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SCIENTIFIC ARTICLE

Society of skeletal radiology position paper – recommendations for contrast use in musculoskeletal MRI: when is non-contrast imaging enough?

Jonathan D. Samet[1] · Hamza Alizai[2] · Majid Chalian[3] · Colleen Costelloe[4] · Swati Deshmukh[5] · Vivek Kalia[6] · Sarah Kamel[7] · Jennifer Ni Mhuircheartaigh[5] · Jimmy Saade[8] · Eric Walker[9] · Daniel Wessell[10] · Laura M. Fayad[11]

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Abstract

The following White Paper will discuss the appropriateness of gadolinium administration in MRI for musculoskeletal indications. Musculoskeletal radiologists should consider the potential risks involved and practice the judicious use of intravenous contrast, restricting administration to cases where there is demonstrable added value. Specific nuances of when contrast is or is not recommended are discussed in detail and listed in table format. Briefly, contrast is recommended for bone and soft tissue lesions. For infection, contrast is reserved for chronic or complex cases. In rheumatology, contrast is recommended for early detection but not for advanced arthritis. Contrast is not recommended for sports injuries, routine MRI neurography, implants/hardware, or spine imaging, but is helpful in complex and post-operative cases.

Keywords Contrast use · Gadolinium administration · MRI

✉ Jonathan D. Samet
jsamet@luriechildrens.org

✉ Laura M. Fayad
lfayad1@jhmi.edu

Hamza Alizai
hamzaalizai@gmail.com

Majid Chalian
mchalian@uw.edu

Colleen Costelloe
ccostelloe@mdanderson.org

Swati Deshmukh
sdeshmuk@bidmc.harvard.edu

Vivek Kalia
vivekkalia@gmail.com

Sarah Kamel
sarah.kamel@jefferson.edu

Jennifer Ni Mhuircheartaigh
jnimhuircheartaigh@gmail.com

Jimmy Saade
drjsaade@gmail.com

Daniel Wessell
wessell.daniel@mayo.edu

[1] Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University, Chicago, USA

[2] CHOP Department of Radiology, Children's Hospital of Philadelphia, Philadelphia, USA

[3] Department of Radiology, University of Washington, Seattle, USA

[4] The University of Texas MD Anderson Cancer Center, Houston, USA

[5] Beth Israel Deaconess Medical Center, Boston, USA

[6] Children's Scottish Rite Hospital, Dallas, USA

[7] Thomas Jefferson University Hospital, Philadelphia, USA

[8] Creighton University School of Medicine, Phoenix Regional Campus, Phoenix, USA

[9] Penn State Health Milton S Hershey Medical Center, Hershey, USA

[10] Mayo Clinic Jacksonville Campus: Mayo Clinic in Florida, Jacksonville, USA

[11] Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins Medicine, Baltimore, USA

Introduction

Gadolinium-based contrast agents (GBCA) have become an integral part of medical practice in the USA, although there are short- and long-term risks associated with their use. The short-term risks include issues with intravenous access including infection, contrast extravasation, and air embolus. There are also acute adverse reactions which are divided into physiologic reactions (metallic taste, nausea, vomiting, vasovagal reaction, shortness of breath) and rare allergic-like reactions (rate of 0.1%). Of the allergic-like reactions, 90% are urticaria (hives), and 10% are anaphylaxis, with a risk of death of 1 per million [1]. GBCA are contraindicated in pregnancy, as they cross the placenta into the fetal circulation, are excreted by fetal kidneys, and remain in amniotic fluid for the length of the pregnancy. Since only a very small percentage of the GBCA that is excreted into breast milk is absorbed by infants' gut, the latest recommendation from the ACR and ACOG is to not interrupt breastfeeding after GBCA administration [2].

Long-term risks from GBCA administration, including nephrogenic systemic fibrosis (NSF), are associated with older linear Group I agents [3]. Macrocyclic agents lack association with NSF. The lack of cases associated with Group II GBCAs led to the ACR's recommendation that eGFR screening is no longer necessary when these types of contrast are administered [4-6].

Despite the safety of Group II agents with respect to NSF, the discovery of retained gadolinium deposition in the brain after the administration of macrocyclic as well as linear agents has led to renewed debate over the administration of GBCA for medical imaging [7, 8]. An unrevised statement issued by the FDA in 2017 indicated that there was no evidence that gadolinium deposition in the brain is clinically harmful, but a new class warning was also issued later that year stating that brain deposition occurs and that the distribution of a new patient medication guide was deemed necessary to properly inform patients of the issue [9].

In addition to the potential side effects of contrast, there is a growing body of literature which states that contrast is not necessary for certain indications [10-13]. Other disadvantages include longer scan times when contrast is administered.

The following White Paper will discuss the appropriateness of gadolinium administration in MRI for musculoskeletal indications. Musculoskeletal radiologists should consider the potential risks involved and practice the judicious use of intravenous contrast, restricting administration to cases where there is demonstrable added value (Table 1).

Oncology: bone lesions

Background

MRI plays a vital role in the evaluation of bone lesions. Non-contrast conventional (T1-weighted (T1W), fluid-sensitive) and advanced (diffusion-weighted imaging (DWI), chemical shift imaging (CSI)) techniques, combined with radiography and clinical data, are often adequate for detection, characterization, and evaluation of the extent of pediatric and adult bone lesions [14, 15].

Added benefit of contrast

Following contrast administration, bone tumors may exhibit a variety of characteristics that can be used for tumor characterization, biopsy planning, and treatment response assessment [16]. Differentiating a solid from a cystic lesion is paramount to bone lesion interpretation and management, with non-neoplastic fluid-containing entities including subchondral cysts, abscesses, and simple bone cysts that may all mimic tumors [17]. In addition, chondroid lesions are inherently T2 hyperintense and could be mistaken for a cystic lesion without contrast. While not always required for bone tumor detection and determination of medullary extent [18-20], contrast can be helpful for assessing soft tissue extent.

