Spectrum of Fat-containing Soft-Tissue Masses at MR Imaging: The Common, the Uncommon, the Characteristic, and the Sometimes Confusing[1]

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Abbreviations: ALT = atypical lipomatous tumor, DDLPS = dedifferentiated liposarcoma, LN = lipomatosis of nerve, WDLPS = well-differentiated liposarcoma, WHO = World Health Organization

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Discuss the WHO classification of adipocytic tumors and describe the characteristic and overlapping MR imaging findings of common fat-containing soft-tissue masses.
- Classify the fat-containing soft-tissue masses at imaging as either clearly benign for which no further workup is warranted or as suspicious features requiring biopsy.
- Understand the role of molecular markers in the proper characterization and classification of fat-containing soft-tissue masses.

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Fat-containing tumors are the most common soft-tissue tumors encountered clinically. The vast majority of fat-containing soft-tissue masses are benign. Lipomas are the most common benign fat-containing masses and demonstrate a characteristic appearance at magnetic resonance (MR) imaging. Less common benign soft-tissue masses include lipoblastoma, angiolipoma, spindle cell lipoma/pleomorphic lipoma, myolipoma, chondroid lipoma, lipomatosis of nerve, lipomatosis, hibernoma, and fat necrosis. Well-differentiated liposarcomas (WDLPSs)/atypical lipomatous tumors (ALTs) are locally aggressive soft-tissue masses that do not metastasize. Biologically more aggressive liposarcomas include myxoid, pleomorphic, and dedifferentiated liposarcomas. At MR imaging, lipomas typically resemble subcutaneous fat but may contain a few thin septa. The presence of thick, irregular, enhancing septa and nonfatty soft-tissue mass components suggests liposarcoma rather than lipoma. However, benign lipomatous lesions and WDLPS/ALT often have overlapping MR imaging findings. Distinguishing WDLPS/ALT from a benign lipomatous lesion or from fat necrosis at imaging can be challenging and often requires histologic evaluation. We present the spectrum of fat-containing masses, using the World Health Organization classification of adipocytic tumors, with an emphasis on commonly encountered lesions, characteristic MR imaging findings associated with specific tumors, and overlapping MR imaging findings of certain tumors that may require histologic sampling. We also briefly discuss the role of molecular markers in proper characterization and classification of fat-containing soft-tissue masses.

Introduction

Fat-containing tumors are the most common soft-tissue tumor encountered clinically (1). The vast majority of fat-containing soft-tissue masses are benign (1). Proper characterization of fat-containing tumors at magnetic resonance (MR) imaging requires careful

TEACHING POINTS

- Distinguishing well-differentiated liposarcoma (WDLPS)/atypical lipomatous tumor (ALT) (themselves synonymous with each other except for location) from a benign lipomatous lesion or from fat necrosis can be challenging and often requires histologic evaluation.
- Lipomas typically resemble subcutaneous fat, but may contain a few thin septa measuring less than 2 mm in thickness.
- Infiltrative intramuscular lipomas may show intermingled bundles of muscle fibers, which are characteristically isointense to normal muscle on T1- and T2-weighted MR images.
- Imaging findings of thickened, irregular septa and nonfatty elements distinguish WDLPS/ALT from lipoma.
- A nonlipomatous mass (intermediate-to-hypointense T1 signal, intermediate-to-hyperintense T2 signal) arising within or adjacent to a WDLPS is suspicious for dedifferentiation.

attention to lesion complexity. For instance, distinguishing well-differentiated liposarcoma (WDLPS)/atypical lipomatous tumor (ALT) (themselves synonymous with each other except for location) from a benign lipomatous lesion or from fat necrosis can be challenging and often requires histologic evaluation. We describe the MR imaging characteristics of common benign and malignant fat-containing soft-tissue masses using the current World Health Organization (WHO) classification of adipocytic tumors (2). We also briefly discuss the role of molecular markers in the proper characterization and classification of the fat-containing soft-tissue masses. It is important for the radiologist to understand the role of molecular markers in the setting of fat-containing soft-tissue masses, as molecular markers are increasingly being used for definitive tumor characterization, to guide targeted therapy, for prognostication, and for monitoring response to treatment in cancer patients (3).

Benign Fat-containing Masses

Lipoma

Lipoma accounts for approximately one-half of all soft-tissue tumors and is the most common subcutaneous neoplasm (1,4). Lipomas occur most commonly in the 5th to 7th decades of life and are more common in obese patients (4).

The majority of lipomas show heterogeneous balanced structural chromosomal aberrations, most involving a breakpoint in the chromosomal region 12q13-15, resulting in expression of truncated HMGA2 protein or a fusion protein (5). Rare, unbalanced chromosomal aberrations can be seen, including chromosome 13 deletions, chromosome 12 duplications, and supernumerary ring chromosomes (Table) (5,6).

Classically, lipoma is a soft-tissue mass composed of homogeneous mature adipose tissue (Fig 1). Lipomas typically resemble subcutaneous fat, but may contain a few thin septa measuring less than 2 mm in thickness (4). The thin septa can enhance after contrast material administration (7). The enhancement is better appreciated at MR imaging than at computed tomography (CT).

Lipomas are categorized as superficial (Fig 1) or deep (Fig 2) on the basis of their location relative to the fascia overlying the deep muscles (4). They are categorized as parosteal when arising on the surface of a bone (4). Lipomas can be encapsulated or unencapsulated and may contain regions of nonadipose tissue including fibrous tissue, cartilage, bone, and myxoid tissue, which can resemble other tumors at imaging (4). Lipomas are usually solitary, but can be multiple in 5%–15% of cases (4). A lipoma usually manifests as a painless soft-tissue mass, although large lipomas can be painful secondary to nerve compression (4).

Intramuscular lipomas can be well-circumscribed and encapsulated (17% of cases) or infiltrative (83% of cases) (8–11). Infiltrative intramuscular lipomas may show intermingled bundles of muscle fibers, which are characteristically isointense to normal muscle on T1- and T2-weighted MR images (8). Rarely, an infiltrative intramuscular lipoma may infiltrate tendons and fascia and may have extramuscular extension (8). Although infiltrating intramuscular lipomas may show features that overlap with those described with varied lipomatosis disorders, these entities are usually easily distinguished by assessing the overall pattern and extent of fat distribution (8,12). Due to their size, deep location, infiltrative growth patterns, tendency to local recurrence, and muscle fibers mimicking internal septa, it may be difficult to differentiate a deep lipoma (especially an infiltrative intramuscular lipoma) from a WDLPS/ALT. At MR imaging, features suggesting a liposarcoma include tumor heterogeneity, thick irregular nodular or interrupted septa, nodular soft-tissue or nonadipose components, and incomplete fat suppression with linear or nodular hyperintense areas on fluid-sensitive images (11).

Fat necrosis demonstrates a highly variable imaging appearance (Fig 3) (13). It is commonly located over pressure points or bone protuberances (14). It may manifest as a fatty mass with cloudlike stranding and surrounding inflammatory changes (13). Fat necrosis within a lipoma may be difficult to differentiate from liposarcoma (13).

