Picture-perfect: imaging techniques in juvenile idiopathic arthritis

Juvenile idiopathic arthritis is a debilitating condition consisting of several categories of arthritis. Early detection, accurate diagnosis and monitoring of changes upon treatment are critical in order to minimize long-term sequelae. Imaging modalities, such as radiography, ultrasound and MRI are commonly employed to evaluate synovial inflammation, joint effusion, bone erosions and other disease manifestations. Challenges in pediatric populations arise from lack of technology appropriate for small joint imaging and the lack of available data for standardization and validation of imaging methods and disease grading. This review describes the optimal utility and advantages and disadvantages of various imaging methods, focusing on an in-depth review of current and novel MRI techniques and suggesting protocols for implementation.

KEYWORDS: imaging, JIA, JRA, MRI, pediatric, rheumatology

Conventional radiography

Conventional radiography remains the primary imaging method for JIA evaluation, at least in part because it is widely available and relatively inexpensive. Plain radiographs are important to exclude fractures, tumors and osteomyelitis, and if the initial evaluation of any of these conditions are clinically suspected, other imaging may be important in initial evaluation. Films may show features of JIA, including swelling of soft tissue, bone loss or erosions, joint space narrowing or misalignment, growth plate disturbances and periostitis [12]. These features are important for baseline assessment of disease severity and joint damage. Although screen films have historically been limited to displays of joint damage that appear late in disease progression, recent advances in digital radiography have improved data display and assessment. A study designed to evaluate the performance of digital radiography versus screen films determined that small, early erosions were visualized equally well by both methods [13]. However, an experiment with artificial erosions concluded that a flat-panel detector was superior to screen films, enabling the detection of bone erosions as small as 0.5 mm.
in diameter and depth [14] at clinical exposures. Ludwig et al. further posit that the exposure dose of ionizing radiation, one of the significant drawbacks of radiography, can be decreased by 50% while maintaining results comparable to typical films [14]. Although these advances are useful, radiography cannot be used to quantify the inflammatory activity of early disease, so other methods of assessment are needed.

Another disadvantage of radiography is standardization of assessment. Standardized tools are critical for evaluation of therapeutic benefit and disease progression; in fact, the US FDA requires evaluation of structural damage as an efficacy measure and states that slowing x-ray progression should be measured with a validated index for adults with rheumatoid arthritis [101]; however, methods validated for adult populations are not necessarily appropriate for pediatrics. Thus, several scoring mechanisms have been developed that are more appropriate for juvenile disease. One early method developed by Poznanski et al. established standards for normal carpal length in healthy children by measuring the ratio between radiometacarpal length and the second metacarpal bone length [15]. Advantages of this method include simplicity and practicality, and because this measurement is not dependent upon the degree of ossification of the carpal bones, it is appropriate for growing children and for those with advanced ossification. However, this system is only useful in those with wrist involvement and is not reliable with advanced erosive disease. More recently, the Dijkstra composite score was suggested as a method of scoring various features of JIA, such as soft tissue swelling, joint space narrowing, growth disturbances, osteopenia/osteoporosis, erosions, subchondral cysts and joint position in several joints [16,17]. As the authors noted, however, this was a somewhat complicated system that requires thorough radiologic knowledge of both normal and diseased joints, but it has the advantages of being sensitive to change and applicable to all joints. Other scoring methods have been developed or adapted to pediatric populations for specific joints, such as hip [18] and wrist/hand [19]. It is generally recognized, however, that other imaging methods are better suited for sensitive detection of very early inflammation and soft tissue changes, or much smaller erosions. Pediatric arthritis often has significant involvement of cartilage and synovium, which radiography is unable to accurately quantify; highly sensitive methods allow earlier assessment of joint damage and more rapid evaluation of therapeutic benefit.

Ultrasound

Ultrasound is a safe, relatively inexpensive and easily implemented method for assessing joint inflammation. Recent advances in resolution due to high frequency (12–15 MHz) linear probes have substantially improved joint visualization. This is extremely helpful for determining joint activity, since swelling and pain can be caused by factors other than JIA effusion. Moreover, the lack of radiation exposure renders sonography useful for longitudinal assessments, such as following treatment response or clinical course, although poor repeatability may require assessments to be conducted by the same sonographer over time. Sonography is also helpful for guiding aspiration or injection of joints.

