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Pictorial review

Follow-up of musculoskeletal tumors

I. Local recurrence

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Abstract. The prognosis for a patient with a musculoskeletal sarcoma has improved considerably over the past two decades largely due to the use of adjuvant chemotherapy. Surgical techniques have become more sophisticated with limb salvage, the preferred management in the majority of cases. Imaging plays an important role in the assessment of suspected local recurrence of tumor. This pictorial essay reviews the different imaging options and highlights various pitfalls in the detection and diagnosis of recurrence. The role of magnetic resonance imaging in this respect is stressed.

Key words: Recurrent sarcoma – MRI

Introduction

The past two decades have seen considerable improvements in the management and prognosis of patients with musculoskeletal tumors. The previously gloomy outlook for most patients with musculoskeletal malignancies, namely amputation followed by the rapid development of metastases and ultimately death, is no longer inevitable. There are now many long-term survivors who have undergone limb-conserving surgery and are able to maintain a good quality of life. The surgery is only one phase in the management of the patient with a musculoskeletal sarcoma. Assuming that the patient does not have stage-III disease (i.e., metastases) [1] either at presentation or developing during preoperative chemotherapy, they are closely monitored for evidence of local recurrence, metastatic disease, and complications of treatment. The purpose of this pictorial essay is to review the experience from two orthopedic oncology centers in the imaging management of the patient with a suspected local recurrence of their tumor. A further pictorial essay will review the imaging assessment in metastatic musculoskeletal sarcoma.

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Recurrence of benign bone tumors

For the majority of benign bone tumors curettage is the most widely accepted therapy. In the locally aggressive tumors, such as giant cell tumor, chemical or thermal cautery of the cavity walls has its advocates. Depending on the size and site of the tumor the surgical defect may be left to consolidate spontaneously or alternatively be packed with either bone graft or bone cement. Total excision may be appropriate if a small bone is involved. Local recurrence in simple bone cyst and aneurysmal bone cyst is unusual. It is a relatively common occurrence in giant cell tumor with a quoted incidence following curettage of 20–50% [2]. The clue to the recurrence is the identification of increasing lysis of the surrounding bone and/or bone graft on comparison of serial radiographs (Fig. 1) [3]. A soft tissue mass is usually a late feature unless there was initial packing of the surgical defect with bone cement. In this situation, because of the durability of the cement, the recurrent tumor takes the line of least resistance and spreads early into the soft tissues. Magnetic resonance imaging of curetted bone lesions can give a confusing appearance with variable amounts of fibrous scar, granulation tissue, and cystic areas occupying the bony defect. Recurrence, within bone can be difficult to identify in the absence of a mass lesion. Fortunately, the time/signal intensity enhancement curve for giant cell tumor is usually sufficiently rapid for a dynamic sequence to distinguish recurrence from scar [4]. Most giant cell tumor recurrences occur within 2 years of initial surgery but may be seen as late as 7 years [2]. If a recurrence is behaving in a particularly aggressive manner, rare secondary malignant change of a giant cell tumor to an osteosarcoma should be considered [5]. The initial histology should also be reviewed to ensure that the original pathological diagnosis was correct.

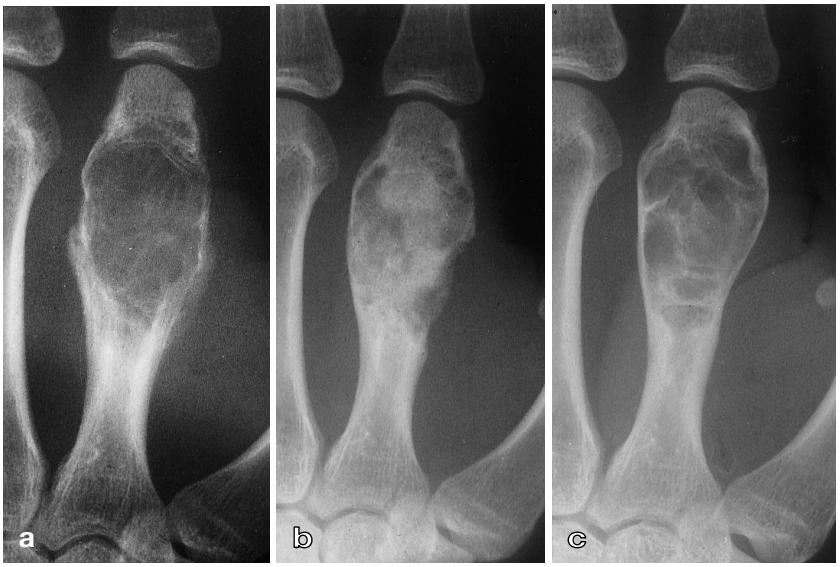


Fig. 1. Giant cell tumor of the distal metaphysis of the second metacarpal **a** at presentation, **b** 4 months postoperative showing satisfactory incorporation of bone graft and **c** 15 months postoperative showing lysis of the graft due to recurrent tumor

Chondroblastoma may also recur in approximately 15% of cases [6] possibly because the surgeons are keen to preserve as much of the epiphysis in order to minimize growth disturbance. Preliminary work with MR imaging has shown that marrow edema, a frequent and non-specific finding in many neoplastic and non-neoplastic conditions [7], can be a useful indicator of the presence of recurrent chondroblastoma [8, 9].

