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ORIGINAL ARTICLE

Maximum intensity projection as a tool to diagnose early rheumatoid arthritis

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Abstract In this study, we investigated the usefulness of contrast-enhanced MRI with maximum intensity projection (MIP) as a convenient tool for detecting early rheumatoid arthritis (RA). A total of 21 patients with undiagnosed arthritis of the hands at the initial visit were enrolled in a prospective study over a 1-year period. The number of swollen joints found during physical examination at this first visit, the results of serological tests and the number of synovitis joints diagnosed on MIP images were compared between the RA group and non-RA group. Of the 21 patients, 17 (81%) from the initial study who were followed up for an additional 1 year entered this study. Of these, 5 met the conditions for diagnosis of RA during follow-up, and 12 did not. MIP images were used to review the arthritis of RA patients, and a significant difference was found in the number of synovitis inflammations detected with MIP images when compared with findings after physical examinations. The two criteria of positive CARF and/or anti-CCP antibody and symmetrical synovitis in bilateral hands on MIP images allowed the prediction of RA with 100% sensitivity and 75% specificity. Thus, MIP is a useful tool for making early diagnosis of RA because it yields clear visualization even with just one image.

Keywords Magnetic resonance imaging · Maximum intensity projection · Rheumatoid arthritis · Diagnosis

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Introduction

Treatment for rheumatoid arthritis (RA) has recently been dramatically improved. With the introduction of newly developed disease-modifying anti-rheumatic drugs (DMARDs) and biological agents, the prevention of future joint deformities and a remission of the disease can be achieved. Therefore, an early diagnosis of RA is becoming more important [5], and improvements in the use of diagnostic tools, such as anticyclic citrullinated peptide antibodies (anti-CCP antibody) and magnetic resonance imaging (MRI), have been made.

The validity of MRI in diagnosing early RA is improving, since it shows greater sensitivity than radiography in detecting synovitis [6, 14, 15]. However, evaluations based on MRI images are occasionally difficult and time consuming. This study was performed to investigate the usefulness of contrast-enhanced MRI with maximum intensity projection (MIP) as a simple tool to diagnose synovitis and detect early RA.

Patients and methods

Between 2002 and 2005, 21 patients with undiagnosed arthritis of the hands at the initial visit were studied prospectively for a 1-year period. Informed consent was

received from the patients in the study after obtaining approval from the local research ethics committee (Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan).

At the initial visit, the number, location, and symmetry of swollen joints observed during physical examination were recorded by an experienced rheumatologist (T.D., JCR; Japan College of Rheumatology senior fellow). A total of 22 joints, including the proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints and wrists (carpi radialis joints, midcarpal joints, and distal radioulnar joints) in the bilateral hands, were investigated.

Posteroanterior and anterior oblique view radiographs of the hands as well as posteroanterior and lateral view radiographs of the wrist joints were taken in the usual manner. Patients with positive erosion or unequivocal cortical demineralization on plain X-rays of the hands and wrists were excluded from the study.

A serological test to examine C-reactive protein (CRP), anti-agalactosyl IgG antibodies (CARF), and anti-CCP antibody was performed and analyzed.

MRI was performed using a 1.5-T superconducting magnet (Signa 1.5T; GE Healthcare, USA) equipped with a 4-channel phased array body coil or QD head coil. Both hands of the patients were imaged. The patients underwent imaging in a prone or supine position, with arms semi-flexed above the head and hands positioned in the center of the coil. Straps kept the palms and the fingers extended, aligning the carpus with the metacarpals. In all patients, an intravenous bolus of 0.1 mmol gadopentetate dimeglumine/kg of body weight (Magnevist, Bayer Japan, Osaka) was injected, and then fat-suppressed gadolinium-enhanced transverse T1-weighted SE and fat-suppressed gadolinium-enhanced 3-D gradient echo images were obtained within 4 min. The 3-D gradient echo image was a plane in the coronal slab and covered both hands and the distal forearms. The overall imaging time was about 20 min.

