Soft Tissue Sarcoma Follow-up Imaging: Strategies to Distinguish Post-treatment Changes from Recurrence

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Abstract

Soft tissue sarcomas encompass multiple entities with differing recurrence rates and follow-up intervals. The detection of recurrences and their differentiation from post-therapeutic changes is therefore complex, with a central role for the clinical radiologist. This article describes approved recommendations. Prerequisite is a precise knowledge of the current clinical management and surgical techniques. We review recurrence rates and treatment modalities. An adequate imaging technique is paramount, and comparison with previous imaging is highly recommended. We describe time-dependent therapy-related complications on magnetic resonance imaging compared with the spectrum of regular post-therapeutic changes. Early complications such as seromas, hematomas, and infections, late complications such as edema and fibrosis, and inflammatory pseudotumors are elucidated. The appearance of recurrences and radiation-associated sarcomas is contrasted with these changes. This systematic approach in follow-up imaging of soft tissue sarcoma patients will facilitate the differentiation of post-therapeutic changes from recurrences.

Keywords

- sarcoma
- recurrence
- aftercare
- magnetic resonance imaging
- postoperative complications

Recurrence Epidemiology

The diagnosis and therapy of patients with soft tissue tumors has improved in recent decades, with a much higher long-term survival rate, requiring an extended follow-up. Consensual interdisciplinary tumor board decisions in dedicated centers help adherence to optimized and standardized procedures for the individual patient.^{1–6}

The local recurrence (LR) rates of soft tissue sarcomas reported in the literature vary considerably, with ~ 8.5% of patients after 2 years,⁷ 17 to 26% after 5 years, and 20 to 32% after 10 years.^{8,9} Well-differentiated liposarcoma was associated with late (> 5 years) local recurrences.¹⁰ Recurrences are more common in truncal sarcomas⁷ with almost 40% of cases after 5 years, compared with ~ 4 to 20% in extremity sarcomas.⁹ In general, localizations in the deep retroperitoneal and head and neck are associated with higher recurrence rates.^{8,11} In extremity sarcomas, radiotherapy further decreases local recurrence.¹² With limb-preserving resection and postoperative radiation, rates of 9% after 5 years and 12% after 10 years^{3,13} can be achieved. LR is observed more often on the upper extremity than on the lower extremity.¹⁴

The influence of positive resection margins on LR rate is under debate. An initial unplanned positive resection margin was shown to result in higher LR rates even after a wide resection and adjuvant surgical therapy¹⁵ and increased the likelihood of earlier recurrence¹⁶ in some studies. Other studies failed to show the same results¹⁷ even in stage 3 sarcomas.¹⁸ Microscopically positive resection margins (termed R1, in contrast to R0 margins, which are defined as microscopically negative) as such resulted in up to a 3 to 5.9 times increased risk of LR.^{7,8,13,17,19–21} Only in retroperitoneal sarcomas and primary fibrosarcoma was the local recurrence-free survival not altered by positive resection margins.²² Similarly, if a patient already has an LR, their future prognosis depends to a large extent on whether the resection margins during reoperation are negative, up to 2 mm or > 2 cm.^{13,23,24} In general, an unintentional R1 resection seems to be more common in myxofibrosarcomas and undifferentiated pleomorphic sarcomas,^{12,25} whereas R0 resection is more common in liposarcomas (apart from special difficulties with retroperitoneal liposarcomas) or generally low-grade sarcomas.²⁴

Various studies indicate that patients benefit from a primary resection in a dedicated sarcoma center; adherence to approved guidelines has especially proved to be a crucial factor.^{26–29} Overall, intermediate and especially high histologic tumor grades as well as large tumors (especially > 10 cm) also show higher LR rates.^{7–10,20,30} Additional unfavorable factors are a patient aged > 64 years and certain tumor entities, such as undifferentiated pleomorphic sarcoma, myxofibrosarcoma, malignant peripheral nerve sheath tumor, angiosarcoma, and epithelioid sarcoma,^{4,7,8,31,32} as well as highly/dedifferentiated liposarcoma in the retroperitoneum.^{33,34} Overall survival in some studies largely depended on the occurrence of distant sarcoma metastases, whereas LRs mainly affected local tumor control.²¹ However, other studies also found that LRs had an impact on overall survival.^{13,31,35,36}

Unfortunately, sarcoma recurrences tend to be deeper seated and higher graded compared with the initial tumor.^{37,38}

Overview of Therapeutic Options in Sarcoma

For a radiologist, an understanding of the expected and unexpected changes following the different treatment options (surgery, in most cases including wide resection; radiotherapy; and chemotherapy) is crucial in interpreting follow-up studies.

