Bone Marrow Edema Is the Most Specific Finding for Rheumatoid Arthritis (RA) on Noncontrast Magnetic Resonance Imaging of the Hands and Wrists: A Comparison of Patients with RA and Healthy Controls

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ABSTRACT. ***Objective.*** To evaluate the sensitivity and specificity of magnetic resonance imaging (MRI) in detecting erosions, bone edema, and synovitis in the metacarpophalangeal and wrist joints for rheumatoid arthritis (RA).

Methods. MRI scans of bilateral hands and wrists of 40 healthy subjects and 40 RA patients were performed using 0.2 T extremity-MRI and read blindly using a modified RA MRI (RAMRIS) system (no contrast injection, imaging in 1 plane only). To determine interreader reliability, images of 10 randomly selected subjects were read independently by a musculoskeletal radiologist.

Results. A total of 3360 bones were evaluated. Patients with RA had significantly more erosions as well as higher scores for bone edema and synovitis than healthy subjects. Age had a significant effect on the number of erosions in both groups. However, when disease duration was factored in, age became insignificant in RA patients. Erosion number correlated with positive rheumatoid factor and higher C-reactive protein values. The intraclass correlation coefficient between the 2 readers was 0.76 for individual joints and 0.88 for total scores. When having a single erosion was used as a positive test for RA, the sensitivity of this test was 90%, but the specificity was only 35%. Presence of bone edema provided 65% sensitivity and 82.5% specificity. Eliminating the lunate from scoring for bone edema increased the specificity to 87.5% while decreasing the sensitivity to 62.5%.

Conclusion. While MRI is a highly sensitive tool for identifying and tracking the progression of erosions, erosions detected by MRI with measures commonly used in a rheumatologist's office (no contrast, imaging in 1 plane) provide low specificity for RA. Bone marrow edema is the most specific MRI lesion for RA in this setting. (J Rheumatol Dec 1 2009; doi:10.3899/jrheum.090062)

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Radiography is a standard imaging technique for assessing destructive joint lesions in rheumatoid arthritis (RA)[1]. It is one of the few objective criteria used for diagnosis of this disease as part of the American College of Rheumatology (ACR) 1987 revised criteria for the classification of RA[2]. Magnetic resonance imaging (MRI) is known to be considerably more sensitive than conventional radiography and clinical examination for the detection of RA joint pathology such as bone erosions, osteitis, or synovitis[3,4]. However, the specificity of MRI findings for the diagnosis of RA has not been well established. The majority of studies assessing the sensitivity of MRI changes in RA patients have failed to include a healthy control population[3-5]. Sensitive techniques can visualize subtle changes of unclear significance, so the possibility of false-positive results due to the potential low specificity of MRI findings should be considered.

There are few published studies assessing bony lesions or synovitis-like changes in healthy subjects. Ejbjerg, *et al* reviewed the literature in 2004 and found 14 publications[6-20]. The authors found that changes resembling mild synovitis and small bone erosions are occasionally found in the metacarpophalangeal (MCP) and wrist joints of healthy subjects when standard MRI sequences are used[6]. Since then, 3 additional articles have been published evaluating the signs of arthritis on MRI in healthy subjects[21-23].

The subject numbers in the previous studies were relatively small and the readers evaluating images were usually not blinded to the subjects' diagnosis, with the exception of only 3 reports[14,21,23]. Also, the majority of the studies were performed using T1-weighted sequences with thick slices

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(3–3.5 mm). The exceptions were Ejbjerg, *et al* who used a T1-weighted 3-dimensional (3-D) gradient-echo sequence with a slice thickness of 1 mm, and Dohn, *et al*, who used a T1-weighted 3-D fast-field echo with slices only 0.4 mm thick[21,23].

An international Outcome Measures in Rheumatology Clinical Trials (OMERACT) MRI working group has developed an RA MRI scoring system (RAMRIS) and published an atlas with recommendations on how to score MR images of patients with RA[24,25]. RAMRIS includes a semiquantitative score for bone erosions, bone edema, and synovitis and has been validated in a multireader, longitudinal setting[24-26].

We assessed the presence of changes resembling bone erosions, osteitis, and synovitis in the MCP and wrist joints of healthy subjects on MRI evaluated using the RAMRIS system and compared them with patients with RA. We also reviewed the practical usefulness of MRI in establishing a positive RA diagnosis by calculating the sensitivities and specificities of these changes in groups of patients with known diagnoses (RA vs healthy controls), although a true diagnostic value should be tested in patients with undifferentiated arthritis. Lastly, interreader reliability for MRI scoring was assessed.