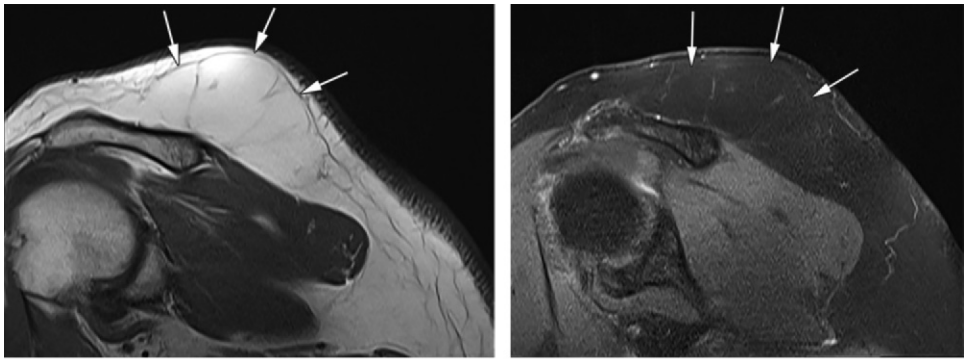
Lipoma Arborescens

Lipoma arborescens is a lipoma associated with the synovial lining of a joint or soft-tissue

Cytogenetic Characteristics of Adipocytic Tumors

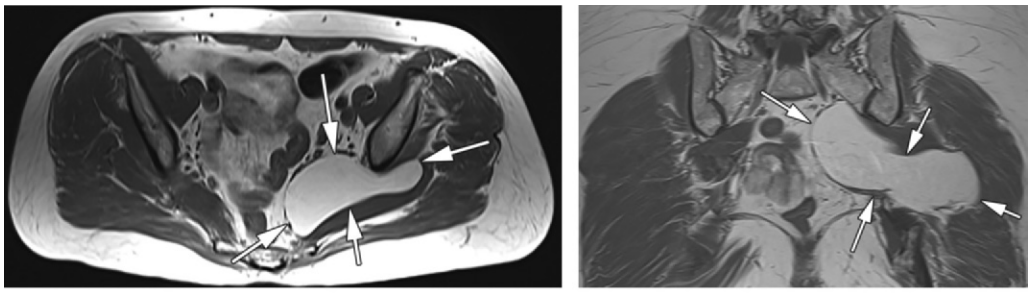
Adipocytic Tumor Type	Characteristic or Common Abnormalities
Benign adipocytic tumors	
Lipoma	12q13-15 breakpoint aberration, with resulting expression of truncated HMGA2 protein or fusion protein 6p21-23 chromosomal aberration 13q12-22 deletions Chromosome 12 duplications Supernumerary ring chromosomes S100-, leptin-, and HMGA2-positive
Lipoblastoma	8q11-13 breakpoint aberration, with resulting upregulation of *PLAG1* gene production S100-, CD34-, and/or desmin-positive
Myolipoma	Desmin- and SMA-positive, HMB45-negative
Chondroid lipoma	t(11;16)(q13;p13) balanced translocation, resulting in the *C11orf95-MKL2* fusion oncogene S100-positive, EMA-negative
Spindle cell lipoma	13q and/or 16q deletions CD34-positive, S100-negative
Lipomatosis	Activating mutations of the phosphatidylinositol-3-kinase/AKT/mTOR pathway
Hibernoma	11q13 structural rearrangements, with resulting deletion of *MEN1* tumor suppressor gene and of *PPP1CA* CD34-negative (except for the spindle cell variant) S100- and UCP1-positive
Intermediate adipocytic tumors	
WDLPS	12q13-15 amplification (supernumerary ring or giant marker chromosomes), with resulting overexpression of *MDM2*, *HMGA2*, and *CDK4* oncogenes S100-, MDM2-, and/or CDK4-positive
Malignant tumors	
DDLPS	12q13-15 amplification (supernumerary ring or giant marker chromosomes), with resulting overexpression of *MDM2*, *HMGA2*, and *CDK4* oncogenes MDM2- and/or CDK4-positive Divergent differentiation
Myxoid liposarcoma	t(12;16)(q13;p11) or t(12;22)(q13;q12) reciprocal translocation, resulting in the *FUS-DDIT3* and *EWSR1-DDIT3* fusion genes, respectively
Pleomorphic liposarcoma	Complex karyotypes without specific structural or numerical aberrations MDM2 and CDK4 negative

Note.—DDLPS = dedifferentiated liposarcoma, mTOR = mammalian target of rapamycin.



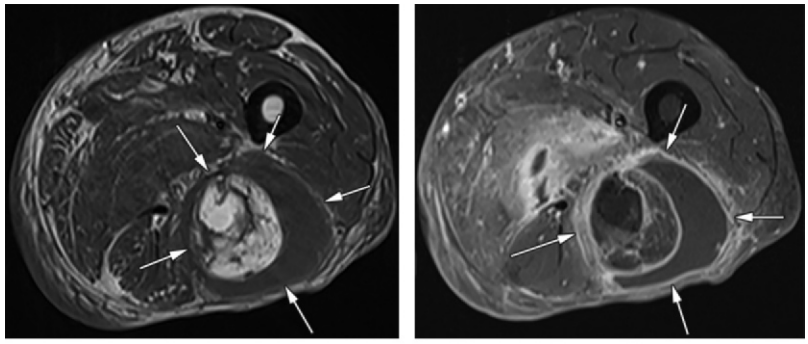
a. **b.**

Figure 1. Superficial lipoma in a 53-year-old man with a left shoulder mass. **(a)** Oblique sagittal T1-weighted MR image of the shoulder shows a homogeneous fat-containing mass (arrows), which is similar in signal intensity to the adjacent subcutaneous fat. Note the presence of a thin capsule and thin (<2 mm) internal septa without a nonadipose component. **(b)** Postcontrast fat-saturated T1-weighted MR image in a similar imaging plane shows complete suppression of fat signal intensity within the mass (arrows), mild enhancement of thin internal septa, and no solid enhancing component.



a. b.

Figure 2. Deep lipoma of the pelvis in a 65-year-old woman. Axial **(a)** and coronal **(b)** T1-weighted MR images of the pelvis show a homogeneous fat-containing extraperitoneal mass (arrows) centered within the left pelvis. The mass is displacing the left piriformis muscle and the neurovascular structures. Note the presence of a thin capsule without nodularity or any nonadipose component.



a. b.

Figure 3. Fat necrosis in a 60-year-old man with left leg pain and swelling. **(a)** Axial T1-weighted MR image shows a heterogeneous mass (arrows) within the posterior compartment of the left thigh with a lobulated hyperintense component centrally suggesting the presence of fat with a peripheral hypointense component. **(b)** Axial postcontrast fat-saturated T1-weighted MR image shows suppression of the fat signal intensity of the mass (arrows), an adjacent peripheral rim-enhancing collection, and heterogeneous enhancement within the adjacent muscles.

structure. It is characterized by mature fatty infiltration of connective tissue underneath the synovial lining (15,16). It usually manifests in adults with gradual painless joint swelling (17). It is most common in the knee, involving the suprapatellar recess. There have been several reports of ankle and hip joint involvement (18,19). Most cases are monoarticular, with rare polyarticular involvement. Cases of extra-articular lipoma arborescens have been reported, involving the peroneal and flexor ankle tendon sheath, subdeltoid bursa, extensor tendon sheath of the hand, and biceps tendon sheath (20–24). It most commonly appears as frondlike, lobulated fat-containing tissue within the joint space and is usually associated with joint effusion. Lipoma arborescens is most likely a reactive process, although other postulated causes include posttraumatic, developmental, and neoplastic (15,19).

