

Low-field MRI *versus* ultrasound: which is more sensitive in detecting inflammation and bone damage in MCP and MTP joints in mild or moderate rheumatoid arthritis?

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Abstract

Objectives

The aim of the present paper is to determine if the ultrasound of hands and feet is comparable to the MRI of the dominant hand to detect erosive disease and inflammation in mild or moderate rheumatoid arthritis (RA).

Methods

Twenty-six patients (14 females; mean age, 48 years) with active mild or moderate RA (mean DAS28, 3.9; mean disease duration, 19 months) were examined clinically, by ultrasound and by gadolinium-enhanced low-field MRI at baseline, after 6 and 12 months (78 examinations). Radiographs from hands and forefeet were taken at baseline and after 12 months. MRI was performed at the clinically most active (dominant) hand or forefoot evaluating the MCP 1-5 or MTP 1-5 joints. Ultrasound examination additionally included all other 2nd, 5th MCP and 5th MTP joints.

Results

MRI and ultrasound detected erosive disease in 67 and 56 of 78 examinations, respectively ($p < 0.01$); radiography only in 8 of 52 examinations ($p < 0.001$). MRI and ultrasound were equally sensitive to detect synovitis (in 64 and 66 examinations). Synovial power Doppler signals were present in 38 ultrasound examinations. Bone marrow oedema was present in 37 MRI examinations. Ultrasound was more sensitive than MRI to detect tenosynovitis (in 30 vs. 15 examinations; $p = 0.001$).

Conclusion

MRI of the dominant hand and bilateral ultrasound of MCP and MTP joints are superior to x-ray to detect erosive disease in mild and moderate RA. MRI is slightly, but significantly more sensitive than ultrasound for erosive disease, while ultrasound is more sensitive to detect tenosynovitis. Ultrasound and MRI are comparably sensitive to detect synovitis.

Key words

ultrasonography, magnetic resonance imaging, radiography, rheumatoid arthritis

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Introduction

Rheumatologists are increasingly aware of early rheumatoid arthritis (RA). Even mild or moderate disease needs to be treated as early as possible. It is important to know if erosions have already developed to estimate the probability of disease progression and, therefore, to decide upon the best treatment for the individual patient who has early, mild or moderate RA. Conventional radiographs of hands and forefeet show erosions only after reasonable damage has occurred. Furthermore, x-ray provides little information on synovitis or tenosynovitis. It has been shown that magnetic resonance imaging (MRI) and musculoskeletal ultrasound are more sensitive than conventional radiography to detect erosions at MCP and MTP joints, due to their ability to provide tomographical information (1-6). Moreover, ultrasound and MRI detect synovitis and tenosynovitis more commonly than radiography and clinical examination (7).

MRI is more sensitive to detect erosions when compared with ultrasound because anatomy behind bones is not accessible by ultrasound (1, 4). Erosions localise more commonly at the radial or ulnar aspects than on the anterior and posterior sides of MCP and MTP joints (2). Therefore, ultrasound fails to delineate erosions particularly at the MCP 3 and 4 joints and at the MTP 2 to 4 joints. Hence, MRI might be more useful than ultrasound to search for erosions in early, radiographically non-erosive rheumatoid arthritis. However, MRI examination is usually restricted to one hand or to one foot. Particularly low-field MRI is time consuming. Ultrasound allows assessment of both hands and feet far more quickly. When comparing MRI with ultrasound for their ability to detect erosive disease in daily rheumatological practice, this may not be done on a single joint basis, but rather on a global basis to determine whether the modality detects erosive disease or not.

Therefore, this study differs from previous studies as it globally compares ultrasound with MRI for its ability to detect the presence of erosions of MCP and/or MTP joints, synovial swelling and tenosynovitis on a patient level. It compares two different approaches:

ultrasound of both hands and feet *versus* MRI of the dominant hand or foot to detect erosions, synovial thickening, synovitis, tenosynovitis and bone marrow oedema. Furthermore, it compares the presence of intra-articular vascularity (presence of power Doppler signals within the synovium) with the presence of bone marrow oedema. Both findings have been found to be independent predictors for the development of erosions in the course of the disease (8-15). The primary hypothesis of the study states that ultrasound of both hands and feet as described above is equally sensitive as MRI of the dominant hand or foot to detect erosive RA.

