Review

Imaging in juvenile idiopathic arthritis with a focus on ultrasonography

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Received on May 13, 2012; accepted in revised form on July 19, 2012.

Clin Exp Rheumatol 2013; 31: 135-148.

Key words: imaging, ultrasonography, MRI, juvenile idiopathic arthritis

Competing interests: none declared.

ABSTRACT

Early therapeutic intervention and use of new highly efficacious treatments have improved the outcome in many patients with juvenile idiopathic arthritis (JIA), but have also led to the need for more precise methods to evaluate disease activity. In adult rheumatology, numerous studies have established the importance of magnetic resonance imaging (MRI) and ultrasonography (US), and MRI is considered the reference standard. Nevertheless, due to differences in disease characteristics and the unique features of the growing skeleton, the findings obtained in adults are not directly applicable to children and adolescents. For paediatric patients, US offers specific advantages over MRI, because it is non-invasive, does not require sedation or general anesthesia (which facilitates repeated examinations for follow-up), is quickly accessible bedside, and is easy to combine with clinical assessment (interactivity). Agitation of the patient is rarely a problem, and hence young children can be seated on a parent's lap or play while being examined, and multiple locations can be assessed during a single session. Furthermore, modern high-frequency US transducers used by experienced US examiners can provide unsurpassed resolution of the superficial musculoskeletal structures in children. US is also the best available technique for imaging guidance of steroid injections. Unfortunately, there are still no validated MRI or US scoring systems for evaluating inflammatory and joint damage abnormalities in JIA, and few US studies have been conducted. Sonographic assessment of disease activity has, however, been proven to be more informative than clinical examination and is also readily available at points of care.

This review summarises the literature on imaging in JIA, focusing on US and the important role this technique will play in JIA in the future.

Introduction

The term juvenile idiopathic arthritis (JIA) encompasses all forms of arthritis that begin before the age of 16 years, persist for more than six weeks, and are of unknown etiology (1, 2). JIA is the most common form of chronic rheumatic disease in childhood, and it causes extensive disability. In high-income countries, the annual incidence is about two to 20 children and the prevalence 16 to 150 cases per 100.000 children (2), and corresponding figures for the Nordic countries are 11 to 15 children and 86 children, respectively (3, 4). Early therapeutic intervention and the use of new, highly effective drugs aiming to prevent structural damage have shifted the attention away from radiographic detectable damage, stimulating a growing need for new imaging modalities more sensitive to the detection of pre-erosive changes and the monitoring of treatment efficacy.

In adult rheumatology, numerous studies have established the important role of magnetic resonance imaging (MRI) and ultrasonography (US), and MRI is considered the reference standard for advanced imaging (5, 6). Nevertheless, due to differences in disease characteristics and the unique features of the growing skeleton such as age-related variations in the articular cartilage thickness, incomplete ossification and bone growth anomalies induced by the disease, the findings of studies in adults are not directly applicable to children and adolescents (7).

Imaging techniques such as US and MRI have not yet been fully evaluated in paediatric rheumatology (8-13), and there are no validated US or MRI scoring systems for the assessment of inflammatory and joint damage abnor-

malities in JIA (14). Nevertheless, with the advances of imaging technology, it is expected that both MRI and US will play an expanding role in the future diagnosis and monitoring of JIA.
This review summarises the published literature on imaging in JIA, with a specific focus on US (15). Attention is also given to the importance of having good knowledge of the normal appearance of each joint at different developmental stages in order to avoid diagnostic errors when performing US examinations in growing subjects (16).

Imaging in JIA

Conventional radiography

Assessing structural damage to joints over time is essential for evaluating the effectiveness of therapeutic interventions for patients with inflammatory arthritis. Although radiography is able to quantify joint damage, the changes found with conventional radiography (CR) early in the disease course are non-specific, and late radiographic changes are often irreversible (11).
CR has been, and still is, the central component of imaging in JIA, and it has also served as the basis for developing specific systems used to score joint damage (17-23). Assessment of structural damage by CR is a key outcome in studies of treatment efficacy in adult arthritis patients (8). The imaging used to evaluate articular disorders in children differs from that applied in adults in several important aspects, and the growing skeleton in young patients makes CR assessment of structural damage in JIA a challenge. Joint space width normally decreases with increasing skeletal maturity, making it difficult to reliably assess cartilage loss in paediatric patients without the availability of normal standards. Furthermore, JIA patients may develop distinctive abnormalities such as disturbance of bone growth and maturation. The scoring systems designed for adults are not directly applicable, although certain paediatric-targeted scoring systems have proven to be reliable and valid (19). A major limitation of CR, in addition to the radiation dose, is that it does not allow direct evaluation of inflammatory changes in soft tissues.

Fig. 1. US examination of the ankle in a young child with JIA.

Table I. Advantages and disadvantages of musculoskeletal US imaging in children.

Advantages
Non-invasive: no ionizing radiation, no need for sedation or general anesthesia, no intra-venous contrast
No complications, no contraindications
Can visualise both soft tissues (inflammatory changes) and bone surfaces (destructive disease manifestations)
Multiregional: possible to examine several joint regions in one session
Potential for guiding interventions (*e.g.* intra-articular steroid injections)
Unsurpassed resolution of superficial musculoskeletal structures
Interactivity with clinical assessment, dynamic tests
Well tolerated by children of all ages, agitation rarely a problem
Results available in real time
Relatively short examination time
Repeatability (follow-up)
Bedside availability
Widely available (all hospitals)
Relatively low cost
Disadvantages
Long learning curve
Operator-dependent (acquisition and interpretation of images)
Incomplete examination: acoustic shadowing from overlying bones; cannot image bone; air, fat, and fibrosis can alter images
Lack of overview (but possible to obtain "panoramic view images")
Limited normative data on children
Doppler-US not validated for use in children, difficult to standardise and to make objective measurements
Difficult to standardise for clinical trials
Machine-dependent
Less objective documentation

Magnetic resonance imaging

MRI provides detailed cross-sectional of all the joint structures involved in inflammatory arthritis: synovial proliferation, joint and extra-articular fluid, cartilage damage, bone erosions, and bone marrow oedema (13, 24-29). A distinctive advantage of MRI compared

Table II. Definitions of musculoskeletal US findings in JIA pathology.

JIA pathology	Definition for US pathology (OMERACT)
Synovial hypertrophy	Abnormal intra-articular tissue that is hypoechoic (relative to subdermal fat) or in some cases isoechoic or hyperechoic, and is non-displaceable and poorly compressible, and may also exhibit a Doppler signal
Joint effusion	Abnormal 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 a Doppler signal
Tenosynovitis	Hypoechoic or anechoic thickened tissue with or without fluid in the tendon sheath that is seen in two perpendicular planes and may exhibit a Doppler signal
Enthesitis	Abnormally hypoechoic (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bony attachment (may contain hyperechoic foci consistent with calcification), seen in two perpendicular planes that may exhibit a Doppler signal and/or bony changes such as enthesophytes, erosions, or irregularities
Bone erosion	Discontinuity of the bone surface visible in two perpendicular planes

Based on: Musculoskeletal ultrasound including definitions for ultrasonographic pathology, R.J. Wakefield, *et al*.; *J Rheumatol*; 2005, 32, 12, pp. 2485-7.

