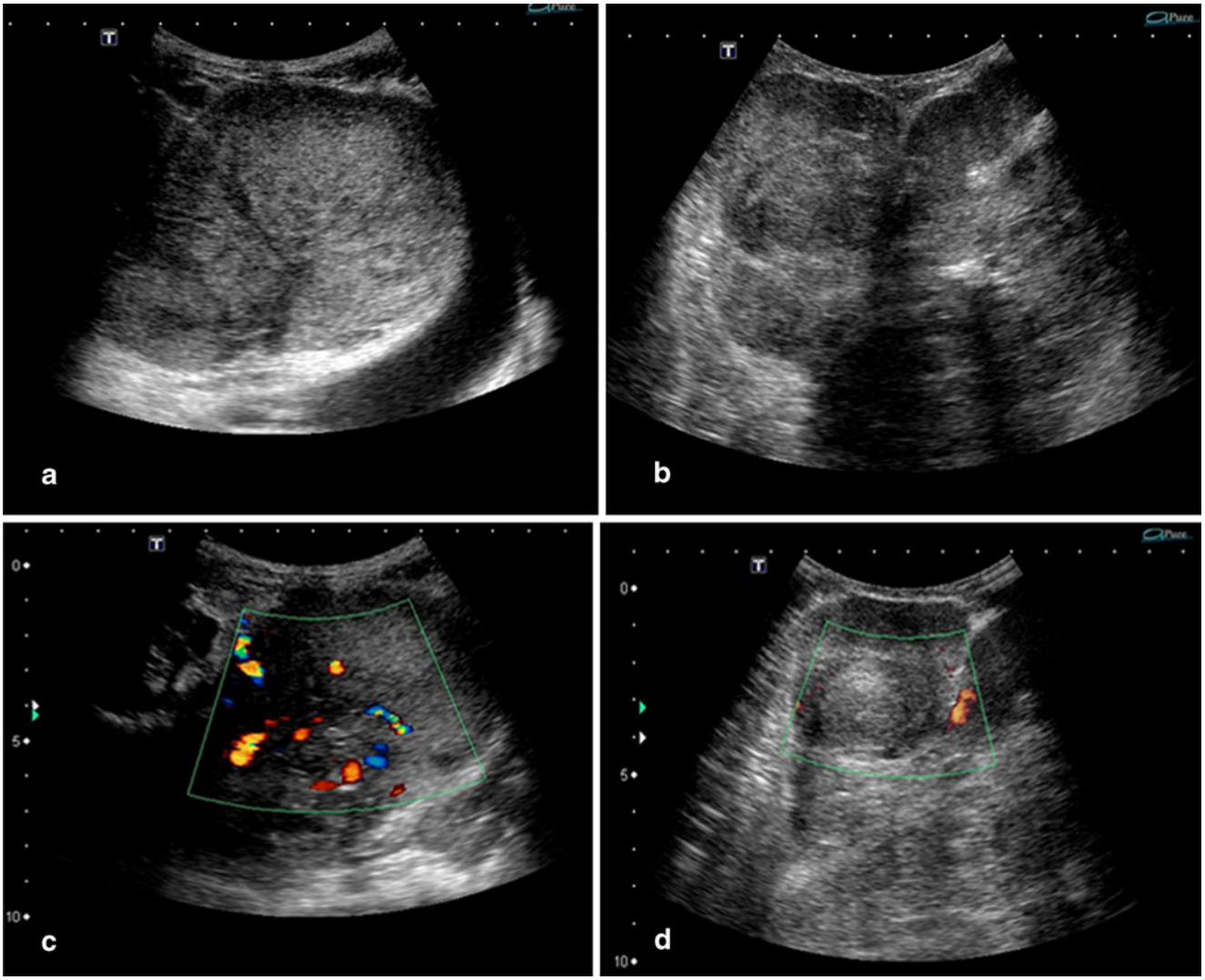

Fig. 2 **a** & **b** Sonographic images showing STS in pelvic (**a**) and left abdominal wall (**b**). **c** & **d** show peripheral tumor perfusion on the color flow imaging