Ultrasound can be used to determine severity of involvement of accessible joints, measuring features such as effusion volume, synovial thickness, bony erosions, and cartilage thinning or erosions. Spannow et al. have calculated normal reference ranges for both sexes for cartilage thickness of several joints, including knee, ankle and wrist, for children aged between 7 and 16 years, along with an algorithm for determining hyaline cartilage thickness [20]. It should be noted that the amount of inter- and intra-observer agreement can vary with ultrasound; one study demonstrated strong or acceptable agreement for several joints, but not for wrist [21]. However, the similarity of joint thickness between right and left extremities in healthy children that was found in this study provides a reference for determining the extent of disease activity in joint cartilage.

A recent study in knees of children with JIA concluded that ultrasound was 90% sensitive and 100% specific in the detection of effusion in clinically active knee joints, and detected effusion in 70% of clinically inactive joints; likewise, a synovial thickness greater than 2.3 mm had 94% positive and 84% negative predictive value for disease activity [22]. In this same study, ultrasound-determined synovial thickness of the knee correlated with disease activity score and articular indices, as well as biomarkers of disease activity, such as sedimentation rate and C-reactive protein level. Similarly, Manzoni et al. detected subclinical synovitis by ultrasound on 5.5% of 1560 clinical ‘normal’ joints [23]. Results from these studies and others [24] suggest that classification of disease based on clinical evaluation of joint involvement may be misleading.

Not all ultrasound studies have yielded such strong results, however. Sureda et al. were only able to document effusion in 60% of known
clinical active knee joints, and similar findings were reported by Frosch et al. [25,26]. Recently, ultrasound was unable to reliably demonstrate ankle joint disease in patients with documented JIA, identifying effusion in less than 33% of clinically active joints [27]. Methods of measurement, such as determining bursa length versus volume, and ultrasound equipment, may play a role in such divergent results. Power and color Doppler ultrasound methods, which detect increases in synovial vascularity by measuring synovial blood flow, have improved the ability to measure inflammatory activity [28,29]. Such methods have been used to predict short-term relapse in patients in apparent clinical remission [30]. Although few studies have been conducted in children, a recent report combining grayscale ultrasound and power Doppler documented ongoing inflammation in children who had been in clinical remission for at least 3 months [31], and other studies have documented relapse in ankle joints [32] and subclinical synovitis in other joints [33] with Doppler ultrasound.

Other disadvantages of ultrasound include difficulty in assessing some joints, such as the temporomandibular joint, and the generally small size of joints in young children. Although inter-observer reproducibility can also play a role in variability of measurement, Magni-Manzoni et al. demonstrated that ultrasound can be a strongly reproducible modality, with inter-observer reproducibilities of 83, 84 and 95% for determining the presence or absence of joint effusion, synovial hypertrophy and power Doppler signal, respectively [34]. It should be noted, however, that even reproducible results may need to be interpreted with caution. A recent MRI-based analysis of wrist joints in healthy children aged 6–15 years demonstrated a high prevalence of bony depressions, signal changes indicating bone marrow edema and significant joint fluid [35], suggesting that developing joints may be variable in appearance. This underscores the need for a baseline assessment in children with JIA.

**MRI**

**MRI introduction**

MRI-based methods have advanced dramatically over the past decade for imaging of JIA, and comprise the optimal imaging modality for assessing very early, pre-erosive stages of disease, and for determining response to therapy. MRI is most important in children with polyarticular disease, while its importance in the child with oligoarticular involvement is generally for exclusion of other diagnoses, such as co-existing trauma or tumor. MRI has its greatest use when radiographs fail to exclude these other conditions. They may be clinically suspected in all children with arthritis because of persisting well-localized bone tenderness on physical examination, and in children with active polyarticular arthritis in whom affected joints show progressive loss of motion or swelling despite optimized treatment. MRI is also important in documenting sacroiliitis in patients with severe enthesitis-related arthritis [36].