Reconstructive Surgery

Myocutaneous flaps can serve to cover defects in extended resections.³⁹ Pedicled flaps allow for a preserved neurovascular supply.^{40–42} Soft tissue sarcomas occur particularly frequently in the lower extremity. Patients with extensive tumors or in whom a prior incomplete surgery necessitate re-resection frequently require soft tissue reconstruction with flaps. Implants in particular need adequate coverage by viable muscular tissue. In the proximal thigh area, the most commonly used muscles for myocutaneous flaps are gluteals, tensor fasciae latae, biceps femoris, rectus femoris, and vertical rectus abdominis flap in the hip area. In the distal thigh, vastus lateralis and gracilis muscle are also used.⁴⁰

Around the knee, the medial or lateral gastrocnemius is often pivoted, and in the case of large defects it may be combined with displacement of the soleus muscle. In areas with high mechanical loads (e.g., the sole of the foot), defect coverage with a well-vascularized neurofasciocutaneous flap such as the sural flap may be indicated.⁴²

For extensive defect coverage or with limited local vascular supply, free flaps can be transplanted, whose vascular supply is reanastomosed. The rectus abdominis or latissimus dorsi muscle is mostly used for this purpose.⁴⁰ The surgical outcome has improved with the use of flaps.⁴³

Radiotherapy

In addition to the wide resection (with the aim of limb salvage), highly malignant sarcomas usually undergo adjuvant irradiation. For certain indications, neoadjuvant radiation is performed. The advantages and disadvantages due to the therapy sequence are further described in the section on imaging findings. The interval between surgery and radiation is currently under debate; it is usually 4 to 6 weeks.^{44–48}

Low-grade sarcomas are typically irradiated if the safety distance of the resection is < 1 cm or marginal and no subsequent resection is planned.^{49,50} In principle, choice of the chronological order of surgery and radiation has largely no influence on the local tumor control, metastasis rate, or overall survival as a result of the disease (except in the case of tumors that would have been difficult to resect anatomically or are primarily unresectable); in most cases, radiation is given postoperatively (adjuvant).^{45,48,51}

Preoperative radiotherapy (RT) has some advantages. A lower dose (50 Gy) can be given compared with postoperative RT, and also the planning of the RT is easier. Two targets have to be defined: the gross tumor volume, as seen on imaging, and the clinical target volume including potential

microscopic disease, usually an additional 2 to 5 cm. Insertion of metalwork also causes problems with postoperative RT. As alluded to earlier, preoperative radiation can make inoperable tumors operable.^{52–54}

However, wound complications are more likely with preoperative RT, with an odds ratio of 2.9 compared with postoperative radiation.⁵⁵ In postoperative radiation, target volumes are significantly larger because they include the entire surgical area. Due to the altered anatomy, the definition of the irradiation target volumes is more difficult. With individual doses of 60 to 66 Gy in the tumor bed and 50 Gy in the operative area, higher radiation doses are used (depending on the location of the tumor bed and the resection margins). In definitive RT of inoperable patients, radiation doses should be increased locally to > 60 Gy whenever possible to achieve better local control.⁵⁶

Chemotherapy

Chemotherapy is not part of the routine treatment of soft tissue sarcomas. It is a preferred option for patients with metastatic disease. If used in LR, it should be combined with radical re-resection, if possible. However, the ability of additional neoadjuvant or adjuvant chemotherapy (usually with ifosfamide and doxorubicin) in reducing the LR rate, rate of metastases, and recurrence-free survival or overall survival^{57,58} is not fully clear. Presumably, patients with large grade 3 limb sarcomas in particular benefit from chemotherapy.⁵⁹

Imaging Strategies for Follow-up

Currently, no evidence-based consensus exists about how regular follow-up imaging influences the outcome of sarcoma patients. Studies have shown that the survival rate of high-risk patients with soft tissue sarcomas can be improved by regular local imaging follow-ups.⁶⁰ LRs of extremity soft tissue sarcomas may already be clinically noticeable due to a palpable lump or pain.⁶¹ However, in several studies, magnetic resonance imaging (MRI) was superior in detecting LR compared with clinical examination⁶² even in extremity sarcoma recurrences.⁶³ Detection of > 50% clinically inapparent nonpelvic LR by MRI was reported.⁶⁴

An exact knowledge of the resection margins is important, and the detection of clinically inapparent high-grade sarcoma LR can be further improved by including a dynamic contrast-enhanced (DCE) sequence.⁶⁵ Moreover, physical examination in terms of tactile findings can be of limited value when post-therapeutic changes are present or in deeper structures. Individual authors advise limiting imaging follow-up to cases that are difficult to evaluate clinically or high-risk patients.^{61,66}

It is useful to bear in mind that the risk of soft tissue sarcoma patients for LR decreases after the first few years.^{67–69} Current guidelines, such as those published by the European Society of Musculoskeletal Radiology (ESSR), recommend regular routine checks with local imaging and chest computed tomography (CT) up to 10 years after the first treatment. Because high-grade soft tissue sarcomas tend to reoccur earlier than intermediate- or low-grade sarcomas (11.2 versus 36.6 and 35.2 months,

Table 1 Examples of follow-up intervals after soft tissue sarcoma

Clinical examination, locoregional MRI, and chest CT scan (no contrast agent)	
Year after first treatment	Follow-up interval
1–3	Grading dependent every 3–4 mo
3–5	Every 6 mo
> 5, up to 10	Annually

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

respectively),⁶⁴ the recommended examination intervals depend on the histologic degree of the sarcoma but also on the site of the primary tumor (extremity/superficial trunk, head/neck, or retroperitoneal/abdominal) and the period since primary therapy.^{70–73} (→ Table 1).⁷²

Depending on the entity, further investigation modalities may be indicated.⁷⁴ Also, depending on the entity, adjusting the time intervals and the overall surveillance period may be needed.⁷⁵ Well-differentiated liposarcomas and myxoid liposarcoma were associated with late LR as long as 15 years from diagnosis.⁷⁶ Nomograms may help in the future to further refine surveillance protocols.

