Magnetic Resonance Imaging of Bilateral Hands Is More Optimal Than MRI of Unilateral Hands for Rheumatoid Arthritis

Ying-Qian Mo, Ze-Hong Yang, Hai-Ning He, Jian-Da Ma, Jin-Jian Liang, Wei-Ke Zeng, Guang-Zi Shi, Jun Shen, and Lie Dai

ABSTRACT. ***Objective.*** To explore the advantages of magnetic resonance imaging (MRI) of bilateral hands in rheumatoid arthritis (RA).

Methods. Consecutive patients with active RA were recruited for clinical assessments, radiographs, and MRI of bilateral hands. Bilateral hands were scanned simultaneously on 3.0 T whole-body MRI system and were scored on synovitis, osteitis, and bone erosion according to the RA MRI scoring (RAMRIS) system.

Results. Among 120 patients included, wrist bones and metacarpophalangeal joint (MCPJ) 2 proximal showed bone erosion in early RA. The second to fifth metacarpal bases and the second to fourth MCPJ distal showed more bone erosion in mid-stage or late-stage RA. When MRI of dominant unilateral hand was analyzed, MRI synovitis and osteitis in 5% of wrists and 3 MRI features in 5–14% of MCPJ were misdiagnosed (McNemar test, all $p < 0.05$). There were 46% wrist synovitis, 29–52% MCPJ2–5 synovitis, 45% wrist osteitis, and 20%–34% MCPJ2–5 osteitis not detected by joint tenderness and/or swelling. When the clinically more severe hand was selected for MRI of unilateral hand according to physical examination, MRI synovitis in 5% of wrists and 3 MRI features in 7–15% of MCPJ were misdiagnosed (all $p < 0.05$). Scatter plots and linear regression analyses were used to illustrate RAMRIS between dominant or selected hand (Y values) and nondominant or nonselected hand (X values). All linear models were markedly different from a $Y = X$ linear model, indicating the dominant or clinically more severe hand could not represent the contralateral hand to evaluate RAMRIS.

Conclusion. MRI of bilateral hands is more optimal than MRI of the unilateral hand in RA. (First Release May 1 2018; J Rheumatol 2018;45:895–904; doi:10.3899/jrheum.171044)

Key Indexing Terms:
ARTHRITIS RHEUMATOID ARTHRITIS MAGNETIC RESONANCE IMAGING RAMRIS

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Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammation in the synovium (synovitis) and bone (osteitis), leading to joint destruction and even deformity. Although conventional radiography is considered the gold standard for imaging articular structure, its sensitivity for RA diagnosis and disease measurement is low and it almost cannot reflect inflammation[1]. Magnetic resonance imaging (MRI), which has advantages in visualizing inflammation and detecting bone erosion without exposure to radiation, can show synovitis, osteitis, and bone erosion in patients with RA. Osteitis is a strong independent predictor for subsequent radiographic progression[2]. Only MRI, not radiography or ultrasound, can detect osteitis. Additionally, physical examination such as tender or swollen joint counts correlated poorly with MRI osteitis[3].

MRI has been increasingly used in diagnosis, disease measurement, and treatment response for research and clinical purposes in RA[4,5]. A validated semiquantitative scoring methodology for MRI synovitis, osteitis, and bone erosion was developed by the Outcome Measures in Rheumatology Clinical Trials (OMERACT): the RA MRI

scoring (RAMRIS) system[6,7,8,9]. In 2003, RAMRIS was generated from databases consisting of images of dominant wrists and/or metacarpophalangeal joints (MCPJ); MRI evaluation of unilateral hands was then recommended by OMERACT[7,8]. In the majority of the succeeding studies, RAMRIS was evaluated for the clinically more severe hand or dominant hand in patients with RA[3,10–23].

RA is characterized by symmetrical joint involvement. Physical examination and radiographs are usually performed on bilateral hands of patients with RA. A study compared radiographs of unilateral and bilateral hands in view of lower cost and exposure to radiation and found that 24–40% of patients would be incorrectly classified as nonerosive when radiographs of unilateral hands were evaluated, and progression would be missed in 21%–31% of patients[24]. A report on a small cohort[25] of patients with RA (n = 35) by low-field (0.2 T) extremity MRI in 2005 was the only published report comparing unilateral and bilateral hands by MRI, in which only bone erosion was evaluated because of lack of T2-weighted and contrast-enhanced images. This study showed that MRI of bilateral hands detected radiological progression in more patients with RA (n = 29) than MRI of unilateral hands did (n = 25); however, the difference was not statistically significant[25]. More recently, high performance of whole-body MRI and multichannel synergic coils enabled bilateral hands to be scanned simultaneously; it makes scanning faster, more accurate, and more convenient than before. Herein we used 3.0 T whole-body MRI for patients with RA to explore the advantages of MRI of bilateral hands.

MATERIALS AND METHODS

Patients. Consecutive patients with RA who fulfilled the 1987 American College of Rheumatology (ACR) revised classification criteria for RA or the 2010 ACR/European League Against Rheumatism classification criteria for early RA, and who had active disease [28-joint count Disease Activity Score using C-reactive protein (DAS28-CRP) ≥ 2.6] were recruited between April 2014 and April 2016 from Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China. Patients were excluded if they refused or had contraindications for MRI examinations or contrast agents. This study was conducted in compliance with the Helsinki Declaration. The Medical Ethics Committee of Sun Yat-sen Memorial Hospital approved the protocol (SYSEC-2009-06) and all patients signed written informed consent.

Clinical assessments and radiographic assessment. Demographic characteristics including sex, age, disease duration, and prior therapy before recruitment were recorded. Clinical assessments and radiographs of bilateral hands (anteroposterior view) were performed just before MRI examination, as described[26,27]. Radiographs were scored according to the modified total Sharp/van der Heijde score (mTSS) of the hands. Subjects with mTSS > 10 were considered as having radiographic joint damage[28].

