Magnetic Resonance Imaging: a Valuable Method for the Detection of Synovial Inflammation in Rheumatoid Arthritis

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ABSTRACT. ***Objective***. Clinical assessment of rheumatoid arthritis (RA) based on pain and swelling and physical examination is limited by observer error and interpretation. We compared magnetic resonance imaging (MRI) and clinical examination to detect synovitis in RA.

Methods. Twelve patients with active RA were assessed according to Ritchie index, swollen joint count and score, swollen joint count of hands and wrists [2 wrists, 10 metacarpophalangeal (MCP), 10 proximal interphalangeal (PIP)], morning stiffness, pain intensity, Disease Activity Score (DAS), erythrocyte sedimentation rate, and C-reactive protein. MR images of hands and wrists were obtained with an adapted device, on T1 weighted (T1W) spin echo (SE) coronal images before and after gadolinium DTPA, T1W SE axial images with gadolinium DTPA, T2* gradient echo recall coronal and axial sequences, and assessed by 2 radiologists (0 = no synovitis, 1 = synovitis).

Results. The swollen joint count on hands and wrists was 59 on clinical examination (mean 5.08 ± 3.15 per patient; 20/24 wrists, 7/120 MCP, 32/120 PIP) and 162 on MRI (mean 13.50 ± 5.65; 22/24 wrists, 70/120 MCP, 70/120 PIP). Statistically significant correlations were found between MRI synovitis count and swollen joint count ($p = 0.015$) and score ($p = 0.019$), Ritchie Index ($p = 0.035$), DAS ($p = 0.02$) and morning stiffness ($p = 0.07$). MRI revealed synovitis significantly more often than clinical examination (162 vs 59; $p = 0.00002$) [2-fold in PIP (70/32) and 10-fold in MCP (70/7)]. Clinical examination and MRI were concordant for 157/264 joints (59.5%). The association of normal MRI with synovitis on clinical examination was observed in 2 cases, the opposite in 105.

Conclusion. MRI is more sensitive than clinical examination to detect synovitis of hands and wrists in RA, especially for MCP and PIP joints, and is valuable for assessment of inflammation in hands and wrists in RA. (J Rheumatol 2001;28:35–40)

Key Indexing Terms:
RHEUMATOID ARTHRITIS MAGNETIC RESONANCE IMAGING SYNOVITIS

Studies of the natural history of rheumatoid arthritis (RA) and assessment of treatment modalities in the early stages of RA have been hampered by the lack of objective criteria to determine outcome and response to therapy. Outcome evaluation in most major therapeutic trials in RA has depended on measurement of a combination of subjective, semiobjective, and objective variables, including physician and patient overall assessment, joint count and index, laboratory data, and radiographic findings. Despite attempts to correlate such information with disease activity or endpoint, this approach has been fraught with problems of observer error and interpretation. The clinical assessment of RA based on evaluation of pain and swelling experienced by the patient and physical examination of the joints has considerable inter- and intraobserver variability[1]. Standard radiographs taken in the early stages of disease are seldom specific, and bone damage is detected only when disease is relatively advanced[2-4] and the clinical pertinence of biological data is disputed[5]. An objective, noninvasive, reproducible, quantitative method to evaluate arthritis activity in RA would be valuable in patient management and in assessment of therapeutic effects.

The excellent soft tissue contrast of magnetic resonance imaging (MRI) makes it a valuable technique to detect changes of RA in joints, especially synovitis, which represents the beginning of irreparable joint destruction[6-16]. MRI allows direct visualization of rheumatoid synovium after intravenous (iv) administration of gadolinium-diethylene-triamine pentaacetic acid (Gd-DTPA), for reliable differentiation between synovial inflammation and effusion[12,14,17,18] and has been proposed for evaluating synovitis[12,15,17,19]. The inter- and intraobserver variability of MRI has been shown to be very low[20].

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We compare MRI and clinical examination to detect synovitis of hands and wrists in RA.

MATERIALS AND METHODS

Patients. This study included patients who fulfilled the 1987 American Rheumatism Association criteria[21] for RA and gave informed consent to participate. The protocol was approved by the Committee of Medical Ethics, Tours University Hospital.