MRI with contrast is currently the gold standard for local follow-up scans. High sensitivities ~ 90% and 100%, and specificities ~ 97% were reported.^{77,78} In easily accessible regions, a follow-up inspection can alternatively be performed with sufficient expertise using ultrasound to exclude a mass.^{79,80}

Fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT imaging was shown to be helpful in assessing possible LR. It has a higher sensitivity and specificity of 100% and 95.6%, respectively, in comparison with 97.2% and 63.5%, respectively, for CT imaging.⁸¹ However, various benign processes such as infectious diseases and postsurgical and post-RT states as well as the use of granulocyte colony-stimulating factors can lead to false-positive results.⁸² According to a study, PET/CT is comparable in sensitivity (95% PET/CT versus 90% MRI) and specificity (95.5% versus 97.7%) in the detection of recurrence and therefore may act as an adjunct to MRI findings.⁷⁷ It may be justified in regions such as the retroperitoneum or in the ear, nose, and throat area if the initial tumor was PET avid,^{70,83} simultaneously offering the advantage of showing distant metastases.

For myxoid liposarcoma, for which PET/CT has a high false-negative rate in detecting LR,⁷⁰ follow-up with whole-body MRI was advocated.⁸⁴ In PET-avid soft tissue sarcomas, PET/MR is promising in detecting LR when compared with MRI alone.⁸⁵ However, PET/MR is only available at a few sites.

MRI Technique

To fully visualize the surgical site, the edges of the postoperative scar should be marked with glued cutaneous markers.⁸⁶ The field of view should be large enough to include all adjacent post-therapeutic signal alterations, and the site should be evaluable in all three dimensions.

The sequence listing should contain a fluid-sensitive sequence and a T1-weighted sequence in the long axis as well as a fluid-sensitive, fat-suppressed sequence in the short axis.⁸⁷ A T2-weighted sequence without fat saturation can offer additional morphological information, especially if it shows hypointense areas, suggesting fibrosis, calcifications (together with projection radiographs), or substance deposits.⁸⁸ The application of a contrast agent is recommended unless clinical or imaging circumstances dictate otherwise.⁸⁷ The postcontrast sequences should include an axial fat-saturated sequence. The use of one T1-weighted Dixon sequence allows for postprocessing with reconstruction of in-phase and out-phase, water-only, and fat-only images, so the number of sequences can be reduced (precontrast, the fat content can additionally be assessed); T2-weighted or proton-density Dixon are also possible. However, motion and breathing artifacts are increased.⁸⁹ Subtraction imaging can increase lesion conspicuity. A dynamic contrast sequence and diffusion are desirable. In special cases, a hemosiderin-sensitive sequence can be added. We generally recommend a protocol as described in the ESSR guidelines.^{72,78,90}

Radiomics MR analysis is promising in better differentiating LR from post-therapeutic alterations in the future.⁹¹ With metallic implants or foreign bodies, a lower field strength magnet (e.g., 1.5 T) and metal artifact reduction sequences are adapted. In the case of significant metal artifacts, expected or otherwise, the implementation of an ultrasound or a PET/CT should be considered alternatively.

Before Starting the Report

Precondition for diagnosis is a precise knowledge of the patient's medical history and clinical examination. It should include these items:

- Knowledge about the initial diagnosis of tumor entity, histologic tumor grade, localization (deep/superficial, as well as the body section), and the size of the tumor. This includes availability of all pre- and post-therapeutic scans (including the first postoperative imaging as an important baseline exam)²⁸ to know the exact location, extent, and morphology of the original tumor because the recurrent tumor is often similar to that of the primary tumor.⁸⁶
- Knowledge of previous therapies (including the resection margins) to be able to classify post-therapeutic changes.
- Knowledge of the current clinical presentation if possible. The physician should carry out a short inspection and palpation of the local site to look for radiation dermatitis, subcutaneous fibrosis, or ulceration and describe the extent of the palpable tumor and reconstruction site,⁹² if possible.

Post-therapeutic Changes

Regular Post-therapeutic Soft Tissue Changes

These changes include edema, inflammatory tissue reaction, granulation tissue, fibrosis, and scars. Postsurgery, immediate diffuse edema is normal, as well as a subsequent diffuse edema-like pattern by granulation tissue (described in more detail in the article by Bloem et al in this issue). Following radiation therapy, increase and longer persistence of those changes is also normal.^{26,93,94}

The initially very variable edema-like signal increases over time with a peak ~ 12 to 18 months after irradiation with photons and ~ 6 months after neutron irradiation. Normalization is less frequent and occurs later after neutrons compared with protons.^{26,93,95}

In the subcutaneous tissue, the collagenous septations typically lead to lattice-like fluid-equivalent signal change, whereas the changes in the muscles (which are observed in ~ 80% of patients after surgery with additional radiation) are more diffuse. The tissue architecture is naturally preserved and the contrast uptake is very low,^{26,96} which is helpful in the differentiation from recurrence. If the tissue is diffusely edematous, but the architecture of the muscles is preserved with muscle pennation visible on all sides on T1-weighted sequences ("texture" or "feathering sign"), tumor recurrence is rather unlikely^{26,96,97} (►Fig. 1). The changes in the intermuscular septa persist significantly longer than in the muscle or adipose tissue. It is important to keep in mind that the thickness of the intermuscular septa and adipose tissue can increase over time⁹³ also without recurrence.