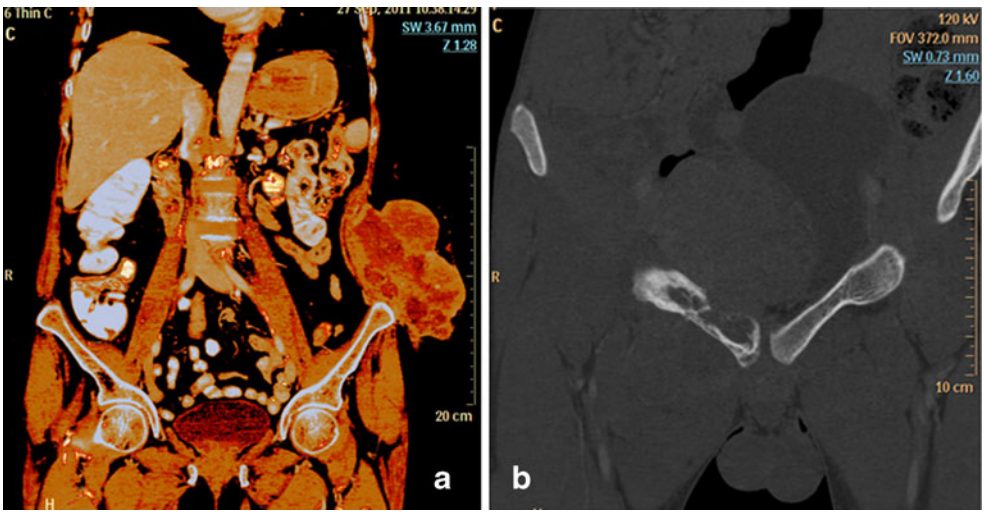

Fig. 3 **a** Volume rendered MDCT image showing anatomical details of the abdominal wall STS **b** Bone window CT image of recurrence of pelvic STS showing involvement of pubic symphisis

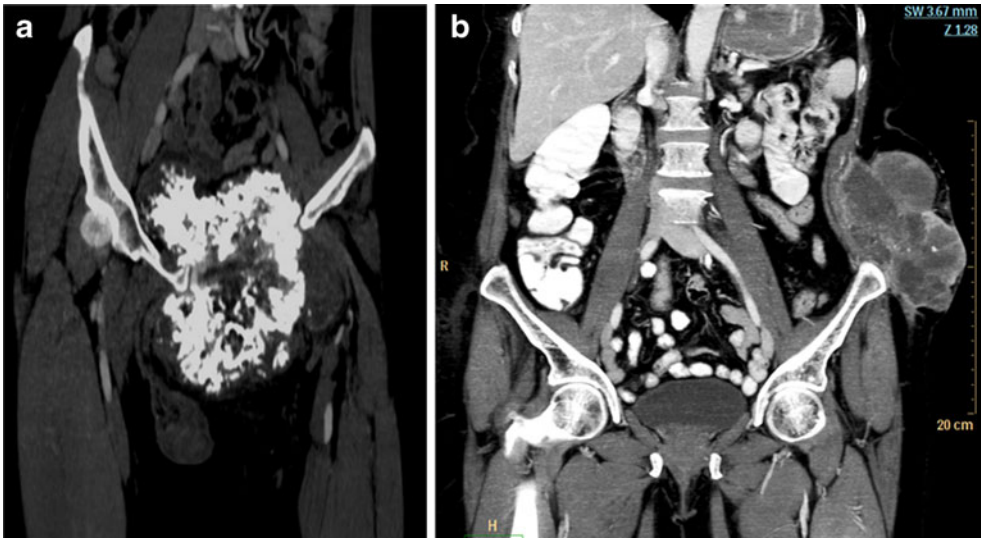

Fig. 4 **a** Plain CT image showing pelvic chondrosarcoma with expensive calcification **b** CT scan image of abdominal wall STS. Underlying iliac bone is not involved

increased temporal resolution. It is ideally suited for evaluation of lesions having complex osseous anatomy. Osseous remodeling, periosteal reaction, and matrix is better detected, also extrinsic osseous erosions, subtle areas of mineralization, or soft tissue gas that may not be apparent on MRI, is better identified. In cases of post-operative patients with metallic hardware, with the efficient usage of the x-ray tube, beam-hardening artifacts can be minimized. Hence there is better visualization of surrounding structures. With the advent of MDCT, CT angiography has become an useful modality to demonstrate vascular anatomy (Figs. 5, 6). CT is also useful in patients in whom MRI is contraindicated. In a multi-institutional study by the National Institute of Health, the Radiology Diagnostic Oncology Group found no statistically significant difference between CT and MRI in determining tumor involvement of muscle, bone, joint, or neurovascular structures [10, 11]. CT is the preferred modality for the identification of pulmonary metastases. CT is also important in aiding in various intervention techniques, aspiration and biopsy procedures. Now with the advent of robotic guidance where an automated apparatus that calculates coordinates on