MRI assessment. Bilateral hands of each patient were scanned simultaneously on 3.0 T whole-body MRI system with an 8-channel sense head coil (Achieva; Philips Medical Systems). Each patient was imaged in a prone position, with pronation of bilateral hands. Hand movement was avoided with the aid of sandbags on forearms. The imaging sequences comprised coronal turbo spin echo fat-suppressed T2-weighted imaging [repetition time (TR) 2718.2 ms, echo time (TE) 30 ms, slice thickness/gap 2.5/0 mm, field of view (FOV) 128 × 128, matrix 312 × 312], coronal spin echo T1-weighted imaging (TR 500 ms, TE 15 ms, slice thickness/gap 2.5/0 mm, FOV 128 × 128, matrix 356 × 275), and axial turbo spin echo fat-suppressed T2-weighted imaging (TR 3443.7 ms, TE 30 ms, slice thickness/gap 5/2 mm, FOV 128 × 128, matrix 312 × 310). Contrast-enhanced imaging was initiated immediately after intravenous injection of 0.2 mmol/kg Gd-DTPA (Magnevist; Bayer Pharma AG), with imaging sequences of axial spin echo fat-suppressed T1-weighted imaging (TR 500 ms, TE 15 ms, slice thickness/gap 5/2 mm, FOV 128 × 128, matrix 190 × 312) and coronal spin echo fat-suppressed T1-weighted imaging (TR 500 ms, TE 15 ms, slice thickness/gap 2.5/0 mm, FOV 128 × 128, matrix 275 × 356).

All MRI images were assessed according to the scoring system of MRI synovitis, osteitis, and bone erosion, as indicated in the definitions and atlas (standardized reference images) of the OMERACT 2002 RAMRIS[6,9,29,30]. For synovitis, each hand was scored in MCPJ2–5 and 3 wrist regions, including distal radioulnar, radiocarpal, and intercarpal-carpometacarpal joints; the scale is 0–3. For osteitis and bone erosion, each hand was scored in 15 wrist bones (8 carpal bones, distal radius, distal ulna, and 5 metacarpal bases), metacarpal heads (proximal), and phalangeal bases (distal) of MCPJ2–5. The scale is 0–3 for osteitis and 0–10 for bone erosion. As a summary, unilateral hand synovitis score ranged from 0 to 21, osteitis score from 0 to 69, and bone erosion score from 0 to 230; bilateral hands synovitis score ranged from 0 to 42, osteitis score from 0 to 138, and bone erosion score from 0 to 460.

All MRI images were scored by 2 experienced radiologists (ZHY and GZS, with 7 and 3 years of experience in musculoskeletal MRI, respectively) who were blinded to the patients' clinical findings and the objectives of our study. Specifically, they did not know dominant hands would be compared to nondominant hands when assessing MRI images. Reliability and agreement were assessed using intraclass correlation coefficient (ICC). The mean ICC of interobserver agreement was 0.852 for synovitis score, 0.739 for osteitis score, and 0.815 for bone erosion score. The mean ICC of intraobserver agreement was 0.837 for synovitis score, 0.763 for osteitis score, and 0.930 for bone erosion score. All the above agreements were considered high (ICC 0.6–0.8) to very high (ICC ≥ 0.8)[31].

Statistical analysis. Statistical analyses were performed with SPSS for Windows 19.0 (SPSS Inc.). Data were presented as frequencies and percentages for categorical variables; or median (interquartile range; IQR) for continuous variables. Spearman rank (r) correlation analysis generated the correlation coefficient. Chi-squared test or Fisher's exact test was used for comparison of categorical variables between 2 independent groups. McNemar test was used for comparison of categorical variables between 2 paired groups. Mann-Whitney rank-sum test was used for comparison between 2 independent groups, and Kruskal-Wallis 1-way ANOVA on ranks among ≥ 3 groups. Linear regression analysis was used to illustrate the relationship between RAMRIS in the dominant or selected hand and RAMRIS in the nondominant or nonselected hand. All significance tests were 2-tailed and were conducted at the 5% significance level.

RESULTS

Demographic characteristics of patients with RA. A total of 138 patients with RA were recruited. All patients finished MRI examinations of bilateral hands, and 18 of them were excluded because their MCPJ could not be imaged in a single coronal view of MRI for severe deformity. Thus 120 patients with RA were included for statistical analyses (Table 1). The median age was 52 years (range 24–79) and 79% were female. There were 52%, 35%, and 13% of patients, respectively, with high, moderate, and low disease activity according to DAS28-CRP. Bony erosions were detected in 97% of patients and radiographic joint damage in 79%. One patient was left-handed and 119 patients were right-handed. Seventy patients (58%) were treatment-naive and never took

Table 1. Demographic and clinical characteristics of the 120 patients with RA. Values are n (%) or median (IQR).

Characteristics	Values
Female	95 (79)
Age, yrs	52 (44–61)
Disease duration, mos	48 (12–120)
Core disease activity indicators	
28-TJC	9 (3–15)
28-SJC	4 (2–9)
PtGA	6 (4–7)
PrGA	6 (4–7)
ESR, mm/h	68 (30–92)
Elevated ESR*	108 (90)
CRP, mg/l	24 (7–53)
Elevated CRP**	97 (81)
RF-positive rate	83 (69)
ACPA-positive rate	83 (69)
DAS28-CRP	5.9 (4.7–6.9)
SDAI	29 (18–42)
CDAI	26 (16–36)
HAQ score	1 (0–2)
Radiographic assessment	
mTSS	36 (15–66)
Joint space narrowing subscore	5 (1–20)
Erosion subscore	26 (11–43)
Bony erosions	116 (97)
Radiographic joint damage, mTSS > 10	95 (79)
Previous medications	
DMARD- and corticosteroid-naive	70 (58)
Low-dose glucocorticoid alone	14 (12)
Low-dose glucocorticoid + DMARD	25 (21)
DMARD alone	11 (9)

