

Submitted: 18.04.2016  
Accepted: 04.05.2016  
Published: 31.03.2017

## Rheumatoid arthritis: what do MRI and ultrasound show

Iwona Sudół-Szopińska<sup>1,2</sup>, Lennart Jans<sup>3</sup>, James Teh<sup>4</sup>

<sup>1</sup> Department of Radiology, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland

<sup>2</sup> Imaging Diagnostic Department, Warsaw Medical University, Warsaw, Poland

<sup>3</sup> Department of Radiology, Ghent University Hospital, Gent, Belgium

<sup>4</sup> Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, Oxford, United Kingdom

Correspondence: Prof. Iwona Sudół-Szopińska, MD, PhD, Department of Radiology, National Institute of Geriatrics, Rheumatology and Rehabilitation, Spartańska 1, 02-637 Warsaw, Poland, tel./fax: +48 22 844 42 41, e-mail: sudolszopinska@gmail.com

DOI: 10.15557/JoU.2017.0001

### Key words

rheumatoid arthritis,  
magnetic resonance  
imaging,  
ultrasonography,  
early arthritis,  
imaging

### Abstract

Rheumatoid arthritis is the most common inflammatory arthritis, affecting approximately 1% of the world's population. Its pathogenesis has not been completely understood. However, there is evidence that the disease may involve synovial joints, subchondral bone marrow as well as intra- and extraarticular fat tissue, and may lead to progressive joint destruction and disability. Over the last two decades, significant improvement in its prognosis has been achieved owing to new strategies for disease management, the emergence of new biologic therapies and better utilization of conventional disease-modifying antirheumatic drugs. Prompt diagnosis and appropriate therapy have been recognized as essential for improving clinical outcomes in patients with early rheumatoid arthritis. Despite the potential of ultrasonography and magnetic resonance imaging to visualize all tissues typically involved in the pathogenesis of rheumatoid arthritis, the diagnosis of early disease remains difficult due to limited specificity of findings. This paper summarizes the pathogenesis phenomena of rheumatoid arthritis and describes rheumatoid arthritis-related features of the disease within the synovium, subchondral bone marrow and articular fat tissue on MRI and ultrasound. Moreover, the paper aims to illustrate the significance of MRI and ultrasound findings in rheumatoid arthritis in the diagnosis of subclinical and early inflammation, and the importance of MRI and US in the follow-up and establishing remission. Finally, we also discuss MRI of the spine in rheumatoid arthritis, which may help assess the presence of active inflammation and complications.

## Introduction

Rheumatoid arthritis (RA) is the most common inflammatory arthritis, affecting approximately 1% of the world's population<sup>(1)</sup>. It is characterized by proliferative, hypervascularized synovitis and osteitis, resulting in bone erosion, cartilage damage, joint destruction and long-term disability<sup>(2)</sup>. Over the last two decades, significant improvement in its prognosis has been achieved owing to new strategies for disease management, the emergence of new biologic therapies and better utilization of conventional disease-modifying antirheumatic drugs<sup>(1)</sup>. Prompt diagnosis and appropriate therapy have been recognized

as essential for improving clinical outcomes in patients with early RA<sup>(1)</sup>.

Diagnosis of RA is based on clinical, laboratory and radiographic findings.

Conventional radiography has been the imaging modality of choice in RA primarily because of its reproducibility and feasibility with respect to detecting structural damage<sup>(1-3)</sup>. However, radiography can provide only indirect information on synovial inflammation, and the technique is insensitive to early inflammatory bone involvement and bone damage<sup>(2)</sup>.

Until recently, the absence of effective treatment to prevent joint destruction has limited the need for more sensitive imaging techniques. This situation changed after the development of new therapeutics for RA, such as anti-tumor necrosis factor (TNF) agents<sup>(2)</sup>. The availability of these potent and expensive drugs has created new demands for radiologists to identify patients with aggressive RA at an early stage<sup>(2)</sup>.

Magnetic resonance imaging (MRI) and ultrasonography (US) are increasingly being used in the assessment of RA in research and clinical practice due to their capacity to provide insight into the pathogenesis of inflammatory joint disease and ability to identify the key pathologic features of this disease entity at presentation, much earlier than they are seen on radiography<sup>(2,3)</sup>. Both modalities are characterized by high sensitivity in depicting local inflammation in the form of synovitis, tenosynovitis and bursitis, which is greater than in clinical examination and conventional radiography and can help establish an early diagnosis in RA<sup>(3)</sup>.

MRI also allows the detection of bone marrow edema, which is thought to be a precursor for the development of erosions in early RA as well as a marker of active inflammation<sup>(1)</sup>, and can be seen neither on radiographs, ultrasound or CT. In addition, the multi-plane, multislice capability of MRI allows visualization of the area of interest in three orthogonal planes. Therefore, MRI has the advantage of providing details concerning both the bone and surrounding tissues of the joint, which is not shared by any other imaging modality, whilst avoiding ionizing radiation<sup>(3)</sup>.

In particular, MRI in RA allows<sup>(4)</sup>:

- assessment of peripheral joints for active inflammation in the form of joint effusions, synovitis, tenosynovitis, BME, as well as subsequent structural lesions, such as articular cartilage damage, cortical bone erosions, and tendons tears;
- assessment of inflammatory changes and post-inflammatory complications in the spine, i.e. assessment of inflammatory activity, atlanto-axial / atlanto-occipital structural lesions (e.g. subluxations);
- qualitative, semi-quantitative and quantitative measurements in dynamic contrast-enhanced MRI (DCE-MRI) of active inflammation.

Advantages of ultrasound include:

- high availability, low cost, and high patient acceptance compared to MRI;
- assessment of peripheral joints for active inflammation in the form of effusion, synovitis, tenosynovitis, as well as subsequent structural lesions, such as tendons tears, whereas cortical bone erosions and articular cartilage damage can be seen to some extent;
- dynamic examination of peripheral joints, useful in the assessment of inflammatory changes, e.g., impingement of the inflamed subacromial bursa with acromion, stability of the ulnar nerve, tendon sublux-

ations and luxations (e.g. extensor carpi ulnaris tendon), tendons tears;

- qualitative, semi-quantitative and quantitative measurements of inflammation (intensity of vascularization, thickness of synovium).