There are a broad range of sequences and protocols available, and it is critical to understand the tissue characteristics and disease pathology of interest to ensure the best protocol for each. Studies have demonstrated the superiority of MRI over radiography and ultrasound in assessment of bone erosions and soft tissue involvement [37–39]. Examples of MRI methods that are generally appropriate by tissue type are displayed in Table 1 (adapted from [40]). One difficulty with MRI is that standardized grading scores for joint disease activity and consensus definitions are not as well validated as in adults, and may be difficult to validate in growing joints regardless of how many patients are studied. Unlike the large body of information gathered and collated into Rheumatoid Arthritis MRI Score (RAMRIS) by the Outcome Measures in Rheumatology Clinical Trials (OMERACT) MRI group [41], pediatric data are more scarce. A recent study aimed to develop and validate a pediatric MRI scoring system for JIA and to compare this system to RAMRIS [42]. Overall, the pediatric MRI scoring system was highly reliable for assessment of erosions and conventional damage assessments.

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**Table 1. Matching of MRI sequences to tissue of interest.**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Measurement</th>
<th>MRI sequence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovium</td>
<td>Fluid</td>
<td>T₁-weighted MRI</td>
</tr>
<tr>
<td></td>
<td>Rate of transfer of contrast between plasma and EES</td>
<td>DCE-MRI</td>
</tr>
<tr>
<td></td>
<td>Restricted water motion (proxy for inflammation)</td>
<td>DTI</td>
</tr>
<tr>
<td>Cartilage</td>
<td>Cartilage degradation assessed by increased water mobility</td>
<td>T₁-weighted MRI</td>
</tr>
<tr>
<td></td>
<td>Glycosaminoglycan content</td>
<td>dGEMRIC</td>
</tr>
<tr>
<td></td>
<td>Proteoglycan depletion</td>
<td>³¹Na MRI</td>
</tr>
<tr>
<td></td>
<td>Proteoglycan content</td>
<td>T₁-rho MRI</td>
</tr>
<tr>
<td>Bone</td>
<td>Erosions</td>
<td>T₁-weighted MRI</td>
</tr>
<tr>
<td></td>
<td>Bone marrow edema</td>
<td>STIR or T₁-weighted FSE</td>
</tr>
<tr>
<td>Muscle</td>
<td>Dermatomyositis or polymyositis</td>
<td>T₂-weighted FSE</td>
</tr>
</tbody>
</table>

**Legend:**
- **DCE:** Dynamic contrast enhanced, **dGEMRIC:** Delayed gadolinium-enhanced MRI of cartilage; **DTI:** Diffusion tensor imaging; **EES:** Extravascular, extracellular space; **FSE:** Fast spin echo.

Adapted from [40].
but did not correlate well with active disease parameters and was not as sensitive to change as RAMRIS. Interestingly, RAMRIS also provided valid and reliable assessments of synovitis. Interpretations from this study are limited by its small sample size (66 patients) and the lack of age-matched healthy controls, but it is a start toward addressing the problem of consistent definitions and MRI-based scoring in pediatric patients.

Generally, disease processes that involve changes in water content, including joint effusion, should be imaged with sequences that are sensitive to increases in proton mobility, such as T2-weighted fast spin echo sequences. In the case of synovitis, a hallmark of disease activity in JIA, the synovium will be visualized as thick and irregular with MRI, and will have high signal intensity on T2-weighted sequences. Differentiation between joint effusion and synovium may be difficult due to similar signal intensity; heavily T2-weighted, fast spin echo sequences may help in this regard [43]. Furthermore, the child with arthritis who has weakness out of proportion to the clinical findings of arthritis may be developing dermatomyositis or polymyositis. MRI with T2-weighted images of the proximal lower extremities can identify sites of affected muscle, which are potential candidates for diagnostic biopsy.

Bone erosions are typical in advanced polyarticular disease and large lesions are easily identifiable by conventional radiography. High-frequency ultrasound has also shown potential to detect changes in adult bone in patients with rheumatoid arthritis [44,45] and erosive osteoarthritis [46]. Erosive disease has been associated with poorer outcomes in JIA patients [47], and erosions that are detectable by radiography or ultrasound may indicate irreversible damage. Thus, early identification of small erosions is extremely helpful in determining prognosis and assessing treatment options. Malattia et al. demonstrated that MRI is superior to both radiography and ultrasound in revealing bone erosions in the wrist and in revealing erosions in patients with less than 3 years’ disease duration [37]. Utilizing a T2-weighted, 3D gradient echo sequence for image acquisition and multiplanar reconstruction was found to be optimal for identification of small erosions. This is consistent with studies in adult RA in which bone erosions were detected on average 2 years earlier with MRI than with conventional radiography [48]. Unfortunately, further data regarding MRI compared with radiography versus ultrasound are lacking in pediatric populations, and further studies are certainly warranted.

