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Diagnostic Modalities of Soft Tissue Tumors

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Abstract: Histopathology is the gold standard for establishing the diagnosis and grade of soft tissue tumours; also radiology-pathology correlation is very important to avoid any diagnostic faults. Imaging helps in localizing the mass and the characterization , staging, and assessment of treatment response of the tumour. It also aids in differentiating the tumour (like hematoma, abscess, ganglia, bursae, tenosynovitis, and myositis) from true neoplasms. Radiography is commonly used in the initial evaluation (especially in extremities) and can show calcification, lucency (corresponding to fat), and associated bony changes. Ultrasound is preferred as an initial investigation for superficially located lesions due to its easy availability, good spatial and contrast resolution, ability to differentiate solid from cystic lesions, and ability to show internal morphology and vascularity. It can even help to characterize some of the soft tissue tumours and differentiate benign from malignant tumours with reasonable accuracy. CT is frequently employed in the evaluation of lesions located in the head and neck, mediastinum, and retroperitoneum. MRI is the imaging gold standard and modality of choice for the evaluation of soft tissue tumours. Based on the age, location, MR signal intensity and morphology, the radiologist may suggest a narrow list of differential diagnoses.

Keywords: *Soft Tissue Tumors*

Introduction.

radiology-pathology correlation is very important to avoid any diagnostic faults [1].

II. Imaging

Imaging helps in localizing the mass and characterizing, staging, and assessing the treatment response of the tumor. It also aids in differentiating the tumor (like hematoma, abscess, ganglia, bursae, tenosynovitis, and myositis) from true neoplasms (Flowchart 1) [2].

1. **Radiography** is commonly used in the initial evaluation (especially in extremities) and can show calcification, lucency (corresponding to fat), and associated bony changes.
2. **Ultrasound** is preferred as an initial investigation for superficially located lesions due to its easy availability, good spatial and contrast resolution, ability to differentiate solid from cystic lesions, and

ability to show internal morphology and vascularity [3, 4]. It can even help to characterize some of the soft tissue tumors and differentiate benign from malignant tumors with reasonable accuracy [4].

3. **CT** is frequently employed in the evaluation of lesions located in the head and neck, mediastinum, and retroperitoneum.
4. **MRI** is the imaging gold standard and modality of choice for the evaluation of soft tissue tumors. Based on the age, location, MR signal intensity, and morphology, the radiologist may suggest a narrow list of differential diagnoses (Flowcharts 1–3) [4, 5].

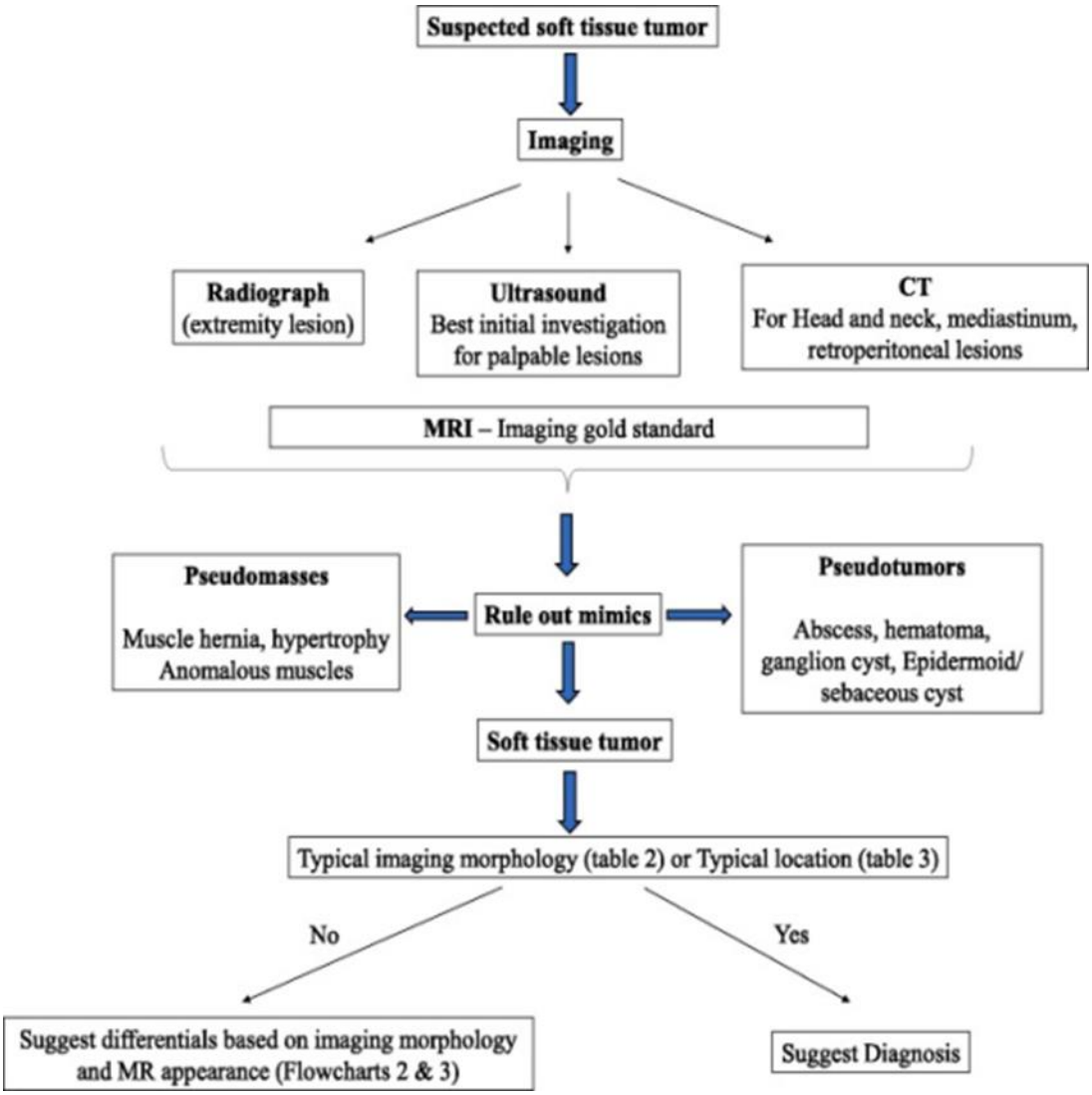

Figure 1: Imaging Approach to soft tissue tumors.