### **Pathogenesis of RA and RA-related pathological phenomena within the synovium, subchondral bone marrow and articular fat tissue in MRI and ultrasound**

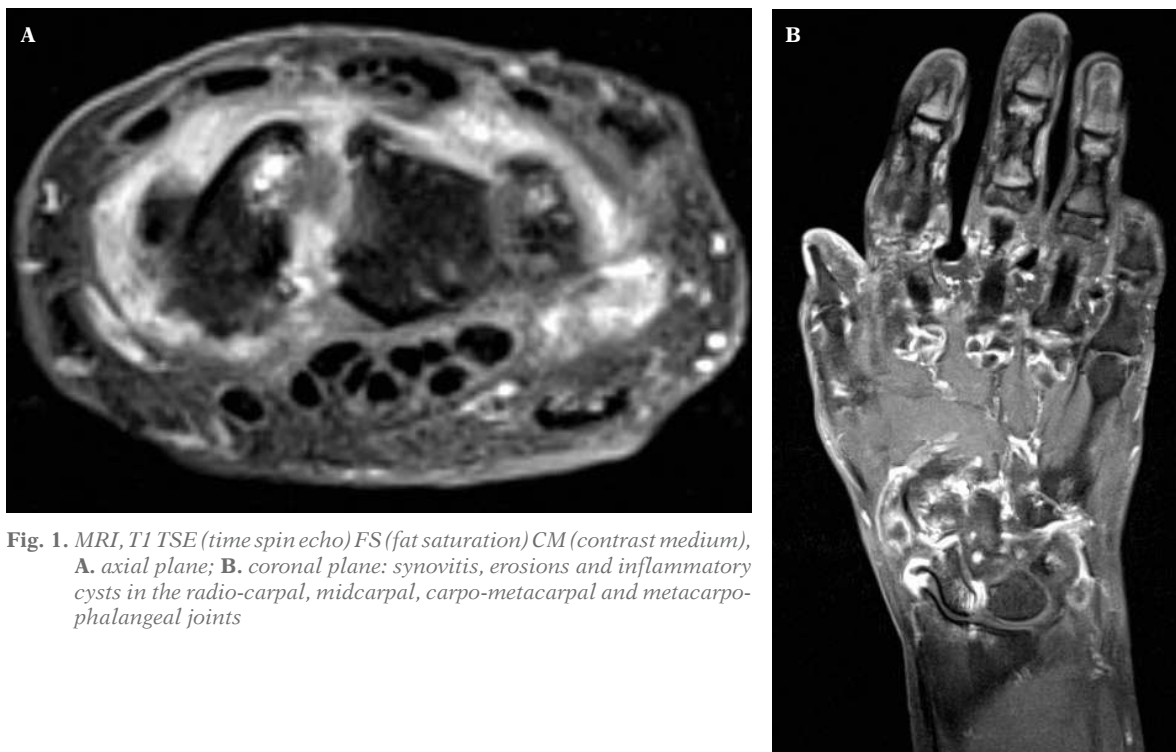
The pathogenesis of RA has been understood to some extent only. However, there is evidence that the process of joint destruction is initiated in the joint cavity and bone marrow. In addition, adipose tissue may also play a pro-inflammatory and pro-destructive role. So far, it has not been determined what triggers the formation of inflammatory infiltrates in the synovial membrane. Environmental factors, such as cigarette smoking and porphyromonas gingivalis, are thought to play a role. In certain predisposed individuals, the synovium may thicken rapidly within a few months due to hyperplasia, which is an increase in the number of fibroblast-like synoviocytes from 1–3 layers to up to 12 layers. The subintima layer, which in healthy individuals is composed of loose connective tissue with blood and lymphatic vessels, nerve fibers and several cell types, may thicken as a result of edema caused by migration and retention of infiltrating cells. This thickened synovium is well-visible on US and MRI scans<sup>(4-7)</sup>.

The thickened synovium is also characterized by increased vascularity, which is a result of angiogenesis. This aspect of the disease is also well-visible on both Doppler ultrasonography and MRI on contrast-enhanced T1-weighted images. DCE-MRI shows increased permeability of neovessels<sup>(8)</sup>.

If RA is recognized early and aggressive treatment is introduced early on (i.e. within the first 3 months, known as a therapeutic window), it is possible to suppress the inflammatory reaction. Otherwise, the disease could take on a more chronic, aggressive form, with joint destruction.

RA does not only involve the synovium. MRI showed that the inflammatory process also takes place within the bone, and that BME reflects inflammatory infiltration in the bone marrow in RA<sup>(1,9)</sup>. When untreated, BME leads to the development of erosions<sup>(10-12)</sup>.

The third compartment with the inflammatory and destructive potential in RA is the adipose tissue. The adipose tissue is infiltrated by immune cells and produces over 50 adipocytokines or adipokines as well as other inflammatory mediators and factors which are secreted into the joint fluid and may influence the metabolism of the cartilage and synovial membrane as well as sustain the inflammatory response<sup>(13)</sup>.



**Fig. 1.** MRI, T1 TSE (time spin echo) FS (fat saturation) CM (contrast medium), **A.** axial plane; **B.** coronal plane: synovitis, erosions and inflammatory cysts in the radio-carpal, midcarpal, carpo-metacarpal and metacarpophalangeal joints

### RA-related pathological phenomena within the synovium, subchondral bone marrow, and peri-articular fat tissue on MRI and ultrasound

Abnormalities in early RA include synovitis, tenosynovitis, bursitis, BME and adipose tissue inflammation. On MR and US images, early RA-related pathologies include thickening of the synovium of the joint capsule, tendon sheaths and bursae. In the next stage of the disease, vascularization of the synovium, resulting from neo-angiogenesis, is observed. Joint effusion is seen early in the disease process in RA and is commonly associated with synovitis, tenosynovitis and bursitis. BME accompanies synovitis in the majority of patients. However, it could be the only area involved in early RA.

### Synovitis

Proliferative synovitis (rheumatoid pannus) is the earliest pathologic abnormality in rheumatoid arthritis, and it is secondarily responsible for bone and cartilage damage<sup>(2)</sup>. It involves peripheral joints, most frequently of the hand and wrist, ankle and foot and cervical spine. In the hand, wrist, ankle and foot it is usually, but not exclusively, bilateral. With the disease progression, neovessels will be seen within the thickened (first hyperplastic and then hypertrophied) synovium.

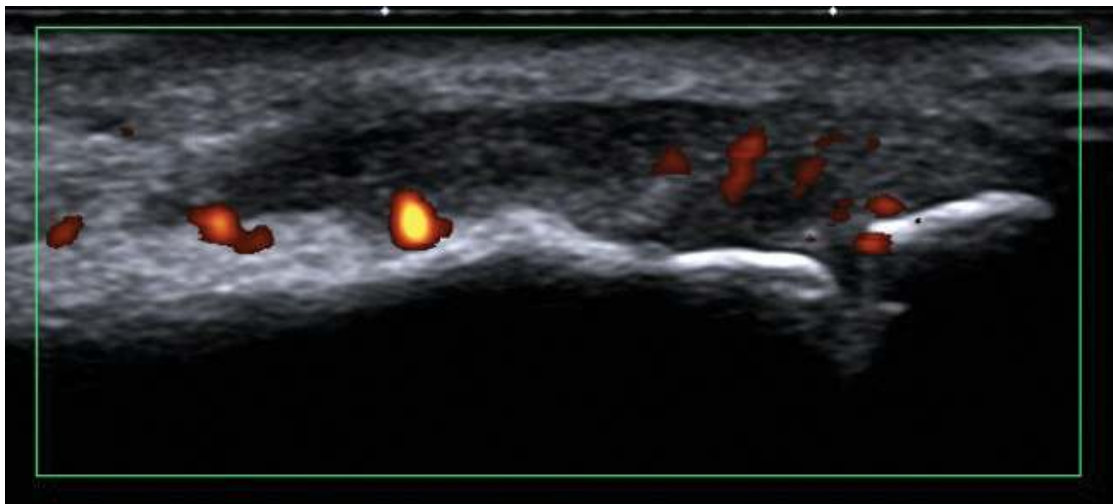
MRI reveals proliferative synovitis as thickening of the synovial membrane, which has intermediate to low signal intensity on T1-weighted images and, due to increased water content of synovitis, high signal intensity

on T2-, PD-weighted and STIR/TIRM images<sup>(1)</sup>. Contrast-enhanced T1-weighted images are more sensitive and specific in the assessment of acute synovitis than non-contrast MRI<sup>(1)</sup>. On post-contrast images, the inflamed synovium shows fast enhancement, which lasts approximately 5 minutes after injection<sup>(1,2)</sup> (Fig. 1).