The acquired gadolinium-enhanced 3-D transverse images were post-processed by means of the MIP method. Two rheumatologists—who were not shown the clinical results—independently reviewed the MIP images and diagnosed whether synovitis was present in any of the joint areas studied. They were requested to diagnose synovitis in cases with significant intra-articular gadolinium enhancement. Periarticular synovial tendinitis was included in synovitis.

A definitive diagnosis was performed at the time of follow-up (more than 1 year after initial visit) according to the American College of Rheumatology (ACR), 1987 classification criteria for RA [1]. The patients who were diagnosed with RA during the follow-up period were categorized as the RA group, the others were categorized as the non-RA group. The number of swollen joints found during physical examination at the first visit, the results of serological tests, and the number of synovitis joints diagnosed on MIP images were compared between the RA group and non-RA group.

Statistical analyses were performed using the repeated-measures analysis of variance with an unpaired *t* test and a chi-square test with Fisher's exact probability test.

Results

Of 21 patients, 17 (81%) in the initial study were followed up for more than 1 year. These included 14 women and 3 men, with a mean age of 57.7 years (range 43–77 years) and a mean follow-up period of 27.4 months (range 13–40 months). During follow-up, 5 patients met the conditions for diagnosis of RA, such as osteoarthritis of the fingers, according to ACR criteria (the RA group), and 12 did not (the non-RA group).

The CRP values at baseline were 0.14 ± 0.16 (0–0.4) mg/dl in the RA group and 0.30 ± 0.52 (0–1.5) mg/dl in the non-RA group (no significant difference). CARF was positive in all patients in the RA group and in 5 of 12 patients in the non-RA group, but this difference was not significant. Anti-CCP antibody was positive in 3 of 5 patients in the RA group (at a concentration of 100 U/ml or more in each case) and in 1 of 12 patients in the non-RA group (33.8 U/ml).

In the RA group, the number of swollen joints diagnosed during a physical examination was 1.0 ± 0.7 (range 0–2), but synovitis was diagnosed by means of contrast-enhanced MRI with MIP in 5.2 ± 1.6 joints (range 4–8). This was a significant difference in the number of these joints. MIP images were used to review the arthritis in RA patients, and a significant difference was found in the number of synovitis inflammations detected with MIP images relative to that with physical examinations (Fig. 1).

In the non-RA group, the number of swollen joints found by physical examination was 3.2 ± 3.2 (range 0–12), and synovitis was found by means of contrast-enhanced MRI with MIP in 2.7 ± 1.8 joints (range 0–8). There was no significant difference in the number of these joints (Fig. 2).

Symmetrical synovitis was observed in 11 cases on MIP—all 5 cases in the RA group and 6 of 12 cases in the non-RA group. All RA patients (5 of 5) and 3 of 12 non-RA patients showed symmetrical synovitis in bilateral hands only by MIP images, despite the fact that they had no symmetrical swelling of bilateral hands at the first medical examination. The difference in the number of these joints was significant (Table 1). In the non-RA group, 3 patients showed symmetrical swelling joints upon physical examinations only, and no symmetrical synovitis on MIP images.

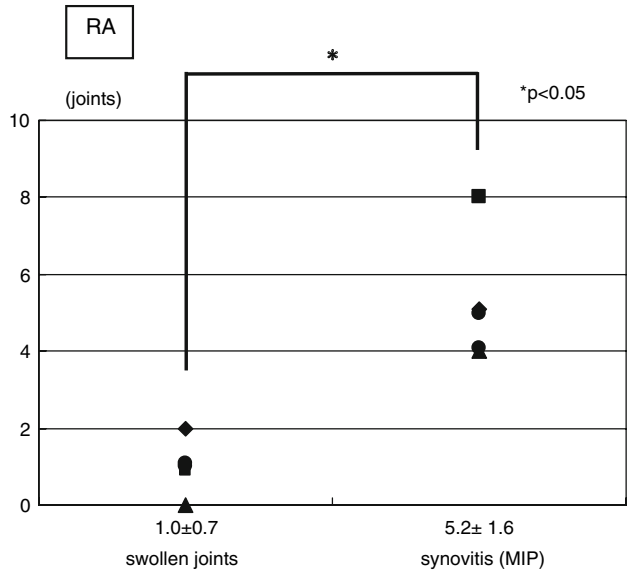

Fig. 1 In the RA group (5 cases), the number of swollen joints found during a physical examination was 1.0 ± 0.7 (range 0–2), and synovitis was found using contrast-enhanced MRI with MIP in 5.2 ± 1.6 joints (range 4–8). There was a significant difference in the number of these joints