MATERIALS AND METHODS

Subjects. Local institutional review board approval was obtained. Patients were recruited consecutively from the Oklahoma Rheumatoid Arthritis Cohort, which is an observational, prospective, cohort study of patients with RA. All patients had to fulfill the revised ACR criteria for RA[2]. Healthy subjects were employees of the Oklahoma Medical Research Foundation. They had no evidence of clinical inflammatory arthritis, including history of morning stiffness or joint swelling.

Clinical assessment. On the day of MRI examination, clinical and laboratory data were collected from patients with RA and healthy controls and included date of birth, sex, disease duration from the diagnosis (patients with RA only), IgM rheumatoid factor (RF) (assessed by ELISA), anti-cyclic citrullinated peptide (anti-CCP), erythrocyte sedimentation rate (ESR), and serum C-reactive protein (CRP). All the laboratory tests were performed and analyzed at the Diagnostic Laboratory of Oklahoma.

Imaging. All the subjects had MRI performed of the wrists and the second through the fifth MCP joints. A 0.2 Tesla dedicated-extremity MRI unit (C-Scan, Esaote, Italy) equipped with a dual phased array wrist coil was used. All MRI examinations (wrists and MCP joints) were carried out in the coronal plane using T1-weighted 3-D gradient echo and short-tau inversion recovery (STIR) sequences with no intravenous contrast. The Coronal Turbo 3D-T1 scanning measures were (1) repetition time (TR) = 50 ms, echo time (TE) = 16 ms, flip angle = 65°; (2) NEX = 1; (3) field of view (FOV) = 160 mm × 160 mm; (4) matrix = 256 freq, 192 phase (100% phase and slice FOV); (5) slice thickness = 0.6–0.9 mm, interslice gap = 0 mm. The Coronal STIR measures were (1) TR = 1780 ms, TE = 24 ms, TI = 80 ms; (2) NEX = 2; (3) FOV = 160 mm × 160 mm; (4) matrix = 192 freq, 160 phase (100% phase FOV); (5) slice thickness = 3 mm, gap = 0.2 mm.

The total examination time, including subject setup, positioning of coil, prescanning, and imaging, was approximately 80 min (60 min image acquisition time).

MRI evaluation. MR images were evaluated for bone erosions, bone edema, and synovitis by the same observer, using a modified OMERACT MRI scoring system (RAMRIS) with no contrast injection and imaging in 1 plane only[24,25]. In order to determine the interreader reliability for MRI scores, images of 10 randomly chosen subjects (6 patients with RA and 4 healthy controls) were read independently by another observer in the same manner. Both assessors were blinded to the subjects' diagnosis.

Modified RAMRIS definitions of joint pathologies and scoring. MRI bone erosion is a sharply marginated bone lesion, with correct juxtaarticular localization, typical signal characteristics, and a cortical break. Since the images were done in only 1 (coronal) plane, the erosion-like lesions were required to be visible in at least 2 adjacent slices. Bone erosions were scored on a scale of 0–10, based on the proportion of eroded bone compared with the assessed bone volume judged on all available images.

MRI bone edema is a lesion within the trabecular bone, with ill-defined margins and signal characteristics consistent with increased water content. The bone edema scale was 0–3, based on the proportion of bone with edema.

Synovitis is an area of increased signal on STIR in the synovial compartment that shows a thickness greater than the width of the normal synovium. Synovitis was assessed in 3 wrist regions, the distal radioulnar joint, the radiocarpal joint, and the intercarpal-carpometacarpal (CMC) joints, and in each MCP joint. The first CMC joint and the first MCP joint were not scored. The scale is 0–3, based on thickness.

The modified RAMRIS scores for 1 wrist can range from 0 to a maximum of 150 for erosions, 0–45 for bone edema, and 0–9 for synovitis. The corresponding ranges for the second through the fifth MCP joints unilaterally are 0–80 for erosions, 0–24 for bone edema, and 0–12 for synovitis.

Statistical analysis. Analysis was undertaken using SPSS Version 11 and SigmaStat Version 3.5. In order to evaluate the interreader reliability, intraclass correlation coefficients (ICC) for individual joints and total scores were calculated. Differences between outcomes were evaluated using the t-test or the Mann-Whitney rank-sum test. MRI results (number of erosions, RAMRIS scores for erosions, bone edema, and synovitis) were compared between the 2 groups using the Mann-Whitney rank-sum test. A multiple linear regression model was used to assess the correlation of MRI scores with demographic characteristics and to explore potential confounding variables. Pearson's correlation coefficients were calculated between various MRI findings and clinical characteristics. The sensitivities and specificities of MRI findings to identify patients with RA were calculated.