* Elevated ESR: > 15 mm/h for males and > 20 mm/h for females. ** Elevated CRP: CRP > 5 mg/l. IQR: interquartile range; 28-TJC: 28-joint tender joint count; 28-SJC: 28-joint swollen joint count; PtGA: patient's global assessment of disease activity; PrGA: provider global assessment of disease activity; HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RF: rheumatoid factor; ACPA: anticyclic citrullinated peptide antibody; DAS28: 28-joint count Disease Activity Score; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; mTSS: modified total Sharp/van der Heijde score; DMARD: disease-modifying antirheumatic drug; RA: rheumatoid arthritis.

any disease-modifying antirheumatic drugs (DMARD) or glucocorticoids before recruitment. Thirty-nine (33%) took low-dose glucocorticoids (equivalent to prednisone ≤ 10 mg/d) alone (n = 14) or with DMARD (n = 15). Eleven (9%) took DMARD without glucocorticoids. DMARD, including methotrexate (n = 30, 25%), leflunomide (n = 18, 15%), salazosulfadimidine (n = 6, 5%), and hydroxychloroquine (n = 7, 6%). None of them took biologic DMARD.

The median disease duration was 48 months (range 3–360). Thirty-three (28%) patients had early RA (< 1 yr). Another 28% of patients (n = 34) had late-stage RA (> 10 yrs), and 53 (44%) patients had mid-stage RA (1–10 yrs).

MRI features and RAMRIS of bilateral hands. The mean imaging time for the entire MRI examination of bilateral hands, including patient positioning and contrast agent injection, was 23 ± 5 min. Figure 1 showed typical MRI images in 2 patients with RA, 1 with early RA and the other with mid-stage RA. Among 240 hands of 120 patients with RA, the occurrence frequencies of each MRI feature in wrist joints or bones were higher than those in MCPJ2–5 (Table 2 and Figure 2). Among all bones of bilateral hands, the top 3 bones with MRI osteitis were triquetrum (76%), lunate (76%), and scaphoid (74%); the top 3 bones with MRI bone erosion were triquetrum, lunate, and capitate (all 93%). The distribution of MRI synovitis was nearly consistent among patients in different stages of RA (Figure 3). Trapezoid and fifth metacarpal base showed more osteitis in mid-stage RA than in early RA. Wrist bones and MCPJ2 proximal showed bone erosion in early RA. The second to fifth metacarpal bases and the second to fourth MCPJ distal showed more bone erosion in mid-stage or late-stage RA (Figure 3).

The mean RAMRIS time for bilateral hands was 10 ± 2 min compared to unilateral hand of 7 ± 2 min. The median RAMRIS of synovitis, osteitis, and bone erosion were, respectively, 18 (IQR 10–26), 34 (11–52), and 58 (18–126). For early RA, median RAMRIS were 14 (10–23), 18 (8–36), and 29 (15–38), respectively. For mid-stage RA, median RAMRIS were 20 (11–30), 45 (16–61), and 90 (21–134), respectively. For late-stage RA, median RAMRIS were 21 (9–31), 36 (14–43), and 121 (40–196), respectively. Among the 3 groups, significant differences were seen in osteitis ($p = 0.036$; mid-stage RA > early RA, $p = 0.018$), and bone erosion ($p < 0.001$; mid-stage RA > early RA, $p = 0.001$; late-stage RA > early RA, $p < 0.001$).

Further analyses of RAMRIS with clinical assessment showed significant correlation of synovitis score with DAS28-CRP ($r = 0.559$, $p < 0.001$), Simplified Disease Activity Index (SDAI, $r = 0.572$, $p < 0.001$), Clinical Disease Activity Index (CDAI, $r = 0.536$, $p < 0.001$), 28-joint swollen joint count (SJC28, $r = 0.467$, $p < 0.001$), 28-joint tender joint count (TJC28, $r = 0.460$, $p < 0.001$), CRP ($r = 0.501$, $p < 0.001$), or erythrocyte sedimentation rate (ESR, $r = 0.449$, $p < 0.001$). RAMRIS bone erosion score was significantly correlated with mTSS ($r = 0.721$, $p < 0.001$) or erosion subscore of radiographic assessment ($r = 0.719$, $p < 0.001$).

Comparison of MRI of bilateral hands with MRI of dominant unilateral hand. MRI images of bilateral hands showed asymmetrical involvement of bilateral hands in certain patients with RA (Figure 1D, Figure 1E, Figure 1F), indicating the possibility of misdiagnosis in the case of MRI of unilateral hands. Dominant hand was recommended for MRI of unilateral hands by OMERACT[7,8]. As shown in Table 2, when MRI of the dominant unilateral hand was analyzed, MRI synovitis in 5% of wrists and 5–11% of MCPJ2–5, MRI osteitis in 5% of wrists, and 9–12% of MCPJ2–5, and MRI bone erosion in 8–14% of MCPJ2–5 were misdiagnosed (McNemar test, all $p < 0.05$). Similarly, when MRI of nondominant unilateral hand was analyzed, MRI synovitis in 12–19% of MCPJ2–5, MRI osteitis in 5% of wrists and

