

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:**

**Follow-up of Malignant or Aggressive Musculoskeletal Tumors**

**Variant 1:**

**Lower-risk patient (low grade). Evaluation for metastatic disease to the lung from musculoskeletal primary.**

Radiologic Procedure	Rating	Comments	<a href="#"><u>RRL*</u></a>
<b>Modality for Baseline Examination</b>			
CT chest without contrast	9	Despite some of the cost analysis studies, the panel believes early diagnosis of lung metastases is critical and that chest CT should be performed. If chest CT is done, chest x-ray is not necessary.	Med
FDG-PET whole body	5	In individual cases, can be a good problem-solving tool. Outcomes data on PET/CT are pending. The CT portion of PET/CT, although unenhanced, can include thin section images through the whole body, which can enhance diagnosis.	High
X-ray chest	3		Min
<b>Modality for Follow-Up Examination</b>			
CT chest without contrast	9		Med
FDG-PET whole body	4	Can be a useful problem-solving tool if another study is equivocal.	High
X-ray chest	3		Min
<b>Timing of First Postoperative Examination</b>			
3-6 months postoperative	9		NS
<b>Frequency of Follow-Up</b>			
Every 3-6 months	9		NS
Every 6-12 months	2		NS
<b>Duration of Follow-Up</b>			
10 years	9	After 5 years, frequency can decrease to every 6-12 months.	NS
5 years	2		NS
<b><u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate</b>			<b>*Relative Radiation Level</b>

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**Clinical Condition:****Follow-up of Malignant or Aggressive Musculoskeletal Tumors****Variant 2:****Higher-risk patient (high grade). Evaluation for metastatic disease to the lung from musculoskeletal primary.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
<b>Modality for Baseline Examination</b>			
CT chest without contrast	9	Despite some of the cost analysis studies, the panel believes early diagnosis of lung metastases is critical and that chest CT should be performed. If chest CT is done, chest x-ray is not necessary.	Med
FDG-PET whole body	7	In individual cases, can be a good problem-solving tool. PET/CT appears to be emerging as a primary diagnostic tool as well for diagnosing metastatic disease in many musculoskeletal tumors.	High
X-ray chest	2		Min
<b>Modality for Follow-Up Examination</b>			
CT chest without contrast	9		Med
FDG-PET whole body	5	Can be a useful problem-solving tool if another study is equivocal.	High
X-ray chest	2		Min
<b>Timing of First Postoperative Examination</b>			
3-6 months postoperative	9		NS
<b>Frequency of Follow-Up</b>			
Every 3-6 months	9		NS
Every 6-12 months	2		NS
<b>Duration of Follow-Up</b>			
10 years	9	After 5 years, frequency can decrease to every 6-12 months.	NS
5 years	2		NS
<b>Rating Scale: 1=Least appropriate, 9=Most appropriate</b>			<b>*Relative Radiation Level</b>

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**Clinical Condition:****Follow-up of Malignant or Aggressive Musculoskeletal Tumors****Variant 3:****Evaluation for osseous metastatic disease from musculoskeletal primary.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><a href="#">RRL*</a></b>
<b>Timing of Baseline Examination</b>  Only if symptomatic	9	Although additional imaging should be provided only if the patient is symptomatic, it should be noted that in many cases, baseline whole-body PET/CT would already have been done, which provides high sensitivity for some bone tumors.	NS
<b>Frequency of Follow-Up</b>  Only if symptomatic	9		NS
<b>Duration of Follow-Up</b>  Only if symptomatic	9		NS
<b>Modality for Follow-up Examination</b>  FDG-PET whole body	7	In individual cases, can be a good problem-solving tool. Sclerotic lesions are more difficult to detect with PET but are well demonstrated on the CT portion of the PET/CT exam.	High
NUC Tc-99m bone scan whole body	5		Med
MRI whole body without contrast	3	Problem-solving tool or staging for second surgery.	None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 4:****Surveillance for local recurrence.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><a href="#">RRL*</a></b>
<b>Timing of Baseline Exams</b>  3-6 months postoperative	9		NS
<b>Frequency of Follow-Up</b>  At 3 months or before 6 months	9		NS
At 6 months or before 9 months	2		NS
At 9 months or before 12 months	2		NS
<b>Duration of Follow-Up</b>  10 years	9	After 5 years, frequency can decrease to every 12 months or be performed earlier if symptomatic.	NS
3 years	1		NS
5 years	1		NS
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