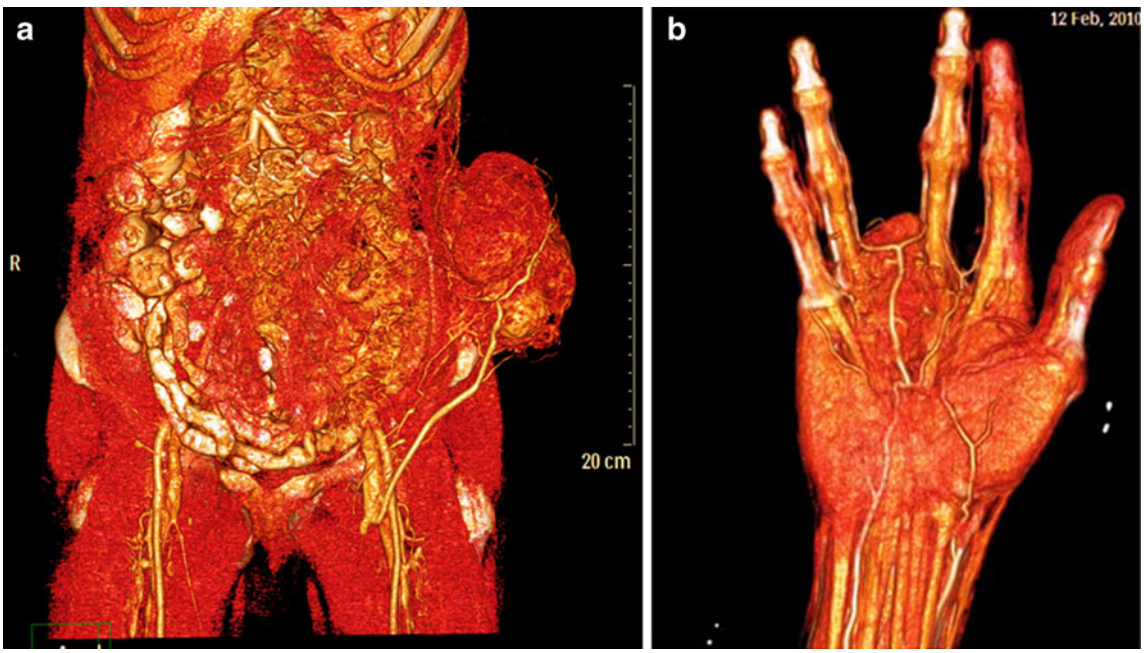

Fig. 5 **a** Volume rendered CT angiography image of abdominal wall STS showing feeder vessels and draining vein of the tumour **b** Synovial sarcoma of hand showing vascular relationship of the lesion