RESULTS

Forty patients with RA and 40 healthy controls were included in the study. Subjects' characteristics are provided in Table 1. The only significant difference between the groups, which was explored in the statistical models, was an age difference, with healthy controls being significantly younger ($p < 0.001$). Except for 1 healthy person with positive anti-CCP, all other controls were RF- and anti-CCP-negative.

Analysis of the individual bones. A total of 3360 (1680 in each group) bones were evaluated and scored. Five hundred fourteen bones with erosion-like lesions were found: 89/1680 (5.3%) in the healthy control group and 425/1680 (25.3%) in patients with RA (Table 2). Erosions were more likely to be found in the wrists (62%) than hands (38%). Overall, there were 177 large erosions (modified RAMRIS > 1), with 19/177 (10.7%) in the healthy control group. Number of erosions, number of erosions scored > 1, modified RAMRIS scores for erosions, bone edema, and synovitis were significantly higher in the RA group than in healthy controls (Table 2). There were no significant differences in the number of erosions, as well as erosion, bone edema, and synovitis scores between dominant and nondominant hands/wrists in both groups (Table 2).

Table 1. Subjects' characteristics.

Characteristics	Healthy Controls, n = 40	RA, n = 40	p
Gender (F:M)	29:11	32:8	
Mean age, yrs, (range)*	36.7 (20–64)	47.3 (19–62)	< 0.001
Median age, yrs	31	49.5	
Positive RF*	0	29 (72.5%)	< 0.001
Positive anti-CCP*	1 (2.5%)	23 (57.5%)	0.001
Mean ESR (range)*	11 (2–40)	29 (0–137)	0.002
Subjects with elevated ESR	3 (7.5%)	16 (40%)	
Mean CRP (mg/dl) (range)*	0.48 (< 0.4–1.2)	1.32 (< 0.4–10.6)	0.027
Subjects with elevated CRP	2 (5%)	11 (27.5%)	
Right hand dominant	36 (90%)	39 (97.5%)	
Mean disease duration, months (range)	0	83.5 (0–367)	
Median disease duration, months	0	47	

* Significant difference between the two groups. RF: rheumatoid factor; CCP: cyclic citrullinated peptide; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

Both groups had the greatest number of erosions (10% of the total erosions) in the third metacarpal head. The highest scores for bone erosions were found also in the third metacarpal head as well as in the second metacarpal head (9% of the total score for erosions each). The highest scores for bone edema were found in the lunate bone (15% of the total score for bone edema). Synovitis scores were greatest in the intercarpal-CMC joint area in both groups (24% of the total score for synovitis).

Analysis of individual subjects. Only 1 RA patient demonstrated no abnormalities on MRI, compared to 11 subjects in the healthy control group.

Twenty-six healthy subjects (65%) had at least 1 erosion-like lesion on MRI of bilateral hand and wrist (Figure 1A). Of these, 14 had at least 1 large lesion (scored > 1) and 4 had 2 such lesions. Bone edema was found in 7 healthy subjects (17.5%) and 17 (42.5%) had detectable changes resembling synovitis. Interestingly, the anti-CCP-positive healthy control was found to have negative modified RAMRIS scores for erosions, bone edema, and synovitis. The total number of erosions as well as the erosion scores were highly correlated with age ($r = 0.47$ and 0.49 respectively, $p < 0.01$; Figure 2). Bone edema and synovitis scores were also associated with age ($r = 0.38$ and 0.37, $p < 0.01$).

Thirty-six (90%) of the patients with RA were found to have at least 1 erosion when both hands and wrists were evaluated. Twenty-four (60%) were found to have at least 1 large erosion (scored > 1) and 14 patients (35%) had 2 or more of them. In addition, 26 subjects with RA (65%) were found to have bone edema and 32 had synovitis (80%). Significant correlations between the different MRI findings were found (Table 3). The total number of erosions correlated with the other components of RAMRIS: erosion, bone marrow edema, and synovitis scores, as well as RF titer, CRP values, and age. While the erosion score was associated with edema and synovitis scores ($p < 0.05$), the strongest correlation was found between edema and synovitis scores ($p < 0.01$). As expected, there was a significant association between disease duration and number of erosions, as well as erosion score (Table 3).

In a multiple linear regression, the total number of erosions was predicted by not only RA diagnosis ($p = 0.001$), but also higher age ($p = 0.005$). However, in patients with RA, when disease duration was factored in, age lost its effect ($p = 0.113$) as compared to disease duration ($p = 0.002$). Bone edema correlated significantly with CRP values ($p = 0.003$) by linear regression ($R = 0.353$).

