ELSEVIER

Seminars in
ULTRASOUND
CT and MRI

Soft Tissue Sarcomas

Rajendra Kumar, MD, FACR

Imaging evaluation of soft tissue masses is essential for diagnosis, preoperative staging, and post-treatment follow-up. Magnetic resonance imaging plays the major role because of its superior resolution that helps in better tissue characterization, and its multiplanar imaging capability in evaluation of soft tissue masses. Additional imaging techniques, such as radiographs, computed tomography, positron-emission tomography-CT, radionuclide scintigraphy and ultrasonography, also play vital roles by providing additional information required in management of soft tissue masses. Knowledge of the usefulness and limitations of these imaging techniques is essential for their judicious selection. This article reviews the current role of various imaging techniques in diagnosis, presurgical planning, and post-treatment follow-up of soft tissue masses.
Semin Ultrasound CT MRI 42:194-200 **© 2020 Elsevier Inc. All rights reserved.**

Introduction

Soft tissue sarcomas comprise of more than 50 different pathologic subtypes of malignant mesodermal tumors, the majority of which are mesenchymal in origin. Neuroectodermal and some other unknown-cell derivative sarcomas, such as Ewing sarcoma and synovial sarcoma, also occur.[1,2] These tumors can arise anywhere in the body, but are most often seen in the soft tissues of the lower extremities. The majority of soft tissue masses are benign, superficial, and <3 cm in diameter. Malignant soft tissue sarcomas are uncommon, and are mostly seen in patients over 50 years of age. The most common soft tissue sarcomas of children are rhabdomyosarcomas, in young adults synovial sarcomas, and in older patients undifferentiated pleomorphic sarcomas. Liposarcoma is the most common sarcoma that occurs in the retroperitoneum. Soft tissue sarcomas tend to be 2-3 times more malignant than primary bone sarcomas, and often metastasize to lungs.[2] The exact predisposing cause in most soft tissue sarcoma is unknown, although secondary soft tissue sarcomas can develop in previously irradiated sites usually 3-15 years following radiation treatment for tumors such as lymphoma, cervical cancer, breast cancer, and testicular cancer. Rarely, angiosarcoma following breast cancer treatment (Stewart-Treves syndrome) may be seen. Virus-related Kaposi sarcoma may occur in AIDS patients. A higher incidence of soft tissue sarcomas is seen with some genetic disorders, such as neurofibromatosis, and Li-Fraumeni syndrome.

Emergence of new imaging modalities in the past few decades and further refinements of many of these imaging procedures have tremendously improved our ability to assess and treat patients with soft tissue sarcomas. These imaging techniques help us not only in preoperative staging of soft tissue tumors, but also in presurgical planning and post-treatment surveillance. Information regarding a soft tissue mass, such as its exact site in body, specific location in specific soft tissue(s), size, margin, matrix mineralization, vascularity, relationship with adjoining structures, and metabolic activity, can help the oncologic team to plan proper treatment and management of patients with soft tissue sarcomas. The ability of magnetic resonance imaging (MRI) for tissue characterization of soft tissue tumor even prior to biopsy assists the pathologist in difficult situations. Radiographs, computed tomography, ultrasonography, radionuclide bone scintigraphy, MRI, and F18 FDG PET-CT, each has specific, limited and, at times, overlapping roles in the localization, diagnosis, presurgical staging and post-treatment of soft tissue masses.

Radiography

Although radiographs have a limited role in evaluation of a soft tissue mass, they can be helpful in the initial work-up as they can provide important information about adjoining bone. Even when a soft tissue mass is not visible, a periosteal

Department of Musculoskeletal Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX.
Address reprint requests to Rajendra Kumar, MD, FACR, Department of Musculoskeletal Imaging, The University of Texas MD Anderson Cancer Center, Unit 1475, 1515 Holcombe Blvd, Houston, TX 77030 E-mail: Rajkumar@mdanderson.org

 https://doi.org/10.1053/j.sult.2020.08.021
0887-2171/© 2020 Elsevier Inc. All rights reserved.

