Reducing Invasiveness, Duration, and Cost of Magnetic Resonance Imaging in Rheumatoid Arthritis by Omitting Intravenous Contrast Injection — Does It Change the Assessment of Inflammatory and Destructive Joint Changes by the OMERACT RAMRIS?

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ABSTRACT. ***Objective.*** Gadolinium (Gd)-enhanced magnetic resonance imaging (MRI) provides highly sensitive assessment of inflammatory and destructive changes in rheumatoid arthritis (RA) joints, but intravenous (IV) Gd injection prolongs examination time and increases cost, invasiveness, and patient discomfort. We explored to what extent RA joint pathologies in wrists and metacarpophalangeal (MCP) joints can be reliably assessed by unenhanced MRI images compared with Gd-enhanced MRI as the reference method.

Methods. MRI data sets from 2 RA substudies were scored according to preliminary OMERACT RA MRI scoring system (RAMRIS): Substudy A included 1.0 T/1.5 T MR images from 40 RA patients, which were scored twice by 2 experienced readers. Substudy B included 0.2 T dedicated extremity MRI (E-MRI) images from 55 patients, scored twice by one experienced reader. The first reading included only unenhanced images, whereas complete image sets were available for the second reading.

Results. Gd contrast injection appeared unimportant to MRI scores of bone erosions and bone edema in RA wrist and MCP joints. However, when post-Gd MRI was considered the standard reference, MRI without Gd provided only moderate to high agreement concerning assessment of synovitis, and omitting the post-Gd acquisitions increased the interreader variation on synovitis scores. Low-field (0.2 T) E-MRI in these exercises provided a lower sensitivity of unenhanced imaging for synovitis than MRI using higher-field strengths.

Conclusion. Omitting IV contrast injection did not change scores of bone erosions and bone edema, but decreased the reliability of synovitis scores. However, this disadvantage may for some purposes be outweighed by the possibility to assess more joints and/or greater feasibility. (J Rheumatol 2009;36:1806–10; doi:10.3899/jrheum.090350)

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Numerous studies have demonstrated that magnetic resonance imaging (MRI) is more sensitive for detection of inflammatory and destructive joint changes in rheumatoid arthritis (RA) than conventional clinical, biochemical, and

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radiographic methods[1,2]. This is true not only for conventional high-field MRI systems, but also for some low-field dedicated extremity MRI (E-MRI) systems[3,4].

The majority of MRI studies of RA joints have obtained T1-weighted MR images before and after intravenous (IV) injection of a gadolinium-containing contrast agent (Gd)[1-4]. Gd increases the T1 relaxation of neighboring protons, and increases the signal intensity on T1-weighted images proportionally to its local concentration. After IV injection, Gd is transported within the plasma and passes into the interstitial space depending on tissue perfusion and local microvascular permeability. Inflamed tissues, such as the synovium in active arthritis, are characterized by increased blood flow, microvascular permeability, and extracellular edema and, consequently, show increased signal intensity (enhancement) on T1-weighted post-Gd injection images[5,6]. Thus, Gd injection is used because the marked postinjection enhancement of inflamed tissues makes them easy to recognize[1-6].

Consequently, IV Gd is generally recommended for MRI assessment of RA joint changes, particularly synovitis[7]. However, the use of IV Gd markedly prolongs the examination time and increases costs, invasiveness, and patient discomfort, and thereby reduces the feasibility of MRI in RA. Further, omission of Gd injection would allow imaging of more joints, which potentially could provide information that reflects the overall disease status better than MRI of 1 or 2 joint regions, i.e., could increase the content validity[8].

Some MRI sequences, such as T2-weighted fat-saturated (T2 FS) sequences and short-tau inversion recovery (STIR) sequences, display areas with a high water content as bright areas. Thus, visualization of inflamed edematous areas of the inflamed synovium should be possible. However, the performance of unenhanced MRI compared with Gd-enhanced imaging for detection of RA joint pathologies is unknown. Further, it is unknown whether E-MRI units, using a lower field strength, would provide the same results.

The aim of our study was, by comparison with Gd-enhanced MRI as the reference method, to explore to what extent RA joint pathologies in wrists and metacarpophalangeal (MCP) joints can be reliably assessed by MRI without Gd injection. Both conventional 1.0–1.5 Tesla MRI and dedicated 0.2 Tesla MRI were investigated.

