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REVIEW ARTICLE

Advanced imaging in rheumatoid arthritis

Part 1: Synovitis

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Abstract Rheumatoid arthritis (RA) is a chronic and progressive inflammatory disorder primarily affecting the synovium. We now recognise that conventional radiographic images show changes of rheumatoid arthritis long after irreversible joint damage has occured. With the advent of powerful disease-modifying drugs, there is a need for early demonstration of rheumatoid arthritis and a need to monitor progress of the disease and response to therapy. Advanced imaging techniques such as ultrasound and MRI have focussed on the demonstration and quantification of synovitis and erosions and allow early diagnosis of RA. The technology to quantify synovitis and erosions is developing rapidly and now allows change in disease activity to be assessed. However, problems undoubtedly exist in quantification techniques, and this review serves to highlight them. Much of the literature on advanced imaging in RA appears in rheumatological journals and may not be familiar to radiologists. This review article aims to increase the awareness of radiologists about this field and to encourage them to participate and contribute to the ongoing development of these modalities. Without this collaboration, it is unlikely that these modalities will reach their full potential in the field of rheumatological imaging. This review is in two parts. The first part addresses synovitis imaging. The second part will look at advanced imaging of erosions in RA.

Keywords Rheumatoid arthritis · Synovitis · Erosion · Magnetic resonance imaging · Ultrasound

Part 2 of this article (Erosions) can be found at http://dx.doi.org/10.1007/s00256-006-0220-3.

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Introduction

This review looks at advanced imaging techniques in rheumatoid arthritis and in particular how they are applied to the monitoring of the disease process. While rheumatoid arthritis manifests itself with many radiological features, the application of modern imaging techniques has principally been in the detection and monitoring of synovitis and erosions. In this first part synovitis will be addressed. The second part will look at erosions.

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown origin characterised by polyarticular synovitis. It affects 1.0% [1] of the population with women affected more frequently.

With the introduction of new drug treatments, such as disease-modifying antirheumatic drugs (DMARDs) capable of halting joint destruction and functional debility, there are new pressures on diagnostic imaging. Early demonstration of pre-erosive inflammatory features and monitoring of the long-term effects of treatment are becoming increasingly important.

In this article, the role of ultrasound (US) and magnetic resonance imaging (MRI) in the detection and monitoring of synovitis will be explored and the current literature reviewed.

Pattern of disease

The early months of rheumatic disease are a critical period during which irreversible joint damage occurs and more than 60% of patients initially present with symmetric arthritis of the small hand joints. The time course of RA progression is not linear and joint involvement is not uniform, particularly with the early administration of DMARDs. In a single individual, various imaging findings may be present in different joints at any one time. This is especially prominent in early-stage disease, and each joint in these patients must be evaluated independently.

Early detection of synovitis offers advantages in terms of allowing early instigation of therapy and may allow the identification of those patients displaying more aggressive disease who might benefit from early intervention with expensive DMARD therapy [2, 3]. The ability to monitor changes in disease status by assessing synovitis allows modification of therapy before such decisions can be made clinically.

A minority of patients demonstrate an atypical pattern of disease, and differentiating patients with RA from those with other joint diseases such as the seronegative spondyloarthropathies can be difficult.

Pathogenesis of synovitis and effusion

Synovitis is initiated by cytokines such as interleukin-1 and tumour necrosis factor (TNF) alpha [4] that mediate synovial inflammation and oedema with increased synovial vascularity (angiogenesis), capillary leakage and joint effusion. Serum concentrations of vascular endothelial growth factor (VEGF), a potent endothelial cell-specific growth factor that is upregulated by proinflammatory cytokines and by hypoxia, are elevated in RA and correlate with disease activity [5]. The disease state in a given joint is correlated with synovial vascularity [6], and while an effusion is a sensitive predictor of joint disease, it is non-specific for RA activity. Synovitis occurs early in the natural history of RA and is considered to be a strong predictor of bone-erosion development [7–10].

Imaging

The traditional signs of RA seen using conventional radiography (CR), such as joint space loss, erosions and subluxations, represent changes that occur at a late stage in the disease process, by which time the joint damage may be substantial. The limitations of CR include its inability to directly visualise key structures such as synovium, cartilage, soft tissue and bone marrow. CR is cheap and readily available and although it is a useful tool in monitoring established disease progression it is not sufficiently precise. Radiographic changes such as cartilage loss and joint space loss develop slowly, but synovitis changes relatively quickly and is potentially reversible, allowing for regular monitoring of changes in response to therapy. Plain film assessments of synovitis such as peri-articular osteopenia and soft-tissue swelling are unreliable and consequently CR has no role in synovitis assessment.

