Musculoskeletal MRI: Contrast and non-contrast applications

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Over the past 10 to 15 years, magnetic resonance imaging (MRI) has had a major impact on musculoskeletal imaging. Excellent soft-tissue contrast, spatial resolution, and multiplanar imaging are among the major advantages of MRI. The majority of applications for musculoskeletal MRI fall into one of three major categories of disease: (1) tumors and tumor-like conditions; (2) infectious processes; and (3) derangement within and about joints. Although non–contrast-enhanced MRI is sufficient for the evaluation of many musculoskeletal conditions, the addition of either intravenous (IV) or intra-articular gadolinium-based contrast agents is, at times, necessary to improve the evaluation of certain disease processes.

Basic principles of gadolinium contrast agents in musculoskeletal imaging

Whether administered intravenously or intra-articularly, gadolinium-based contrast agents cause T1 shortening, due to their paramagnetic properties, which enhances relaxation rates of nearby protons. When administered intravenously, gadolinium contrast compounds, just as iodinated contrast agents, distribute rapidly within the intravascular space, diffuse within the extracellular space, and are excreted by the kidneys. T1-weighted sequences depict areas of contrast enhancement. Contrast-enhanced T1-weighted sequences with chemical fat suppression will increase the conspicuity of the area of contrast enhancement and may help to differentiate regions of enhancement from fatty tissue.

When administered intravenously, the standard dose of contrast for musculoskeletal applications is 0.1 mmol/kg of body weight. Standard static or dynamic images can be performed. Static postcontrast images are obtained at a set time interval shortly after IV contrast administration. Dynamic postcontrast imaging is utilized primarily in evaluating neoplastic processes. Typically, ultra-fast T1-weighted snapshot sequences are performed during the first 3 minutes following bolus contrast injection. Images are obtained at an optimal rate of one image per 3.5 to 7 seconds through a preselected slice, which optimally represents the tumor. Utilizing postprocessing software, signal intensity-to-time curves can be obtained and analyzed. The multiple images obtained during the period of contrast enhancement can also be viewed in a cine format.

MR arthrography is an emerging technique, utilized to evaluate pathology in and about joints. MR arthrography can be performed either directly or indirectly. In the direct technique, gadolinium is injected directly into the joint space. A 20- or 22-gauge needle is placed within the joint of interest (with or without fluoroscopic guidance, depending on the joint). If using fluoroscopic guidance, a small amount of iodinated contrast can be injected to confirm needle position. Depending on the joint involved, a variable amount of gadolinium-saline solution (typically a 1:200 to 1:250 ratio of gadolinium to saline), with or without lidocaine, is
injected into the joint space. The joint can then be imaged immediately following contrast injection, and ideally within 30 to 45 minutes, to maximize distention of the joint space and to minimize absorption of contrast from the joint space. Typically, T1-weighted sequences with fat suppression and T2-weighted sequences are utilized.5,6

In contrast to direct MR arthrography, indirect MR arthrography utilizes an IV injection of gadolinium. Following a delay of 5 to 20 minutes and exercise of the joint to optimize distribution of gadolinium, the contrast will have diffused from the synovium into the joint fluid.6

Gadolinium contrast agents are relatively safe, with the most common reactions reported to be headache, nausea, dizziness, and injection-site symptoms. Serious reactions, such as death due to anaphylaxis, are rare. The overall reaction rate, with a 0.1 mmol/kg dose, is reported to be 2.4%. The most frequent symptoms included nausea (0.4%) and headache (0.4%).7 No known reported deaths rates due to intravenous gadolinium-based contrast agents have been published.