Radiographs may show increased soft-tissue opacity in the suprapatellar recess, a nonspecific finding. Advanced cases may show findings of subchondral erosions, subchondral cysts, or secondary osteoarthritis (17). At MR imaging, findings of intra-articular frondlike fat-containing masses with associated joint effusion are pathognomonic for lipoma arborescens (Fig 4) (15). It is usually treated with arthroscopic or open synovectomy (17).

Lipoblastoma

Lipoblastoma is a rare childhood neoplasm, predominantly occurring in infants and young children less than 3 years of age (25,26). The tumor can be well-circumscribed (lipoblastoma) or, less commonly, infiltrative (lipoblastomatosis) (4). These tumors most commonly occur in the extremities (25). A lipoblastoma typically presents as a rapidly enlarging, painless mass with occasional reports of Horner syndrome, respiratory compromise, spinal cord compression, extremity weakness, and hemiparesis (4,26–30).

Lipoblastomas are benign tumors consisting of embryonal (immature) fat cells (2). Several histologic features of a lipoblastoma (myxoid stroma, plexiform capillary network, mitotic

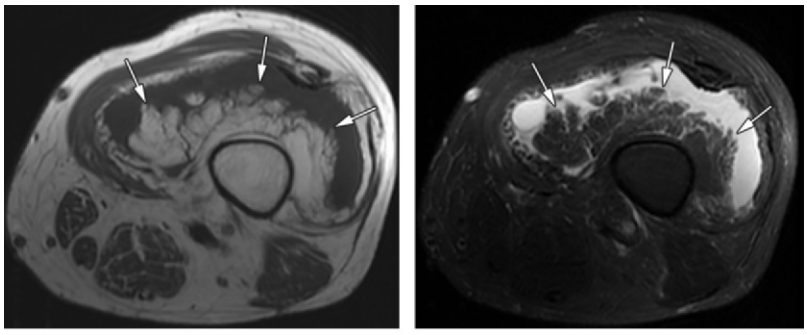


Figure 4. Lipoma arborescens of the knee in a 62-year-old man. **(a)** Axial T1-weighted MR image of the knee shows a frondlike lobulated fat-containing (hyperintense) mass (arrows) in the suprapatellar recess. **(b)** Axial fat-saturated T2-weighted MR image shows suppression (arrows) of fat signal intensity within the mass. Note the presence of a moderate joint effusion.

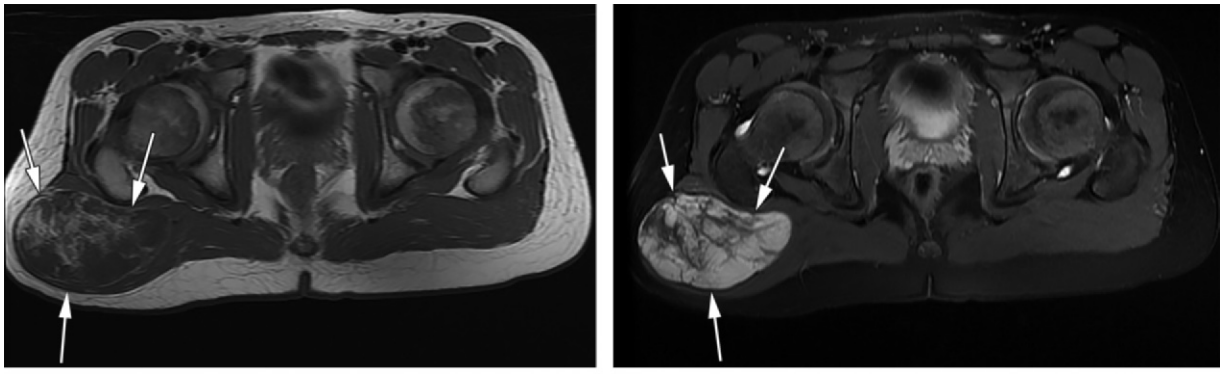


Figure 5. Lipoblastoma in a 13-year-old boy with a painless right gluteal mass. **(a)** Axial T1-weighted MR image shows a heterogeneous, well-circumscribed mass (arrows) in the right gluteus maximus muscle. Patchy and wispy areas of hyperintense signal within the mass suggest the presence of fat; however, the hyperintense signal is less intense than that of normal subcutaneous fat. **(b)** Axial fat-saturated proton density–weighted MR image shows markedly hyperintense signal within the mass (arrows), likely reflective of myxoid stroma. Surgical excision and pathologic evaluation allowed confirmation of a lipoblastoma.

figures) can overlap with those of liposarcoma (27). However, liposarcoma is extremely rare in children less than 5 years of age (27). Additionally, lipoblastoma shows a characteristic lobulation, absence of hyperchromasia, and lack of nuclear atypia, unlike liposarcoma (27). Lipoblastomas show breakpoint abnormalities of chromosomal region 8q11-13, which is involved in the upregulation of *PLAG1* gene production (25,31).

At MR imaging, lipoblastoma shows heterogeneous T1- and T2-hyperintense signal due to a variable proportion of fat and myxoid and fibrous tissue (Fig 5). Of note, the T1-hyperintense signal in lipoblastoma is characteristically less intense than that of mature fat (27). The nonfat component of the tumor shows marked heterogeneous enhancement. Lipoblastoma is usually treated with complete surgical excision (27). Unlike with lipoblastomatosis, local recurrence after surgical excision is rare. However, because of the reported possibility of maturation into lipoma, spontaneous regression, and absence of malignant transformation, it is worthwhile to consider avoiding extensive mutilating surgery done in an attempt to ensure complete surgical excision (29,30,32).

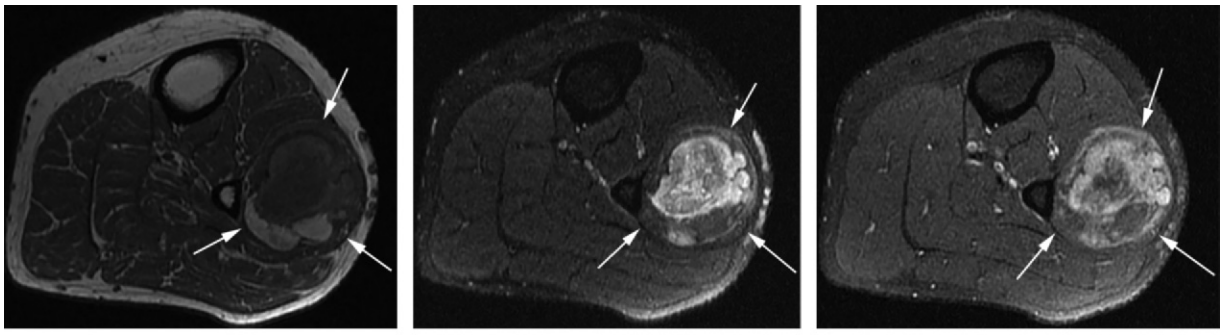
Angiolipoma

Angiolipoma is a benign neoplasm composed of mature adipose cells and small blood vessels (2). It usually occurs in the 2nd and 3rd decades of life (4). It most commonly presents as multiple, small (<2 cm), subcutaneous, tender nodules located in the forearm (the most common site), trunk, or upper arm (4).