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**Clinical Condition:****Follow-up of Malignant or Aggressive Musculoskeletal Tumors****Variant 5:****Osseous tumor, without significant hardware present. Local recurrence.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><a href="#">RRL*</a></b>
X-ray area of interest	9	Both MRI and x-ray are indicated.	NS
MRI area of interest with or without contrast	9	Both MRI and x-ray are indicated. Contrast administration helpful for further evaluation of equivocal findings. See comments regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body	4	Can be a useful problem-solving tool if another study is equivocal.	High
CT area of interest without contrast	4	On a case-by-case basis, CT may be useful. Useful for osseous tumors when better definition of bony anatomy is needed.	NS
US area of interest	1		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 6:****Osseous tumor, with significant hardware present. Local recurrence.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><a href="#">RRL*</a></b>
X-ray area of interest	9		NS
MRI area of interest with or without contrast	7	Can use metal suppression techniques. Contrast administration helpful for further evaluation of equivocal findings. Since fat suppression is inhomogeneous with adjacent hardware, pre- and post-contrast subtraction postprocessing is recommended. See comments regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body	5	Can be a useful problem-solving tool if another study is equivocal.	High
CT area of interest without contrast	5	Can be useful if MRI not informative. Alter technique to decrease metal artifact.	NS
US area of interest	2		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

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**Clinical Condition:****Follow-up of Malignant or Aggressive Musculoskeletal Tumors****Variant 7:****Soft-tissue tumors; presume no significant hardware. Local recurrence.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
MRI area of interest with or without contrast	9	Contrast administration helpful for further evaluation of equivocal findings. See comments regarding contrast in text under "Anticipated Exceptions."	None
FDG-PET whole body	6	Can be a useful problem-solving tool if another study is equivocal. Outcomes data on PET/CT are pending. The CT portion of PET/CT includes thin-section images through the whole body, which can enhance diagnosis.	High
X-ray area of interest	2	Problem solver if needed to interpret findings on MRI.	NS
CT area of interest without contrast	2	Postoperative scarring can obscure local recurrence.	NS
US area of interest	2		None
<b><u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate</b>			<b>*Relative Radiation Level</b>

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# FOLLOW-UP OF MALIGNANT OR AGGRESSIVE MUSCULOSKELETAL TUMORS

Expert Panel on Musculoskeletal Imaging: Catherine C. Roberts, MD<sup>1</sup>; Richard H. Daffner, MD<sup>2</sup>; Barbara N. Weissman, MD<sup>3</sup>; D. Lee Bennett, MD<sup>4</sup>; Judy S. Blebea, MD<sup>5</sup>; Jon A. Jacobson, MD<sup>6</sup>; William B. Morrison, MD<sup>7</sup>; Charles S. Resnik, MD<sup>8</sup>; David A. Rubin, MD<sup>9</sup>; Mark E. Schweitzer, MD<sup>10</sup>; Leanne L. Seeger, MD<sup>11</sup>; Mihra Taljanovic, MD<sup>12</sup>; James N. Wise, MD<sup>13</sup>; William K. Payne, MD.<sup>14</sup>

## Summary of Literature Review

This topic specifically excludes: 1) metastatic disease from other primaries; 2) head and neck tumors; 3) spine tumors; 4) chest wall tumors; 5) multiple myeloma; 6) benign or nonaggressive bone or soft-tissue tumors; and 7) evaluation for chemotherapy or radiation therapy effectiveness, preoperatively after such induction therapy.

It should be noted that there is a lack of controlled studies in the literature that directly address the issue of tumor follow-up, and the recommendations are based mostly on consensus, are subject to changes later if new data come out, and should be used only as a guideline, with generous opportunity for modification in individual circumstances.

This topic addresses two issues of follow-up for tumor therapy: the timing of the follow-up examination, and the type of imaging best used for follow-up.