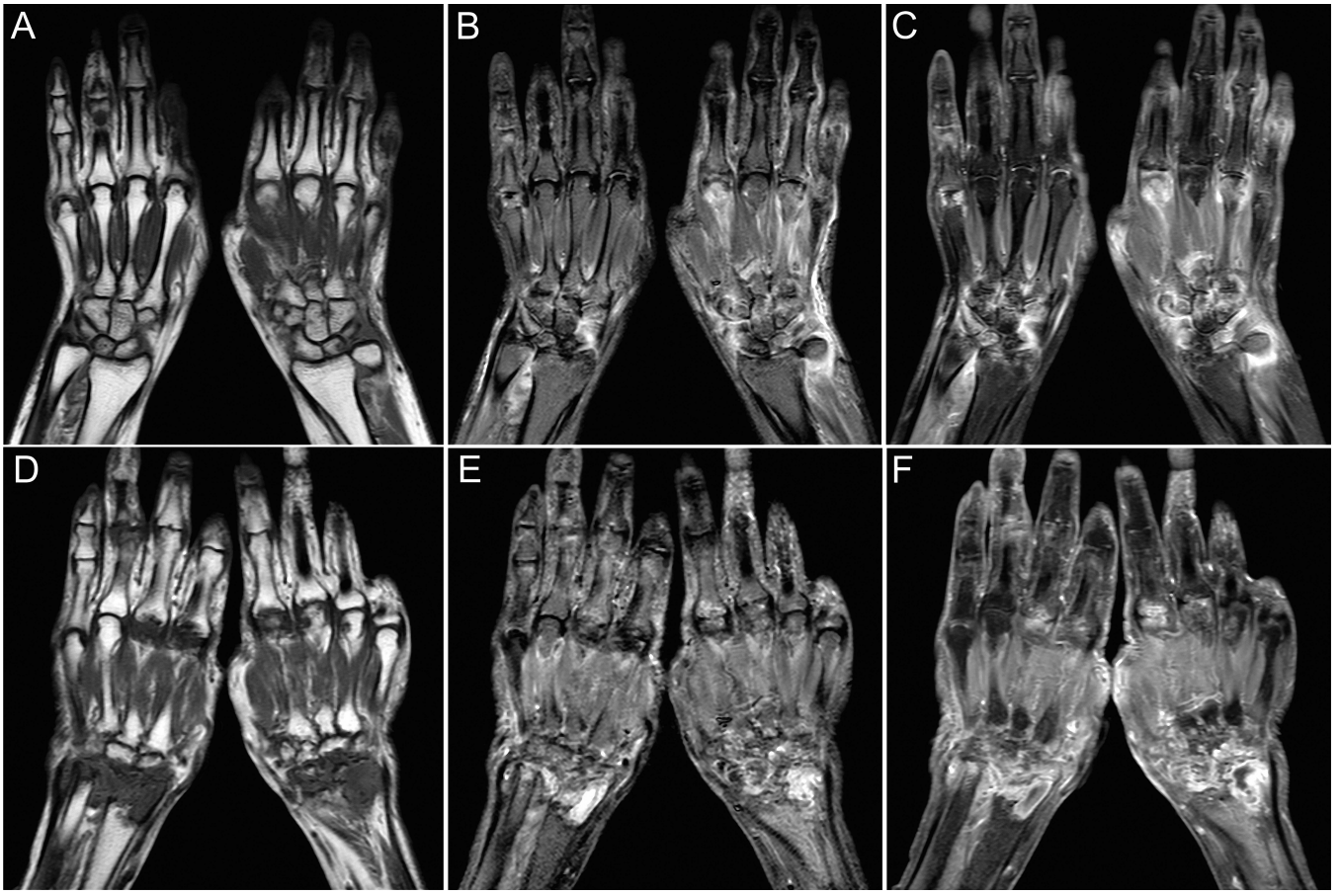

Figure 1. Typical MRI images of bilateral hands in 2 patients with RA. One was a 44-year-old woman and diagnosed with early RA (7 mos disease duration). Marked synovitis, osteitis, and bone erosion were shown in MRI (A–C). The other patient was a 64-year-old woman with 84 months of disease duration. Synovitis, osteitis, and bone erosion were shown as more severe in the nondominant hand versus the dominant hand (D–F). A and D. Coronal spin echo T1-weighted imaging. B and E. Coronal turbo spin echo fat-suppressed T2-weighted imaging. C and F. Contrast-enhanced coronal spin echo fat-suppressed T1-weighted imaging. MRI: magnetic resonance imaging; RA: rheumatoid arthritis.

12%–18% of MCPJ2–5, and MRI bone erosion in 12–19% of MCPJ2–5 were misdiagnosed (McNemar test, all $p < 0.05$).

Scatter plots in Figure 4 (top panels) were drawn with Y values of RAMRIS in dominant hands, and X values of RAMRIS in nondominant hands. Linear regression analyses showed significant constants (all $p < 0.01$), and 95% CI of regression coefficients (B values) did not cover 1.000. Specifically, the linear models were markedly different from a Y = X linear model, indicating that dominant hands were different from nondominant hands and could not represent nondominant hands to evaluate RAMRIS. In fact, there were 41%, 47%, 39% of dominant hands, respectively, having lower RAMRIS than nondominant hands. A similar trend could be seen in patients with early RA (Supplementary Figure 1A, available from the authors on request).

Comparison of bilateral-hands MRI with selected unilateral-hand MRI. The clinically more severe hand was usually selected for MRI of the unilateral hand, according to patients' complaints and physical examination[3,10–23]. In our study, the right hands of 42 patients (35%) and left hands of 28 patients (23%) were selected for clinically more severe involvement, and dominant hands (right hands of 49 patients and left hand of 1 patient) of 50 patients (42%) were selected for equal involvement of bilateral hands. Among 240 wrists, 98% showed MRI synovitis and 95% showed MRI osteitis (Table 2), but only 24% had swelling and 46% had tenderness (Supplementary Figure 2, available from the authors on request). There were 46% of wrist synovitis and 45% of wrist osteitis that were not noticed by joint tenderness and/or swelling. Among MCPJ, MCPJ2 showed the highest TJC (25%) and the highest SJC (23%). There were 33% of MCPJ2 synovitis and 20% of MCPJ2 osteitis not noticed by joint tenderness and/or swelling.