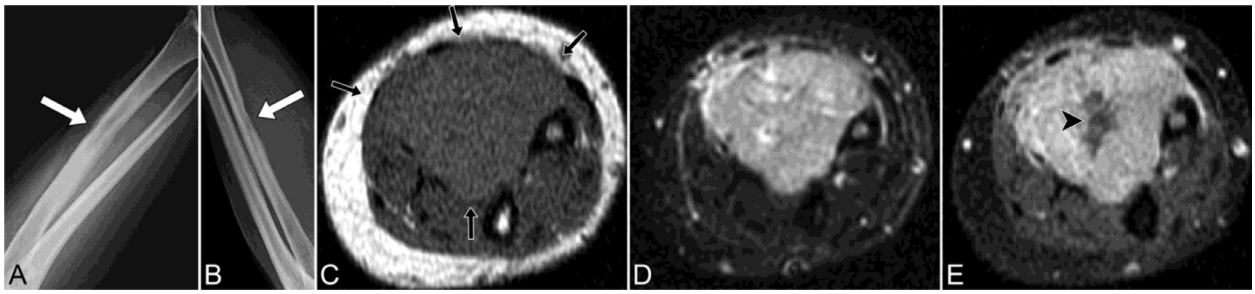

Figure 1 Undifferentiated pleomorphic soft tissue sarcoma with bone erosion in right forearm of a 57-year-old man. AP (A) and lateral (B) radiographs of the right forearm with superficial cortical erosion at mid radial shaft (arrows). The soft tissue mass is isointense to muscle on axial T1-WI (C), heterogeneously hyperintense on axial fat-suppressed (FS) T2-WI (D) and demonstrates heterogeneous enhancement with central necrosis (arrowhead) on axial postcontrast FS T1-WI (E).

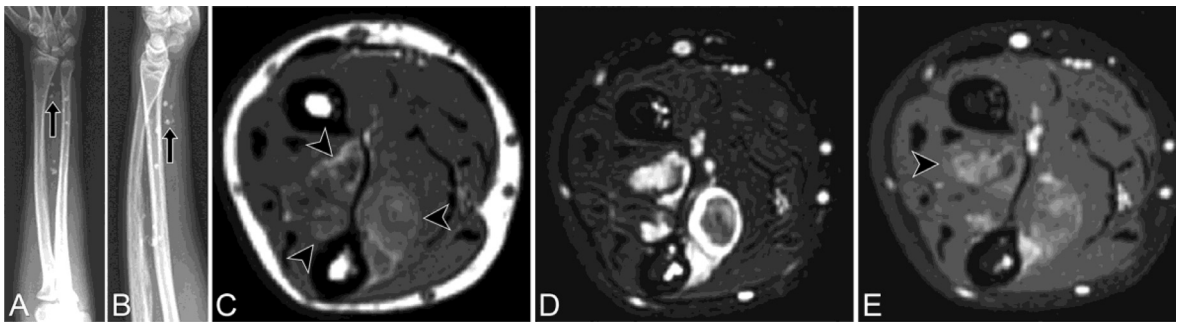

Figure 2 Hemangioma in the left forearm of a 38-year-old woman. AP (A) and lateral (B) radiographs show numerous calcified phleboliths scattered in the soft tissues (arrows). The infiltrating soft tissue mass containing high signal intensity fat is heterogeneously hyperintense on axial T1-WI (C), heterogeneously hyperintense on axial FS T2-WI (D), and shows mild heterogeneous enhancement with several small tubular and serpiginous structures, representing blood vessels on axial FS T1-WI following intravenous gadolinium contrast administration (E, arrowhead).

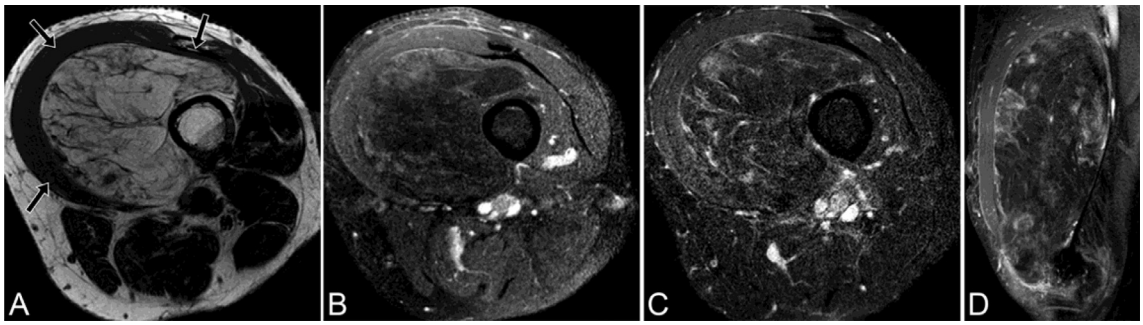

Figure 3 Well-differentiated liposarcoma (atypical lipomatous tumor) in right thigh of a 76-year-old man. Axial T1-WI (A) shows a well-circumscribed, large lobulated lipomatous soft tissue mass with predominately high T1 signal (arrows). Axial FS T2-WI (B) shows diffuse heterogeneous hypointense MR signal indicative of suppressing fat and confirming the presence of a lipomatous tumor. Axial (C) and coronal (D) postcontrast FS T1-WI show mild heterogeneous enhancement.