MATERIALS AND METHODS

MRI data sets from 2 substudies were integrated in the present report: an intermediate/high-field MRI substudy of 40 RA patients, and a low-field dedicated E-MRI substudy of 46 RA patients and 5 healthy controls. All RA patients fulfilled the American College of Rheumatology (ACR) 1987 criteria for RA[9].

Exercise A. MRI image sets from 40 RA patients [23 women/17 men; median age 59 yrs (range 26–80)] were collected, 20 from Copenhagen University Hospital at Hvidovre, Denmark, and 20 from Leeds General Infirmary, UK. Image sets comprised 10 sets of wrist joints (all from Hvidovre) and 30 sets of 2nd–5th MCP joints (20 from Leeds, 10 from Hvidovre).

Hvidovre MRI were obtained using a 1.0 T Impact MRI unit (Siemens, Erlangen, Germany) and Leeds MRI using a 1.5 T Gyroscan ACS NT system (Philips Medical Systems, Best, The Netherlands). Both these machines were conventional clinical whole-body MRI units. See Table 1 for acquired sequences.

The image sets (Figure 1) were scored twice by 2 experienced readers (MØ and POC) blinded to patient details. The first reading ("–Gd") included only images obtained without IV Gd (coronal and axial T1-weighted images, plus either coronal STIR or coronal T2-weighted FS images. For the second reading ("+Gd"), which was done after –Gd scores were collected from readers and images were reordered with new numbers (to ensure that readers could not compare with the scores of the first reading), complete image sets including post-Gd coronal and axial T1-weighted images were available. The images were scored in accordance with preliminary suggestions by the OMERACT-MRI in RA group (erosions and edema: each bone scored 0–10; synovitis: each MCP joint and each of 3 wrist joint areas scored 0–3)[10]. Mixed-effects model intraclass correlation coefficients (ICC) were used to assess agreements between scores.

Exercise B. In this low-field dedicated E-MRI study, MRI image sets (wrist and 2nd–5th MCP joints) from 45 patients with RA [36 women/11 men; median age 54.5 yrs (range 24–78)] and 9 healthy controls [8 women/1 man; median age 43 yrs (range 29–53)] obtained on a 0.2 T low-field dedicated MRI unit (Artoscan, Esaote Biomedica, Genoa, Italy) were collected. The patients were recruited from the Department of Rheumatology, Copenhagen University Hospital at Hvidovre. See Table 1 for sequences.

The MRI image sets were scored twice by one experienced reader (BE). The first reading (–Gd set) included only nonenhanced images: coronal and axial T1-weighted gradient-echo images and coronal STIR images. At the second reading, complete image sets (+Gd set), i.e., nonenhanced as well as contrast enhanced images, were assessed. The images were scored for bone erosion and synovitis as described above.

Statistics. In exercises A and B, the sensitivity, specificity, and accuracy of unenhanced MRI were calculated with Gd-enhanced MRI as the standard reference method. Mixed-effects model ICC were used to assess agreements between scores.

RESULTS

Substudy A. The main results are summarized in Table 2. Concerning bone erosions, the agreement between –Gd and +Gd readings was very high for bone erosions with respect to sensitivity, specificity, accuracy, and ICC. Further, interreader agreements were all high [ICC = 0.85–0.92 (MCP); 0.73–0.74 (wrists)] and were practically identical on –Gd and +Gd readings.

Scores for bone edema showed very high specificities of –Gd, and high sensitivities and ICC. Further, we found good +Gd interreader agreements (ICC = 0.71–0.79), and –Gd interreader agreements were only slightly lower (0.63–0.77). Agreements between –Gd and +Gd scores were high (0.70–0.93) for both readers.

Synovitis: The sensitivity of –Gd MRI was high, but the specificity only moderate. +Gd interreader agreements were high (ICC = 0.60–0.88), whereas –Gd interreader agreements (0.59–0.60) were somewhat lower.

Substudy B. The main results are summarized in Table 3. For erosions, both the sensitivity and specificity were very high. For synovitis, sensitivity of –Gd was only moderate (0.60), while specificity was high.