Proton density (PD) images are used for anatomical information to assess joint integrity. These two image sets are usually collected simultaneously as dual echo PD-, T2-weighted sequences collected in both the sagittal and axial planes [49]. A typical imaging protocol at 1.5 Tesla (T) for knee joint evaluation can be seen in Table 2. Representative PD-, T2-weighted images are shown in Figure 1.

Table 2. 1.5 Tesla MRI protocol for evaluation of the juvenile knee.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>FA (degrees)</th>
<th>NA</th>
<th>BW Hz/pixel</th>
<th>FOV (mm)</th>
<th>Resolution (mm)</th>
<th>ST (mm)</th>
<th>ETL (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AXIAL FSE/PDW/FS</td>
<td>3000</td>
<td>20.6</td>
<td>90/180</td>
<td>2</td>
<td>163</td>
<td>160</td>
<td>256 x 192</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>SAG FSE/PD/T2W/FS</td>
<td>4000</td>
<td>16, 80</td>
<td>90/180</td>
<td>2</td>
<td>81</td>
<td>180</td>
<td>256 x 192</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>SAG T2 Map</td>
<td>1500</td>
<td>9, 18, 99</td>
<td>90/180</td>
<td>1</td>
<td>244</td>
<td>180</td>
<td>256 x 160</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>SAG T1, postcontrast</td>
<td>350</td>
<td>8</td>
<td>90</td>
<td>2</td>
<td>122</td>
<td>180</td>
<td>256 x 128</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>T1-perfusion</td>
<td>3.8</td>
<td>1.5</td>
<td>60</td>
<td>0.5</td>
<td>244</td>
<td>180</td>
<td>128 x 128</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

BW: Bandwidth; ETL: Echo train length; FA: Flip angle; FOV: Field of view; FS: Fat saturation; FSE: Fast-spin echo; NA: Number of averages; PDW: Proton density weighted; SAG: Sagittal; ST: Slice thickness; T1w: T1 weighted; TE: Echo time; TR: Time to relaxation.

Figure 1. Representative sagittal, fast-spin echo dual echo images with fat saturation MRIs of a knee of a 13-year-old male with mild juvenile idiopathic arthritis. The field of view = 180 mm, the data matrix was 256 x 256, slice thickness = 3 mm, slice gap = 1 mm, repetition time = 4000 ms, number of averages = 2, echo train length = 8, pixel bandwidth = 81 Hz, total acquisition time = 3 min 12 s. (A) Proton density image with echo time = 16 ms. (B) T2-weighted image with echo time = 80 ms.
Contrast-enhanced MRI
Although $T_1$-weighted fast spin echo sequences are helpful for imaging inflamed synovium, the best method is with contrast-enhanced MRI [50,51]. The rate of enhancement of synovium with contrast is dependent in part on tissue vascularization and capillary permeability, both of which are highly correlated with synovial inflammation [52–54]. Assessing rate of enhancement (dynamic contrast-enhanced [DCE] MRI) is also useful for helping to distinguish between joint effusion and synovitis, both of which are disease attributes with high water content. Since the contrast agent can quickly diffuse into the synovial fluid and confound differentiation, a $T_1$-weighted, fat-suppressed image should be acquired between 5 and 10 min post-contrast injection (Figure 2). A precontrast $T_1$-weighted image can be used for subtraction to increase conspicuity. The volume of synovium can be calculated from the post-contrast images or from the subtracted images and can then be used to monitor treatment response as shown in Figure 3 [55]. If chemical shift saturation or water excitation gives incomplete or poor fat saturation, short-tau inversion recovery imaging, another water-sensitive technique that nullifies the fat signal, can be used for $T_1$-weighting. DCE-MRI has been demonstrated to be both valid and reliable, with excellent inter-class correlation coefficients for inter-reader agreement of synovial inflammatory activity of wrist and hip joints [50]. It has also demonstrated early hip involvement in JIA patients without clinical evidence of disease activity [56].