Sensitivity and specificity of MRI lesions. The sensitivities and specificities of various MRI findings for RA were calculated and are presented in Table 4. If having 1 erosion on MRI of bilateral hand and wrist was a positive test for RA, the sensitivity of this test would be 90%, but specificity only 35%. While the finding of more erosions and a higher erosion score increased the specificity, the sensitivity decreased markedly. The presence of synovitis provided 57.5% specificity, but having a synovitis score > 2 was 70% sensitive and 80% specific.

The presence of bone edema appears to be a better single test for RA, with 82.5% specificity and 65% sensitivity. Since none of the controls had bone edema in the MCP joints, finding bone edema in those joints was 100% specific. The highest scores for edema in our study were found in the lunate, which according to the literature is the most frequent wrist and hand bone to be involved in wrist impingement syndromes[27]. Ulnar impaction syndrome on MRI looks similar to inflammatory osteitis seen in RA (Figure 1B). Because of the high prevalence of ulnar impaction syndrome in the general population, we eliminated the lunate from the bone edema scoring. After exclusion of the lunate, the specificity increased to 87.5% and the sensitivity was slightly lower at 62.5%.

Interreader reliability. Characteristics and results of the 10

Table 2. Comparison of MRI results between healthy and RA subjects.

Results	Healthy, n = 40	RA, n = 40	p
Total number of erosions (D wrist)	29	125	
Total number of erosions (D hand)	21	82	
Total number of erosions (ND wrist)	23	140	
Total number of erosions (ND hand)	16	78	
Total number of erosions (D hand/wrist)	50	207	
Total number of erosions (ND hand/wrist)	39	218	
Total number of erosions (B hand/wrist)	89	425	
Mean number of erosions (range)	2.2 (0–9)	10.6 (0–45)	
Median number of erosions	1.5	8.5	p < 0.001*
Number of erosions scored > 1 (D wrist)	4	42	
Number of erosions scored > 1 (D hand)	3	43	
Number of erosions scored > 1 (ND wrist)	6	50	
Number of erosions scored > 1 (ND hand)	6	23	
Number of erosions scored > 1 (D hand/wrist)	7	85	
Number of erosions scored > 1 (ND hand/wrist)	12	73	
Total number of erosions scored > 1 (B hand/wrist)	19	158	
Mean number of erosions scored > 1 (range)	0.5 (0–3)	4.0 (0–35)	
Median number of erosions scored > 1	0	1.0	p = 0.004*
Erosion score (D wrist)	40	286	
Erosion score (D hand)	23	221	
Erosion score (ND wrist)	41	307	
Erosion score (ND hand)	25	126	
Erosion score (D hand/wrist)	63	507	
Erosion score (ND hand/wrist)	66	433	
Total erosion score (B hand/wrist)	129	940	
Mean erosion score (range)	3.2 (0–14)	23.5 (0–289)	
Median erosion score	2	10	p < 0.001*
Edema score (D wrist)	13	101	
Edema score (D hand)	0	41	
Edema score (ND wrist)	8	112	
Edema score (ND hand)	0	43	
Edema score (D hand/wrist)	13	142	
Edema score (ND hand/wrist)	8	155	
Total edema score (B hand/wrist)	21	297	
Mean bone edema score (range)	0.5 (0–5)	7.5 (0–78)	
Median bone edema score	0	2	p < 0.001*
Synovitis score (D wrist)	31	81	
Synovitis score (D hand)	12	90	
Synovitis score (ND wrist)	19	91	
Synovitis score (ND hand)	13	73	
Synovitis score (D hand/wrist)	43	171	
Synovitis score (ND hand/wrist)	32	164	
Total synovitis score (B hand/wrist)	75	335	
Mean synovitis score (range)	1.8 (0–14)	8.3 (0–38)	
Median synovitis score	0	5	p < 0.001*
Total RAMRIS (B hand/wrist)	225	1572	

* Mann-Whitney rank sum test. D: dominant; ND: non-dominant; B: bilateral; RAMRIS: rheumatoid arthritis magnetic resonance imaging scoring system.

randomly chosen subjects whose images were used for interreader reliability calculations are presented in Table 5. The mean and median age of the controls in this subgroup was higher than the entire healthy group (44.5 and 43.5 vs 36.7 and 31 years, respectively). Both of the subgroups (healthy and RA) had higher erosion numbers as well as erosion, edema, and synovitis scores compared to the whole groups.

Interreader reliability was found to be good, with ICC between the 2 readers being 0.76 for individual joints (0.81 for erosions, 0.69 for bone edema, 0.73 for synovitis) and 0.88 for total scores (0.9 for erosions, 0.84 for bone edema, 0.86 for synovitis).