Ideally, the timing of follow-up for tumor recurrence or metastatic disease would be individualized for each tumor type and each patient. To design a follow-up protocol, one would generally wish to know the following: 1) How good is the imaging test to be used for detecting the presence of tumor? 2) How important is early detection of relapse, related to salvage effectiveness (utility/risk analysis)? and 3) When is the relapse most likely to occur (hazard rate)? Individual hazard rate is related to tumor type, grade, size, and central location; patient age and gender; tumor stage; type of treatment; and surgical margins. Overall, the goal of an imaging protocol is to concentrate testing when the relapse is most likely to occur. This presumes that testing frequency should gradually decrease over time. There are outstanding reviews of model development for such protocols in

lymphoma and other tumors [1,2]. However, such models do not exist for extremity tumors.

Because models relating to the hazard rate and utility/risk analysis do not exist for individual extremity tumor types, we will consider the sarcomas as a group and try to evaluate general local recurrence rate and timing as well as metastatic rate and timing. The most helpful general information can be found in several articles [3-8]. The information most commonly agreed to among these authors is that approximately 80% of patients who recur locally or systemically will do so within 2 years of their primary treatment. This suggests that the most aggressive follow-up should occur in the first 2 years, with tapering of imaging after that time.

## **Timing and Frequency of Follow-Up**

The incidence of metastatic disease varied considerably in the large studies quoted above. The incidence of metastatic disease only to the lung ranged from 18%-52% [4,6]. In one study, 31% of patients had metastatic disease, of whom 42% previously had a local recurrence [7]. In at least some of these studies, it appears as though the incidence of local recurrence is less frequent than the occurrence of metastatic disease in high-grade sarcomas. Therefore, local failure may not be the initiating factor in most systemic metastases. This finding suggests that follow-up studies should include systemic surveillance as well as imaging for local recurrence.

Of the systemic metastases, lung metastasis is by far the most frequent. It is generally accepted that computed tomography (CT) is more accurate in diagnosing lung parenchymal metastatic disease than is chest radiography [9]. However, that increased accuracy may not translate to a positive cost-benefit analysis. One excellent review article quotes a retrospective study of 125 consecutive patients in which, for low-risk patients (primary tumor <5 cm), the incremental cost was \$59,722 per case of synchronous pulmonary metastases when chest CT was added to chest radiography. This suggested to the authors that the yield for an added CT scan is low when a good quality chest radiograph does not reveal any suspicion for lung metastases [3]. Based on this, those authors recommend surveillance for lung metastases in the low-risk patient (primary tumor <5 cm) by chest radiography alone. In the high-risk category (primary tumor >5 cm), this study found that initial staging chest CT was cost-effective, but recommended follow-up only by chest radiography [3]. However, given the higher accuracy of CT, as well as the fact that pulmonary metastases from sarcomas are frequently cured by surgical excision, it is likely that the use of CT for staging and surveillance for lung metastases will continue.

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In terms of frequency of follow-up, some experts recommend that high-risk patients be followed with chest radiography every 3 months for 2 years, every 4 months for the next 2 years, every 6 months for the fifth year, and annually after that [3]. The recommendation from another review based on the experiences of two large tumor centers for low-risk patients is similar, calling for chest radiograph for pulmonary metastatic surveillance every 3-4 months for 2 years, every 4-6 months for the next 2 years, and yearly after that [10]. Six-month imaging is widely regarded by other experts as a suitable compromise between intense surveillance and early lesion detection [11]. The optimal frequency and modality of follow-up imaging have not been scientifically established.

The frequency of other distant metastatic disease ranges from 14%-20%. It is debatable whether surveillance for osseous metastases or lymphatic metastatic disease is cost-efficient. If required, technetium bone scan is most frequently used; with care, whole-body magnetic resonance imaging (MRI) can detect osseous metastases with reasonable sensitivity and specificity [12,13]. Opposed phase gradient echo sequences may be used to improve specificity when equivocal marrow changes are seen on MRI [14].

The use of 2-fluorine-18 fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) has been shown to be effective in localizing metastases from many bone sarcomas, though it may be nonspecific and produces false negatives in osteosarcoma bone metastases [15-18]. Although bone scan, FDG-PET, and MRI may detect osseous metastases, these studies are generally not advocated as part of the initial workup or follow-up for osseous metastases in asymptomatic cases.