Multiplanar imaging modalities such as magnetic resonance imaging (MRI) and ultrasound (US) have subsequently gained importance during the early stages of disease and have enabled visualisation of synovitis and bone erosion long before the changes are visible on CR [11–14]; they have been shown to be more sensitive than clinical examination for identifying synovitis [15, 16].

Techniques of synovial assessment

Synovitis represents a potential surrogate measure of disease activity that can be monitored using either MRI or US; the techniques have generally focussed on monitoring synovial volume or quality as assessed by its vascularity.

Assessment of synovial quantity can be achieved using semiquantitative techniques, for example, scoring the amount of synovium with a simple 0–3 scale. Alternatively a quantitative approach can be used where the volume of synovium is actually measured.

MRI measurement of synovial volume can be undertaken using both manual and computer-assisted techniques. Synovitis enhances on MRI with intravenous gadolinium (Gd-DTPA), and Gd-DTPA-enhanced T1-weighted imaging (usually with fat suppression) is generally accepted as the most reliable technique to visualise synovium using MRI. Volume measurements are difficult to make with ultrasound and reproducibility is consequently poor. As a result, ultrasound techniques to assess synovial volume have focussed on semiquantitative methods.

Synovial vascularity can be assessed with MRI by assessing the rate of enhancement using dynamic MRI, which is the basis of measurement of synovial quality. With US, an indication of synovial inflammation can be obtained using colour or power Doppler sonography (PDS) to assess synovial vascularity either semiquantitatively or with quantitative techniques.

Standardisation of technique

OMERACT (Outcome Measures in Rheumatoid Arthritis Clinical Trials) is an international, multidisciplinary group set up with the aim of standardising techniques, joint pathology definitions and scoring systems for the use of imaging in RA [17]. It determines the validity, reliability

and feasibility of each imaging modality leading to a higher degree of international consensus. The group has developed an MRI scoring system for rheumatoid arthritis and is now addressing other areas and disease entities and is also looking at outcome measures using ultrasound. Anatomical coverage of the RA score is currently restricted to the wrists and hands, but the method may provide a basis for a more comprehensive score [17].

MRI

The OMERACT definition of synovitis on MRI is an area in the synovial compartment that shows above normal, post-gadolinium enhancement of a thickness greater than the width of the normal synovium [18]. Unfortunately no indication of the width of normal synovium is given for those wishing to apply this definition.

MRI provides simultaneous assessment of osseous (including bone marrow) and soft-tissue structures (both intra- and extraarticular) and can differentiate between synovium and cartilage. Thus it is often considered to be the gold standard for synovial imaging [10, 11].

On T1 imaging, the intraarticular synovial tissue is of intermediate signal, and of high signal on T2 imaging. Pre- and post-intravenous Gd-DTPA T1-weighted imaging is excellent in assessing the synovium, and synovial enhancement allows distinction from fluid (Fig. 1).

MR does detect synovial enhancement in normal volunteers [19]. No strategy for differentiating this "normal" synovial enhancement from a pathological one has been proposed in the literature.

Volume of synovial proliferation

Inflamed synovium enhances immediately, and Gd-DTPA then diffuses rapidly to the adjacent joint fluid [20, 21]. This causes a blurring of the margins of the synovium, which can lead to an overestimation of synovial volume. Early scanning after administering gadolinium minimises this problem, but there is debate regarding optimal timing for quantification of synovial volume. One study suggests