The delay between contrast administration and scanning is important as the volume of enhancing synovitis increases initially before stabilizing after about 4 min. After 6–11 minutes, contrast reaches the synovial fluid, obscuring the synovium / fluid interface<sup>(1,13,14)</sup>. Imaging is then best performed between these times. Images obtained more than 10 minutes after contrast injection may not accurately delineate the extent of synovitis since gadolinium may diffuse into the synovial joint fluid<sup>(1)</sup>. This diffusion may blur the margins of the inflamed synovium, which can lead to overestimation of synovial volume<sup>(1)</sup>. The use of fat-suppressed gadolinium-enhanced T1-weighted images increases the contrast between the inflamed synovium and adjacent structures on T1 FS (fat saturated) sequences following contrast administration<sup>(1,2)</sup>.

Sonography shows abnormal thickened and hypoechoic (relative to subdermal fat) intraarticular tissue that is poorly compressible and that exhibits Doppler signal with color or power Doppler imaging<sup>(2)</sup> (Fig. 2).

Joint effusion occurs early in RA and is commonly associated with synovitis. In some patients, it is the first sign of inflammation, even if the thickness and signal of the synovium are normal or only slightly increased.



**Fig. 2.** Ultrasound: synovitis in the PIP (proximal interphalangeal) 2 joint

On MR images, this fluid shows high signal intensity on T2-weighted and PD MR images, it is hypointense on T1-weighted images and has a low signal intensity on fat-suppressed gadolinium-enhanced T1-weighted MR images<sup>(2)</sup>. On unenhanced MR images, synovitis and joint fluid are usually difficult to differentiate. However, heavily T2-weighted images (TE > 140 msec) can be helpful in identifying synovitis, which has lower signal intensity than joint effusion<sup>(1)</sup>.

On sonography, the fluid appears anechoic, with no evidence of flow on Doppler imaging, and can be displaced from the region by compression with the transducer<sup>(2)</sup>.

## Tenosynovitis

Tenosynovitis predominates over joint synovitis in some patients<sup>(1)</sup>, or can even be the only pathological finding in RA. Tenosynovitis in RA is usually bilateral. Although any tendon may be affected, at the wrist level the extensor tendon sheaths from I to VI compartments are more frequently involved than flexors. At the ankle level, the tibialis posterior, flexor digitorum longus, flexor hallucis longus tendons and peroneal tendons are more frequently involved than extensors. At the hand and foot level, only flexor tendon sheaths are involved as extensors do not have tendon sheaths at these levels. Some amount of fluid may be associated with tenosynovitis with imaging features identical as in case of joint effusion.

MRI features of inflamed synovium of tendon sheaths are the same as in joint space synovitis, and the use of FS T1-weighted MR imaging is recommended to delineate the extent of inflammatory changes in tendon sheaths more accurately<sup>(1)</sup>. MRI reveals thickening of the synovial sheath with marked enhancement on fat-suppressed gadolinium-enhanced T1-weighted images<sup>(2)</sup> (Fig. 3).

Sonography shows hypoechoic and thickened synovial sheath with or without hyperemia on Doppler imaging<sup>(2)</sup> (Fig. 4).

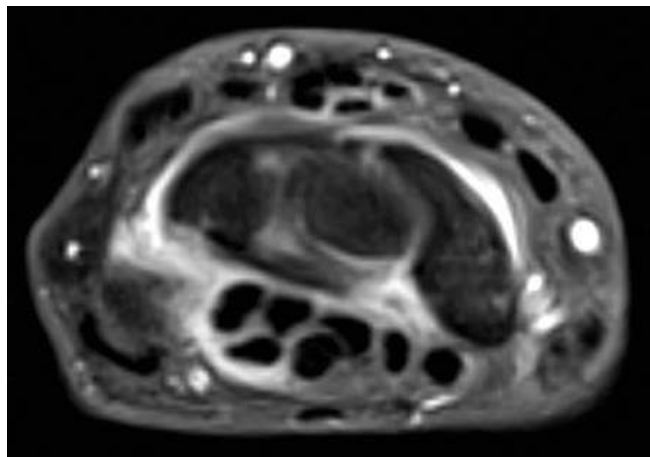
In less favorable conditions, inflammation will be seen also in tendons (tendonitis secondary to tenosynovitis), which – if not treated – may lead to tendon rupture related both to invasion of the tendon by the tendon sheath synovitis and frying of the tendon against eroded bone margins<sup>(1)</sup>. Inflammatory changes representing tendonitis show increased and usually heterogeneous signal intensity on both T1- and T2-weighted MR images<sup>(1)</sup>. On ultrasound, inflamed tendons are focally thickened, of low echogenicity and show vessels of inflammatory and reparative process. Thickening, thinning, intratendinous tearing or complete discontinuity of tendons on MR and ultrasound imaging are all indicative of partial or complete tear<sup>(1)</sup>.

## Bursitis

Bursitis is not a common finding in patients with early rheumatoid arthritis as synovitis and tenosynovitis. In hands, it is rarely seen between the extensor tendons and metacarpal heads, between the first and second compartment of extensors. In feet, there is intermetatarsal and submetatarsal bursitis (located between or beneath the metatarsal heads). Other locations include: Achilles tendon bursitis, subacromial bursitis, olecranon bursitis and gluteus maximus bursitis.

The signal from inflamed synovium of bursae is identical compared to joint space synovitis or tenosynovitis, thus showing significant enhancement on MRI after IV gadolinium injection due to inflammation (Fig. 5).

On sonography, inflamed bursae may contain exudate only or in more chronic cases exudate with fibrotic septa. In RA-typical cases, they show thickened hypertrophied synovium with exudate. Hyperemia of the synovial lining can be seen on Doppler sonography. Secondary involvement of tendons in the case of Achilles tendon bursitis or subacromial bursitis is a common complication, as well as heel bone erosions in chronic achillobursitis. Moreover,



**Fig. 3.** MRI, T1 TSE FS CM, axial plane: midcarpal joint synovitis, tenosynovitis of the flexors and 4<sup>th</sup> compartment of extensor tendons

ruptured semimembranous-gastrocnemius bursa of the popliteal fossa is easily diagnosed on ultrasound (Fig. 6).

### Bone marrow edema (BME)

The ability to image BME is an advantage of MRI over ultrasound and radiography<sup>(15)</sup>. BME is seen as hyperintense T2 signal area within trabecular bone with ill-defined margins and signal characteristics consistent with increased water content, i.e. high signal on PD FS/SPAIR, T2 FS/SPAIR, STIR/TIRM images, and increased signal intensity after the administration of gadolinium-based contrast material<sup>(2,14)</sup>. With T1-weighted sequences, BME has low signal intensity, but changes are less conspicuous compared to other pulse sequences<sup>(2,14)</sup>. In early RA, BME is usually located in the subchondral bone. However, in e.g. carpal bones, it may involve a great proportion of bone at some distance from the subchondral bone<sup>(1)</sup> (Fig. 7). Intraosseous cysts are similar to BME in terms of signal characteristics, but are better delineated com-

pared to ill-defined areas of BME. From the pathological point of view, they represent areas of damaged bone. This makes them visible on plain radiography, contrary to BME which is not seen.