Metastatic disease from primary extremity liposarcoma deserves special note. A study retrospectively looking at 122 patients with extremity liposarcoma found that the myxoid type (86% of liposarcomas in this series) tended to metastasize to extrapulmonary sites, frequently involving the trunk or retroperitoneum [10]. A biopsy-proven "primary" myxoid liposarcoma in the trunk or retroperitoneum should prompt a rigorous search for an occult extremity primary.

Local recurrence can be as low as 10%-20% using multimodality therapy as well as limb-sparing surgery [6] and may be routinely as low as 10% in patients with high-grade sarcomas smaller than 5 cm at the time of diagnosis. Local recurrence ranged from 20%-52% in the two largest studies [4,6]. Different studies have related local failure to tumor grade and size as well as to type of resection [6]. A multivariate analysis of 15 factors demonstrated marginal excision, tumor necrosis, and extracompartmental location to be the greatest factors relating to local recurrence, but the greatest factors

relating to survival include local recurrence, high grade, male gender, and extensive necrosis [5]. Stotter et al [7] found that local recurrence does not correlate with tumor size, although metastatic disease does. Similarly, local recurrence does not correlate with location proximal to the original tumor or grade, but the likelihood of metastatic disease does. Local recurrence in this study related most strongly to the "quality" of local treatment. In another study, long-term survival was influenced only by positive surgical margins [19]. Another study noted specifically that, compared with ablative surgical procedure, limb-sparing surgery itself has a three- to five-fold increased risk of local relapse, which significantly worsens the prognosis [15].

Because of the different findings, it would seem reasonable to establish a routinely suggested timing sequence for evaluating local recurrence, with the caveat that for marginal excision, in the presence of large regions of necrosis and high-grade or site evaluation, more frequent follow-up may be efficacious. One retrospective analysis drawing on a review of 1,500 patients from the Memorial Sloan-Kettering Cancer Center and the M.D. Anderson Cancer Center, recommended follow-up of adult soft-tissue sarcomas [3] based on low and high risk of recurrence. Risk stratification was based on size of primary neoplasm (T1: low risk <5cm; T2: high risk >5cm). For local recurrence in low-risk patients the recommendation was for "cross-sectional imaging of choice" individualized for patient and location of primary tumor. The implication is that for extremity primaries the clinical examination may obviate the need for routine cross-sectional imaging follow-up in the low-risk group. Cross-sectional imaging follow-up for less accessible areas (trunk or retroperitoneum) would be required at 3-4-month intervals for 2 years, 4-6-month intervals for 2 years and yearly thereafter. Within the low-risk group, surveillance could stop after 5-10 years.

Within the high-risk group local recurrence rate was noticeably higher, and the analysis recommended cross-sectional imaging every 3 months for 2 years, every 4 months for the next 2 years, every 6 months for the fifth year, and then annually [3]. A study looking at long-term follow-up (greater than 5 years) of patients with primary extremity sarcoma [19] showed that 21% of patients alive at 5 years will die of their disease in the next 5 years. In a multifactorial analysis, a positive surgical margin was the only factor that showed positive predictive value for long-term recurrence. Size, grade, age, and depth were not shown to increase long-term recurrence, and local recurrence did not correlate with increased mortality after 5 years. These data may necessitate a more tailored approach to follow-up of patients with bone or soft-tissue sarcoma. Patients with T2 primaries need to be followed more closely than those with T1 primaries, and those with

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positive surgical margins may need longer surveillance than those with complete excision.

### **Implications of Tumor Type and Therapy**

The specific type of imaging for follow-up for local recurrence will depend on the site of the original tumor (osseous vs soft tissue), as well as the type of therapy used (curettage with bone graft vs resection with allograft vs soft-tissue resection, all taking into account the presence or absence of hardware) [20-22]. The following comments relate to each of these situations.

One reference suggests that patients treated with curettage and bone chip allografts can be followed by MRI [23]. It suggests that most cases will have a speckled bright signal on T2 imaging and that if signal intensity on both T1 and T2 imaging is predominantly low, there is a reasonable likelihood that this does not represent recurrence. Richardson et al [24] discuss MRI follow-up of patients with curettage and bone grafting plus cryosurgery. Many of these cases showed a zone beyond the surgical margins that is low signal on T1 and high signal on T2, the thickness of which ranges from 1 to 17 mm, varying within a single patient.