Inclusion criteria comprised age between 18 and 70 years; active disease defined by at least 3 criteria of: ≥ 3 swollen joints, ≥ 6 tender joints, duration of morning stiffness > 45 min, erythrocyte sedimentation rate (ESR) ≥ 28 mm/h, and functional capacity class I to III according to Steinbrocker[22].

Exclusion criteria were: contraindication for MRI [pacemaker, ferromagnetic vascular clip, metallic cardiac valve, cochlear prosthesis, any badly placed metallic foreign agent (intraocular, in contact with vessels, in hand or wrist ...), claustrophobia or conditions impeding the interpretation of MRI (wrist or hand prosthesis)]; and radiation synovectomy of wrist or phalangeal joint in the previous 4 weeks and iv administration of glucocorticosteroids in the previous 3 months.

Methods. All evaluations were performed on the same day for each patient.

Clinical evaluation. Each patient was assessed for age, sex, disease duration, concomitant medication, Ritchie articular index[23], tender joint count, swollen joint count and score (0: none, 1: minor, 2: moderate, 3: marked), swollen joint count of hands and wrists [22 joints per patient (2 wrists, 10 metacarpophalageal, MCP, 10 proximal interphalangeal, PIP; total in 12 patients: 264 joints], mean duration of morning stiffness, global pain intensity self-assessment during the previous week on 100 mm visual analog scale, and Disease Activity Score (DAS) (Ritchie index for function, swollen joint count, and ESR)[24] by an experienced physician.

Laboratory measurements. ESR was determined by the Westergren method (mm/h), C-reactive protein by nephelometry (normal < 8 mg/l), and rheumatoid factor (RF).

Magnetic resonance imaging. The same protocol was followed by an MRI specialist assisted by a radiologist for all patients. MRI was performed on hands and wrists only. All MR images were obtained on a 1 Tesla superconducting magnet system (Magneton SP, Siemens, Erlangen, Germany), using a 20 cm diameter supple surface coil and a 256 × 230 matrix. The following 5 sequences were performed on each side for each patient: (1) one T1 weighted (T1W) spin echo (SE) coronal image, field of view (FOV) 22 cm, contiguous 4 mm slice thickness, repetition time TR = 500 ms, echo time TE = 20 ms, acquisition time = 1 min 58 s; (2) the T1W sequence was also performed immediately after gadolinium DTPA injection; (3) one T1W SE axial image, FOV 18 cm, 6 mm slice thickness, TR = 500 ms, TE = 20 ms, acquisition time = 1 min 58 s with gadolinium DTPA injection; (4) T2* gradient echo recall coronal and (5) axial sequences, FOV 18 cm, 6 mm slice thickness, TR = 420 ms, TE = 18 ms. The patient was supine with the hand always placed in the same position on a piece of wood with the surface coil wound round the hand.

The sequences were performed first on the right side and then on the left side. Two experienced radiologists blind to the clinical pattern independently reviewed each case; each joint (2 wrists, 10 MCP and 10 PIP) was scored on a 0–1 scale (0 = absence of synovitis, 1 = synovitis) providing an MRI synovitis count (0 to 22) (discordance between the 2 radiologists necessitating a further reading together). Inflammation proliferation was characterized by low-to-intermediate signal intensity on T1W images, high signal intensity on T2W images, and marked signal intensity enhancement on post-contrast T1W images.

Statistical analysis. Three tests were performed systematically to compare clinical examination and MRI: Shapiro-Wilk test to verify data normality and Student and Wilcoxon tests. Student test was used when data had a normal distribution, otherwise the Wilcoxon test was used. Statistical significance was fixed at $p < 0.05$. To analyze correlations between MRI data and disease activity variables, Shapiro-Wilk test was performed upon each variable to verify data normality. When there was normality, Pearson correlation coefficient was calculated; otherwise the Spearman correlation coefficient was retained. Statistical significance was set at $p < 0.05$. Analysis of concordance between MRI and clinical examination was performed using the efficiency coefficient, corresponding to the observed concordance; the kappa coefficient corresponding to the real concordance was then used (eliminating the random concordance)[25]. The interpretation of the real concordance, expressed by the kappa coefficient, is as follows: $k < 0$, poor; $0 < k < 0.20$, insignificant; $0.21 < k < 0.40$, weak; $0.41 < k < 0.60$, fair; $0.61 < k < 0.80$, good; $0.81 < k < 1$, excellent.