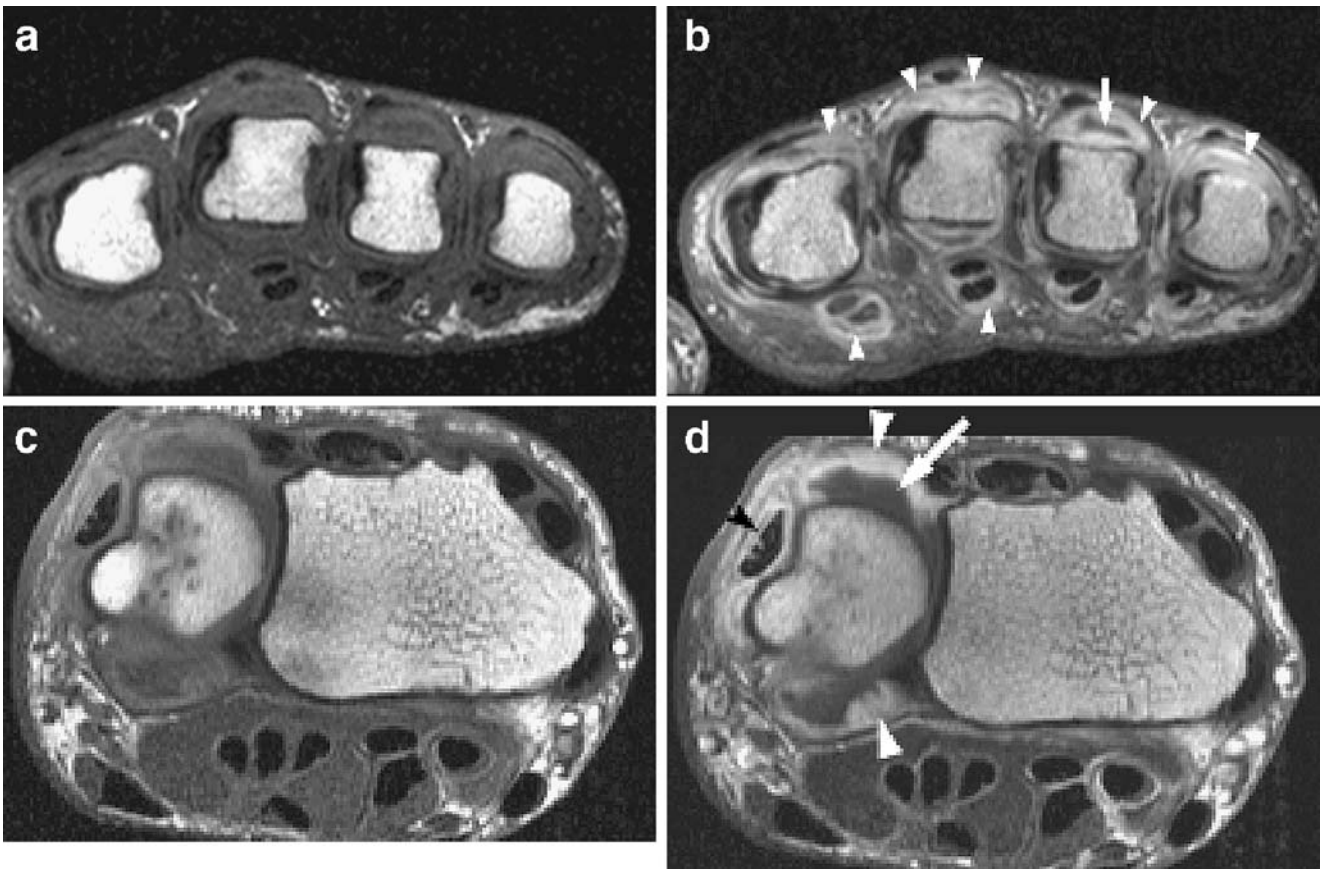

Fig. 1a–d Transverse T1-weighted MR imaging pre- and post-gadolinium (Gd-DTPA) through the MCP joints and wrist in a patient with RA. **a** Pre-Gd-DTPA and **b** post-Gd-DTPA in the same axial section through the MCP joints. The thickened enhancing synovium is clearly shown surrounding the joints and the flexor tendons (*arrowheads*). Some non-enhancing joint fluid is seen within the ring MCP joint (*arrow*). **c** Pre-Gd-DTPA and **d** post-Gd-DTPA in the same axial section through the wrist. Enhancing synovitis is seen at the distal radio-ulnar joint (*arrowheads*) and surrounding the flexor tendons. Non-enhancing fluid is also seen (*arrow*). Further synovitis is seen surrounding the extensor carpi ulnaris tendon, a common site for synovitis in RA (*black arrowhead*)

the first few seconds post-injection [22], another 5 min [15], and a further study states that MR imaging should be performed within the initial 10 min and that small time variations are insignificant [23]. The authors feel that waiting as long as 10 min can be problematic and aim to image within 5 min. Using established image-processing techniques such as manual outlining of the synovium, aided by subtraction images and computer processing of the data, the volume of enhancing synovial tissue can be quantified [7, 24, 25].

Several studies have shown that synovial volume correlates with joint swelling and tenderness and is predictive of clinical disease activity [24, 26, 27]. Comparison with synovial membrane histopathology has verified the relationship between synovial membrane volumes and current synovial inflammatory activity [28, 29].