Synovitis, tenosynovitis and bursitis can be assessed with qualitative, semi-quantitative and quantitative methods. As for quantitative methods, inflammatory activity can be estimated by quantifying an increase in signal intensity at DCE-MRI within inflamed tissues<sup>(1,13,15)</sup> (Fig. 8). DCE-MRI consists in imaging of the same slices at intervals of several seconds after *iv* contrast administration for a period of 2–5 min. Absolute and relative early enhancement rate (RER) of the synovium can be obtained from the analysis, reflecting synovial perfusion and permeability of capillary vessels within the inflamed tissue. This is correlated with the degree of synovial vascularization which may be useful in treatment monitoring<sup>(4)</sup>.

On ultrasound, CFR (color flow ratio) can be calculated after introducing the ROI to the most representative area of high vascularization (Fig. 9)

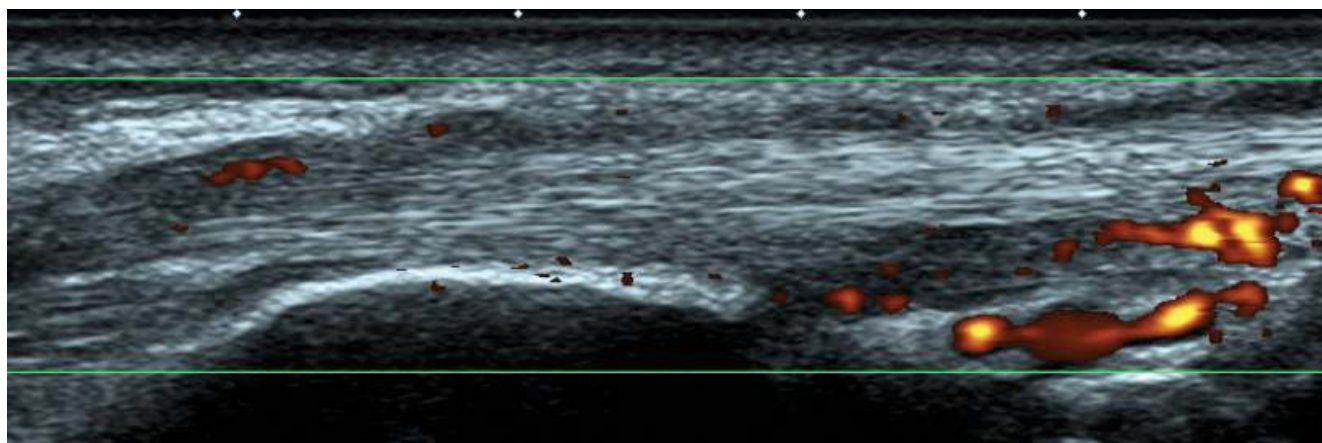
### Adipose tissue inflammation

On MRI, increased signal on T2-weighted images and enhancement on post-contrast images of the intra- or extra-capsular fat tissue may be seen.

On ultrasound, inflamed fat tissue is of high echogenicity. Additionally, some individuals present vascularization (Fig. 10).

### Erosions

The clinical relevance of synovitis and BME in terms of their role as erosion precursors is well-studied<sup>(3)</sup>. It has been shown that initial erosions are marginal, result from destructive activity of the synovial pannus and are well-seen on plain radiography, ultrasound and



**Fig. 4.** Ultrasound, longitudinal view of tenosynovitis of the extensor carpi ulnaris tendon

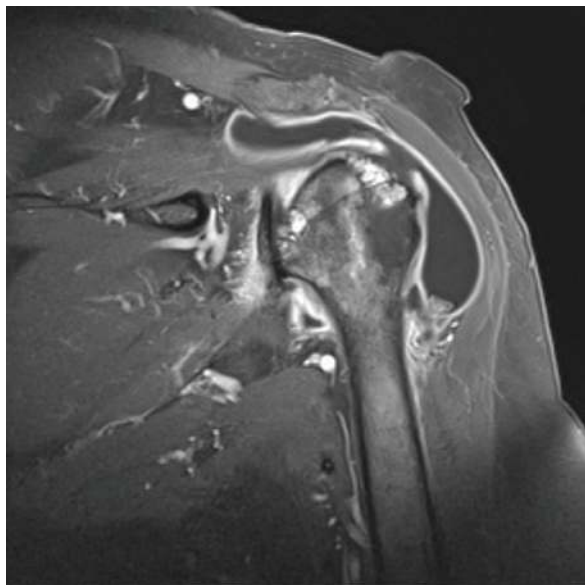


Fig. 5. Subacromial bursitis in MRI, T1 TSE FS CM

MRI (however, the first two methods show only some erosions due to the summation on radiographs and limited access to some articular areas on ultrasound). With RA progression, the invasion of the pannus on the joint hyaline cartilage and its subsequent damage is seen as subchondral bone erosion formation. Joint space narrowing is a radiographic sign cartilage damage. MRI allows direct visualization of joint cartilage. The cartilage of even small joints can be depicted on MRI but requires high-end equipment and the acquisition of pulse and high-resolution sequences. However, cartilage assessment is not included in the current recommendations for RA joint assessment<sup>(16)</sup>. Bone destruction also occurs in the course of inflammation of the subchondral bone marrow, which may cause subcortical bone destruction. It is initially seen on radiographs and ultrasound as inflammatory cysts and later as erosions.

On MRI, erosions are sharply margined trabecular bone defects with disrupted cortical bone continuity. They are seen in at least 2 planes with low signal intensity on T1-weighted images, high signal intensity on T2-weighted and STIR images and may show enhancement after administration of gadolinium-based contrast material, especially well-seen with thin-partition 3D gradient-echo sequences<sup>(1,2,4)</sup>. Erosions may be difficult to differentiate from focal regions of BME, although they tend to have clearly defined margins and clear cortical break<sup>(1)</sup> (Fig. 11).

On sonography, bone erosions are seen as intraarticular discontinuities of the bone surface that are visible in two perpendicular planes<sup>(2)</sup>. High signal on Doppler imaging suggests the presence of hypervascularized pannus tissue in the erosion<sup>(2)</sup> (Fig. 12). Compared with MRI, sonography cannot visualize all erosions because of limitations of probe positioning and restricted access to all cartilage surfaces.

## The significance of MRI and ultrasound findings in rheumatoid arthritis

According to ESSR<sup>(4)</sup> and EULAR recommendations, MRI is currently considered the best, non-invasive, observer-independent imaging modality to evaluate inflammation of joints, tendons, entheses and bone marrow. The main indications for MRI in patients with RA include:

- assessing inflammatory lesions that are not detected on clinical examination;
- assessing early signs of inflammation (synovitis, tenosynovitis, bursitis, BME) and establishing prognosis (synovitis and bone marrow edema in particular are risk factors for the progression to structural changes);
- assessing treatment response / monitoring disease activity and progression;
- assessing remission;
- identification of disease complications.

