Dynamic Contrast-enhanced Magnetic Resonance Imaging of Articular and Extraarticular Synovial Structures of the Hands in Patients with Psoriatic Arthritis

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ABSTRACT. ***Objective.*** Dynamic, contrast-enhanced magnetic resonance imaging (DCE-MRI), the quantification of enhancement within the synovial membrane and bone by extracting curves using fast T1-weighted sequences during intravenous administration of contrast agent, evaluates synovitis and bone marrow edema in psoriatic arthritis (PsA). In this pilot study, we looked at possible differences between joint synovitis and tenosynovitis in PsA as compared with rheumatoid arthritis (RA).

Methods. Seven patients with PsA and 10 with RA were studied. After DCE-MRI was performed on 3 axial slices of the wrist, the enhancement ratio was calculated on 6 different regions of interest (ROI) of the synovial membrane outlined by the operator: the wrist compartment, 3 extensor tendon compartments, and 2 flexor compartments. DCE-MRI results were quantitatively analyzed using the Dynamika software, a computer-aided semiautomated method.

Results. In PsA, the area of the ROI outlined around the first and second extensor compartments was larger than in RA; the opposite was true for the extensor carpi ulnaris region. The volume of inflammation was significantly higher in RA than in PsA for all the extensor compartments except the second, and in the joint synovial membrane. The DCE-MRI indicators of the degree of inflammation were higher for PsA in the joint synovial membrane ($p = 0.002$ and $p < 0.001$, respectively). There was a significant correlation between volume of inflammation but not its degree and 28-joint Disease Activity Score at the level of the wrist joint ($r = 0.6$; $p = 0.01$).

Conclusion. DCE-MRI can reveal useful and potentially clinically important information on the characteristics of different types of arthritis. (J Rheumatol 2012;39 Suppl 89:44–48; doi:10.3899/jrheum.120242)

Key Indexing Terms:
PSORIATIC ARTHRITIS RHEUMATOID ARTHRITIS SYNOVITIS TENOSYNOVITIS MAGNETIC RESONANCE IMAGING DYNAMIC MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) is widely used to assess the joints of patients with seronegative spondyloarthritides[1]. It allows early diagnosis of undifferentiated spondyloarthritides by showing bone marrow edema (BME) of the sacroiliac joints and of the vertebrae[2]. In psoriatic arthritis (PsA), MRI can also help in the evaluation of peripheral joints and reveal synovitis, BME, erosions, tenosynovitis, enthesitis, periostitis, and soft tissue edema. These findings could be useful for diagnosis and for the followup of treatment[3]. The Outcome Measures in Rheumatology study group for MRI has developed a scoring system to evaluate lesions in the metacarpophalangeal and interphalangeal joints, called the PsA MRI scoring system[4]. The performance of this scoring system is good for assessing erosions and BME but only

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Supported in part by a grant from Progetti di Ateneo, University of Genoa. The OAK Foundation supported Dr. Boesen's research through the Parker Institute with an unrestricted grant.

Dr. Kubassova is founder and managing director of Image Analysis, producer of the software used in this study. Dr. Boesen has acted as an independent unpaid adviser to Image Analysis. Dr. Cimmino acted as an independent unpaid adviser to Esaote.

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modest for other features[4]. In addition, the wrist, which is often involved in PsA[5], is not included among the studied joints. An alternative method to evaluate synovitis and possibly BME in PsA is the quantification of enhancement within the synovial membrane and bone by extracting curves using a fast T1-weighted sequence during intravenous administration of gadolinium contrast agent[6]. This method, known as dynamic, contrast-enhanced MRI (DCE-MRI), showed that in PsA the degree of synovitis is similar to that observed in rheumatoid arthritis (RA)[6]. Automated analysis of the resulting curves has been developed to further increase the speed and objectivity of the examination[7].

In our pilot study, DCE-MRI of the wrist in patients with PsA is performed and studied to look at possible differences between joint synovitis and tenosynovitis, and to compare the results with those seen in RA.

MATERIALS AND METHODS

Seven patients (5 women) with PsA according to the CASPAR criteria[8] were studied. The mean age was 61.7 ± 14 years. The MRI examination was repeated in 3 patients after 3 months of anti-tumor necrosis factor-α (TNF-α) treatment (infliximab in 1 patient and etanercept in 2). For comparison, 10 patients with RA diagnosed according to the 1987 American College of Rheumatology criteria[9] were also studied. There were 8 women and the mean age was 44.7 ± 11.4 years. Clinical and laboratory characteristics, including number of swollen and tender joints, pain visual analog scale (VAS), and C-reactive protein (CRP), were recorded at the time of MRI examination.