The evaluation of large allografts used in treating sarcomas is discussed in several articles [23,25-29]. Most of these studies used only radiographs [23,25,28,29]. They indicate that there is a high complication rate (40%-57%). The complications include infection (6%-25%), usually occurring in the first 12 months; the patient may present with a mass. Fracture is a common complication as well, ranging from 15%-27% and occurring in the first 3 years. Tumor recurrence in these series ranged from 0%-16% and generally occurred in 12-24 months. After 4 years, there is late development of articular degeneration if the graft is an osteoarticular type. Technetium bone scanning may reflect the physiology of allograft incorporation [30,31], but it has not been advocated to detect local recurrence. Also, specific CT appearance is described, showing initial thinning of the cortex and very prominent subcortical cyst formation as well as a differential in attenuation between the graft and host bone [32]. One extremely small study of MRI of allografts showed a very heterogeneous T1 and T2 signal but was inadequate in scope for further information to be derived. It seems that radiographs are usually used for follow-up of massive allografts because of the large amount of hardware that is generally present. However, the authors note that multislice CT with reformatting in coronal or sagittal planes can minimize metallic artifact and can be extremely useful in evaluating for either union or allograft to host bone or for osseous complications. Most of the complications relate to failure of the graft or infection.

Recurrence involving only the soft tissues could be detected by ultrasound (US) if too much hardware is present to evaluate with other imaging modalities. PET

has emerged as a powerful tool for evaluating local recurrence in the face of suboptimal cross-sectional imaging because of large amounts of metal. PET and its possible applications are addressed separately below.

### **Magnetic Resonance Imaging, Computed Tomography, and Ultrasound**

Two studies evaluated MRI of both soft tissue and bone tumors in follow-up [32,33]. Both emphasized that high signal intensity on T2 can be seen for a number of non-neoplastic reasons. These include presence of a postoperative seroma, hematoma, changes related to radiation therapy, fat necrosis, packing material, allograft, scar tissue, and bowel or bladder herniation. Although the timing of the study and knowledge of details of the case can be very valuable in sorting out these possibilities, in some cases they did not obviate biopsy [32]. The larger of the studies [33], with 60 patients in follow-up, showed that if there is a lesion of low signal intensity on T2, it generally does not represent recurrent tumor (sensitivity 96%). If there is a lesion with high signal intensity on T2 and surgery was the only therapy used, tumor recurrence is a high likelihood. If radiation therapy as well as surgery has been used, high signal intensity is nonspecific for distinguishing between radiation-induced inflammation and recurrent tumor. In that study, 66% of patients had high signal intensity on T2, and the overall sensitivity for detecting tumor recurrence was only 70%.

In evaluating whether CT or MRI is more efficacious in follow-up of sarcomas, one should discount the Radiology Diagnostic Oncology Group<sup>®</sup> (RDOG<sup>®</sup>) report in which no statistical difference was found between CT and MRI in determining tumor involvement of bone, muscle, joints, or neurovascular structures because this study did not address questions of follow-up [31]. However, one study demonstrated that CT does not differentiate between tumor recurrence and scar, since both enhance [34].

Few studies advocate the use of US in follow-up for soft-tissue masses. A study performed in 1991 compared MRI and US in follow-up of soft-tissue sarcoma [35]. The sensitivity and specificity of MRI for local recurrence were 83% and 93%, respectively, while those for US were 100% and 79%, respectively. These differences were not statistically significant. It was noted that acute postoperative changes make US diagnosis difficult (particularly in the first 3-6 months postoperatively). Note was also made that US may be particularly helpful in detecting recurrences that have short T2 relaxation times. This particular article recommends baseline US and MRI, followed by US. If subsequent US scans are inconclusive, MRI with contrast is recommended. The findings of these and other articles are difficult to apply, as MRI has dramatically improved over the years since the studies were performed. Another article [36] is biased, without cross-sectional imaging comparison but with favorable

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statistics on a prospective study of 50 consecutive patients with clinical suspicion of local recurrence. Twenty-four of 26 patients were confirmed as having recurrence, and 22 of 22 were accurately classified as no recurrence or benign masses (abscesses or lipoma) based on US examination. Discrete, hypoechoic, well-defined lesions were labeled as recurrence. Although these studies did not include osseous sarcoma follow-up, US in the presence of extensive hardware may be useful for follow-up for soft-tissue mass in that situation. Color Doppler flow imaging may also help differentiate recurrent tumor mass from fibrous tissue or other nonvascular tissue in the postoperative tumor site; this may be particularly helpful in the presence of hardware and if there is a baseline postoperative Doppler study [37]. These problem-solving utilities of US are useful in the absence of FDG-PET.