Recurrence of musculoskeletal sarcomas

Incidence

The risks of local recurrence will vary from patient to patient depending on the initial management and the histological type of the primary tumor. Prior to the introduction chemotherapy all attempts to locally resect the commonest bone sarcoma, osteosarcoma, resulted in unacceptably high rates of local recurrence. With chemotherapy limb-salvage surgery has been shown not to adversely affect the eventual outcome when compared with early amputation [10, 11]. The local recurrence rate for osteosarcoma treated with chemotherapy and surgery ranges from 4.5 to 11% [10–12] increasing to 19% if the patient sustained a pathological fracture [13]. For Ewing's sarcoma the rate can be as high as 36% if the primary treatment is radiotherapy with or without chemotherapy, but this reduces to between 4 and 17% if treatment also includes surgical excision [14–16]. Pelvic Ewing's sarcoma is associated with a considerably higher local recurrence rate because of the large size at presentation and the difficulties of achieving tumor-free surgical margins [17]. The local failure rate for sarcomas where the initial surgical margins were inadequate range from 67% for chondrosarcoma [18] to in excess of 90% with a high-grade soft tissue sarcoma [19].

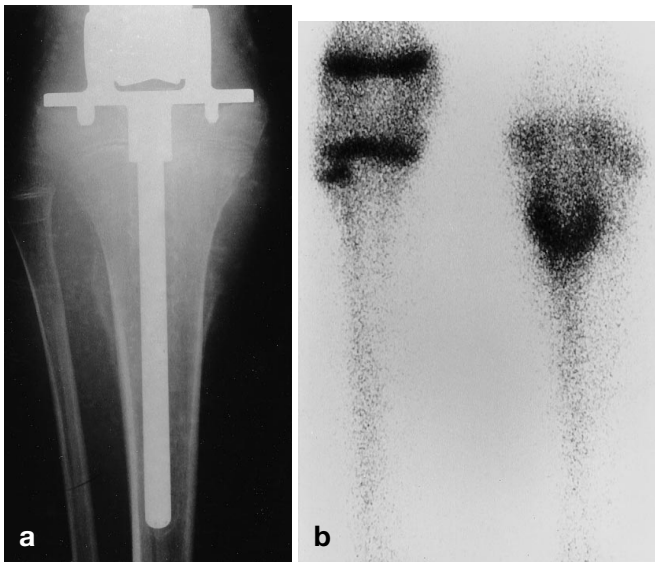
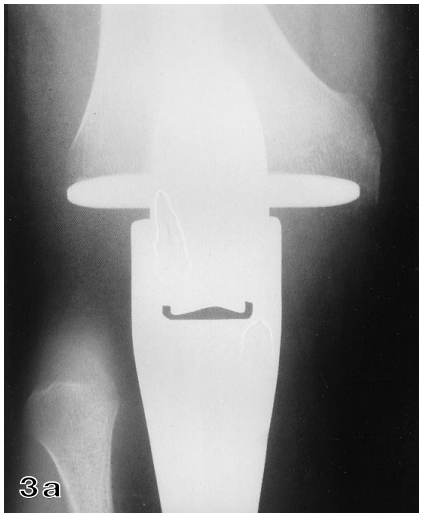
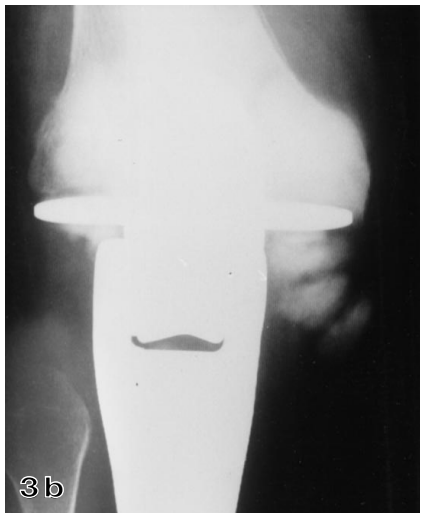


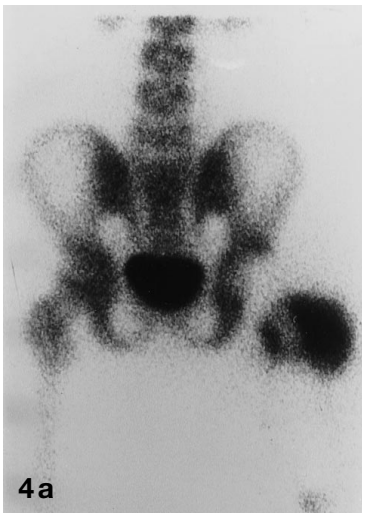
Fig. 2 a, b. A 22-year-old male 18 months following distal femoral endoprosthetic replacement for an osteosarcoma. **a** Anteroposterior radiograph showing lysis and periosteal newbone formation indicating local recurrence in the proximal tibia. **b** Three-hour posterior bone scintigraphy showing increased activity at the site of the recurrence

Site

Local recurrence of a sarcoma may occur at any site within the initial surgical field. Following an intralesional or marginal excision this usually corresponds with the site of the original tumor. Wide or radical excisions by definition involve more extensive surgery and as a result local recurrence may arise relatively remote from the primary site. Because the affected bone is excised most bone sarcoma recurrences also occur in the soft tissues. The exceptions are those cases where the bone sarcoma recurs within the bone at the junction with a prosthesis (Fig. 2). Recurrence in an amputation stump can also