MRI of the more severely involved wrist was performed with a 0.2T extremity-dedicated machine (Artoscan C, Esaote, Genoa, Italy) equipped with a permanent magnet and with a dedicated hand and wrist coil, as described[10]. The hand was fixed in the neutral position, with fingers extended and the thumb up, using several supporting foam pillows. The field of view was 120 mm and allowed evaluation of the carpal bones, the proximal metacarpal heads, and the distal radius and ulna. Starting exactly at the time of the intravenous injection of 0.2 ml/kg body weight gadopentetic acid contrast medium (Magnevist, Bayer Schering Pharma, Berlin, Germany) in 30 s through a 21–mm butterfly needle into a cubital vein, 20 consecutive acquisitions of 3 prepositioned 5-mm axial T1-weighted spin echo images (TR 100 ms, TE 16 ms, 160 × 128 matrix, 150 × 150 FOV, NEX 1) were obtained. The first of the 3 axial prepositioned DCE-MRI slices with no interslice gap was positioned tangentially to the radius. Each slice was obtained every 18 s, for 360 s.

The enhancement ratio was calculated on 6 different regions of interest (ROI) of the synovial membrane outlined by the operator: the wrist compartment, 3 extensor tendon compartments (the first including the extensor pollicis brevis and abductor pollicis longus, the second including the extensor carpi radialis brevis and longus, the extensor pollicis longus, the extensor digitorum communis, extensor indicus proprius, and extensor digiti quinti proprius, and the third including the extensor carpi ulnaris), and finally 2 flexor tendon compartments, including the ulnar bursa with the flexor digitorum profundus and superficialis, the flexor pollicis longus, and the flexor carpi radialis in the first compartment and the flexor carpi ulnaris in the second (Figure 1). DCE-MRI results were analyzed using the Dynamika software version 3.1.2, a computer-aided semiautomated method for quantitative analysis (Image Analysis Ltd., www.imageanalysis.org.uk)[11]. It includes motion reduction functionality algorithms able to reduce artifacts associated with hand movement during the examination. The imaging processing software analyzes dynamic slices on a voxel-by-voxel basis for the whole slice or in a user-defined ROI. The signal intensity vs time curves are extracted from each voxel and automatically assigned to 1 of 4 patterns of contrast uptake described as either "no enhancement," "persistent," "plateau," or "washout." The no enhancement and persistent patterns are typical for disease-unaffected tissues and background. The plateau and washout are typical for tissues with large perfusion such as inflamed synovial membrane or blood vessels. Further, measures characterizing contrast uptake dynamics are extracted, such as maximum enhancement (ME), calculated as maximum increase in the postcontrast signal intensity divided by the baseline signal intensity, and initial rate of enhancement (IRE), calculated as increase in signal intensity in percent/second from time of onset of enhancement until ME is reached. The highest values for ME and IRE are shown in the color map superimposed on the MRI image in bright yellow/white and lower values in redder colors. From each set, the following measures were used for further analysis: the sum of voxels with the patterns of persistent, plateau, and washout enhancement (Ntotal), IRE, and ME. The Ntotal represents a measure of the volume of inflammation, whereas IRE and ME reflect the severity or degree of inflammation, as previously described[12]. To compare the results between diseases, absolute values were used. To compare them within patients with PsA, figures were divided by the area of the compartments.

RESULTS

Patients with RA had a higher number of tender (18.1 ± 5.8 vs 5.4 ± 10.1; $p = 0.005$) and swollen (14 ± 5 vs 3 ± 2.7; $p < 0.001$) joints than those with PsA, but were similar for pain VAS (62.6 ± 28 mm vs 44 ± 26.6 mm; $p = 0.19$) and C-reactive protein concentration (18.3 ± 15.4 mg/dl vs 12.4 ± 12.8 mg/dl; $p = 0.41$). The 28-joint Disease Activity Score (DAS28) CRP was 6.2 ± 1 in RA and 3.7 ± 1.4 in PsA ($p = 0.001$). The main MRI results of the study are reported in Table 1. The area of the ROI outlined around the different compartments examined was similar for PsA and RA in the joint synovial membrane and flexor tendons. Conversely, the area was significantly higher in PsA for the first and second extensor compartments, and for RA in the extensor carpi ulnaris region (Figure 1). In both PsA and RA, disease activity measured by DCE-MRI gave similar results in the synovial joint compartment and in the synovial sheaths. The volume of inflammation, measured by Ntotal, was significantly higher in RA than in PsA for all the extensor compartments, except the second. Conversely, IRE and ME, i.e., the indicators of the degree of inflammation, were similar in both diseases in this location. IRE was higher for PsA in the first flexor compartment ($p = 0.04$). Both IRE and ME were higher for PsA in the joint synovial membrane ($p = 0.002$ and $p < 0.001$, respectively). Ntotal ($p = 0.002$), including all its components, was higher for RA in the joint synovial membrane. There was a significant correlation between Ntotal, but not ME and IRE, and DAS28 at the level of the wrist joint ($r = 0.6$; $p = 0.01$). The number of swollen joints correlated with IRE ($p = 0.03$) and Ntotal ($p = 0.002$). After treatment, the decrease in synovial enhancement was slightly more evident in the extensor tendon sheath in comparison to the flexor tendons and joint compartments (Figure 2).