Several MRI studies have refined the methodology for evaluation and for detecting recurrence of soft-tissue sarcomas [30,37,38]. On the basis of a large number of examinations (511 examinations, 182 patients), Vanel et al [38] showed that of the 102 examinations showing no high-signal-intensity mass, 101 had no recurrence. Seventy-nine of the patients had a high signal intensity in the surgical bed on T2 but no mass; of these, only two had a local recurrence. Seventy-eight patients had high signal intensity on T2 with the presence of a mass. Sixty of these were proven to have recurrence, 24 had a seroma, and four had a radiation-induced pseudomass. Further evaluation with contrast showed that seromas do not enhance, whereas recurrences and radiation changes do enhance. A caveat here is that if there is a large area of necrosis, then tumor may not enhance. It was also noted that generally (with some areas of overlap), recurrences enhance earlier in a dynamic study than does a radiation-induced pseudomass. Another report suggested that in regions of high signal intensity on T2-weighted imaging, T1-weighted images should be reviewed for normal “texture” of muscle to help differentiate recurrence from other etiologies of high signal intensity.

Very few follow-up protocols have been advocated. However, Vanel et al [37] suggest an algorithm for following soft-tissue tumors postoperatively. This algorithm starts with T2 imaging. If a mass is present on T2-weighted imaging, it should be followed by T1-weighted sequences with and without contrast. This procedure generally distinguishes hematoma and seroma from tumor or inflammation. If necessary, this can be followed by dynamic enhanced imaging with subtraction postprocessing, which further helps differentiate tumors from inflammation. In this algorithm, if a region of high signal intensity is seen on T2-weighted imaging but there is no mass present; further evaluation with contrast imaging is not recommended. Reasonably enough, it is stated that there will be some exceptions to the above recommendations. This algorithm is supported by a recent

article reporting 98 patients with seven local recurrences and three inflammatory pseudotumors [39]. All but one recurrence was detected by T2-weighted imaging, indicating that it is a logical way to start the examination. Although enhanced MRI with subtraction postprocessing characterizes recurrences better than routine sequences in most patients, it is advocated only if contrast injection is required for diagnosis [39]. Contrast may be particularly helpful when assessing for recurrence in the presence of postoperative hematoma [40]. Based on these authors’ experience, they advocate delaying the postoperative baseline scan for at least 6-8 weeks to allow postoperative changes to subside; they acknowledge that 3- or 6-month follow-up MRI examinations may be too costly but reiterate that close follow-up is mandatory, especially if the surgical resection was intralesional or marginal [41].

#### **FDG-PET and PET/CT**

There has been a significant amount of literature exploring the utility of FDG-PET in evaluating recurrent soft-tissue and osseous sarcoma [15-18,42-47]. The literature seems to support using FDG-PET in three scenarios: 1) as a problem-solving tool in equivocal cases of local recurrence detected by MRI in patients who have undergone limb salvage surgery and have postoperative and/or radiation change confounding accurate MRI assessment, 2) as a primary evaluation for local recurrence in patients with overwhelming metallic artifact precluding accurate assessment with MRI, and 3) as a confirmatory tool in equivocal cases of distant metastases.

First, FDG-PET has been shown to have a high sensitivity and specificity for local recurrence in those patients in whom postoperative change or significant hardware causes equivocal or nondiagnostic MR findings. For evaluating local recurrence FDG-PET sensitivity ranges from 88%-100% [18,46] and specificity ranges from 92%-100% [18,46]. Specifically in nine patients with equivocal or technically inadequate MRI, sensitivity and specificity were 100% for recurrence using FDG-PET scanning [42]. Situations in which PET was falsely negative were in tumors of low histologic grade (two low-grade liposarcomas and one low-grade chondrosarcoma), and one false positive was caused by inflammation [47]. Postradiation or postoperative inflammation did not seem to cause diagnostic difficulty due to significant differences in specific uptake values (SUV) between benign and malignant causes. Mean SUV of malignant recurrence ranged from 3.0-5.0, and benign etiologies ranged from <1-1.35 [18,42,47].