Pharmacokinetic parameter mapping
Information gleaned from DCE-MRI can be enhanced even further using pharmacokinetic (Pk) modeling for quantitative mapping [51,57,58]. In this physiologically based model, signal enhancement time courses are described by a plasma compartment and the extracellular–extravascular space. Pk parameters that are representative of tissue signal enhancement patterns include $K_{trans}$ (the rate of contrast transfer from plasma to extravascular space), $K_{ep}$ (the rate constant denoting the rate of contrast transfer from extravascular space to plasma), and $V_p$ (the fraction of plasma space per unit volume of tissue) [51]. These are obtained by iteratively fitting...
the data to model equations by nonlinear least-squares curve fitting on a pixel-by-pixel basis. To obtain the required data, dynamic images can be acquired every 5 s while the contrast agent is being injected (Figures 4 & 5). Overall, approximately 40 images are acquired. The first four are used as a baseline of precontrast steady-state of signal intensity. The fourth precontrast image (after T1-relaxation saturates) can be subtracted from the 40th image (post-contrast) to indicate areas of contrast agent uptake and synovitis (Figure 6). Color-coded parameter maps are generated, as shown in Figure 7. The parameters for each pixel are coded depending on their magnitudes, with minimum values as blue and maximum values as red, to facilitate visual comparisons during longitudinal assessments. Pk parameters have been shown to decrease in children under treatment over time, and provide specific, local information on synovial inflammation [58]. The total time for acquisition is approximately 3 min, so this dynamic methodology does not increase the total examination time and the software required is generally available on commercial imaging platforms.

**T2 mapping**

T2 relaxation mapping is another parametric technique that can be easily implemented to assess cartilage hydration or collagen orientation in normal as well as immature or diseased cartilage [59,60]. Typically, there is a general decrease in T2 during longitudinal assessments.}

**Figure 4. Dynamic contrast-enhanced MRI.** These are 3D gradient echo images of the hand. Each 3D volume takes 5 s to acquire. Four datasets are acquired prior to contrast agent injection. Thirty-six more volumes are collected postinjection for a total of 40 datasets. The field of view = 180 mm, the data matrix was 128 x 128, slice thickness = 8 mm, slice gap = 0 mm, repetition time = 3.8 ms, echo time = 1.5 ms, number of averages = 0.5, pixel bandwidth = 244 Hz, total acquisition time = 5 s per volume.

**Figure 5. Dynamic contrast-enhanced MRI of the hand.** (A) A color-coded pharmacokinetic parameter map of the permeability constant, kp. (B) A normalized signal intensity versus time curve of the color-coded region of interest from the permeability map.
relaxation from the cartilage surface to the deeper layers [61,62], but cartilage degradation that occurs with JIA has been shown to increase T₂ relative to age-matched controls [63]. T₂ relaxation maps are calculated from a series of multislice multiecho images (Figure 8). Magnitude, gray and color scale T₂ maps are produced for evaluation (Figure 9). Typical maps showing elevated T₂ in a 10-year-old girl with JIA compared with a healthy 10-year-old boy are shown in Figure 10. The T₂ change from the subchondral bone to the articular surface is graphed in Figure 11 for a girl with JIA, a healthy boy and for a healthy adult. T₂ mapping is performed before contrast agent injection to preclude the effects of T₁ and T₂ shortening, although the effects of contrast on T₂ are minimal [DARDZINSKI, B, ...]

**Figure 6. 3D subtraction image from a dynamic contrast-enhanced MRI series of the knee.** The 4th volume image (precontrast) has been subtracted from the 40th volume image (post-contrast). This increases the conspicuity of regions of update of contrast agent. The hyperintense regions indicate perfusion of the distal femoral and proximal tibial physes (yellow arrows) as well as areas of synovitis (red arrows). Perfusion of physes is normal in children and can complicate segmentation of synovial volume.