reaction and/or bone erosion can suggest its presence (Fig. 1). A calcified soft tissue mass can be easily detected on radiographs, and specific types of soft tissue calcification, such as phleboliths in soft tissue hemangioma, can even suggest definitive diagnosis (Fig. 2). Recognition of fat within a soft tissue mass on radiographs indicates a lipomatous tumor (Fig. 3). Similarly, a soft tissue mass with calcification near a joint in a young adult often indicates synovial sarcoma (Fig. 4). Thus, radiographs should be an essential part of the initial work-up of a patient with a soft tissue mass.[3]

Magnetic Resonance Imaging

MRI is the mainstay of evaluation of soft tissue masses in current clinical practice.[3-8] MRI is an exceptional modality

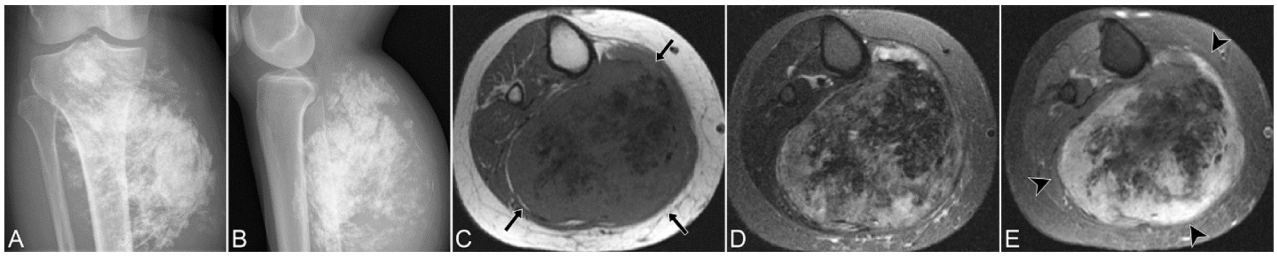

Figure 4 Calcified synovial sarcoma in right upper calf of a 43-year-old woman. AP (A) and lateral (B) radiographs of the right lower leg show a calcified, large soft tissue mass. Axial T1-WI (C) shows a heterogeneous hypointense soft tissue mass (arrows). Axial FS T2-WI (D) shows that the soft tissue mass is heterogeneously hyperintense. Postcontrast FS T1-WI (E) shows heterogeneous enhancement of the noncalcified component of tumor (arrowheads).

because of its superior tissue resolution (differentiating different tissues such as fat, muscle, ligament, tendon, bone, etc.), and multiplanar imaging capability. It provides information such as lesion size, location, and relationship to adjoining bone and neurovascular structures. In most cases, it can also determine the main constituent tissue type of a soft tumor, whether lipomatous, fibrotic, vascular, hemorrhagic or myxomatous (Fig. 3). Despite this, MRI has limitations in providing specific tissue diagnoses, and is generally unable to differentiate benign from malignant soft tissue masses.[8,9] Thus, it is important that the MR imaging of a soft tissue mass must be consistently of optimal quality, and should be obtained for specific information regarding localization, characterization and staging prior to treatment. MRI is highly sensitive, but nonspecific in detection of bone marrow lesions. Contrast-enhanced MRI following intravenous injection of gadolinium is routinely used in preoperative evaluation, but also postoperatively for surveillance for tumor recurrence (Figs. 5-7).[3,10-13] Diffusion-weighted MR imaging (DWI) of soft tissue masses can help to provide better tumor border delineation and to distinguish tumor margin infiltration from extensive peritumoral edema.[14] It can characterize tumors for the presence of restricted diffusion (intact cell membranes as can be seen with viable tumor that is refractory to therapy). It can determine whether a soft tissue mass is predominantly cystic or solid.[14] Gadolinium (Gd)-