1. **PET** is being used more frequently to assess the metabolic activity and, presumably, the biologic aggressiveness of a lesion.
2. **Angiography** to evaluate any vascular involvement by soft tissue tumors has essentially been replaced by MRI [6].

3. **Nuclear scintigraphy**, in contrast to X-ray, CT, and MRI, is a functional examination that reflects various metabolic activities including bone turnover, sodium-potassium pump activity, and mitochondrial metabolism [7]. Bone scintigraphy is commonly used as a screening test for metastatic bone tumors in cancer patients [8].

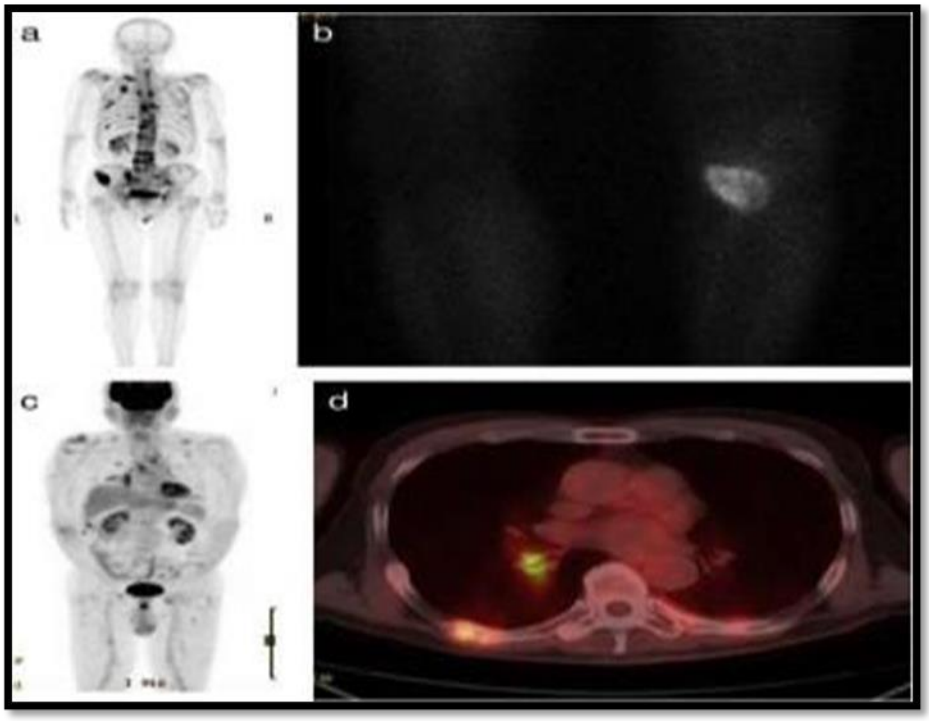

Figure 2: Nuclear scintigraphy; a. Bone scintigraphy, b. 201Thallium scintigraphy. Osteosarcoma of distal femur, c. Multiple metastases of angiosarcoma, d. PET-CT. Metastatic tumor of rib (Miwa et al., 2013).

III. Laboratory Investigations

Other than histologic and cytogenetic analysis, no specific laboratory tests exist for diagnosing soft-tissue tumors [9].

The Most Prevalent Soft Tissue Masses

1. Lipoma

Definition:

Lipomas are benign soft tissue tumors composed of mature adipose tissue. These lesions are the most common soft tissue tumor, making up nearly 50% of all soft tissue tumors [10].

Location:

Lipomas are most commonly located within the superficial soft tissues of the extremities, back, and neck.

Lipomas may occur deep to the superficial fascia, but much less frequently. They may be intramuscular or intermuscular and most frequently occur in the lower extremity. They may also be found rarely within certain locations, i.e., the retroperitoneum, hands, feet, and chest wall, and alternative diagnoses should also be considered for lesions in these locations [10].

Presentation:

Usually asymptomatic, but due to the superficial location, these lesions commonly present less than 5 cm in size [10].

Diagnosis:

Superficial lipomas can almost always be diagnosed clinically.

Radiological findings:

- **Radiography:** Large lipomas may appear as a radiolucency on radiographs, but the finding is not diagnostic.
- **Sonography:** Appear as well-defined, oblong, echogenic masses without posterior acoustic enhancement. In the larger lesions, fine linear striations may be seen coursing parallel to the skin [11].
- **Non-contrast CT:** The classic appearance of a lipoma is a circumscribed, homogeneously low (fat) density mass ranging from -120 to -65 Hounsfield units [10].
- **MRI:** The characteristic lipoma is an encapsulated lesion isointense to the subcutaneous fat on all MRI sequences. Intramuscular lipomas may not be encapsulated and instead may insinuate within the skeletal muscle [12].

Histopathologically: Lipomas are encapsulated tumors composed of mature adipocytes. Fibrous connective tissue may be seen which correlates with the thin septa seen on imaging. Lipomas have a rich vascular supply, though the tenuous vessels are often compressed by the large adipocytes.