The validity of synovial volumes has been assessed in several studies. Contrast-enhanced, fat-suppressed, 3D spoiled-gradient-recalled-acquisition (SPGR) MR imaging allowing thin slice and high tissue contrast between enhancing synovium and non-enhancing tissue in wrists showed a reduction in inflamed synovial volume in patients in remission following DMARDs [30]. A further study showed that synovial volume decreased within only 2 weeks of treatment with low dose methotrexate [31].

The prognostic value of pre-treatment synovial volumes is documented in several studies. A close relationship between baseline synovial membrane volumes and increase in the MRI bone erosion score was found at 1 year [7, 32–34]. In one study, the synovial enhancement rate was compared with the static synovitis score, which combines scores of synovial thickening and synovial enhancement, and the latter was shown to be more predictive of bone erosion on follow-up imaging at 1 year [34].

Unenhanced synovial volumes, which may include active and inactive synovial tissue, effusion and fibrous tissue, have been analysed in the finger joints and are also predictive of bone erosion on follow-up imaging after 1 year [35].

Early identification of patients who are likely to progress rapidly has important therapeutic implications, allowing early implementation of DMARDs.

Dynamic enhanced MRI (DEMRI)

In addition to quantifying the amount of synovium and joint fluid in arthritic joints, gadolinium-enhanced MRI can also provide objective information regarding the severity of inflammation.

This technique involves obtaining rapid serial T1-weighted images at different time intervals after injection of a bolus of contrast. An S-shaped curve of intensity against time is typical of inflamed synovium from which rates of enhancement can be extrapolated [33]. The ‘E-ratio’ has been proposed as a measure of synovitis, calculated by dividing the rate of increase of synovial enhancement after contrast injection by the baseline signal intensity of the synovial membrane. A significant correlation between the E-ratio and features of synovitis on biopsy has been found [33]. Gaffney et al. re-evaluated the calculations used to measure synovitis in their study of 21 patients with knee synovitis and proposed that the initial rate of synovial enhancement be used as an absolute measure, rather than relative to a baseline that was highly variable. This study was limited by the poor temporal resolution of the dynamic scans and blind biopsy gold standard [36].

The rate and magnitude of synovial enhancement on sequential MR images after bolus intravenous injection of gadolinium have been shown to correlate with the histological severity of inflammation in the synovium and with clinical markers of disease activity [29, 34]. The optimum time for enhancement measurements is 30 s to 1 min after Gd-DTPA injection, as the maximum correlation coefficients to histological inflammation were observed in this interval [29]. Moderate and severe inflammation identified on histology could not be differentiated on MR imaging [29].

Reece et al. demonstrated the validity of DEMRI in detecting changes in synovial enhancement in response to treatment. This randomised controlled clinical trial measured rate of synovial enhancement at baseline and after 4 months of treatment with leflunomide or methotrexate. Although only a small number of patients were included, a statistically significant difference between the two treatment groups was seen. Of particular interest was the finding that the change detected at MRI was not detectable clinically, indicating the sensitivity of this technique [37]. The histological findings from synovial biopsies of the same joints corresponded well with the MRI results. In this study, the regions of interest used for DEMRI curve generation were matched to the biopsy sites by the arthroscopist [38].

Several debated issues remain regarding the optimum technique for DEMRI: which part of the joint to image, what plane of section to use, how to manage the intrinsic heterogeneity of inflammation in the synovial compartment and which variable of enhancement to use [34]. An automated data analysis system is needed for DEMRI to become a widespread practice. A study compared manual outline method and automated data analysis and found the areas of enhancing synovium to be identical, which is encouraging as the latter is far less time consuming [39].

Reproducibility and reliability

MRI must be able to detect change and must be reliable and reproducible. International initiatives such as OMER

ACT and EULAR (European League Against Rheumatism) have addressed issues of standardisation and reliability [18, 40–42]. Consensus MRI definitions of important joint pathologies and a 'core set' of basic MRI sequences have been suggested [18]. T1-imaging pre- and post-gadolinium and T2 or STIR imaging with fat saturation in at least two plane (axial and coronal) or three-dimensional projections with a maximum slice thickness of 3 mm are recommended [17, 18].

Based on data from iterative multicentre studies [18, 40–42], a semiquantitive OMERACT RA MRI scoring (RAMRIS) system has been developed for assessment of synovitis, bone erosions and bone oedema in RA hands and wrists [18]. The EULAR–OMERACT RA MRI reference image atlas creates a new tool for standardised assessment of RA joints thereby allowing semiquantative scoring of MR image sets for inflammatory and destructive changes guided by standard reference images [43]. It is hoped that this will improve the consistency of MRI scoring among different centres and different studies.