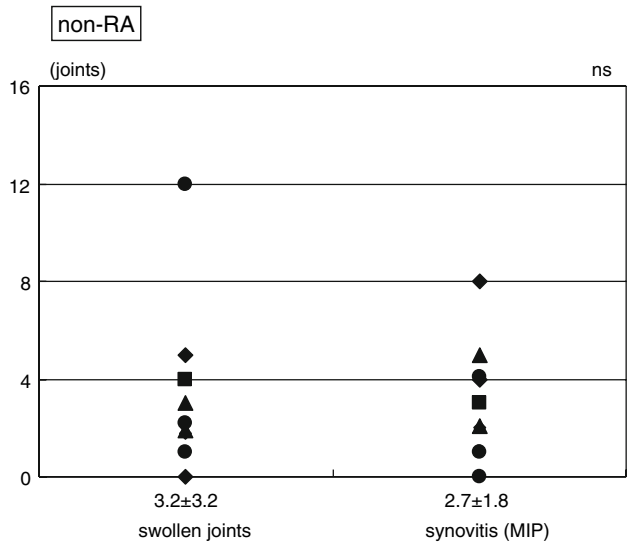

Fig. 2 In the non-RA group (12 cases), the number of swollen joints found during physical examination was 3.2 ± 3.2 (range 0–12), and synovitis was found using contrast-enhanced MRI with MIP in 2.7 ± 1.8 joints (range 0–8). There was no significant difference in the number of these joints

Discussion

Recently, there have been several reports about the usefulness of contrast-enhanced MRI for early diagnosis of RA [4, 6, 8, 10, 12, 16, 18, 19, 22]. In a study by McQueen et al. [12] MRI revealed carpal erosions in 45% and synovitis in 70% of a group of RA patients at 4 months from the onset of symptoms, only 15% of whom had erosions on plain radiographs [11]. Tamai et al. [20, 21] reported that, at the first visit, a total score of 2 or more on three objective criteria (anti-CCP antibody and/or IgM-RF; symmetric synovitis on MRI; bone-marrow edema and/or bone erosion on MRI) predicted RA with 82.5% sensitivity and 84.8% specificity. It is significant for a diagnosis of early RA that symmetrical synovitis is visible on MRI. In a study by Haavardsholm et al. [7], ten sets of the first visit and a 1-year follow-up on MR images of the wrists of patients with progressive changes on conventional hand radiographs were scored independently by four readers on two consecutive days, preceded by reader training and calibration.

Table 1 Symmetrical synovitis on MRI (MIP), and all RA patients (5 of 5) and 3 of 12 non-RA patients showed symmetrical synovitis in bilateral hands only by MIP images, despite the fact that they had no symmetrical swelling of bilateral hands at the first medical examination

	Symmetrical synovitis with MRI (MIP)		Symmetrical synovitis only with MRI (MIP) and no symmetrical swelling joints	
	(+)	(−)	(+)	(−)
RA	5	0	5*	0*
Non-RA	6	6	3*	9*

NS not significant

* $P < 0.05$

MRI has the greatest sensitivity for detecting and monitoring synovitis, bone erosions, and bone-marrow edema, and it can also detect and follow pre-erosive features of RA. MRI has become the new golden standard for an assessment of RA joints. But it must be noted that diagnostic imaging takes time and requires experienced readers because of multiple articular inflammation. Recently, in the EULAR recommendations for the management of early arthritis, MRI and ultrasonography were proposed as promising techniques that may become valuable in the diagnosis, prognosis, and therapeutic monitoring of early arthritis. However, the report also mentioned that their use is still experimental and sometimes controversial, and their merits in routine clinical practice have yet to be defined [2].

