

# Imaging of Juvenile Idiopathic Arthritis

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## KEYWORDS

- Juvenile idiopathic arthritis • Juvenile spondyloarthropathies • Radiography • Ultrasound
- MR imaging • MR imaging scoring system

## KEY POINTS

- Multimodal imaging analysis plays a key role in the diagnosis and treatment monitoring of juvenile idiopathic arthritis (JIA).
- A concrete knowledge of normal joint anatomy throughout pediatric age groups is important.
- A reproducible, accurate, and established scoring system for use in international routine clinical care for monitoring and predicting long-term response to therapeutic interventions is still to be developed for any joints on MR imaging.

## INTRODUCTION

JIA is an umbrella term covering several distinct categories that share common features.<sup>1</sup>

The term JIA replaced, in the 1990s, the older terms, juvenile rheumatoid arthritis (used commonly in the United States) and juvenile chronic arthritis (preferred in Europe). As defined by the International League of Associations for Rheumatology (ILAR), JIA diagnosis relies on the presence of arthritis that persists for at least 6 weeks, begins before the age of 16 years, and is of unknown origin.<sup>2</sup> The classification, established in Durban in 1997 and revised in Edmonton in 2001, defines different subtypes characterized by their clinical, demographic, and genetic features, translating into different responses to treatment (Box 1).

Modern multimodal imaging, including conventional radiographs (CRs), ultrasound (US), and MR imaging, plays a key role in the diagnosis, follow-up, and treatment monitoring of JIA. Unlike imaging of rheumatoid arthritis and other

inflammatory joint conditions in adults, extensively studied in the past 2 decades, the available literature for JIA is more limited, and consensus articles about the role of imaging of the different manifestations of JIA have been published only recently.

The European League Against Rheumatism and the Pediatric Rheumatology European Society have recently published a consensus article with recommendations to guide radiologists and clinicians in choosing the best imaging technique for each particular clinical setting.<sup>3</sup> Specific scoring system for each joint may contribute to make the staging and the follow-up more reproducible.

## EPIDEMIOLOGY OF JUVENILE IDIOPATHIC ARTHRITIS

Based on the current classification established by the ILAR in 2001, the incidence of JIA in European children is approximately 3 to 15 individuals per

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**Box 1****International League of Associations in Rheumatology classification criteria for juvenile idiopathic arthritis**

1. Systemic
2. Oligoarthritis
  - a. Persistent
  - b. Extended
3. Polyarthritis (RF negative)
4. Polyarthritis (RF positive)
5. Psoriatic arthritis
6. ERA
7. Undifferentiated arthritis
  - a. Fits no other category
  - b. Fits more than 1 category

100,000 individuals younger than 16 years.<sup>4</sup>

Chronic arthritis seems worldwide in distribution, but the reported incidence and prevalence vary considerably throughout the world. Ethnic differences have been reported to have a significant influence on JIA epidemiology, whites being more affected than African American and Asian individuals.<sup>5,6</sup>

Age at disease onset and gender ratio depends on clinical subset. In most published series of patients with JIA, the female/male ratio is of 2/1 to 3/1, although equal gender ratios have been reported in certain ethnic groups, such as Indian and black South African children.<sup>5</sup> JIA onset occurs at approximately 6 years of age in patients with polyarticular disease in both genders, whereas young patients with oligoarticular disease have a mean age of approximately 4 years in girls and 10 years in boys.<sup>7</sup> Gender has a high influence in determining some features of JIA. As an example, oligoarticular JIA has a female preponderance as high as 8:1 in children younger than 8 years, mainly in a subset of patient with antinuclear antibodies positivity and associated iridocyclitis.<sup>8</sup>

## **PATHOGENESIS**

The etiology and pathogenesis of JIA are unclear but thought to be the result of a combination of genetics and environmental factors. Twin and family studies suggest a role of genetic factors in the predisposition to JIA. Numerous associations between HLA alleles and JIA categories have been reported in multiple populations. Although the juvenile spondyloarthropathies or enthesitis-related arthritis (ERA) is strongly associated with the

HLA-B27, other associations have been described for both HLA or non-HLA susceptibility loci with some JIA categories, in particular, *HLA-DRB1:01* and *PTPN22* or *STAT4* variants with oligoarticular or RF-negative polyarticular JIA, shared epitope encoding *HLA-DRB1* with RF-positive polyarticular JIA. Some alleles that predispose to the risk of category might be also protective against another JIA category.<sup>9</sup>

In combination with genetic factors, environmental triggers are also described as involved in the pathogenesis of JIA. Infectious viral or bacterial agents are mainly considered potential triggers. It has been reported an interaction between the immune system and microbiome which may play a role in the autoimmunity or contributing in the development of JIA.<sup>10</sup>