DISCUSSION

Our preliminary data emphasize the possibility to discriminate between different localizations and components of

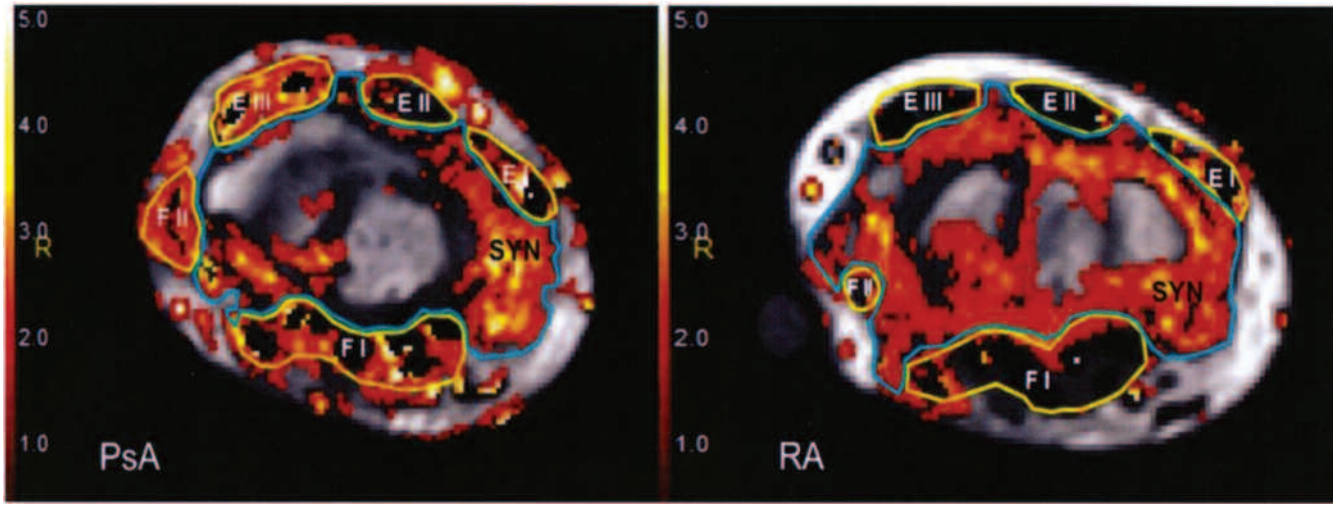

Figure 1. Representative parametric maps of dynamic, contrast-enhanced magnetic resonance imaging (MRI) data of maximum enhancement superimposed on an axial T1-weighted dynamic MRI of the wrist in a patient with psoriatic arthritis (PsA) and another patient with rheumatoid arthritis (RA). The region of interest containing the wrist synovial membrane is outlined in light blue; regions around the tendon sheaths are yellow. The different synovial compartments evaluated are outlined (SYN = joint synovial membrane; EI-III = first to third extensor compartment; FI-II = first and second flexor compartment). In this example, tenoynovitis prevails in PsA and joint synovitis in RA.