As shown in Table 2, when selected MRI of unilateral hands were analyzed, MRI synovitis in 5% of wrists, 7–12% of MCPJ except for MCPJ4, MRI osteitis in 8–13% of MCPJ2–5, and MRI bone erosion in 11–15% of MCPJ2–5 were misdiagnosed (McNemar test, all $p < 0.05$). Similarly, when MRI of nonselected unilateral hands were analyzed, MRI

Table 2A. The occurrence frequencies of MRI features per joint, comparing dominant versus nondominant hand. Values are % unless otherwise specified.

MRI Joint	Bilateral Hands	Unilateral Hand			Misdiagnosis by MRI			
					Unilateral Dominant Hand		Unilateral Nondominant Hand	
		Dominant	Nondominant	p*	Rate	p*	Rate	p*
Synovitis								
Wrist	98	93	94	1	5	**0.031**	4	0.063
MCPJ2	70	59	58	1	11	**< 0.001**	12	**< 0.001**
MCPJ3	62	52	46	0.281	10	**< 0.001**	16	**< 0.001**
MCPJ4	66	61	47	**0.002**	5	**0.031**	19	**< 0.001**
MCPJ5	77	69	63	0.230	8	**0.002**	14	**< 0.001**
Osteitis								
Wrist	95	90	90	1	5	**0.031**	5	**0.031**
MCPJ2	53	44	35	0.071	9	**< 0.001**	18	**< 0.001**
MCPJ3	48	38	33	0.362	10	**< 0.001**	15	**< 0.001**
MCPJ4	44	33	32	0.851	11	**< 0.001**	12	**< 0.001**
MCPJ5	55	43	42	0.856	12	**< 0.001**	13	**< 0.001**
Bone erosion								
Wrist	98	98	98	1	0	1	0	1
MCPJ2	59	48	40	0.132	11	**< 0.001**	19	**< 0.001**
MCPJ3	48	34	36	0.856	14	**< 0.001**	12	**< 0.001**
MCPJ4	33	25	18	0.122	8	**0.002**	15	**< 0.001**
MCPJ5	49	38	32	0.311	11	**< 0.001**	17	**< 0.001**

Table 2B. The occurrence frequencies of MRI features per joint, comparing selected versus nonselected hand. Values are % unless otherwise specified.

MRI Joint	Unilateral Hand			Misdiagnosis by MRI of Unilateral Selected Hand		Missed Diagnosis by MRI of Unilateral Nonselected Hand	
	Selected	Nonselected	p*	Rate	p*	Rate	p*
Synovitis							
Wrist†	93	94	1	5	**0.031**	4	0.063
MCPJ2	58	60	0.701	12	**< 0.001**	10	**< 0.001**
MCPJ3	53	44	0.071	9	**< 0.001**	18	**< 0.001**
MCPJ4	63	45	**< 0.001**	3	0.125	21	**< 0.001**
MCPJ5	70	63	0.108	7	**0.008**	14	**< 0.001**
Osteitis							
Wrist◊	91	89	0.774	4	0.063	6	**0.016**
MCPJ2^	40	38	1	13	**< 0.001**	15	**< 0.001**
MCPJ3^	35	35	1	13	**< 0.001**	13	**< 0.001**
MCPJ4^	36	29	0.185	8	**0.002**	15	**< 0.001**
MCPJ5^	44	41	0.585	11	**< 0.001**	14	**< 0.001**
Bone erosion							
Wrist◊	98	98	1	0	1	0	1
MCPJ2^	44	44	1	15	**< 0.001**	15	**< 0.001**
MCPJ3^	33	38	0.362	15	**< 0.001**	10	**< 0.001**
MCPJ4^	21	22	1	12	**< 0.001**	11	**< 0.001**
MCPJ5^	38	31	0.175	11	**< 0.001**	18	**< 0.001**

* P value was generated from McNemar test for comparing occurrence frequencies of each MRI feature per joint between dominant and nondominant hand, between selected and nonselected hand, and between MRI of bilateral hands and unilateral hand (dominant, nondominant, selected, or nonselected hand) considered as paired groups. P values in bold face are statistically significant. † Distal radioulnar joint, radiocarpal joint, and intercarpal-carpometacarpal joints were evaluated. ◊ 15 wrist bones were evaluated. ^ Metacarpal heads (proximal) and phalangeal bases (distal) were evaluated. MRI: magnetic resonance imaging; MCPJ: metacarpophalangeal joints.

synovitis in 10–21% of MCPJ2–5, MRI osteitis in 6% of wrists and 13–15% of MCPJ2–5, and MRI bone erosion in 10–18% of MCPJ2–5 were misdiagnosed (McNemar test, all $p < 0.05$).

Scatter plots in Figure 4 (bottom panels) were drawn with Y values of RAMRIS in selected hands and X values of RAMRIS in nonselected hands. Three linear models showed significant constants (all $p < 0.01$), and 95% CI of regression coefficients (B values) did not cover 1.000. Specifically, the linear models were markedly different from a Y = X linear model, indicating that selected hands were different from nonselected hands and could not represent nonselected hands to evaluate RAMRIS. There were 37%, 48%, and 44% of