Detection and extent of disease

For the detection and determination of the extent of bone lesions, a non-contrast T1W sequence (SE/FSE) is often sufficient and forms the foundation of a bone tumor MRI protocol by offering excellent contrast resolution between the tumor and the background of normal fatty marrow. In the presence of abundant red marrow, the detection and evaluation of the extent of the tumor may be limited. In this case, the addition of DWI and in-phase (IP) and opposed-phase (OP) imaging reveals the bone tumor extent. Bone marrow imaging is especially challenging in the pediatric population due to a drastically changing proportion of red marrow with age. However, this, too, can be improved by the use of DWI and chemical shift imaging [18, 19, 21]. The Dixon method can achieve uniform fat suppression and is useful for detecting pathology on post-contrast imaging [22].

Characterization

For the characterization of bone lesions, conventional MRI lacks adequate specificity. For this reason, intravenous contrast is often administered during the workup of an unknown lesion to differentiate cysts from solid lesions, to

Table 1 Summary of recommendations for contrast use in musculoskeletal MRI

	Contrast recommendation	Explanation, exceptions, and considerations
Oncology – bone lesions		
Detection	No	Utilize DWI, CSI if possible
Disease extent	No	Utilize DWI, CSI if possible
Characterization	Yes	Utility: -Cyst vs. solid -Benign vs. malignant -Biopsy planning
After neoadjuvant therapy and surgery	Yes	Utility: -Diagnose recurrent tumor
Oncology – soft tissue lesions		
Detection	No	Non-contrast imaging sufficient
Disease extent	Yes	DWI may serve the same role as contrast
Characterization	Yes	Utility: -Cyst vs. solid -Benign vs. malignant -Low vs. high flow -Biopsy planning (-DWI may be sufficient for some histologies)
After neoadjuvant therapy and surgery	Yes	Utilize DCE for recurrent tumor vs. scar and post-operative collections
Infection – adults		
Routine acute and chronic osteomyelitis	No	T1w and T2w images typically adequate
Complications of subacute and chronic osteomyelitis	Yes	Utility: -Detect bone and soft tissue abscesses -Detect ulcers, sinus tracts
Neuropathic joint with superimposed infection	Yes	Utility: -Highlight ulcer and sinus tracts as signs of infection
Extent of soft tissue infection	Yes	Utility: -Highlight devitalized tissue
Rheumatology		
Extremities		
Early arthritis detection	Yes	Utility: detect synovitis (Consider for follow-up of synovitis)
Advanced arthritis	No	Utility: -Erosions and marrow edema well seen on non-contrast MRI -Difficult to distinguish synovitis related to joint damage from active disease
Inflammatory myositis	No	
Axial skeleton		
Sacroiliitis	No	Subchondral marrow edema, erosions, and sclerosis well seen on non-contrast MRI
Cervical, thoracic, lumbar	Controversial	Utility: detect synovitis
Osteonecrosis		
Femoral head – adult	No	
Femoral head – pediatric	Yes	Utility: Perthes diagnosis
Scaphoid fracture AVN evaluation	-No for advanced AVN -Controversial for early AVN	Contrast may be helpful for the diagnosis of early AVN, although physiologic and technical factors confound the post-contrast MRI appearance of the bone
Pediatrics		
Perthes disease of femoral head	Yes	Note: image bilateral to detect asymmetry in perfusion
Vascular anomaly	Yes	Utilize DCE-MRI to distinguish high vs. low flow

Table 1 (continued)

	Contrast recommendation	Explanation, exceptions, and considerations
Infection	Yes in infants No in older children	Utility: -Detect infection of unossified bone -Improve reader confidence
Tumor	Same as adult recommendations	
Rheumatology	Same as adult recommendations	
Sports injuries		
Routine injury	No	Non-contrast is first line
Labral tear	No	MR arthrogram if high-resolution MRI not available or inconclusive
Cartilage	No	dGEMRIC may be considered if other non-contrast techniques not available
Neurography		
Routine evaluation	No	Contrast may be helpful for peripheral tumors, polyneuropathies, and post-operative collections Contrast may be helpful for suppression of background signal
Implants/hardware		
Routine use	No	
Tumor prosthesis	Yes	DCE especially helpful Subtraction is recommended if contrast used
Infection	Yes	Subtraction is recommended if contrast used
Recurrent hemarthrosis	Yes	Subtraction is recommended if contrast used
Spine		
General back pain	No	
Fracture/trauma	No	
Degenerative disease vs. discitis/osteomyelitis	Yes	
Post-operative – cervical	No	
Post-operative – lumbar	Yes	
Abnormality in the canal	Yes	Utility: demyelinating, oncologic, infectious, and vascular conditions

help differentiate benign and malignant solid lesions, and to aid in biopsy planning. However, there is a significant overlap between enhancement characteristics of benign and malignant lesions on conventional post-contrast anatomic imaging [23, 24]. This overlap can be reduced with DCE-MRI dynamic contrast-enhanced MRI (DCE-MRI) [25].

Treatment response assessment and post-surgical evaluation

Following treatment (after neoadjuvant therapy or after surgical resection), the administration of contrast is routinely performed to identify post-treatment necrosis, viable tumor, and enhancing recurrence. DCE-MRI is the preferred method for such assessments when available, as the features of post-treatment fibrosis/granulation tissue overlap with a residual or recurrent tumor on static post-contrast imaging [14, 16, 26, 27], and is especially valuable in the presence of surgical reconstruction hardware [28, 29].