**Figure 7. Quantitative parameter maps from pharmacokinetic modeling of dynamic contrast-enhanced MRI data.** (A) The volume transfer coefficient (K₅₀), which is the rate of transfer of the contrast agent from plasma to the extravascular, extracellular space. (B) The rate constant Kₑ, which is the rate of transfer of contrast agent from the extravascular, extracellular space to the plasma. (C) Displays vₚ, the fraction of plasma space per unit volume of tissue. This modeling permits early quantitative assessment of disease activity and treatment response.
Other techniques used to evaluate cartilage include contrast-free $T_1$-rho or delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) [64–66]. Parameter maps from these techniques evaluate proteoglycan content, which is critical in adults for maintaining cartilage stiffness and is decreased with disease. However, the importance of proteoglycan abnormalities in children with JIA has not been established.

**Unpublished Data.**

### Alternative techniques: diffusion tensor imaging & $^{23}$Na MRI

Diffusion tensor- or diffusion-weighted imaging (DWI) is a technique that measures the Brownian motion of water [67,68], which is freely isotropic in pure liquid, but is anisotropic in tissue [69]. Diffusion is hindered by cellular membranes and organelles. By applying magnetic field gradients in multiple directions, the...
anisotropic behavior in the tissue compartment of interest can be assessed. The appeal of DTI is that it is contrast-free, thus avoiding possible adverse events with administration of gadolinium-based contrast agents. This technique has been applied to the brain to map fiber tract trajectories in white matter and to perform diffusion tractography [70]. The use of DTI to assess cartilage in knee joints is limited due to the short $T_2$ relaxation time of cartilage (30–70 ms) [61], although a 3D steady-state DWI sequence has been proposed [71]. Conventional $T_2$ relaxation time mapping provides a measure of cartilage hydration and reflects collagen orientation and breakdown [59]. One study in adults demonstrated that DTI performed as well as $T_2$-weighted contrast-enhanced MRI at detecting synovial inflammation [72]. Another study found that DWI was able to identify cartilage maturation post-chondrocyte transplantation [73]. Although the contrast-free approach is a desirable one, challenges in implementation and analysis currently limit the utility of this technique.

Another alternative MRI method is $^{23}$Na MRI [74], which identifies areas of proteoglycan depletion through bonding of the positively charged sodium with negatively charged glycosaminoglycan molecules [75] and specific protocols have been suggested for cartilage assessment [76]. The major limitation of this technique is the low overall sodium content in cartilage, which limits the signal-to-noise ratio (SNR). MRI protocols using systems with higher (7 T) field strengths are being evaluated to help overcome this significant challenge [77–79].

![Figure 10](image1.png)
**Figure 10.** Gradient echo images and $T_2$ relaxation time maps from the patellar cartilage of a 10-year-old girl with juvenile idiopathic arthritis compared with a 10-year-old healthy boy. Although the gradient echo images do not reveal structural differences, the $T_2$ maps show clear biochemical differences indicative of disease activity, indicated by yellow and red dashed ellipses. GRE: Gradient recalled echo; JIA: Juvenile idiopathic arthritis.

![Figure 11](image2.png)
**Figure 11.** $T_2$ relaxation profiles across the patellar cartilage from the images in Figure 10. Note that the profiles across the cartilage are similar for a healthy boy and a healthy adult, but the profiles for the girl with JIA are elevated and relatively homogeneous from the subchondral bone to the articular surface. JIA: Juvenile idiopathic arthritis.
The use of 3 T systems has increased over the past several years for small joint imaging [50–82]. The increase in field strength can be used to decrease scan time or increase resolution. This is due to the increase in SNR (Figure 12). Contrast to noise is also increased (Figure 13). For 3 T systems, protocols need to be modified from those implemented with 1.5 T systems due to increases in $T_1$ and potential decreases in $T_2$, depending on tissue type (Figures 14 & 15) [83]. For conventional sequences, repetition time (TR) needs to be increased and echo time (TE) needs to be decreased. The echo train length (ETL) can also be increased to shorten imaging time. A knee protocol consisting of three planes of fat-saturated intermediate-weighting (IW) can be implemented in 10 min if contrast is not needed (Figure 16). To suppress the fatty marrow, inversion time needs to be increased at 3 T due to the increase in $T_1$, and should also be adjusted to the

![](image)