–Gd MRI detected synovitis in 39% of MCP joints with

Table 1. MRI acquisitions in Exercises A and B.

Center/MRI unit	Sequence	Plane	FS	Gd	TR (ms)	TE (mm)	ST (mm)	TI (ms)	Gap (mm)	FOV (mm)	Matrix	Time (min)
Exercise A												
Leeds	T1 SE	Cor	–	–	485	20	1.5	–	0.1	100 × 50	256 × 256	4.10
1.5 T Philips	T2 TSE SPIR	Cor	+	–	2000	100	2.0	–	0.2	100 × 100	198 × 256	3.44
Gyroscan	T1 SE	Ax	–	+/–	485	20	1.5	–	0.1	100 × 50	205 × 256	3.21
	T1 SPIR	Cor	+	+	450	20	1.5	–	0.1	100 × 100	192 × 256	8.44
Copenhagen	T1 SE	Cor	–	+/–	600	15	3.0	–	0.0	109 × 145	192 × 256	3.53
1.0 T Siemens	T1 SE	Ax	–	+/–	600–700	15	3.0	–	0.0	109 × 145	192 × 256	3.53–4.32
Impact	STIR	Cor	–	–	4500	30	3.0	150	0.0	108 × 145	182 × 256	5.5
Exercise B												
Copenhagen	3D-GE	Cor/Ax	–	+/–	30	18	1.0	–	0.0	140 × 140	256 × 256	6.5
0.2 T Esaote Artoscan	STIR	Cor	–	–	1100	24	3.0	85	0.3	140 × 140	192 × 160	5.5

FOV: field of view; FS: spectral fat saturation (+: yes; – no); Gd: IV injection of gadolinium contrast (–: sequence obtained before injection; +: sequence obtained after injection); GE: gradient echo; 3D-GE: T1-weighted 3-dimensional gradient echo sequence with subsequent multiplanar reconstruction. The flip angle was 65°. SPIR: spectral prepulse inversion recovery; ST: slice thickness; STIR: short-tau inversion recovery; T: tesla; T1-SE: T1-weighted spin-echo; TE: echo time; TI: inversion time; TR: repetition time.