Controversies/gaps in knowledge/future direction

The use of DCE-MRI is not widespread, with varied technical considerations for the implementation of qualitative, semi-quantitative, and quantitative analysis. Qualitative DCE-MRI increases diagnostic confidence in characterizing malignant tissue through the visual display of arterial phase enhancement [25]. Non-contrast techniques, including DWI with apparent diffusion coefficient (ADC) mapping, have been shown to offer benefits for some applications such as characterization, but lack spatial resolution. As advances in non-contrast techniques progress, the role of intravenous contrast may decrease.

Quantitative DCE-MRI is more complicated and requires post-processing time [14] and is thus not routinely used clinically. Future directions include research regarding optimal acquisition parameters, MRI sequences, and analytic methods for tumor perfusion imaging and the incorporation of such data into radiomics analysis for the assessment of tumor character and treatment. Machine learning algorithms

may provide information for various tumor applications and also reduce the time constraints of performing quantitative DCE-MRI [30]. Finally, an additional consideration is the role of MRI for imaging tumor prostheses and the role of intravenous contrast in this setting. However, the role of non-contrast techniques such as DWI and CSI, among others, may limit the need for contrast in the future.

Recommendations

Intravenous contrast administration is typically not required for the detection of bone lesions or the evaluation of their extent in the medullary canal, especially with the advent of DWI and CSI. Contrast, in particular DCE-MRI, is recommended for the characterization of lesions (for distinguishing cystic from solid lesions and benign from malignant lesions) and biopsy planning when alternative non-contrast sequences (DWI) are not available. The administration of contrast is recommended for the assessment of response after neoadjuvant therapy, and for the detection of recurrence after surgery, with DCE-MRI providing the highest specificity for differentiating post-treatment fibrosis from the viable tumor.

Oncology: soft tissue lesions

Background

Contrast reveals the internal vascular composition of soft tissue lesions, which in turn may help decide if a biopsy is needed [31]. Avascular non-enhancing lesions of the musculoskeletal system are less likely to be malignant yet still may need to be surgically managed.

Added benefit of contrast

Soft tissue tumor detection is often detected clinically without imaging. Intravenous contrast helps with characterization, distinguishing cystic from solid lesions. Lesions with solid enhancement may be malignant, and DCE-MRI offers greater insight into lesion hemodynamics than static imaging, distinguishing high flow/arterial phase enhancement from low flow/venous phase enhancement [32]. This distinction is particularly useful in vascular anomaly workup and guides management [33, 34].

When planning a biopsy, contrast enhancement can help guide needle placement by identifying the most vascular/cellular portion of the lesion, increasing the likelihood that the sample will accurately reflect the histology of the tumor [6].

In oncologic imaging, malignant soft tissue tumors are more likely to have early arterial enhancement with fast wash-out (high flow), whereas benign lesions or post-operative scar/granulation tissue will show delayed wash-in and delayed wash-out [35-38]. Similarly, DCE-MRI can facilitate the early detection of recurrent sarcoma nodules as they will have early arterial enhancement compared with nodular-appearing scar [6, 25, 36, 39, 40].

Characterization

On static post-contrast T1-weighted imaging, ganglion cysts and lymphatic malformations demonstrate thin rim and/or septal enhancement as key distinguishing post-contrast features [24]. In the instance of a hematoma which is intrinsically hyperintense on T1, contrast with subtraction images are useful to document the lack of internal enhancement that would otherwise be seen with a tumor [35]. Non-cystic soft tissue tumors will have some degree of solid, nodular, or thickened septal contrast enhancement. In particular, the presence of pre-therapeutic central necrosis, as demonstrated on contrast-enhanced MRI, has been found to be a prognostic indicator of high histologic grade in soft tissue sarcomas [41].

When available, DCE allows for the analysis of tumor perfusion characteristics which can provide additional useful information [42]. DCE can identify high or low perfusion areas of a tumor due to the high temporal resolution of the scan [25]. Malignant soft tissue tumors will appear in the early phase due to tumor neovascularity [36], while many benign lesions demonstrate delayed initial perfusion as well as protracted wash-out [6]. Venous malformations will have variable enhancement depending on the timing of imaging, but will progressively fill in on delayed phase images [34], while arteriovenous malformations will show early enhancement by DCE-MRI.

Extent

The extent of a soft tissue tumor is often defined on non-contrast T1-weighted and fluid-sensitive sequences. When the margin of the tumor is not well defined on fluid-sensitive sequences or there is an accompanying perilesional signal, intravenous contrast administration and DWI are helpful for defining the true extent of the lesion.

Therapeutic assessment (surgical and systemic)

Prior to surgical resection, a tumor in situ undergoing systemic therapy may diminish in enhancement following successful therapy, particularly with the development of post-therapeutic necrosis [6]. It should be noted that tumors which develop post-treatment granulation tissue and scarring rather than necrosis still enhance with contrast administration.

In the post-resection follow-up of soft tissue malignancies, static contrast administration and DCE have been shown to detect early recurrences [6, 25, 39]. DCE can also help distinguish nodular enhancing foci of post-operative granulation tissue or scar (delayed enhancement) from the recurrent tumor (early arterial enhancement) [36, 39, 40, 43]. Both static and dynamic enhancement distinguish recurrent tumor (solid enhancement) from post-operative fluid collections (thin peripheral and no central enhancement) [6].

Controversies/gaps in knowledge/future direction

Diffusion-weighted imaging (DWI) with ADC maps has been shown to be a useful non-contrast oncologic biomarker in initial characterization, assessment of the extent, and monitoring of soft tissue tumors after treatment. Therefore, as DWI techniques improve, the role of contrast enhancement may diminish. For example, for peripheral nerve tumors, ADC values help distinguish benign and malignant disease [44-46].