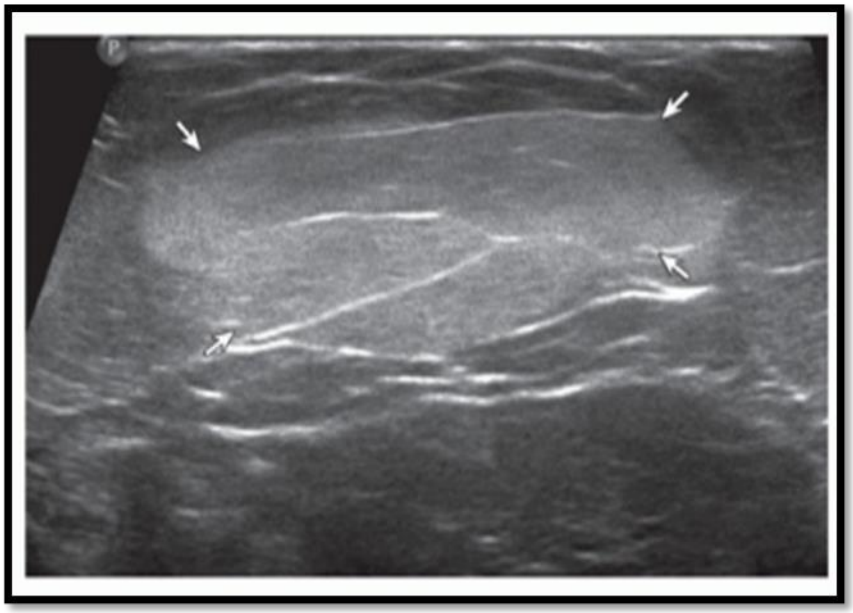

Figure 3: Lipoma. Ultrasound image shows oval hyperechoic subcutaneous lipoma (arrows) with internal linear hyperechoic fibrous tissue (pathologically proven) [10].

2. Schwannoma

Definition:

Schwannomas are the most common benign nerve sheath neoplasms that arise from the Schwann cells of the peripheral nerves. Schwann cells are glial cells that provide insulation for both the motor and the sensory neural signal in the peripheral nervous system [13].

Location:

Schwannomas are considered rare and involve the upper extremities twice as often as the lower extremities. Constituting approximately 0.8-2.0% of all hand tumors, neurofibromas, ganglion cysts, tumors, lipomas, and xanthomas need to be considered as possible differential diagnoses [14].

Presentation:

Schwannomas present as palpable solitary, painless lesions on the volar aspect of the wrist causing entrapment syndrome with paresthesia, hypoesthesia, and pain.

Radiological findings:

- **Radiography:** Can be performed to rule out any bony involvement or abnormalities.
- **Sonography:** The imaging modalities should include ultrasonography first. Ultrasonography will typically show a solid, sharply delineated, ovoid, hypoechoic homogeneous mass [13].

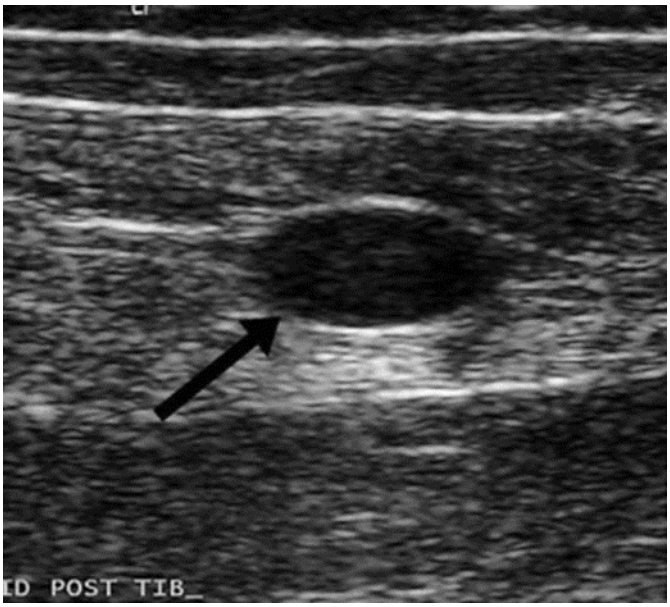

Figure 4: Ultrasound image of the schwannoma. Arrow indicates solid hypoechoic nodule displacing muscle.

- **MRI:** On MRI, schwannomas show intermediate to low signal on T1-weighted images and increased diffuse signal on T2WI. Contrast enhancement on T1WI is particularly helpful in their diagnosis, with diffuse enhancement and central areas of low signal being characteristic

Occasionally on MR images, a schwannoma can be distinguished from a neurofibroma by its location relative to the nerve: The schwannoma can be eccentric to and separable from the nerve, whereas the neurofibroma is intrinsic to it. The "split fat sign" can be associated with PNSTs: As the tumor enlarges, a surrounding rim of normal fat is maintained [15].

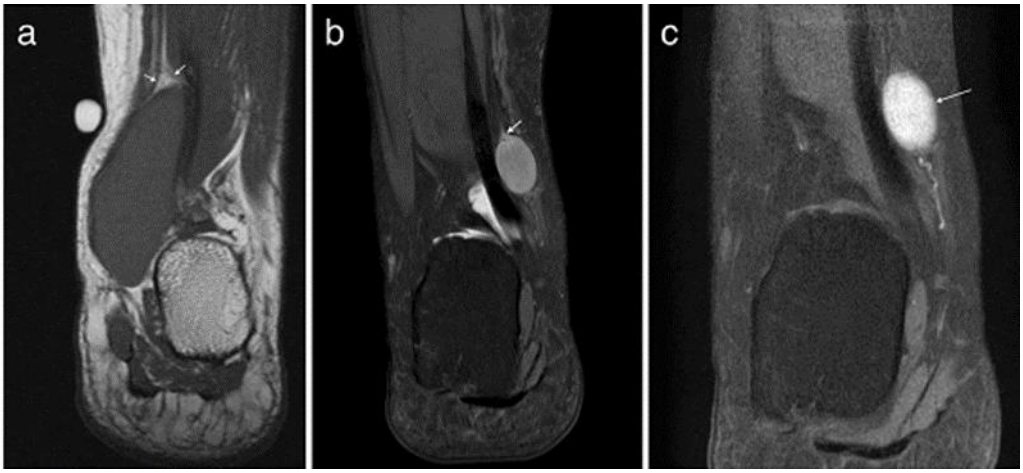

Figure 5: Schwannoma; a) Coronal T1W image demonstrating a well-defined homogeneously T1 isointense lesion with the split fat sign (arrows). b) Coronal T2FS image of another schwannoma showing a homogeneously hyperintense lesion with a "ball on a string" sign denoting origin from the posterior tibial nerve (arrow). c) The same lesion demonstrates avid enhancement on the post-contrast T1FS image [15].