Ultrasound is commonly performed to evaluate peripheral joints, tendons sheaths and bursae in RA due to its availability and lower cost. The main indications for ultrasound include:

- assessment of inflammatory lesions that are not detected on clinical examination;
- assessment of early signs of inflammation (synovitis, tenosynovitis, bursitis);
- assessment of treatment response / monitoring disease activity and progression;
- assessment of remission;
- identification of disease complications in peripheral joints.

## Subclinical inflammation

RA has a period of preclinical disease, and MRI and US appear valuable in identifying joints and tendon sheaths

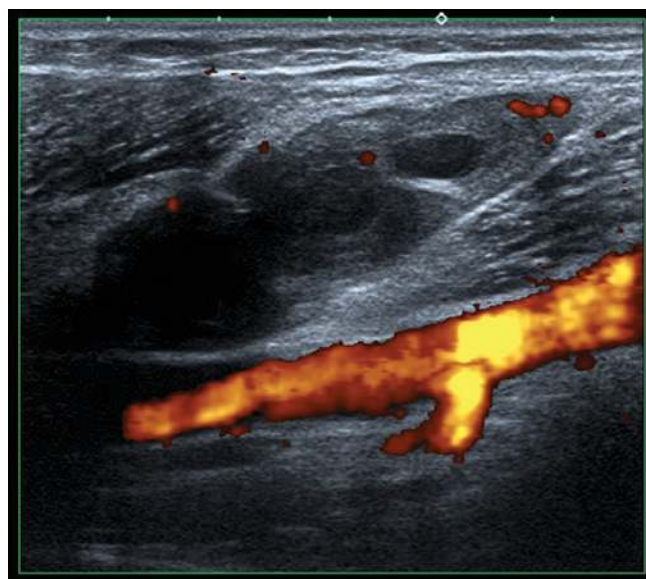


Fig. 6. Ultrasound: gastrocnemius-semimembranous bursitis



Fig. 7. MRI, bone marrow edema in the distal radius

with subclinical inflammation (synovitis, tenosynovitis, bursitis, BME) despite normal physical examination (no edema, no pain). This has clinical implications since imaging can help confirm subclinical RA. It also has a prognostic value for the subsequent appearance of erosions during follow-up<sup>(1)</sup>.

In a study by van Steenberg<sup>(17)</sup>, MRI diagnosed subclinical inflammation in 44% of patients clinically suspected to progress to RA (non-swollen, non-painful joints, only arthralgia). 35% of them progressed to clinically evident inflammation within 4 months. Krabben et al.<sup>(18)</sup> found subclinical inflammation (BME, synovitis, tenosynovitis) in 26% of asymptomatic joints. Radiographic progression was observed in 4% of those joints within 1 year, in comparison to 1% progression of asymptomatic joints and without abnormalities in MRI. Inflammation seen on MRI was therefore a prognostic factor of progression.

## Early diagnosis

The clinical impact of MRI and US in early diagnosis of RA needs to be determined<sup>(4)</sup>.

Although imaging is not a mandatory part of the current American College of Rheumatology ACR/EULAR classification criteria for RA, MRI and ultrasonography can be used to count involved joints in the case of diagnostic uncertainty<sup>(4)</sup>. In the joint involvement domain, which can provide up to 5 of the 6 required points for an RA diagnosis, MRI and US can be used to determine joint involvement<sup>(4)</sup>.

Also, these modalities can help to differentiate patients with aggressive disease in early RA, allowing the targeting of expensive therapies to those with a poor prognosis<sup>(16)</sup>.

On the other hand, however, early inflammatory features, such as synovitis, tenosynovitis, bursitis or exudate, could be nonspecific, and we are unable to differentiate early inflammation from overuse, early osteoarthritis or other connective tissue. This also concerns BME, which is well-documented in traumatic, neoplastic, and degenerative processes. However, BME is reported to represent a distinctive MRI finding in patients with RA, especially in the earlier phase of the disease<sup>(1)</sup>. In most cases, it coexists with synovitis. However, in some cases, BME may precede synovitis or it may be the only feature of the disease. This suggests a potential role of MRI in the diagnosis of early stages of the disease, for instance in patients with no pathologies seen on ultrasonography. BME was found in 39% of cases of early arthritis (<3 years duration) and in 68% of cases of established RA (>3 years duration)<sup>(1)</sup>.

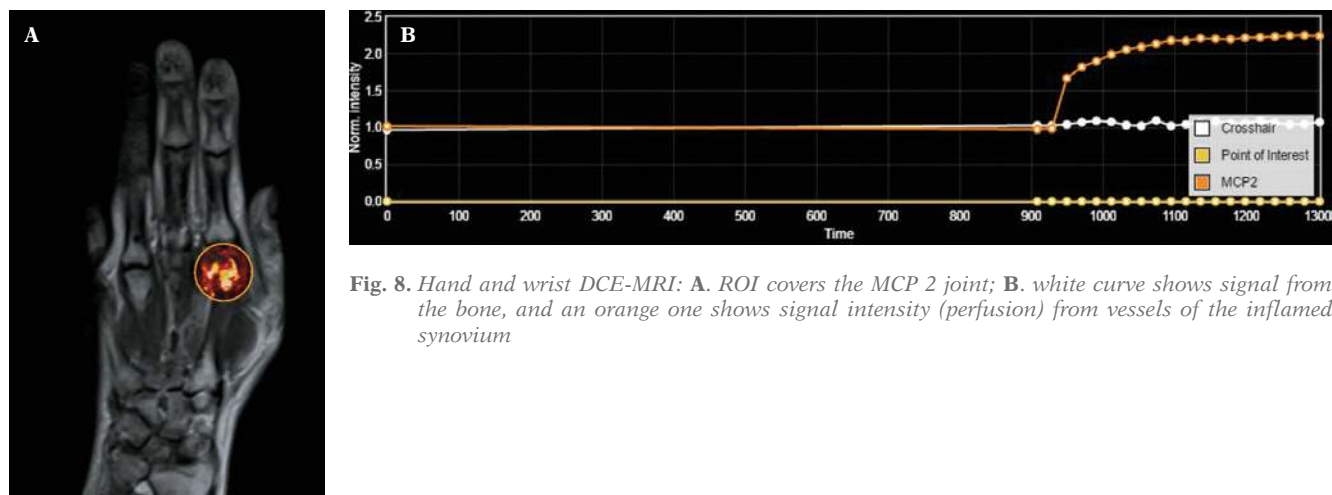
BME is also an independent predictor of subsequent radiographic progression in early RA, which means that it may precede erosion formation. The risk of erosion formation is 6 times higher in areas in which BME had been noted earlier.

In addition, MRI helps to detect more bone erosions in the wrist and hand in early RA than radiography and ultrasonography. Detection of bone erosions in the early phase of RA indicates irreversible joint damage and correlates with poor long-term radiographic and functional outcome<sup>(1)</sup>. In early RA, MRI helps identify bone erosions in 45–72% of patients with disease of less than 6-month duration<sup>(1)</sup>, compared with 8–40% for radiography.