Tumor perfusion imaging with more robust quantification of vascularity will help to refine the characterization of lesions and monitor response to therapy, especially with the incorporation of radiomics and, perhaps, machine learning algorithms. Investigations of additional biomarkers for soft tissue tumor characterization and assessment of viable malignancy are needed and may emerge with advances in DWI, MRI spectroscopy, and susceptibility-weighted imaging [37].

Recommendations

Intravenous contrast is recommended for the initial assessment of uncharacterized soft tissue lesions and for post-therapeutic evaluation. DCE, if available, is recommended as a routine sequence to accompany static post-contrast imaging. Of note, DWI may be sufficient for the characterization of some histologies without intravenous contrast.

Non-spinal musculoskeletal infection in adults

Background

Musculoskeletal infections are commonly imaged with MRI and are classified by the areas affected as soft tissue, joint, and bone infections. Early diagnosis of infection is necessary to prevent the serious complications of joint damage, limb deformity, and a requirement for amputation, among other less serious complications [47].

Added benefit of contrast

Soft tissue infection

Cellulitis will typically enhance on post-contrast MRI, helping to distinguish it from non-infectious soft tissue edema [47, 48]. Similarly, pyomyositis will enhance on post-contrast imaging, and fascial enhancement will be a sign of fasciitis, even present in the early stages of necrotizing fasciitis. While abscesses are readily visible on non-contrast T2-weighted images, they will be increased in conspicuity on post-contrast imaging with rim enhancement leading to higher levels of diagnostic confidence for radiologists [13]. Intravenous contrast can also highlight the margins of ulcers and sinus tracts, as there is a peripheral enhancement in these regions [48]. Importantly, devitalized or ischemic tissue is detectable by MRI as an area lacking contrast enhancement and could indicate necrotic tissue which needs to be debrided [48].

Joint infection

Joint effusion and synovitis are hallmarks of septic arthritis. The effusion is easily seen on non-contrast T2-weighted images. However, on post-contrast imaging, there is synovial thickening and hyperenhancement, characteristic of the accompanying synovitis.

Osteomyelitis

In acute osteomyelitis, there is hyperenhancement of the medullary space which often parallels hyperintensity on T2-weighted images.

In subacute or chronic osteomyelitis, contrast can help delineate sinus tracts, intra-osseous abscesses, and necrotic bone [47, 49]. A sequestrum, or focus of dead bone in chronic osteomyelitis, will be non-enhancing centrally and have peripheral enhancement related to granulation tissue [49, 50].

One common clinical challenge is distinguishing neuropathic arthropathy from osteomyelitis. Contrast can help identify ulcers and sinus tracts to underlying bone surfaces which are key features of osteomyelitis in this setting [48].

Controversies/gaps in knowledge/future direction

While contrast may increase the confidence of a radiologist and help highlight pathologic findings, many of the imaging findings of musculoskeletal infection can be adequately diagnosed without contrast [10, 13]. Osteomyelitis can be confidently diagnosed when there is a confluent low T1 signal and corresponding high T2 signal in the medullary space [48]. In fact, poorly enhancing tissue

is not necessarily necrotic and may be ischemic or due to venolymphatic congestion [48], features which could lead to misinterpretation. Furthermore, abscesses demonstrate restricted diffusion on diffusion-weighted imaging, negating the need for contrast [51]. Additionally, small abscesses that may be missed on non-contrast imaging alone may be too small to be clinically relevant [13].

Contrast does not typically add significant value in non-spinal musculoskeletal infection to justify its use in every MRI exam. Studies are needed to assess whether contrast may be helpful in non-routine difficult cases such as infection refractory to medical treatment, infection around hardware, or chronic foreign bodies [10]. Rapid imaging is growing for a variety of indications, and future studies are needed to validate its use in MSK infection.

Recommendations

Non-contrast MRI is typically sufficient for routine acute and chronic osteomyelitis and septic arthritis, although contrast may improve reader diagnostic confidence. Contrast is recommended to detect the complications of subacute and chronic osteomyelitis and for the detection of superimposed infection in the setting of a neuropathic joint. Contrast is often useful for soft tissue evaluation to help delineate abscesses, sinus tracts, and devitalized tissue.

Rheumatology

Background

Treatment of rheumatic disorders has changed drastically in the past three decades, evolving from symptomatic relief using NSAIDs to the current use of biologic response modifiers which can target key steps during the pathogenesis of the disease. Early treatment of rheumatic disorders such as rheumatoid arthritis and spondyloarthropathies offers a better prognosis and can delay or prevent severe joint damage [52]. It is important to treat a patient before the formation of bone erosions, usually considered as irreversible damage [53]. Timely diagnosis of these conditions is therefore vital, and MRI provides an unparalleled evaluation of inflammation in the bone and adjacent soft tissues.

Added benefit of contrast

Extremities

Early manifestations of inflammatory arthritis include joint effusion, synovitis, and tenosynovitis. Synovitis and tenosynovitis will have thick hyperenhancement of the joint synovium and tendon sheath, respectively, indicating active inflammation which can be seen in early and recurrent disease. Gadolinium contrast administration can further help distinguish between joint effusion and synovitis [54]. Contrast improves sensitivity and specificity for detecting synovitis and tenosynovitis in patients with early inflammatory arthritis and subtle imaging findings, with T2 fat saturation sequences shown to be deficient compared with post-contrast imaging [54-56]. Bursitis is not an early feature of rheumatoid arthritis, but the inflamed synovium of bursae will show similar enhancement on post-contrast imaging as synovitis [57].

