Complete Summary

GUIDELINE TITLE

Follow-up of malignant or aggressive musculoskeletal tumors.

BIBLIOGRAPHIC SOURCE(S)

Manaster BJ, Petersen B, Dalinka MK, Rubin DA, Rosen G, Lackman R, Janjan N, Expert Panel on Musculoskeletal Imaging. Follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 11 p. [46 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Radiology (ACR), Expert Panel on Musculoskeletal Imaging. Follow-up examinations for bone tumors, soft-tissue tumors, and suspected metastasis post therapy. Reston (VA): American College of Radiology (ACR); 2002. 10 p. (ACR appropriateness criteria).

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Musculoskeletal tumors
- Metastatic disease

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Oncology
Radiology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of follow-up radiologic examinations for patients with malignant or aggressive musculoskeletal tumors

TARGET POPULATION

Patients with malignant or aggressive musculoskeletal tumors

Note: These guidelines are not intended for use in the following patients:

- Patients with routine metastatic disease from other primaries
- Patients with head and neck tumors
- Patients with spine tumors
- Patients with chest wall tumors
- Patients with multiple myeloma
- Patients with benign or nonaggressive bone or soft-tissue tumors
- Patients evaluated for chemotherapy or radiation therapy effectiveness, preoperatively after such induction therapy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Timing, frequency, and duration of follow-up examinations
2. Computed tomography (CT)
3. Positron emission tomography (PET)/CT, whole body
4. X-ray
5. Nuclear medicine (NUC), bone scan
6. Magnetic resonance imaging (MRI), whole body
7. Ultrasound (US), alone or with color Doppler flow imaging

MAJOR OUTCOMES CONSIDERED

Utility of radiologic examinations in differential diagnosis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of recent peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed to reach agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as

developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

It is generally accepted that computed tomography (CT) is more accurate in diagnosing lung parenchymal metastatic disease than is chest radiograph. 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 effectiveness ratio was $59,722 per case of synchronous pulmonary metastases when CT chest was added to chest radiograph. 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. Based on this, the authors recommend surveillance for lung metastases in the low-risk (primary tumor <5 cm) patient by chest radiograph 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 radiograph. However, given the higher accuracy of CT, as well as the fact that sarcoma pulmonary metastases are frequently candidates for potentially curative surgical metastasesectomy, it is likely that the argument for staging and surveillance for lung metastases by CT will retain strength.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Foreword

Questions of musculoskeletal tumor follow-up require decisions on both method and timing of follow-up, for both 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 modality and timing of follow-up for osseous metastatic disease from a musculoskeletal primary.
- Variant 4 addresses timing of follow-up for local recurrence.
- Variants 5, 6, and 7 address modality for follow-up in osseous tumors without hardware, osseous tumors with hardware, and soft-tissue tumors, respectively.

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. (This presumes an average "hazard rate" for recurrence; individual variations [e.g., histologic evidence of tumor at margin, etc.] may mitigate this choice.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Lungs: Modality for Baseline Examination		
CT, chest	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.
PET/CT, whole body	4	In individual cases, can be a good problem solving tool.
X-ray, chest	3	
Lungs: Modality for Follow-Up Examination		
CT, chest	9	
X-ray, chest	3	

Radiologic Exam Procedure	Appropriateness Rating	Comments
PET/CT, whole body	3	Can be a useful problem solving tool if another study is equivocal.
Lungs: Timing of First Postoperative Examination		
3-6 months postoperative	9	
Lungs: Frequency of Follow-Up		
Every 3-6 months	9	
Every 6-12 months	2	
Lungs: Duration of Follow-Up		
10 years	9	After 5 years, frequency can be decreased to every 6-12 months.
5 years	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Higher risk patients (high grade). Evaluation for metastatic disease to the lung from musculoskeletal primary. (This presumes an average "hazard rate" for recurrence; individual variations [e.g., histologic evidence of tumor at margin, etc.] may mitigate this choice.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Lungs: Modality for Baseline Examination		
CT, chest	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.
PET/CT, 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