Histopathologically:

Histologic and pathologic analyses will demonstrate that schwannomas are fusiform masses and have true capsules composed of epineurium. Therefore, the mass can be found in an eccentric location regarding the affected nerve, with the nerve moved to the periphery of the mass. Microscopic assessment shows that schwannomas consist of 2 distinctive tissues, the Antoni A region, which is densely cellular and orderly

arranged in short bundles or interlacing fascicles, and the Antoni B region, which has fewer cells and disorganized areas with a greater myxoid component arranged in a loose stroma [13].

3. Hemangioma

Hemangiomas are predominantly found in younger patients, occur more often in females, and feature a period of rapid growth with endothelial cell proliferation followed by stagnation and eventually spontaneous involution, a fact that allows distinction from vascular malformations that grow proportionally with the child [16].

Presentation:

Superficial hemangiomas present with characteristic skin discolorations, and can therefore usually be easily diagnosed by visual inspection alone.

Radiological findings:

- **Sonography:** On US, an infantile hemangioma during the proliferative phase usually appears as a well-defined mass located in subcutaneous tissue showing variable echogenicity and color Doppler shows increased internal vascular flow. After reaching its maximum size, the infantile hemangioma starts an involuting phase characterized by a decrease in size, increase in echogenicity, and decrease of internal vascular flow as a result of fibro-fatty replacement [16].

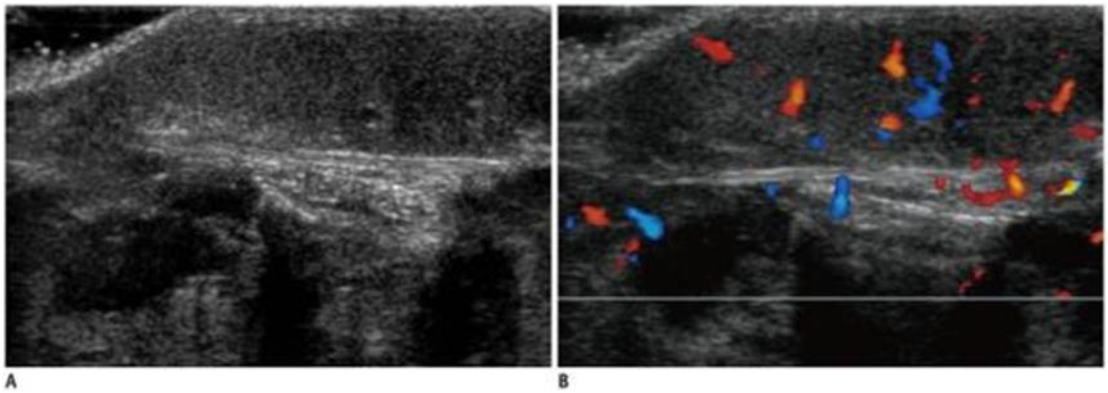

Figure 6: Infantile hemangioma in 8-month-old girl with enlarging foot mass. US (A) shows a well-defined ovoid hypoechoic mass confined to subcutaneous fat. Color Doppler scan (B) shows increased vascular flow [16].

- **MRI:** Hemangiomas are usually hyperintense on T2WI as a result of decreased blood flow and subsequent increased fluid content, and frequently display lobulations and septations [17]. Masses are iso to hyperintense to muscle on T1WI, with larger lesions containing fat, smooth muscle, myxoid tissue, thrombi, hemosiderin, and fluid levels. As a distinct feature, muscle atrophy in the periphery of the lesion has been described secondary to chronic ischemia due to a shunting phenomenon caused by the mass [18].

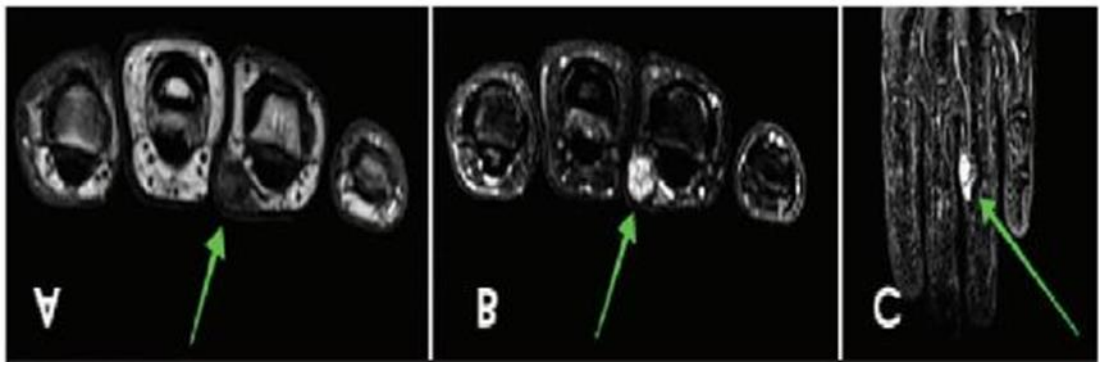

Figure 7: Hemangioma. 30-year-old woman with a lobulated mass centered in the subdermal and superficial subcutaneous soft tissues along the volar radial aspect of the fourth digit at the level of the proximal interphalangeal joint. Mass demonstrates T1W isointense signal, heterogeneously hyperintense T2W fat-saturated signal, and hyperintense short T1 inversion recovery signal (A-C). Pathologically proven to be a hemangioma. Clinically, the mass was tender to palpation and increased in size with prolonged use of the hand. Histologic examination of the surgically resected lesion demonstrated hemangioma [19].