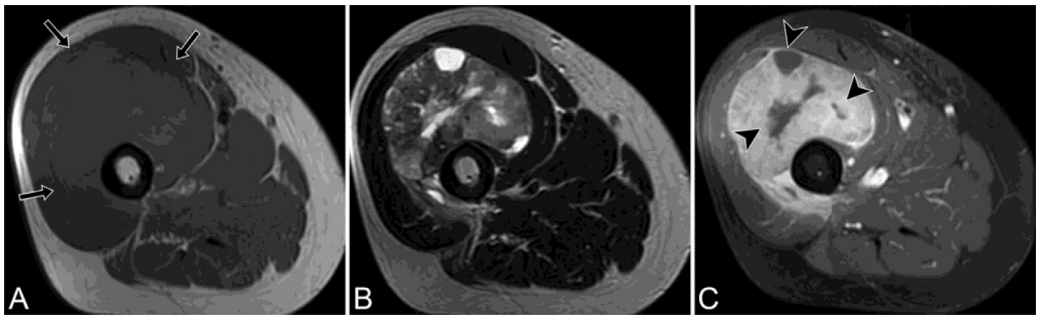

Figure 5 A 48-year-old woman with a myxoid liposarcoma of the distal right thigh. The soft tissue mass in the anterior thigh is isointense to the muscle on T1-WI (A, arrows), compressing and displacing the vastus lateralis muscle. The well-circumscribed mass is heterogeneously hyperintense on axial FS T2-WI (B). Postcontrast axial FS T1-WI (C) shows heterogeneous enhancement with foci of central necrosis (arrowheads).

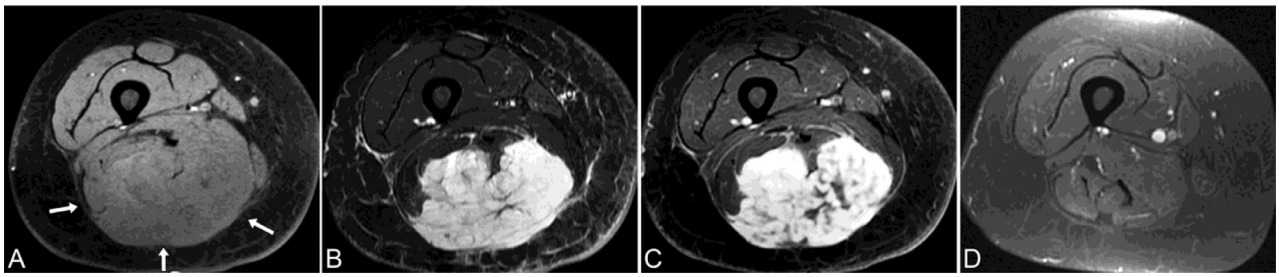

Figure 6 Myxoid liposarcoma in the left thigh of a 35-year-old woman. Pretreatment MRI shows an indistinct soft tissue mass in the posterior compartment of the left thigh with signal intensity that is isointense to the adjacent normal muscle on axial FS T1-WI (A, arrows). The lesion is heterogeneously hyperintense on axial FS T2-WI (B). Postcontrast axial FS TW1-WI (C) shows heterogeneous tumor enhancement. Follow-up MRI after treatment with 6 cycles of chemotherapy (D) shows complete resolution of the soft tissue tumor on axial postcontrast FS T1-WI.