The first multicentre study (OMERACT 2001) to test the interreader agreement on MR images of RA joints used a global score (0–3) for synovitis, which takes into account synovial thickness and Gd-DTPA enhancement. Kappa values of interreader agreement that take into account the presence or absence of absolute agreement were in the poor to fair range (0.12–0.36). Intraclass coefficient (ICC) values take into account the level of disagreements among scores and were considered to be more representative. The mean ICC value of synovitis global score was higher at 0.58, which is considered to be a moderate level of agreement [40].

The OMERACT 6 group (2003) found that interreader reliability was high for scoring synovitis with ICC at wrists and MCP joints, ranging from 0.68–0.89 [44]. However the smallest detectable difference (SDD), an absolute measure of agreement, ranged from 25–35%. Intrareader reliability was tested for one trained reader and was found to be high for all variables, with an ICC of 0.78 for synovitis [44].

A recent longitudinal study assessed the intra- and interreader reliability and the sensitivity to change of the OMERACT RAMRIS on digital images. The intrareader ICC for synovitis was 0.8 showing good correlation, but the SDD was similar at 26.5% [45].

The importance of selecting magnet type and sequence to reduce further errors has been stressed [40]. Recently there has been an increase in rheumatology departments acquiring low-field-dedicated extremity MRI units that are largely unvalidated. There have been three studies comparing low- and high-field MRI units [46, 47]. Ejbjerg et al. compared a low-field unit (0.2T) with a high-field unit in the detection and grading of erosions, synovitis and bone marrow oedema. The mean sensitivity, specificity, accuracy, and ICC of low-field MRI for detection of synovitis, when high-field MRI was considered the standard, were 90%, 96%, 94%, and 0.923 ($P<0.05$), respectively [47]. It is worth noting that the high-field unit used as a gold standard in this study was only a 1.0T system, which would not be considered a gold standard in many centres. However the results do reflect Savnik's other work using a 1.5T system [46].

Lindegaard et al. have shown that low-field-strength extremity systems are better than clinical examination for the detection of synovitis [48]. It is noteworthy that Ejbjerg et al. found the overall sensitivity for detection of bone marrow oedema on the low-field scanner was only 39%, which may limit the usefulness of this type of scanner in RA if bone marrow oedema is proved to be a pathological event of major prognostic significance, as has been proposed by several authors [27, 49]. The study also used only a binary scoring assessment for the presence or absence of synovitis and a single observer. Further studies are required to assess the reproducibility of results obtained using low-field MRI units. Interscanner reproducibility for DEMRI synovitis assessment has not as yet been adequately assessed.

MRI has important implications for the diagnosis and correct management of patients with early unclassified polyarthritis. MRI detected perientheseal high signals representing fluid or oedema in all spondyloarthropathic patients in several studies, but these signs were found to be a minor feature of RA [50]. Also specific features of small joint osteoarthritis at MRI have been identified and recently described [51].

Ultrasound

The OMERACT definition of synovitis on US is hypoechogenic thickened intraarticular tissue that is non-displaceable and poorly compressible and that may exhibit Doppler signals [52].

US is increasingly considered an extension of the clinical examination, and in many centres in Europe and North America is being undertaken by rheumatologists at the time of clinic appointment without reference to the radiology department. It provides direct visualisation and assessment of synovitis, the primary site of disease in RA, and can thereby aid in RA diagnosis. Treatment response or disease activity can be assessed and US can be used to guide therapy. Real-time dynamic imaging, close clinical correlation and excellent spatial resolution allow symptom-based, anatomical and functional assessment. A good representation of the patient's disease can be achieved by multiple joint assessment during one session, an advantage US has over MRI, particularly if contrast-enhanced MRI is to be used.

US can evaluate several features of both intra- and extraarticular disease. The US markers of intraarticular disease are effusion, synovial hypertrophy and vascularity, erosions and proliferative new bone formation. Extraarticular manifestations including tenosynovitis, enthesopathy, tendon rupture and bursae can also be assessed.

Normal synovium is not visualised sonographically. When thickened, it appears as intraarticular tissue of variable echogenicity depending on the degree of synovial oedema. Oedematous synovium is of low echogenicity and can even be anechoic, making it difficult to differentiate from effusion. Two techniques can aid the diagnosis: compression will move the fluid but not the synovium, and using colour or power Doppler sonography (PDS) may detect vascular flow in synovitis that will not be seen in fluid (Fig. 2).