Musculoskeletal tumors
Although conventional radiographs remain the most reliable predictor of tumor histology,4 MRI can be a powerful tool in the evaluation of tumors of soft tissue and bone. When determining the intra- or extracompartmental extent of a tumor and its relationship to neighboring structures, for example, MRI is the modality of choice.6 The indications for IV gadolinium in augmenting the MRI evaluation of tumors is not entirely clear, since a great deal of information can be obtained from non–contrast-enhanced T1- and T2-weighted, as well as other non–contrast-enhanced sequences. Studies have shown that contrast adds further significant information in only ≤10% of patients evaluated.6 Non–contrast-enhanced MRI scans can characterize most lesions accurately, including lipoma, nerve sheath tumor, pigmented villonodular synovitis, and many sarcomas.6 This section will review the broad categories of tumor evaluation and how they might benefit from the IV administration of gadolinium. These categories include local staging/biopsy planning, tissue characterization, evaluating response to chemotherapy, and detecting recurrence.2

Local staging/biopsy planning
Evaluating the local extent of a tumor is the most important role for MRI in tumor evaluation.11 Bone, joint, muscle, and neurovascular involvement must all be defined accurately before biopsy can be performed and subsequent therapy planned. Unenhanced MRI is generally quite good at delineating the relationship between these structures and the tumor (figure 1). Most tumors have low signal on T1-weighted sequences, which are best for evaluating marrow involvement. Generally, tumors and peritumoral edema have high signal on T2-weighted images, and thus are readily distinguishable from adjacent muscle or bone.11 However, the use of contrast can assist in determining the extent of tumor versus non-neoplastic peritumoral edema.3 Accurate delineation of tumor margins may be helpful in surgical planning, particularly when limb-sparing surgery is contemplated.11

One area in which gadolinium...
appears to be of particular value is in assisting in biopsy. This may be especially important in bulky tumors with large areas of necrosis. Biopsy can thus be targeted to the solid, enhancing tissue, which is presumed to be viable.2

**Tissue characterization**

Contrast-enhanced MRI is limited in its ability to distinguish benign from malignant tumors.12 Malignant tumors are thought to possess a greater degree of enhancement, as well as more rapid uptake of contrast.2 Static and dynamic postcontrast imaging have been studied, but despite these techniques, there is a high degree of overlap between the appearance of many malignant and benign tumors. In fact, the correct histological diagnosis can be made in only 25% to 30% of lesions, when based on MRI alone.12 Rim-to-center differential enhancement ratios have been proposed as a method for histologic evaluation,11 but more research needs to be performed in this area before MRI can be used to distinguish benign from malignant tumors accurately.

Although contrast-enhanced MRI may not be optimal for distinguishing benign from malignant tumor, it can assist in determining several other potentially important tissue characteristics.

Contrast-enhanced MRI can be used to differentiate solid from cystic lesions, especially when signal characteristics on non–contrast-enhanced sequences do not clearly make this distinction. Cystic or partially cystic lesions are identified readily due to their lack of internal enhancement.12 Patterns of rim enhancement (thin versus thick), as well as enhancing internal septations, also assist in diagnosis. Benign and malignant lesions that may appear cystic on non–contrast-enhanced sequences include synovial or ganglion cyst, lymphoceles, seroma, abscess, bursitis, chondrosarcoma, myxoid lesions (benign and malignant), sarcomas, and metastases.14 Administration of gadolinium may help in differentiating these entities, when the diagnosis is not clear on non–contrast-enhanced images.

Another application for utilizing contrast is in the evaluation of hematomas. In rare circumstances, sarcomas may present within muscle hematoma. Administration of gadolinium will reveal small enhancing foci of tumor, which would go undetected on non–contrast-enhanced imaging. The only caveat is that fibrovascular tissue in organizing hematomas may show enhancement.2,12