Histopathologically:

A multinodular pattern fed by a single arteriole can be seen. The nodules are composed of hyperplastic endothelial cells, pericytes with and without lumens, and prominent basement membranes [20].

4. Soft Tissue Sarcomas

Epidemiology:

Soft tissue sarcomas account for 1% of all adult malignancies, with more than 80 different histologic and molecular subtypes [21].

Incidence:

STS grows with age, with a median age of approximately 60 years [22]. However, some STSs are more frequent in young patients, such as rhabdomyosarcoma and alveolar soft-part sarcoma in children and young adults [23].

Risk factors:

Although most STS are sporadic without obvious predisposing conditions, risk factors have been identified.

The main exogenous factor is ionizing radiations. Endogenous risk factors of STS comprise several genetic disorders such as neurofibromatosis type 1, or hereditary retinoblastoma syndromes [24].

Clinical presentation:

STS generally presents as a slowly-growing painless mass. STS mostly occurs in the lower limbs (40–50%), followed by upper limbs (15–20%), trunk wall (20%), retroperitoneum (10–15%), and head and neck (10%), with a deep location with regard to the superficial muscle fascia in 75% of patients.

Moreover, synovial sarcoma and epitheloid sarcoma are the most frequent STSs of the foot and hand [22].

Diagnosing soft tissue sarcomas: initial radiological assessments:

First-line imaging: ultrasonography and conventional radiographs.

Conventional radiography remains suggested by the American College of Radiology Appropriateness Committee, even for superficial masses, to look for the mineralization and bone erosion. Conventional radiography can also help orienting towards primary bone origin with secondary extension to soft tissue. According to the European Society for musculoskeletal Radiology [25].

Ultrasonography should: [26]

- Confirm the presence of a tumor.
- Determine its relationship to the superficial muscle fascia enabling to distinguish superficial versus deep tumors (i.e., below the fascia or invading the fascia);
- Estimate the dimensions of the tumor in each axis;
- Identify the precise anatomic location;
- Analyze the relationships to vessels, nerves, bones, and joints;
- Determine the internal content of the lesion (i.e., cystic component, necrosis, bleeding, mineralization, or vascularized tissue with color Doppler ultrasonography);
- Describe its margins; and
- Report the presence of similar satellite lesions defining multifocality. Of note, axillary, subclavian, inguinal, and popliteal regions are considered as deep regions.

When and how to complete with MRI and when to address to sarcoma reference centers

Any undetermined/doubtful lesion on ultrasonography, deep tumor, superficial tumor invading the fascia, tumor incompletely seen on ultrasonography, and tumor > 5 cm should be further investigated using magnetic resonance imaging (MRI).

Contrast-enhanced (CE) MRI is the best modality to characterize a soft-tissue tumor (STT). Quantitative sequences are not necessary at this step. In addition to the assessment of the tumor location, anatomical relationships, and dimension, MRI enables to depict the tumor content (or matrix), its margins, and the surrounding tissues [26].

Undifferentiated/Unclassified Sarcomas (Malignant Fibrous Histiocytoma)

Twenty percent of soft-tissue sarcomas show no lines of differentiation and are classified as undifferentiated sarcomas. These lesions are most often undifferentiated pleomorphic sarcoma (previously known as pleomorphic malignant fibrous histiocytoma). Undifferentiated pleomorphic sarcomas are often large at the time of diagnosis and invade adjacent anatomic structures [27].

Location:

Undifferentiated sarcomas (USTS) may occur in any location; however, it most commonly occurs in the extremity (lower > upper).

Presentation:

USTS has an aggressive clinical behavior, presenting as a deep-seated, often intramuscular, painless solid mass. Up to 5% of cases demonstrate extensive hemorrhage, presenting as a fluctuant mass and may be misinterpreted as a hematoma. Tumors can be between 5–15 cm and >20 cm when in the retroperitoneum [28].

Imaging:

- **Radiography:** Radiographs may be normal or reveal a non-specific soft tissue density, which is often greater than 5 cm in diameter. Radiographs can detect periosteal reaction, cortical erosion, and pathologic fracture. Calcification or ossification can be detected in 5–20% of patients [28].

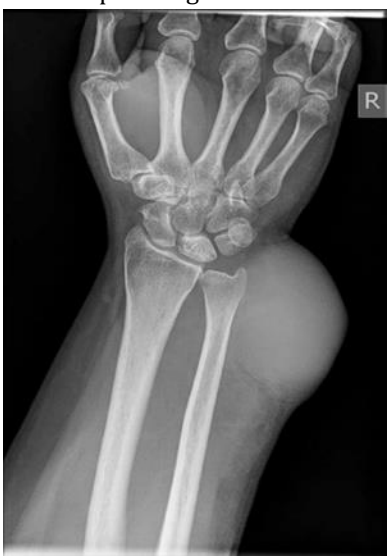

Figure 8: Radiograph of biopsy-confirmed USCS. The radiograph demonstrates a bulging dense solid mass at the wrist [28].

- **Sonography:** Ultrasound is non-specific, but typically is a well-defined heterogeneous mass. Hyperechoic areas represent a cellular composition, and hypoechoic regions represent necrotic or hemorrhagic tissue. USTS demonstrates increased Doppler signal. Ultrasound is the modality of choice for image-guided biopsy and can be used to target suitable areas for biopsy, avoiding necrotic components and the feeding vessels [28].