RESULTS

Twelve patients (8 female, 4 male) with a mean age of 53 years (range 41–65) were studied, and mean disease duration was 5.2 years (range 1–11). Therapeutic regimens included nonsteroidal antiinflammatory drugs (NSAID) in 10 patients, corticosteroids in 8 (mean dosage 9.2 mg/day, range 5–13), and disease modifying antirheumatic drugs (DMARD) in all patients (sulfasalazine, 6; methotrexate, 5; gold salts, 1). All but one had class II functional capacity according to Steinbrocker.

The mean value for the Ritchie index was 9.83 ± 3.97 (range 6–19), the mean value for the tender joint count was 16.42 ± 9.16 (range 6–35), the mean values for swollen joint count and score were 6.25 ± 2.80 (range 3–11) and 6.67 ± 3.65 (range 3–15), and the mean value for the swollen joint count in hands and wrists was 5.08 ± 3.15 (range 1–11). The synovitis count in hands and wrists on clinical examination was 59 (20/24 wrists, 7/120 MCP, 32/120 PIP) (Tables 1 and 2). The mean overall pain intensity self-assessment during the previous week on 100 mm VAS was 39.2 mm (range 29–75), mean duration of morning stiffness was 62 min (range 45–120), mean DAS was 3.10 ± 0.63 (range 2.1–4.3), mean ESR 21.4 mm (range 1–63), and mean CRP 23.7 mg/l (range 2–80). RF was present in 6 patients. The mean synovitis count on MRI of hands and wrists was 13.50 ± 5.65 (range 3–21) and the number of joints with synovitis was 162/264 (22/24 wrists, 70/120 MCP, 70/120 PIP) (Tables 1 and 2).

Table 1. Number of joints with synovitis detected by clinical examination and magnetic resonance imaging (MRI) in hands and wrists in 12 patients with RA (22 joints per patient, total of 264 joints).

Patient	Clinical Examination	MRI
1	11	19
2	8	21
3	8	17
4	5	19
5	2	7
6	8	17
7	4	13
8	6	10
9	1	3
10	2	7
11	2	15
12	2	14
Total	59	162

Table 2. Number of joints with synovitis detected by clinical examination and magnetic resonance imaging (MRI) in hands and wrists of 12 patients with RA (2 wrists, 10 MCP, and 10 PIP per patient, total of 264 joints).

	Clinical Examination	MRI
Wrists (0–24)	20	22
MCP (0–120)	7	70
PIP (0–120)	32	70
Total (0–264)	59 (22%)	162 (61%)

Statistically significant correlations were found between MRI synovitis count and swollen joint count ($p = 0.015$; $\rho = 0.73$) and score ($p = 0.019$; $\rho = 0.71$), Ritchie index ($p = 0.035$; $\rho = 0.64$), DAS ($p = 0.02$; $\rho = 0.68$) and duration of morning stiffness ($p = 0.07$; $\rho = 0.55$) but not with the tender joint count, VAS pain, ESR, or CRP.

MRI revealed significantly more synovitis in hands and wrists (Figures 1 and 2) than clinical examination [162 joints (61%) vs 59 joints (22%); $p = 0.00002$]. More joints with synovitis were detected by MRI than by clinical examination in 12/12 patients (Table 1). The interpretation of the 2 radiologists was discordant in 24/264 (9%) joints and concordance was obtained after second reading. The performance of MRI and clinical examination for the wrists was similar (22/20). MRI detected twice as many joints with synovitis in PIP (70/32) (Figure 3) and 10 times as many (70/7) in MCP (Figure 4) (Table 2). Clinical examination and MRI were concordant for 157 of 264 joints, discordant for 107 (Table 3). The finding of "normal MRI with synovitis on clinical examination" was observed in only 2 cases (1 wrist, 1 PIP), versus positive findings in 105 cases (3 wrists, 63 MCP, 39 PIP). The concordance observed was 0.83 for wrists, 0.67 for PIP, and 0.48 for MCP. However, use of the kappa coefficient (real