Axial skeleton

Spondyloarthropathies may have synovitis of spinal joints such as the C1-2 articulation, facet joints, and sacroiliac joints, for which contrast can be used to highlight the synovitis. Enthesitis and endplate inflammation can also be accentuated with contrast. The use of contrast for spinal spondyloarthropathy may improve the identification of subtle soft tissue inflammatory changes and differentiation of synovitis from joint fluid during the initial evaluation for axial spondyloarthropathies [58-60]. Contrast is helpful from a practical standpoint as many standard spinal MRI protocols for the evaluation of disc disease may not include fat suppression of the T2-weighted sequences necessary for providing sensitivity for the inflammatory features of axial spondyloarthropathy [61, 62]. STIR sequences and contrast-enhanced imaging may be complementary rather than mutually exclusive in both assessment of disease activity and treatment response in axial spondyloarthropathy [62].

Controversies/gaps in knowledge/future direction

Extremities

Synovial thickening on contrast-enhanced MRI has been seen in patients unaffected by clinical arthritis, which may lead to overdiagnosis [63]. While contrast is helpful in the initial detection of early inflammatory arthritis, its utility in MRI follow-up of patients with an established diagnosis of inflammatory arthropathy and substantial joint damage needs to be established. Joints with chronic arthritis may have some degree of synovial enhancement which could confound the ability to assess for active disease. In addition, the detection of bone marrow edema and osteitis on post-contrast T1-weighted sequences is comparable to T2-weighted fat-saturated or STIR sequences, and non-contrast-enhanced T1-weighted sequences are recommended to assess erosions in the peripheral joints [54, 64].

Axial skeleton

Several studies have concluded that non-contrast MRI with fluid-sensitive sequences is sufficient for the diagnosis of inflammatory sacroiliitis, while other manuscripts claim the use of contrast may better demonstrate inflammation in subchondral bone and adjacent soft tissues as well as the differentiate synovitis from fluid in the sacroiliac joints and is beneficial to ensure maximum diagnostic confidence [65-71]. While there is some utility for contrast in the assessment of myonecrosis, the use of contrast otherwise does not add to the MRI evaluation of non-infectious myositis [72, 73].

DCE-MRI allows for the measurement of absolute and relative perfusion values of the synovium, which may be useful for quantitative assessment of response to treatment [74]. However, studies have shown promise regarding non-contrast techniques such as DWI and T2/fluid-attenuated inversion recovery (FLAIR) imaging as an alternative to contrast for the diagnosis of synovitis [75, 76].

Recommendations

Extremities

Contrast is recommended in early inflammatory arthritis to help detect synovitis and tenosynovitis. Contrast should be considered for post-treatment follow-up of synovitis. In advanced arthritis, contrast is not recommended as morphologic osseous findings can be assessed on non-contrast sequences alone, and contrast may complicate the interpretation. Contrast is not recommended for inflammatory myositis.

Axial skeleton

Contrast is not routinely recommended for sacroiliitis. Contrast may be considered for other spondyloarthropathy affecting the remainder of the spine.

Osteonecrosis

Background

Avascular necrosis (AVN) (osteonecrosis at articular surfaces) and bone infarcts (osteonecrosis in non-articular areas) manifest as geographic areas with central normal marrow signal demarcated by a double line sign best seen on T2-weighted images. Histologically, the double line sign is the interface between the viable (granulation tissue = hyperintense inner line) and devitalized (sclerosis = hypointense outer line) bone [77]. MRI without contrast is sensitive and specific for the detection of osteonecrosis with accuracy rates reported as high as 97–100% [78, 79].

Added benefit of contrast

Contrast administration has an intuitive appeal to better assess bone perfusion. The lack of enhancement in a segment of bone suggests ischemia or developing infarction. However, normal bone marrow has low levels of enhancement, and areas of osteonecrosis show variable enhancement patterns following contrast administration. Although some studies have shown an association between increased peak enhancement and the progression of osteonecrosis, enhancement has also been demonstrated in areas of bone repair, limiting the utility of this finding [80, 81].

Contrast may be more useful in the pediatric population. Legg-Calve-Perthes disease is detected earlier using contrast-enhanced MRI than with non-contrast MRI, and contrast is useful in defining the extent of the disease [82].

Controversies/gaps in knowledge/future direction

Scaphoid AVN

Evaluation of AVN of the scaphoid proximal pole in the setting of fracture is often a clinical dilemma. Advanced AVN is confidently diagnosed without contrast due to sclerosis that is observed in the proximal pole, while early AVN is challenging to diagnose. Studies have compared the detection of scaphoid AVN using unenhanced, contrast-enhanced MRI, and DCE-MRI with disparate results. Some studies show that contrast-enhanced MRI is the most reliable to assess scaphoid proximal pole vascularity and AVN [83, 84]. However, there is controversy about which type of contrast-enhanced study is better at detecting scaphoid viability, with some studies showing the superiority of DCE-MRI and others favoring CE-MRI [85-87]. Other studies have shown that unenhanced MRI is adequate and more sensitive and accurate than contrast-enhanced MRI at detecting scaphoid AVN [88-90]. The discrepancy in diagnosing scaphoid AVN in the prior studies may be related to how enhancement is interpreted [90]. Specifically, heterogenous enhancement between the center and periphery of the proximal scaphoid pole may skew qualitative assessment. In addition, the effects of hyperemia in adjacent tissue may exaggerate perceived scaphoid enhancement due to partial volume averaging and slice thickness. Finally, nonviable bone has been noted to enhance, with proposed mechanisms including the growth of fibrous tissue or diffusion of GBCA into the necrotic bone [91, 92].