## Follow-ups

Modern drug therapies reportedly decrease synovial proliferation and BME and prevent the development of bone erosions. MRI and sonography can qualitatively, semi-quantitatively and quantitatively evaluate the synovium and bone marrow inflammation, and identify treatment response as a reduction in synovial volume and a decrease in the rate of synovial enhancement or area of inflamed bone marrow<sup>(2)</sup>. Semi-quantitative scoring methods of early rheumatoid arthritis features advancement (i.e. synovitis, bone erosions and bone edema) at the wrist and metacarpophalangeal joints have been developed and standardized for MRI by the OMERACT (Outcome Measures in Rheumatology Clinical Trials) and EULAR (European League Against Rheumatism) groups<sup>(2)</sup>. However, they are rarely used in everyday clinical practice.

One of the most exciting applications for MRI is monitoring of the response to treatment, including biologics, with MRI-diagnosed synovitis and BME acting as imaging biomarkers for measuring patient responses to therapy. The first randomized therapeutic trial using MRI as an outcome measure in early RA was published by Conaghan<sup>(3)</sup>. MRI was used to follow synovitis and erosions in patients randomized to methotrexate +/- intraarticular corticosteroid<sup>(3)</sup>.



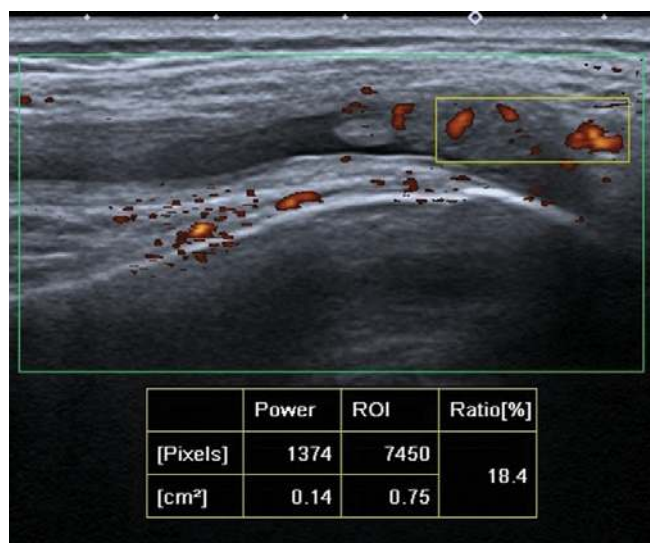
**Fig. 8.** Hand and wrist DCE-MRI: **A.** ROI covers the MCP 2 joint; **B.** white curve shows signal from the bone, and an orange one shows signal intensity (perfusion) from vessels of the inflamed synovium

## MRI of the spine in RA

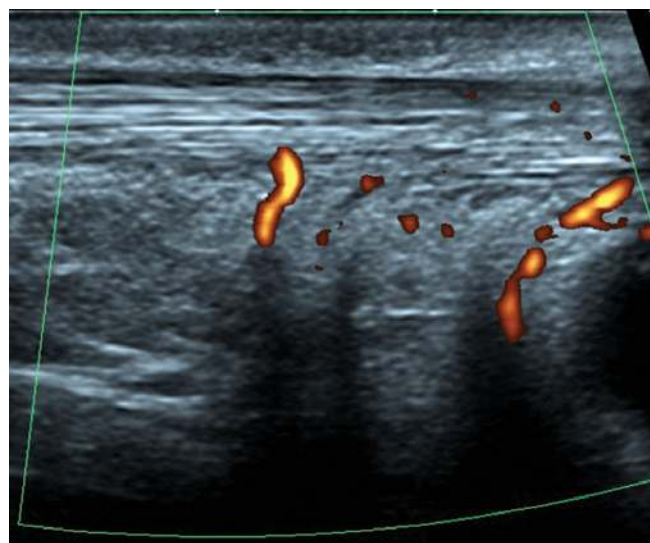
The spine is a common target of rheumatoid arthritis, ranking the third after the hands and feet<sup>(19)</sup>. The proportion of patients who experience cervical spine involvement at some point of their disease ranges from 14% to 88%<sup>(19)</sup>. Cervical spine involvement in patients with RA may lead to clinical manifestations varying from pain to neurologic deficits or even death from acute respiratory failure due to brainstem compression. These cervical spine lesions include: atlanto-axial subluxation (AAS), subaxial subluxation (SSA), C1–C2 arthritis, erosions and discitis<sup>(20,21)</sup> (Fig. 13).

MRI offers the most comprehensive evaluation of rheumatoid lesions in the spine. In RA patients, MRI is usually performed in order to assess the presence and activity of inflammation (pannus) and possible complications in the atlanto-axial, atlanto-occipital and subaxial areas, especially brainstem and/or spinal cord compression<sup>(20)</sup>.

The main abnormality at the upper CS is AAS (including anterior, vertical, lateral, rotatory and posterior) which is caused by the development of C1–C2 pannus and rupture or luxation of the transverse ligament<sup>(20)</sup>. At the lower CS, the main lesion is subaxial subluxation, and 10–50% of patients are asymptomatic<sup>(19)</sup>. Other MRI features of RA are: dens and atlas erosions secondary to pannus destructive activity, brainstem compression, subarachnoid space encroachment not only at the level C1/2 but also more distally, abnormal fat pad caudal to the clivus (present, displaced, reduced, absent), basilar invagination and subaxial spinal stenosis<sup>(21)</sup>. Subarachnoid space encroachment was found to be associated with a 12-fold increased risk of neurological complications in a study by Reijnierse et al.<sup>(20)</sup> This enhancing tissue leads to stenosis, and presumably represents pannus and may lead to cord compression, with resultant irreversible cord atrophy<sup>(20)</sup>. Dynamic flexion–extension MRI scanning in evaluating RA involvement of the cervical spine was found to diag-