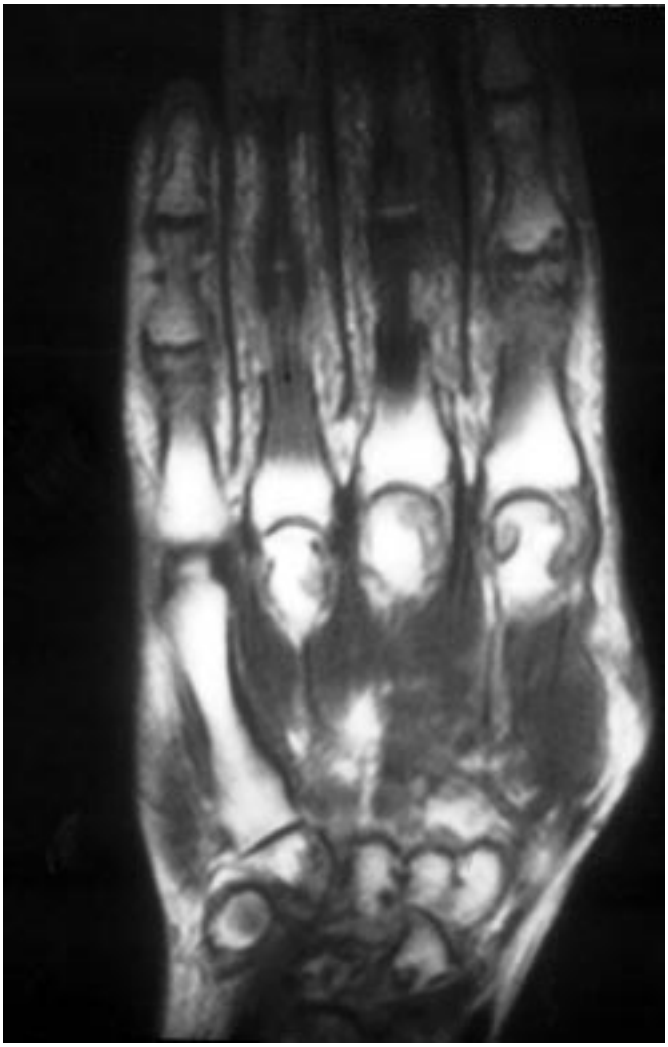

Figure 1. MRI T1 weighted spin echo coronal image (field of view 22 cm, contiguous 4 mm slice thickness, repetition time 500 ms, echo time 20 ms, acquisition time 1 min 58 s) after gadolinium DTPA injection: synovitis of the wrist, MCP 2–4, and PIP 2.