Imaging is rarely performed, given the subcutaneous location of the tumors (4). The tumor shares signal intensity characteristics with mature adipose tissue. There may be internal areas of T1-hypointense and T2-hyperintense signal, corresponding to vascular elements, which enhance after contrast material administration (4). Surgical resection is curative, without reported recurrence or malignant transformation (2).

Myolipoma

Myolipoma, also known as lipoleiomyoma, is a rare benign neoplasm composed of mature adipose tissue and mature smooth muscle cells (2). It is most common in adult women (2). Most commonly, it arises within the abdominal cavity, retroperitoneum, or inguinal regions (2), but may arise within the body wall, extremities, and



a. b. c.

Figure 6. Chondroid lipoma in a 21-year-old man with a slowly enlarging left leg mass. **(a)** Axial T1-weighted MR image shows a heterogeneous mass (arrows) within the peroneal compartment of the left leg. The majority of the mass is hypointense with a smaller hyperintense portion, suggesting intralesional fat. **(b)** Axial fat-saturated T2-weighted MR image shows lobulated hyperintense signal (arrows) reflective of chondroid or myxoid matrix. Loss of signal intensity in the posterior portion of the mass confirms the presence of intralesional fat. **(c)** Axial postcontrast fat-saturated T1-weighted MR image shows heterogeneous enhancement of the mass (arrows). Surgical excision and pathologic evaluation confirmed chondroid lipoma.

subcutaneous fat (2). Due to its deep location, it is usually large at presentation and is completely or partially encapsulated (4).

At MR imaging, these tumors are heterogeneous, with areas of fat and soft-tissue signal intensity corresponding to muscle elements (intermediate on T1-weighted images, intermediate-to-hyperintense on T2-weighted images) (4). Preoperative imaging diagnosis is difficult, and most tumors are diagnosed at pathologic evaluation (4). The imaging appearance of a myolipoma overlaps with that of a WDLPS, the most common retroperitoneal fat-containing neoplasm (4). Surgical resection is curative, without reported recurrence or malignant transformation (2).

Chondroid Lipoma

Chondroid lipoma is a rare, benign, slow-growing neoplasm (2). The tumor is usually well-circumscribed and encapsulated, arising in the superficial or deep soft tissues (33). The most common location is in the proximal extremities or limb girdles (34). It usually manifests in the 3rd or 4th decade and is more common in women (male-to-female ratio, 1:4) (33).

Histologically, the tumor is composed of rounded cells in a myxoid or hyalinized chondroid matrix and a variable amount of mature fat (2). There is usually no notable mitotic activity or nuclear pleomorphism (33). The tumor may show areas of hemorrhage, fibrin deposition, inflammation, calcification, and/or bone formation (33). Histologically, the tumor can be difficult to differentiate from a myxoid liposarcoma or extraskeletal myxoid chondrosarcoma (2). The tumor characteristically shows a t(11;16)(q13;p13) balanced translocation, resulting in the *C11orf95-MKL2* fusion oncogene (33,35).

Chondroid lipoma may show calcification on radiographs (4). CT typically shows a well-circumscribed, heterogeneously enhancing mass with areas of fat attenuation (4). Additionally, CT shows areas of matrix mineralization (chondroid or osteoid). MR imaging typically shows a well-defined mass with lobulated areas of T2-hyperintense and/or fluidlike signal intensity, which may resemble a myxoid liposarcoma or extraskeletal myxoid chondrosarcoma (Fig 6) (36). On T1-weighted MR images, the mass is primarily isointense or hypointense to muscle, with focal hyperintense areas that are representative of fat (33,36,37). The tumor enhances heterogeneously after contrast material administration and can show hypermetabolic activity at PET/CT (38). The tumor cannot be definitively distinguished from malignant neoplasms; excision or biopsy is often needed for diagnosis (39).

The treatment of choice is complete surgical excision. No examples of local recurrence or metastasis have been reported in the literature (33).

Spindle Cell or Pleomorphic Lipoma

Spindle cell lipoma (SCL), or pleomorphic lipoma, is a benign, well-circumscribed subcutaneous or superficial mass lesion (2). The majority are located in the posterior neck, shoulder, and upper back in middle-aged men (40). SCLs may express androgen receptors, accounting for their predominance in men (41).

Histologically, SCLs are composed of varying proportions of mature adipocytes, spindle cells without atypia arranged in typical "school of fish" parallel arrays, myxoid stroma, and rope-like collagen bundles (42). SCLs exhibit 13q and/or 16q deletions, CD34 positivity, and, unlike nerve sheath tumors, S100 negativity (40). Intramuscular SCL may be well-circumscribed or can be infiltrative with a striated appearance due to interspersed muscle fibers (40).

The imaging and pathologic diagnosis can be very challenging, as the lesion contains a variable

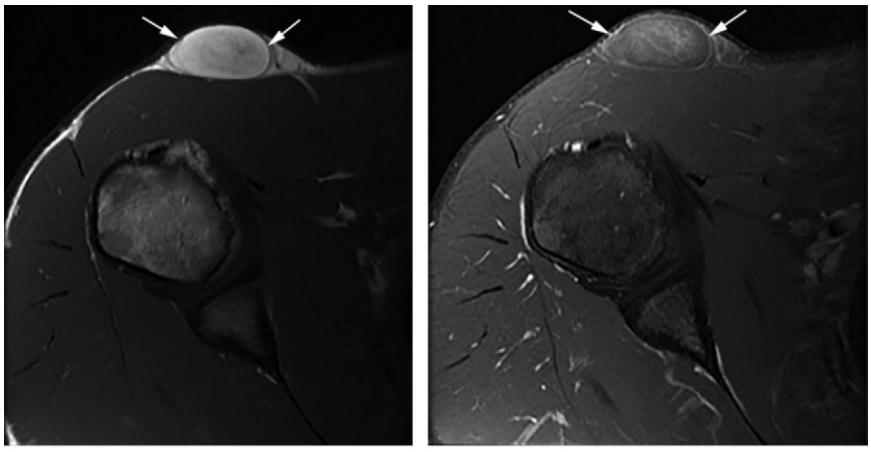


Figure 7. Spindle cell (pleomorphic) lipoma in an 18-year-old woman with a painless right shoulder mass. **(a)** Axial T1-weighted MR image shows a superficial, encapsulated fat-containing mass (arrows) in the anterior shoulder. There is indistinct, wispy hypointense signal within the mass. **(b)** Axial postcontrast fat-saturated T1-weighted MR image shows suppression of the fat signal intensity and mild enhancement of the indistinct hypointense areas. Surgical excision and pathologic evaluation confirmed spindle cell lipoma.

amount of fat and frequently little or no macroscopic or microscopic fat (40). At MR imaging, the nonfat portion is usually isointense to muscle on T1-weighted images and variable in signal intensity on T2-weighted images (40). There is delayed homogeneous or heterogeneous enhancement, which depends on the relative proportion of fat (Fig 7) (40). SCLs tend to show hypermetabolic activity at PET/CT (40). Local recurrence after surgical excision can occur (2). As the imaging appearance overlaps with liposarcoma, preoperative image-guided biopsy may be considered when SCL is in the differential diagnosis, so as to prevent morbidity associated with more aggressive surgery for liposarcoma (4,40).