Postinflammatory tissue or fibrosis after surgery can be bulky, and the presence of nodular enhancement neither predicts nor excludes microscopic residual tumor.¹⁶ As opposed to recurrence, post-therapeutic tissue almost never shows arterial enhancement on the DCE sequence (specificity of 97% for recurrence).⁷⁸ A visual impression of the clinical severity of cutaneous changes such as the presence of cellulitis or ulceration can be helpful in the image assessment of deeper changes.

Muscular flap plastic surgery also initially shows an edema-like signal (►Fig. 2) that normalizes in about a third of the patients within 2 years. In ~ 75% of the patients, there is an initial contrast enhancement of the flap that is no longer detectable in about a third of the patients after 1.5 years.³⁹ For development of atrophy, see the article by Bloem et al.⁹⁵

In the final state, the post-therapeutic scar tissue is ideally hypointense on all sequences.^{89,98} As a rule of thumb, the size and complexity of the entire postoperative scar tissue correlate with the size of the resected tissue and the entire surgical field.⁹⁴ On T2-weighted sequence, if only hypointense tissue is found, recurrence can be excluded in 99% of the cases.⁹⁶ The irradiated bone also shows MR signal alterations, in particular after additional chemotherapy and mostly focal in various patterns and with subsequent dose and location-dependent fatty marrow conversion,^{99–102} as described in more detail by Bloem et al.⁹⁵

Occurrence and Imaging of Complications

Local complications must be distinguished from these regular post-therapeutic changes. In addition to defined postoperative seromas and hemorrhages, these also include post-therapeutic infections, tissue necrosis, and failure of flap reconstructions. The risk of postoperative local complications increases with additional radiation.^{26,96,103}

Acute wound healing disorders such as wound dehiscences, seromas, or infections occur more frequently with neoadjuvant radiation (34–35%) than with adjuvant radiation (16–17%).^{52,54} They can also be observed increasingly in patients with diabetes,

Fig. 1 Post-therapeutic changes and T1-weighted “texture” or “feathering sign” in a 74-year-old male patient, 12 years after myxofibrosarcoma of the lower leg (initial intralesional resection at another institution; revision and radiation therapy; recurrence after 9 years with isolated limb perfusion and subsequent wide resection, partial resection of the gastrocnemius and soleus, and soleus muscle flap). (a) In the follow-up magnetic resonance imaging 2 years later, the coronal T1-weighted sequence shows the typical texture or feathering sign of fatty muscular atrophy (arrow). In the (b) axial proton-density fat-saturated (FS), (c) T2-weighted, and (d) T1-weighted FS postgadolinium sequences, minor edema and enhancement in the operative site, including the remnants of gastrocnemius and soleus muscle, is also depicted (open arrows).

large tumors (different limit values of 5 or 10 cm are described in the literature), surgeries requiring vascular pedicle flaps, and split-thickness skin coverage.^{54,104}

However, patients who received postoperative radiation with large target volumes are more likely to experience late complications than patients with neoadjuvant radiation. These include edema (23.2% in postoperative versus 15.1% in neoadjuvant radiation), fibrosis (48.2% versus 31.5%), and joint stiffness in cases where the joint was irradiated (23.2% versus 17.8%).⁴⁷ This applies particularly to patients with postoperative wound complications, with tumors in the groin or on the thigh, and with radiation doses > 60 Gy.⁵⁴

Seroma

Characteristically, frequently occurring postoperative seromas demonstrate a smooth lining, with homogeneous fluid intensity contents (► Fig. 2). However, they appear lighter on T1-weighted sequences when protein is abundant. Seromas

can be inhomogeneous when debris is included and rarely have fluid levels. The serum content typically does not show contrast enhancement.^{26,105}

Seromas are usually surrounded by a mostly thin pseudocapsule that takes up moderate and late contrast enhancement.¹⁰⁵ Seromas with small nodular areas (► Figs. 3 and 4), which are often relatively hypointense, may mimic organized hematomas. LRs within seromas are rare.¹⁰⁶ Most seromas regress within 3 to 18 months.^{26,94}

Hematoma

Recurrence exclusion can be more difficult if there is a postoperative hematoma (► Fig. 5). The contained hemosiderin can be detected more sensitively by means of gradient echo sequences due to its paramagnetic effect (“blooming”). In general, however, hematomas appear inhomogeneous due to different blood products. If you give contrast agent (KM) and then examine T1-weighted subtraction images (postcontrast agent minus

Fig. 2 Post-therapeutic changes and “texture” or “feathering sign” in a 64-year-old male patient with initial unintended intralesional resection of myxofibrosarcoma (“whoops”) at an outside institution. In-house radiation therapy and revision with wide resection and osteoligamentous allograft (arrow), wound healing disorder with debridement, cutaneous flap and partial soleus flap, and split-thickness skin graft. Magnetic resonance imaging 3 months later. (a) Coronal T1-weighted sequence, (b) axial proton-density fat-saturated (FS), (c) T2-weighted, and (d) T1-weighted FS postgadolinium images show extensive edema-like signal of the flap. The feathering sign is best depicted in sequences with high contrast between fluid and muscle (open arrows). The adjacent tissue shows diffuse inflammatory changes and muscle atrophy.