The secondary hypotheses are: a) ultrasound and MRI are equally sensitive in detecting synovitis/synovial thickening and tenosynovitis, b) ultrasound shows synovial vascularity in joints that display bone marrow oedema in MRI and *vice versa*, c) findings of ultrasound and MRI are sensitive to change after escalation of treatment in patients with active RA, d) inter-observer agreement is good for both imaging modalities, and e) ultrasound and MRI are more sensitive than conventional radiography to detect erosive RA.

Methods

The recruited patients had mild or moderate RA, fulfilling the American College of Rheumatology (ACR) classification criteria for RA (16). At study entrance they had active disease, and a new disease modifying anti-rheumatic drug (DMARD) or biologic was added to the existing treatment.

The patients were examined clinically, by ultrasound and by low-field MRI at baseline, after 6 months (± 2 months) and after 12 months (± 2 months). Radiographs from both hands and forefeet were taken in two planes at baseline and after 12 months (± 2 months).

The clinical examination included the 28-joint count Disease Activity Score (DAS 28) and history for medication at baseline and after 6 and 12 months.

IgM-rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) were calculated at baseline. Baseline and follow-up visits included evaluation for ESR and C-reactive protein (CRP).

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Competing interests: none declared.

Gadolinium-enhanced low-field MRI (0.2 Tesla; C-Scan, Esaote S.p.A, Genua, Italy) was performed at the dominant (clinically most active) hand or forefoot including either MCP joints 2–5 or MTP joints 1–5. It was repeated after 6 and 12 months at the same anatomical area. Images were evaluated and interpreted according to the RAMRIS score and the EULAR OMERACT RA MRI reference image atlas (17, 18). Dual array coils were used.

All MRI examinations included the following sequences:

- coronary Short Time Inversion Recovery (STIR) sequence; slice thickness, 3 mm; field of view, 120 mm x 120 mm;
- coronary T1 weighted turbo spin echo sequence; slice thickness, 2 mm; field of view, 120 mm x 120 mm;
- axial T1 weighted turbo spin echo sequence; slice thickness, 2 mm; field of view, 120 mm x 120 mm;
- high resolution three dimensional (3D) echo sequence with 1 mm slice thickness before application of contrast agent; field of view 120 mm x 120 mm; secondary reconstruction of the data in axial, coronary and sagittal planes;
- high resolution 3D gradient echo sequence with 1 mm slice thickness starting two minutes after intravenous injection of 0.2 ml/kg gadolinium; field of view 120 mm x 120 mm; secondary reconstruction of the data in axial, coronary and sagittal planes.

The RAMRIS score evaluates the following parameters with MRI (17): a) erosions (grades 0–10), b) synovitis (grades 0–3), c) tenosynovitis (present or absent), and d) bone marrow oedema (grades 0–3).

B-mode and power Doppler ultrasound were performed on the same day after the MRI examination using a linear probe (LA 523, 5–13 MHz, Esaote Technos MPX, Esaote S.p.A, Genua, Italy) at the same joints that had been examined by MRI. In addition, ultrasound examination always included the 2nd and 5th MCP joints and the 5th MTP joints of both hands and feet. All sonographically accessible regions of the joints were examined circumferentially

in longitudinal and transverse plains in neutral joint position. The following standard settings were used for the ultrasound examinations: Grey scale frequency, 13 MHz; focus point position, 5 mm; power Doppler frequency, 10 MHz; pulse repetition frequency (PRF), 750 Hz; power Doppler gain just below disappearance of artefacts (19–21).