JIA is an immune-mediated disease. In a majority of JIA subset, errors of adaptive immunity (mistakes by antigen-specific T and B cells) initiates an inflammatory response because a defect in normal self-inhibitory mechanisms. Conversely, systemic JIA could be considered an autoinflammatory disorder involving pathways associated with innate immunity. Several cells types, including monocytes/macrophages, T lymphocytes or B lymphocytes, or specific cytokines, such as tumor necrosis factor (TNF)- $\alpha$ , interleukin-6, and interleukin-1, play an important role in the pathophysiology of JIA. Therapeutic advances with biologics agents are known to be efficient for specific categories of JIA, suggesting a specific role of these cells or cytokines in the disease with a different way. Polyarticular and oligoarticular JIA are better responders to TNF- $\alpha$  blocking agents compared with systemic JIA, where anti-IL-6 or anti-IL-1 blocking agent is more efficient. Further insights into the disease pathogenesis will be provided by the continuous advances in understanding of mechanisms related to the immune response and inflammatory process implicated in JIA.

## **CURRENT CLASSIFICATION**

1. The most frequent clinical subtype of patients with JIA is oligoarthritis (27%–60%).<sup>4</sup> By definition, the oligoarthritis subtype involves fewer than 4 joints within the 6 months of onset of the disease. It occurs typically in very young girls and is often associated with the presence of antinuclear antibodies. The patients of this subtype are at increased risk of asymptomatic uveitis and should be monitored closely to detect it early. Most patients in this group are first referred for an episode of arthritis of the knee. The second most frequent clinical

- presentation in this group of patients is an inflamed ankle (up to 40% of patients). Ankle involvement often occur in girls ages less than age 5 years.<sup>11</sup> Some patients develop a polyarticular involvement after the first 6 months and are considered as having extended oligoarthritis.
- The subset of patients with a polyarticular presentation ( $\geq 5$  joints affected within the first 6 months after the onset) and negative rheumatoid factor (RF) accounts for 11% to 28% of all JIA patients.<sup>4,12</sup> In this subgroup, girls are more frequently affected than boys (2:1). Two age peaks can be observed: an early peak between 2 years and 4 years and a later peak between 6 years and 12 years.<sup>4</sup> Small joints are symmetrically involved, but large joints can also be affected in the early stage of the disease.
  - Patients with a polyarticular presentation ( $\geq 5$  joints affected within the first 6 months after the onset) and positive RF account for only 2% to 7% of all patients with JIA. Girls are more affected than boys.<sup>4</sup> Almost all patients in this group develop bone erosions during the first 5 years after the onset, leading to joint damage. Hand and wrist are typical locations. Uveitis, lung, and aortic involvement are rarely observed in this subgroup of patients.
  - Psoriatic arthritis is a form of JIA found in 2% to 11% of patients with JIA.<sup>4</sup> Arthritis is associated with psoriasis or with a familial history of psoriasis. Dactylitis, nail pitting, and psoriasis are specific features of this subset of patients. In 50% of this subgroup, arthritis occurs before the skin changes, whereas skin and joint are simultaneously affected in only 10% of patients. In patients with psoriatic arthritis, both large and small joints may be involved. At the early stage, the involvement is mostly oligoarticular but a symmetric polyarticular evolution may eventually occur. Sternoclavicular joint inflammation has been reported as typical in these patients.<sup>13</sup>
  - Patients with ERA account for only 3% to 11% of all patients with JIA. It occurs mostly in boy aged more than 10 years, which will develop first peripheral arthritis and entesopathies, and probably evolve to spondylarthritis with axial involvement. They are often HLA-B27 positive. Up to one-third of these patients develop an inflammation of sacroiliac (SI) joints. Patients with fewer than 4 joints involved usually have a better prognosis.
  - Systemic arthritis is the most severe form and refers to Still disease of adults. Arthritis is accompanied by prolonged high fever associated with

a typical rash, adenopathies, hepatosplenomegaly, or serositis. This subtype is classified as an autoinflammatory syndrome and has a different pattern of response to biologics. This subtype includes only 4% to 17% of patients with JIA.<sup>4</sup> Life-threatening acute complications can occur as macrophage activation syndrome (5%–10% of cases). Amyloidosis can be observed as a late complication due to chronic uncontrolled inflammation.

- The undifferentiated subtype includes those patients (11%–21%) who do not match the criteria to be included in the subsets (discussed previously) of patients or who could be included in more than 1 of the previous 6 subtypes.<sup>4</sup>

### IMAGING IN JUVENILE IDIOPATHIC ARTHRITIS: GENERAL FEATURES

JIA shares the same imaging findings of inflammatory joint disease in adults, including soft tissue swelling, joint effusion, periarticular osteopenia, erosions, synovitis, and bone edema.