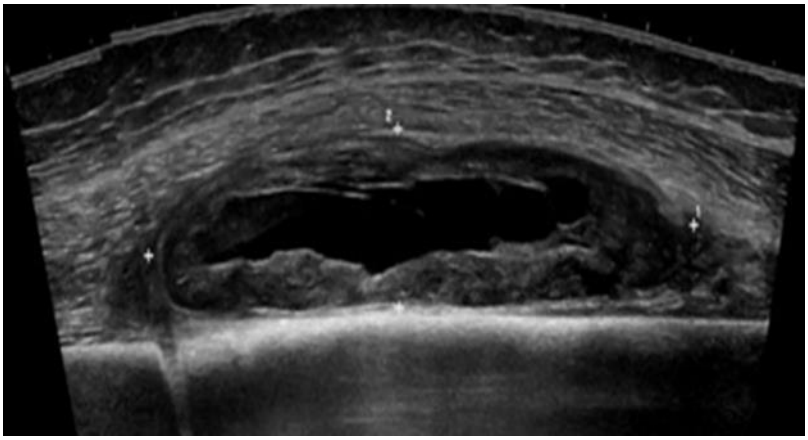

Figure 9: UPS of the thigh. Longitudinal panoramic ultrasound of a deep soft tissue mass in the thigh demonstrates a heterogeneous solid mass with a hypoechoic center. This represents hemorrhage/necrosis [28].

- **Non-contrast CT:** On unenhanced CT, USTS is often a large, lobulated, soft tissue mass, hypo- to isodense to muscle. There are intralesional areas of low attenuation (hemorrhage or necrosis). Fat attenuation is not observed in these tumors, and its presence is suggestive of a liposarcoma. CT may be used to evaluate the internal matrix and assess underlying bony structures for cortical erosion or periosteal reaction. Approximately 10% of retroperitoneal lesions demonstrate calcification [28].
- **MRI:** MRI is the modality of choice for assessing soft tissue sarcomas, as it is best able to locally stage a tumor. These tumors are typically relatively well-circumscribed, located within or adjacent to muscle, exerting a positive mass effect on surrounding structures due to their (usual) large size at presentation. On T1WI, it displays intermediate (to low) signal intensity, similar to adjacent muscle, heterogeneity if hemorrhage, calcification, and necrosis material present with prominent enhancement of its solid component at post-contrast study. On T2WI, the mass displays intermediate to high signal intensity [27].

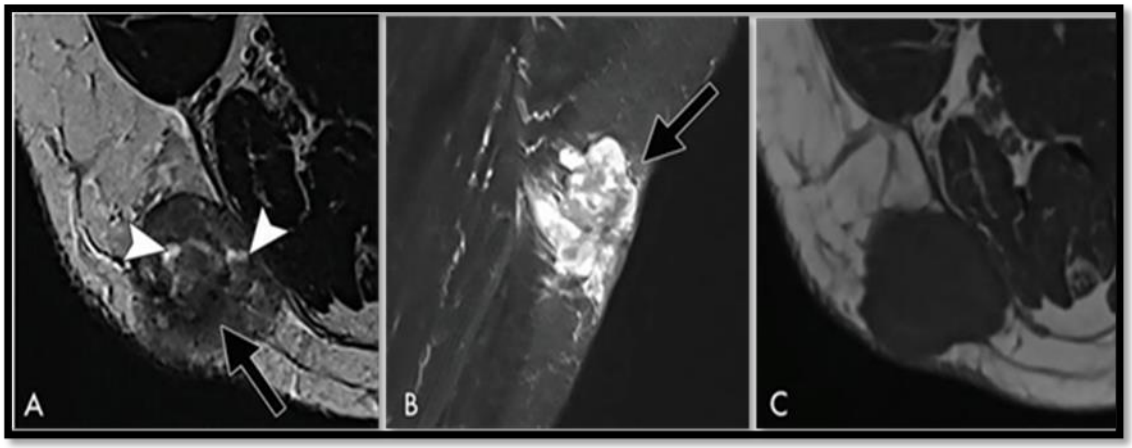

Figure 10: 64-year-old woman with undifferentiated pleomorphic sarcoma. Tumor was located in superficial and aponeurotic tissues of the thigh. A) axial T2-weighted imaging, B) sagittal T2-weighted imaging with short TI inversion-recovery fat-suppression method, and C) axial T1-weighted imaging. Lesion exhibited heterogeneous signal intensities on at least 50% of tumor volume on T2-weighted images (black arrows), foci of necrosis [29].

Histopathology:

USTS can be subdivided according to the cellular morphology into spindle cell morphology, pleomorphic morphology, round cell morphology, epithelioid morphology, and not otherwise specified. There is no specific characteristic feature between the subsets apart from their lack of an identifiable line of differentiation [28].

Liposarcoma

The main differential consideration for lipomas are liposarcomas, as some of these lesions can have a similar imaging and histologic appearance. Liposarcoma makes up 10–35% of soft tissue sarcomas, second only to undifferentiated pleomorphic sarcomas (malignant fibrous histiocytoma) [10].

Liposarcomas have been further subcategorized by the World Health Organization (WHO) into: well-differentiated, myxoid, pleomorphic, mixed, dedifferentiated types.

The most common liposarcoma subtype is a well-differentiated liposarcoma, which makes up approximately half of these lesions [10].

Location:

Deep-seated areas are common sites for liposarcomas, such as the retroperitoneum, which accounts for 20–33% of lesions [10].

Presentation:

These often painless, slow-growing masses do not pose a metastatic risk, but may dedifferentiate into a malignant lesion.

Imaging:

- **Sonography:** Usually, for superficial lipomas, the first diagnostic tool is ultrasound, and it will present as a homogenous hyperechogenic mass with well-defined margins. Conversely, in the US, LPS appears as a heterogeneous, multi-lobulated, and typically well-defined mass. However, compared to lipoma, the possibility of characterizing LPS in the US is limited [30].
- **MRI:** MRI allows a quality assessment of the lesion with the identification of the signs that can indicate malignancy as:

(A) Nodular non-fatty areas within the mass or nodular fatty areas with different densities or signals than the subcutaneous fat.

(B) Presence of thick septa (> 2 mm) or irregular or nodular septations with enhancement after contrast injection.