The following parameters were assessed by ultrasound according to OMERACT definitions (22): a) erosions, b) synovial thickening, c) synovial perfusion measured by power Doppler, and d) tenosynovitis.

Erosions, synovial thickening and tenosynovitis were evaluated for presence or absence. Erosions were considered to be present if they had a diameter of ≥ 1 mm in each direction (longitudinal, transverse and depth) according to previous suggestions to define significant erosions for the presence of RA (23–26).

Conventional radiographs of the hands and feet were done in two planes (anterior – posterior and in 30° oblique position) and scored for the presence or absence of erosions.

MRI, ultrasound examiners and radiologists who read the radiographs were blinded for the other study results.

In order to obtain data for inter-observer variability, 11 ultrasound examinations were independently performed by two experienced ultrasonographers (M. Walther and W.A. Schmidt). In addition, 13 sets of MRI examinations were independently read by two rheumatologists experienced in MRI examinations of hands and feet (M. Walther and B. Ostendorf) and by one experienced radiologist (A. Scherer).

The study was approved by the ethical committee of the Heinrich-Heine Uni-

versity, Düsseldorf. The patients gave written informed consent before entering the study.

Statistical analysis was done with SPSS, Version 17 (Chicago, Illinois, USA). Statistical tests included the chi-square test and the calculation of kappa values. The Cohen's kappa coefficient (kappa value) describes the inter-rater agreement. It characterises values <0 as indicating no agreement, 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1 as almost perfect agreement (27).

Results

Twenty-six patients participated in the study; 14 were female. The mean age was 48 (21–73 years) years. The mean disease duration was 19 months (1–78 months). RF was positive in 46% and anti-CCP antibodies were positive in 42% of patients. All patients attended all visits. Table I shows the clinical data at baseline and at follow-up.

Eight patients were DMARD-naïve at study entrance; the other patients had at least one DMARD. One patient who was on DMARD monotherapy stopped methotrexate because of elevated liver enzymes 9 months after study entrance; therefore, he did not receive a DMARD at 12 months.

MRI was performed at 14 hands and at 12 forefeet. Table II shows the results of imaging with regard to the presence of erosions, synovitis, intra-articular vascularity, bone marrow oedema and tenosynovitis in at least one joint. Figure 1 provides representative examples of MRI and ultrasound findings. Conventional radiography detected erosions only in 4 patients both at baseline and at follow-up, whereas MRI and

Table I. Clinical data and medication at baseline (T0), after 6 $\pm$ 2 (T1) and 12 $\pm$ 2 (T2) months with standard deviations in brackets.

	T0	T1 (6 months)	T2 (12 months)
DAS 28	3.9 ($\pm$ 1.6)	3.2 ($\pm$ 1.1)	2.7 ($\pm$ 0.9)
ESR (mm/h)	22 ($\pm$ 21.5)	13 ($\pm$ 7.1)	11 ($\pm$ 6.1)
CRP (mg/l)	12.6 ($\pm$ 17.8)	7.6 ($\pm$ 11.6)	5.4 ($\pm$ 6.1)
Prednisolone (mg/d)	9 ($\pm$ 9.1)	4 ($\pm$ 3.9)	3 ($\pm$ 3.6)
DMARD mono	14	21	18
Biologic mono	0	0	0
DMARD combo	3	3	3
DMARD and biologic	1	2	4
No DMARD or biologic	8	0	1

ultrasound detected erosions in most patients. The number of patients with erosive disease found by MRI or ultrasound increased slightly but not significantly over time. There was a slight albeit not significant decrease of patients who had synovitis, tenosynovitis, bone marrow oedema or synovial perfusion at follow-up.

When comparing all 78 examinations as shown in Table III, significantly more MRI examinations than ultrasound examinations detected erosive disease in contrast to the primary hypothesis of this study. Ultrasound and MRI were both significantly more sensitive than conventional radiography to detect patients with erosive disease. Ultrasound was significantly more sensitive to detect tenosynovitis than MRI. Both ultrasound and MRI had a comparable sensitivity when examining for the presence of synovitis and when comparing the presence of colour Doppler signals with bone marrow oedema. The correlation between the presence of colour Doppler signals and bone marrow oedema seen by MRI was slight (κ , 0.37; agreement, 73%).