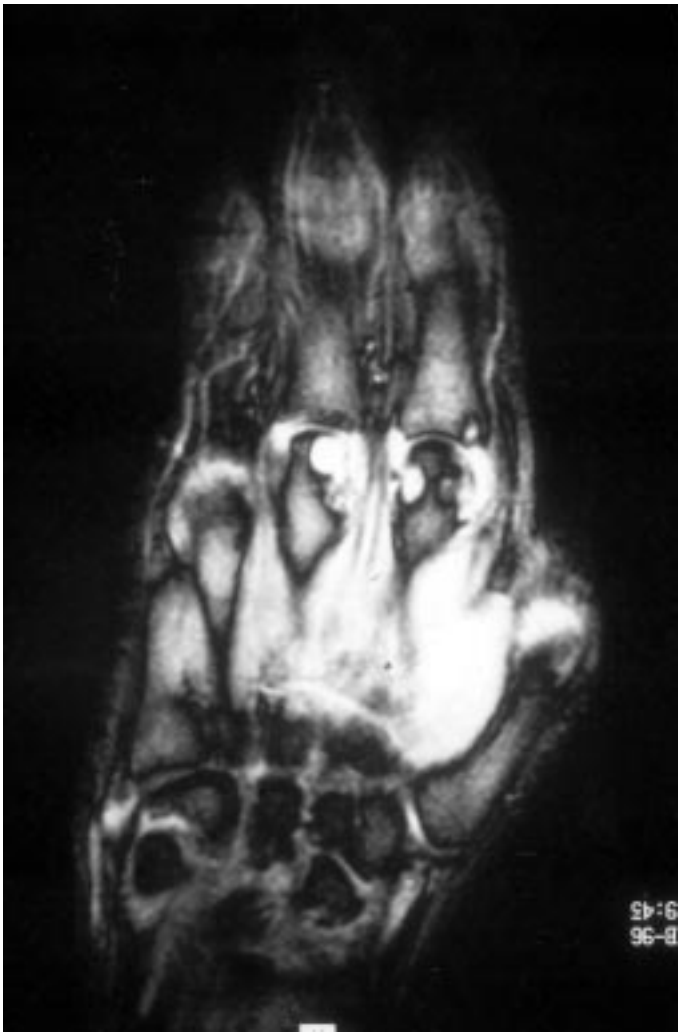

Figure 2. MRI T2* gradient echo recall coronal sequence (field of view of 18 cm, 6 mm slice thickness, repetition time = 420 ms, echo time = 18 ms): synovitis of the wrist, MCP 1-4, PIP 2, 3, and flexor tendons.

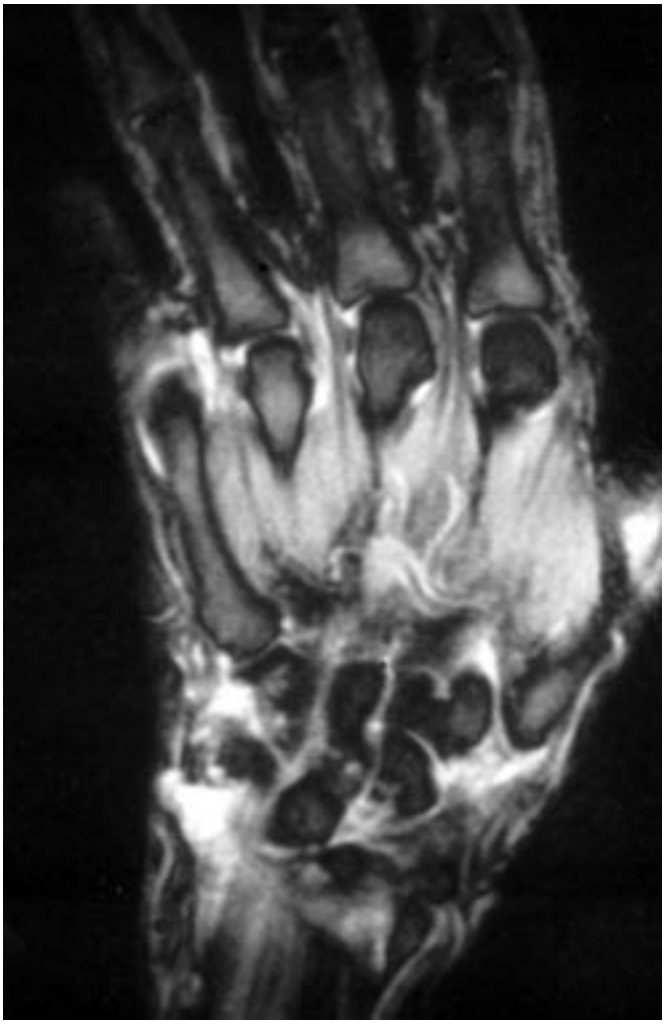

Figure 3. MRI T2* gradient echo recall coronal sequence (field of view 18 cm, 6 mm slice thickness, repetition time 420 ms, echo time 18 ms): synovitis of the wrist and MCP 2–5.