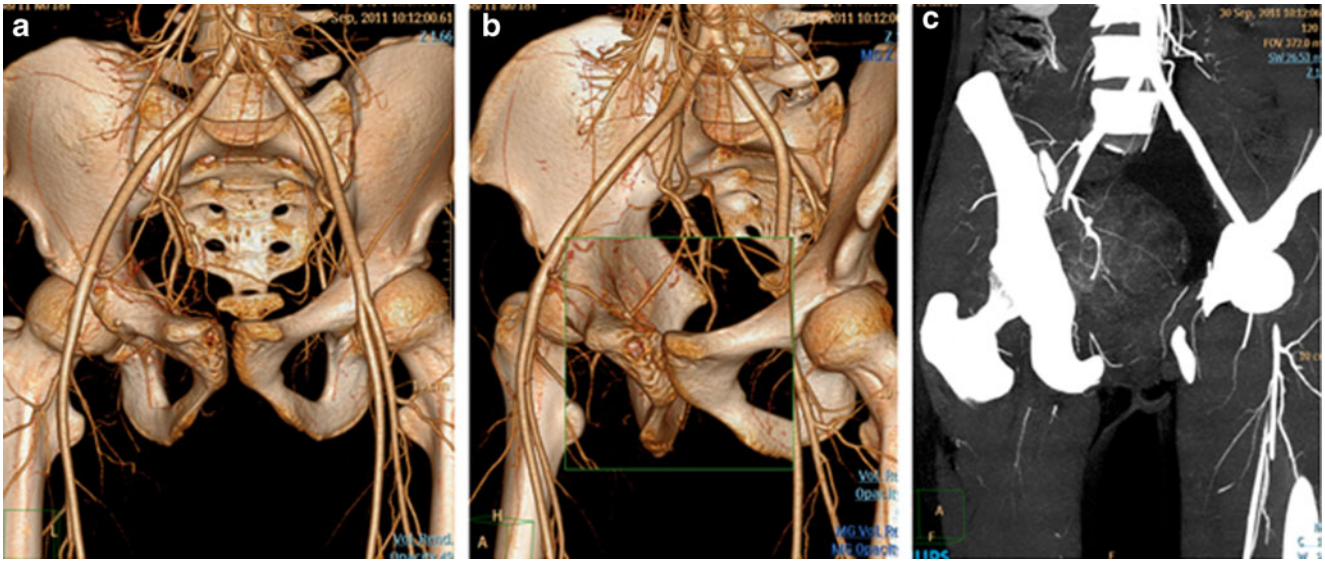

Fig. 6 CT angiographic images (volume rendered, **a** & **b** and MIP, **c**) showing vascular anatomy in case of pelvic STS. Bony involvement can also be accurately demonstrated

DICOM images from a CT scanner and guides the placement of a needle accurately within the body after insertion, the yield rate in cases of difficult biopsies has also gone up.

Magnetic Resonance Imaging

MRI has the ability to give accurate information about both bones and soft tissue, providing valuable information to assist in both diagnosis and staging. It has thus emerged as the preferred modality for evaluating soft tissue tumors. Image quality has been markedly improved by the use of improved gradient strength and speed, coupled with specialized coils that provide increased signal-to-noise ratios.

Accurate anatomical location of a lesion as well as neurovascular relationship, and adequate assessment of bone and soft tissue is the hallmark of MRI. Striking soft tissue contrast resolution of MR facilitates image interpretation however it has limited ability in demonstrating patterns of soft tissue calcification [9]. Sequences usually used in MR imaging include routine T1 and T2 weighted images, inclusion of fluid sensitive and fat saturated sequences help in increasing the specificity (Figs. 7 & 8). Literature has shown MRI to be more superior in detecting tumor involvement of one or more individual muscles that appeared normal on CT.

Though not advocated as a primary screening modality, MRI has been shown to be an important diagnostic tool in staging especially when surgical management has been planned. It is also useful in providing a road map, as well as being helpful in predicting need for development of myocutaneos flaps for wound coverage and in planning adjuvant radiation therapy. It has an edge over CT in the form of image quality, ease of tumor detection and clarity of lesion boundaries. Studies have shown that when a treatment plan includes en bloc wide excision with preservation of limb function, MR is the most valuable imaging technique for preoperative anatomic staging [12]. In MR imaging characterization of soft tissue masses is based on information obtained by comparison of signal characteristics on various sequences, together with morphologic features. Lesions are frequently considered benign when they are small sized with smooth, well-defined margins and homogeneous appearance. However, some malignant masses may also appear as well-defined homogeneous masses.

Larger and more heterogeneous masses should be considered suspicious as only five percent of benign soft tissue tumors measure more than five cm [13]. Combinations of signal intensities reveal the different tumor components (e.g. fat, melanin, water, and blood), thus providing information about the pathologic nature of soft tissue masses. MR signal intensity characteristics of the majority of the soft tissue lesions, including soft tissue sarcomas are nonspecific. They tend to exhibit intermediate signal intensity on T1-weighted images compared to skeletal muscle and high signal intensity on T2-weighted images. Differentiation of different histologic types of soft tissue sarcoma based on MR appearance alone is impossible. However, specificity of MR imaging increases when characteristic imaging features are observed, such as high signal intensity on T1-weighted images or low signal intensity on T2-weighted images.