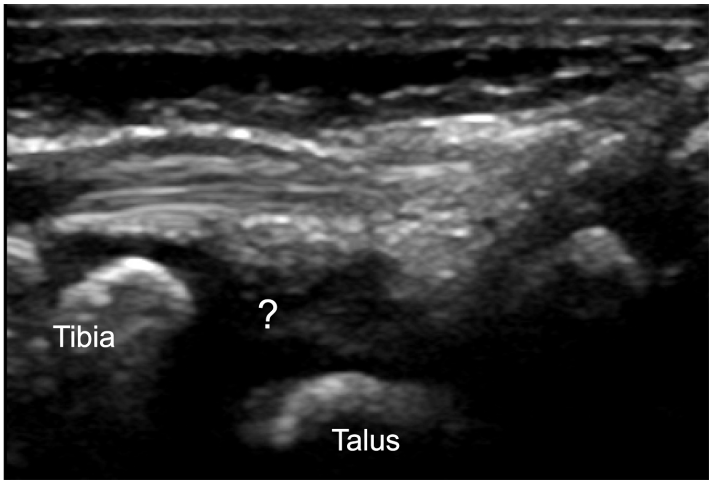


Fig. 2. Anterior longitudinal US scan of the ankle in a child with JIA. The hypoechoic structure (?) between the tibia and talus may be either cartilage or hypertrophied synovium, which have similar echogenicity.

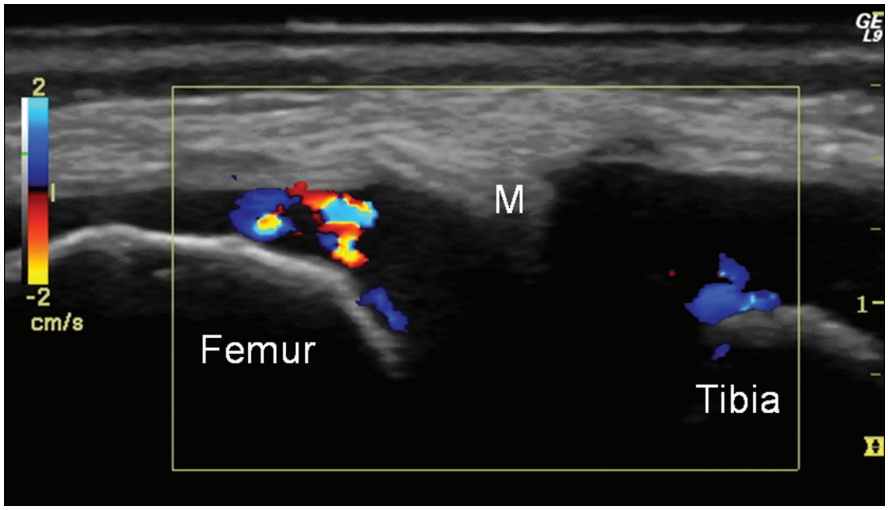


Fig. 3. Medial longitudinal color Doppler examination of the knee in a young healthy child. The vascularised cartilage of the epiphysis is almost anechoic. M=hyperechoic medial meniscus.

to other imaging modalities is the capability to visualise bone marrow oedema, which is a key predictor of erosive joint damage in rheumatoid arthritis (RA) (30). Such oedema is either rare or absent in healthy adults, whereas MRI findings in healthy children have been reported to show physiological bone marrow oedema at the iliac crest, in the wrist, and in the ankle region (31-35). To date, there is no data on the prognostic meaning of bone marrow oedema in JIA. Until longitudinal studies will clarify the prognostic significance of these abnormalities, it would not be advisable to make treatment recommendations based on this finding in children and adolescents.

MRI reveals an erosion as a break in the cortical bone, and studies of adults with RA have demonstrated the significant prognostic value of MRI-detected bone erosions (36). Predicting prognosis in children with newly diagnosed JIA is of key importance. A major issue in this age group is the difficulty of discriminating growth-related bony depression from disease related erosive damage. Thus far only a few studies have been conducted to evaluate MRI assessment of JIA, and all of them have used different methodologies (8, 26, 37-39).

The MRI-RA group of the Outcome Measures in Rheumatology Clinical Trials (OMERACT) has devised a semi-quantitative scoring system for the assessment of inflammatory and joint damage abnormalities in RA, and has also suggested a core set of basic MRI sequences (40). The so-called Rheumatoid Arthritis MRI Scoring (RAMRIS) system has been validated in the wrist and MCP joints of adult subjects and has been recently tested on wrists in a paediatric population, and it may provide a standard for forthcoming JIA studies (41).

No normal reference values are available for individual joints at different developmental stages during childhood, and there are no validated MRI scales or standardised MRI protocols targeting children, and thus it is difficult to draw firm conclusions regarding the value of MRI assessment in JIA (42, 43). Furthermore, no long-term MRI studies of JIA have been performed,

and the significance of MRI abnormalities over time is still unclear.

MRI imaging requires intravenous injection of a contrast medium to distinguish between synovial tissue and effusion, and this is a disadvantage when dealing with paediatric patients. The main disadvantages of MRI, besides the considerable cost of the equipment, are that it is often unavailable, it cannot be integrated with the clinical assessment, and it requires sedation of young children, an age group with a high prevalence of JIA. Despite these limitations, the advances in MRI assessment of findings in JIA have strongly influenced current views on this disease. MRI imaging has contributed greatly to strengthening the perceptions that synovitis is the primary inflammatory focus of JIA, that synovitis is associated with damage, and that patients in apparent clinical remission may still have persistent synovitis (8).

US in the assessment of JIA

Musculoskeletal US (MSUS) has emerged as an indispensible tool for physicians involved in musculoskeletal medicine, and lately it has become more attractive to paediatric rheumatologists as well. Two important aspects have resulted in increased interest in using MSUS in JIA: a) the evolution of high-frequency linear transducers that depict superficial musculoskeletal structures with unsurpassed resolution, and b) the need for imaging techniques that can detect the slightest traces of soft tissue inflammation. So far, only a few studies have investigated both grey-scale and Doppler assessments of children with JIA (31, 44-55).

In daily clinical practice, the diagnosis of "active arthritis" in JIA is based primarily on clinical evaluation. However, it is often difficult to clinically determine whether a perceived joint swelling is secondary to synovitis with joint effusion, or if it is due to soft tissue oedema and/or tenosynovitis (44, 47, 56, 57). Similarly, pain and limitation of mobility in a joint are not always the result of active arthritis (27). In JIA, clinically assessing disease activity in the small joints of the hand is a particularly complex task (58).