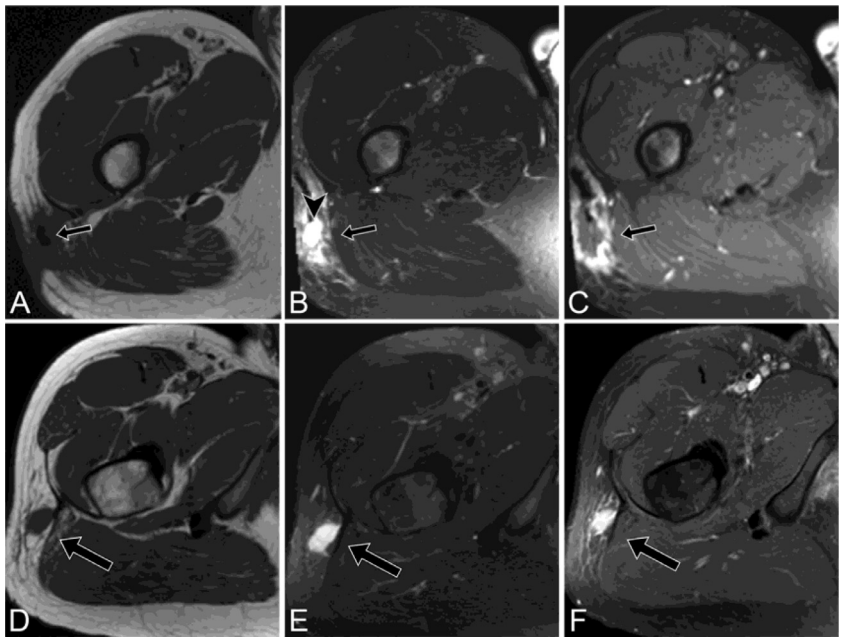

Figure 7 Recurrent subcutaneous undifferentiated pleomorphic sarcoma in the upper right lateral thigh in a 42-year-old man. The tumor was surgically resected in October 2015. Postoperative axial T1-WI (A) shows hypointense scar at the resection site (arrow). Axial FS T2-WI (B) shows heterogeneous hyperintense granulation tissue in surgical bed (arrow), surrounding the homogeneously high signal of the postoperative fluid collection (arrowhead). Axial postcontrast FS T1-WI (C) shows peripheral enhancement around the small postoperative fluid collection (arrow). Follow-up MRI of the right thigh in May 2016 now shows a small soft tissue nodule in the surgical bed. The nodule is isointense on axial T1-WI (D), hyperintense on axial FS T2-WI (E) and shows homogenous enhancement on axial postcontrast FS T1-WI (F, large arrows), consistent with tumor recurrence.

enhanced MRI is routinely used for postoperative evaluation for residual or recurrent soft tissue tumor in the presence of metallic hardware as it has fewer susceptibility artifacts as compared with CT. MR spectroscopy can be useful in assessment of chemotherapy response of unresectable or recurrent soft tissue tumors.[15] However, MRI is poor for detection of calcification and air in a soft tissue mass, whereas radiography and CT imaging can depict them easily.[3] An important advantage of MRI is that it involves no ionizing radiation.

Technique

Most soft tissue masses are evaluated with conventional T1-weighted imaging (WI), fat-suppressed (FS) T2-WI and postcontrast FS T1-W fast-spin-echo images in axial and coronal planes.[3-8] Additional images in sagittal and oblique planes can be obtained, when required. Gradient recall echo imaging can aid lesion characterization by detecting hemosiderin, which produces conspicuous magnetic susceptibility effect within applicable soft tissue masses, such as pigmented villonodular synovitis.[3] Short tau inversion recovery (STIR) imaging can potentially depict hyperintense lesions with high conspicuity against a homogenous, dark, suppressed-fat background. STIR imaging can produce more robust fat suppression than conventional fast-spin echo sequences in the presence of artifacts and can be used routinely for the evaluation off-centered lesions, such as in the upper arms. It is also an excellent technique for assessment of bone marrow lesions, and also when evaluating soft tissue lesions in presence of orthopedic hardware.

Routine use of intravenous Gd for contrast-enhanced imaging of soft tissue masses, despite being controversial, is ubiquitous and often advantageous.[3,10-13] Gd-enhanced MRI can differentiate solid soft tissue masses, such as myxoma, that simulate cysts due to homogeneous high T2 signal, from simple cysts by demonstrating central enhancement in solid tumors and only rim enhancement in cysts. It also highlights the location of viable tumor tissue by distinguishing it from unenhanced necrotic tissue, thereby facilitating biopsy of the viable regions. The change in enhancement on follow-up scans is useful for the assessment of tumor response to treatment (Fig. 6). However, the use of Gd adds extra cost and increased imaging time. Occasionally, mild anaphylactic adverse reactions, such as hives and bronchospasm, with the use of Gd may be seen, but rare serious adverse reactions, such as systemic nephrogenic fibrosis, also can occur and even a few deaths have been reported. Newer Gd-contrast agents with fewer adverse reactions, such as agents with macrocyclic rather than linear ligands, should be preferred, especially in patients with reduced renal function.[16]

Field of view should be large enough to include the entire tumor as well as the entire area for tumor staging purposes, including regional lymph nodes. A skin marker, usually a vitamin E capsule, is routinely placed gently on the skin to indicate area of interest.

MR angiography can be performed to evaluate vascular soft tissue tumors and arteriovenous malformation in soft tissues. Magnetic resonance angiography can be used without and with intravenous contrast administration in the multiplanar assessment of vascular anatomy and vascular perfusion of a soft tissue tumor.[17] Proton spectrum spectroscopy, DWI, and other MR imaging techniques can be used for both qualitative and quantitative assessments.[18]