Femoral head AVN

Compared to non-contrast MRI, contrast-enhanced MRI improved inter-observer correlation for the diagnosis of femoral head AVN [93], but this study did not demonstrate increased diagnostic accuracy. Enhancement patterns may help distinguish transient bone marrow edema and subchondral insufficiency fractures from AVN, and contrast may help to differentiate between these entities in this specific diagnostic dilemma [94, 95]. There is conflicting evidence regarding the efficacy of contrast-enhanced MRI in identifying early osteonecrosis. Two different studies evaluated the role of contrast-enhanced MRI in the setting of surgical reduction of developmental dysplasia of the hip: One study found that globally decreased enhancement in the femoral head was a significant risk factor for the development of AVN [96], while another study showed no difference in enhancement pattern or percent enhancement in predicting the development of AVN [97]. DCE and perfusion mapping have shown more promise, as MR perfusion sequences have demonstrated different patterns of perfusion between bone marrow edema and osteonecrosis [95].

Osteonecrosis as a complication of infection

As discussed earlier, a sequestrum is a fragment of devitalized bone separated from the surrounding intact bone in the setting of chronic osteomyelitis. This bone fragment is readily identified with a non-contrast MRI, although intravenous contrast could help highlight enhancing peripheral granulation tissue [50].

Larger prospective studies comparing unenhanced to contrast-enhanced MRI are needed to clarify the utility of contrast in the evaluation of scaphoid and femoral head AVN, particularly in the post-treatment setting.

Recommendation

In the adult population, intravenous contrast is not routinely recommended for osteonecrosis of the extremities or for detecting devitalized bone in the setting of infection, although it may be useful for the diagnosis of early scaphoid ischemia/AVN. Caution should be used for the interpretation of scaphoid proximal pole viability on a contrast-enhanced MRI due to technical and physiologic factors that affect the enhancement of the bone marrow.

In the pediatric population, intravenous contrast is recommended for the diagnosis of Perthes disease.

Pediatrics

Background

Adding contrast to a pediatric MRI examination is not a trivial decision. It requires the placement of an IV and is a source of pain for children [98]. Although rare, pediatric allergic-like reactions to gadolinium-based contrast have been reported [99]. Furthermore, post-contrast sequences extend the MRI acquisition time as well as duration under sedation if anesthesia is needed.

Added benefit of contrast

As in adults, for soft tissue mass characterization, DCE-MRI with time-resolved MR angiogram technique can distinguish high flow from low flow vascular malformations, assess the potential for malignancy, and help distinguish post-operative scar from recurrent soft tissue sarcoma [35, 100]. In Perthes disease (idiopathic femoral head AVN), unlike for adults, routine contrast-enhanced MRI has been shown to be a more reliable method than non-contrast to assess the extent of femoral head involvement [101], and diagnosis in the early stages is very important for management and prognosis. Contrast is useful in juvenile idiopathic arthritis to detect synovitis [102]. Particularly in infants and young children, infection (and other pathologies) can be occult on non-contrast sequences in the unossified cartilage and marrow, and contrast may be necessary for diagnosis [103].

Controversies/gaps in knowledge/future direction

There is a growing body of pediatric MRI literature showing that contrast may not be necessary for a variety of clinical indications. Recent studies have concluded that non-contrast MRI was sufficient to diagnose pediatric sacroiliitis [12]. In a study of pediatric musculoskeletal infection, adding contrast did not change the diagnosis, and the authors recommended against routine use, although intravenous contrast may potentially aid the reader's confidence in assessing for subperiosteal abscess. Furthermore, although contrast is helpful for the detection of synovitis, synovial thickening on contrast-enhanced MRI can be seen in children unaffected by clinical arthritis, which may lead to overdiagnosis.

Further studies are needed to rigorously assess which indications truly need contrast for diagnosis in pediatric musculoskeletal MRI. For example, the criteria for assessment of synovitis on contrast-enhanced MRI need to be optimized to avoid overdiagnosis and treatment. Further investigation and optimization of non-contrast techniques, such as DWI, for assessing indications, such as Perthes and subperiosteal abscesses, is needed. In addition, no systematic study exists analyzing the true time penalty of adding contrast to a pediatric MRI exam. This information is essential to understand the true burden to the health care system, including overutilization of resources, cost, and, most importantly, the risk to children.

Recommendations

Contrast recommendations parallel those for adult patients for bone and soft tissue tumors, rheumatology, and infection. However, while intravenous contrast may not be necessary for routine musculoskeletal infection imaging, it may improve the detection of osteomyelitis in infants and young children as well as improve reader diagnostic confidence. Intravenous contrast is recommended for the diagnosis of Perthes disease.

Radiologists should be judicious in administering contrast; assessment of the acquired pre-contrast images before proceeding with contrast may optimize its usage.

Sports injuries

Background

Many sports-related injuries result in edema in the soft tissues and bone marrow, often with joint effusions. There is a sufficient intrinsic resolution by MRI to detect sports-related injuries, limiting the need and utility of intravenous contrast administration.

Added benefits of contrast

The main utility of contrast for sports medicine applications is direct MR arthrography (MRA). The most common indications for direct MRA are joint instability, shoulder and hip labral pathology, or rotator cuff pathology, comprising 85.1% of cases [104]. In such instances, intra-articular contrast may improve the sensitivity of MRI by increasing joint distension and better delineating certain soft tissue injuries. Contrast coating of tear surfaces may allow for easier diagnosis of novel tears and re-tears of the post-operative rotator cuff [105], has increased accuracy for detection of ligamentous injuries at the wrist compared to conventional MRI [106], and has been shown to be superior to conventional MRI for detecting acetabular labral tears [107]. Recurrent meniscal tears can represent a diagnostic challenge in the post-operative setting as granulation tissue and scarring can mimic the appearance of a tear; in such cases of diagnostic confusion, intra-articular contrast can improve diagnostic accuracy [108, 109].