Lipomatosis of Nerve

Lipomatosis of nerve (LN) is a rare and incompletely understood benign condition, which has been variably described using terms such as fibrolipomatous hamartoma and fibrofatty proliferation of a nerve (43). LN most commonly occurs in the wrist and hand, involving the median nerve and its branches (43). However, LN has been reported in multiple other nerve distributions, including the ulnar, radial, digital, sciatic, intercostal, and medial plantar nerves as well as the cervical, brachial, and lumbosacral plexus (44–46).

LN represents a spectrum of nerve disorders ranging from nerve-associated lipoma to lipomatosis (47). LN can involve single or multiple nerves in an extremity and can be unilateral or bilateral (43). LN is frequently associated with varying degrees of localized mesenchymal overgrowth in the territory of nerve distribution (45). This ranges from minimal digital enlargement to extensive bone and soft-tissue hypertrophy, referred to as macrodystrophia lipomatosa (44).

LN is characterized by diffuse nerve enlargement secondary to interfascicular fibrofatty infiltration (2). The intervening nerve fibers are intact. The fibrofatty proliferation associated with LN is histologically benign, but may progress even after surgical resection (48). The growth is usually most rapid in childhood and can outpace skeletal growth. The growth continues after skeletal maturation, but usually slows down in late adulthood (48).

LN most commonly presents as a painless, slowly enlarging mass (43). A retrospective review of 180 cases of median nerve lipomatosis demonstrated a mean age of presentation of 21 years (range, 1 month–67 years), with 71% of patients presenting before 30 years of age (43). The most common presentation was an enlarging distal forearm or hand mass (88%) followed by sensory symptoms of median neuropathy, including paresthesia, numbness, and/or tingling. Motor median nerve deficit was present in 27% of patients (43).

There is no curative treatment for LN (2,43). The treatment goal includes symptomatic relief and cosmetic and functional improvement of the deformity (43). Carpal tunnel release aims to provide symptomatic relief from compressive median neuropathy (43). In patients with marked median nerve enlargement, carpal tunnel release can be performed prophylactically (43). Surgical resection of LN can result in serious neurologic dysfunction. Interfascicular surgical decompression can result in recurrent painful neuromas (49).

The MR imaging findings of marked diffuse nerve enlargement with T1-hyperintense fat interspersed between normal T1-hypointense nerve fascicles are pathognomonic (47) (Fig 8). Since the MR imaging findings are diagnostic and because of the risk of neurologic deficit from surgery, biopsy is not recommended (47).

Lipomatosis

Lipomatosis is an incompletely understood rare and heterogeneous group of benign fat deposition disorders (2). Lipomatosis is characterized by diffuse infiltrative overgrowth of mature fatty tissue

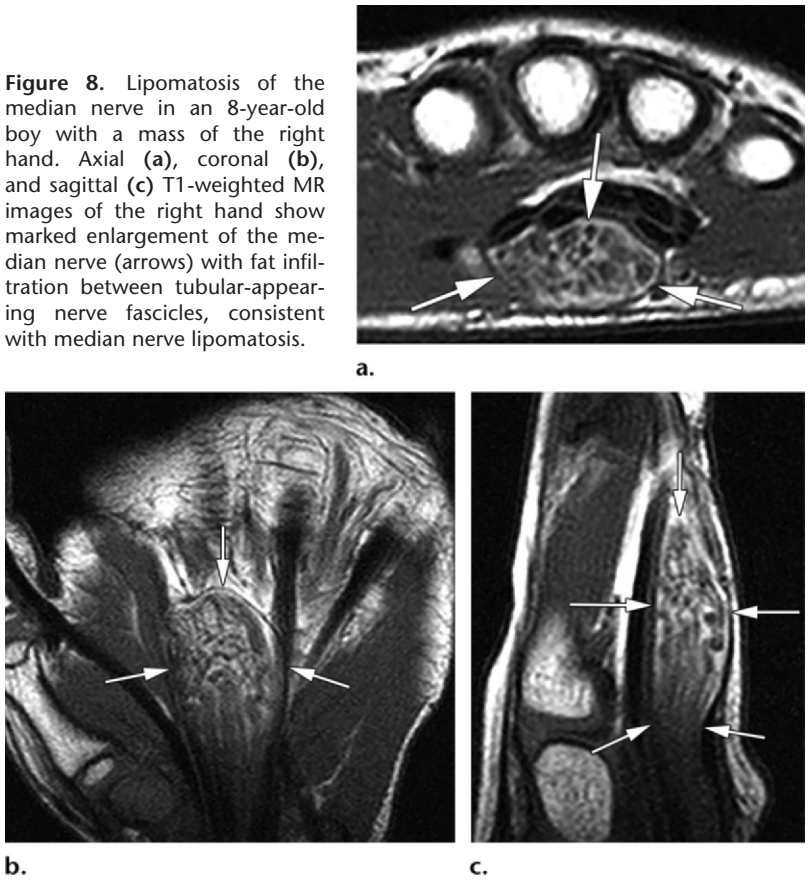


Figure 8. Lipomatosis of the median nerve in an 8-year-old boy with a mass of the right hand. Axial **(a)**, coronal **(b)**, and sagittal **(c)** T1-weighted MR images of the right hand show marked enlargement of the median nerve (arrows) with fat infiltration between tubular-appearing nerve fascicles, consistent with median nerve lipomatosis.

involving the subcutaneous and/or deep soft tissues (2). It can be localized, multifocal, or diffuse (4). MR imaging shows infiltration of unencapsulated fat in subcutaneous or deep soft tissue, with characteristic T1- and T2-hyperintense signal that suppresses at fat-suppressed sequences (4).

A heterogeneous phenotypic spectrum of somatic segmental overgrowth syndromes has recently been described to be associated with activating mutations of the *PIK3CA* gene (50,51). These disorders can be associated with varying degrees, location, and distribution of lipomatous overgrowth (51).

Hibernoma

Hibernoma is an uncommon benign tumor of brown fat (2). The tumor usually manifests in adults as a painless, slow-growing mass (2). It is most commonly located in the thigh, shoulder girdle, back, or neck (52).

Hibernomas are well-circumscribed, partially encapsulated hypervascular masses (2). Four histologic variants have been described: typical hibernoma, lipoma-like variant, myxoid variant, and spindle cell variant (52). Lipoma-like variant can be difficult to differentiate from WDLPS/ALT or myxoid liposarcoma, especially when manifesting retroperitoneally (52). Myxoid variant hibernoma can be difficult to differentiate from myxoid liposarcoma (52). The spindle cell variant has overlapping features with spindle cell lipoma and may represent a hybrid neoplasm (2). Most hibernomas are positive for S100 and most, except spindle cell variant, are negative for CD34 (2). Hibernomas may show 11q13 and 11q21 chromosomal rearrangements (52).