Joint level analysis showed that both ultrasound and MRI most commonly detected erosions at the MCP 2 ($n=18$, 31) and MTP 5 joints ($n=26$, 28) followed by the MCP 3 ($n=3$, 26), MTP 1 ($n=10$, 20) and MCP 5 joints ($n=5$, 14). In 6 patients, erosions were only detected by MRI, 2 with RAMRIS grade 1, 3 with RAMRIS grade 2 and 1 with RAMRIS grade 3 at an MCP 3 joint. In 2 patients, ultrasound detected erosions that were not seen by MRI at MTP 5 joints, 1 with ultrasound grade 1 and the other one with ultrasound grade 2. How does ultrasound compare with MRI, and how are the inter-observer agreements? Table IV provides the results. Inter-observer agreement was substantial or almost perfect both for ultrasound and for MRI, except for the evaluation of tenosynovitis by ultrasound.

Discussion

MRI and ultrasound are valuable diagnostic tools in early and mild or moderate RA particularly for two scenarios: firstly, when it appears clinically dif-

Table II. Patients with positive findings in at least one joint at baseline, after 6 and 12 months (26 patients examined).

	Ultrasound			MRI			x-ray	
	T0	T1	T2	T0	T1	T2	T0	T2
Erosions	17	19	20	23	23	24	4	4
Synovitis	22	21	21	26	22	18	NA	NA
Tenosynovitis	12	10	8	9	4	2	NA	NA
Doppler/bone-marrow oedema	14	14	10	15	9	13	NA	NA

NA: not applicable.