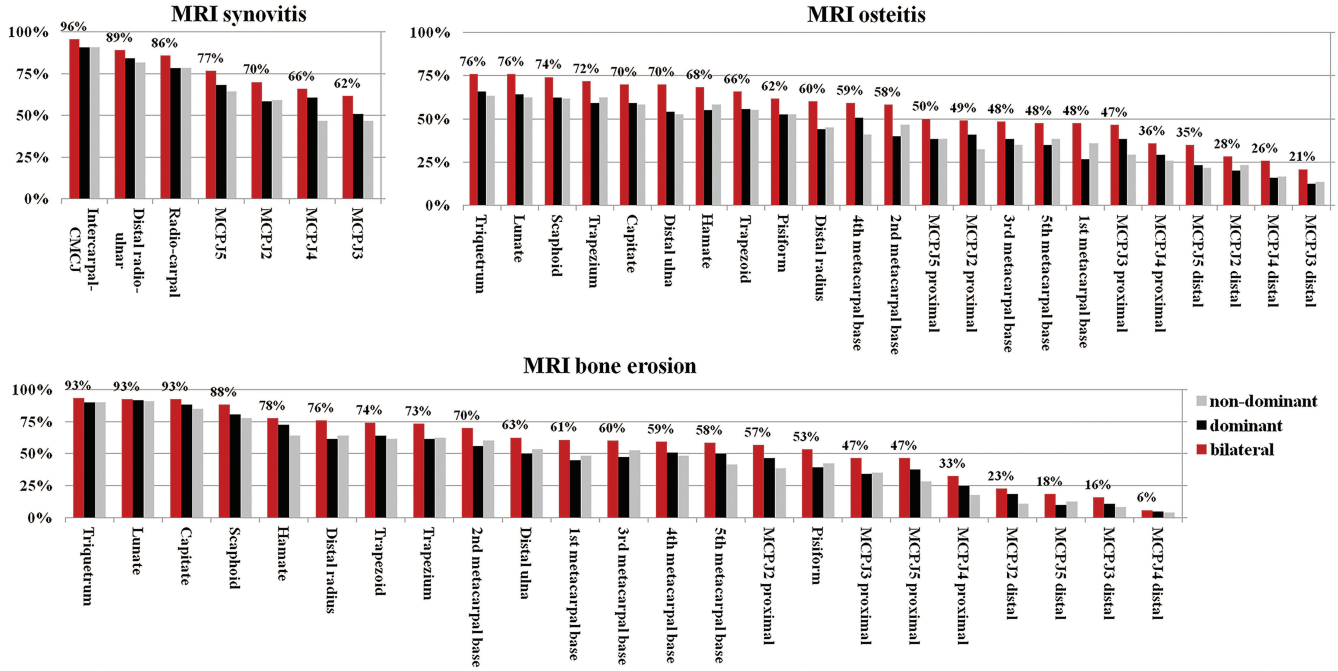

Figure 2. Distributions of MRI features in bilateral hands, dominant hands, and nondominant hands among 120 patients with RA. For MRI synovitis in wrist, the distal radioulnar joint, radiocarpal joint, and intercarpal CMCJ were evaluated. For MRI osteitis and bone erosion in wrist, 15 wrist bones were evaluated. For MRI osteitis and bone erosion in MCPJ, metacarpal heads (proximal) and phalangeal bases (distal) were evaluated. MRI: magnetic resonance imaging; CMCJ: carpometacarpal joints; MCPJ: metacarpophalangeal joints.

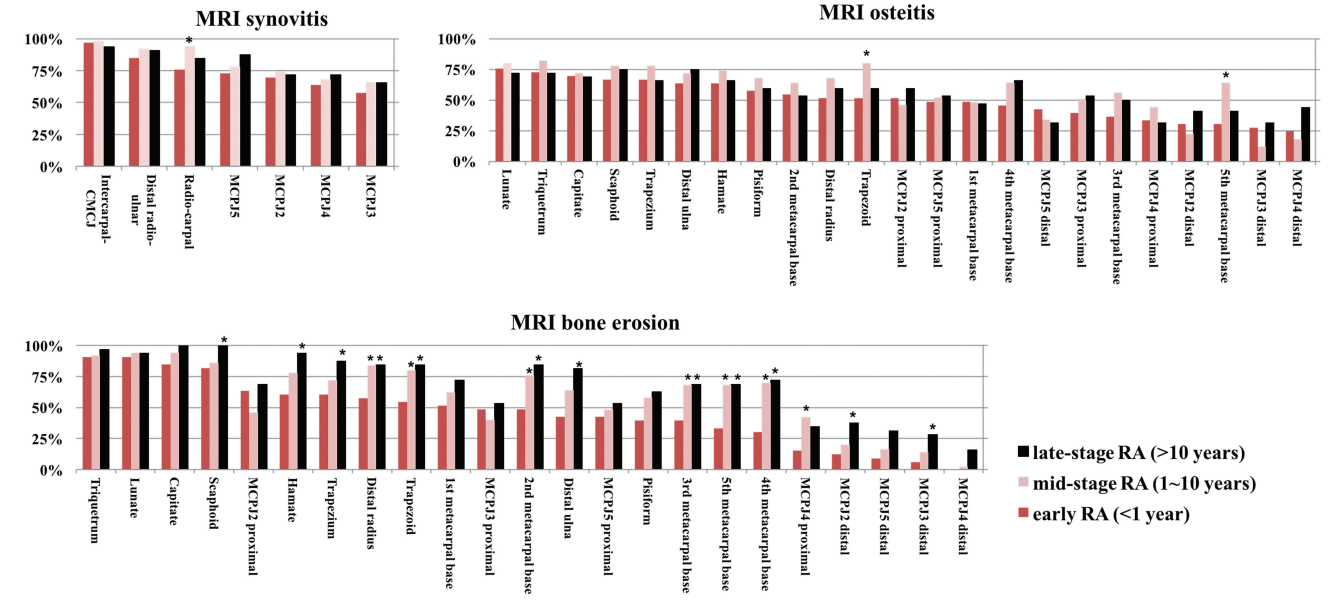

Figure 3. Distributions of MRI features per joint or bone among patients with early RA (< 1 yr, n = 33), mid-stage RA (1–10 yrs, n = 53), and late-stage RA (> 10 yrs, n = 34) based on bilateral-hands MRI. RA: rheumatoid arthritis; MRI: magnetic resonance imaging; CMCJ: carpometacarpal joints; MCPJ: metacarpophalangeal joints.