Although hibernoma is a fat-containing lesion, it is associated with prominent vascularity and septa (53). The fat often appears similar but not identical to mature fat (53). At MR imaging, hibernoma appears as a well-defined mass with T1 signal intensity that is greater than that of skeletal muscle and less than that of subcutaneous fat (Fig 9) (54). The tumor may fail to suppress on fat-suppressed images (55). It is heterogeneously hyperintense on T2-weighted images and shows intense enhancement after contrast material administration (53). Hibernoma tends to show hypermetabolic activity at PET/CT (53,55–57). Surgical resection is curative, with very rare local recurrence, due to incomplete excision (54).

Liposarcoma

Liposarcoma accounts for 17.1% of all soft-tissue sarcomas (58). Liposarcoma is a heterogeneous group of disorders categorized by the

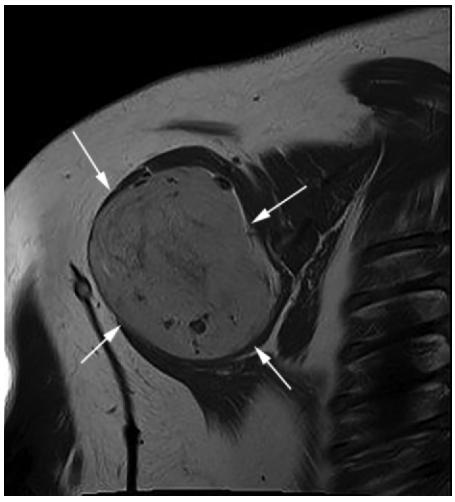


Figure 9. Hibernoma. Oblique coronal T1-weighted MR image shows a well-circumscribed mass (arrows) of the shoulder. The mass shows hyperintense signal that is less intense than that of the subcutaneous fat.

2013 WHO Classification (2) as intermediate (WDLPS/ALT) or malignant (DDLPS, myxoid liposarcoma, and pleomorphic liposarcoma). Liposarcoma usually manifests in the 6th decade as an enlarging painless mass and is equally common in men and women (59).

Intermediate (Locally Aggressive) Fat-containing Masses

WDLPS/ALT

WDLPSs/ALTs are the most common liposarcomas (60). The most common location is in the extremities, followed by the retroperitoneum, paratesticular region, and mediastinum (1). It typically is an asymptomatic slow-growing mass and does not metastasize (2). Large tumors can be symptomatic due to local mass effect. WDLPSs/ALTs are locally aggressive and show a propensity for local recurrence, especially when the primary tumor arises within the mediastinum or retroperitoneum (59). Occasionally, they can undergo dedifferentiation into high-grade sarcoma, resulting in an unfavorable prognosis due to more aggressive local behavior and acquisition of metastatic potential (59). The presence of supernumerary ring chromosomes or giant marker chromosomes is the cytogenetic hallmark of a WDLPS (5). This results in amplification and overexpression of *MDM2*, *HMGA2*, and *CDK4* oncogenes (chromosomal region 12q13-15), which are important molecular markers that may differentiate liposarcoma from lipoma and other soft-tissue sarcomas (5,61).

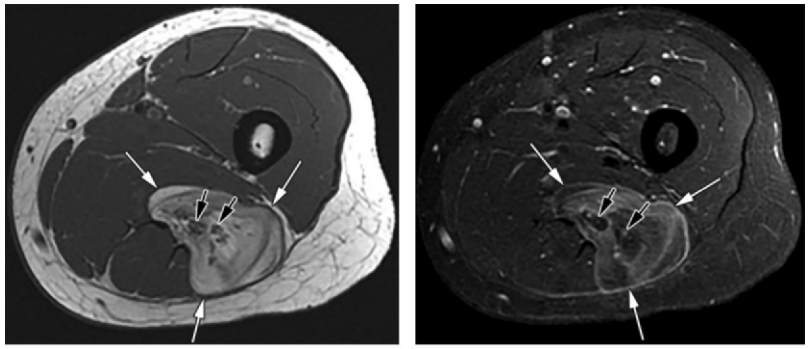
WDLPS/ALT usually manifests as a predominantly fat-containing mass with thick irregular septa (linear, nodular, or swirled), septal enhancement, and nonadipose areas (7,60,62). These tumors can appear as soft-tissue or fat-attenuation masses on radiographs, especially when arising within the extremities. Calcification or ossification can be seen in 10%–32% of tumors at radiography or CT (60). CT or MR imaging typically shows a predominantly fat-containing mass with thick enhancing septa (>2 mm) or nonfatty areas that are typically <2 cm in size (Figs 10, 11) (62). Imaging findings of thickened, irregular septa and nonfatty elements distinguish WDLPS/ALT from lipoma (62). However, imaging features can resemble a benign lipomatous lesion or involutional change in a lipoma. Therefore, histologic diagnosis is often required. Lipomas rarely arise in the mediastinum or retroperitoneum. Therefore, a predominantly fat-containing mass arising in the mediastinum or retroperitoneum most likely represents WDLPS (60).

WDLPSs/ALTs are treated with wide local excision to prevent local recurrence (63). The nomenclature used to categorize these tumors has been subject to debate (7). Although WDLPS and ALTs are similar morphologically, karyotypically, and in their biologic potential, the 2013 WHO classification recommends terminology based principally on tumor location and resectability (2). Lesions arising in the extremities and trunk have better prognosis than retroperitoneal liposarcomas, due to the relative ease of obtaining clear surgical margins and are referred to as ALTs (62). In contrast, tumors located within the mediastinum and retroperitoneum are relatively large at presentation and encase vital organs, complicating surgical excision (63). The local recurrence rate is higher for these tumor locations with notable morbidity and mortality due to the need for repeated surgeries (63). The 2013 WHO classification categorizes such lesions arising in the mediastinum, retroperitoneum, and spermatic cord as WDLPS (2). As ALT and WDLPS are synonyms, it is vitally important for all members of the clinical team to use agreed-on terminology that promotes universal comprehension and appropriate treatment (2,7).