precontrast), misinterpretation of hyperintense blood products as contrast enhancement can be avoided. However, hematomas can also take up small amounts of contrast due to organizational processes, and their appearance can change during hematoma organization (→ Fig. 2e–i). Organized hematomas can liquify.¹⁰⁷

According to a study, the diffusing capacity in hematomas is significantly higher than in soft tissue sarcoma relapses or pseudotumors.⁷⁸ The so-called chronic expanding hematoma is a particular problem. It appears inhomogeneous (due to a mixture of different blood products, granulation tissue with injecting capillaries, inflammatory tissue, necrotic debris, and fibrin¹⁰⁸) and usually has a pseudocapsule (made of fibrin, hemosiderin deposits, and macrophages).¹⁰⁷ The diffusion-weighted sequence can again be helpful because the apparent diffusion coefficient (ADC) is also significantly higher in chronic expanding hematomas than in soft tissue sarcoma tissue.¹⁰⁹

The chronic expanding hematoma grows slowly, presumably due to an irritation of the blood products that repeatedly leads to capillary injuries and new bleeding.¹¹⁰ It can therefore have nodular contrast-enhancing parts. But recurrences can also bleed slowly, and therefore a reliable exclusion of recurrence may only be possible through a biopsy.¹⁰⁷

Infection/Abscess

Infections after resection of musculoskeletal tumors occur in ~ 12.2% of patients with malignant tumors (→ Fig. 6) and only in ~ 0.32% with benign tumors. The likelihood increases with a long duration of surgery, greater blood loss, preoperative chemotherapy (the effects of radiation have not been investigated), and after implants. Three to four of these risk factors increase the likelihood of developing an infection to 38.5%.¹¹¹

Fig. 3 Seroma with small dark pseudotumor. Magnetic resonance imaging of the left thigh 1 year after resection of an spindle cell sarcoma in a 68-year-old female patient. (a) Axial proton-density, (b) T2-weighted, as well as (c) dynamic contrast-enhanced (DCE) and (d) axial and (e) coronal T1-weighted fat-saturated postgadolinium images show a small persisting nonenhancing nodule (arrows) within a small postoperative seroma (small arrow points at curve in DCE). The fibrotic capsule of the retention still enhances, and there are minor adjacent postoperative muscle changes.

The tissue (e.g., muscle flaps) can be destroyed by infection spread or become necrotic due to increased metabolism.¹⁰³ The MR morphology of soft tissue abscesses after tumor resection generally corresponds to that of abscesses of another cause, with circumscribed fluid retention, hypo or intermediate intense signal on T1-weighted sequence, hyperintense signal on T2-weighted sequence without central enhancement, with a hypointense, thick, irregular, enhancing marginal border.^{112,113}

However, the differential diagnosis compared with seromas is difficult due to the already existing post-therapeutic diffuse changes. Individual studies report at least initially restricted diffusion in the abscess compared with seromas.¹¹⁴ It is important to know the clinical condition of the patient and their laboratory values. A precise knowledge of the irradiated field helps differentiate it from postradiation noninfectious changes.¹¹⁵

Inflammatory Pseudotumor, Hypertrophic Scar, Neuroma, and Nerve Swelling

So-called inflammatory pseudotumors have also been described after radiation with a prevalence between 5% and 12.5% and after radiation doses of ~ 55 Gy^{95,116} (**Fig. 7**). These pseudotumors can occur at variable time intervals after the start of therapy, in one study after 38 months on average, with isolated cases between 1 and 12 years after

resection and radiation.¹¹⁶ They are described as oval lesions that are signal rich on fluid-sensitive sequences and less signal rich on T1-weighted sequences compared with the muscles. These are often confined and not very bulky. The contrast uptake is clearly heterogeneous, but in contrast to tumor recurrences it is delayed in dynamic sequences. The contrast enhancement takes place only 3 to 9 minutes after administration of contrast, compared with recurrences that typically show early contrast enhancement after 1 to 2 minutes.^{90,96,116} Histologically, they should correspond to vascular ectasia and fibrosis.¹¹⁶

Hypertrophic scar tissue (**Fig. 8**) presents as a postoperative growing palpable lump. Histologically, there is increased cellularity, enlarged arterioles and capillaries, excessive collagen, inflammatory changes, and bleeding. In individual cases, T2-weighted images can therefore also be hyperintense in some cases.¹¹⁷

Both tumor recurrence and fibrosis can lead to nerve compression with denervation edema and fatty muscle atrophy (**Fig. 9**).²⁶ After nerve reconstruction with a graft, for example with an autologous sural nerve interposition, a neurologic deficit often remains. Even with a very good clinical result, local changes (e.g., small neuromas) may be visible (**Fig. 3**)^{118,119} and should not be confused with nodular recurrence.