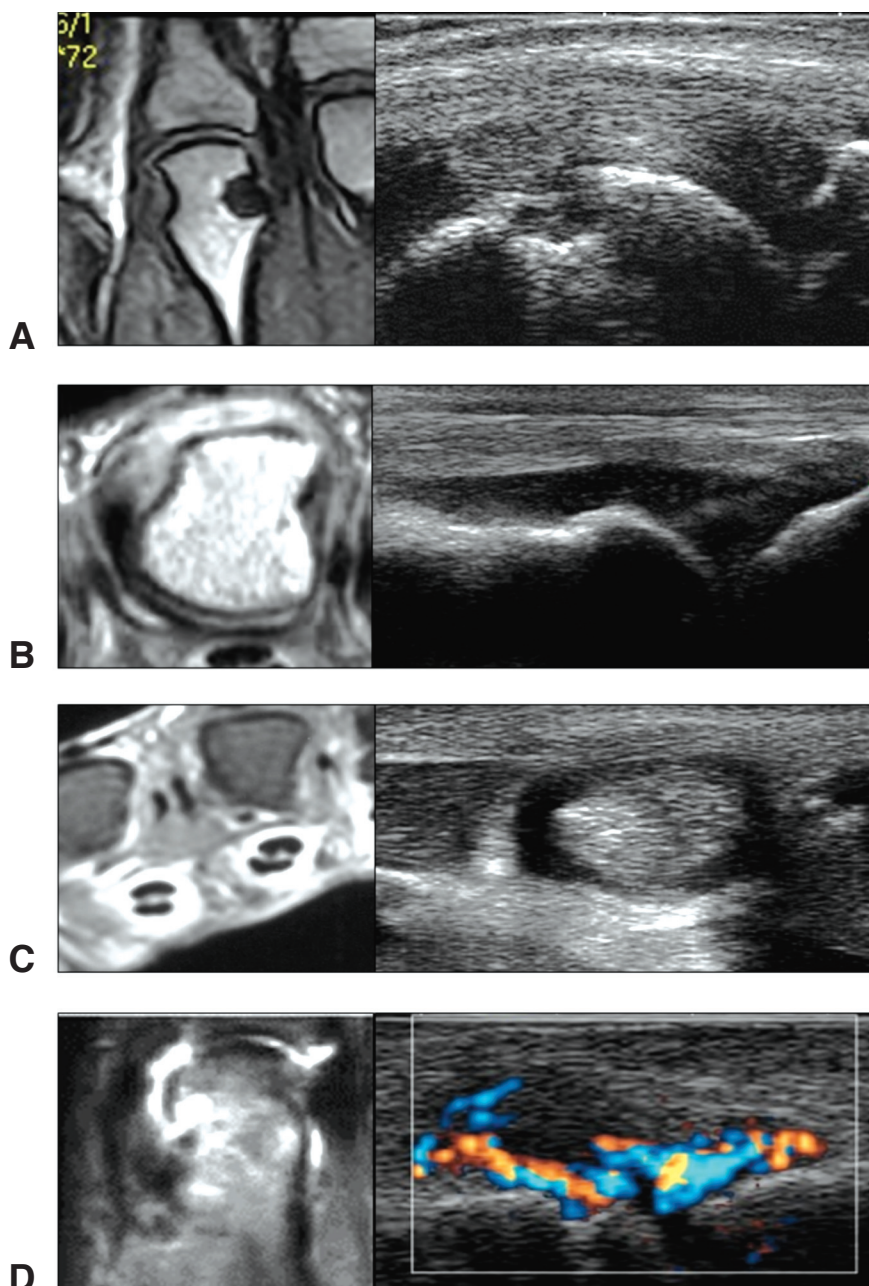


Fig. 1. MRI (left) and ultrasound findings (right) at the level of the MCP joints in RA: **A)** erosion (T1 weighted MRI sequence; grey scale ultrasound); **B)** synovitis (gadolinium enhanced T1 weighted MRI sequence; grey scale ultrasound); **C)** finger flexor tendon tenosynovitis (gadolinium enhanced T1 weighted MRI sequence; grey scale ultrasound); **D)** bone marrow oedema (STIR MRI sequence) and synovial hypervascularity (power Doppler ultrasound).

Table III. Abnormalities in at least one joint detected by ultrasound and MRI, respectively (78 examinations).

	Ultrasound+ MRI+	Ultrasound+ MRI-	Ultrasound- MRI+	Ultrasound- MRI-	Significance (<i>p</i> -value)
Erosions	49	7	21	1	<0.01
Synovitis	56	8	10	4	n.s.
Tenosynovitis	12	18	3	45	<0.01
Doppler/bone marrow oedema	23	15	14	26	n.s.

Table IV. Inter-observer agreements (kappa values).

	Ultrasound vs. ultrasound (single joints)	MRI vs. MRI (single joints)
Erosions	0.81	1.0
Synovitis	0.74	1.0
Tenosynovitis	0.38	0.79
Doppler / bone marrow oedema	0.79	0.68

difficult to decide whether arthritis or tenosynovitis are present or absent, and secondly, when it is important to decide if erosions have already developed despite negative findings on radiographs of hands and forefeet. Both the detection of inflammation and bone damage may lead to an escalation of immunosuppressive treatment, particularly as the presence of bone marrow oedema, the detection of synovial vascularity by power Doppler ultrasound and the presence of erosions have been shown to be strong predictors for further bone damage in RA (8-15). Therefore, we also compared the presence of power Doppler ultrasound signals with the presence of bone marrow oedema detected by MRI.

Since it does not make sense to use both ultrasound and MRI in this setting it is important to compare the value of both methods. In previous studies, this was done on a single joint basis. However, when to decide whether to intensify DMARD or biologic treatment it is important for the rheumatologist to know if inflammation or erosive disease is present or absent in the particular patient as a whole.