Because of the specific lesions of bone and joints in children, some additional pathologic features can be revealed by imaging in JIA not present in adults, including epiphyseal growth disturbances, premature physeal fusion, limb length inequality, and abarticular periosteal reaction.

Due to the heterogeneity of imaging findings in JIA, there is not a stand-alone imaging modality to assess all the different features of JIA.

CR, US, and MR imaging are the current imaging modalities used in clinical and are analyzed later.

Other techniques, such as PET and scintigraphy, have been proposed in the past but are not currently performed in clinical settings. CT is used but is limited by the high radiation dose (although it might be helpful in the evaluation of facet joints in cervical spine as well cone-beam CT evaluates bony changes in temporomandibular joints [TMJs]).

After the discussion of each imaging modality, recommendations for the use of imaging in JIA are summarized based on expert consensus literature.

#### Conventional Radiology

CRs in the early stages of JIA are often normal.<sup>14–16</sup> The first radiographic changes consist of soft tissue swelling, joint effusion, periarticular osteopenia, epiphyseal remodeling–widening, periostitis, and osseous overgrowth. A CR of the knee may be the first examination requested by clinicians facing an asymmetric inflammatory swelling.

On CR, persistent inflammation and synovial hypertrophy will result in destruction of epiphyseal cartilage and plate, and the erosive changes after significant cartilage loss will be apparent. Higher prevalence of the bony erosions as also progressive joint destruction<sup>17</sup> is observed<sup>18</sup> in children) with polyarticular than oligoarticular JIA.

Periostitis resulting in an enlarged squared-off appearance more commonly involves phalanges, metacarpal, and metatarsal bones and less frequently any long bone (Figs. 1–4).

Carpal crowding and squaring of the carpal bones and “balloon-like” epiphyses of the lower extremities are more observed in JIA.

Periarticular osteopenia is most commonly observed in the systemic subtype and is due to bone hyperemia.

CR also allows visualizing late complications of JIA like ankylosis, joint misalignment, enlarged epiphysis due to bone growth disturbance, premature physeal fusion causing limb length inequality, and spine deformities (Fig. 5).

CRs are of limited use in some conditions.

On CR, TMJ involvement may be overlooked. As another example, periarticular swelling is particularly difficult to detect on CR at the level of metacarpal/metacarpophalangeal joints.

Anatomic variations may be misinterpreted as bone erosions on CR, especially in the wrist joint, because of the large number and variation of the vascular channels, cortical irregularities, and recent ossified bones at the level of secondary ossification centers.<sup>19–21</sup>

Periosteal apposition observed on CR also occurs in children, in the bone adjacent to an inflammatory joint. This feature is characteristic in children and is not found in inflammatory chronic diseases of adults, such as rheumatoid arthritis. This finding can be speculated in children because they present a much high bone turnover reconstruction.

Pathologic fractures depending on treatment must be ruled out.<sup>18,22–24</sup>

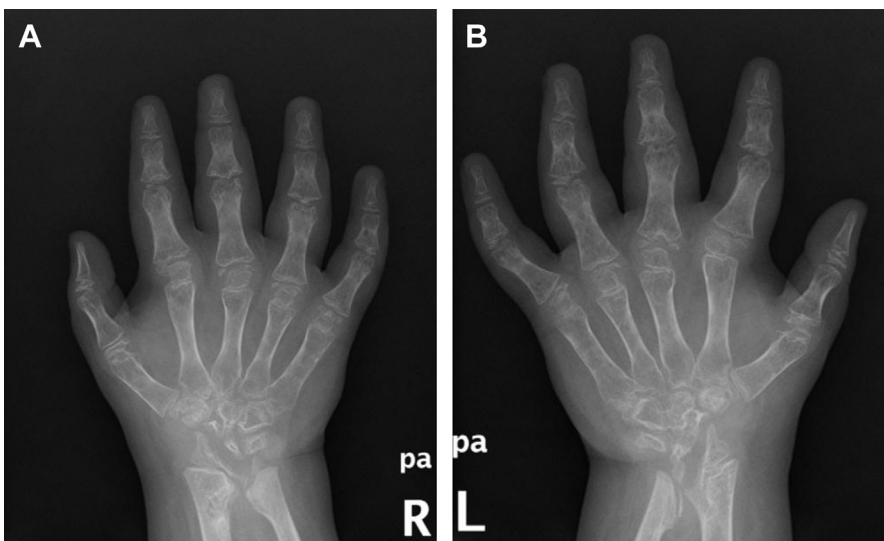
Severe muscular atrophy can be also observed on CR on the latest stage of the disease as a complication of chronic functional joint impairment.