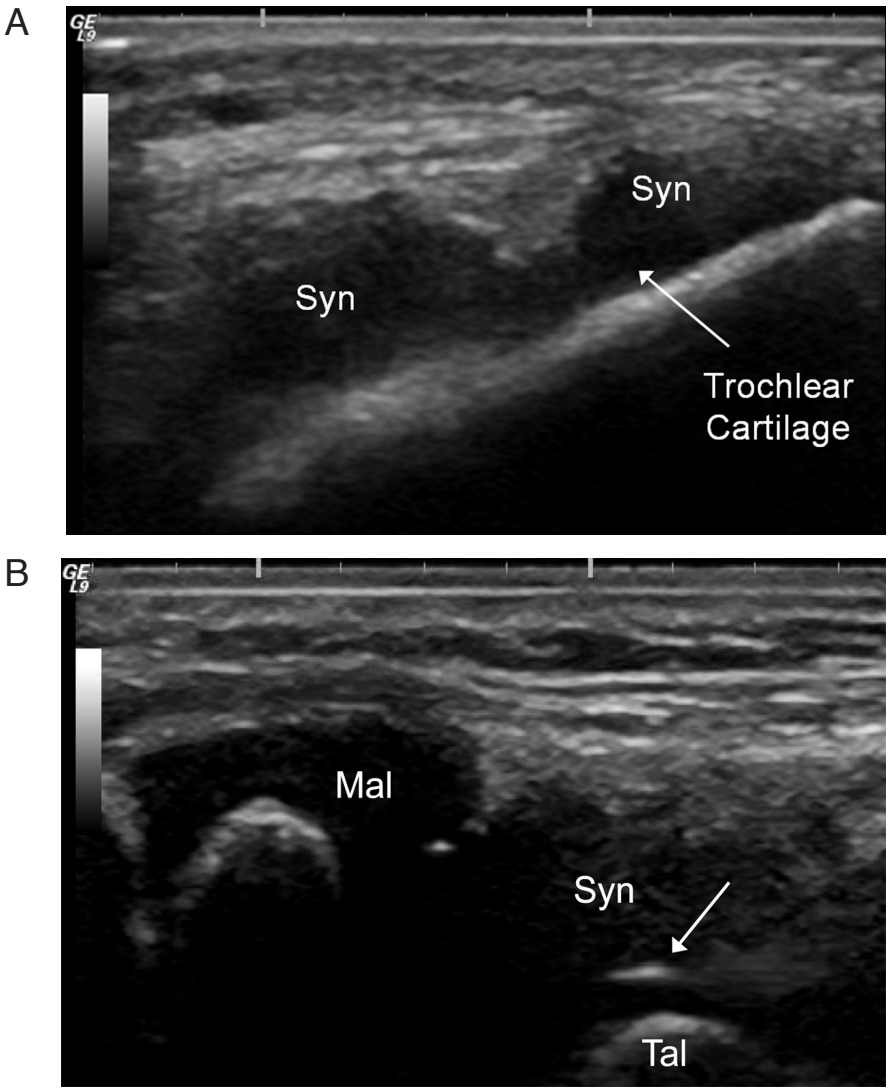


Fig. 4. The importance of transducer position when performing US of the ankle in a child with JIA. **(A)** Due to the obliquity of the ultrasound beam, the anisotropic artifact prevents differentiation between synovial hypertrophy and the cartilage of the talus. **(B)** Perpendicular scanning enables visualisation of the surface of the trochlear cartilage of the talus (arrow). Mal=lateral malleolus; Syn=synovial hypertrophy; Tal=talus.

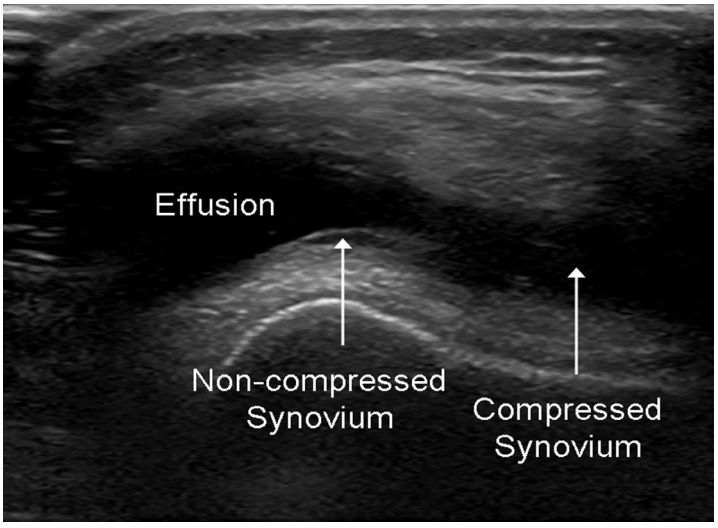


Fig. 5. Axial US scan of the suprapatellar recess of the knee in a child with JIA.
The compression by the transducer transmits the effusion to the left, while the residual hypoechoic, hypertrophied synovium remains on the right in the US image.

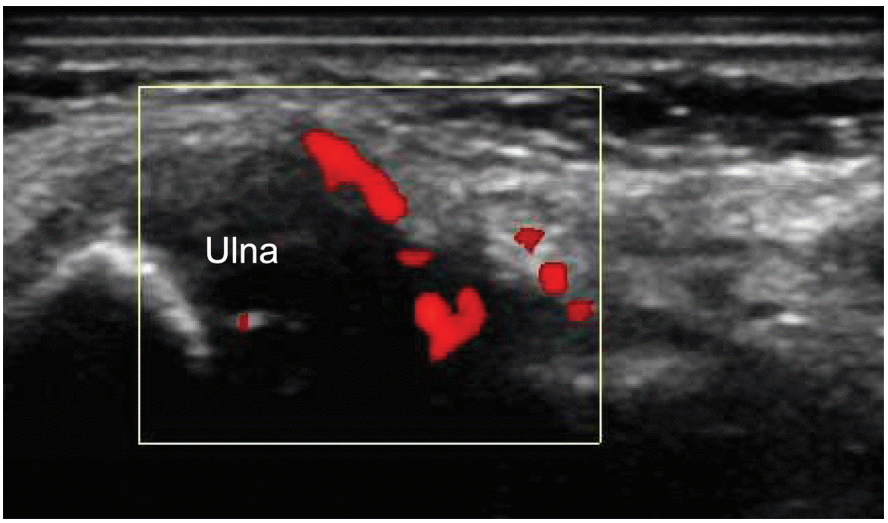


Fig. 6. Ulnar longitudinal US scan of the wrist in a child with JIA.
Synovial vascularisation detected by colour Doppler reflects disease activity.

