Use of Imaging Prior to Referral to a Musculoskeletal Oncologist

Abstract

The Musculoskeletal Tumor Society and American Academy of Orthopaedic Surgeons recently collaborated on a clinical practice guideline Use of Imaging Prior to Referral to an Orthopaedic Oncologist. The complete manuscript is available on OrthoGuidelines (www.orthoguidelines.org) and the Musculoskeletal Tumor Society website (www.msts.org). This clinical practice guideline is designed to assist practitioners without specialization in musculoskeletal tumors to determine the most efficacious imaging modalities for establishing an accurate diagnosis and treatment plan when confronted with a bone or soft-tissue lesion of unknown etiology. A panel of experts with interest and expertise in orthopaedic surgery, orthopaedic oncology, and musculoskeletal radiology created relevant questions and synthesized existing literature into 12 topics and 27 recommendations. The group considered several common clinical and radiographic features often seen at the initial presentation of a bone or soft-tissue tumor of the pelvis or extremities. This guideline is intended to inform front-line practitioners to give insight into imaging modalities that are of minimal clinical utility, as well as those that are critical to establishing an accurate diagnosis and assessing the urgency of referral to an oncologic specialist. In addition to a summary of the primary findings of the report, we included three cases that illustrate clinical scenarios in which the guidelines can assist in determining the most appropriate first-line management. The strengths of the relevant guidelines are noted.

Overview and Rationale

Orthopaedic tumors are generally considered to be rare entities seldom encountered by non–oncology-trained orthopaedic surgeons, primary care physicians, pediatricians, and surgeons. This notion is supported by the small number of fellows trained in orthopaedic oncology, typically 12 to 15 annually, the smallest of all of the orthopaedic subspecialties. A recent estimate of the distribution of orthopaedic oncologists suggests that there is one specialist per 1.6 million people in the United States (US). Furthermore, sarcoma, the quintessential primary malignancy of the connective tissue, accounts for only 1% of all cancers in adults and 15% in children. However, these numbers underestimate the true burden of all extremity tumors (including sarcoma, metastatic disease of bone, benign tumors, and tumor-like non-neoplastic conditions) and the commonality of encountering lesions of unknown
etiology in a community clinical practice. The American Cancer Society estimates that 12,750 new soft-tissue sarcomas would be diagnosed in the US in 2019. The American Academy of Orthopaedic Surgeons (AAOS) estimates that 50% of the new carcinoma cases in the US (approximately 1.2 million) will eventually metastasize to bone. A case series documenting the annual procedural volume of early-career orthopaedic oncologists suggested that the malignant entities, sarcoma and metastatic disease of bone, account for a minority of clinical evaluations by orthopaedic tumor specialists because 59% of the procedures are performed for benign entities. Additional reports of consecutive referrals to orthopaedic oncology practices found 70% to 72% of referrals were for lesions felt to be benign or non-neoplastic. This also underestimates the number of clearly benign lesions in the population at large, such as lipomas and asymptomatic enchondromas, which are either unrecognized and therefore not evaluated, or managed without specialist referral. This substantial burden of musculoskeletal abnormality and the possibility of inappropriate use of healthcare resources or delayed diagnosis of an unrecognized or misinterpreted malignancy were the primary motivators for creating this guideline.

Three prospective case series over the last 2 decades have attempted to comment on the most appropriate imaging modalities to be done by referring practitioners before evaluation by a specialist in orthopaedic tumors. This question is important to avoid over-imaging tumors of low-risk and quiescent biology, as well as recognizing tumors that are inherently aggressive and a threat to the survival of the afflicted. These previous reports demonstrated general agreement in the overuse of advanced imaging in orthopaedic tumors (MRI, CT, bone scan, and positron emission tomography [PET]), with benign bone tumors as the most common entity over-imaged. In addition, the studies' results demonstrated agreement in the propensity for physicians with orthopaedic training to overuse advanced imaging at the same rate as those without orthopaedic training, namely primary care practitioners, internists, pediatricians, general surgeons, and specialty surgeons. Finally, each report recommended that defined guidelines would assist practitioners to choose the best imaging modalities depending on the clinical presentation, physical examination, and appearance on plain radiographs.