MIP is an image-processing method of contrast-enhanced MRI [13]. It is used to visualize high-intensity structures within volumetric data. At each pixel, the highest data value encountered along a corresponding viewing ray is depicted in 3-D, thus allowing clear visualization and easy diagnosis with one image (Fig. 3). Fishman et al. [3] reported a comparison of volume rendering versus MIP using CT angiography.

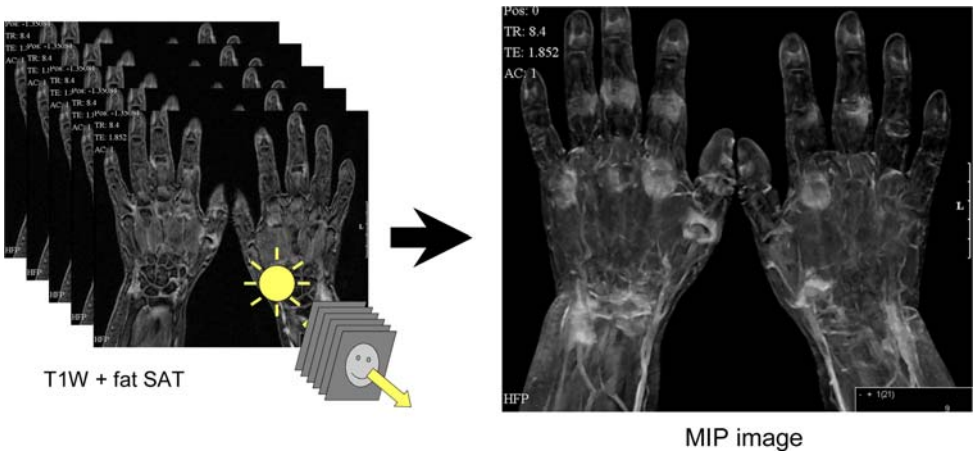

Fig. 3 Fat-suppressed, gadolinium-enhanced transverse T1-weighted SE images and gadolinium-enhanced transverse images were obtained, and the highest data value for each pixel encountered along a corresponding viewing ray is rendered for a 3-D image

Table 2 Criteria for predicting RA: positive CARF and/or anti-CCP antibody and symmetrical synovitis in bilateral hands on MIP images

	CARF(+) and/or anti- CCP ab(+) and symmetrical synovitis with MRI(MIP)	
	(+)	(−)
RA	5*	0*
Non-RA	3*	9*

Sensitivity 100%, specificity 75%

* $P < 0.05$

In this study, there was a significant difference between the numbers of synovitis inflammations found with MIP images and with physical examinations of RA patients.

All RA patients and 5 of 12 non-RA patients had positive CARF and/or anti-CCP antibodies. There was no significant difference in the number of patients. The criteria of positive CARF and/or anti-CCP antibodies and symmetrical synovitis in bilateral hands on MIP images allowed the prediction of RA with 100% sensitivity and 75% specificity. There was a significant difference in the number of patients (Table 2).

MIP is a useful tool for making an early diagnosis of RA because it yields clear visualization even with only one image. It allows easy and early diagnosis of RA and will reduce inter-reader errors due to its high sensitivity. We must also note that contrast-enhanced MRI is expensive, and the drawback of MIP images is that they do not depict small changes, which can occasionally make diagnosis of RA difficult. For the more accurate diagnosis, conventional X-rays, computed tomography [9, 15], ultrasonography, and MRI should all be used. Nonetheless, it is obvious that MIP will be very useful in the diagnosis of RA.

The limitations of this study are that we could not define the reproducibility of diagnosis using MIP and the errors between doctors who evaluated the findings. Furthermore, quantitative analysis of the synovitis shown in MIP images should have been performed.

It has recently been suggested that future MRI studies for assessing both inflammatory and destructive changes in RA joints should at least include imaging in two planes with T1-weighted images before and after intravenous gadolinium contrast and a T2-weighted fat-saturated sequence or STIR (short TI inversion recovery) by OMERACT (outcome measures in rheumatology). Furthermore, OMERACT has proposed a scoring system for contrast-enhanced MRI, named RAMRIS (rheumatoid arthritis magnetic resonance imaging scoring system) [7, 17]. We believe that MIP should also have a scoring system, and this should be the subject of future MIP research.

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