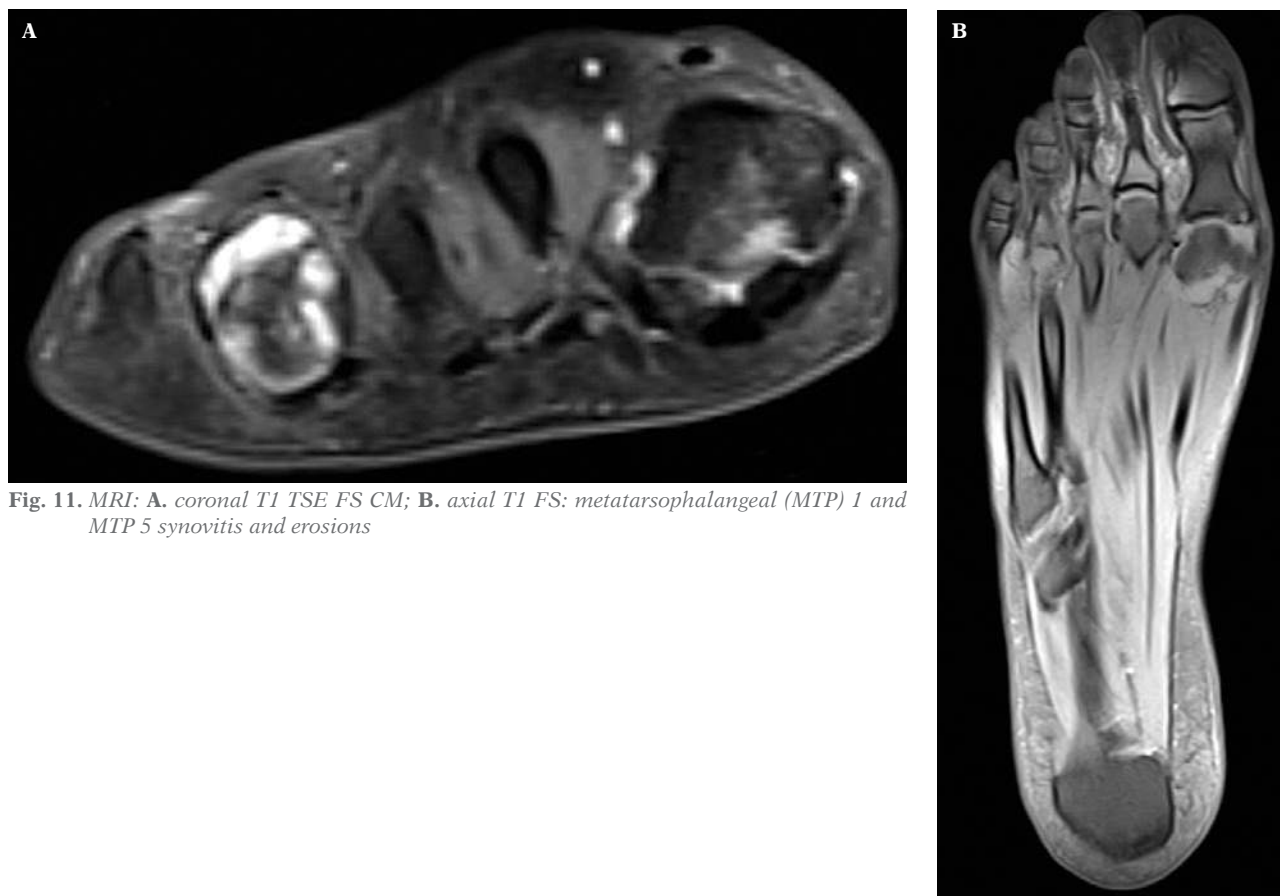


**Fig. 9.** Quantifying inflammation in the radiocarpal joint with the use of the vascularity index



**Fig. 10.** Ultrasound, increased echogenicity and vascularization of the Kager's fat pad





**Fig. 11.** MRI: **A.** coronal T1 TSE FS CM; **B.** axial T1 FS: metatarsophalangeal (MTP) 1 and MTP 5 synovitis and erosions

nose subarachnoid encroachment in flexion that was not evident on neutral MRI<sup>(21)</sup>.

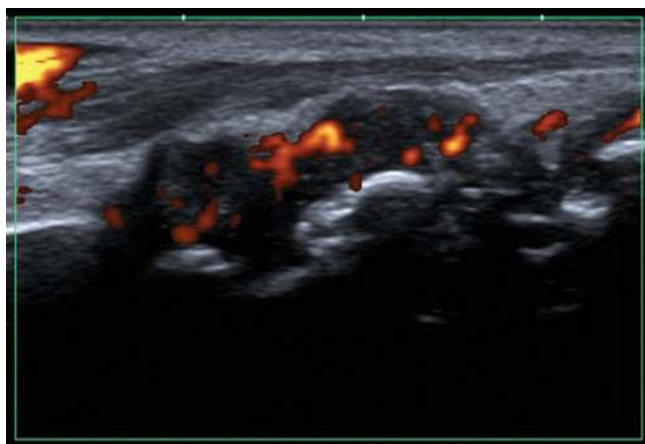
### Remission

MRI and US may sensitively detect residual synovitis or BME that could persist even in the face of a clinical response. This takes us back to the concept of imaging remission, which may be the target of future therapy<sup>(22)</sup>. It has been shown that many patients with RA who are in the stage of clinical remission continue to have persistent inflammatory processes at the cell level. In successfully treated cases, MRI and US will show fibrotic pannus which usually presents in end-stage RA and appears relatively hypovascular after iv administration of gadolinium-based contrast material or in Doppler studies. On T2-weighted MRI sequences, fibrous pannus with intermediate to low signal intensity can be distinguished from acute synovitis and joint fluid<sup>(1)</sup>.

### Differential diagnosis

The diagnosis of early RA is often difficult, especially when laboratory tests do not indicate any specific entity. Hyperplastic and even slightly vascularized synovium can be seen in overuse injuries, osteoarthritis or soft tissue impinge-

ments. Also, other connective tissue diseases can be notoriously hard to differentiate with early RA. For example, in patients with psoriatic arthritis (PsA), MRI and ultrasound may show synovitis and tenosynovitis. In the later course, they may reveal erosions and periosteum irregularities. In addition, MRI can show a number of cervical spine pathologies, resembling RA (active pannus, dens erosions, subluxations). Predilective areas include DIP joints and



**Fig. 12.** Ultrasound, longitudinal view of the radiocarpal and midcarpal joints: synovitis and erosions



**Fig. 13.** Cervical spine: **A.** CT and MRI; **B.** sagittal T1-weighted image; **C.** sagittal T2-weighted image; **D.** axial T2-weighted image: dens erosions, vertical subluxation (basilar invagination), multilevel instability with a tendency to C4-C6 kyphosis and spinal cord compression

one digit tendon sheath (sausage finger, dactylitis). BME in peripheral joints and in the subchondral part of entheses was found to be more extensive in PsA than in RA. Also, extracapsular inflammation is suspected to be specific for PsA. MRI may therefore show extensive signal intensity changes in the bone marrow and beyond joint capsule on STIR T2-weighted, fat-suppressed T2-weighted, or fat-suppressed gadolinium-enhanced T1-weighted sequences<sup>(2)</sup>.

The latest data, however, show that even osteoarthritis may manifest with extensive BME and extracapsular inflammation on MRI<sup>(23)</sup>.

In patients with systemic lupus erythematosus, MRI may show abnormalities similar to those of patients with early RA (e.g., synovitis, tenosynovitis and bone erosions), and it might be impossible to differentiate patients with early RA

from those with systemic lupus erythematosus on MRI<sup>(2)</sup>. We also observe fibrotic degeneration of tendons, involving the intramuscular part of tendons, which may lead to a tear, and seems specific for lupus. Such changes are very-well seen in ultrasound.

In 2014, Stomp et al.<sup>(24)</sup> conducted the first study to determine whether patients who are clinically classified with RA differ in MRI features from patients with other diseases. Although patients with RA had higher scores of MRI inflammation than patients without RA and ACPA-positive patients had more BME than ACPA-negative, the severity of MRI inflammation assessed according to RAMRIS did not accurately differentiate patients with RA from other early arthritis patients. Because BME is a predictor of progression of joint destruction, this observation is in line with ACPA-positive RA being a more severe disease.

## Summary

MRI and ultrasound enable early diagnosis, follow-up, treatment and postinflammatory joint damage assessment of synovial joints in patients with RA. MRI additionally shows bone marrow inflammation and axial spine involvement.