DISCUSSION

We evaluated MRI of bilateral MCP and wrist joints in 40

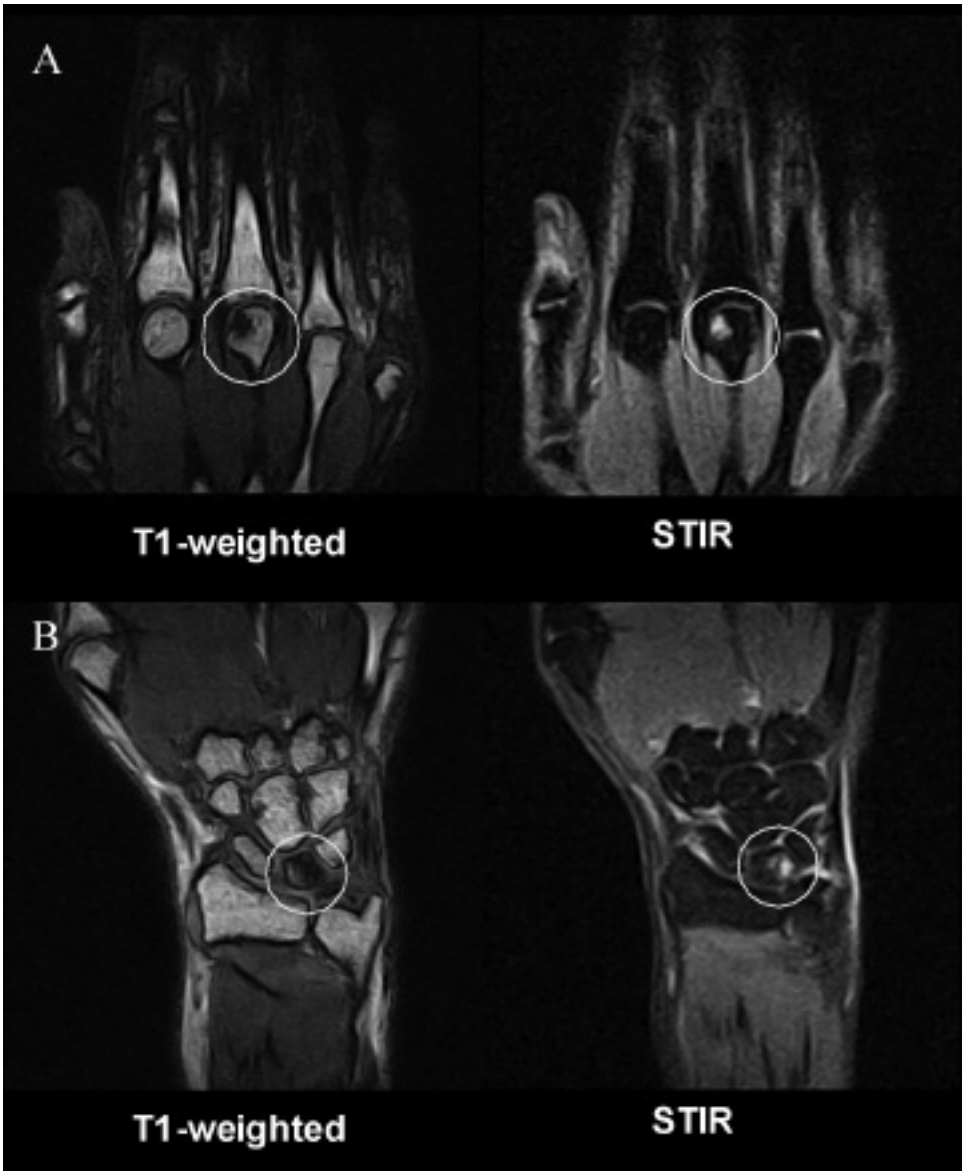

Figure 1. Examples of erosion-like lesions and bone edema in healthy controls. A. Erosion-like lesion in the right third metacarpal head. B. Bone edema in the right lunate. This could also represent ulnar impaction syndrome.

healthy subjects and 40 patients with RA using a 0.2 T extremity-MRI and employing noncontrast T1-weighted 3-D with thin slices (0.6–0.9 mm) and STIR sequences in the coronal plane. Images were read blindly using a modified RAMRIS system (no contrast injection, imaging in 1 plane only), and in order to assess interreader reliability, the images of 10 subjects were read independently by a musculoskeletal radiologist. A total of 3360 bones were examined. The primary conclusion of this study is that changes resembling RA pathologies can be frequently found in the MCP and wrist joints of healthy individuals. Further, the morphologic appearance of these findings is not different from those seen in RA. However, the overall number of lesions and the associated scores were significantly lower in the healthy controls as compared to the RA population.