**Figure 12.** Signal-to-noise ratio measurements in the pediatric knee of an 11-year-old boy as a function of field strength and receiver bandwidth. The SNR is calculated as the signal from the tissue of interest divided by the standard deviation of the background noise. The increase in SNR at 3 T is 30–100% higher than at 1.5 T and varies with tissue type. The field of view = 160 mm, the data matrix was $256 \times 192$, 75% phase field of view, slice thickness = 3 mm, slice gap = 0 mm, repetition time = 3000 ms, echo time = 13 ms, number of averages = 1, echo train length = 7 (1.5 T) and 6 (3 T), pixel BW = 122, 244 Hz at 1.5 T 125, 250 Hz at 3 T. MRI Systems: 1.5 T GE Signa, 3 T Siemens Trio.

BW: Bandwidth; ROI: Region of interest; SNR: Signal-to-noise ratio.

![](image)

**Figure 13.** Contrast-to-noise ratio measurements in the pediatric knee of an 11-year-old boy as a function of field strength and receiver bandwidth. The CNR is calculated by the difference in signal between two tissues of interest divided by the standard deviation of the background noise. The CNR is increased in most tissue types with increasing field strength. The field of view = 160 mm, the data matrix was $256 \times 192$, 75% phase field of view, slice thickness = 3 mm, slice gap = 0 mm, repetition time = 3000 ms, echo time = 13 ms, number of averages = 1, echo train length = 7 (1.5 T) and 6 (3 T), pixel BW = 122, 244 Hz at 1.5 T 125, 250 Hz at 3 T. MRI Systems: 1.5 T GE Signa, 3 T Siemens Trio.

BW: Bandwidth; CNR: Contrast-to-noise ratio; ROI: Region of interest.
amount of fat present due to skeletal maturity (Figure 17). The receiver bandwidth also needs to be increased to reduce chemical shift artifact. With the increased SNR, high resolution images can be acquired in 3D and can be reformatted in any plane. The key to successful reformatting is to keep the in-plane resolution below 0.4 mm and the slice thickness below 0.7 mm (Figure 18). Along with the MRI protocol, coil type is also critical. Coils should provide a high SNR.

**Figure 14.** $T_1$ relaxation time map in the pediatric knee showing field strength effect at 1.5 and 3 T. Top image: color-coded $T_1$ relaxation time maps. Bottom table: quantitative $T_1$ relaxation times for four tissue types at 1.5 and 3 T. The $T_1$ relaxation time increases range from 8–40% depending on tissue type. Single slice saturation recovery images used to calculate $T_1$. The field of view = 160 mm, the data matrix was 256 x 160, slice thickness = 3 mm, repetition time = 50, 67, 100, 200, 400, 750, 1250, 2000 and 3000 ms, echo time = 10 ms, number of averages = 1, echo train length = 3, pixel BW = 250 Hz, echo train length = 3. MRI Systems: 1.5 T GE Signa, 3 T Siemens Trio. ROI: Region of interest.

<table>
<thead>
<tr>
<th>ROI</th>
<th>1.5 T</th>
<th>3 T</th>
<th>% Δ at 3 T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>321 ± 88</td>
<td>430 ± 57</td>
<td>34</td>
</tr>
<tr>
<td>Cartilage</td>
<td>1159 ± 533</td>
<td>1252 ± 311</td>
<td>8</td>
</tr>
<tr>
<td>Muscle</td>
<td>934 ± 86</td>
<td>1270 ± 131</td>
<td>36</td>
</tr>
<tr>
<td>Fat</td>
<td>272 ± 28</td>
<td>380 ± 25</td>
<td>40</td>
</tr>
</tbody>
</table>

**Figure 15.** $T_2$ relaxation time map in the pediatric knee showing field strength effect at 1.5 and 3 T. Left image: color-coded $T_2$ relaxation time maps. Right table: quantitative $T_2$ relaxation times for four tissue types at 1.5 and 3 T. The $T_2$ relaxation times are generally constant but demonstrate small decreases in cartilage. Imaging parameters were the same as those in Figure 8. MRI Systems: 1.5 T GE Signa, 3 T Siemens Trio. ROI: Region of interest.
and there are choices available for most joints, including temporo-mandibular, shoulder, knee, and ankle; however, the size of the coil should match the anatomy to maintain a high SNR, and as most coils are sized for adults, this can require some creativity in pediatrics. For example, it is possible to use an adult wrist coil on the elbow of a small child. The size of the coil is important, especially in the pediatric setting where the anatomy is typically small.