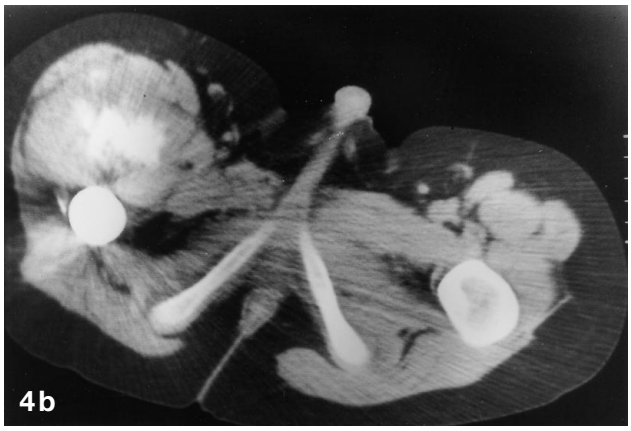


Fig. 3a, b. A 16-year-old male with endoprosthetic replacement of the proximal tibia for an osteosarcoma. **a** Postoperative anteroposterior radiograph showing normal appearances. **b** Anteroposterior radiograph 1 year later showing local recurrence indicated by the mineralization in the soft tissues and increased sclerosis in the remnant of the medial distal femoral metaphysis

Fig. 4. A 14-year-old male with a soft tissue recurrence of an osteosarcoma anterior to a proximal femoral endoprosthesis. **a** Three-hour posterior scintigraphy showing increased activity in the recurrence and photopenia from the prosthesis. **b** CT of the proximal femora showing a large, partly mineralized soft tissue recurrence lying anteriorly in the right upper thigh. Only minor beam hardening artifact from the titanium prosthesis

be considered local as this represents the nearest remaining tissue, albeit usually remote from the primary tumor.

Imaging

Radiographs

The majority of soft tissue tumors, including local recurrence, are of water density similar to that of muscle and are, therefore, only revealed by virtue of mass effect. This includes displacement or disruption of the adjacent fat planes, distortion of the skin contour, and involvement of bone. Obliteration of the fat planes is normal after the trauma of surgery such that only sizeable local recurrences are likely to be identified unless there is evidence of matrix mineralization or bone changes. Baseline radiographs should be obtained after insertion of a prosthesis. Occasionally, bone cement may become "displaced" and it is one of the few materials which can show an amorphous density on radiographs mimicking malignant bone formation (Fig. 3).

Scintigraphy

Recurrent tumors with the propensity to mineralize will typically exhibit increased activity on bone scintigraphy, but it is rarely used for this purpose (Fig. 4a). The low specificity of bone scintigraphy can also be a problem when trying to differentiate local recurrence in bone from infection or aseptic loosening associated with a prosthesis (Fig. 2b). Scintigraphy will reveal evidence of bone stress in a remarkably high percentage of patients who have undergone surgery for osteosarcoma which should not be mistaken for bone metastases [20]. Bone scintigraphy is indicated as part of re-staging when local recurrence of a bone sarcoma, but not a soft tissue sarcoma, is proven.

Computed tomography

The spatial resolution of CT, of the order of 1–2 mm, allows for masses as small as 1–2 cm to be detected, depending on differential attenuation between tumor and the surrounding soft tissues. Viewing of the images on narrow window settings will be required if density differences are small. This can be a problem if the recurrence is deep within muscle where tumor tissue can exhibit an attenuation similar to that of the muscle. Intra-

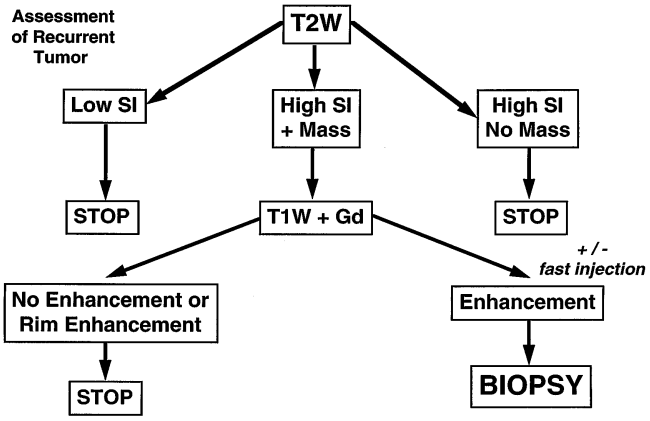


Fig. 5. Algorithm for the management of a suspected recurrent musculoskeletal sarcoma

venous contrast medium will help to accentuate tumor conspicuity. Local recurrence is easily demonstrated if it mineralizes (Fig. 4 b) or arises within the subcutaneous scar. Changes to adjacent bones can also be readily detected. Although MR imaging is now the technique of choice in the investigation of a suspected recurrence, CT is of comparable accuracy if the tumor volume is greater than 15 cc [21]. Computed tomography is unable to differentiate residual tumor from hematoma and granulation tissue following excisional biopsy [22]. As the prostheses used are principally manufactured from titanium, metal artifact is not a major problem except around the joint replacements. Routine re-staging of a patient with chest CT is required when local recurrence of a sarcoma is proven.

Ultrasound

Ultrasound is a low-cost, easily obtained examination that can readily differentiate solid from cystic musculoskeletal masses. Choi and co-workers, when comparing US and MR imaging, concluded that US could be equally useful in the detection of soft tissue local recurrences, routine follow-up and in guiding needle biopsies, but can be difficult to interpret in the early postoperative period [23]. Although US does have some attractions, MR imaging should be used if US is inconclusive and will be required for pre-operative evaluation if a recurrence is identified. For these reasons the authors tend to use MR imaging in preference to US as their first-line investigation.