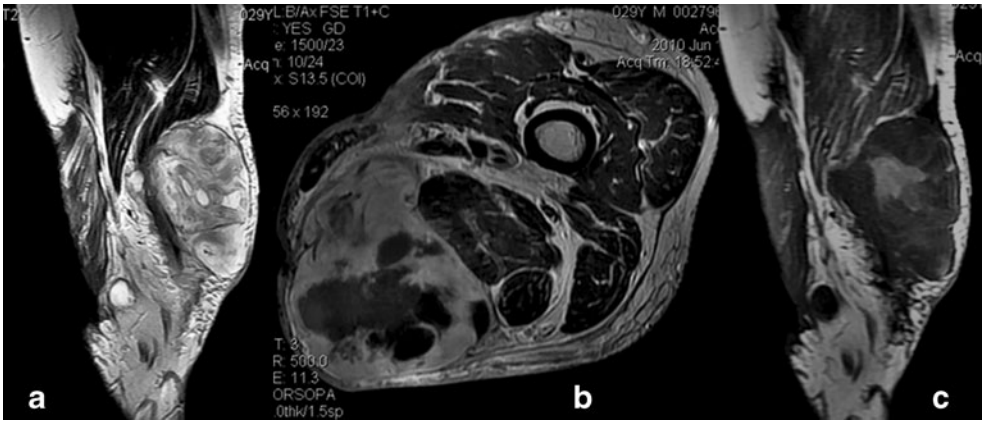

Fig. 7 **a**, **b** and **c**. MR T1W (**a**), T2W (**b**) and contrast enhanced (**c**) images showing a lower limb fibrosarcoma

Contrast-Enhanced MR imaging

Administration of intravenous contrast agent (Gd-DTPA) has increased the potential of MRI. Comparison of signal characteristics on non-enhanced and enhanced images after intravenous administration of Gd-DTPA improves morphologic distinction between different areas within the tumor. Static contrast-enhanced images usually taken in association with fat saturated sequences generally assist in identifying solid enhancing tumor parts, opposed to non-enhancing cystic or necrotic components. Though not specific however high-grade soft-tissue sarcomas frequently tend to demonstrate a peripheral enhancing zone with a non-enhancing necrotic center (Figs. 7 & 8). Dynamic contrast-enhanced MR studies with rapid image acquisition after intravenous bolus administration of Gd-DTPA is a valuable tool in distinguishing benign from malignant soft tissue tumors, monitoring response to (chemo)therapy, guiding biopsy procedure, and early detection of local tumor recurrence [13, 14]. This technique provides an indication