- Limitations of MRI in pediatrics

Although MRI is a powerful and flexible technology for the assessment of joint disease in...
children, there are limitations. One such challenge, the lack of standardized grading systems for joint activity and the lack of consensus on definitions, has been addressed above. Natural variability in joint development \[35\] poses another difficulty, both in standardizing joint activity definitions and in evaluating disease. As suggested previously, baseline assessments for each child are very important in understanding joint involvement and changes over time. Another limitation is the inability to image more than one joint in a session; several sessions may be required to assess various joints with different MRI protocols. Bone scintigraphy may be helpful in cases where it is not possible to define the region for imaging. For example, children with nonlocalized extremity pain may have occult osteomyelitis. Scintigraphy can elucidate the involved areas, pointed to regions for further studies. Similarly, in children with chronic fever and lower extremity pain, bone scan may show changes typical of neuroblastoma, such as adrenal uptake or metastatic uptake in ribs.

Finally, sedation during MRI may be required in small children; however, the advent of video-compatible MRI systems has alleviated this concern. In the authors’ experience, children as young as 3 years of age can watch engaging videos while being scanned, and frequently are reluctant to leave the scanner until the video is over! Finally, although anaphylactic or injection site reactions to contrast agent are rare, they have been reported in post-licensure experience \[84\], and safety in children younger than 2 years of age has not been established.

Conclusion
It is clear that there are several options for pediatric imaging in the context of JIA, from widely available, low-cost methods such as radiography and ultrasound, to more complex MRI-based techniques. As with adults, the earlier the disease is caught, the better the clinician is able to render an accurate diagnosis and assess treatment and follow-up options and avert long-term disability. Thus, the accessibility of conventional radiography and ultrasound may be outweighed by the need to gather as much information about affected joints as early as possible in the disease course, and to assess progress with treatment. Several MRI-based techniques are available for these purposes.

It is also clear that data in pediatric patients are sorely lacking for validation and standardization of imaging methods, especially in MRI. Coils and protocols are generally developed for adults with RA or osteoarthritis and assumed to be translatable to the pediatric population. The field would benefit tremendously from larger pediatric studies or pooled data analyses to assist with protocol validation and standardization of MRI-based disease grading. However, large strides in pediatric research have certainly been made over the past decade, and continued improvements in both treatment options and in sensitive methods for imaging disease progression will undoubtedly improve the lives of many children living with JIA.

Future perspective
As 3 T and 7 T imaging systems are being introduced into mainstream imaging (7 T mainly for research), resulting increases in SNR and in resolution will facilitate enhanced imaging of small joints \[85\]. At 7 T it will also be possible to image sodium signal from cartilage \[86\]. With the improved SNR from higher field strengths, what
is important for small joint imaging will be dedicated transmit–receive RF coils that will increase the SNR while reducing the specific absorption rate. Specific absorption rate becomes a problem for whole body transmit and phased array receive and will pose more of a challenge on 3 T systems as 7 T systems remain research only and lack body RF coils for excitation. Another important advance in MRI would be to have dedicated extremity gradient coils to increase resolution and speed as compared with fixed whole body gradients and that do not cause peripheral nerve stimulation.

An intriguing option in the future will be the use of optical imaging to probe angiogenesis with nonspecific fluorescent probes. Such studies are currently being performed in adult rheumatoid arthritis. The use of idocyanine green contrast agent allows for nonspecific, fast and longitudinal imaging of disease activity. First applications are in the hands and wrist since the thickness of the hand does not severely limit depth penetration of photons. In the future it is likely that this technique can be used with specific probes to target the disease process of interest (e.g., integrins and proteases) and with handheld systems for other joints [87–95].

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References
14 Ludwig K, Henschel A, Bernhardt Tm et al. Performance of a flat-panel detector in the


46 Magni-Manzoni S, Rossi F, Pistorio A et al. Prognostic factors for radiographic progression, radiographic damage, and


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