In June 2015, the Evidence Based Medicine Committee of the Musculoskeletal Tumor Society identified the topic of imaging before referral to a musculoskeletal oncologist as one of interest and importance to orthopaedic surgeons, general surgeons, primary care physicians, advance practice providers, and any healthcare professional who may encounter a bone or soft-tissue tumor of unknown etiology in their practice. The Musculoskeletal Tumor Society secured matching funds in November 2015 from the AAOS Board of Specialty Societies Quality and Patient Safety Action Fund, designed to identify important quality and patient safety initiatives, thus allowing the project to be financially secured through completion.

In April 2016, we formed a working group of representatives from the AAOS, the Musculoskeletal Tumor Society, and the American College of Radiology. The working group was selected after soliciting volunteers from the relevant societies, ensuring that no participant had any financial conflicts of interest consistent with AAOS policy. The first task for this group was to formulate our questions of interest using the standard “population, intervention, comparison, and outcome” (eg, “PICO”) format. Once these 12 questions were agreed upon, an extensive literature review was performed by a medical librarian to identify all potentially relevant primary research manuscripts. The AAOS Evidence Based Medicine Unit then reviewed all abstracts and identified pertinent full-text articles for additional analysis and review of methodology and strength. In total, 9,978 abstracts were reviewed, 1,707 full-text articles were analyzed, and 158 articles were included to create the guidelines. Each recommendation contains the specific articles relevant to the question, the quality of the study, and comments from the workgroup regarding how they were interpreted. Readers are encouraged to access the complete guideline for a more comprehensive discussion.

We included articles of primary data only; review articles were excluded. Registry studies were included, given that they satisfied the other a priori inclusion criteria. We included retrospective noncomparative case series and case series of nonconsecutive enrollment; these were considered very low-quality data. The quality of evidence for each included report was assessed using modified versions of participating societies: Musculoskeletal Tumor Society, American Academy of Orthopaedic Surgeons, American College of Radiology. Guideline development participants: Benjamin J. Miller, MD, MS (Chair), Kenneth R. Gundie, MD, Carlos M. Pereira Betancourt, MD, Ahmet Salduz, MD, Ana Cecilia Belzarena Genovese, MD, Mark D. Murphy, MD, Michael Mulligan, MD, Kurt R. Weiss, MD, Lukas M. Nystrom, MD, Matthew R. DiCaprio, MD, Eric R. Henderson, MD, and Catherine C. Roberts, MD. Staff of the AAOS: Kaitlyn Sevarino, MBA, Jayson N. Murray, MA, Kyle Mullen, MPH, Anne Woznica, MLIS, AHIP, and Mary DeMars.
the GRADE and QUADAS instruments. We then determined the strength of the recommendation depending on the quality of the scientific reports from which the recommendation was drawn. For instance, if a recommendation was supported by two or more high-quality studies, the strength of the recommendation would be strong. In contrast, if the best evidence were from two or more moderate-quality studies, the strength of the recommendation would be moderate. Support from low-quality and very low-quality data would result in a limited strength of recommendation. Further detailed discussion on the methodology of assigning quality of literature and strength of recommendations is available in the full guideline.1 If there was no reliable supporting evidence, the working group had the opportunity to create a consensus statement based primarily upon expert opinion. The explanation of each topic also includes a section on future research with suggestions on how the data may be improved with further investigation.

These guidelines were created with the generalist, front-line practitioner in mind. The guidelines do not apply to imaging studies that may be necessary to completely characterize a known malignancy or clarify a subtle management decision; these decisions are left to the expertise of oncologic specialists at the treating centers. The target audience includes physicians, but also advanced practice practitioners (physician assistants and nurse practitioners), nurses, physical therapists, and anyone who may be involved in the initial evaluation of patients. Nonphysician providers are becoming increasingly important in modern delivery of care, and the recommendations apply to anyone making management decisions in patients with a musculoskeletal tumor.

Recommendations

**Indications for Plain Radiographs**

**Bone Tumors**
Moderate evidence supports using conventional radiographs in the initial evaluation of a bone tumor of unknown etiology.

*Strength of Recommendation: Moderate*

*Implication: Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.*

**Soft-Tissue Tumors**
In the absence of reliable evidence, it is the opinion of the work group that conventional radiographs are a reasonable diagnostic test and may be considered during the initial evaluation of a soft-tissue tumor.

*Strength of Recommendation: Consensus*

*Implication: In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.*

**Indications for Advanced Imaging Based on Radiographic Findings**

**Cortical Irregularity or Periosteal Reaction**
Moderate evidence supports the use of an MRI scan (or CT if MRI is not available) for evaluation of a cortical irregularity or periosteal reaction in patients with a potentially malignant bone tumor.