Since accurate assessment of synovial volume is difficult using ultrasound, many studies have concentrated on the use of Doppler techniques to provide a measure of disease activity by assessing the vascularity of the inflamed synovium. PDS offers greater sensitivity than colour Doppler and has been shown to assess synovial blood flow reliably [53, 54]. PDS ignores the velocity of the signal but estimates the total signal strength; it can therefore demonstrate less flow in smaller vessels, and there is no aliasing effect. PDS can reliably depict soft-tissue hyperaemia associated with tendons and bursae [53] (Fig. 3).

There are several potential pitfalls that the operator should be aware of when applying PDS, as findings are influenced by the examiner, the spatial and temporal resolution of the machine, and the acoustical conditions involved in image processing. The probe must be used with minimal pressure to avoid compressing vessels, obliterating flow and thereby obtaining false-negative results.

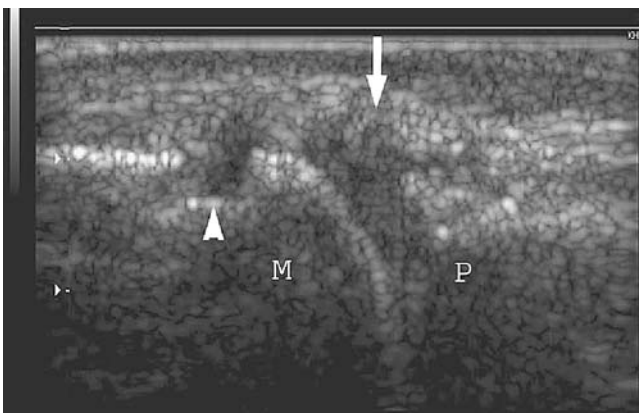

Fig. 2 Dorsal sagittal US image of MCP joint synovitis. The low-reflective thickened synovium (*arrow*) is seen at the MCP joint between the metacarpal (*M*) and proximal phalanx (*P*). Synovium is also seen within a small erosion (*arrowhead*) on the dorsum of the metacarpal

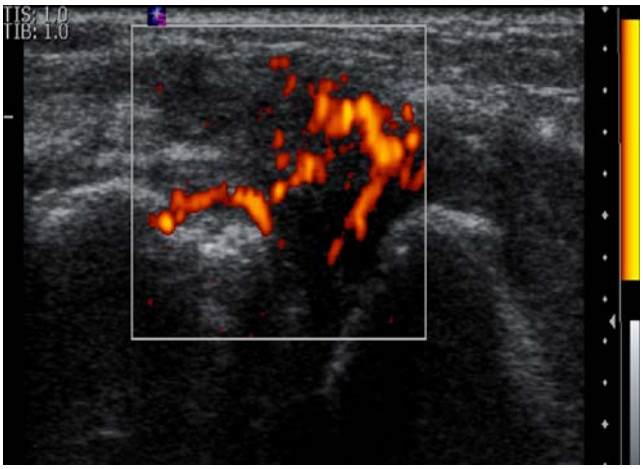

Fig. 3 Dorsal sagittal power Doppler ultrasonography image of MCP joint synovitis. The thickened low-reflective synovium shows extensive vascularity in the form of a Doppler signal

Several artifacts, including those of noise and movement, can occur. Another type is the edge artifact, which is related to strong specular reflectors and appears as steady colour along the rim of cortical bone or tendons. This can make adjustment of the gain-setting difficult. The gain threshold should be set so that there is no observed signal in bone [55].

The flash artifact manifests as a colour signal caused by tissue motion. This motion is most commonly seen when there is surrounding hypoechoic effusion and is more of a problem when using PDS than when using colour Doppler. Artifacts may be distinguished from true flow by the stable location of the artifact and absence of pulsation.

PDS with contrast agent Levovist (Schering, Germany) has been shown to be concordant with MRI in all cases [56]. With arthroscopy as reference, contrast-enhanced PDS (CEPDS) was found to be more accurate than PDS in demonstrating increased synovial vascularity in knees [57]. This study showed that CEPDS offered more-reproducible PD signal scores as well as higher sensitivity (80 vs. 30%), but lower specificity (62 vs. 87%). When increasing the sensitivity of PDS, factors such as additional costs, time, and invasiveness must be considered.

Much of the available data in this field are preliminary, often with lack of consensus regarding standard examination technique or technical parameters. However there are studies that have attempted to quantify synovial inflammation from Doppler imaging. The objective quantification of PD (QPD) signal by counting pixels in a specific area of interest has been used to demonstrate a significant decrease in QPD following intravenous steroid treatment [58]. This study unfortunately had limitations: the single observer was aware that all patients had received IV steroids and that they were being rescanned when they reported an improvement in symptoms. The observer was also aware of the pre-therapy imaging findings at the time of the second scan.