Radiologic Exam Procedure	Appropriateness Rating	Comments
		tumors.
X-ray, chest	2	
Lungs: Modality for Follow-Up Examination		
CT, chest	9	
PET/CT, whole body	4	Can be a useful problem solving tool if another study is equivocal.
X-ray, chest	2	
Lungs: Timing of First Postoperative Examination		
3-6 months postoperative	9	
Lungs: Frequency of Follow-Up		
Every 3-6 months	9	
Every 6-12 months	2	
Lungs: Duration of Follow-Up		
10 years	9	After 5 years, frequency can be decreased to every 6-12 months.
5 years	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Evaluation for osseous metastatic disease from musculoskeletal primary.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Bone Metastasis: Timing of First Examination		
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

Radiologic Exam Procedure	Appropriateness Rating	Comments
		for lung, which provides high sensitivity for some tumors.
Bone Metastasis: Frequency of Follow-Up		
Only if symptomatic	9	
Bone Metastasis: Duration of Follow-Up		
Only if symptomatic	9	
Modality for Detecting Osseous Metastatic Disease		
PET/CT, whole body	7	In individual cases, can be a good problem solving tool.
NUC, bone scan	3	
MRI, whole body	3	Problem solving tool or staging for secondary surgery.
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Surveillance for local recurrence.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Timing of Baseline Exams for Local Recurrence		
Postoperative evaluation at 3-6 months	9	
Local Recurrence: Frequency of Follow-Up		
At 3 months or before 6 months	9	
At 6 months or before 9 months	2	
At 9 months or before 12 months	2	
Local Recurrence: Duration of Follow-Up		

Radiologic Exam Procedure	Appropriateness Rating	Comments
10 years	9	After 5 years, frequency can decrease to every 12 months or earlier if symptomatic
3 years	1	
5 years	1	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Osseous tumor, without significant hardware present. Local recurrence.

Radiologic Exam Procedure	Appropriateness Rating	Comments
X-ray	9	Both MRI and x-ray are indicated.
MRI	9	Both MRI and x-ray are indicated.
PET/CT, whole body	4	Can be a useful problem solving tool if another study is equivocal.
CT	4	On a case by case basis, CT may be useful. Useful in osseous tumor when better definition of bony anatomy is needed.
US	1	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: Osseous tumor, with significant hardware present.

Radiologic Exam Procedure	Appropriateness Rating	Comments
X-ray	9	

Radiologic Exam Procedure	Appropriateness Rating	Comments
MRI	7	
PET/CT, whole body	5	Can be a useful problem solving tool if another study is equivocal.
CT	4	Can be useful if MRI not informative.
US, with color Doppler flow imaging	2	
US	1	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: Soft-tissue tumors; presume no significant hardware.

Radiologic Exam Procedure	Appropriateness Rating	Comments
MRI	9	
PET/CT, whole body	5	Can be a useful problem solving tool if another study is equivocal.
X-ray	4	Problem solver if needed to interpret MRI
CT	1	
US	1	
US, with color Doppler flow imaging	1	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

This topic specifically excludes 1) routine 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 (This is a very rapidly evolving field and is unlikely to be a clinical situation in which most general radiologists will find themselves unless they are practicing in a tumor center.)

It should be noted that there are 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 comes out, and should be used only as a rough guideline with a lot of room for modification in individual circumstances.

This topic deals with 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. First, we must acknowledge that most currently used surveillance protocols are ad hoc and not based on rigorous theoretical foundations. With rigorous examination some prove inefficient and costly.

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? 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. However, such models do not exist for most 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. 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.

Let us consider follow-up timing and frequency for metastatic disease first.

The incidence of metastatic disease had a surprisingly wide range in the large studies quoted above. The incidence of metastatic disease only to the lung ranged from 18%-52%. In another study, 31% of patients had metastatic disease, of which 42% previously had a local recurrence. 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 occurrences. This finding suggests that follow-up studies should include systemic surveillance as well as imaging for local recurrence.

Of the systemic diseases, lung metastasis is by far the most frequent. It is generally accepted that CT is more accurate in diagnosing lung parenchymal

metastatic disease than is chest radiograph. 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 effectiveness ratio was $59,722 per case of synchronous pulmonary metastases when CT chest was added to chest radiograph. 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. Based on this, the authors recommend surveillance for lung metastases in the low-risk (primary tumor <5 cm) patient by chest radiograph 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 radiograph. However, given the higher accuracy of CT, as well as the fact that sarcoma pulmonary metastases are frequently candidates for potentially curative surgical metastasectomy, it is likely that the argument for staging and surveillance for lung metastases by CT will retain strength.