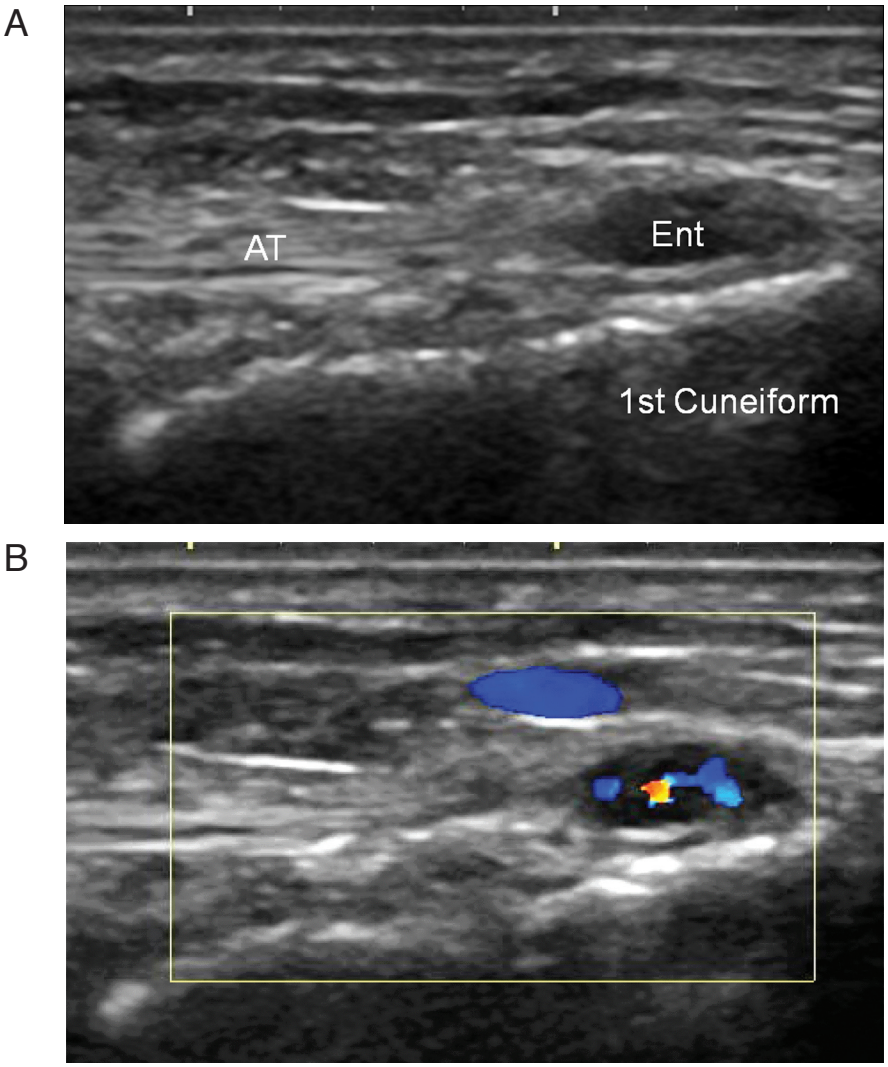


Fig. 7. Longitudinal US scan of the dorsal aspect of the foot in a child with JIA and enthesitis-related arthritis.
(A) Hypoechoic thickening of the anterior tibial tendon (AT) enthesis (Ent). **(B)** Colour Doppler examination reveals vascularisation indicating disease activity at the enthesis.

In JIA, it has been proven that US assessment of disease activity is more informative than clinical examination (59). US images are analysed in real time, and the information that is acquired can be used directly to adjust the clinical assessment, which can be particularly useful if there are few verbal complaints, *e.g.* in infants (60). Subclinical synovitis is frequently detected by US, particularly in the hands and feet (51, 56, 61, 62). The prognostic significance of such subclinical inflammation still needs to be determined.

A recent study of JIA patients with a clinical history of unilateral wrist involvement has shown that 50% of previously unaffected wrists had abnormal grey-scale findings, but no Doppler signals, which indicates that the initial clinical assessment may have falsely described the disease involvement as unilateral (49). The clinical implication of such US detected inflammatory changes is not known, but grey-scale abnormalities of this kind have not been detected in healthy children (31, 49, 63). US can also detect subclinical enthesitis in JIA, as demonstrated in another recent investigation in which Doppler-US revealed enthesitis in 50% of clinically normal entheses (46).

The issue of subclinical disease may be particularly relevant in JIA (59). In the current ILAR classification, oligoarthritis *versus* polyarthritis is defined by the number of affected joints in children with JIA. The classification of a JIA patient has important implications for treatment management and follow-up. US allows to classify as having polyarthritis patients who were previously labeled as having oligoarthrtitis, based solely on clinical findings (51). Furthermore, US allows precise identification of the site of inflammation (including the differentiation between synovial, tendineous and enthesal inflammation) and to classify as having oligoarthritis some patients who were previously labeled as having extended oligoarthritis or polyarthritis (57). Active disease in at least five joints is a prerequisite for the diagnosis of polyarticular JIA, which in turn is a requirement for inclusion in clinical trials of second-line or biological agents (8, 11, 64-66).

MSUS is easy to perform on children of all ages, because agitation of the patient is rarely a problem (Fig. 1). The time factor is also important in dealing with young children. Only a relatively short amount of time is required to examine each anatomical structure, and thus it is a simple matter to assess multiple locations during a single session. Sonographic reference values have not been established for most paediatric joints, and there is no consensus regarding what constitutes "normal" grey-scale and Doppler findings at the single-joint level in children or in adults, which represents a limit to US examination. The advantages and disadvantages of MSUS imaging in children are summarised in Table I.

US pathological findings in JIA includes the following: non-compressible hypoechoic synovial hypertrophy, compressible hypoechoic/anechoic joint effusion, hypoechoic/anechoic tissue within the tendon sheath, hypoechoic and/or thickened tendons, ligaments, capsules or fasciae on bony insertions, and erosions seen as localised cortical defects. In addition, the Doppler technique is used to detect hyperaemia. Definitions of JIA pathology have varied in different US studies. In our investigations, we defined US synovitis/tenosynovitis as synovial hypertrophy with or without synovial vascularisation, and with or without effusion (67, 68). Table II summarises the pathology of JIA and the corresponding OMERACT definitions of US signs of the disease (68).

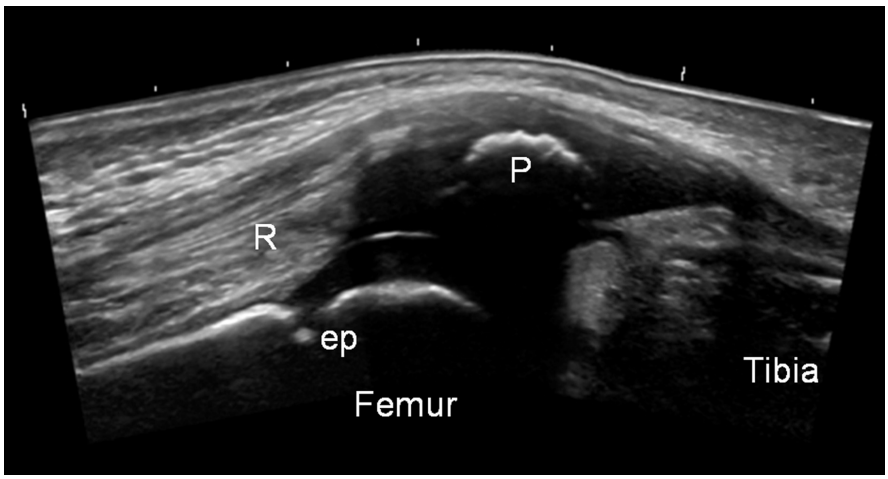


Fig. 8. Anterior longitudinal US scan of the knee in a healthy 4-year-old child. The echogenic anterior structure (P) is the cartilaginous patella ossification centre. The communication between the suprapatellar recess (R) and the joint line of the knee and the epiphysis (ep) can be seen.

Synovial thickening

The synovial membrane is a thin layer of soft tissue that lines joint cavities, tendon sheaths, and bursae, and it is the location of the primary inflammation that occurs in arthritis. The characteristics of such inflammation include hypertrophy and oedema caused by proliferation of the capillaries and postcapillary venules, and also increased perfusion. US is a sensitive method for detecting synovial thickening and synovial cysts (69), and it shows synovial hypertrophy as a solid, non-compressible, abnormally thickened hypoechoic tissue associated with joint lines or surrounding tendons (68, 70). A semi-quantitative system for grading synovial hypertrophy is used most frequently in adult rheumatology, but no such system has been validated in JIA (71).