*Strength of Recommendation: Moderate*

*Implication: Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.*

**Tumor Interface**
Moderate evidence suggests that characterizing the tumor interface (borders and zone of transition) on MRI and CT may assist with obtaining a diagnosis or planning further diagnostic studies or treatment for bone or soft-tissue tumor of unknown etiology.

*Strength of Recommendation: Moderate*

*Implication: Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.*

**History of Pain**
Moderate evidence supports that both radiographs and MRI have weak sensitivity in determining malignancy but moderate to strong specificity in determining benignity of bone tumors in patients reporting pain.

*Strength of Recommendation: Moderate*

*Implication: Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.*

Limited evidence supports that a Tc99 bone scan may assist with obtaining a diagnosis or planning further diagnostic studies or treatment in patients with a bone tumor of unknown etiology and pain in the area of the tumor.

*Strength of recommendation: Limited*

*Implication: Practitioners should feel little constraint in following a recommendation labeled as Limited, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the
balance between benefits and potential harm. Patient preference should have a substantial influencing role.

In the absence of reliable evidence, it is the opinion of this work group that an MRI of a bone or soft-tissue tumor of unknown etiology should be considered and is the preferred advanced imaging study in patients with a report of pain at the site of the identified tumor.

**Strength of recommendation:** Consensus

Implication: In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

In the absence of reliable evidence, it is the opinion of this work group that contrast-enhanced CT scan of the site should be considered in patients with pain at the site of a bone or soft-tissue mass when there are patient-specific contraindications to MRI, such as a pacemaker or cerebral aneurysm clips.

**Strength of recommendation:** Consensus

Implication: In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

In the absence of reliable evidence, it is the opinion of this work group that contrast-enhanced CT scan of the site should be considered in patients with a report of pain at the site of the identified but undiagnosed tumor, CT of the chest/abdomen/pelvis, PET-CT, and Tc99 bone scan may assist with the diagnostic workup but should be used at the discretion of the treating oncologic specialists.

**Strength of recommendation:** Consensus

Implication: In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

**History of Growth**

Moderate strength evidence supports that, in patients suspected of soft-tissue tumor recurrence, an MRI of the tumor site can reliably identify neoplastic tissue and differentiate between solid and cystic areas.

**Strength of Recommendation:** Moderate

Implication: Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.

In the absence of reliable evidence, it is the opinion of this work group that an MRI should be considered, and is the preferred advanced imaging study, in patients with a clear history of rapid growth of a bone or soft-tissue mass.

**Strength of recommendation:** Consensus

Implication: In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

**Tumor size:**

Strong evidence supports the use of MRI imaging for a bone or soft-tissue tumor of unknown etiology with a size greater than 5 cm to assist with obtaining a diagnosis and planning further treatment.

**Strength of recommendation:** Strong

Implication: Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.

In the absence of reliable evidence, the work group recommends that, in aggressive-appearing bone or soft-tissue tumors, advanced imaging studies be requested with the guidance of an orthopaedic oncologist or musculoskeletal radiologist.

**Strength of recommendation:** Consensus

Implication: In the absence of reliable evidence, practitioners should
remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

**Indications for Staging Studies**

**Chest Radiograph Before Chest CT**

In the absence of reliable evidence, it is the opinion of the work group that a chest radiograph is not necessary before a chest CT in the staging of a bone or soft-tissue malignancy.

**Strength of recommendation:** Consensus

**Implication:** In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

**Technical Aspects of Cross-Sectional Imaging Studies**

**Use of Contrast in MRI**

Strong evidence supports that contrast enhancement on MRI can assist in determining whether a soft-tissue tumor is benign or malignant.

**Strength of recommendation:** Strong

**Implication:** Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.

Strong evidence supports that a heterogeneous signal in a contrast-enhanced MRI can assist in determining whether a soft-tissue tumor is benign or malignant.

**Strength of recommendation:** Strong

**Implication:** Practitioners should follow a Strong recommendation unless a clear and compelling rationale for an alternative approach is present.

In the absence of reliable evidence, the opinion of the work group that a magnet of at least 1.5 Tesla should be used when imaging musculoskeletal neoplasms.

**Strength of recommendation:** Consensus

**Magnet Strength in MRI**

**Area to Visualize in MRI and CT**

In the absence of reliable evidence, it is the opinion of the work group that MRI or CT scans performed to visualize a potentially malignant bone tumor should include a detailed assessment of the tumor and surrounding soft tissue, with additional sequences that visualize the entire bone compartment, from the proximal joint to the distal joint.