Malignant Fat-containing Masses

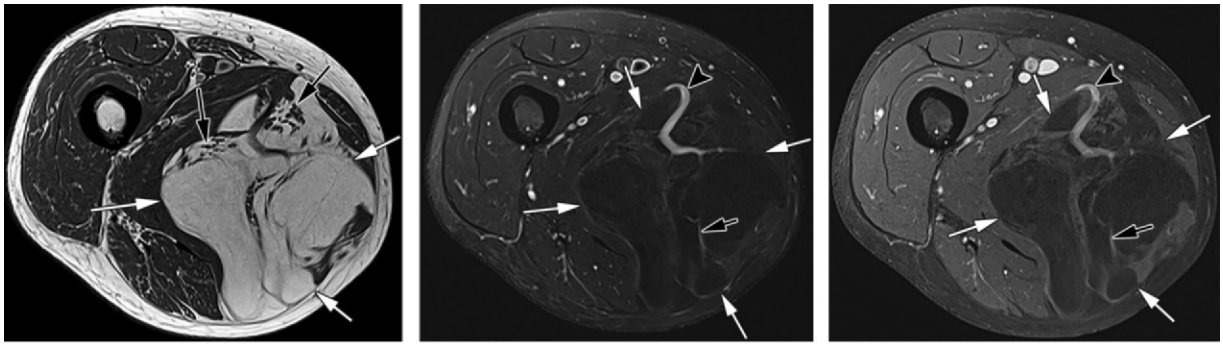
DDLPS

DDLPS, by definition, is a high-grade sarcoma secondary to progression in a primary or recurrent WDLPS/ALT (2). The majority (90%) of these tumors are dedifferentiated at the time of presentation (referred to then as de novo DDLPSs) or develop as a late complication of WDLPS (10%) (2,64). There is, approximately, a 17% risk of dedifferentiation for retroperitoneal



a. b.

Figure 10. ALT in a 52-year-old woman with a painless left posterior thigh mass. **(a)** Axial T1-weighted MR image shows a heterogeneous fat-containing mass (white arrows) with thickened internal septa in linear and swirled configurations within the posterior compartment. Note the tibial and common peroneal nerves (black arrows) encased by the mass. **(b)** Axial postcontrast fat-saturated T1-weighted MR image shows suppression of fat signal intensity and enhancement of the capsule (white arrows) as well as thickened internal septa. Note the tibial and common peroneal nerves (black arrows) encased by the mass.

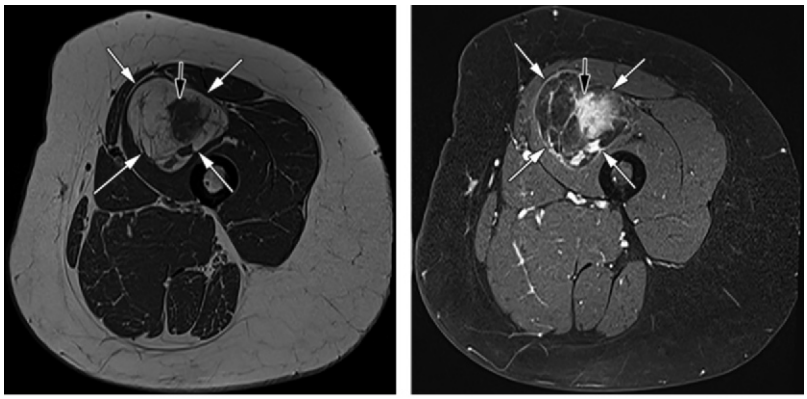


a. b. c.

Figure 11. ALT in an 82-year-old man with a painful right medial thigh mass. **(a)** Axial T1-weighted image shows a large, fat-containing, predominantly intramuscular mass (white arrows) with muscle bundles (black arrows) traversing through the mass and thickened internal septa. **(b)** Axial T2-weighted fat-saturated image shows the mass (white arrows) with suppression of fat signal intensity, mildly hyperintense internal septa (black arrow), and an enlarged vessel (black arrowhead). **(c)** Axial postcontrast fat-saturated T1-weighted image of the mass (white arrows) shows suppressed fat signal intensity, thick enhancing internal septa (black arrow), and an enlarged vessel (black arrowhead).

WDLPS and a 6% risk of dedifferentiation for extremity WDLPS/ALT (64). The risk of dedifferentiation increases with recurrent retroperitoneal WDLPS (20% for first-time recurrence, 44% for second-time recurrence) (65). Like WDLPS, 90% of DDLPSs show amplification and overexpression of the *MDM2*, *HMGA2*, and *CDK4* oncogenes (chromosomal region 12q13-15) (63). DDLPSs and WDLPSs/ALTs biologically represent a spectrum of the same disease with similar underlying chromosomal alteration (63). However, DDLPSs are more aggressive, with metastatic potential. DDLPS commonly manifests in the 7th decade of life as a painless enlarging mass or with abdominal pain (66). The most common location is the retroperitoneum (67).

Histopathologically, DDLPSs show a well-differentiated component, with a dedifferentiated component such as an undifferentiated pleomorphic sarcoma, rhabdomyosarcoma, leiomyosarcoma, osteosarcoma, or chondrosarcoma (66). A DDLPS is usually large at presentation and at imaging manifests as a well-circumscribed round or lobulated mass (66). The imaging findings of DDLPS can overlap with WDLPS and are best evaluated at MR imaging. A nonlipomatous mass (intermediate-to-hypointense T1 signal, intermediate-to-hyperintense T2 signal) arising within or adjacent to a WDLPS is suspicious for dedifferentiation (Fig 12) (66). Hong et al (66) reported four morphologic categories of retroperitoneal DDLPS: category I, predominantly fatty mass with small nonfatty component; category II, predominantly nonfatty mass with small fatty component; category III, adjacent well-defined fatty and nonfatty masses; and category IV, two adjacent predominantly



a. b.

Figure 12. DDLPS in a 58-year-old woman with a painful left anterior thigh mass. **(a)** Axial T1-weighted image shows a primarily fat-containing mass (white arrows) within the quadriceps musculature with multiple irregular septa and a large, irregular, hypointense nodule centrally (black arrow). **(b)** Axial postcontrast fat-saturated T1-weighted image of the mass (white arrows) shows intense enhancement of the central nodule (black arrow) and internal septa.

nonfatty masses (66). DDLPS with a predominantly nonfatty mass or masses (Hong's categories II and IV, respectively) can be difficult to differentiate from pleomorphic liposarcoma and other retroperitoneal liposarcomas at imaging (66). Retroperitoneal WDLPS and DDLPS can be multifocal at initial presentation or at recurrence (67). The incidence of multifocality may be related to some underlying genetic defect, and the entire retroperitoneal/intra-abdominal fat may be at increased risk for disease development (67). Due to pathologic variations, biopsy should be directed toward the nonlipomatous component (66).

The mainstay of treatment is complete surgical resection (63). However, due to difficulty in obtaining clear surgical margins, especially in retroperitoneal WDLPS and DDLPS, outcomes remain poor (63).

Myxoid Liposarcoma

Myxoid liposarcoma is the second most common type of liposarcoma (68,69). Myxoid liposarcoma and round cell liposarcoma show similar chromosomal translocation and are considered to represent a histologic continuum (2). Pure myxoid liposarcoma is considered to be a low-grade sarcoma with <10% metastasis risk (2). Myxoid liposarcoma with >5% round cell component is considered to be a high-grade sarcoma, which is associated with a higher risk of metastasis and poorer prognosis (2,68). Fat usually comprises less than 25% of the tumor mass (68). The chromosomal translocation t(12;16)(q13;p11) is highly sensitive and specific for myxoid liposarcoma (68). It occurs mainly in the deep soft tissues of the extremities, most commonly in the thigh musculature, and can rarely occur in the retroperitoneum (2). It tends to manifest in a younger age group than that for WDLPS and DDLPS, with no gender predilection (2). Myxoid liposarcoma shows a high propensity for local recurrence and distant metastasis (70,71). Unlike other soft-tissue sarcomas, it shows a high incidence of extrapulmonary metastasis to the soft tissues and bones (71). The incidence of bone metastasis (17%) has been reported to be even higher than pulmonary metastasis (14%) (70,71).