MR imaging

Imaging strategy. Magnetic resonance imaging is currently the most useful technique for studying cases with a suspected local recurrence of their sarcoma, be it a bony or soft tissue primary tumor. An easy-to-follow algorithm, developed by one of the authors (D. V.) and coworkers, is proposed when faced with one of these challenging cases (Fig. 5) [24, 25]. The somewhat simplistic principle behind the use of MR imaging in this context relies on the mass effect and high water content of tumor with respect to the surrounding soft tissues. A T2-weighted (+ fat saturation if available) or short tau inversion recovery (STIR) sequence is the most useful in demonstrating a high signal intensity mass. In the absence of a high signal intensity mass the likelihood of recurrence is remote. The exceptions are detailed in the pitfalls section below. Scar tissue is typically of low signal intensity due to its fibrous content.

Diffuse high signal intensity is frequently seen shortly after surgery or can be prolonged following radiation therapy [25–27]. Typically, a feather-like pattern of high signal intensity, without mass effect, is seen extending along fascial planes and separating muscle fibers (Fig. 6). This change can be best appreciated in the lower limbs if the contralateral normal limb is included for comparison within the scan field. A similar inflammatory response may be found surrounding a recurrence and so care should be taken when reviewing the images to exclude an underlying mass.

A high signal intensity mass on T2-weighted or STIR images is suggestive, but not conclusive, for local recurrence, as it may be seen in a variety of other postoperative entities [28]. These include hematomas and seromas. Subacute hematoma may be confidently diagnosed within weeks of surgery on T1-weighted MR imaging due to the characteristic halo of high signal intensity extracellular methemoglobin surrounding an intermediate signal intensity cavity with a thin low signal intensity outer rim (Fig. 7). The identification of a hematoma does not exclude the presence of microscopic residual disease following a marginal excision. The hematoma may need to be re-excised together with a generous cuff of normal tissue if an adequate surgical margin is to be achieved.

The commonest cause of a high signal intensity mass on T2-weighted or STIR images following surgery for a sarcoma is a localized fluid collection (seroma/hygroma). A seroma typically exhibits a relatively homogeneous high signal intensity on T2-weighted images due to the fluid content with a very low signal intensity rim due to hemosiderin-laden macrophages (Fig. 8 a). Occasionally, some debris may be identified within the seroma (Fig. 9 a) together with fluid–fluid levels if there is the settling out of old blood products (Fig. 10 a). The fluid is usually of lower signal intensity on T1-weighted images in comparison with surrounding muscles (Fig. 8 b) but may appear hyperintense if the fluid is proteinaceous or in the presence of blood products (Fig. 10 b). In cross section a seroma is usually rounded, oval, or angular in shape conforming to the surgical defect in the soft tissues (Figs. 8–10). The longitudinal extent of a seroma is characteristically greater than transverse reflecting the plane of surgical exposure. As a result, seromas typically show a flame-shaped appearance on sagittal or coronal MR imaging (Fig. 9 b). The size of seroma may remain unchanged or show gradual resolution with time in contradistinction to local recurrence of tumor which would be expected to increase in size. If there is any doubt as to the nature of the mass, T1-weighted im-