It is more challenging to assess synovial hypertrophy in younger children than in adolescents and adults, even though image quality is actually better in children, because they have less fat and fibrosis and more cartilaginous joints. The explanation for this is that, in children, the synovial tissue is difficult to distinguish from the hypoechoic cartilage of the epiphyses (Fig. 2). Doppler examination is generally not a solution to this problem, since vascularisation can be present in both hypertrophic synovial membranes and cartilaginous epiphyses during growth (Fig. 3). Therefore, to avoid diagnostic errors, it is important to have good knowledge of the normal US appearance of each joint at different stages of development, and it is also imperative to use a meticulous scanning technique that allows clear interpretation of possible anisotropic artifacts (Fig. 4). For the most part, it is easier to differentiate synovial tissue from effusion. In short, effusion is often anechoic or more hypoechoic than synovial tissue, and it can be mobilised by compression with the transducer; by comparison, synovial tissue is solid and non-compressible (Fig. 5).

Effusion

Physiological joint effusion is common in children, but there is no consensus concerning the normal amount of synovial effusion in healthy individuals in this age group. Notably, in a recent MRI study, the wrists of healthy children were found to contain fluid in relatively large amounts that had previously been considered to be pathological in adults (32, 72). Even in a large and easily palpable joint such as the knee sonography is more sensitive than both CR and clinical examination for detecting effusion (69, 73). US can detect volumes as small as one milliliter, and interobserver agreement of 79% was found in an analysis of effusion in joints of the hands and feet (74). As mentioned above, sonopalpation entails compression with the transducer, and it is useful for distinguishing effusion from synovial proliferation (Fig. 5). In a prospective study, it was noted that US detection of a knee effusion in JIA was highly correlated with clinical disease activity, although the correlation was lower for the hip, probably because that joint is less accessible to clinical investigation (75).

Synovial perfusion

When using grey-scale US, it can be difficult to differentiate between active synovitis and inactive synovial thickening, because both may appear as non-specific hypoechoic synovial hypertrophy. Doppler-US techniques depict the increased vascularity of the hypertrophied synovium, and they are considered to be superior in distin-

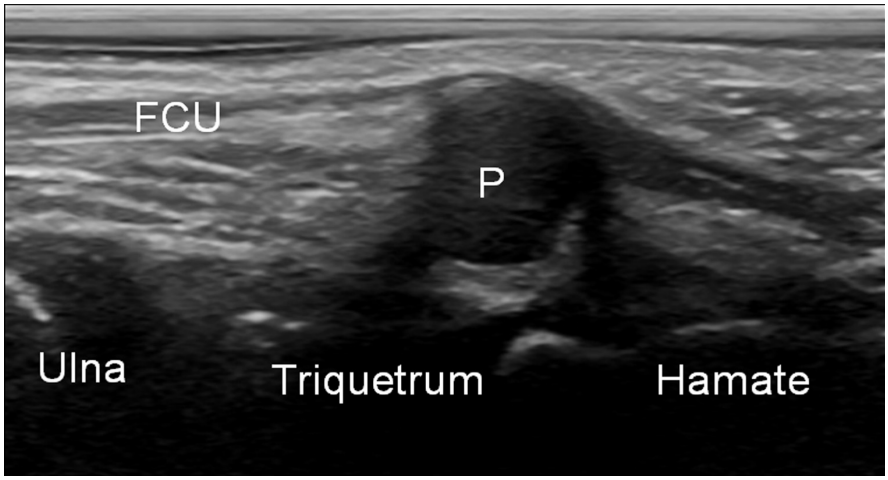


Fig. 9. Anterior longitudinal US scan of the ulnar aspect of the wrist in a healthy 5-year-old child. The anechoic oval structure (P) is the cartilaginous pisiform bone, not a ganglion cyst. FCU=flexor carpi ulnaris tendon.

guishing between active and inactive synovial thickening (76-79). Studies have shown that the Doppler signal is correlated with clinical and laboratory data, MRI results, and histology, and it also reflects disease activity in adult RA (78-80). Furthermore, investigations of JIA have demonstrated that the Doppler signal is correlated with clinical activity and with serum levels of IL-6 (45, 50, 53, 55, 81). Various systems using quantitative or semi-quantitative methods have been proposed to evaluate Doppler flow in synovial tissue in adults, but none of those techniques have been validated in JIA (71). In our research, we have never detected any Doppler flow in healthy children, which agrees with a recent US study in which no Doppler signal was observed in healthy controls, and the presence of Doppler flow was significantly associated with clinical synovitis in JIA (31, 45). In a growing child, juxta-articular Doppler flow can represent either the well-vascularised cartilage of the epiphysis or synovial hyperaemia reflecting disease activity (Fig. 6), which underlines that it is necessary for the investigator to have good anatomical knowledge of the area that is examined.

In three recent studies (31, 44, 47), Doppler flow was detected in 86–91% of clinically affected joints that exhibited synovial hypertrophy on grey-scale US, and this was done using the same definition of synovial hyperaemia and the same US equipment and Doppler settings. That observation concurs with other investigations in which hyperaemia was found in 93% of symptomatic MCP joints and 77% of symptomatic knees in JIA patients (53, 55).

Use of intravenous contrast media in Doppler-US to diagnose inflammatory joint disease has not yet been validated in adults or children (82).

Enthesitis and tenosynovitis

Enthesitis is defined as inflammation of the sites where tendons, ligaments, capsules, or fascia are attached to bone. Conventional radiography visualises mainly the bony changes at an enthesis (*i.e.* calcifications, enthesophytes, and bony erosions) and thus reveals only the late stages of disease (83). MRI or US can demonstrate the early soft tissue signs of inflammatory enthesitis in adult SpA and in JIA (46, 48).

The OMERACT definition of US signs of enthesitis stipulates an abnormally hypoechoic and/or thickened tendon or ligament at its bony attachment seen in two perpendicular planes that may exhibit Doppler signal and/or bony changes (Table II) (68), and the US appearance of enthesitis is the same irrespective of age (46, 84, 85). Other recognised US signs include focal or diffuse loss of normal tendon or ligament fibrillar structure, effusion, intratendinous or intraligamentous calcifications, bone erosions, enthesophytes, and associated abnormalities of adjacent bursae. US is more sensitive than clinical assessment for diagnosing enthesitis in adult SpA patients and in JIA, and Doppler-US has been shown to be a sensitive method for detecting abnormal blood flow in and around peripheral entheses (46, 86).

The US appearance of tenosynovitis is the same in patients of all ages, showing effusion and/or synovial hypertrophy in a tendon sheath. Recent JIA studies have demonstrated that tenosynovitis in swollen ankles is detected by US more often than previously assumed (Fig. 7) (47, 57, 62).