(C) Significant increase in size over time by either clinical or radiological examination.

(D) Intra-tumoral calcifications.

(E) Mediastinal, retroperitoneal, intra-abdominal, or pelvic/spermatic cord origin.

(F) Most extensive length is over 10 cm for superficial localization and 5 cm for deep location.

Areas of active tumor enhancement on post-contrast MRI indicate areas of viable tumor that should be targeted for biopsy [30].

Differentiation from lipoma:

Because the clinical examination is usually not helpful, the Italian Association of Medical Oncology and European Society of Medical Oncology (ESMO) guidelines suggest imaging with magnetic resonance imaging (MRI) for deep masses of any size, surface masses > 5 cm, or rapidly growing masses. They should be considered suspicious of sarcoma and treated as such or referred to the Centers of High Specialization.

MRI allows the study of the anatomical relationships of the tumor with the adjacent structures for optimal surgical planning and guides biopsy; therefore, the first diagnostic step is to classify the tumors as either “deep” or “superficial”, depending on the location of the investing fascia [30].

Histopathology:

Histologically, these lesions are further separated into five categories, though distinctions between these cannot be identified by imaging [10].

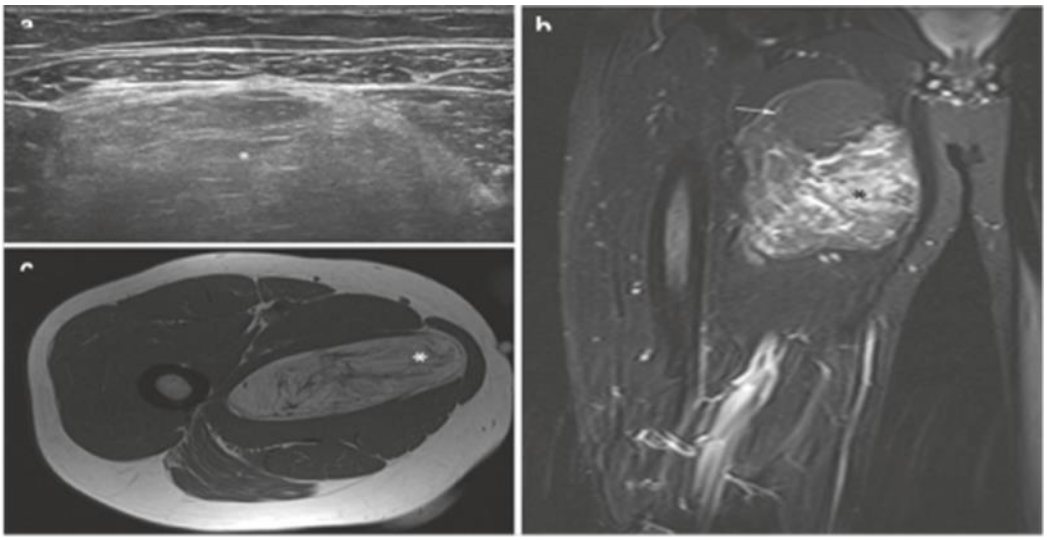

Figure 11: Well-differentiated liposarcoma of the right thigh. (a) Ultrasound. (b) Coronal fat-suppressed SE T2-weighted MR image. (c) Axial SE T1-weighted MR image [28].

Rhabdomyosarcoma

Definition:

Rhabdomyosarcoma is a primitive malignant soft tissue sarcoma with a skeletal muscle phenotype. Metastases occur to the lymph nodes, lungs, and bones. It is the most common soft tissue tumor in children, accounting for 5–8% of all childhood cancers. It is very rare in adults. There are four main histological subtypes: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing [28].

- **Radiography and CT:** Plain radiographs and CT may show local bone invasion, which is seen in about 25% of cases. Bone metastases may occur and are usually lytic and more rarely mixed [28].
- **Sonography:** US findings of rhabdomyosarcoma are nonspecific.
- **MRI:** MRI demonstrates a lesion that is iso- to hyperintense to muscle on T1W, heterogeneously hyperintense on T2W with moderate to marked enhancement with contrast (fig. 28). Prominent serpentine flow voids are often a feature of these highly vascular lesions, as is internal hemorrhage [31].

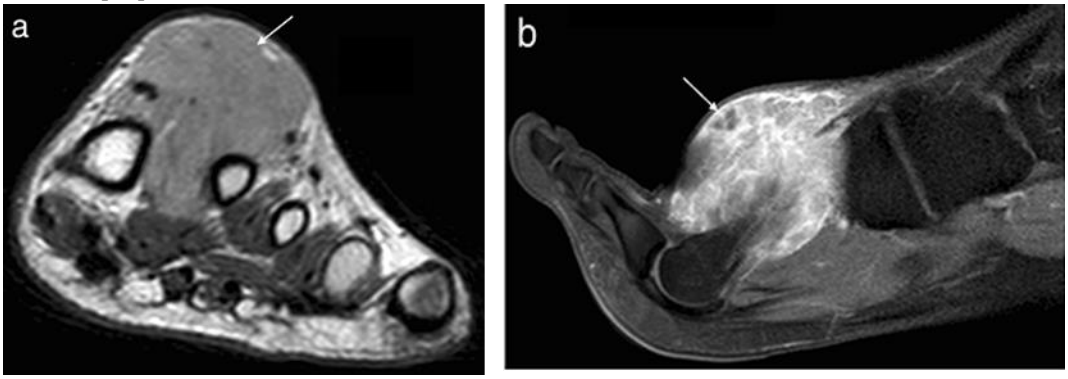

Figure 12: Rhabdomyosarcoma. Short axis T1 image (a) of the foot of a 14-year-old girl demonstrating a hyperintense mass in the first webspace with avid enhancement on post-contrast T1FS imaging (b) [15].