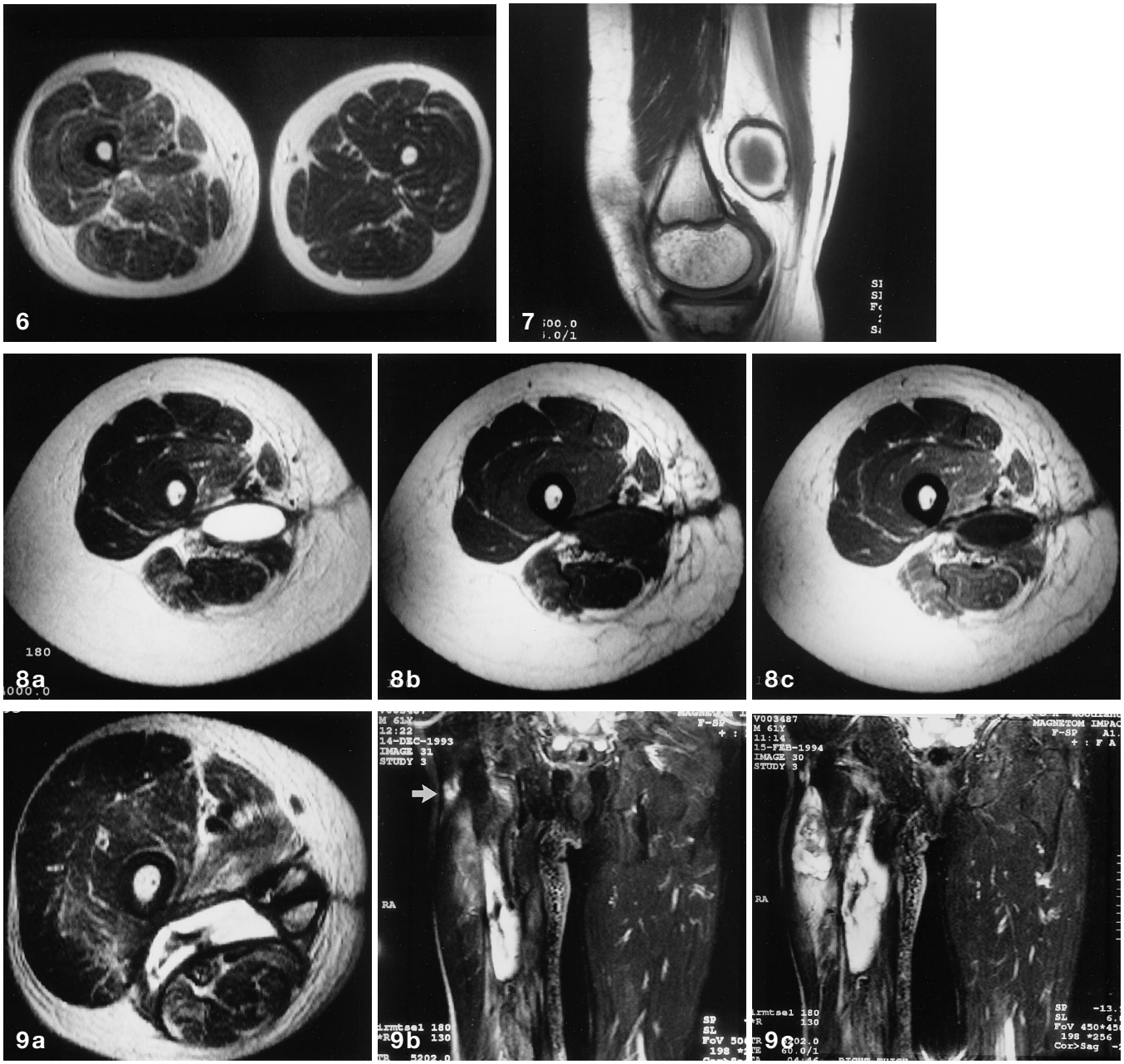


Fig. 6. A 32-year-old female 2 years after surgical excision and postoperative radiotherapy for soft tissue sarcoma right thigh. Axial T2-weighted image through both thighs showing diffuse swelling and edema of the right thigh secondary to the radiotherapy

Fig. 7. An 11-year-old boy complaining of lump behind the knee 2 weeks after excision of a rhabdomyosarcoma. The sagittal T1-weighted image shows a low signal rim lining a high signal intensity zone around a lower signal intensity center typical of a subacute hematoma

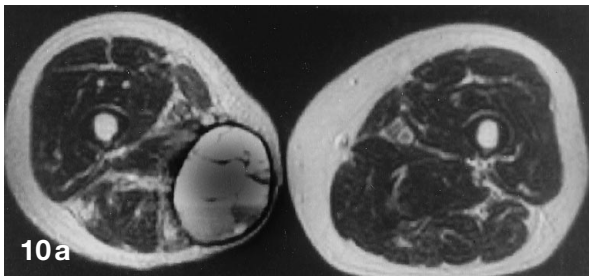
Fig. 8 a–c. A 27-year-old female 18 months after excision of a soft tissue sarcoma from the adductor compartment. **a** Axial T2-weighted image shows an oval high signal intensity mass deep to the subcutaneous scar. Axial T1-weighted images, **b** precontrast and **c** postcontrast, show only minor rim enhancement indicating that the mass is a seroma

Fig. 9 a–c. A 61-year-old male 5 months following excision of soft tissue sarcoma from right thigh. **a** Axial T2-weighted image showing a seroma behind the femur containing low signal debris. **b** Contemporary coronal STIR image showing a flame-shaped seroma. The small focus of signal change *(arrow)* was overlooked. **c** Coronal STIR image 6 weeks later showing that the seroma persists and that the focus has enlarged considerably due to an extensive local recurrence of soft tissue sarcoma

ages should be obtained following the intravenous injection of a gadolinium chelate. Seromas will either not enhance or show only minor rim enhancement (Fig. 8 b, c).

Identification of a probable solid mass of high signal intensity on the initial T2-weighted or STIR images should prompt the use of a gadolinium chelate for further evaluation. If the mass enhances, the likelihood is that it represents recurrent tumor and biopsy of the mass together with full re-staging of the patient is indicated (Fig. 11). In this respect MR imaging is important

Fig. 10 a, b. A 58-year-old female 15 months after resection of soft tissue sarcoma right thigh and postoperative radiotherapy. Oval seroma showing a fluid–fluid level on **a** the axial T2-weighted image and relatively hyperintense contents on **b** the coronal T1-weighted image