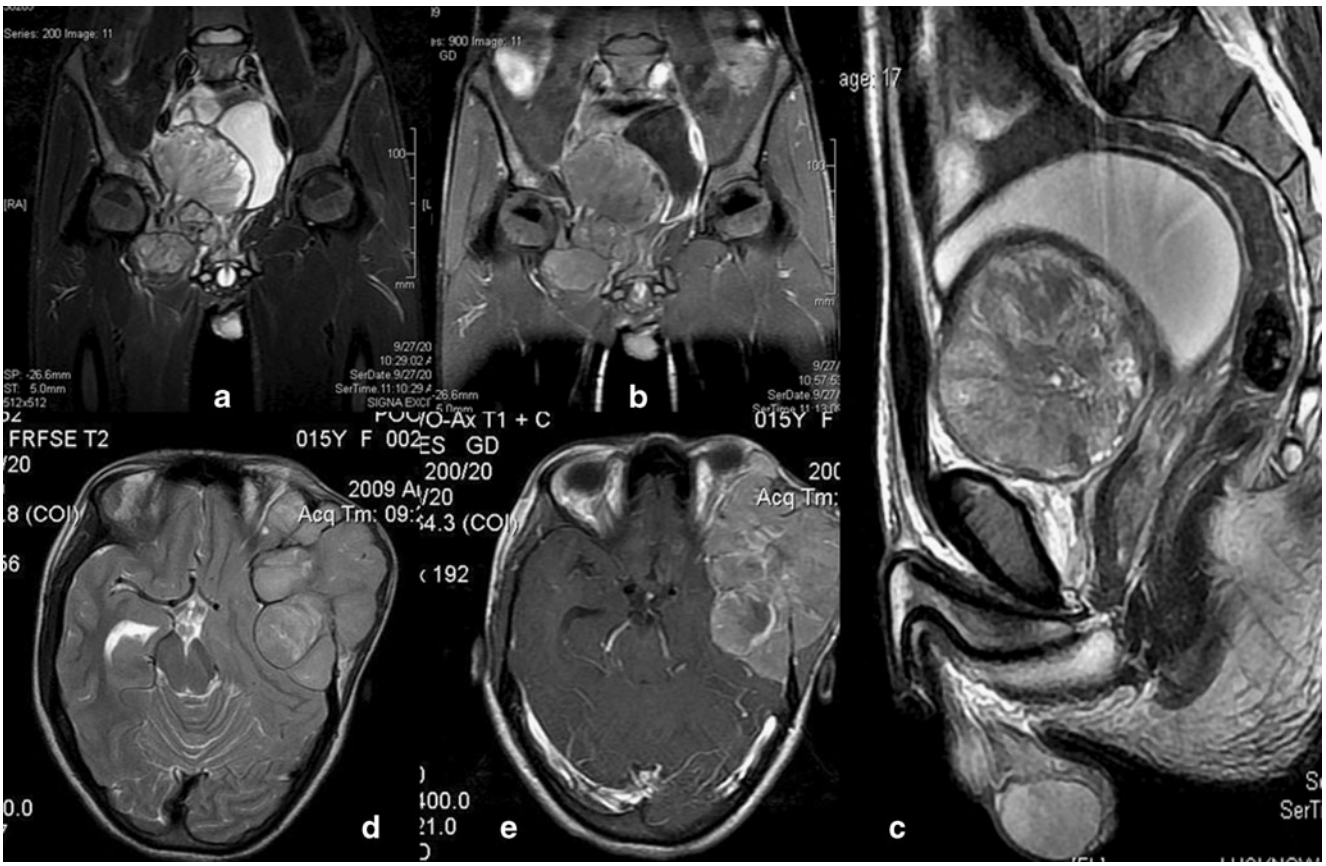

Fig. 8 **a**, **b**, **c** Fat saturated T2W coronal (**a**), CE MR coronal (**b**) and T2W sagittal (**c**) images showing recurrence of pelvic STS 8 d, e T 2 W and CEMR image showing infra - temporal fossa pleomorphic sarcoma

of tissue vascularization, perfusion, capillary permeability and composition of the interstitial space.

There have been various indicators of the malignant potential STS like the start of tumoral enhancement, pattern of tumoral enhancement (peripheral versus diffuse) and slope values Despite some overlap between highly vascularized benign lesions (e.g. nodular fascitis, schwannomas etc.) and malignant lesions, dynamic contrast-enhanced MR imaging seems to be a promising technique in distinguishing benign from malignant soft tissue tumors [15]. Early, rapidly progressive and peripheral enhancement favor the diagnosis of soft tissue malignancy, whereas late and gradual or absent dynamic enhancement more likely occurs in benign lesions. Soft tissue sarcomas can be treated preoperatively, either systemically (neoadjuvant chemotherapy) or locally (isolated limb perfusion with tumor necrosis factor α and melphalan), in an attempt to reduce initial tumor load. Hence in patients with high-grade bone sarcoma, dynamic contrast-enhanced MR imaging may also be useful in evaluating the effects of systemic or local chemotherapy in selected patients with soft tissue sarcoma [14]. Areas or foci showing rapidly progressive enhancement may represent remnant viable tumor, whereas reactive changes such as peritumoral edema will show a more gradual pattern of enhancement.

MR Angiography (MRA)

MRA can also be performed with or without gadolinium to accurately depict vascular anatomy and detection of aneurysms and pseudoaneurysms (Fig. 9). Newer techniques utilizing bolus administration of gadolinium with fast sequences timed at peak contrast concentration in the affected region can reveal vascular anatomy with remarkable detail.

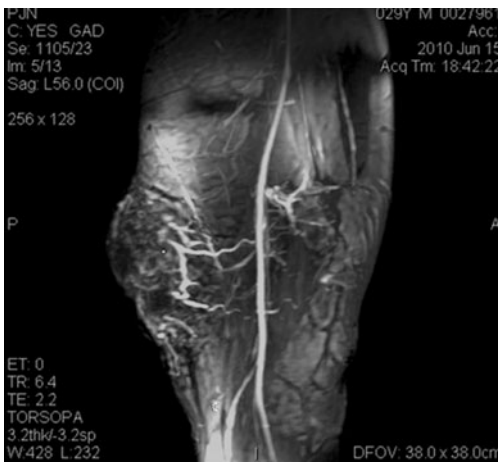

Fig. 9 MR TOF angiographic image showing vascular supply of the tumor

MR Spectroscopy (MRS)