Cartilage thinning

The cartilaginous ends of long bones are responsible for the enchondral ossification that occurs during growth in childhood. Therefore, children have a large amount of cartilage tissue, whereas adults have only a thin layer of avascular articular cartilage, and this has implications for the interpretation of MSUS images. The ends of the bones comprise three zones called the epiphysis, the metaphysis, and the physis. At birth, the epiphysis is completely cartilaginous, except at the distal end of the femur. Over time, one or several epiphyseal ossification centres appear and enlarge until the entire epiphysis has been ossified, with the exception of the thin layer of articular cartilage. Thus, during childhood, there are three vascular systems in the long bones: the epiphyseal, the metaphyseal/intramedullary, and the periosteal blood supply. When a growing child is examined by Doppler-US, any juxta-articular flow must be thoroughly analysed, because the Doppler signal can represent either normal cartilaginous vascularisation or synovial hyperaemia indicating inflammation (47). In adulthood, the articular cartilage of the epiphysis is avascular, and any juxta-articular Doppler flow suggests inflammation. Consequently, when performing US examinations in growing subjects, it is important to have knowledge of the normal appearance of each joint at different developmental stages in order to avoid diagnostic errors (Fig. 8-9) (16, 47).

On US, the articular cartilage is normally seen as a hypoechoic structure

creating a smooth outline of the bone surfaces. Age- and sex-related reference intervals for US measurements of cartilage thickness in large and small joints of healthy children have been proposed, and validated by comparison with MRI results (87-89). Some early US studies of JIA patients have reported cartilaginous changes involving early thickening or late thinning with blurred surfaces (69, 90, 91).

Bony erosions

A relevant proportion of JIA patients who do not receive treatment will develop progressive joint destruction and serious physical disability (10). The occurrence of erosions early in the course of JIA is associated with a higher risk of progressive disease, and it is an indicator of poor long-term outcome (92, 93). In RA, US is equal or superior to CR in detecting cortical erosions in areas that are accessible to the sound waves (Fig. 10). Notably, US has been found to be comparable to MRI in some studies but not in others, and this discrepancy might also be related to whether the investigated sites were accessible to US examination (10, 94-96).

US-guided steroid injections

Steroid injections constitute an important form of treatment in JIA (97, 98), and the clinical effect that is achieved depends on accurate placement of the drug in the diseased compartment. However, it has been shown that up to 50–70% of palpation-guided joint injections are placed incorrectly in adult rheumatology (99-101). Importantly, the accuracy can be significantly improved by use of imaging guidance, as compared to palpation guidance, and US is the best available technique for this purpose (100, 102-110). US guidance can be static or dynamic. In static guidance, the structure of interest is identified, and the angle required for the needle is noted, with the point of entry marked on the skin. In dynamic guidance, US visualises the needle in real time which provides quicker and more accurate guidance and is generally preferred by experienced users (60). In JIA patients with wrist swelling, it is common clinical practice to perform palpation-guided injections in the radiocarpal joint, whereas injection of the midcarpal joints or tendon sheaths is done less frequently (44). When clinical ankle swelling is present, a palpation-guided injection is usually given in the talocrural joint, and less often in the subtalar joints (Fig. 11) or tendon sheaths. Misdiagnosing of ankle swelling or malplacement of injected steroid might explain the poor outcome of steroid injections in ankle disease in JIA, but no study has been comparing the effect of US guided and palpation-guided steroid injections in this group of patients (47, 51, 110-112).

Subcutaneous atrophy due to extravasation of steroid is a well-recognised adverse effect of intra-articular steroid injections, and it is most likely to occur in small or complex joints such as the wrist or ankle in children under 4 years of age, or when a larger volume is injected (113, 114). Employing US guidance makes it easier to ensure that the tip of the needle is correctly positioned before injecting the drug, which potentially minimises the risk of extravasation of steroid into the subcutaneous tissue.

US follow-up of treatment efficacy and disease remission

In studies evaluating grey-scale US follow-up of treatment efficacy in JIA, it

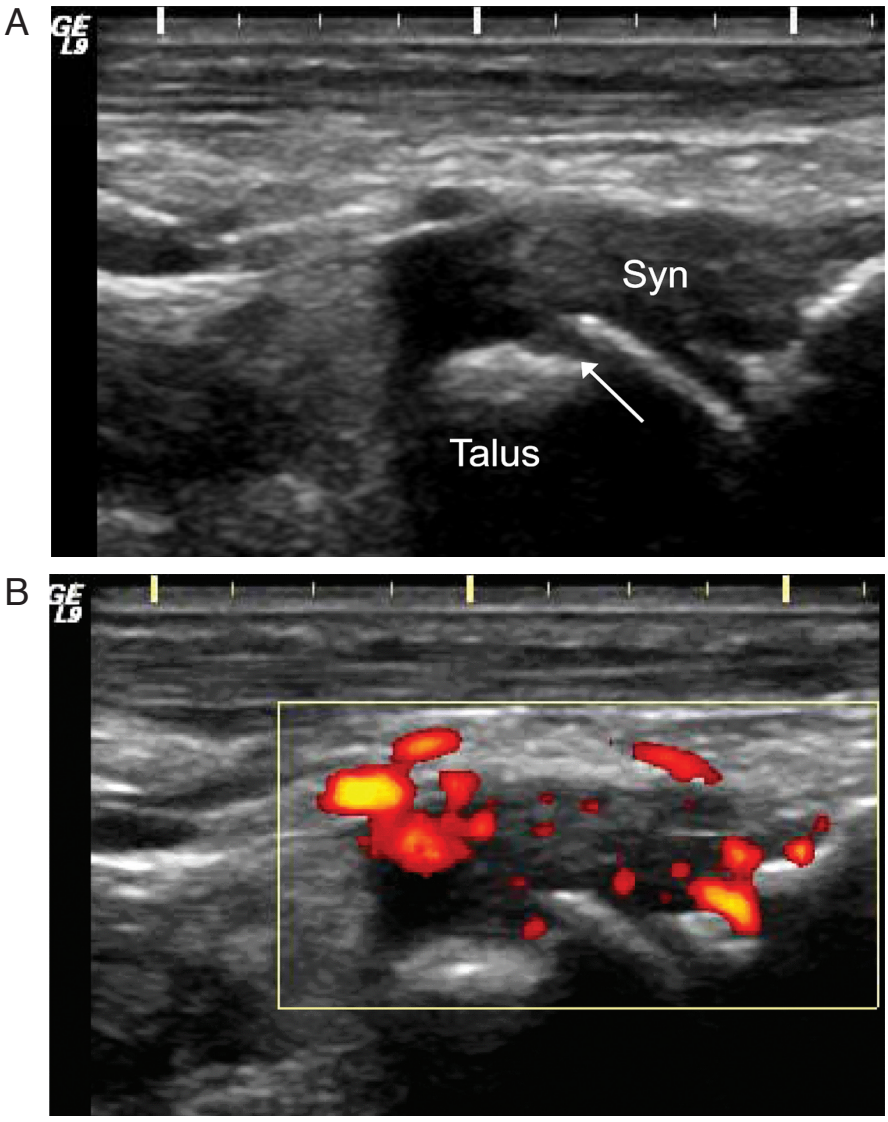
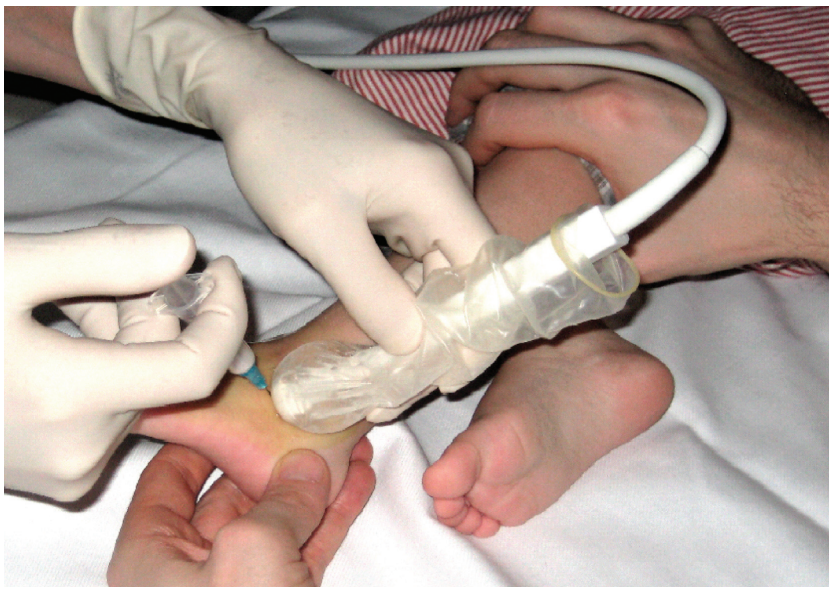