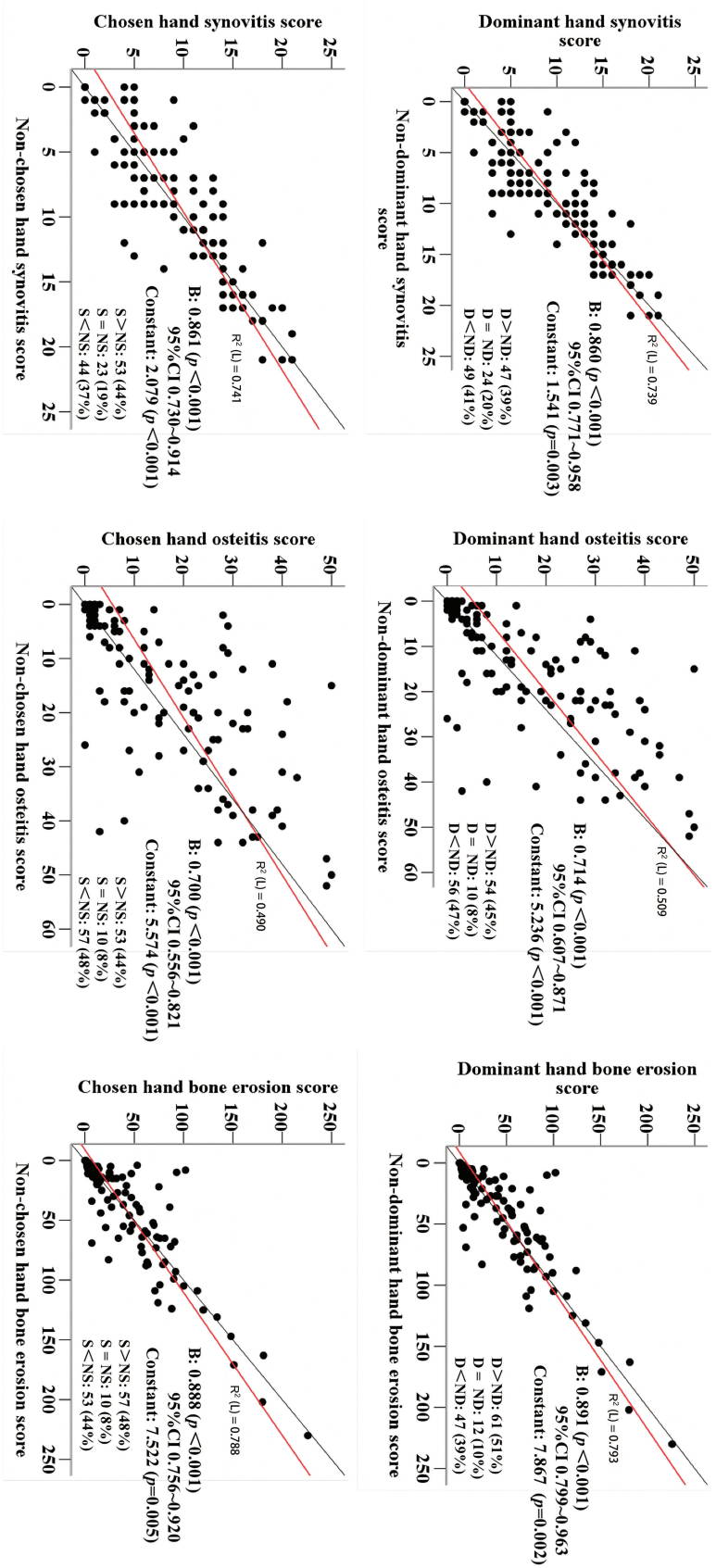

Figure 4. Scatter plots of RAMRIS in dominant and nondominant hands (top panels) and selected and nonselected hands (bottom panels). The black lines indicate Y = X linear model. The red lines indicate the real linear model by linear regression analyses for each scattered plot, of which R^2, constant, and regression coefficient (B) and its 95% CI are shown. D: dominant; ND: non-dominant; S: selected; NS: nonselected; RAMRIS: rheumatoid arthritis magnetic resonance image scoring.

selected hands, respectively, having lower RAMRIS than nonselected hands. A similar trend could be seen in patients with early RA (Supplementary Figure 1B, available from the authors on request).

DISCUSSION

In our study, bilateral hands of 120 consecutive patients with RA were assessed by high-field (3.0 T) whole-body MRI with an 8-channel sense head coil, which took 23 min for imaging and 10 min for scoring. First, we reported the distribution and occurrence frequencies of MRI synovitis, osteitis, and bone erosion in different stages of RA resulting from complete sequences of MRI of bilateral hands. A strength of our study is the detailed comparison of MRI features and RAMRIS between MRI of bilateral hands and MRI of dominant or selected (clinically more severe) unilateral hands. We also reported on the significant correlation of RAMRIS synovitis score of bilateral hands with major disease activity indicators, including DAS28-CRP, SDAI, CDAI, SJC28, TJC28, CRP, or ESR, and significant correlation of RAMRIS bilateral hands bone erosion score with mTSS or erosion subscore.

In most clinical situations, MRI of the unilateral hand has been performed using extremity MRI with 100-mm coils[15,16,17]. Limited by 100-mm FOV, all sequences need to be acquired separately for the wrist and MCPJ[32], which doubles the imaging time (e.g., 25 min for unilateral wrist[33] and 58 min for unilateral wrist and MCPJ[15]). More recently, knee coils that can provide sufficient FOV to cover the wrist and MCPJ have been used for MRI of the unilateral hand, greatly reducing the imaging time[34].