A very rare postamputation finding is sciatic nerve swelling proximal to the surgical stump (**Fig. 10**). The pathomechanism is still unclear. It has been attributed to

Fig. 4 Seroma with small enhancing pseudotumor. Magnetic resonance imaging (MRI) of the right distal thigh of a 79-year-old patient after initial unintended intralesional resection of leiomyosarcoma (“whoops”) at an outside institution, revision, and radiation therapy. In the follow-up MRI, the (a) coronal short tau inversion recovery, (b) axial T2-weighted, (c) coronal, and (d) axial postcontrast T1-weighted fat-saturated sequences demonstrate a large postoperative seroma (arrow). In the proximal part of the retention, adjacent to the capsule, are small partly nodular solid intralesional components with minor contrast enhancement (open arrows), representing a pseudotumor. Histology revealed necrosis and granulation tissue.

hyperplasia of the neuronal fascicles (and was initially termed “paradoxical diffuse hypertrophy”) with fiber disorganization and perineural fibrous tissue. Clear discrimination from neuroma is not possible so far. The swelling may also be related to hindrance of axonal transport. It is most pronounced distally. Continuity with the sciatic nerve proximally is a key finding in differentiation from tumor recurrence at the surgical stump. In contrast to typical stump neuroma or recurrence, the usually painless thickening is diffuse and without contrast enhancement.¹²⁰

Bone complications after radiation and chemotherapy, such as osteoporosis and insufficiency fractures or osteonec-

rosis, are covered elsewhere.¹²¹ We also refer to the article by Bloem et al.⁹⁵

Appearance of Local Recurrences and Radiation-associated Sarcomas

Local Recurrences

LRs typically appear as masses or nodular soft tissue changes (►Fig. 4) and are usually hyperintense on fluid-sensitive sequences.⁹⁶ However, LR of low-grade myxofibrosarcoma and of undifferentiated pleomorphic sarcoma may appear plaque-like or show tail-like infiltration.^{122,123}

Fig. 5 Postoperative hematoma. Magnetic resonance imaging of the left thigh 1 month after resection of an undifferentiated pleomorphic sarcoma G3, in a 68-year-old male anticoagulated patient (after pulmonary embolism). Continuous bleeding from a small wound dehiscence. (a) Coronal short tau inversion recovery, (b) axial T2-weighted images, and (c) apparent diffusion coefficient map show a large hematoma with hemorrhagic elements of different ages (white arrows) and sedimentation phenomena (small white arrows). (d) Coronal T1-weighted hyperintense components can be depicted (white open arrow). In the postcontrast sequence (e) without and (f) with fat saturation, there is only minor intralesional enhancement due to minor organization but an enhancing capsule and adjacent postoperative muscle changes (dashed white arrow).

A new lesion compared with the baseline post-therapeutic examination and slowly enlarging tissue alterations are highly suspicious¹²⁴ (► **Figs. 11** and **12**). The recurrence is often similar to the primary tumor¹²⁵; for example, a myxoid tumor on liquid-sensitive sequences can look almost like a seroma (► **Figs. 5** and **6**). The morphology of the current lesion should therefore be correlated with that of the original tumor.^{86,126}

Circumscribed hyperintense lesions should be further clarified with T1-weighted sequences and gadolinium administration,¹²⁷ preferably with the inclusion of subtraction images (► **Fig. 13**). The contrast-enhanced sequences prove the presence of solid tissue. The detection of arterial flooding in the tumor on the dynamic contrast sequence is particularly specific and excludes 97% of postoperative inflammatory altered or fibrotic tissue.^{78,90} Of note, myxoid

liposarcoma may almost lack contrast enhancement and FDG-PET avidity (► **Fig. 14**), so small recurrences may be overlooked.

As another pitfall, granulation tissue can also initially show an early contrast uptake, but after 2 to 6 months only a slow contrast uptake should then be detectable.¹²⁸ A post-therapeutic baseline examination after 6 to 8 weeks therefore seems sensible, so immediate florid post-therapeutic changes can somewhat subside.⁷⁰

The ADC is known to depend heavily on the tissue composition. Moreover, absolute values are highly machine dependent. The evaluation of the ADC in sarcoma follow-up MRI is therefore complex. Cell-rich sarcoma tissue usually shows a low ADC. However, the same is true for fibrosis, and myxoid sarcoma components show high ADCs. But an improvement in the specificity of the recurrence detection

Fig. 6 Infection in a 62-year-old female patient 4 months after neoadjuvant radiotherapy and wide resection of a myxoid liposarcoma. Magnetic resonance imaging of the thigh shows postoperative wound healing disturbance with necrosis that required wound revision. (a) Coronal short tau inversion recovery, (b) axial proton-density fat-saturated (FS), (c) axial T2-weighted imaging, and (d) apparent diffusion coefficient map of diffusion-weighted imaging show the retention and a fistula (arrows) within surrounding inflammation (open arrow in (a)). (e) In the dynamic contrast-enhanced image, the diffuse enhancement of surrounding organizing inflammatory tissue (dashed arrows) is slower and begins later than the arterial curve (dotted arrow). (f) The retention does not enhance, demonstrated in the static T1-weighted FS postgadolinium sequence (small arrow).