## References

- Narváez JA, Narváez J, De Lama E, De Albert M: MR imaging of early rheumatoid arthritis. *Radiographics* 2010; 30: 143–165.
- Boutry N, Morel M, Flipo RM, Demondion X, Cotton A: Early rheumatoid arthritis: a review of MRI and sonographic findings. *AJR Am J Roentgenol* 2007; 189: 1502–1509.
- Freeston JE, Bird P, Conaghan PG: The role of MRI in rheumatoid arthritis: research and clinical issues. *Curr Opin Rheumatol* 2009; 21: 95–101.
- Sudol-Szopińska I, Jurik AG, Eshed I, Lennart J, Grainger A, Østergaard M *et al.*: Recommendations of the ESSR Arthritis Subcommittee for the Use of Magnetic Resonance Imaging in Musculoskeletal Rheumatic Diseases. *Semin Musculoskelet Radiol* 2015; 19: 396–411.
- Singh JA, Arayssi T, Duray P, Schumacher HR: Immunohistochemistry of normal human knee synovium: a quantitative study. *Ann Rheum Dis* 2004; 63: 785–790.
- Humbly F, Bombardieri M, Manzo A, Kelly S, Blades MC, Kirkham B *et al.*: Ectopic lymphoid structures support ongoing production of class-switched autoantibodies in rheumatoid synovium. *PLoS Med* 2009; 6: e1.
- Xu X, Hsu HC, Chen J, Grizzle WE, Chatham WW, Stockard CR *et al.*: Increased expression of activation-induced cytidine deaminase is associated with anti-CCP and rheumatoid factor in rheumatoid arthritis. *Scand J Immunol* 2009; 70: 309–316.
- Walsch DA: Angiogenesis and arthritis. *Rheumatology (Oxford)* 1999; 38: 103–112.
- McQueen FM, Benton N, Perry D, Crabbe J, Robinson E, Yeoman S *et al.*: Bone edema scored on magnetic resonance imaging scans of the dominant carpus at presentation predicts radiographic joint damage of the hands and feet six years later in patients with rheumatoid arthritis. *Arthritis Rheum* 2003; 48: 1814–1827.
- Hetland ML, Ejlertsen B, Horslev-Petersen K, Jacobsen S, Vestergaard A, Jurik AG: MRI bone edema is the strongest predictor of subsequent radiographic progression in early rheumatoid arthritis. Results from a 2-year randomized controlled trial (CIMESTRA). *Ann Rheum Dis* 2009; 68: 384–390.
- Tamai I, Kawakami A, Uetani M, Takao S, Arima T, Iwamoto N *et al.*: A prediction rule for disease outcome in patients with undifferentiated arthritis using magnetic resonance imaging of the wrists and fingers and serologic autoantibodies. *Arthritis Rheum* 2009; 61: 772–778.
- Sudol-Szopińska I, Kontny E, Zaniewicz-Kaniewska K, Prohorec-Sobieszek M, Saied F, Maśliński W: Role of inflammatory factors and adipose tissue in pathogenesis of rheumatoid arthritis and osteoarthritis. Part I: Rheumatoid adipose tissue. *J Ultrason* 2013; 13: 192–201.
- Hodgson RJ, O'Connor P, Moots R: MRI of rheumatoid arthritis image quantitation for the assessment of disease activity, progression and response to therapy. *Rheumatology* 2008; 47: 13–21.
- Stomp W, Krabben A, van der Heijde D, Huizinga TW, Bloem JL, van der Helm-van Mil AH *et al.*: Aiming for a shorter rheumatoid arthritis MRI protocol: can contrast-enhanced MRI replace T2 for the detection of bone marrow oedema? *Eur Radiol* 2014; 24: 2614–2622.
- Axelsen MB, Ejlertsen B, Hetland ML, Skjødt H, Majgaard O, Lauridsen UB *et al.*: Differentiation between early rheumatoid arthritis patients and healthy persons by conventional and dynamic contrast-enhanced magnetic resonance imaging. *Scand J Rheumatol* 2014; 43: 109–118.
- Østergaard M, Duer A, Møller U, Ejlertsen B: Magnetic resonance imaging of peripheral joints in rheumatic diseases. *Best Pract Res Clin Rheumatol* 2004; 18: 861–879.
- van Steenberg HW, van Nies JA, Huizinga TW, Bloem JL, Reijnen M, van der Helm-van Mil AH: Characterising arthralgia in the preclinical phase of rheumatoid arthritis using MRI. *Ann Rheum Dis* 2015; 74: 1225–1232.
- Krabben A, Stomp W, van Nies AB, Huizinga TWJ, van der Heijde D, Bloem JL *et al.*: MRI-detected subclinical joint inflammation is associated with radiographic progression. *Ann Rheum Dis* 2014; 73: 2034–2037.
- Kroft LJ, Reijnen M, Kloppenburg M, Verbist BM, Bloem JL, Buchtem MA: Rheumatoid arthritis: epidural enhancement as an underestimated cause of subaxial cervical spinal stenosis. *Radiology* 2004; 231: 57–63.
- Reijnen M, Dijkmans BA, Hansen B, Pope TL, Kroon HM, Holscher HC *et al.*: Neurologic dysfunction in patients with rheumatoid arthritis of the cervical spine. Predictive value of clinical, radiographic and MR imaging parameters. *Eur Radiol* 2001; 11: 467–473.

The spectrum of features seen on MRI and ultrasound corresponds well with histopathological stages of RA progression.

Ultrasound is a quick and inexpensive way to detect synovitis, tenosynovitis, tendon tears and bursitis. However, it is operator-dependent and also depends on the quality of a US machine. MRI allows a more global approach to all joints, both small and large, and the spine. It is more sensitive and more specific than ultrasound. However, stage 1–2 tendon tears are much better appreciated on ultrasound. Also, for maximal sensitivity, accurate scoring and sensitive evaluation of changes over time, T1w sequences with contrast injection are mandatory. Unenhanced MRI using STIR sequences is only moderately reliable for assessing synovitis and tenosynovitis. Contrast injection, field strength, and coil type influence MRI scan assessment, and should be considered before performing MRI in clinical trials and practice<sup>(4)</sup>.

## Conflict of interest

Authors do not report any financial or personal links with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

21. Reijnierse M, Breedveld FC, Kroom HM, Hansen B, Pope TL, Bloem JL: Are magnetic resonance flexion view useful in evaluating the cervical spine of patients with rheumatoid arthritis? *Skeletal Radiol* 2000; 29: 85–89.
22. McQueen FM: The MRI view of the synovitis and tenosynovitis in inflammatory arthritis: implications for diagnosis and management. *Ann NY Acad Sci* 2009; 1154: 21–34.
23. McGonagle D, Hermann KG, Tan AL: Differentiation between osteoarthritis and psoriatic arthritis: implications for pathogenesis and treatment in the biologic therapy era. *Rheumatology* 2015; 54: 29–38.
24. Stomp W, Krabben A, van der Heijde D, Huizinga TW, Bloem JL, van der Helm-van Mil AH *et al.*: Are rheumatoid arthritis patients discernible from other early arthritis patients using 1,5T extremity magnetic resonance imaging? A large cross-sectional study. *J Rheumatol* 2014; 41: 1630–1637.