Anatomical imaging techniques including radiography, ultrasound, CT and MRI currently play a dominant role in the evaluation of suspected and known soft tissue sarcomas. However these imaging techniques fall short of estimating the degree of tumor variability. Functional imaging methods that measure biological properties within sarcomas may be better able to determine true tumour response to chemotherapy or radiotherapy.MR spectroscopy gives information regarding the cellular chemistry. MRS can estimate the marker for membrane phospholipid like phosphatidyl-choline and hence provide information about increased cellularity and aid in differentiating malignant tumors (Fig. 10) [16] MRS is done as an adjunct to dynamic contrast enhanced MR imaging, correct positioning of the volume of interest for suspicious lesions is guided by the use of enhanced images. Use of MRS along with anatomical imaging can be useful in differentiating benign versus malignant lesion, in guiding biopsies and in follow up of patients subjected to chemotherapy, radiotherapy and surgery.

PET

PET is an imaging technique which utilizes radioisotopes that undergo positron emission decay. Paired gamma photons released as a consequence of decay are detected by a sophisticated ring detector and the interaction is registered in the form of an image. PET has proven to be the "gold standard" in metabolic imaging. The radionuclide most commonly utilized for PET is [18 F]-fluoro-2-deoxy-D-glucose (FDG). In vivo, FDG behaves like glucose and provides a means of quantifying glucose metabolism. However unlike glucose, the metabolite of FDG is not a substrate for glycolytic enzymes. Hence the radioactive tracer is trapped in the cell, allowing subsequent imaging. The tissue's metabolism is reflected by the amount of tracer accumulated. The use of PET in the diagnosis of sarcoma is still being defined. Many types of tumors especially high grade sarcomas have higher rates of glycolysis than uninvolved tissue, hence are FDG avid than low grade malignancies and benign lesions (Fig. 11). Time taken for whole-body scan is approximately 40 to 60 min. It is considered positive when uptake is greater than that of the contralateral side or than in adjacent tissues. Advantages of PET over other conventional nuclear medicine techniques are rapid imaging and interpretation, with results available in as little as 2 hours, and multiplanar imaging with higher resolution than with other nuclear medicine techniques. Also PET is an inherently quantitative imaging method that allows treatment monitoring [17].

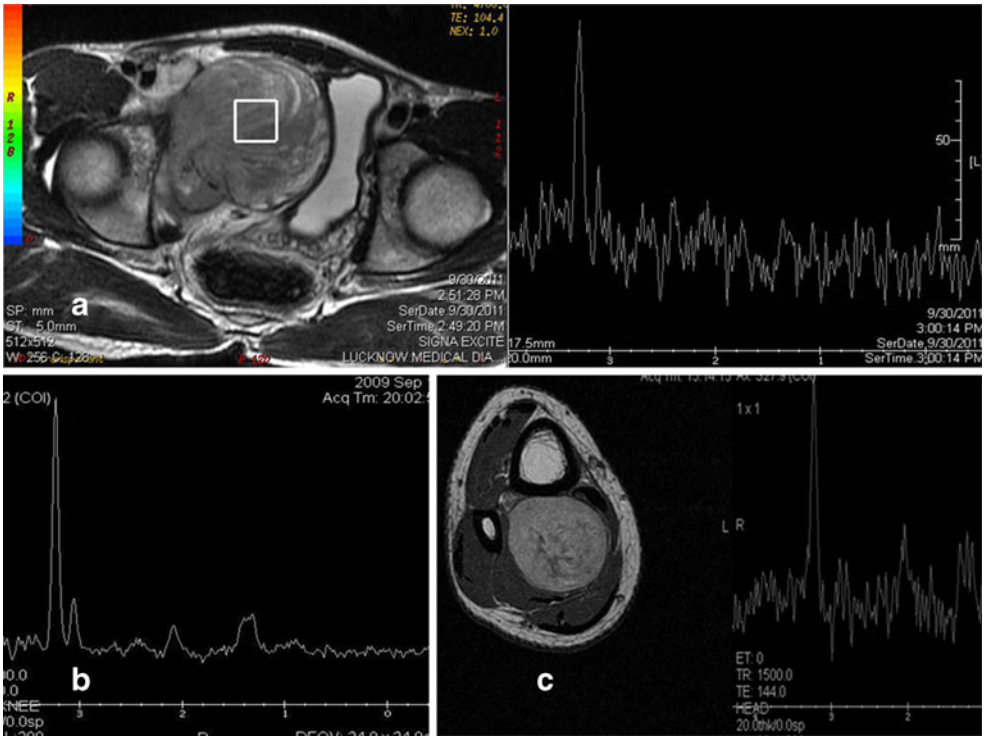

Fig. 10 **a**, **b** & **c** MR spectroscopy images taken at 144 TE in three different patients of STS showing choline peak characteristic of malignant lesions