Few studies have been performed to assess inflammatory joint pathology in healthy control subjects, and in most cases these involved small numbers of patients[14-23]. Additionally, to our knowledge there have only been 3 studies with the MRI assessors blinded to the diagnosis[14,21,23].

Our study evaluated the largest number of healthy subjects to date. In addition, we examined many joints of the subjects (bilateral hand and wrist), which probably led to the high number of people with positive MRI findings. The images in our study were obtained using a low-field extremity-dedicated MRI machine. High-field MRI machines have

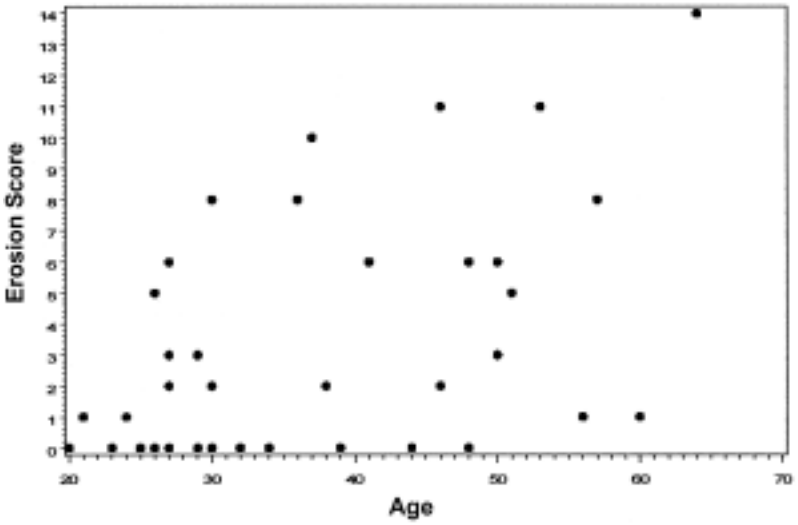

Figure 2. Plot of total erosions score by age in healthy controls (correlation coefficient = 0.47, $p < 0.01$).

Table 3. Association between different MRI findings and clinical characteristics of RA patients (correlation coefficients R).

Patient Characteristics	Erosion Score	Edema Score	Synovitis Score	RF	Anti-CCP	ESR	CRP	Age	Disease Duration
Erosion number	0.73**	0.59**	0.51**	0.41**	0.02	0.03	0.32*	0.35*	0.53**
Erosion score	X	0.38*	0.35*	0.15	–0.13	–0.03	0.25	0.1	0.45**
Edema score	X	X	0.66**	0.34	0	0.1	0.31	0.3	0.21
Synovitis score	X	X	X	0.27	0.23	0.16	0.28	0.08	0.15
RF	X	X	X	X	0.31*	0.2	0.23	0.26	0.08
Anti-CCP	X	X	X	X	X	0.30	0.12	0.05	0.04
ESR	X	X	X	X	X	X	0.8**	–0.1	–0.18
CRP	X	X	X	X	X	X	X	0.06	0.09
Age	X	X	X	X	X	X	X	X	0.27

* $p < 0.05$, ** $p < 0.01$. RF: rheumatoid factor; CCP: cyclic citrullinated peptide; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

Table 4. Sensitivity and specificity of MRI findings for RA.

Test	Sensitivity	Specificity
One erosion (bilateral hand/wrist)	90%	35%
One erosion (dominant hand/wrist)	87.5%	42.5%
One erosion (dominant wrist)	72.5%	57.5%
> 5 erosions (bilateral hand/wrist)	55%	90%
At least 1 erosion scored > 1 (bilateral hand/wrist)	60%	65%
At least 2 erosions scored > 1 (bilateral hand/wrist)	35%	90%
Erosion score > 8 (bilateral hand/wrist)	57.5%	90%
Bone edema (bilateral hand/wrist)	65%	82.5%
Bone edema (bilateral MCP joints)	32.5%	100%
Bone edema (bilateral hand/wrist, excluding lunate)	62.5%	87.5%
Synovitis (bilateral hand/wrist)	80%	57.5%
Synovitis score > 2 (bilateral hand/wrist0	70%	80%
Synovitis score > 7 (bilateral hand/wrist)	40%	92.5%

MCP: metacarpophalangeal.

a better signal-to-noise ratio and could be hypothetically more sensitive in the evaluation of bone and joint lesions. However, the literature suggests that low-field extremity-MRI can provide similar information on bone erosions and synovitis as high-field MRI units[28,29]. A perceived weakness of our study may be that we did not use contrast media, which could have a significant effect on the specificity of the MRI findings. However, according to some authors, STIR/T2-weighted fat-suppressed images have lower sensitivity and higher specificity for detection of synovitis than do contrast-enhanced T1-weighted images[30]. Given our findings, the lower sensitivity and higher specificity technique might be preferred.