In terms of frequency of follow-up, some experts recommend that high-risk patients be followed with chest radiograph every 3 months for 2 years, every 4 months for the next 2 years, every 6 months for the 5th year, and annually after that. However, the recommendation from a recent 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. Six-month imaging is widely regarded by other experts as a suitable compromise between overinvestigation and early lesion detection. 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 MRI can detect osseous metastases with reasonable sensitivity and specificity. This screening MRI generally uses a combination of T1-weighted imaging and inversion recovery, screening the spine in the sagittal plane, the proximal arms, the pelvis in the coronal plane, and the proximal femora. Opposed phase gradient echo sequences may be used to improve specificity when questions arise. The use of 2-(fluorine-18)fluoro-2-deoxy-D-glucose (FDG) PET has been shown to be effective in localizing metastases in many bone sarcomas, though it may be nonspecific and produces false negatives in osteosarcoma bone metastases. Although bone scan, FDG PET, and MRI may detect osseous metastases, these studies are generally not advocated as part of the initial work-up 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. 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 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. Different studies have related local failure to different factors. It has been related to tumor grade and size as well as to type of resection. 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. One study found that local recurrence does not correlate with tumor size, although metastatic disease does. Similarly, local recurrence does not correlate with proximal location 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. Another study noted specifically that, compared with ablative surgical procedure, limb-sparing surgery itself has a 3- to 5-fold increased risk of local relapse, which significantly worsens the prognosis.

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 Memorial Sloan-Kettering Cancer Center, recommended follow-up of adult soft tissue sarcomas 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 exam 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 5th year, and then annually. A study looking at long-term follow-up (greater than 5 years) of patients with primary extremity sarcoma showed that 21% of patients alive at 5 years will die of their disease in the next 5 years. In a multifactorial analysis, 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 to 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 closer than those with T1 primaries, and those with positive surgical margins may need longer surveillance than those with complete excision.

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). 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. 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 represents recurrence. One study discusses the 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. Most of these studies used only radiographs. 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, 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. One extremely small study of MRI of allografts shows a very heterogeneous T1 and T2 signal but is 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 US if too much hardware is present to evaluate with other imaging. PET has emerged as a powerful tool for evaluating local recurrence in the face of suboptimal cross-sectional imaging because of large allografts. PET and its possible applications are addressed separately below.

Two studies evaluated MRI of both soft tissue and bone tumors in follow-up. Both emphasize that high signal intensity on T2 can be seen for a number of nonneoplastic 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 this did not deter biopsy. The larger of the studies, with 60 patients in follow-up, showed that if there is a lesion that is 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 radiation-induced inflammation versus recurrent tumor. In that study, 66% of patients had high signal intensity on T2 and the overall sensitivity for detection of 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 (RDOG) report in which no statistical difference was found between CT and MRI in determining tumor involvement of bone, muscle, joints, or neurovascular structures; this study did not address questions of follow-up. However, one study demonstrates that CT does not differentiate between tumor recurrence and scar, since both enhance. A more biased study showed CT sensitivity only at 69% for recurrence.

Three studies advocate the use of US in follow-up for soft-tissue masses. One is a biased study that showed 100% of detection mass by US and 77% accuracy in diagnosing the malignant masses. A less biased study compared MRI and US in follow-up of soft-tissue sarcoma. 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 is noted that acute postoperative changes make ultrasound 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 ultrasound and MRI, followed by US. If subsequent ultrasounds are inconclusive, MRI with contrast is recommended. The third article is biased, without cross-sectional imaging comparison but with favorable 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). Discrete, hypoechoic, well-defined lesions were labeled as recurrence. Although theses 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. These problem solving utilities of US are useful in the absence of FDG-PET.

Recent MRI studies have refined the methodology for evaluation and for recurrence of soft-tissue sarcomas. On the basis of a large number of examinations (511 examinations, 182 patients), one study 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 on T2 but no mass; of these, only two of these 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 hygroma, and four had a radiation-induced pseudomass. Further evaluation with contrast showed that hygromas 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 radiation- induced pseudomass. Another report suggested that in regions of high signal intensity on T2 imaging, T1 examinations should be reviewed for normal "texture" of muscle to help differentiate recurrence from other etiologies of high signal.