Recently, Ravelli and Martini<sup>4</sup> adapted the Sharp/van der Heijde system for JIA to evaluate the modification in erosions and joint space narrowing scores.

### Ultrasound

US as a cost-effective, easily accessible and non-irradiating modality and plays a significant role in the evaluation of JIA. In addition, US allows a dynamic evaluation and makes easily possible a comparison with the contralateral side without supplementary irradiation.

US evaluates the presence of synovial thickening, synovitis, joint effusion, tenosynovitis, enthesitis and bone erosions (Fig. 6).<sup>25</sup> Synovial thickening and synovitis can be seen during the ultrasonographic examination as a solid, non-compressible, abnormally hypoechoic tissue associated with joint lines or surrounding tendons.



**Fig. 1.** (A, B) CRs of the hand of a young girl with severe periarticular osteopenia, diffuse space loss with erosions, and bony destructions. Epiphyseal remodeling carpal crowding and squaring of the carpal bones is a characteristic feature of chronic JIA due to periostitis.



**Fig. 2.** Epiphyseal remodeling and marked periarticular osteopenia on an anteroposterior knee CR of a young child with JIA.

In young children, where synovial tissue may be difficult to distinguish from adjacent hypoechoic epiphyseal cartilage, evaluation of the synovium is difficult. A better visualization of the synovial



**Fig. 3.** Radiograph of the right shoulder of a young girl with chronic features of JIA, such as the pronounced epiphyseal remodeling–widening, severe bony destruction of epiphyseal cartilage, and periarticular osteopenia.



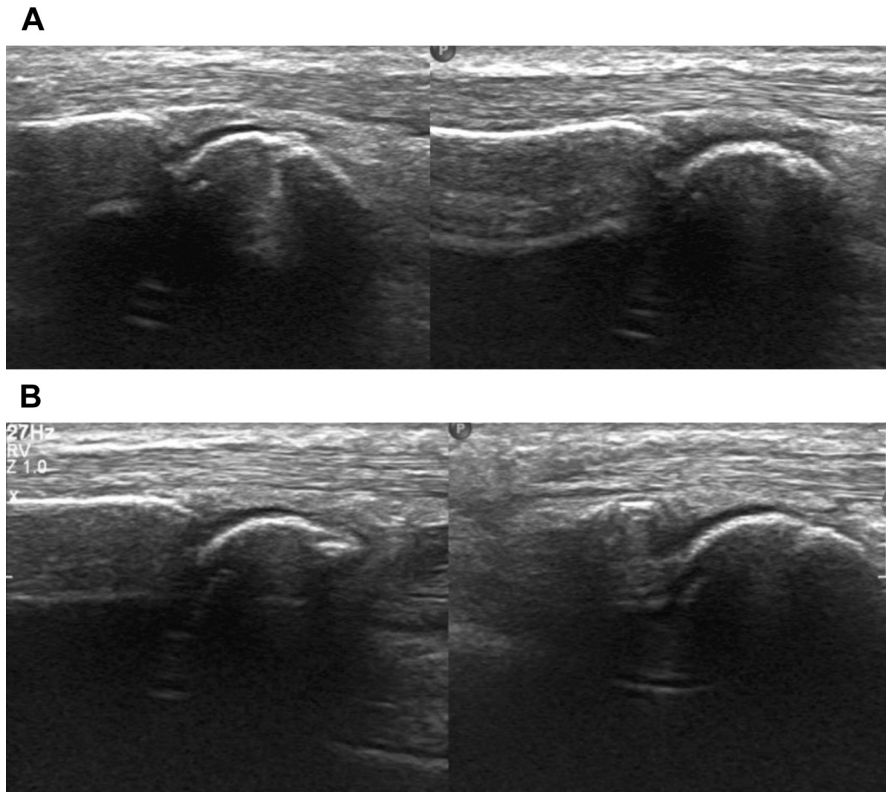
**Fig. 4.** Ankylosis of the posterior elements of C2-C4 visible in the lateral view radiograph of the cervical spine in a young child with JIA.

thickening when associated with a similar echogenicity of joint effusion is acquired after a bit of pressure through the transducer, which displaces the effusion. Color and power Doppler US techniques show a superiority to gray-scale US in observing active disease. Doppler US analyzes synovial blood flow, suggestive of active disease. A potential pitfall can be the physiologically synovial vascularization of the in healthy children.<sup>26,27</sup>



**Fig. 5.** Chronic radiographic changes of JIA. Radiograph of the pelvis in a child with long-lasting JIA, showing the bilateral hip joint chronic changes with severe bony destruction and marked epiphyseal remodeling. Bilateral widening of SI joints suggesting their involvement.