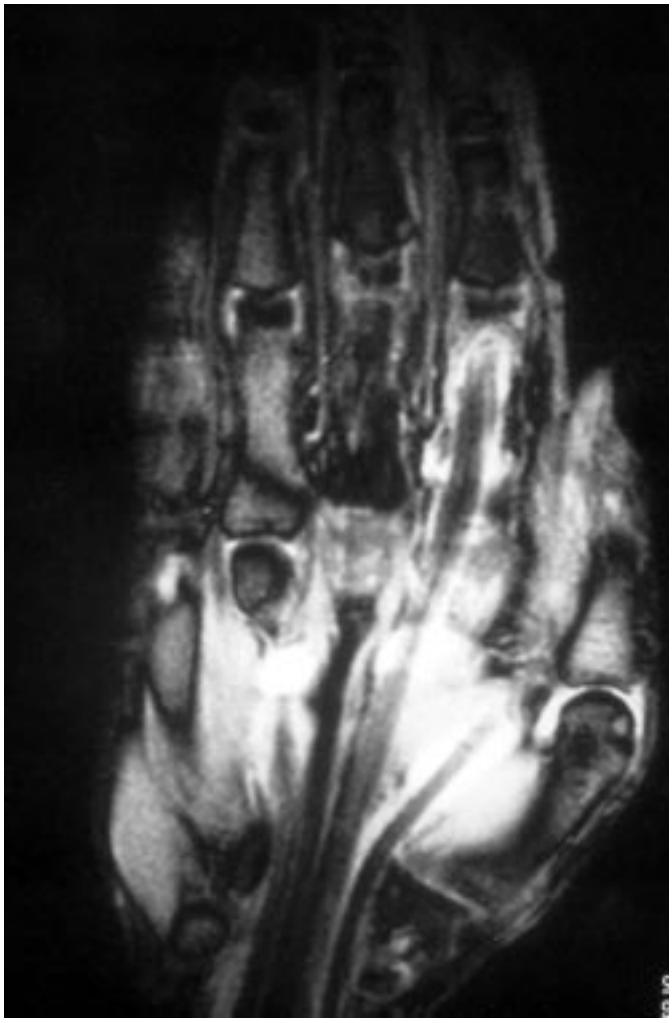

Figure 4. MRI T2* gradient echo recall coronal sequence (field of view 18 cm, 6 mm slice thickness, repetition time 420 ms, echo time 18 ms): synovitis of MCP 1,4, 5, PIP 1–4, and flexor tendons.

Table 3. Concordance between clinical examination (CE) and magnetic resonance imaging (MRI) for the detection of synovitis of wrists and hands in 12 patients with RA.

	Concordance MRI+/CE+	Concordance MRI–/CE–	Discordance MRI+/CE–	Discordance MRI–/CE+	Efficiency Coefficient Observed Concordance	Kappa Coefficient Real Concordance
Wrists (24)	19	1	3	1	0.83	0.25
MCP (120)	7	50	63	0	0.48	0.08
PIP (120)	31	49	39	1	0.67	0.38
Total (264)	57	100	105	2	0.59	0.28

concordance) showed k = 0.25 for wrists, k = 0.38 for PIP, and k = 0.08 for MCP. The overall concordance between the 2 methods was weak (kappa coefficient = 0.28).

DISCUSSION

In this study, MRI was a more sensitive method than clinical examination for the detection of synovitis of hands and wrists

in RA, especially for MCP and PIP joints. This method, performed with a special device to allow satisfactory comfort for these disabled patients, may be useful to assess inflammation in hands and wrists during RA.

RA was not very active in this group of patients [relatively low swollen joint count (6.25 ± 2.80; total of 59/264 joints, 22%) and score (6.67 ± 3.65), mean DAS of 3.1 ± 0.63, and moderate level of inflammation (ESR 21.4 mm; CRP 23.7 mg/l)] and was predominant in the hands and wrists. However, all patients had active RA according to our inclusion criteria and were being treated with DMARD, corticosteroids, and NSAID. Statistically significant correlations were found between MRI synovitis count and swollen joint count and score, Ritchie index, DAS, duration of morning stiffness, all classical criteria of RA assessment. However, the correlation between MRI count and swollen joint count and score or DAS may be due to predominance of synovitis in the hands and wrists in these patients. Such a correlation was not observed in other studies[7,8,10,11,20]. Corvetta, *et al* found no correlation between MRI score and disease duration, morning stiffness, swollen joint count, ESR, and CRP[7]. Gaffney, *et al* failed to show a relationship between the quantitative assessment of synovial inflammation on MRI and Ritchie index, swollen joint count, overall pain intensity, morning stiffness, ESR, and CRP[8].