In clinical practice, MRI is only performed on a single hand or foot, whereas ultrasound can be performed at multiple anatomical regions in a much shorter time. The MRI equipment that is applied in this study is relatively widely used in rheumatological practice. The protocol described in

this study corresponds to OMERACT recommendations to perform MRI examinations in RA. However, using this technology and applying this protocol takes 45 minutes for an examination of one hand or forefoot. The examination of another hand or forefoot is not feasible in the same patient for clinical practice. Therefore, it is common to examine the clinically most affected joint.

Low-field MRI equipment is far cheaper than high-field MRI in terms of acquisition and maintenance. Patients can stay in a more comfortable position during image generation in low-field MRI. Low-field MRI of hands and feet has been shown to perform comparably well as high-field MRI in terms of sensitivity and specificity to detect synovitis and bone erosions in rheumatoid arthritis (5, 28). Low-field MRI is less sensitive than high-field MRI to delineate bone marrow oedema (5). It needs a longer time for image acquisition and has a rather small field of view, which makes it impossible to depict the whole hand including wrist and all finger joints in one examination.

Ultrasound may be performed at multiple joints in which clinical findings are ambiguous. In order to detect erosions ultrasound has been found to be particularly useful at the 2nd and 5th MCP and 5th MTP joints, where no other bones obstruct the view on a larger bony surface (2-4, 26, 27). "Whole body" ultrasound scores with up to 78 examined joints (7) are interesting but not fea-

sible in daily clinical practice. When concentrating on the most important joints ultrasound has the advantage of being cheaper. Furthermore, ultrasound is more commonly available in rheumatological practice than MRI. On the other hand, it is less sensitive, particularly when being compared with MRI on a single joint basis, and concern has been expressed about its dependency on the examiner.

In this study, both MRI and ultrasound examination for erosive disease involved the MTP 1 joints in cases with dominant foot involvement. Inclusion of MTP 1 joints in search for erosions was previously suggested (29). Erosions at MTP 1 joints may frequently occur in other diseases like hallux valgus, osteoarthritis or gout. However, only 2 out of 78 MRI examinations and none out of 78 ultrasound examinations detected erosions exclusively at the MTP 1 joints.

Ultrasound detected tenosynovitis more commonly than MRI in this study. Low-field MRI has been shown to be inferior to high-field MRI in detecting tenosynovitis (28). However, the ultrasound finding of tenosynovitis had only a fair inter-observer agreement with different results in 4 out of 11 patients. Inter-rater agreements for other findings were substantial, to almost being perfect both for ultrasound and MRI in this study.

MRI detected more erosions than ultrasound. However, this study has not investigated if all erosions shown by MRI are true erosions with regard to the diagnosis of RA. Inter-reader agreements were higher for MRI than for ultrasound. However, testing for agreements included both image acquisition and interpretation for ultrasound, but only image interpretation for MRI. We choose to perform MRI at the dominant hand or foot. MRI of the feet has a high diagnostic value in early RA, particularly if imaging of the metacarpophalangeal joints of the hands remains normal (29). Previously suggested ultrasound scores involve both MCP and MTP joints (26).

All patients received additional DMARDs or biologic treatment at baseline. Clinical parameters such as

DAS28, CRP and ESR significantly improved, and the corticosteroid dose could be reduced. However, the number of patients who had synovitis, tenosynovitis, synovial hyperperfusion or bone marrow oedema has not significantly changed both at 6 and 12 months. This contradiction can be explained by the study design. The study investigates the presence or absence of such abnormalities on a patient level. Using scores such as the US-7 score or the OMERACT score, both ultrasound and MRI showed sensitivity to change with treatment (24, 30).

We conclude that both ultrasound and low-field MRI are valuable diagnostic tools to detect erosive disease in early and mild to moderate RA in radiographically negative cases. MRI is slightly but significantly more sensitive to detect erosions than ultrasound. Both imaging modalities show synovitis and tenosynovitis comparably well. In clinical practice either ultrasound or MRI may be performed in early and mild or moderate RA when it is important to decide if the patient has inflammation or erosive disease.

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