Fig. 10. Anterior longitudinal US scan of the ankle in a 15-year-old girl with JIA. **(A)** Bone erosion of the head of the talus (arrow) filled with hypertrophied synovial tissue (Syn). **(B)** Colour Doppler examination showing hyperaemia with vascularisation in the erosive lesion and in the synovium.

A



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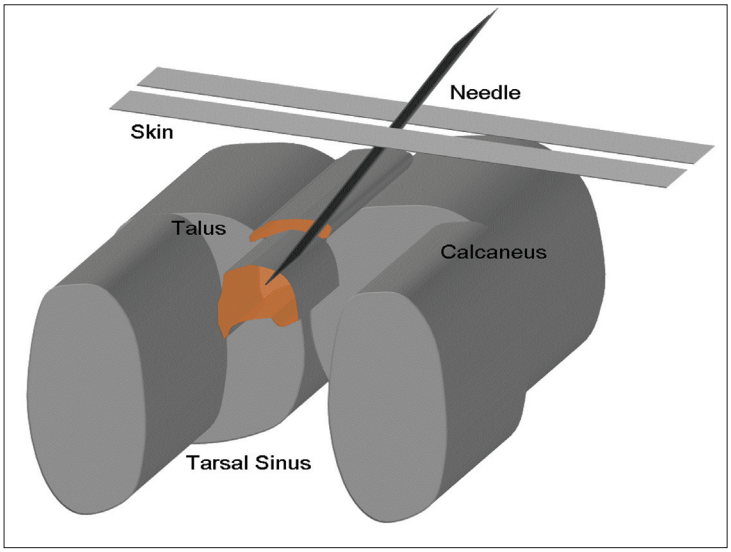

C

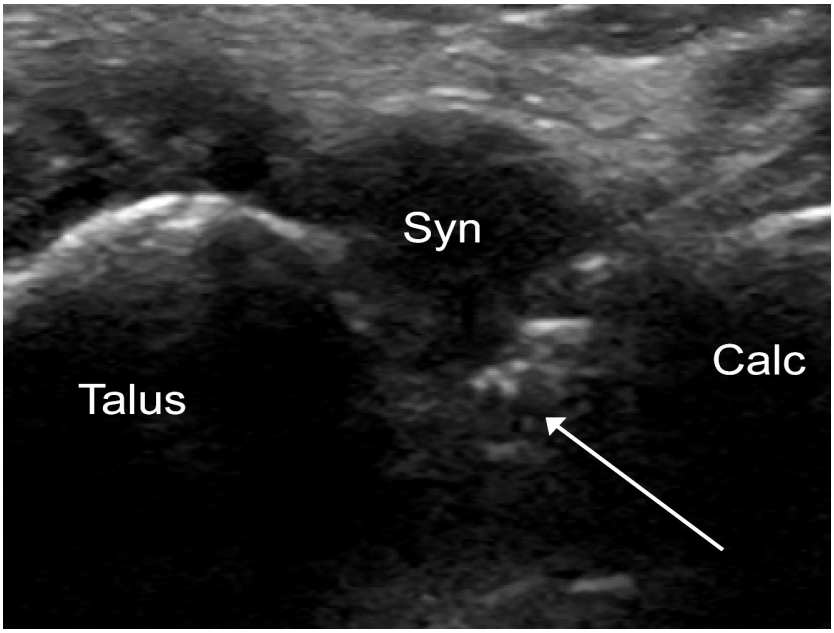

Fig. 11. US-guided injection in the anterolateral recess of the posterior subtalar joint.
(A, B) Lateral oblique longitudinal scanning plane at the level of the posterior tarsal sinus. **(C)** The tip of an injection needle (arrow) is seen in the enlarged hypoechoic anterolateral recess (Syn), which is bulging into the hyperechoic fat of the tarsal sinus between the talus and calcaneus (Calc).

was found that the technique was sensitive enough to detect decreases in joint effusion and synovial hypertrophy in knees treated with NSAIDs, DMARDs, or oral or intra-muscular steroids, and also in knees and hips after intra-articular steroid injection (90, 91, 115, 116). In addition, the rate of decrease was faster for effusion than for synovial hypertrophy (90, 91).

In adult rheumatology, US with Doppler is widely used for follow-up. However, only four studies have concerned corresponding US-Doppler in JIA, and they found the technique valuable to evaluate the efficacy of steroid injections in the ankle or wrist region, or in knee synovitis after systemic corticosteroids and NSAIDs (Fig. 12) (44, 47, 52, 55).

Several investigations have established that MRI and US can improve the accuracy of remission measurement in RA (117-120). Using more stringent remission criteria resulted in reduced signs and symptoms of inflammation, but the majority of the RA patients in the mentioned studies continued to exhibit signs of active inflammation. These data suggest that clinical criteria are sufficiently insensitive to detect low but clinically relevant levels of inflammation accurately (117). Furthermore, such low-grade inflammation has been shown to predict subsequent radiographic deterioration in RA patients treated with DMARDs (119, 121).

In JIA, it is now possible to induce permanent remission in an increasing proportion of affected children, but this cannot be reliably demonstrated by clinical examination alone (2, 9, 49). In a study related to that context, Doppler-US was found to reveal ongoing inflammation in the wrist and ankle joints of some JIA patients who met the current clinical criteria for remission; in that investigation, there was complete con-

cordance between the clinical and US assessments of the knee joint, whereas it was judged that US was particularly beneficial for assessment of the anatomically complex wrist and ankle regions (49).

Thus, inasmuch as clinical criteria cannot exclude disease activity, it seems that the current remission criteria are more appropriate for defining low disease activity. In short, it appears that determination of true remission cannot rely solely on clinical examination, but must include repeated imaging to confirm the absence of subclinical inflammation (49).