It is generally assumed that separate MRI of the unilateral hand may have higher image quality than simultaneous MRI of bilateral hands. Thus we set up 4 major measures to guarantee high image quality in our study. First, sandbags were put on forearms to avoid movement and to ensure bilateral hands lay horizontally in the center of the coil. Second, the field strength was 3.0 T, which could offer a higher signal-to-noise ratio[23]. Third, the matrix values were appropriate, considering resolution, imaging time, and motion artifacts. Coronal and axial short-tau inversion recovery imaging sequence was used to suppress fat, which could guarantee homogeneous fat saturation with bilateral hands. The numbers of acquisitions were 3 for T1-weighted imaging and 2 for T2-weighted imaging. All these improved image quality. Finally, the multichannel synergic coils provided suitable coverage to enable bilateral hands to be scanned simultaneously, ensure the center positioning of bilateral hands, and reduce magnetic field heterogeneity in 3.0 T MRI. There are other coils of whole-body MRI that can be used for bilateral hands, such as dedicated extremity coil, wrist coil, knee coil, or cardiac coil (except flex coil, which is suboptimal for 3.0 T MRI because of its small coverage)[35]. In addition, high-solution 3D scans can also be used in MRI of bilateral hands. There have been 2 major clinical trials in RA: 1 was a randomized, controlled trial of denosumab[36]; the other was a recently abstracted trial of tocilizumab in ACR 2017[37]. Both these studies successfully imaged bilateral hands separately with protocols that included thin-section, 3-D gradient-echo sequences, providing higher resolution than that achieved in our study. However, this MRI scan protocol nearly triples or quadruples the imaging time and thus has a lot of challenges in clinical use.

The occurrence frequencies of each MRI feature based on MRI of bilateral hands in our study were higher than those based on MRI of unilateral hands in a review of 4 major clinical trials of RA[38]. The general distributions were similar, except for a few discrepancies. MCPJ2 showed the most frequent synovitis in a published study[38], but MCPJ5 did in our current study. Trapezium was the seventh wrist bone for osteitis in a published study[38], but it was the fourth in our study, perhaps because of osteitis in nondominant hands, which was higher than osteitis in dominant hands. Further analyses were performed among patients in different stages of RA and showed the distribution of MRI synovitis and osteitis was nearly consistent. Wrist bones and MCPJ2 proximal showed bone erosion in early RA. The second to fifth metacarpal bases and the second to fourth MCPJ distal showed more bone erosion in mid-stage or late-stage RA.

The dominant hand has been recommended for RAMRIS by OMERACT since 2003. One explanation is that RAMRIS originated from databases consisting of MRI images of dominant wrists and/or MCPJ[7,8]. Another explanation may be that the joints of dominant hands could be more heavily affected than the nondominant hand because of mechanical burden. The published studies on the comparison between dominant and nondominant hands were mainly based on radiographs[24,35,39]. A prospective study in 2013 showed that both mTSS at single points and radiographic progression over time in patients with RA were highly correlated between dominant and nondominant hands[24]. There was only 1 MRI study that enrolled 46 bilateral wrists (MCPJ not included) and showed no significant differences of baseline erosions and erosive progression between dominant and nondominant hands, but MRI synovitis or osteitis could not be evaluated because of lack of T2-weighted and contrast-enhanced images[40]. In our study, MRI images of bilateral hands showed that dominant hands were not always more severe than nondominant hands. There were 41%, 47%, and 39% of dominant hands, respectively, having lower RAMRIS than nondominant hands. When MRI of dominant unilateral hands were analyzed, MRI synovitis in 5% of wrists and 5–11% of MCPJ2–5, MRI osteitis in 5% of wrists and 9–12% of MCPJ2–5, and MRI bone erosion in 8–14% of MCPJ2–5 were misdiagnosed. Further linear regression analyses showed dominant hands could not represent nondominant hands to evaluate RAMRIS.

The clinically more severe hand was also usually selected for MRI of unilateral hands according to patients' complaints

and physical examination[3,10–23]. MRI synovitis and osteitis were reported in clinically noninflamed joints[3]. In our study, we found that 46% of wrist synovitis, 29–52% of MCPJ2–5 synovitis, and 45% of wrist osteitis, 20–34% of MCPJ2–5 osteitis were not noticed by joint tenderness and/or swelling. Because of the poor concordance between physical examination and MRI, MRI synovitis in 5% of wrists, 7–12% of MCPJ except for MCPJ4, MRI osteitis in 8–13% of MCPJ2–5, and MRI bone erosion in 11–15% of MCPJ2–5 were misdiagnosed in the case of selected MRI of unilateral hands. Further linear regression analyses confirmed that clinically more severe hands could not represent the contralateral hands to evaluate RAMRIS.

There are 3 major limitations in this study. First, it was cross-sectional with only 1 timepoint MRI scan and it lacked prospective followup. The longitudinal behavior of putative erosions adds specificity to their diagnosis, because vascular channels and enthesis insertion sites do not change very much over time and can otherwise mimic erosions. Second, our study method is suboptimal because simultaneous MRI of bilateral hands and separate MRI of unilateral hands were not compared directly. However, it is difficult to do the contrast inspection twice because that may pose an ethical problem — another injection of contrast is harmful to the patient. Third, the most important advantage of MRI is for early RA, especially with normal radiographs, but there was only a small cohort of patients with early RA in our study. The comparisons between MRI of bilateral hands and MRI of unilateral hands need more data from patients with early RA. In addition, the interslice gap in axial view in our study is 2 mm, which is suboptimal compared to other trials typically using contiguous slices with no gap. This limitation may diminish the sensitivity and specificity for bone erosions.

MRI of bilateral hands is more optimal than MRI of unilateral hands for RA, particularly with the improved performance of high-field whole-body MRI.

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