FDG-PET is now the standard of care in initial staging, monitoring the response to therapy and management of various malignancies (e.g., breast cancer, lung cancer and lymphoma). However, the paucity of anatomical landmarks on PET images makes a consistent hardware fusion to anatomical cross-sectional data extremely useful. The introduction of combined PET-computer tomography (CT) scanners, which provide not only functional, but also structural information leading to a detection of sub centimeter lesions, made this technique useful in the early detection of the disease process and decreasing false-positive lesions. Few studies and clinical trials have found PET/CT to be useful in the identification of unknown primary and in the detection of unsuspected and unusual metastatic sites of a variety of sarcomas. It has been seen to be a useful adjunct in monitoring the response to chemotherapy, radiation therapy, and radiofrequency ablation and in the postoperative evaluation of these tumors. Recent literature has shown that PET-CT may play an important role in guidance of biopsies from primary lesion and especially from metastases to get the representative sample from a metabolically active tissue.

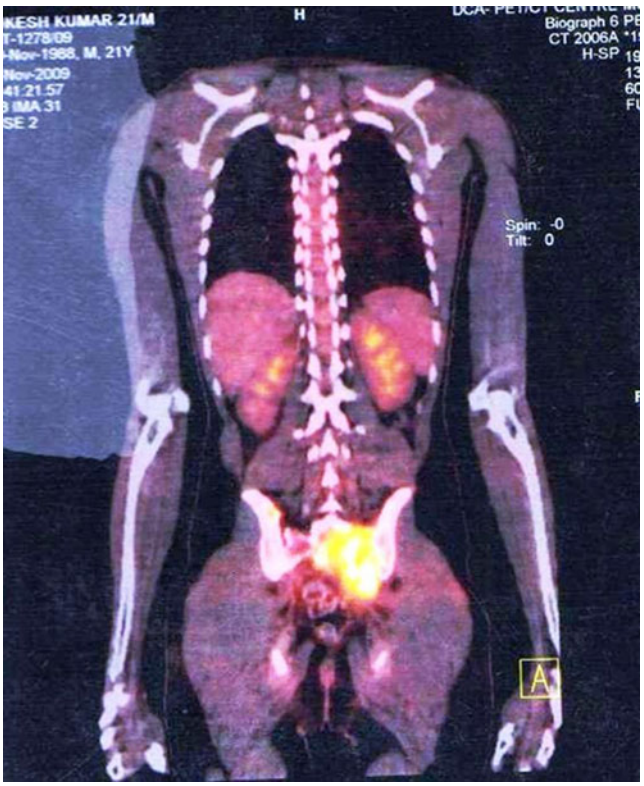

Fig. 11 PET–CT image showing FDG avid lesion indicative of a pelvic STS

Tumor Follow-up Imaging

Stage and grade of the initial lesion usually decide the follow-up protocol. Usually initial base-line postoperative imaging is done at 3 months, by which time post-operative changes have adequately resolved. Follow-up at 3–6 months interval is advocated for high grade lesions, while low-grade lesions may be followed annually. Large lesions, or those in which a wide margin could not be

obtained, may be followed more frequently. Follow-up imaging is continued for 5 years.

Imaging-Guided Biopsy

CT or US are important tools to assist in guided biopsies. Several principles are important for biopsy of suspected sarcomatous lesions, most important being coordination of the biopsy approach with the surgeon who will perform the definitive resection. An incorrect biopsy may violate the compartmental anatomy, leading to the risk of tumor seeding, and may change a wide excision to an amputation. Ideally, the needle track should be placed in the plane of the future incision. Coaxial needle system may be used to used to decrease needle seeding, in this a coaxial needle is placed at the edge of the lesion and then the biopsies are taken through this coaxial needle. In this manner, the needle traversing the superficial soft tissue is not exposed to the cells from the area of biopsy. Core biopsies typically offer higher yield than fine-needle aspirations.

The field of radiology has been revolutionized by new and improved imaging technology. The day is not far when cellular characterization may be possible by imaging, which will be of unparalleled benefit to the patient and clinician for planning various strategies of treatment and prognosticating the outcome.

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