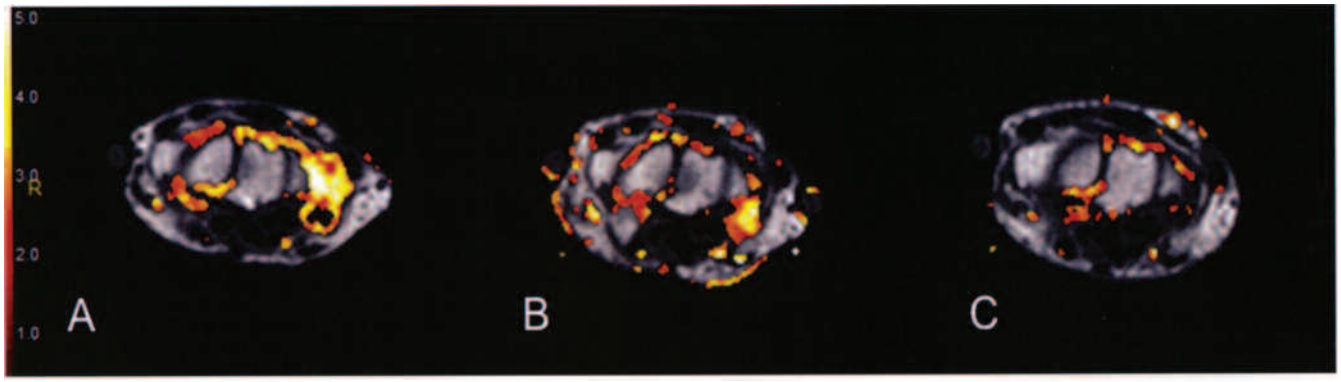

Figure 2. Dynamic, contrast-enhanced magnetic resonance imaging maps of the wrist in a patient with psoriatic arthritis during anti-tumor necrosis factor-α treatment, at baseline (A), and after 1 month (B) and 6 months (C) of therapy. Note the clear decrease of enhancement in the joint synovial membrane and in the synovial sheath of the flexor carpi radialis.

inflammation in the arthritic synovial membrane. No difference was observed in the volume and degree of inflammation between tenosynovitis, with extensor and flexor tenosynovitis in the different compartments, and joint synovitis. Posttreatment decrease in synovial inflammation tended to be more pronounced in the extensor tendon sheath, although not significantly. MRI surface calculations highlighted the wrist synovial sheaths that are more frequently involved in PsA (first and second compartments of the extensor tendons) and RA (extensor carpi ulnaris)[13]. These significant differences in tendon compartment areas were independent from the activity of the included synovial membrane. In the synovial membrane of the wrist joint, a peculiar pattern was observed when comparing PsA and RA: the volume of inflammation was higher in RA but its degree was higher in PsA. This is particularly intriguing because disease activity, measured by DAS28, was significantly higher in RA compared to PsA. It is possible that DAS28 is a surrogate of the amount of inflammation rather than of its intensity, as demonstrated by the significant direct correlation between DAS28 and Ntotal. This finding is different from that observed in our previous comparison on DCE-MRI in PsA and RA, where a similar degree of inflammation was observed, after correction for general disease activity[6]. However, in that study a user-designed ROI was analyzed in the wrist where the maximum enhancement was visually identified and only the equivalents of IRE and ME were studied. It is possible that more advanced and precise tools for quantification of the different measures of DCE-MRI, such as the Dynamika software, could reveal the different aspects of synovitis in greater detail. As an example, pixels with the washout pattern were more often seen in

Table 1. Results of dynamic, contrast-enhanced magnetic resonance imaging analysis in patients with psoriatic arthritis (PsA) and rheumatoid arthritis (RA), according to the different sites of synovitis and tenosynovitis. Statistical significance was not calculated for values normalized to the area because only comparisons within diseases were used.