from 52% to 97% was described when there was a region with a visually low ADC, even if this sign only occurred in 60% of the recurrences. Interestingly, the diffusion capacity of soft tissue sarcoma recurrences in one study was between that of hematomas and pseudotumors. According to this study, the ADC in pseudotumors with contrast uptake is lower than in tumor recurrence, as well as in the surrounding subcutaneous tissue (the latter presumably due to the pseudo-inflammation around the relapse tissue).⁷⁸ However, other studies plausibly describe a lower diffusion in relapse than in post-therapeutic seromas or edematous changes.¹²⁹

Some tumors show special MR morphology and known high recurrence rates for which knowledge of the original tumor is vital. An example of this is the high-/dedifferentiated liposarcoma that occurs particularly in the retroperitoneum. Complete resection of the biphasic tumor is essential,

that is, also the highly differentiated portion (indistinguishable from normal adipose tissue) that can also dedifferentiate in 15%.^{33,34,130}

In aftercare, any nonlipomatous nodule formation in the retroperitoneum and mesentery is suspicious for recurrence. Relapses of retroperitoneal high-/dedifferentiated liposarcoma tend to invade the colon, diaphragm, pancreas, and small intestine.¹³¹

Radiation-associated Sarcomas

Radiation-associated or postradiation sarcomas as a differential diagnosis are rare (0.03–0.2%)¹³² and found more often in the soft tissues than in the bones (2.3:1).¹³³ They occur after a dose of ~ 50 Gy on average and, according to the literature,^{132,134} typically long after radiation (on average 8–15.5 years) (► **Fig. 15**). Very different intervals are given: between 2 and 65 years. The latency period is somewhat

Fig. 7 Inflammatory pseudotumor in a 47-year-old woman with a history of sarcoma at the anterior aspect of the left calf, resected 3 years earlier and radiotherapy completed 2 years ago. (a) T1-weighted axial, (b) short tau inversion recovery sagittal, and (c) contrast-enhanced T1-weighted fat-saturated axial images. Diffuse edematous changes are seen at the postoperative/postradiation bed. A small nodule, with no discrete margins, projects over the skin (arrow). It is T1 hypointense (a), T2 hyperintense (d), and presents vivid delayed uptake of gadolinium (c). There are also edematous changes at the adjacent tibialis posterior and peroneal muscles (b) and mild atrophy of the gastrocnemius muscle (a). The magnetic resonance imaging study did not include dynamic administration of contrast. The nodule was resected, and histology revealed an inflammatory pseudotumor.

Fig. 9 Perineural fibrosis in a 31-year-old woman with a history of resected liposarcoma of the distal thigh 14 months earlier, followed by radiation therapy. A sagittal short tau inversion recovery image shows hypointense and thickened contour of the sciatic nerve, consistent with perineural fibrosis (arrow). Note the hyperintense "feathery sign" of the adjacent adductor magnus muscle.

Fig. 8 Hypertrophic scar in a 60-year-old woman presented with a palpable mass at the site of a resected undifferentiated sarcoma. The resection had been performed 8 months earlier with adjuvant radiotherapy after 6 weeks. (a) T1-weighted axial image shows a homogeneous, hypointense mass-like lesion with thorny outer contour. (b) On axial T2 fat-saturated (FS) image, the lesion is mainly hypointense with moderately hyperintense transverse streaks. (c) Contrast-enhanced T1 FS image documents mild diffuse enhancement of the abnormal area with no discernible nodules. (d) The diffusion-weighted image/apparent diffusion coefficient map shows no restricted diffusion. The lesion was interpreted as hypertrophic fibrosis. Repeat surgery revealed fibrotic/granulation tissue.

Fig. 10 Sciatic nerve swelling after amputation. Coronal magnetic resonance imaging sequences for liposarcoma in a 57-year-old male patient who underwent above-knee amputation 10 years ago, showing swelling of the distal end of the sciatic nerve (white arrow) on (a) T1-weighted, (b, c) short tau inversion recovery sequences, and the outline of the sciatic nerve (black arrows).

Fig. 11 Recurrence after R1 resection without adjuvant therapy in a 52-year-old female patient presenting with recurrence of an undifferentiated small round cell sarcoma, who had been treated externally with R1 resection without adjuvant therapy. Magnetic resonance imaging of the initial tumor at the dorsolateral aspect of the thigh had shown a sharply demarcated epifascial mass with broad contact to and minor edema-like alteration along the fascia. It was not specifically hypointense on (a) T1 and hyperintense on (b) the short tau inversion recovery (STIR) image. Follow-up 4 months postoperative, the surgical bed was hypointense on (c) T1-weighted and (d) STIR, with minor diffuse postoperative edema but with (e) nodular enhancement after contrast administration. Ten months postoperative, there is extensive local and now extracompartmental recurrence. The signal intensity is similar to the primary on (f) T1-weighted and the (g) STIR, and (h) enhances heterogeneously.

shorter in the soft tissues than in the bones.^{132,134–136} They express themselves as progressively growing masses.^{134,136}

The most common radiation-associated soft tissue sarcomas are undifferentiated pleomorphic sarcomas (or the entire group of the former “malignant fibrous histiocytoma”) constituting ~ 68%, followed by extraosseous osteo-

sarcoma with 13%. They are often poorly differentiated with a corresponding heterogeneous MR appearance^{132,134,136} (►Fig. 7). If new masses occur in the soft tissues or if there is bone destruction in the radiation field, after prolonged latency, differential diagnosis of sarcomas should also be considered.