According to the OMERACT definition of an MRI erosion, a lesion should be visible in 2 planes with a cortical break seen in at least 1 plane. The 2-plane criterion was used

Table 5. Characteristics and results of the 10 subjects whose images were used for inter-reader reliability calculations.

	Healthy Controls n = 4 (2 Women, 2 Men)			RA Patients n = 6 (3 Women, 3 Men)		
	Mean ± SD	Median	Range	Mean ± SD	Median	Range
Age, yrs	44.5 ± 16.1	43.5	27–64	48 ± 9.59	46.5	33–59
Disease duration, months	NA	NA	NA	73 ± 87.54	52.5	0–243
Number of erosions	5.0 ± 3.9	5.5	0–9	22.7 ± 12.1	19.0	12–45
Erosion score	7.5 ± 5.97	8	0–14	45.7 ± 48.2	29.5	13–141
Bone edema score	1.0 ± 1.15	1.0	0–2	31.3 ± 30.0	16.0	7–78
Synovitis score	3.3 ± 2.9	3.0	0–7	22.3 ± 13.9	24.0	1–38

NA: not applicable.

to mitigate the partial voluming artifacts inherent in thick (3 mm) slices and may not be necessary with slice thickness substantially smaller than erosion diameters (< 1 mm). In our study, images were done in only 1 coronal plane and we used a modified version of the OMERACT erosion definition: an erosion-like lesion was required to be visible in at least 2 adjacent slices. Also, multiplanar reconstructions were not performed. It is not clear whether including multiplanar reconstructions in the evaluation of images would change the results. Multiplanar reconstructions rely on the same imaging data, merely manipulated by a computer. However, it is possible that this modified approach may increase the risk of misinterpretations, particularly because of partial volume artifacts being wrongly interpreted as erosive changes, and may reduce specificity.

The OMERACT MRI in RA group recommendations of a core set of basic MRI sequences include intravenous gadolinium contrast injection for assessment of synovitis. Our study did not use contrast injection, which also may severely influence the specificity of the method.

Our control group was younger than the RA patients. Given our results that age affected MRI findings, the overall number of lesions and scores would be higher in the control group if they were of similar age. The creation of age-matched standards and establishment of norms for the given age might improve the specificity of RA diagnosis, especially in young patients.

Using the technique presented here, which can be done reproducibly in a rheumatologist's office and did not require contrast injection, 65% of healthy people had at least 1 erosion-like change. They were found in 4.3% of all MCP joint bones studied, 5.8% of the wrist joints, and 5.3% of the total bone areas. This is more than has been found in most of the previous reports, where very few or no erosions were seen in normal controls[6,12,16]. Parodi, *et al* found 26.1% of healthy individuals with at least 1 erosion in studies of the bilateral hand and wrist[22]. Those lesions occurred in 1% of the wrist bones and in 0.2% of MCP joint bones. The T1-weighted sequence with a slice thickness of 3.5 mm and with a 0.3 mm interslice gap in the coronal and axial plane was used in that study. The authors used original RAMRIS definitions, which require an erosion to be visible in 2 planes, with a cortical break seen in at least 1 plane[22]. Ejbjerg, *et al* reported 2.2% eroded MCP joint bones and 1.7% wrist joint bones in their healthy subjects (1.9% of all the bone areas assessed)[6]. They also used sequences with traditional 3 mm slices in 2 planes and original RAMRIS. In the other study from the same group, in which a 3-D T1-weighted sequence with a slice thickness of 1 mm and subsequent multiplanar reconstruction was used, low-grade erosion-like bone changes were found in 2 out of 9 (22.2%) controls by the "few-joints approach" (only 1 dominant hand/wrist) and in 5 (55.6%) by the "many-joints approach" (bilateral hand and wrist plus unilateral metatarsophalangeal joints)[21].

In the Tonnolli-Serabian study, 15 RA and 10 healthy subjects' T1-weighted images with 3 mm slices in the coronal plane only of the unilateral wrist were read blindly to the diagnosis. No erosion scoring was performed. The mean number of erosions per healthy subject was 4.8, more than twice that in our study[14]. In Dohn's study, 1 plane with thin cuts, subsequent multiplanar reconstruction, and a blinded reader were used, and no erosions were found in healthy subjects. However, this was in the MRI examination of unilateral second through fifth MCP joints in only 4 healthy controls[23]. Taking these data together, we hypothesize that a thin slice-thickness sequence and imaging in only 1 plane with no multiplanar reconstruction (therefore modified RAMRIS), as well as having the reader blinded in regards to the diagnosis, contributed to the relatively high prevalence of erosions in healthy subjects in our study.