MRI Characteristics of Soft Tissues

The majority of soft tissue tumors display nonspecific hypointense T1 and hyperintense T2 signal (relative to muscle) with variable enhancement on postcontrast fat-suppressed T1-W MR images (Figs. 1 and 5). In addition, in most cases, MRI cannot distinguish benign from malignant soft tissue tumors.[3-8] MRI is unable to provide a specific tissue diagnosis, with the exception of lipomatous, fibrous, or vascular soft tissue masses, thus necessitating biopsy of the tumor for definitive diagnosis. In general, a superficial small soft tissue mass is likely to be benign as only 5% of benign soft tissue masses tend to be larger than 5 cm in diameter. Larger deep-seated tumors with increased vascularity and heterogeneous enhancement are usually malignant. Actively growing large soft tissue tumors without treatment often outpace their blood supply, and show intratumoral necrotic areas of nonenhancement. However, the size and location of a soft tumor cannot predict its behavior. Similarly, vascularity and intensity of enhancement of a soft tissue tumor are poor criteria for distinguishing benign from malignant soft tissue masses.[8,9] In clinical practice, a heterogeneously enhancing soft tissue tumor, which is >33 mm in diameter with heterogeneous hyperintense signal on T2W or STIR MR images and involvement of adjoining bone and entrapment of adjacent neurovascular bundle has the highest probability of being malignant.[4]

Computed Tomography (CT)

CT is the best imaging modality to study cortical bone and mineralized soft tissue masses.[3,19-22] CT can easily demonstrate cortical bone erosion, periosteal reaction, tumor matrix, and cortical breakthrough caused by an adjacent soft tissue mass. CT imaging is ideal for assessment in complex bones in pelvis, face, and spine, which can be facilitated by 3-dimensional reconstructions, and even cine CT images, thus assisting surgeons with preoperative planning. With newer metal reduction imaging techniques, X-ray beam hardening artifact from orthopedic hardware can be minimized for postsurgical follow-up. Contrast-enhanced CT is an alternative imaging procedure in situations where MRI cannot be performed. Lately, dual-energy CT has been used to distinguish gouty tophus from other calcified soft tissue mass.[3] However, CT exposes the patient to ionizing radiation, and has poor soft tissue contrast in comparison with MRI.[20]

Positron-Emission Tomography (PET)

PET imaging is based on glucose metabolism, and thus, it determines the metabolic activity of a soft tissue tumor.[23,24] In PET imaging, 2-fluoro-2-deoxy-D-glucose (FDG), a glucose analog, is tagged with radioactive F-18, and is administered intravenously in the body. The FDG has same initial metabolic pathway as glucose, but unlike glucose, it accumulates within tissue cells without undergoing the normal rate of breakdown. A PET scanner detects the 2 gamma photon beams emitted by radioactive F18 in the cells, and generates images of the entire body. Thus, a hypermetabolic soft tissue tumor with higher radiotracer uptake can be detected on PET imaging (Fig. 8). PET is routinely combined with CT for more precise anatomical correlation with the FDG-avid lesions than can be achieved with PET imaging alone. PET-CT, and more recently, PET-MRI have proved useful in the assessment of tumor response to treatment, and for detection of tumor recurrence.[25]

Bone Scintigraphy

Bone scintigraphy using Tc99m MDP is a highly sensitive, but nonspecific imaging technique that is routinely used for staging to detect distant bone metastases.

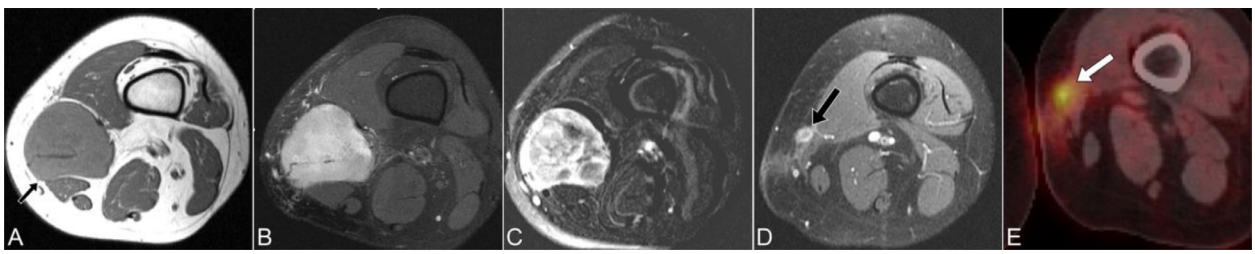

Figure 8 Extra-skeletal Ewing sarcoma in left distal thigh of a 31-year-old woman with recurrence following resection of the primary tumor. Axial T1-WI (A) shows a minimally hyperintense, large soft tissue mass in vastus medialis muscle (arrow), which is diffusely hyperintense on FS T2-WI (B) and enhances heterogeneously on postcontrast FS T1WI (C) in December 2011. The tumor was surgically resected. She was followed up with serial MRI. The scan performed in December 2014 revealed a heterogeneously enhancing, small soft tissue nodule in the surgical bed on axial FS T1-WI (D, black arrow). On the axial fused PET-CT image, the small soft tissue nodule is intensely ^{18}F FDG avid (E, white arrow). The nodule was excised and was confirmed as recurrent tumor on histopathology.