Very few follow-up protocols have been advocated. However, in an outstanding new textbook, one study suggests an algorithm for following soft-tissue tumors postoperatively. This algorithm starts with T2 imaging. If a mass is present on T2

imaging, it should be followed by T1 imaging with and without contrast. This procedure generally distinguishes hematoma and hygroma from tumors or inflammation. If necessary, this can be followed by dynamic subtraction scanning, which helps to differentiate tumors from inflammation. In this algorithm, if a region of high signal intensity is seen on T2 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. All but one recurrence was detected by T2 imaging, indicating that it is a logical way to start the examination. Although subtraction MRI characterizes the recurrences better than routine sequences in most patients, it is advocated only if contrast injection is required. Based on these authors' considerable experience, they advocate delaying the postoperative baseline scan for at least 6-8 weeks to let surgical trauma subside; they acknowledge that three or six monthly 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.

In recent years there has been a significant amount of literature exploring the utility of FDG-PET in evaluating recurrent soft-tissue and osseous sarcoma. 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 which postoperative change or significant hardware cause equivocal or nondiagnostic MR findings. For evaluating of local recurrence FDG-PET sensitivity ranges from 88%-100% and specificity ranges from 92%-100%. Specifically in nine patients with equivocal or technically inadequate MRI, sensitivity and specificity were 100% for recurrence. Situations in which PET was falsely negative were in tumors of low histologic grade (2 low-grade liposarcomas and 1 low-grade chondrosarcoma), and one false positive was caused by inflammation. 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.

Evaluation of distant metastases with FDG PET has been compared to technetium bone scanning for osseous metastases and osseous recurrence, and to CT for lung metastases. For Ewing's sarcoma bony metastases (n=49) FDG-PET showed a sensitivity and specificity of 100% and 96%, respectively, compared to 71% and 92% for technetium bone scan. Interestingly FDG-PET was falsely negative in all 6 osteosarcoma bony metastases. This was in contrast to evaluation of recurrent osteosarcoma which showed PET to be effective (n=6) in correctly identifying these lesions. FDG-PET failed to equal CT in sensitivity for pulmonary metastases, 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 all the literature cited PET and not combined PET/CT. Virtually all clinical studies done today are 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.

In summary, FDG-PET 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 primary recurrence in patients with orthopedic hardware that precludes 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 physician. Routine use of PET/CT beyond a problem-solving role has not been widely advocated in the literature, though individual and anecdotal experiences are increasing rapidly. The panel feels that this emerging technology deserves recognition at least as a problem solving tool and more likely 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 multi-center evaluation of its clinical value in the diagnosis, staging, response to therapy, and value in 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 sarcoma. 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.

Abbreviations

- CT, computed tomography
- MRI, magnetic resonance imaging
- NUC, nuclear medicine
- PET, positron-emission tomography
- US, ultrasound

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate selection and timing of radiologic exam procedures for follow-up of patients with malignant or aggressive musculoskeletal tumors

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- 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 comes out, and should be used only as a rough guideline with a lot of room for modification in individual circumstances.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Manaster BJ, Petersen B, Dalinka MK, Rubin DA, Rosen G, Lackman R, Janjan N, Expert Panel on Musculoskeletal Imaging. Follow-up of malignant or aggressive musculoskeletal tumors. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 11 p. [46 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 (revised 2006)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

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GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Musculoskeletal Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: B. J. Manaster, MD, PhD; Brian Petersen, MD; Murray K. Dalinka, MD; David A. Rubin, MD; Gerald Rosen, MD; Richard Lackman, MD; Nora Janjan, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Radiology (ACR), Expert Panel on Musculoskeletal Imaging. Follow-up examinations for bone tumors, soft-tissue tumors, and suspected metastasis post therapy. Reston (VA): American College of Radiology (ACR); 2002. 10 p. (ACR appropriateness criteria).

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 6, 2001. The information was verified by the guideline developer as of June 29, 2001. This summary was updated by ECRI on May 22, 2003. The updated information was verified by the

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