A retrospective study of 150 shoulders without prior surgery looked at conventional shoulder MRI and MRA exams performed on the same patient on the same day. There was added benefit of the MR arthrogram, enabling pre-arthroscopic detection of full-thickness rotator cuff tears in six additional patients (113 on conventional MR vs. 119 on MRA) [110].

Intravenous injection of gadolinium contrast can also be useful in the context of cartilage evaluation, specifically for quantitative compositional evaluation of cartilage via dGEMRIC (delayed gadolinium-enhanced magnetic resonance imaging of cartilage) sequences, which show areas of low glycosaminoglycan content in diseased cartilage and high glycosaminoglycan content in healthy cartilage. However, other techniques which do not require the injection of contrast are more commonly used for cartilage ultrastructure evaluation, such as T1-rho imaging or T2 mapping.

Controversies/gaps in knowledge/future direction

In the majority of cases, non-contrast MRI is highly accurate in the evaluation of sports injuries by MRI [111, 112]. Data are available showing that injuries, even to small intra-articular structures such as the hip labrum, can be accurately assessed on non-contrast MRI when performed optimally [113]. Several studies have demonstrated that non-contrast MRI at 3.0 Tesla can have similar or even higher accuracy compared with MRA [114-116]. However, if high clinical concern persists after non-contrast examination, an MR arthrogram may provide further diagnostic information.

As MRI quality continues to improve, future studies should strive to show that non-contrast techniques are equal or superior to MR arthrogram, which would eliminate the need for this invasive exam. This would be especially impactful for pediatric patients.

Recommendations

Contrast administration is not recommended for routine sports injuries. Direct MR arthrography is effective and should be used if a high-resolution MRI is not available or is inconclusive. The dGEMRIC technique may be considered in the evaluation of articular cartilage if non-contrast cartilage techniques are unavailable.

Neurography

Background

High-resolution MR imaging of peripheral nerves, referred to as “MR neurography” (MRN), can accurately characterize primary and secondary signs of neuropathy. Normally, peripheral nerves do not enhance on post-contrast imaging, with the exception of the dorsal nerve root ganglion, an anatomic area of deficiency in the blood-nerve barrier [117, 118].

Added benefit of contrast

Nerve pathology can readily be identified in non-contrast MRN by alterations in nerve signal, morphology, and the

presence of perineural scarring [118]. Following contrast administration, peripheral nerve enhancement is observed when the blood-nerve barrier has been disrupted, such as with acute inflammation, post-radiation injury, or tumor [119]. Limited prior retrospective investigations have concluded that contrast did not alter the imaging diagnosis [120] and, other than for evaluation of nerve masses, was of little added benefit [121].

For the characterization of mass lesions [117, 118, 122], it is important to note that traumatic neuromas demonstrate variable enhancement, and as such, only a lack of enhancement may be helpful for distinguishing a neuroma from a peripheral nerve tumor [122-124]. Using DCE-MRI is beneficial to detect early arterial enhancement in malignant peripheral nerve sheath tumors [125].

In cases of diffuse polyneuropathy, contrast may be helpful for the diagnosis of lymphomatous infiltration, which manifests as diffuse nerve enlargement with intense enhancement [122]. In addition, contrast can be used to distinguish some acute from chronic disorders, as enhancement of the cauda equina, nerve roots/plexus, and peripheral nerves is seen in Guillain-Barre syndrome and subtypes, while contrast enhancement is not a typical feature of chronic inflammatory demyelinating polyneuropathy (CIDP) [118, 122].

Following nerve repair, MRN can distinguish operative success from failure without necessarily requiring intravenous contrast [126, 127], as post-operative perineural fibrosis and neuromas are easily identified on non-contrast imaging [121, 128]. However, contrast may be of benefit for the evaluation of post-operative fluid collections (abscess/hematoma) [129].

Controversies/gaps in knowledge/future direction

Given the challenge of differentiating nerves from vessels, a contrast-enhanced 3D SPACE-STIR technique that utilizes the T2-shortening effect of gadolinium to suppress background signal was developed to optimize the visualization of nerves [130-135]. The added value of this technique, in light of the intravenous contrast requirement, remains debatable, especially given the availability of alternative non-contrast 3D MRN techniques [136]. A recent study assessing diagnostic contribution supported the potential application of the contrast-enhanced 3D technique for brachial plexus imaging but suggests that non-contrast 2D protocols are sufficient for lumbosacral plexus and extremity neurography [137].

Prior research regarding intravenous contrast for MRN is limited, largely anecdotal, and lacks applicability to a wide variety of nerve pathology. Future directions include the study of nerve-selective contrast agents, such as supramagnetic iron oxide and gadafluorine M [119].

Recommendations

Intravenous contrast administration is not recommended for MRN, but may be helpful for the evaluation of peripheral nerve tumors, atypical or diffuse polyneuropathy, and post-operative fluid collections. While the use of contrast for background signal suppression to improve nerve visualization is promising, alternative non-contrast 3D techniques can be considered.

Implants/hardware

Background

With recent advancements in metal artifact reduction techniques, MRI can be utilized for diagnostic evaluation in patients with orthopedic hardware. Strategies to optimize imaging in the presence of metal include using a lower field strength magnet, high receiver bandwidth, small slice thickness, a large matrix size, and STIR rather than fat-suppressed sequences [138, 139]. Advanced metal artifact reduction sequences include the use of view angle tilting (to reduce in-plane distortion) and multispectral techniques (to reduce through-plane distortion) [140]. These advances may further enable the evaluation of subtle periprosthetic pathology, whether utilized with non-contrast or contrast-enhanced sequences.