Synovial Sarcoma

Despite its name, it is in fact a lesion of mesenchymal origin and is named for its histological resemblance to synovial tissue. It occurs in young adults, typically between 15 and 45 years of age. It is typically related to tendon sheaths, bursa, and less frequently aponeuroses, fascia, and ligaments [14].

Presentation:

The most typical presentation is that of a palpable deep-seated soft tissue mass. It is usually associated with pain or tenderness and may cause functional impairment of the adjacent joint. Severe functional disturbances and weight loss are infrequent. Although uncommon, involvement of nearby nerves may cause pain, numbness, or paresthesia [28].

Radiological findings:

- **Radiography:** The majority of synovial sarcomas present on radiographs as round or oval, lobulated masses usually located close to a large joint, particularly the knee joint. In 5–30% of cases, there is periosteal reaction, bone erosion (related to pressure from the adjacent tumor), or even bone invasion. The most characteristic finding is the presence of multiple small densities caused by focal calcifications or ossifications seen in about 20–30% of cases, typically in the periphery of the lesion, which differentiates synovial sarcoma from liposarcomas and myxoid chondrosarcomas. The irregular shape of the calcifications helps to make the differentiation from hemangioma. Cases with extensive calcification have been reported to have a better prognosis, with higher survival rates [28].
- **Sonography:** Ultrasound characteristics are those of a well-defined, solid vascular tumor with prominent arterial and venous components. There may be internal cystic components due to internal hemorrhage. Internal calcifications are noted in 20–30%. Ultrasound appears useful as a detection method of local recurrence, in the guidance of fine-needle biopsy, and in the examination of children [28].
- **Non-contrast CT:** CT shows a soft tissue mass, which may infiltrate adjacent structures, having a slightly higher density than muscle. Joint invasion is present when the soft tissue mass projects into the expected confines of a joint capsule or when an intra-articular ligament or tendon is involved. Although bony involvement can be identified on both MR and CT imaging, cortical bone erosion or invasion is better depicted on CT. Intratumoral calcification or ossification is also more easily seen on CT than on MR imaging. Because of its extensive vascular supply, synovial sarcoma enhances markedly after injection of contrast medium [28].
- **MRI:** The MRI appearance is variable depending on size and rate of growth but is typically a T1 hypointense and T2 hyperintense mass with enhancement of viable tumor on post-contrast imaging [14].

Slow-growing masses are well defined, whereas rapidly growing lesions tend to have a more infiltrative appearance. Smaller tumors may have the appearance of simple cysts, and attempted aspiration of these lesions can lead to disruption of the capsule and compromise of the subsequent surgical resection bed [32].

Large lesions may contain solid, cystic, necrotic, and hemorrhagic components and will therefore appear heterogeneous on all sequences and may demonstrate the “triple sign” (low, intermediate, and high signal within the lesion on T2W sequences). Septations within a large lesion can give the classic “bowl of grapes” appearance.

Lesions arising within muscle may demonstrate a “split fat” sign, although this is true of any intramuscular lesion. Fluid-fluid levels are present in 10–25% cases [15].

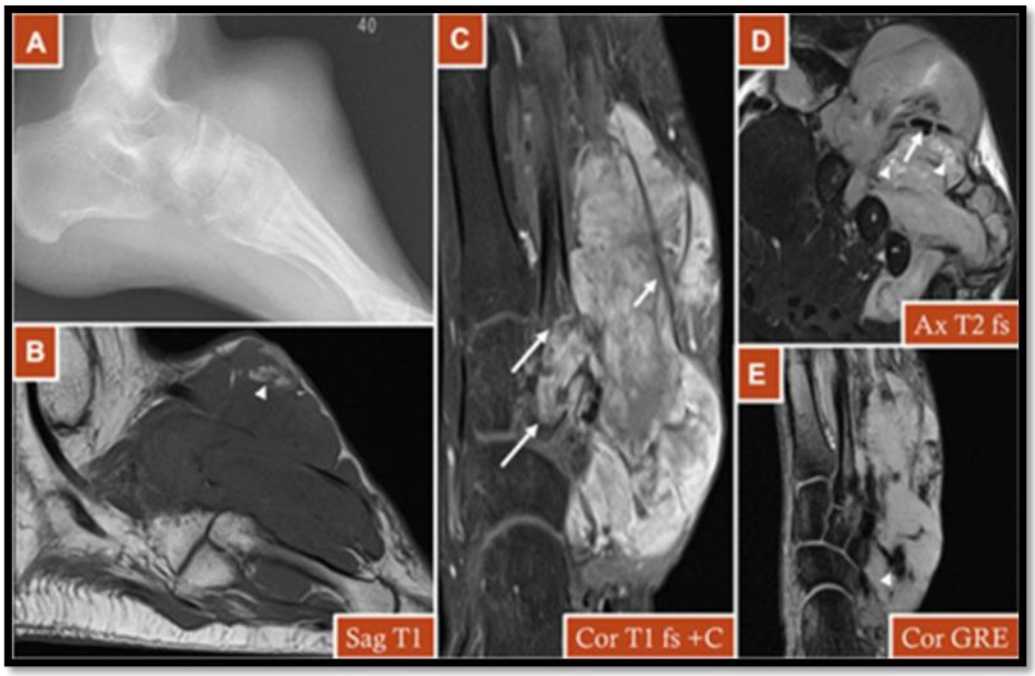

Figure 13: A 37-year-old man with a synovial sarcoma of the left foot. A, Lateral radiograph suggests a large, lobulated mass on the dorsum of the left foot. Multiplanar MRI confirms the heterogeneous mass with hyperintense T1 areas that may correspond to hemorrhagic foci (B, arrowhead), hyperintense T2 areas (D, arrowheads) that may reflect cystic change or cellular/myxoid components, and blooming low-signal foci on gradient sequences (E, arrowhead) suggesting calcification. The mass encases extensor tendons (C and D, short arrows) and invades the second metatarsal and middle cuneiform (C, long arrows) [33].

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