These factors introduce an unavoidable degree of bias into the study findings.

Spectral Doppler resistive index (RI) aims to provide a more quantitative objective assessment of synovial vascularity although its reproducibility is unknown. The Doppler spectrum of three random synovial arteries was electronically traced in five wrists and the RI calculated. Following injection of intraarticular steroid, the RI increased in four patients, consistent with decreased synovial blood flow [59].

Validity of US

For US measures of synovitis, the most convincing comparator or gold standard is microscopic or macroscopic evidence of synovial inflammation.

Angiogenesis is evident on microscopic examination of synovial biopsies from the earliest stages of disease evolution [6], and at arthroscopy is observed as a fine network of vessels over the rheumatoid synovium. US has been compared to the gold standard of microscopic or macroscopic pathological evidence of synovitis [54, 60, 61], but studies exist for larger joints rather than smaller joints. Walther et al. [54, 62] have found a close correlation between histological vascularity and semiquantative grades of PD signal in the synovium of knee joints (n=23) and hip joints (n=24) in patients undergoing arthroplasty for either RA or OA. Both studies showed a highly significant correlation between power Doppler US findings and histopathological findings. B-mode US-detected synovial thickness and arthroscopic grade of synovitis in knee joints also showed significant correlation [60].

MRI has been used as a gold standard in many studies evaluating the use of US in synovial assessment as there is much evidence documenting agreement between pathologic and MRI findings of synovitis [28, 29, 36, 63].

Studies comparing US and MRI in RA finger joints have shown a high level of agreement for synovitis assessed by B mode [60, 64] and particularly PDS [59, 65].

A prospective study of 60 patients showed that US was more sensitive than MRI in detecting synovitis, whereas MRI was more sensitive for detection of small erosions [66]. PD signal and early MRI enhancement in rheumatoid MCP joints have been shown to be closely correlated; the sensitivity and specificity of PDS, with MRI as a reference, were 0.89 and 0.98 respectively [65]. Both these studies however use only a binary score for assessment of synovitis (present or absent).

Szkudlarek et al. used a semiquantative, volume-based grading of MTP joint synovitis (grades 0–4) to compare B-mode US and T1-weighted contrast-enhanced MRI. With MRI considered the reference method, the sensitivity, specificity, and accuracy of B-mode US for the detection of synovitis were 0.87, 0.74, and 0.79 [64]. The authors suggest that the visualised inflammatory changes are similar or identical using both modalities [64].

However the results of the above studies must be treated with caution as few patients were involved in the studies [64, 65], and there was only a single observer in each, resulting in a lack of intraobserver agreement values [64–66].

Longitudinal studies

The use of US in longitudinal studies has demonstrated changes consistent with current theory. PD signal and B-mode synovial thickness decrease when steroids [58, 67–69] or TNF antagonists [70–72] are administered.