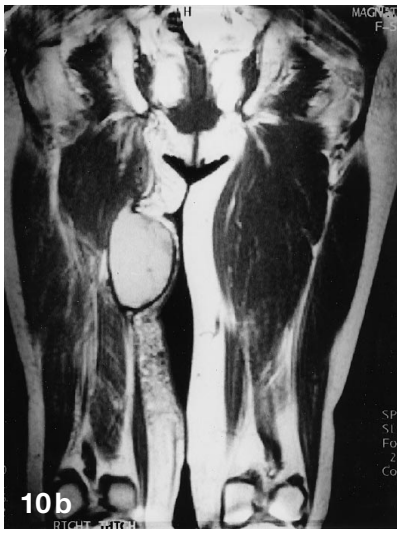
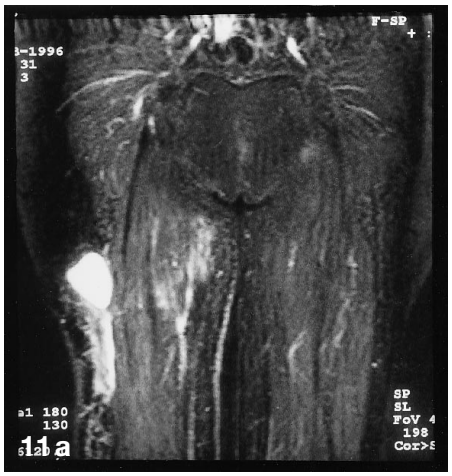
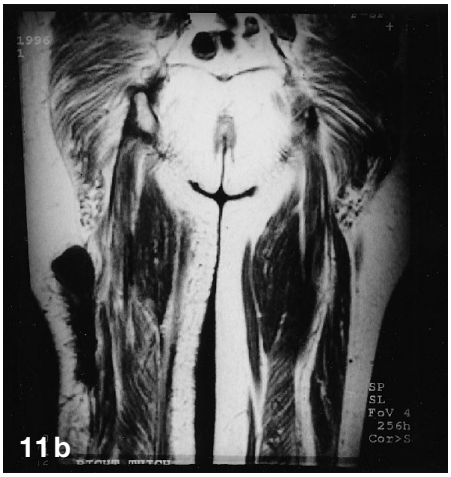
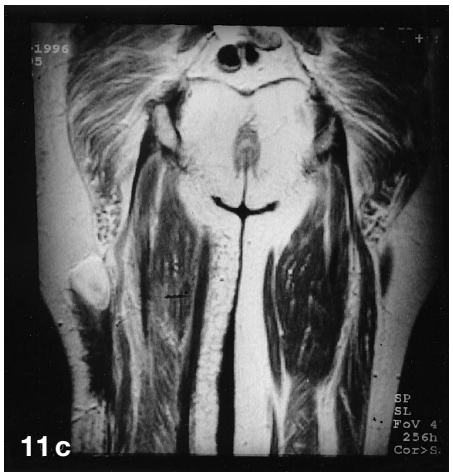


Fig. 11 a–c. A 43-year-old female 2 years following resection of soft tissue sarcoma right thigh. She now complains of fullness deep to scar. **a** The coronal STIR image shows an oval focus of increased signal intensity with a distal tail. Coronal T1-weighted images, **b** pre- and **c** post-Gd-DTPA enhancement, show the oval mass to enhance but the tail is unchanged. The final diagnosis was recurrent tumor with a small linear seroma







in assessing whether the local recurrence is surgically resectable. This depends on the site and size of the tumor together with involvement of critical structures such as the neurovascular bundle. Seroma and recurrent tumor may be present on the same examination (Fig. 11).

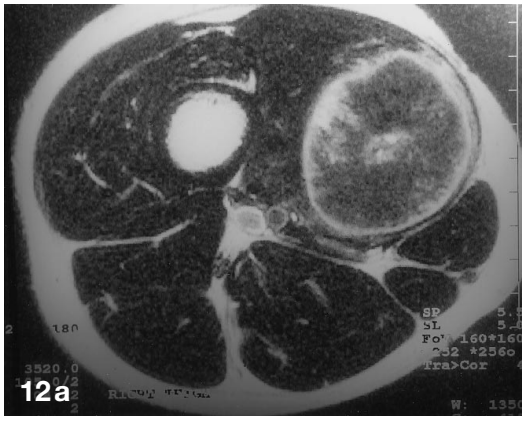
MR imaging pitfalls. There are pitfalls to the stringent application of any algorithm (Fig. 5). It is important that anyone working in this area is fully conversant with the traps for the unwary. If the recurrent tumor contains few mobile protons due to being densely mineralized (e. g., osteosarcoma) (Fig. 12) or hypocellular (e. g., fibromatosis) (Fig. 13) there will be mass effect, but the predominant signal intensity on the T2-weighted images will be low. If the tumor is relatively hypovascular, such as the lobules of cartilage in recurrent chondrosarcoma, there will be a high signal intensity mass on the T2 weighted images but only rim enhancement following injection of a gadolinium chelate simulating seromas. Knowledge of the preoperative imaging characteristics of the primary tumor is clearly valuable together with contemporary radiographs to confirm or exclude mineralization.

High signal intensity masses on T2-weighted images may occur in the presence of infection with abscess for-

Fig. 14. Axial T2-weighted image of the pelvis in a 17-year-old male undergoing radiotherapy for a Ewing's sarcoma of the right ilium. The rounded mass of high signal intensity is a soft tissue spacer surgically inserted to displace the bowel from the radiotherapy field. The subcutaneous metal artifact is from the portal device which allows for saline to be added or removed

Fig. 15a–c. A 63-year-old female 8 years after resection of a soft tissue malignant fibrous histiocytoma. Although on clinical examination there was no evidence of recurrence, the patient felt there had been a recent change in symptoms. **a** An axial T2-weighted image of the thigh was thought to show two possible soft tissue nodules posteriorly *(1, 2)*. **b** A dynamic sequence was performed and regions of interest applied to one of the late images from the sequence (nodules *1* and *2,* normal muscle *3* subcutaneous fat *4*). **c** A time–intensity curve was plotted showing rapid enhancement of the two nodules in comparison with muscle. Biopsy confirmed both to be recurrent tumor