**Fig. 6.** (A, B) Mode B US of the right knee of a 6-year-old girl showing a bony erosion on the distal epiphysis of the tibia. Comparative image with the left nonaffected knee is seen on the right picture.

A joint effusion is described as an abnormal intra-articular finding, which is hypoechoic or anechoic (relative to subdermal fat) or in some cases isoechoic or hyperechoic, intra-articular material that is displaceable and compressible but does not exhibit Doppler signal. Physiologic fluid is common in children, and differentiation between normal amounts of joint fluid from a joint effusion is sometimes subtle.<sup>28</sup>

Epiphyseal cartilage shows a relative hypoechoogenicity and it might be misinterpreted as a joint effusion in unexperienced pediatric ultrasonographers.

Tenosynovitis can be demonstrated as anechoic or hypoechoic thickened tissue with or without fluid in the tendon sheath, which may show Doppler signal and it must be observed in 2 orthogonal planes to eliminate the possible artifact of anisotropy. Tenosynovitis in children is most frequently seen along the extensor tendons of the wrist and along the ankle joint.<sup>29</sup>

Enthesitis is observed as an abnormally hypoechoic or thickened tendon or ligament, associated with a loss of the expected fibrillary architecture, at the tendinous or ligamentous insertion at its bony attachment that is seen in 2 perpendicular planes. This finding may contain foci of calcification and

may show abnormal Doppler signal or bony modifications like enthesophytes, erosions, or cortical irregularities, even though these associated findings are seen less commonly in children. US is found to have a high false-negative rate in detection of subtalar disease.<sup>30,31</sup>

A bone erosion is defined as a discontinuity of the bony cortex visible in 2 orthogonal planes. Identifying an erosive change in a child is challenging, because there are physiologic irregularities in recently ossified bone that can be mistaken as cortical erosions.<sup>6</sup>

The reliability of US in detecting bone erosion compared with CR has not been made in JIA although these techniques are considered equivalent in large meta-analysis performed in adult patients of rheumatoid arthritis.

US evaluates epiphyseal cartilage integrity and detect cartilage erosion and thinning as obliteration and blurring of the normally well-defined margins of its surface. Epiphyseal cartilage changes from anechoic to hypoechoic and thickens with maturation. A recent study established the age-related and gender-related normal reference standards for cartilage thickness of the knee, ankle, wrist, and metacarpophalangeal and proximal

interphalangeal joints for children between the ages of 7 years and 16 years. This work was further evaluated by showing good agreement between MR imaging and US for the measurement of cartilage thickness in healthy children. JIA patients has a thinner cartilage when compared with age-matched and gender-matched controls, although interestingly this finding is observed in both clinically affected and nonaffected joints.

US as a more sensitive diagnostic tool than clinical examination differentiates synovitis from tenosynovitis with evident classification and therapeutic implication.<sup>29,32–34</sup> Additionally, sub-clinical enthesitis can be detected by Doppler US.<sup>35</sup>

The differentiation between joint effusion (and its modification in volume) with inflamed synovium (and its size and distribution changes) is useful for monitoring the disease.<sup>30,36–39</sup>

Color Doppler also evaluates/differentiates the degree of disease activity by the assessment of synovial vascularity.<sup>18</sup>

Contrast-enhanced US has been shown to improve detection and evaluation of the synovial vascularity.<sup>40–42</sup>

A special help of US imaging is the possibility of guiding precisely the joint aspiration or injection of anti-inflammatory agents. Thus avoid complications of extra-articular diffusion of these agents (eg, soft tissues calcifications).

### Ultrasound Limitations

To be able to perform the correct diagnosis, an ultrasonographer should be familiar with the changes occurring in a healthy developing joint; for example, modification of the thickness of epiphyseal cartilage should be compared with a healthy child of the same gender and age.<sup>43,44</sup>

Another limitation of US, Color Doppler, CEUS is the non-documentation by research of the normal appearance of the entheses and tendons changes of the developing skeleton through age and sex which is essential to compare to patients with JIA.<sup>45,46</sup>

Notwithstanding the inherent limitation of US, namely the low inter and intra observer reproducibility in evaluations the synovial thickening as a semi quantitative score was proposed for JIA, but it has not been validated yet.<sup>47</sup>

Evaluation of bone marrow edema, TMJ, and SI joints and active subtalar disease is limited by US.<sup>24,30,31</sup>

### MR Imaging

MR imaging examination accesses and evaluates the inflammatory process in regions where US cannot reach.