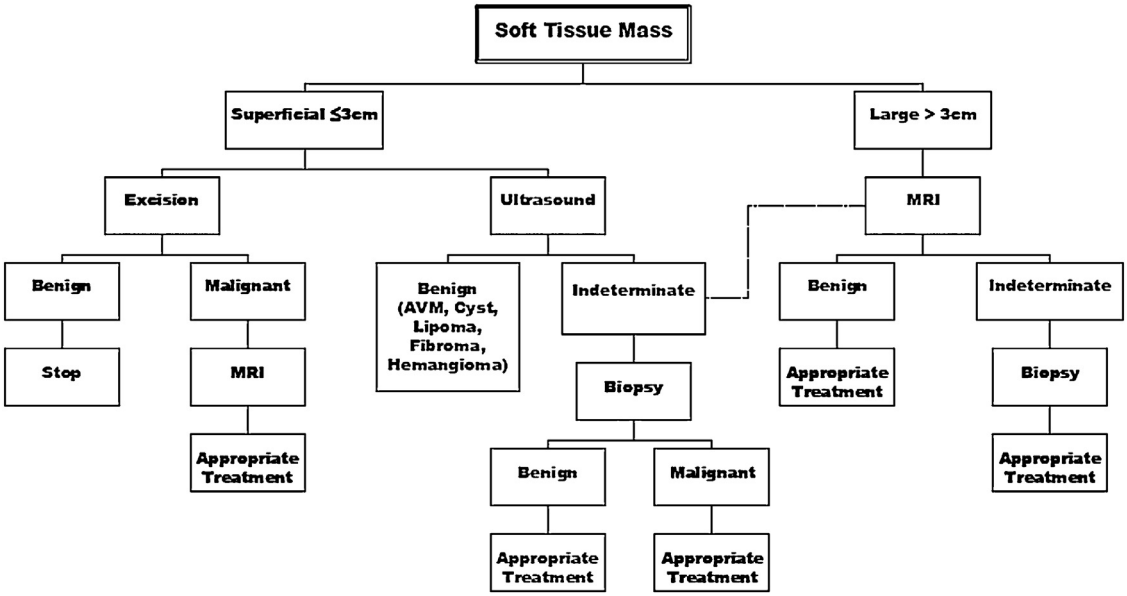

Figure 9 Flow chart for work-up of patients with soft tissue sarcomas.

Ultrasonography

Ultrasonography is useful in evaluation of superficial small soft tissue masses, and is used routinely for needle guidance for biopsy of soft tissue lesions.[26] This economical imaging technique is ideal for distinguishing solid from cystic soft tissue lesions. Doppler ultrasound can be used in the diagnosis of vascular tumors. Dynamic Doppler study of intratumoral blood flow alterations may be helpful for distinguishing benign from malignant soft tissue masses.[27]

Chest Radiographs and Chest CT

Because sarcomas commonly metastasize to the lungs, chest radiographs and chest CT are routinely performed in the work-up of patients with soft tissue sarcomas for initial staging and during follow-up after treatment.

The flow chart (Fig. 9) provides a general outline of the work-up of patients with soft tissue masses.

Conclusion

Imaging of soft tissue masses has been greatly enhanced with the advent of MRI, which is not only useful for preoperative staging, but also in surveillance following treatment to assess tumor recurrence. Other imaging techniques, such as radiographs, CT, PET-CT, radionuclide scintigraphy, and ultrasound are more often complementary to MRI, providing further information required for the initial work-up for staging, and in post-treatment surveillance. Understanding of the roles and limitations of these imaging modalities is essential for the cost effective maximization for diagnosis and management of patients with soft tissue sarcoma.