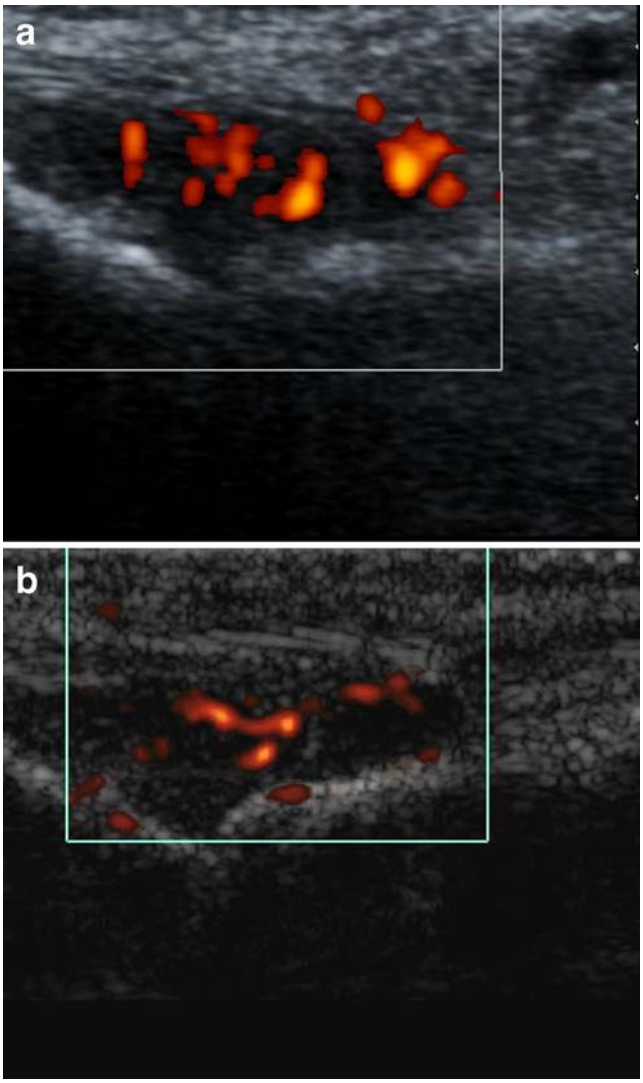

Fig. 4a, b Interscanner comparison between two different manufacturers' ultrasound machines. **a** and **b** show the same MCP joint scanned on the same day in the same room. Scans were obtained immediately one after the other on two different manufacturers' machines of comparable specification. Similar settings were used. Note the obvious difference in amount and location of PD signal between the two machines

Again this evidence is based upon studies that contain relatively few patients and often only one observer. One study relied upon subjective visual scale readings of one sonographer [69].

Generally, a weak correlation has been found between US measures and clinical examinations and biochemical markers [59, 70–72].

Reproducibility

To detect change reliably, US must be reproducible. The problems with reproducibility are based on variations among results obtained by different observers and different US machines. The intra- and interobserver variations of the used measures in US have not been widely tested [70, 73], and the interscanner variation remains untested. Interscan variability poses a significant problem. Results for the same patient scanned at different time intervals using a different scanner may not be comparable (Fig. 4a,b).

Studies have shown good interobserver agreement for assessment of hand- and foot-joint synovitis. A four-grade semiquantative evaluation of synovitis, joint effusion and power Doppler signal by two sonographers revealed ICCs of 0.81, 0.61 and 0.72 respectively and unweighted kappa estimations of 0.63, 0.48 and 0.55 respectively showing moderate to good correlation [73].

Only one study involving RA small joints included both reproducibility and longitudinal data. In this study, intra- and interobserver variations on B-mode US-determined synovial thickness in wrist, MCP and PIP joints of 11 patients were assessed with intraobserver coefficients of variation of 1.9–2.6% and interobserver coefficients of variation of 10.2–11.0% [70]. Treatment with a TNF antagonist changed the synovial thickness more than the coefficient of variation in most joints, suggesting this measure is sensitive to change in clinically relevant situations [70].

Predictive validity

The prognostic value of US in RA is unknown. There is only one study with data on the importance of US findings with respect to later radiographic or functional status [74]. This recent randomised, controlled trial of TNF antagonist therapy in early RA showed that baseline US-determined synovial thickening and degree of vascularity in the MCP joints correlated with the radiographic joint damage in the following year in the placebo group, but not in the group receiving biological therapy.

The prognostic value of MRI regarding development of erosions is not directly transferable to US. Correlation between US and MRI findings of synovitis has been demonstrated, but several studies have shown that the strongest MRI predictor of future erosive damage is presence of bone-marrow oedema [7, 8, 27, 49, 75], and this cannot be visualised by US.

Diagnostic value

Although US can detect intra- and extraarticular changes, the actual ability of US to distinguish RA from other relevant differential diagnoses has not been tested or verified. Studies have shown that US in RA demonstrates signs of intraarticular rather than entheseal inflammation, as is the case for seronegative spondyloarthropathies [50, 76].

Conclusion

Efficient methods for diagnosis, monitoring and determining prognosis are essential in early RA. While CR only visualises the late signs of disease activity, there is evidence that MRI and US are highly sensitive to early inflammatory and destructive changes in RA joints, and that MRI findings are sensitive to change and are of predictive value for future progressive damage.

MRI and US will be increasingly important in routine clinical management of patients in diagnosis, in monitoring whether a treatment satisfactorily suppresses joint inflammation or whether treatment modification is needed, and in prognosis in order to stratify patients into different therapeutic regimens [77]. Prognosis of the disease depends substantially on the appropriate and timely administration and targeting of drug therapy. As improved therapies are likely to reduce progressive structural joint damage to a minimum, MRI synovitis measures may become the main outcome measure in clinical trials [77].

However to achieve these goals, standardisation and validation of US and MRI are required to ensure accurate diagnosis, reproducibility and reliability.

Each modality has different strengths and weaknesses and levels of validation. The clinicians and radiologists need to be aware of these when determining future research and formulating clinical practice and clinical trial strategy for imaging synovitis.

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