MR imaging findings are more specific for a pure myxoid liposarcoma, which manifests as a T1-hypointense and markedly T2-hyperintense encapsulated mass (Fig 13) (60). It can resemble an intramuscular myxoma, and in some cases, the appearance may even resemble a cyst or cystic lesion (60). However, unlike a cyst or cystic lesion, myxoid liposarcoma shows marked or heterogeneous enhancement (68). Additionally, identification of an associated fatty component helps in the differentiation.

High-grade myxoid liposarcoma tends to have an atypical appearance with heterogeneous signal intensity on T1- and T2-weighted images due to nonfatty nonmyxoid component mixed with myxoid and fatty component (68). The nonfatty nonmyxoid (round cell) component shows intermediate T2 signal intensity unlike the markedly T2-hyperintense signal of the myxoid component and variable enhancement (68). Although MR imaging features are nonspecific, the imaging findings of vascular and bone invasion, circumferential vascular encasement, absence of a pseudocapsule, and presence of tumor necrosis are more commonly associated with higher-grade myxoid liposarcoma (68).

The percentage of round cells is a strong negative prognostic factor for local recurrence, metastasis, and survival (69). Other negative risk factors include microscopic residual tumor, greater age, and tumor size >10 cm (69).

Pleomorphic Liposarcoma

Pleomorphic liposarcoma is a high-grade liposarcoma that tends to occur in the extremities

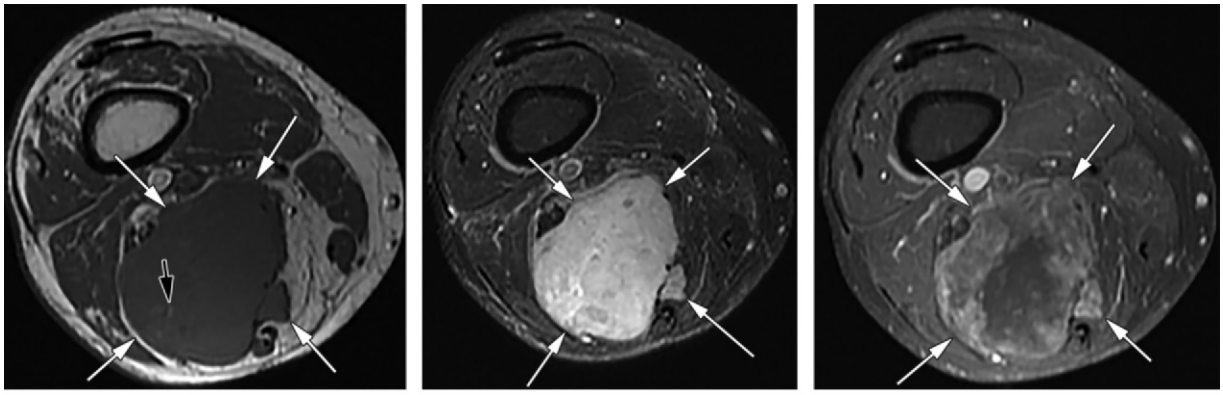


Figure 13. Myxoid liposarcoma in a 65-year-old woman with a right posterior thigh mass. **(a)** Axial T1-weighted image shows a large predominantly hypointense mass (white arrows) in the posterior compartment, with small areas of subtle hyperintense signal (black arrow) suggesting intralesional fat or hemorrhage. **(b)** Axial fat-saturated T2-weighted image shows markedly hyperintense signal throughout the mass (arrows). **(c)** Axial postcontrast fat-saturated T1-weighted image shows heterogeneous enhancement of the mass (arrows). Surgical excision and pathologic evaluation helped to confirm myxoid liposarcoma. No round cell areas were reported at pathologic analysis.

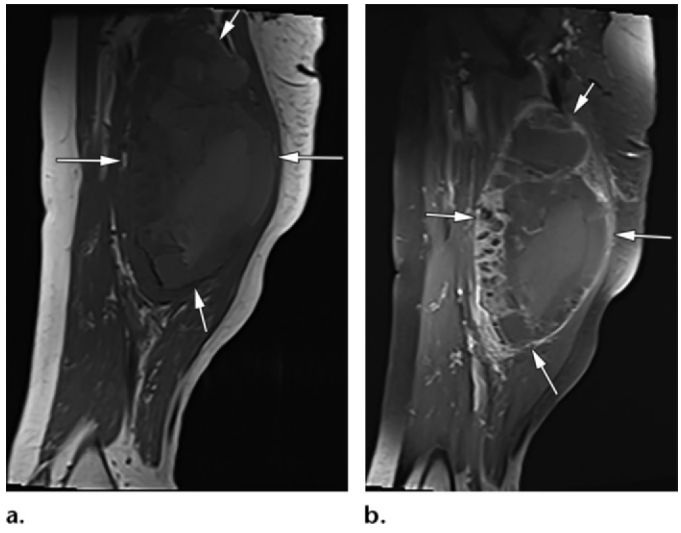


Figure 14. Pleomorphic liposarcoma in a 71-year-old woman with a left thigh mass. **(a)** Sagittal T1-weighted MR image shows a large heterogeneous mass (arrows) within the posterior compartment of the left thigh, with no identifiable intralesional fat. **(b)** Sagittal postcontrast fat-saturated T1-weighted MR image shows peripheral heterogeneous enhancement of the mass (arrows), with a large central nonenhancing area indicating necrosis or cystic degeneration. Surgical excision and pathologic evaluation helped to confirm pleomorphic liposarcoma.

(2,59). Other less-common sites include the trunk and retroperitoneum (2). It is the least common type of liposarcoma, accounting for 5%–15% of all cases (62). It usually occurs in older patients (>50 years of age) (62). It is usually an aggressive, rapidly growing neoplasm with high rates of local recurrence (30%–50%), distant metastasis (30%–50%), and tumor-associated mortality (59). The lung is the most common site of distant metastasis (59).

Pathologically, pleomorphic liposarcoma is a large (>10 cm) heterogeneous myxoid mass with areas of necrosis and/or hemorrhage and small focal areas of fat (62). The imaging findings typically are of a large, relatively well-defined, nonspecific soft-tissue mass (60,62). However, the tumor margins can be infiltrative (60,62). At MR imaging, the tumor shows heterogeneous signal intensity due to the presence of hemorrhage and/or necrosis (Fig 14). The signal intensity of intralesional fat may be less than that of subcutaneous fat (60,62). However, fat-suppressed sequences are helpful in differentiating fat from hemorrhage (60). The absence of fat within the neoplasm can make the imaging diagnosis difficult (60,62).

Conclusion

There are multiple subtypes of benign and malignant fat-containing tumors, many with overlapping MR imaging features. Lipomas typically have a characteristic MR imaging appearance that is independent of location. Thick irregular septa and nonfatty elements distinguish a WDLPS from a lipoma at MR imaging. Histologic evaluation is often recommended for lesions that cannot be confidently characterized as lipomas or a benign process such as lipomatosis of the nerve or fat necrosis.

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