The standard MR imaging protocol includes a T1 spin-echo (SE) sequence, T2 fat-suppressed sequence or short tau inversion recovery (STIR), and T1 fat-suppressed sequence precontrast and postcontrast. The DIXON fat-suppression sequence is being used more frequent than STIR as it allows a very good evaluation of the joint and with a better signal-to-noise ratio.<sup>48</sup>

MR imaging is the only modality that allows the study of all relevant structures in JIA.

The joint can be easily examined in all possible plans with the multiplanar reconstructions and, with its excellent contrast resolution of bone and soft tissues, it is considered the most sensitive imaging technique when contrast-enhanced sequences are performed for detecting synovitis<sup>43</sup> (Figs. 7–9).

MR imaging is the only modality which can objective bone marrow edema (so called in the case pre-erosive osteitis)<sup>49–51</sup> (Fig. 10), which is probably a possible predictor of future erosions in adults.

Bone marrow edema (especially when it involves the epiphysis, when it is located in the areas of synovial reflection, and when it is more diffused) is an indication for treatment to avoid permanent joint destruction.<sup>43</sup> Longitudinal studies need to be done and distinguish the bone marrow edema seen in healthy children compared to the bone marrow edema which is going to evolve to erosions in JIA patients.<sup>26,51</sup>

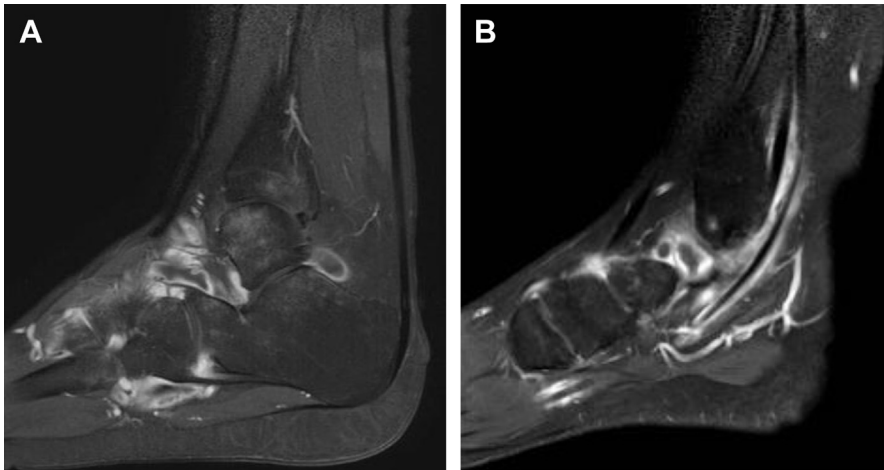
MR imaging is a more sensitive modality which it allows to detects double the number of erosions at the wrist and even more at the SI joint.<sup>45,52</sup> Detection of erosions is also done earlier and with more confidence than US or radiographic examinations.<sup>45</sup>

Weirdly these late complications of a prolonged JIA pathology do occur in chronic recurrent multifocal osteomyelitis where inflammatory modifications are observed around the metaphysis and growing cartilage.

Cartilage and bone damages also are seen and evaluated by MR imaging.

### MR Imaging Limitations

An important limitation of MR imaging is the need for sedation for children younger than 4 years to 6 years old for a correct examination. The low availability and the high costs of this examination should also be taken in consideration. During one MR imaging examination, just 1 joint can be examined with all the requested sequences (contrast-enhanced sequences that raise the potential for allergic reaction and stressful conditions for the children). As in all the other imaging modalities,



**Fig. 7.** (A, B) Sagittal T1 fat-suppressed sequence after contrast enhancement of an ankle with a long-standing arthritis showing on the left picture an inhomogeneous, patchy synovial enhancement indicating fibrotic and active synovitis and, on the right, tenosynovitis of the tibiotalar posterior and flexor digitorum tendons.

MR imaging is limited in distinguishing the normal findings in a developing joint from pathology.

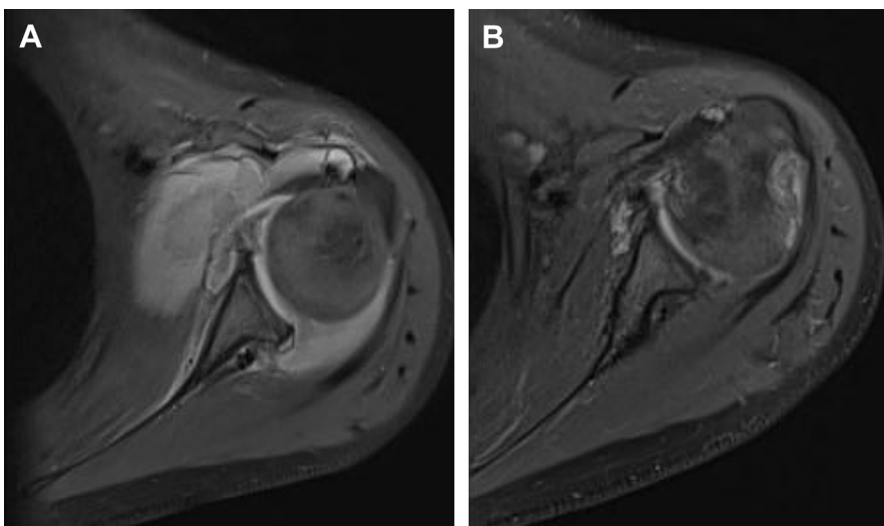
#### CURRENT OPINIONS ON IMAGING ROLE IN CLINICAL MANAGEMENT OF JUVENILE IDIOPATHIC ARTHRITIS: AN UPDATE