References

1. Kransdorf MJ: Malignant soft-tissue tumors in a large referral population: Distribution of diagnoses by age, sex, and location. AJR 164:129-134, 1995
2. Vilanova JC, et al: In: Vanhoenacker, et al., et al (ed): 4th ed, Cham, Switzerland: Springer, 187-196, 2017
3. Kransdorf M, Murphey MD: Imaging of soft-tissue masses: Fundamental concepts. Radiographics 36:1931-1934, 2016
4. De Schepper AM, De Beuckeleer L, Vandevenne J, et al: Magnetic resonance imaging of soft tissue tumors. Eur Radiol 10:213-222, 2000
5. Vilanova JC, Woertler K, Narvaez JA, et al: Soft-tissue tumors update: MR imaging features according to the WHO classification. Eur Radiol 17:125-138, 2007
6. Sundaram M, McGuire MH, Herbold DR: Magnetic resonance imaging of soft tissue masses: An evaluation of fifty-three histologically proven tumors. Magn Reson Imaging 6:237-248, 1988
7. Totty WG, Murphy WA, Lee JKT: Soft-tissue tumors: MR imaging. Radiology 160:135-141, 1986
8. Berquist TH, Ehman RL, Ding BF, et al: Value of MR imaging in differentiating benign from malignant soft-tissue masses: Study of 95 lesions. AJR 155:1251-1255, 1990
9. Chhabra A, Soldatos T: Soft-tissue lesions: When can we exclude sarcoma? AJR 199:1345-1357, 2012
10. Beltran J, Chandnani V, McGhee RA, et al: Gadopentetate dimeglumine-enhanced MR imaging of the musculoskeletal system. AJR 156:457-466, 1991
11. Benedikt RA, Jelinek JS, Kransdorf MJ, et al: MR imaging of soft-tissue masses: Role of gadopentetate dimeglumine. J Magn Reson Imaging 4:485-490, 1994
12. Amini B, Murphy WA, Miner HT, et al: Gadolinium-based contrast agents improve detection of recurrent soft-tissue sarcoma at MRI. Radiology 2:1-8, 2020
13. Costelloe CM, Amini B, Madewell JEM: Risks and benefits of gadolinium-based contrast-enhanced MRI. Semin Ultrasound CT MRI 41:170-182, 2020
14. Hong JH, Jee W-H, Jung C-K, et al: Soft tissue sarcoma: Adding diffusion-weighted imaging improves MR imaging evaluation of tumor margin infiltration. Eur Radiol 29:2589-2597, 2019
15. Vaidya SJ, Payne GS, Leach MO, et al: Potential role of magnetic resonance spectroscopy in assessment of tumour response in childhood cancer. Eur J Cancer 39:728-735, 2003

16. Mathur M, Jones JR, Weinreb JC: Gadolinium deposition and nephrogenic systemic fibrosis: A radiologist primer. Radiographics 40:153-162, 2020
17. Dumoulin CL, Hart HR: Magnetic resonance angiography. Radiology 161:717-720, 1986
18. de Mello R, Ma Y, Ji Y, et al: Quantitative MRI musculoskeletal techniques: An update. AJR 213:524-533, 2019
19. Weekes RG, McLeod RA, Reiman Pritchard DJ: CT of soft-tissue neoplasms. AJR 144:355-360, 1985
20. Panicek DM, Gatsonis C, Rosenthal DI, et al: CT and MR imaging in the local staging of primary malignant musculoskeletal neoplasms: Report of the Radiology Diagnostic Oncology Group. Radiology 202:237-246, 1997
21. Demas BE, Heelan RT, Lane J, et al: Soft-tissue sarcomas of the extremities: Comparison of MR and CT in determining the extent of disease. AJR 150:615-620, 1988
22. Rajiah P, Sundaram M, Subhas N: Dual-energy CT in musculoskeletal imaging. AJR 213:493-505, 2019
23. Bredella MA, Caputo GR, Steinbach LS: Value of FDG positron emission tomography in conjunction with MR imaging for evaluating therapy response in patients with musculoskeletal sarcomas. AJR 179:1145-1150, 2003
24. Bastiaannet E, Groen H, Jager PL, et al: The value of FDG-PET in the detection, grading and response to therapy of soft tissue and bone sarcomas: A systematic review and meta-analysis. Cancer Treat Rev 30:83-101, 2004
25. Grueneisen J, Schaarschmidt B, Demircioglu A, et al: ^{18}F FDG PET/MRI for therapy response assessment of isolated limb perfusion in patients with soft tissue sarcomas. J Nucl Med 60:1537-1542, 2019
26. Carra BJ, Bui-Mansfield LT, O'Brien Chen DC: Sonography of musculoskeletal soft-tissue masses: Techniques, pearls, and pitfalls. AJR 202: 1281-1290, 2014
27. Bodner G, Schocke MF, Rachbauer F, et al: Differentiation of malignant and benign musculoskeletal tumors: Combined color and power Doppler US and spectral wave analysis. Radiology 223:410-416, 2002