Comparison of US and MRI

In adult rheumatology, numerous studies have established the important role of MRI and US, and MRI is considered the reference standard for advanced imaging (5, 6). Nevertheless, no MRI or US scoring systems have been validated for assessment of joint inflammation and joint damage in JIA, and little is known about the normal US and MRI reference values of each joint at different developmental stages in children. In our studies, we elected to use the OMERACT (68) and the RAMRIS (40) definitions for US and MRI pathology, respectively (31, 44, 47, 48).

The comparison of US and MRI in JIA is summarised in Table III.

Conclusion and future perspectives

In JIA, it seems that US can provide useful imaging information, and hence this technique might represent a viable option in many cases in daily clinical practice. At points of care, it is likely that US will play an increasingly significant role in assessment of the disease activity in JIA patients, in analogy with the use of this method in adult rheumatology. Clinical examination, clinical laboratory criteria, and imaging will be combined to confirm, or reject, the presence of inflammation and damage in JIA, and US will be of increasing importance in that context. We believe that US guidance of steroid injections, especially in anatomically complex areas, will soon be a routine approach, and that the two imaging modalities MRI and US will be widely used to evalu-

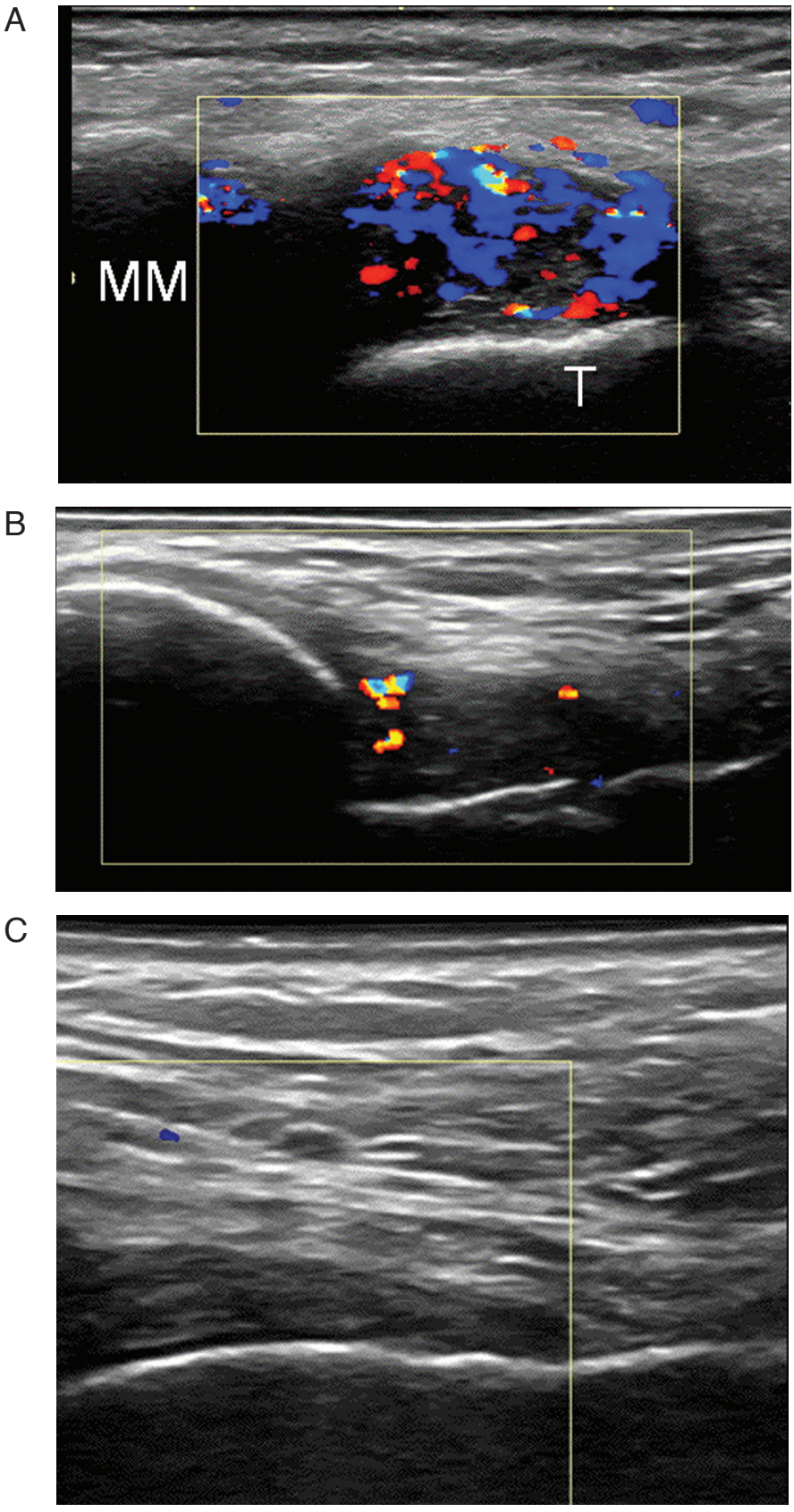

Fig. 12. Effect of US-guided steroid injection in the talocrural joint.
Synovial thickening (Syn) anterior to the medial malleolus (MM), as shown by US before **(A)**, 1 week after **(B)**, and 4 weeks after **(C)** steroid injection. Regression of synovial hypertrophy without complete normalisation can be seen. T=talus.

Table III. US *versus* MRI in JIA.

US	MRI
Early diagnosis	Early diagnosis
Soft tissues	Soft tissues
Hyperaemia/Doppler	Hyperaemia/contrast enhancement
Available at point of care	Poor availability
Non-invasive	IV contrast Sedation/general anesthesia
Quick	Time-consuming
"Focal" imaging	Overview
Bone surface only	Bone, bone marrow oedema
Machine- and operator-dependent	Machine- and operator-dependent
Limited normative data	Limited normative data
Not validated	Not validated

Table IV. Major roles of US in JIA in the future.

Improved evaluation and classification: number of joints involved, tenosynovitis *versus* arthritis, presence of enthesitis (together with MRI)
Guidance of steroid injections, especially in anatomically complex areas
Following the course of the disease, monitoring of treatment efficacy, and assessment of disease remission (together with MRI)
Identification of predictors of damage (together with MRI)
Evaluation of the disease-modifying potential of new drugs in randomised controlled trials (together with MRI)

ate disease and will complement each other.

The role of US in JIA is still under investigation. It is possible that a large part of the knowledge obtained in US studies in adult rheumatology can be applied to children as well, but US must be further validated in all fields of paediatric rheumatology, in close collaboration between radiologists with a special interest in paediatrics and paediatric rheumatologists, to establish reference values for all US aspects of various joints and tendons in children at different stages of development. Specific training in US should be introduced for paediatric rheumatologists and should also be integrated in the educational programs for new specialists in paediatric rheumatology. US is a valuable tool for detecting synovitis in JIA, and demonstrated higher sensitivity in assessing synovitis as compared to clinical examination. However, further studies are needed for evaluating the reliability and responsiveness to assess synovitis changes over time (14).

The potential major roles of US in JIA in the future are summarised in Table IV.

Acknowledgements

Figures 11 and 12 are published with the permission of BioMed Central (47). The authors are grateful to the Norrbacka-Eugenia Research Foundation for financial support.

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