**Response to chemotherapy**

The initial response to chemotherapy is an important predictor in determining eventual treatment outcome. Treatment protocols (including chemotherapy regimen, surgery timing, and radiation therapy) are often influenced by determination of the initial response to therapy.2 Unfortunately, conventional radiographs, computed tomography (CT), radionuclide studies, and static contrast-enhanced MRI have not been shown to be effective in measuring response to initial chemotherapy. Several studies have shown that dynamic contrast-enhanced MRI is a promising technique in measuring initial tumor response to therapy.4 As described earlier, tumor enhancement curves with respect to time are obtained following bolus administration of contrast, using fast low-angle shot (FLASH) sequences. Curves are obtained both before and during initial chemotherapy. Responders will show a decrease in the slope of the curve following treatment.2,4 The limitations are that dynamic contrast MRI is not widely available, it is time-consuming, and is not yet completely reliable.12

**Detecting tumor recurrence**

MRI is extremely useful in the follow-up of patients following treatment for bone tumors. Low signal on both T1- and T2-weighted sequences in the previous site of tumor is a good indicator of no tumor recurrence. In certain instances, high T2 signal regions may persist within the post-treatment site. The appearance, however, is nonspecific and may represent necrosis, edema, hemorrhage, granulation tissue, or recurrent edema.2 Static postcontrast images may be helpful in this instance, but reactive tissue and residual tumor may both enhance to a similar degree on the static postcontrast images. Dynamic contrast-enhanced MRI may play a role in these situations.2,4 Tumors will enhance quickly, whereas reactive tissue will enhance more slowly.

**Musculoskeletal infection**

Musculoskeletal infections, including cellulitis, fascitis (including necrotizing fasciitis), myositis/pyomyositis, septic arthritis, septic tenosynovitis, and osteomyelitis, may affect a variety of structures, including skin, fascia, muscle, joints, tendon sheaths, and bone.15 Such infections are usually detected clinically with symptoms that include local or diffuse swelling, erythema, pain, and fever. Laboratory tests, including erythrocyte sedimentation rate, white blood cell count, and blood cultures, can help confirm the diagnosis.16 The most common pathogens include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*. When the skin is disrupted due to trauma, surgery, or vascular compromise, the risk of osteomyelitis is greater. Imaging is usually obtained when osseous infection is suspected, in complex soft-tissue infections, or if response to antibiotic therapy is poor.15

The initial imaging of osteomyelitis typically consists of conventional radiographs; however, this method is insensitive and may take up to 10 days to reveal an abnormality. Radionuclide studies can be helpful, but are often nonspecific, and cannot differentiate neoplasm, infection, and trauma reliably. Non–contrast-enhanced MRI is a cost-effective, sensitive, and specific study for detecting osteomyelitis (figure 2). The reported rates of sensitivity and specificity for MR detection of osteomyelitis range from 86% to 98% and 77% to 100%, respectively.16 Standard sequences may include a combination of T1-weighted, T2-weighted, and/or short tau inversion recovery (STIR) or
T2-weighted sequences with chemical fat suppression. T1-weighted images are generally best for evaluating marrow infection. T1-weighted sequences will show infection as intermediate or low signal within the bone marrow. Infection is high in signal on T2-weighted and STIR images. Chronic and acute osteomyelitis can be distinguished, as well. Acute disease causes poor definition of soft-tissue planes, lack of cortical thickening, and indistinct transition between normal and abnormal bone marrow. Chronic osteomyelitis will show cortical thickening and a more readily defined distinction between the normal and abnormal tissues.

In both osteomyelitis and soft-tissue infections, MRI can depict the extent of infection accurately. Determining the presence of necrotic tissue or abscess is also important in treatment planning. Necrotic tissue is treated surgically, whereas viable tissue is treated with antibiotics. The addition of IV contrast will readily demonstrate areas of necrosis or abscess (figure 3). Distinguishing viable from necrotic tissue will also aid in biopsy or fine-needle aspiration for culture. If surgery is contemplated, the excellent spatial resolution of MRI will aid in surgical planning.
MRI is also very sensitive for detection of septic arthritis. Very small joint effusions are detected readily. The addition of contrast may reveal enhancement and hypertrophy of the synovium. These findings may also be seen in transient synovitis, but the presence of adjacent signal abnormality within the bone is more specific for septic arthritis.16