Fig. 16. Axial T2-weighted image through the upper calf in a 15-year-old male 9 months following proximal tibial endoprosthetic replacement for an osteosarcoma. There is a signal void from the titanium prosthesis with marked increased signal intensity involving the soft tissues medially and anteriorly. These are the normal postoperative appearances of a gastrocnemius muscle flap reflected anterior to the prosthesis to improve the soft tissue cover



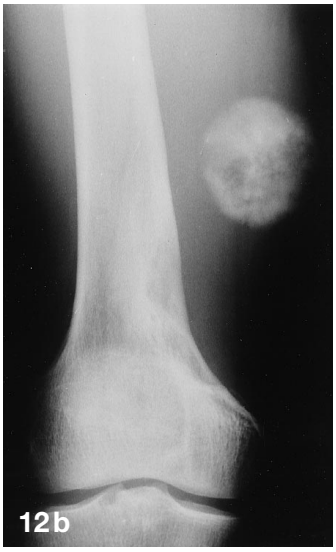
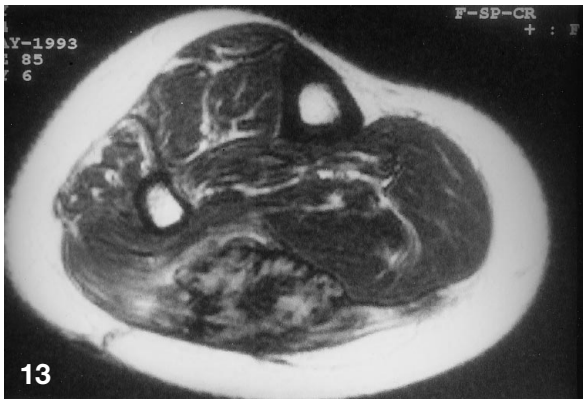


Fig. 12 a, b. A 29-year-old male 10 months following resection of parosteal osteosarcoma distal femur. **a** Axial T2-weighted image showing a large, predominantly low signal intensity, soft tissue recurrence. **b** A contemporary antero-posterior radiograph shows the mass to be densely mineralized. The surgical defect in the medial aspect of the distal femoral metaphysis indicates the site of the primary tumor



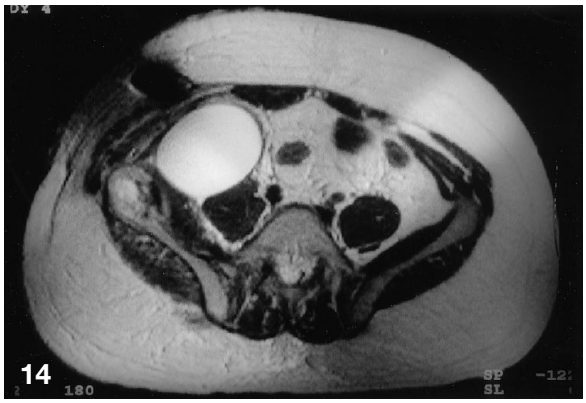
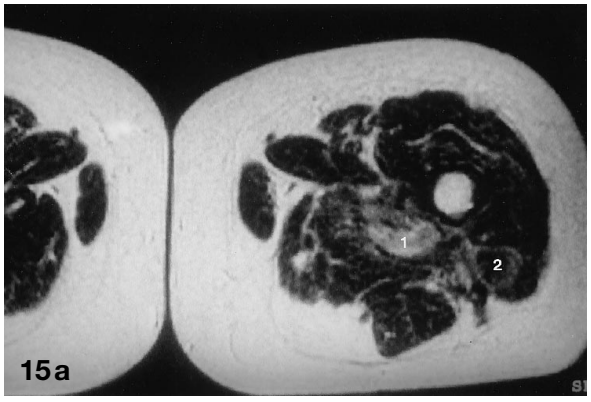
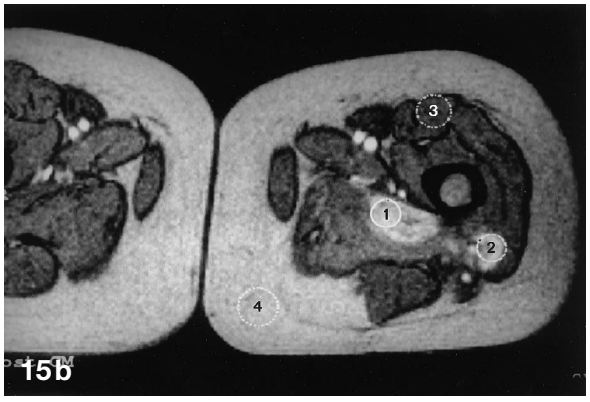
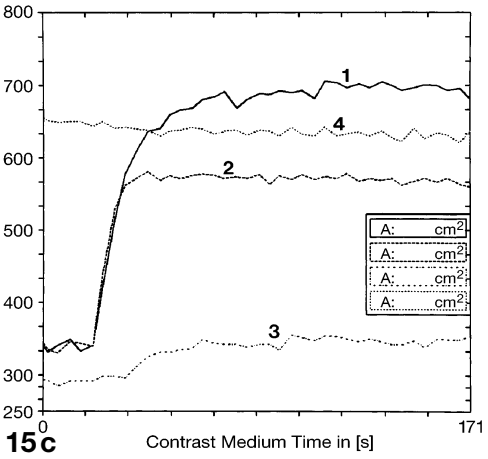
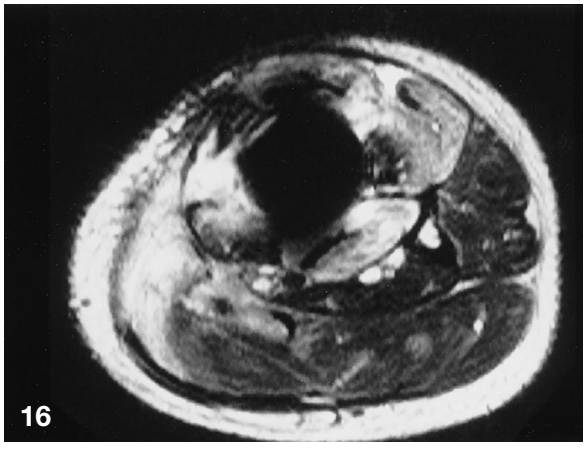