If the presence of at least 1 MRI erosion was used as a positive test for RA, this method would be only 35% specific. To our knowledge, the only previous study calculating sensitivity and specificity of MRI erosions for RA was Tonolli-Serabian, *et al*[14]. Sensitivity was 87% and specificity was 70%. The authors, however, assessed sensitivity and specificity of "having at least 1 gadolinium-enhanced lesion." Therefore, it is possible that gadolinium improves the specificity of RA erosions and it may be useful to use contrast if MRI is done for diagnostic purposes.

The presence of bone edema appears to represent an

important factor in the pathogenesis of RA. Studies suggest that bone edema represents the earliest bone lesion in RA, and related to the progression of joint damage 1 to 6 years later[31-34]. Bone edema was the strongest predictor of radiographic progression after 2 years in 130 patients with early RA in the CIMESTRA study[35]. Moreover, bone edema scores have consistently been found to correlate with clinical and laboratory indicators of disease activity including CRP, ESR, and pain score[36,37] and importantly, these scores have been shown to decrease in response to anti-tumor necrosis factor therapy[38,39]. In a study of MRI prior to finger joint replacement surgery in patients with longstanding RA, visualized bone marrow edema was confirmed to correlate with bone marrow inflammation on histology of the corresponding region[40]. However, although MRI bone edema seems to represent an important pathologic milestone in RA, it also occurs in osteoarthritis, where it has been linked to pain and radiographic progression[41-43]. Ulnar impaction syndrome is very common and indistinguishable from osteitis in the lunate of patients with RA[27]. Bone edema can also be associated with trauma or heavy manual activities[42]. Neither of the above clinical variables were exclusions in our study but should be considered when evaluating MRI findings of patients in the clinical setting.

Few studies have evaluated bone edema in healthy subjects, especially in comparison to patients with RA. In the study reported by McGonagle, *et al* in a healthy population, 10% had bone edema in the second to the fifth dominant MCP joints[8]. In contrast, bone marrow edema-like changes were not seen in any of the joints examined in Ejbjerg's report[6]. Parodi, *et al* found bone edema in 2/23 subjects (8.7%). In our study, we found bone edema in the wrists of 17.5% of the controls and in 12.5% after exclusion of the lunate. Importantly, from a diagnostic point of view, no healthy person had bone edema in the MCP joints. Of the 3 MRI findings (erosions, bone marrow edema, and synovitis) evaluated in our study, edema was the most specific for RA. It also provided reasonable sensitivity. These results suggest that bone marrow edema is the most useful single MRI finding for the diagnosis of RA, especially after eliminating the lunate from bone edema scoring. In studies comparing low- to high-field MRI systems, bone marrow edema on low-field MRI had high specificity with only moderate sensitivity[28,41]. Therefore, the presence of bone edema on high-field MRI may offer higher sensitivity for RA than our results.

The most prevalent joints for erosions, bone edema, and synovitis were similar in both healthy volunteers and RA patients. Also, there was no difference between the dominant and nondominant hand/wrist in both groups. This suggests that the characteristic location of early lesions of RA could be related to normal physiology and perhaps even that some degree of characteristic early RA-like change arises as a normal component of bone homeostasis.

Overall, our study does not support the use of noncontrast MRI as a sole tool for making the diagnosis of RA, although it may help to provide perspective on findings in individual patients, which could contribute to diagnostic accuracy. High sensitivity and good interrater reliability of the MRI readings suggest an important value of this tool in patients with RA to determine a baseline degree of bone injury and to follow patients over time. MRI can provide an objective assessment of treatment effects and help with therapy optimization. In addition, clinicians can use MRI to insure that patients have both clinical remission and lack of progression or reversal of bone injury. This is important, as 19% of RA patients in clinical remission have ongoing joint destruction, which is missed unless they are followed by appropriate imaging[44].

MRI abnormalities are relatively frequent in normal individuals and their presence increases with age. This observation suggests that caution should be used in the interpretation of joint lesions on MRI, especially in early arthritis, and emphasizes the necessity for a careful integration of clinical, laboratory, and imaging results in diagnostic decisions. In addition, before MRI is further considered as a tool for the diagnosis of RA, it may be important to determine whether gadolinium enhancement can reliably improve its diagnostic capability, and to establish age-relevant norms in healthy control populations. Our data suggest that bone marrow edema is the most specific sole MRI finding for RA, especially after eliminating the lunate from the bone edema scoring. There is a need for validation studies of MRI findings in the early diagnosis of RA.

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