Fig. 12 Recurrence. Magnetic resonance imaging of the right thigh in a 49-year-old female patient with a high/dedifferentiated liposarcoma, with (a) sagittal short tau inversion recovery (STIR), (b) axial T2-weighted, (c) T1-weighted, and (d) T1-weighted fat-saturated (FS) postgadolinium (dashed arrows). The dedifferentiated parts of the lesion show nonfatty signal and intense contrast enhancement (arrow). The patient underwent resection and adjuvant radiotherapy. Regular follow-ups showed post-therapeutic seroma with a fibrous capsule (small arrow) and severe fatty atrophy of the quadriceps muscle. However, 6 years postsurgery, magnetic resonance imaging also reveals a recurrence that was nonpalpable (open arrows). In the (e) coronal STIR, (f) axial T2-weighted, (g) T1-weighted, and (h) T1-weighted FS postgadolinium images, the new solid nodule demonstrates signal similar to the dedifferentiated primary.

Fig. 13 Recurrence and subtraction in a 33-year-old male patient, 2 years after rhabdomyosarcoma, with isolated limb perfusion and surgery, with resection, osteomyocutaneous reconstruction, and osteosynthesis (a, projection radiography). (b) Positron emission tomography/computed tomography was inconclusive (small arrows). (c) On magnetic resonance imaging, the axial fat-suppressed T1-weighted subtraction postgadolinium shows the enhancing nodular recurrence (open arrow) and metal artifacts (arrowhead). (d) Postprocessing T1 subtraction with elimination of the fat signal helps better evaluate the tissue adjacent to the metallic implants.

Fig. 14 Recurrence of myxoid liposarcoma in a 47-year-old woman. Magnetic resonance imaging follow-up 4 years after resection of a myxoid liposarcoma, adjuvant radiation, and wound revisions. The operation site still shows diffuse chronic inflammatory changes, a small seroma (small arrow), and fibrosis (open arrows) in the (a) proton-density (PD) fat-saturated (FS), (b) T2-weighted, and (c) T1 postcontrast FS images. (d) In the dynamic contrast-enhanced (DCE) image, the enhancement starts as late as the muscle enhancement (dashed arrow; as reference: artery with rapid wash-in, muscle enhancement with least enhancement). However, in the gluteal muscles, there is a nonpalpable recurrence (formerly soft tissue metastasis, arrow) with the typical hyperintense signal of a myxoid matrix in the (e) PD FS and (f) T2-weighted images, and no diffusion restriction in (g) the apparent diffusion coefficient map. (h) The lesion shows contrast enhancement in the T1-weighted FS sequence that starts later than the external iliac artery in the DCE sequence (d) (dotted arrow), but the wash-in curve is steep. (i) In corresponding fused fluorodeoxyglucose-positron emission tomography/computed tomography, the myxoid liposarcoma (arrowheads) is typically photopenic. The patient moved a lot, leading to diffuse PET avidity of muscle groups such as the gluteals.

Fig. 15 Radiation-associated soft tissue sarcoma in a 71-year-old woman. Presumably radiation-associated soft tissue sarcoma (spindle cell sarcoma with highly malignant osteosarcoma component) after vulvar cancer > 10 years ago treated with primary radiochemotherapy. (a) Projection radiography shows a large tumor with extensive calcification. Magnetic resonance imaging (MRI) of the hip and pelvis (for surgical planning) reveals local tumor extent and shows reportedly long-standing extensive lymphedema. (b) Coronal short tau inversion recovery, (c) axial T2-weighted, and (d) postcontrast fat-saturated T1-weighted images with infiltration of the pubic bone (dashed arrows) and the ischiac nerve (small arrow). The patient underwent wide resection with left-sided hemipelvectomy with gluteal flap reconstruction. One year later, magnetic resonance imaging with (e) sagittal and (f) axial T2-weighted, (g) axial diffusion-weighted, and (h) axial postgadolinium T1-weighted fat-suppressed images reveals extensive postoperative changes with postoperative seroma and fatty atrophy of the flap. A small nonspecific hypointensity (small arrow) is seen on all sequences. (i) In the corresponding fluorodeoxyglucose-positron emission tomography/computed tomography, the small lesion was mineralized and highly PET avid. Histology proved recurrence.

Conclusion

As a rule of thumb in the recurrence detection of soft tissue tumors, the following can apply: If you first consider a T2-weighted sequence with frequency-selective fat saturation, a short tau inversion recovery sequence, or the water image of a Dixon sequence, you can exclude recurrence in 99% of the cases in these situations:

- No hyperintensity is visible (such as with fibrosis in scar tissue); caution is advised for lesions such as the desmoid or the tenosynovial giant cell tumor that demonstrated hypointensity in the primary tumor;
- There is only an “edema-like” diffuse hyperintensity without a circumscribed lesion, as with post-therapeutic changes or inflammation;
- The “texture” or “feathering” pattern of muscles is visible without any other architectural disturbance, and the picture remains completely unchanged from the preliminary examination.

Conflict of interest
None declared.

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Erratum: This article has been corrected in accordance with the Erratum published on January 7, 2021. Figures 1a-b and 2a-b have been corrected.