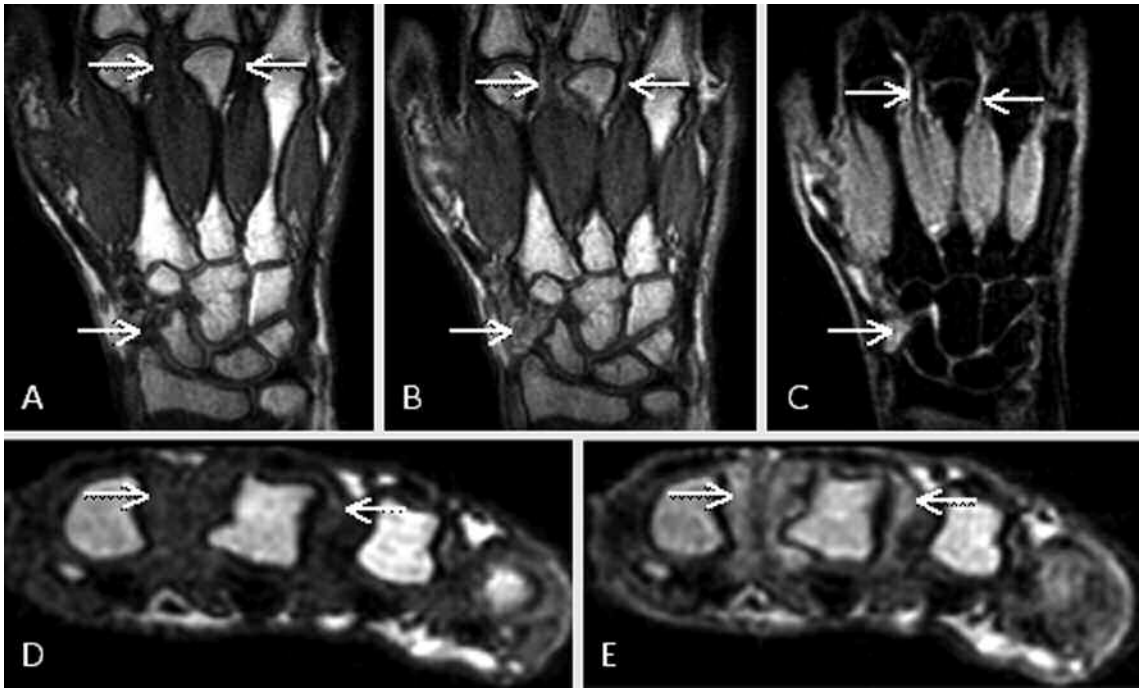

Figure 1. Low-field dedicated E-MRI of RA wrist and 2nd–5th MCP joints. Coronal (a-b) and axial (d-e) T1-weighted gradient-echo images and coronal STIR image (c) of the wrist and MCP joints before (a, c, and d) and after (b and e) IV contrast injection. Synovitis in 2nd and 3rd MCP joints and in the wrist (arrows) is seen both on STIR images and on contrast-enhanced images (arrows).

synovitis grade 1 at enhanced MRI, while 50% of grade 2 synovitis and 80% with grade 3 synovitis, i.e., the sensitivity of –Gd MRI was markedly higher for detecting high-grade synovitis on enhanced MRI. Bone edema was not studied.

DISCUSSION

Our study investigated to what extent omitting IV Gd contrast injection changes the assessment of inflammatory and destructive joint changes when MRI scans of RA joints are scored with the OMERACT RA MRI Score (RAMRIS). Gd injection appeared to be unimportant to MRI scores of bone erosions and bone edema in RA wrist and MCP joints. When post-Gd MRI was considered the standard reference, MRI without Gd provided only moderate to high agreement concerning assessment of synovitis. Further, omitting the post-Gd acquisitions increased the interreader variation on synovitis assessments. In the present exercises, low-field (0.2 T) MRI demonstrated a lower sensitivity of unenhanced imaging for synovitis than MRI using higher field strengths.

Table 2. Exercise A: detection of synovitis, bone erosion, and bone edema by unenhanced MRI, when gadolinium-enhanced MRI is considered the gold standard reference, and interobserver agreement evaluating MR images without and with gadolinium injection.

Type of Pathology	Joints	Image Sets	Performance of Unenhanced (–Gd) MRI*						Interobserver Agreement**	
			Sensitivity	Specificity	PPV	NPV	Accuracy	ICC	ICC –Gd†	ICC + Gd†
Bone erosion	MCP	All	0.94	0.94	0.95	0.94	0.94	0.92	0.85	0.92
	MCP	1.5 T, T2 FS	0.95	0.93	0.95	0.93	0.94	0.91	0.81	0.95
	MCP	1.0 T, STIR	0.91	0.96	0.93	0.95	0.94	0.95	0.92	0.87
	Wrist	All	0.89	0.84	0.83	0.93	0.87	0.87	0.74	0.73
Bone edema	MCP	All	0.71	0.88	0.73	0.88	0.83	0.75	0.63	0.71
	MCP	1.5 T, T2 FS	0.74	0.84	0.76	0.83	0.79	0.74	0.58	0.66
	MCP	1.0 T, STIR	0.72	0.95	0.70	0.96	0.92	0.78	0.73	0.81
	Wrist	All	0.83	0.96	0.80	0.97	0.94	0.91	0.77	0.79
Synovitis	MCP	All	0.90	0.49	0.90	0.47	0.84	0.67	0.61	0.88
	MCP	1.5 T, T2 FS	0.93	0.31	0.93	0.38	0.78	0.69	0.72	0.88
	MCP	1.0 T, STIR	0.86	0.79	0.83	0.54	0.77	0.63	0.40	0.87
	Wrist	All	0.87	0.42	0.83	0.49	0.77	0.76	0.59	0.60

* Values are means of values for observer 1 and observer 2. No major or systematic differences between observers were observed. ** ICC: single measures intraclass correlation coefficient between readings on unenhanced and enhanced MRI (can be considered a "worst-case scenario" intraobserver ICC). † ICC –Gd: ICC for intraobserver agreement based on assessment of unenhanced images only; ICC + Gd: ICC for intraobserver agreement based on assessment of entire image sets, including Gd-enhanced images. PPV: positive predictive value of presence of pathology on unenhanced MRI, with Gd-enhanced MRI as the gold standard reference; NPV: negative predictive value of absence of pathology on unenhanced MRI, with Gd-enhanced MRI as the gold standard reference; MCP: metacarpophalangeal joints; STIR: short-tau inversion recovery; T: tesla; T2FS T2-weighted images with spectral fat saturation.