**Strength of recommendation:** Consensus

**Implication:** In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

In the absence of reliable evidence, it is the opinion of the work group that MRI or CT scans performed to visualize a soft-tissue tumor should include a detailed assessment of the tumor and surrounding soft tissue, including complete visualization of enhancement along fascial planes and peritumoral edema.

**Strength of recommendation:** Consensus

**Implication:** In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.
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**Use of Ultrasonography in Extremity Tumors**

Moderate evidence supports that ultrasonography helps to distinguish benign from malignant soft-tissue tumors.

**Strength of Recommendation:** Moderate

**Implication:** Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.

In the absence of reliable evidence, it is the opinion of the work group that ultrasonographies in large (>5 cm), deep soft-tissue tumors are unlikely to adequately assess the benign or malignant nature of the lesion and should not be the imaging modality of choice.

**Strength of recommendation:** Consensus

**Implication:** In the absence of reliable evidence, practitioners should remain alert to new information because emerging studies may change this recommendation. Practitioners should weigh this recommendation with their clinical expertise and be sensitive to patient preferences.

**Case Examples**

**Case Example: Incidental Finding in a Patient With Knee Pain**

**Presentation**

A 54-year-old woman had a 9-month history of medial-sided left knee pain. She stated that the pain was exacerbated by activity, was not present with rest, and did not wake her at night. She took acetaminophen and nonsteroidal anti-inflammatories as needed with relief of symptoms.

**Management**

Given a clinical presentation suggestive of mild knee degenerative joint disease, a plain radiograph was obtained (Figure 3). The radiographs demonstrated a radiodense lesion in the distal femoral diaphyseal-
metaphyseal junction, most consistent with a low-grade cartilaginous neoplasm, favoring benign enchondroma. No concerning features such as a periosteal reaction, poorly defined borders, or a soft-tissue mass was present. Clinically, her pain was explained by early and mild degenerative changes and was unlikely to be due to this lesion. None of the characteristics of her radiographic or clinical presentation justify advanced imaging. The most appropriate management is another plain radiograph in 3 months with continued surveillance to confirm stability every 3 to 6 months for 2 years.9 Discussion with a musculoskeletal radiologist or orthopaedic oncologist should be considered.

Case Example: Soft-Tissue Mass in a Thigh

Presentation
A 67-year-old woman had a subtle fullness in her right thigh. She stated that she first noticed this about 2 months ago and thought it may be enlarging. It was not painful at rest but was tender when compressed. On examination, there was a palpable mass on the medial aspect of the thigh >5 cm in diameter. The mass flattened when the knee was extended and there were no over-riding skin changes.

Management
Plain radiographs may be obtained during the initial evaluation of soft-tissue tumors (Figure 4). In this case, they revealed a soft-tissue density that was isointense with muscle, did not show any internal calcifications, and did not demonstrate an adjacent cortical reaction. At this point, the differential diagnosis remains wide and further imaging is warranted. Ultrasounds are a cost-effective and noninvasive intervention that can distinguish between benign and malignant entities (moderate evidence). However, they are more accurate in superficial lesions and may be inadequate in deep or large tumors such as this one. An MRI would be the study of choice in tumors larger than 5 cm (strong evidence) because it is able to reliably identify neoplastic tissue and distinguish between solid and cystic areas (moderate evidence) (Figure 5). If there is a question about the aggressiveness of the lesion, intravenous contrast may be used to determine whether the tumor is benign or malignant (strong evidence) because malignant tumors routinely demonstrate a heterogeneous signal (strong evidence). CT scans may be used in place of MRI in patients with contraindications (pacemaker, cerebral aneurysm clips). In this case, the MRI is highly suggestive of a malignancy, and the patient was referred to a sarcoma center before biopsy or additional imaging. A core needle biopsy was done, in line with the anticipated limb-sparing incision with guidance from the treating surgeon, and demonstrated a high-grade undifferentiated pleomorphic sarcoma. The patient was enrolled in a clinical trial and treated with

Figure 3
Radiograph of the distal femur demonstrating modest degenerative changes of the knee joint and a calcified intramedullary lesion consistent with an enchondroma.

Figure 4
Radiograph of the distal femur demonstrating a subtle soft-tissue mass without internal calcification.

Figure 5
MRI of the thigh demonstrating a heterogeneous mass that should cause concern for a soft-tissue sarcoma.

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neoadjuvant radiation before surgical excision.

References

References printed in **bold type** are those published within the past 5 years.