Added benefit of contrast

Non-contrast MRI can adequately assess the majority of potential hardware-related complications including periprosthetic fracture or adverse local tissue reaction [139, 141, 142]. A single study of 47 patients imaged with metal-on-metal hip implants following gadolinium administration determined that contrast did not detect any additional hardware-associated complications when compared to routine sequences, but findings of osteolysis and soft tissue masses were more conspicuous and easier to characterize; the authors conclude that this may potentially increase sensitivity to early findings of adverse local tissue reaction [143]. Administration of intravenous contrast is helpful if there is clinical suspicion of infection, such as soft tissue abscess or osteomyelitis, or neoplasm/tumor recurrence [39, 40, 144, 145]. Contrast-enhanced MR angiography may be indicated for evaluation of recurrent hemarthrosis following total knee arthroplasty [146, 147].

Controversies/gaps in knowledge/future direction

In the presence of metallic hardware, fat-suppression techniques are hampered by disruption of the homogeneous

static magnetic field from susceptibility artifact which contributes to geometric distortion and signal loss [138]. This particularly impacts imaging following contrast administration where fat-suppressed T1-weighted sequences are necessary to highlight areas of gadolinium enhancement. Given this limitation, subtraction of the pre-contrast T1-weighted pulse sequence from the post-contrast image is critical to identify areas of enhancement in the absence of fat suppression [138, 146]. Furthermore, the choice of specific metal artifact suppression methods for implementation with contrast-enhanced sequences is unclear, and the utility of DCE-MRI for some indications, such as for detecting recurrence around a tumor prosthesis, is emerging [29].

There is a paucity of literature on the use of contrast with metal artifact reduction sequences. Further research is needed to determine the role of contrast in the evaluation of hardware-associated complications with attention to earlier detection and potential impact on clinical management decisions. For example, current United States Food and Drug Administration recommendations regarding metal-on-metal prostheses specify surveillance for hypersensitivity reactions in the appropriate clinical context by non-contrast MRI [148]. If the addition of contrast may potentially provide earlier detection of hypersensitivity reaction, more research is needed regarding the long-term outcomes in these patients based on MRI performed with and without contrast. Continued advancements in imaging techniques to minimize susceptibility artifact from metallic hardware are also needed.

Recommendations

Intravenous contrast is not recommended for routine MRI evaluation in the setting of implants/hardware. However, it is helpful for detecting recurrent tumor in the setting of a tumor protheses and may be helpful for suspected infection or in rare cases of recurrent hemarthrosis following total knee replacement. When intravenous contrast is administered, subtraction imaging is recommended.

Spine imaging

Background

Spine MRI is routinely performed without contrast for chronic back pain to assess for degenerative disc disease (DDD), facet arthropathy, and nerve impingement. In the setting of trauma, non-contrast MRI can assess for marrow edema, fracture, and spinal cord edema/hemorrhage. Contrast has traditionally been used to help distinguish DDD from infectious discitis-osteomyelitis, post-operative evaluation, and spinal canal abnormalities.

Added benefit of contrast

Contrast utilization in the spine is specifically supported in cases of known or suspected malignancy or infectious causes of myelopathy [149-154]. There is also supportive evidence for contrast use in the assessment of acute spinal cord ischemia, as there is typically no enhancement in early ischemia [155]. For demyelinating conditions such as multiple sclerosis and neuromyelitis optica, contrast can help detect spinal cord lesions [156-158]. Contrast may also be necessary when differentiating post-operative spine complications including abscess, hematoma, or recurrent disc herniation from compressive epidural fibrosis [65, 70, 150]. In specific instances of trauma where there is a concern for arterial injury, contrast administration for an MR angiogram is also indicated [159].

Controversies/gaps in knowledge/future direction

While many studies do not support contrast in the evaluation of degenerative disease, the addition of contrast may highlight inflammatory changes associated with the degeneration of the posterior elements which could be clinically significant [160]. Particularly in the setting of differentiating Modic type 1 degenerative endplate changes and early infectious spondylitis, contrast may be useful to elucidate epidural inflammation or early inflammatory changes in the soft tissues to support infection [66, 151].

While there is a role for contrast in post-operative imaging of the lumbar spine when differentiating recurrent disc herniation from epidural fibrosis, several studies indicate no impact on clinical outcomes and poor correlation of post-contrast findings with clinical symptoms [67, 161, 162]. Additionally, regarding post-operative cervical spine imaging, most surgeries are performed from an anterior approach without violation of the epidural space and, therefore, granulation tissue which would be highlighted by contrast administration is expected to be minimal. More literature is needed on the role of contrast in patients with posterior approach cervical fusion/decompression, as most of the current literature is based on the lumbar spine [68].

There are several studies exploring the utility of DCE-MRI for spinal tumor vascularity or in the assessment of osseous lesions, particularly in the setting of pathologic vertebral fracture [69, 149]. Larger scale studies with pathologic correlation are needed prior to the integration of these sequences into routine contrast imaging protocols. Studies assessing the utility of diffusion and opposed-phase imaging sequences versus contrast administration are needed to determine if there is a difference in the diagnostic potential of these imaging techniques.

Recommendations

Contrast is not recommended for general back pain or fractures. Contrast is recommended to help distinguish degenerative disc disease from discitis-osteomyelitis. Contrast is recommended for post-operative imaging of the lumbar spine, but not of the cervical spine. Contrast is recommended for abnormalities in the spinal canal such as demyelinating, oncologic, infectious, and vascular conditions.

Declarations

Conflict of interest The authors declare no competing interests.

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