Table 3. Exercise B. Detection of synovitis and bone erosion by unenhanced low-field E-MRI, when gadolinium-enhanced MRI is considered the gold standard reference.

Type of pathology	Joints	Performance Unenhanced (–Gd) MRI*			
		Sensitivity	Specificity	Accuracy	ICC**
Erosion	Wrist and MCP	0.93	0.99	0.97	0.99
Synovitis	Wrist and MCP	0.60	0.96	0.76	0.61

* Values are means of values for observer 1 and observer 2. No major or systematic differences between observers were observed. ** ICC single measures intraclass correlation coefficient between readings on unenhanced and enhanced MRI (this value can be considered a "worst-case" scenario intraobserver ICC).

Assessment of synovitis by unenhanced MRI was not quite as reliable using high-field MRI, and the reliability of synovitis assessments was further reduced when low-field E-MRI was employed. However, the unenhanced E-MRI still detected the majority of the most severe synovitis (80% of grade 3 synovitis scores), and these severely involved joints may be particularly clinically important. The disadvantage of unenhanced MRI not optimally detecting synovitis may, depending on the purpose of the MRI examination, be outweighed by the advantage of the ability to assess more joints and/or higher feasibility (reduced invasiveness, duration, and cost).

It is noted that the specificity of synovitis by the STIR sequence was high, in both the low-field E-MRI study and the high-field study, whereas using the T2 FS sequence provided lower specificities (albeit the highest sensitivity). Although it should be remembered that the patient materials differed between the subsections of this study, this may suggest that the STIR sequence is more robust and does not lead to overestimation of synovitis, albeit at the expense of a somewhat lower sensitivity. Reasons contributing to a lower specificity of T2 FS sequences could be susceptibility to noise from vessels and, in particular, incomplete fat suppression in some patients. The fat saturation in FS sequences is based on "turning off" the fat signal by applying a radio frequency pulse with exactly the same frequency as the precession frequency of the protons in fat, and this requires a very homogenous magnetic field. This makes the sequence more susceptible to inhomogeneities in the magnetic field than the STIR sequence, within which the image contrast is based on relaxation time differences. The fact that the STIR sequence appears to provide fairly robust and specific results is convenient, because STIR sequences can be obtained by both high and low-field machines, whereas T2 FS sequences can only be obtained by high-field units.

The assessments of bone erosions and bone edema were, as expected, not markedly affected by omitting the contrast-enhanced images, as these pathologies are recommended to be scored mainly on T1-weighted precontrast images and STIR/T2 FS images, respectively. However, exact knowledge of whether synovitis was present in a joint or not could theoretically affect the assessment of erosions and

bone edema. However, our study showed that this was not the case, or only to a very limited extent.

Some limitations of our study should be mentioned. The "intermediate/high-field MRI" were obtained on 1.0 and 1.5 T units in 1998–2002. It is likely that using state of the art high-field units today would provide a higher agreement between unenhanced and Gd-enhanced assessments. Further, other technical developments, such as 3-Tesla imaging, may provide additional options. In exercise A, bone edema was scored from 0 to 10 according to the 2001 OMERACT recommendations[10], while later recommendations have suggested using a 4-step scale (score 0–3)[7]. However, this difference is not expected to have markedly affected our results.

In conclusion, our study showed that Gd contrast injection appeared to be unimportant to MRI scores of bone erosions and bone edema in RA wrist and MCP joints. However, when post-Gd MRI was considered the standard reference for assessing synovitis, MRI without Gd provided only moderate to high agreement, and omitting the post-Gd acquisitions increased the interreader variation. Low-field (0.2 T) E-MRI in these exercises provided a lower sensitivity of unenhanced imaging for synovitis than MRI using higher field strengths. However, these disadvantages of unenhanced MRI may for some purposes be outweighed by the advantage of the ability to assess more joints and/or greater feasibility.

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