**Evaluation of internal joint derangement**

MRI evaluation of the bones and soft tissues around the joints has been a major advance in musculoskeletal imaging. The normal anatomy, as well as pathology of joints, can be evaluated in exquisite detail. The role of non–contrast-enhanced MRI in imaging suspected joint injuries is well established. MRI will often confirm clinically suspected injuries such as meniscal tears and ligament or tendon injuries (figure 4). It can also uncover unsuspected pathology, which may either guide arthroscopy or would have been difficult to detect with arthroscopy. Recent studies in the orthopedic literature on the impact of shoulder MRI on clinical decision making showed that MR evaluation made statistically significant changes in clinical management.18

When gadolinium is used in the evaluation of joint injury, it is primarily used for direct MR arthrography. Direct MR arthrography with gadolinium is an emerging technique that relies on the improved visualization of the articular structures when intra-articular fluid is present. Distention of the joint space by the intra-articular injection of gadolinium is a key contributor to the improved assessment of complex intra-articular structures.5,19

A detailed discussion of all current indications for direct MR arthrography is beyond the scope of this paper; however, some situations where it is advantageous over conventional MRI include the evaluation of labral abnormalities of the hip, osteochondral injuries, intra-articular loose bodies, postoperative evaluation of the knee after meniscal repair, characterization of ankle/elbow ligament injuries, and evaluation of glenohumeral joint instability (figure 5).20 The most common studies performed are for evaluation of shoulder joint instability and the post-operative knee.6

Drawbacks of direct MR arthrography, aside from patient discomfort, include that it is invasive and time-consuming and has the potential for complications. Morbidity with MR arthrography, however, appears to be low, with one study reporting an adverse reaction rate of 3.6%.21 The most common side effects included pain, vasovagal reaction, and urticaria.21 Another recent study found that the majority of patients undergoing the procedure found it acceptable, in that they were willing to undergo pain, anxiety, and potential complications in order to achieve a potentially more accurate diagnosis.20

Indirect MR arthrography is an alternative to the direct method. Indirect arthrography involves IV injection of contrast and imaging the joint after a...
5- to 20-minute delay, as described earlier. Following the delay, the joint fluid will enhance, creating an arthrogram. Advantages of this technique over direct MR arthrography are that it is less invasive and less time-consuming to perform. However, one major disadvantage is that if no native effusion is present, the diagnostic advantage of a distended joint space is not present, as it is in direct MR arthrography. Studies comparing the efficacy of indirect MR arthrography to conventional MRI and direct MR arthrography are ongoing. Preliminary studies suggest that indirect MR arthrography may be superior to non-contrast MRI in detecting similar types of pathology that are more readily detected with direct MR arthrography. However, further studies need to be performed in order to more clearly define the role of indirect MR arthropathy and in which circumstances it may be an acceptable alternative to direct MR arthrography.

Conclusion

MRI is well established as an important tool in evaluating a variety of musculoskeletal disorders. Conventional non–contrast-enhanced MRI provides an excellent means of evaluating the above-mentioned major musculoskeletal disease categories, as well as potentially many others. The role of the use of gadolinium contrast agents is under ongoing investigation. However, there are numerous situations in which its use is beneficial. In tumor imaging, the routine use of gadolinium is not necessarily warranted, but it can assist in biopsy planning and more accurate delineation of tumor margins. Dynamic contrast-enhanced MRI has potential roles in gauging tumor response and recurrence. The routine diagnosis of osteomyelitis does not require administration of gadolinium. Imaging of more complicated osseous and soft-tissue infections, especially where infection extent and necrosis are of concern, will benefit from IV contrast. Finally, in the evaluation of suspected articular injuries or postoperative joints, MR arthrography is an emerging technique, which is superior to non–contrast-enhanced MRI in certain clinical scenarios.

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REFERENCES


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