Many efforts have been made by several groups worldwide to improve MR imaging of JIA.

In JIA, TMJ joint inflammation is detected mostly by MR imaging with contrast medium injection. Patients younger than 4 years old are at higher risk developing TMJ lesions.<sup>53,54</sup> Active

inflammation of TMJ is characterized by joint effusion, synovial enhancement, and bone marrow edema. Guidance treatment is usually done by CT or fluoroscopy but some studies have been conducted using MR imaging.<sup>55,56</sup>

The TMJ joint monitoring damages are better done by MR imaging than US because MR imaging detects 25% of lesions whereas US detect only 17%.<sup>53</sup> MR imaging with gadolinium is superior in detecting TMJ inflammation than US (35.7% vs 86.7%, respectively).<sup>57</sup> The joints that are preferentially damaged in the earlier and in the late changes are the wrist and the hip.



**Fig. 8.** (A, B) Synovial enhancement, joint effusion, marginal and central erosions, and bone marrow edema are seen at the images of a child with JIA on these MR imaging axial plane images acquired with STIR sequence and T1 fat-suppressed sequence with contrast.





**Fig. 9.** Sagittal T1 SE fat-suppressed with contrast enhancement of a 15-year-old boy knee shows synovial enhancement evocative of synovitis of the anterior and the posterior compartment.

### Cervical Spine

Cervical spine MR imaging is more useful than clinical examination in the detection of joint damage.<sup>58</sup> According to Tzaribachev and colleagues,<sup>59</sup> although only 20% of patients



**Fig. 10.** Sagittal T2 SE fat-suppressed image of a 15-year-old boy knee reveals joint effusion with synovial thickening. Hoffa fat is infiltrated and bone marrow edema is slightly visible in the proximal metaphysis of the tibia.

presented clinical symptoms, such as pain or movement limitation, 87% of the MR imaging examinations showed abnormalities, which suggests that cervical spine involvement is usually silent.

### Sacroiliac Joint

SI joint inflammation is seen in 30% of patients with the ERA subtype of JIA, especially men with a later age onset of the disease, acute anterior uveitis, and bone marrow edema, all of which indicate active inflammation of the disease. SI joint inflammation is detected better by MR imaging than clinical examination<sup>60,61</sup>; 5 years to 10 years after the onset of symptoms, SI joint abnormalities can be seen.<sup>52,62</sup> MR imaging detects 80% of acute inflammation damages whereas CR cannot.<sup>63</sup>

The evaluation of disease activity and differentiation of active synovitis to fibrotic changes is done by the aspect and characteristics of synovial enhancement. Dynamic contrast-enhanced (DCE) MR imaging sequences and the quantification of permeability values could be supportive tools in treatment decisions and disease management.<sup>64–66</sup> A pixel-by-pixel DCE–MR imaging time intensity curves analysis method can distinguish clinically active disease with asymptomatic patients. Recent studies showed that DCE MR analysis correlate well with the rheumatoid arthritis MR imaging scoring system.<sup>67,68</sup>

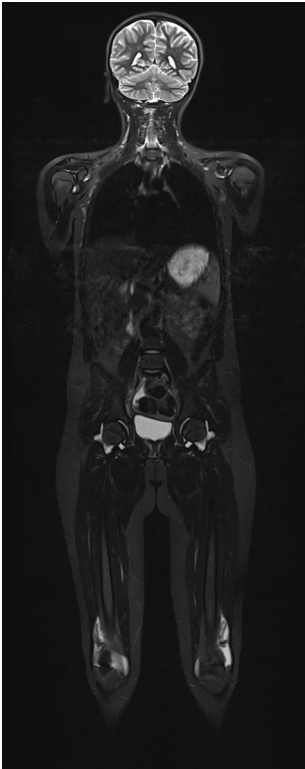
T2 relaxation time mapping as a recent MR imaging technique gives more information about the joint cartilage.