Fig. 13. A 33-year-old female 4 years after surgery to the posterior calf. The axial T2-weighted image shows an ill-defined heterogeneous mass of predominantly low signal intensity within the posterior muscles due to recurrent fibromatosis









mation. Another cause of a high signal intensity mass that can be anticipated is when the surgeons have inserted a soft tissue spacer. These saline filled spacers are used in the management of pelvic sarcomas to displace bowel out of the proposed radiotherapy field. The clue to the correct diagnosis is the homogeneous appearance of the fluid together with the small subcutaneous metal artifact from the portal device (Fig. 14). If the spacer is left in situ for some months and then removed, the potential space may fill with fluid to form a seroma rather than the loops of bowel which had originally been displaced. The use of hemostatic material (Avitene) has also been reported as causing a high signal intensity mass on T2-weighted images [28].

Enhancement per se does not guarantee the presence of recurrent tumor as it may be seen with inflammation shortly after surgery and with soft tissue infection as well as in the rare radiation-induced pseudomass [25]. The latter can be confidently excluded by scanning promptly after the injection of a gadolinium chelate in that recurrent tumor enhances rapidly (< 2 min), whereas a radiation-induced pseudomass enhances relatively slowly (> 4 min). Employing a dynamic sequence in which repeated rapid gradient-echo images are obtained following a bolus injection of a gadolinium chelate will typically show a steep enhancement slope on a time–intensity plot in recurrent tumor in comparison with the surrounding soft tissues (Fig. 15). Rapid enhancement may also be identified in inflamed tissues secondary to recent surgery or infection, but this is typically relatively diffuse with little true mass effect. Various dynamic gadolinium chelate techniques have been developed [29]. These include the region-of-interest technique [30, 31] which uses a preselected part of the image to plot time/intensity curves, factor analysis [32] which allows a pixel by pixel evaluation of the contrast agent uptake in the entire image, and first-pass images [33] which display the slope of uptake signal after the injection on the entire image.

Limb-salvage surgery for bone sarcomas frequently requires the use of allografts or endoprostheses. The authors have little experience with the former but note the contribution of Hoeffner and coworkers who conclude that the heterogeneous appearance on MR imaging of allograft revascularization should not be interpreted as recurrent tumor or infection [34]. Most endoprostheses used are largely constructed of titanium and result in only minor image artifacts, but problems can occur around the joint components where moderate to extensive metal artifact may obscure a small recurrence. Other forms of imaging may be required at these sites to supplement the MR examination.

Familiarity with normal anatomy is a fundamental requisite of image interpretation. Considerable distortion of the anatomy may result from the extensive surgery thereby causing problems with image interpretation. For example, following hindquarter amputation the bladder will deviate from midline to the ipsilateral side to produce a high signal intensity "mass" on T2-weighted images. The disposition of muscles may be deliberately altered at the time of surgery. In order to minimize postoperative infection proximal tibial endoprostheses can be covered anteriorly with a gastrocnemius muscle flap. Subsequent MR imaging will reveal an edematous "mass" anterior to the prosthesis with further edema in the soft tissues at the original site of the muscle flap (Fig. 16). If a muscle is denervated as a result of surgery, it will also appear edematous and enlarged on early follow-up MR imaging with later fatty atrophy.

Timing of follow-up imaging

Optimal scheduling of follow-up MR examinations after surgery for a musculoskeletal sarcoma is contentious. Local recurrence may occur within weeks of surgery in high-grade sarcomas and up to 15 years later in low-grade sarcomas, such as parosteal osteosarcoma. The cost and resource implications of employing regular, 3 or 6 monthly, follow-up MR examinations in all patients are considerable. There can be little doubt that close follow-up of patients in whom the original surgical resection was intralesional or marginal is mandatory. It is always worthwhile listening to the patient as he/she is often aware of subtle changes in their condition well before there is any clinical evidence of recurrence (Fig. 15).

A baseline MR examination can be helpful in interpreting subsequent scans, but the examination should be delayed for 6–8 weeks in order to allow the features secondary to surgical trauma to subside as there are major problems using MR imaging to distinguish residual disease early after inappropriate excision [35].

Conclusion

The team approach to the management of musculoskeletal sarcomas including radiologists, orthopedic surgeons, oncologists, and pathologists is well recognized. With the improving survival of these patients centers specializing in their treatment can expect to have increasing numbers requiring follow-up. A follow-up imaging strategy needs to be determined which takes into account both the efficacy of the investigations and cost constraints. Early detection of recurrence is desirable if local surgical control is to be achieved, even if this does not influence the ultimate prognosis for the patient. The prudent radiologist will ensure that he/she has all the relevant clinical details and previous imaging to hand when supervising and reporting a follow-up examination.

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