Most other studies have assessed MRI for early detection of inflammation and ability to quantify synovial inflammation, or compared its performance with standard radiography. Few studies have compared MRI and clinical examination for detection of synovitis[10,12].

Several studies have suggested that MRI allows early detection of erosions (before standard radiographs) and synovial inflammation in RA[2,3,7,9,11,14,26,27]. Synovial membrane uptake of Gd-DTPA (enhancement) is dependent on tissue perfusion and microvascular permeability, and manifests as increased signal intensity (brightness) on T1 weighted images[4-11,20]. Therefore, since both increased tissue perfusion and microvascular permeability are cardinal features of all acute inflammatory processes, quantification of the rate of synovial membrane enhancement may provide a reliable indirect assessment of acute synovial inflammation. The actively inflamed synovium and pannus are hypervascular, explaining accumulation of iv administered Gd-DTPA in the extracellular space[7,8,10], thus distinguishing it from joint effusion[17–19,28–35]. Several studies quantified synovial inflammation with MRI[8,12,15,20,32,36]. Measurement of the thickness of inflamed synovium is a quantifiable variable; the use of volume determination of synovial proliferation as well as qualitative evaluation of the degree of inflammation using dynamic imaging should improve the effectiveness of MRI in the assessment of joint inflammation and its response to therapy.

Only 2 studies assessed the prognostic value of contrast enhanced Gd-DTPA MRI to evaluate the development of erosive bone changes in RA[37,38], and showed that progression of bone-destructive changes can be expected in joints in which inflammatory active pannus is shown. Other studies have shown that MRI has value in the assessment of the response to local treatment[20,32,33].

In our study, more joints with synovitis were detected by MRI than by clinical examination (162/59) in all patients, especially for PIP and MCP. This could be explained by the difficulties of detecting synovitis of MCP by clinical examination, as has been shown for dorsal and flexor tenosynovitis[38], suggesting that mild involvement of any compartment may not cause clinically detectable swelling, although involvement can be detected by MRI. The concordance between MRI and clinical examination was weak; of the 107 discordant cases, the great majority showed a finding of "synovitis on MRI-normal clinical examination," which is unlikely to be a false positive. The best proxy for the real value of MRI would be to follow patients over time with both clinical examination and repeat MRI. Indeed, for ethical reasons, we did not perform synovial biopsy in this study, but significant correlations have been shown between MRI and histological data[8,12, 15]. A limitation of our study is that we did not study a control group with the same technique. Thus, we cannot affirm that the joints scored as positive on MRI are not due to an artifact (false positive), but the specificity of MRI for the detection of synovitis has been shown in many studies performed in the hands from normal subjects and patients with osteoarthritis[6,11-13,16,26,31,39].

In this study, we used a simple, reproducible, low cost device allowing satisfactory comfort for these disabled patients, immobilization of the hands, and images of good quality [the classical position (prone with arms in anterior elevation of 180˚ above the head) for MRI of hands and wrists is very uncomfortable]. We assessed MRI for the detection of synovial inflammation of hands and wrists in RA. Therefore, the only question asked of the radiologists for each of 264 joints was whether synovitis was present or absent, and we did not study the erosions and tendon sheaths. Because of the necessity to obtain a view of PIP, MCP, and wrists on the same image, we used a relatively large surface coil. It might be useful to use smaller coils allowing more precise analysis. Newly available specialized coils for hand and wrist imaging or dedicated small-body-part imagers and reduced scan time with faster imaging techniques will improve patient comfort, the quality of the examination, and the cost/benefit ratio. However, the cost of this technique remains high in France (about 400 US dollars) and limits its use in practice.

We found MRI is a more sensitive method than clinical examination to detect synovitis of hands and wrists in RA, especially for MCP and PIP joints. MRI could be performed in these disabled patients with a special device allowing satisfactory comfort.

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