Evaluation of distant metastases with FDG-PET has been compared to technetium bone scanning for osseous metastases [17,48] and osseous recurrence [44], and to CT for lung metastases [16]. For Ewing’s sarcoma bony metastases (n=49) FDG-PET showed a sensitivity and specificity of 100% and 96%, respectively, compared to

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71% and 92% for technetium bone scan [17]. Interestingly FDG-PET was falsely negative in all six osteosarcoma bony metastases [17]. This was in contrast to evaluation of recurrent osteosarcoma [44], which showed PET to be effective (n=6) in correctly identifying these lesions. FDG-PET failed to equal CT in sensitivity for pulmonary metastases [16], but there were no PET positive lesions that were CT negative, implying that FDG-PET could be used to confirm lesions suspicious by CT.

It should be noted that the literature cited above is for PET and not combined PET/CT. Virtually all clinical studies done today are done with PET/CT, which is reasonably expected to be a more powerful tool than either PET or CT alone, at least for selected musculoskeletal tumors. PET/CT may eventually rival MRI for local and distant tumor surveillance due to the increased information obtained from thin-slice CT through the entire body. Potential limitations of the CT portion of a PET/CT study include lack of intravenous (IV) contrast and lack of breath-hold technique [49]. Bone lesions identified on PET are not always visible on CT [27,50]. Although PET/CT has a high positive predictive value when findings are concordant, the positive predictive value has been shown to markedly decrease when findings are discordant [51]. Additional outcomes data for PET/CT are expected in the future as a result of the National Oncologic PET Registry ([www.cancerpetregistry.org](http://www.cancerpetregistry.org)).

In summary, FDG-PET/CT is an area of robust growth and research, with current evidence supporting its use as a problem-solving tool in equivocal cases of local or distant recurrence detected on MRI or CT. In addition it may have high utility in evaluating tumor recurrence in patients with orthopedic hardware that limits accurate use of MRI or CT. Low sensitivity for low-grade neoplasms and insensitivity for bony metastases of osteosarcoma are exceptions that need to be considered by the interpreting and ordering physician. Routine use of PET/CT beyond a problem-solving role has not been widely advocated in the literature, though anecdotal experiences are increasing rapidly. The panel feels that this emerging technology deserves recognition as a problem-solving tool and as a primary diagnostic tool for metastatic lesion detection and surveillance, at least in high-grade musculoskeletal tumors. Furthermore, the results of current studies and recent experience warrant a systematic prospective multicenter evaluation of its clinical value in diagnosis, staging, response to therapy, and detecting recurrence and metastatic disease of bone and soft-tissue sarcomas. Any such study must include its influence on outcome as well as a cost-benefit analysis. The same might be said for much of the other imaging recommended in this document. The desired evidence-based data are difficult to obtain for bone and soft-tissue sarcomas. We therefore

strive for a logical consensus that allows for optimizing patient and cost benefit. The result must allow for some nonuniformity, since clinical judgment remains of paramount importance in these cases.

### Preface to the Tables of Variants

Musculoskeletal tumor follow-up requires decisions regarding imaging method and timing, when assessing for local recurrence and metastatic disease.

- Variants 1 and 2 address modality and timing of follow-up for metastatic disease to the lung from a musculoskeletal primary (low and high grade, respectively).
- Variant 3 addresses the modality and timing of follow-up for osseous metastatic disease from a musculoskeletal primary.
- Variant 4 addresses the timing of follow-up for local recurrence.
- Variants 5, 6, and 7 address the modality for follow-up in osseous tumors without hardware, osseous tumors with hardware, and soft-tissue tumors, respectively.

### Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF), also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF [52-54], a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (eg, >0.2mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued a “black box” warning concerning these contrast agents ([http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca\\_200705HCP.pdf](http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf)).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m<sup>2</sup>), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s) [53].

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## Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level*	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

\*RRL assignments are not included for some examinations. The RRL assignments for the NS (not specified) exams cannot be made because the RRL depends on the region of the body exposed to ionizing radiation, and the body part will vary as a function of the clinical situation.

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