The pathological changes induced by JIA such as an increased permeability of the cartilage matrix, increased water content, water distribution in inflammatory tissues, results in a higher T1 and T2 relaxation times. These early changes after inflammatory process of JIA can evaluate the microstructural and reversible modification of the cartilage, allowing an early and more aggressive plan of treatment.<sup>69,70</sup>

In addition to a contrast-enhanced acquisitions, diffusion-weighted imaging could be helpful in differentiating synovitis for joint effusion.<sup>71</sup>

Whole-body MR imaging evaluates not only the activity but also the extent of the disease in the same examination (Fig. 11).

What is needed for a precise monitoring and treatment response is a standard validated and feasible scoring system for the use of MR imaging in JIA (even for knee arthritis<sup>27,72,73</sup>). The existing Juvenile Arthritis MRI Scoring system which assesses the synovial enhancement can differentiate JIA patients from asymptomatic control at group level, but needs extra adaptations to distinguish synovitis to synovial enhancement in unaffected



**Fig. 11.** Whole-body MR imaging, STIR sequence in the coronal plane demonstrates joint effusion in the both shoulders, hips, and knees. Synovial thickening is also seen in both knees. The shoulders and hips involvement in the disease was revealed by imaging and not by the clinical examination.

children. A potential pitfall, mild enhancement of synovium in asymptomatic children, can eventually be eliminated with the standardized acquisition of contrast.

New studies have showed that the diagnosis and synovitis grading by contrast enhancement are influenced by time of postcontrast acquisition used for the grading, a reason why an MR imaging scoring system should be based on a standardized protocol of 1 joint at a time with a standard interval between intravenous contrast injection and postcontrast acquisition.<sup>71</sup>

For differentiation of synovial enhancement an improved MRI scoring with a standardize protocol for MRI acquisition and a consensus on imaging interpretation is still needed to further establish MRI as an accurate monitoring tool for JIA disease activity.

For the wrist, there are already some proposed MR imaging scoring systems,<sup>43</sup> but they are not yet clinically accepted.

Nusman and colleagues<sup>74</sup> proposed an MR imaging protocol of the wrist after the

recommendations from the Outcome Measures in Rheumatology Clinical Trials (OMERACT) MR imaging in JIA Working Group and the Health-e-Child project.<sup>75</sup>

## ROLE IN PROGNOSIS AND MONITORING

In JIA, CR is useful for predicting further joint damage. In terms of prognosis, persistent inflammation on US or MR imaging is a prediction of subsequent joint damage. CR is useful for the prediction of progression: at 5 years with a wrist CR baseline with a Sharp/van der Heijde score greater than 1, patients with erosions and joint space narrowing in the first 6 months of the study spent more time with clinically active disease and were less likely to achieve clinical remission or medication.<sup>74</sup>

US and MR imaging are useful in monitoring disease activity. MR imaging is superior in detecting knee inflammation than US.<sup>36,76,77</sup> They also are better making the differential diagnosis between pannus and effusion.

## ROLE IN TREATMENT AND REMISSION

The treatment guidance of intra-articular injection is usually done by US. US allows accurate assessment of the needle placement during intra-articular injection of medication.<sup>78</sup> According to Parra and colleagues,<sup>56</sup> verified by CT an accurate intra articular placement of the needle under US guidance in 91% of patients. According to Sauremann and colleagues,<sup>79</sup> TMJ injections guided by MR imaging confirmed that 65% of injections were accurately placed. A similar study confirmed that 100% of injections were accurate in the treatment of SI joints.<sup>80</sup>

US and MR imaging are useful in the follow up of asymptomatic patients during remission periods to rule out subclinical inflammation. Synovitis is seen in US B mode in patients with clinical remission in up to 84.1% of joints and power Doppler activity in up to 48.6% of joints.<sup>40</sup>

Examination of clinically inactive joints can reveal on MR imaging a knee inflammation in 50% of patients and bone marrow edema in 33.3%.<sup>81,82</sup>

In recent studies, asymptomatic patients with a positive MRI and signs of inflammation at US are more likely to develop an active disease or show a disease progression at 6-month follow-up.<sup>82</sup>

## SUMMARY

Multimodal imaging contributes to diagnosis and treatment monitoring of JIA.

The importance of an early diagnosis and adjustment of the treatment are critical to avoid joint deformities and ankylosis.

A thorough knowledge of normal joint anatomy throughout pediatric age groups is important. Based to this knowledge, an imaging scoring system could be created, as it exists for adults suffering from RA. An imaging scoring systems could be created that can be used as a powerful tool in clinical trials for new therapies monitoring. Standard MR imaging protocols and scoring systems should be validated in the near future for a reliable evaluation of drug effects and clinical course in clinical trials. In addition these protocols and scoring systems should be tailored for each joint.

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