	PsA	RA	p	PsA	RA	p
First extensor compartment				First flexor compartment		
IRE	0.015 (0–0.06)	0.003 (0–0.02)	0.04	0.015 (0–0.06)	0.003 (0–0.02)	0.04
IRE/area	3.9×10^{-5} ($0–1.1 \times 10^{-4}$)	7×10^{-6} ($0–8 \times 10^{-5}$)		3.9×10^{-5} ($0–1.1 \times 10^{-4}$)	7×10^{-6} ($0–8 \times 10^{-5}$)	
ME	1.67 ± 0.75	1.60 ± 0.22	0.79	1.67 ± 0.75	1.60 ± 0.22	0.79
ME/area	0.004 ± 0.002	0.005 ± 0.002		0.004 ± 0.002	0.005 ± 0.002	
Ntotal	55.6 ± 90.4	71.7 ± 49.9	0.64	55.6 ± 90.4	71.7 ± 49.9	0.64
Ntotal/area	0.027 (0–0.47)	0.19 (0.008–0.55)		0.027 (0–0.47)	0.19 (0.008–0.55)	
Persistent	1.28 ± 1.89	9 ± 6.32	0.007	1.28 ± 1.89	9 ± 6.32	0.007
Plateau	36.4 ± 58.9	37.6 ± 27.2	0.96	36.4 ± 58.9	37.6 ± 27.2	0.96
Washout	17.9 ± 30.2	28.3 ± 19.3	0.40	17.9 ± 30.2	28.3 ± 19.3	0.40
Area	460.4 ± 74.5	374.7 ± 100.6	0.08	460.4 ± 74.5	374.7 ± 100.6	0.08
Second extensor compartment				Second flexor compartment		
IRE	0.028 ± 0.04	0.004 ± 0.004	0.05	0.004 ± 0.005	0.004 ± 0.003	0.87
IRE/area	$9 \times 10^{-5} \pm 10^{-4}$	$4 \times 10^{-5} \pm 3 \times 10^{-5}$		0 ($0–2.5 \times 10^{-4}$)	3.7×10^{-5} (0–0.016)	
ME	1.58 ± 0.51	1.31 ± 0.53	0.38	0.83 ± 1.08	1.37 ± 0.53	0.18
ME/area	0.004 ± 0.002	0.014 ± 0.007		0.015 ± 0.02	0.024 ± 0.01	
Ntotal	57.9 ± 75.2	31.6 ± 24.5	0.32	11.8 ± 27.1	22 ± 9.5	0.37
Ntotal/area	0.13 ± 0.16	0.18 ± 0.18		0.15 ± 0.29	0.34 ± 0.15	
Persistent	1.7 ± 2.1	2.9 ± 4.1	0.5	0.14 ± 0.38	2.60 ± 2	0.006
Plateau	39.3 ± 51.2	17.6 ± 15	0.22	9.14 ± 20.4	10.9 ± 7	0.80
Washout	16.8 ± 25	11.1 ± 9.3	0.5	2.57 ± 6.8	6.8 ± 5.8	0.19
Area	455.7 ± 106.4	115.6 ± 48.3	< 0.001	58.6 ± 29.1	59 ± 12.6	0.97
Third extensor compartment				Joint synovial membrane		
IRE	0.013 ± 0.016	0.004 ± 0.002	0.07	0.013 ± 0.006	0.005 ± 0.004	0.002
IRE/area	$2 \times 10^{-4} \pm 3 \times 10^{-4}$	$2 \times 10^{-5} \pm 1 \times 10^{-6}$		$5.7 \times 10^{-6} \pm 1.5 \times 10^{-6}$	$2 \times 10^{-6} \pm 1.6 \times 10^{-6}$	
ME	1.46 ± 1.05	1.52 ± 0.16	0.86	1.85 ± 0.2	1.51 ± 0.12	< 0.001
ME/area	0.02 (0-0.05)	0.008 (0.005-0.02)		$9 \times 10^{-4} \pm 2 \times 10^{-4}$	$6 \times 10^{-4} \pm 1 \times 10^{-4}$	
Ntotal	4.43 ± 6.4	74.1 ± 58.5	0.007	366.4 ± 347.3	971.9 ± 323.6	0.002
Ntotal/area	0.09 ± 0.18	0.35 ± 0.21		0.15 ± 0.13	0.41 ± 0.12	
Persistent	0	6 ± 5.2	0.008	5 (0–23)	22 (8–113)	0.014
Plateau	3.43 ± 4.89	39.1 ± 33.5	0.02	238.7 ± 215.6	518.1 ± 188.9	0.013
Washout	1 ± 1.53	29 ± 26.7	0.01	119.3 ± 136.7	417.6 ± 214.1	0.006
Area	76 ± 21.4	190.4 ± 52.2	< 0.001	2181.1 ± 536.4	2341.1 ± 472.5	0.53

IRE: initial rate of enhancement; ME: maximum enhancement; Ntotal: Persistent + plateau + washout enhancement.

RA in most of the compartments studied. In our study, we tried to dissect the inflammatory component of joint synovitis from that of tenosynovitis to look at possible differences within and between diseases. In clinical trials the focus is on 1 joint region without inclusion of tenosynovitis. However, including tenosynovitis in the analysis might be an advantage, as this feature is part of the inflammatory load of the individual patient. This is supported in a recent publication showing that the combination of RA MRI scoring synovitis, BME, and a novel tenosynovitis score revealed higher standardized response mean during anti-TNF-α treatment than each measure alone[14].

There are a few limitations in our study. First, the number of examined patients is small, which could account for the lack of significance in the comparison of the different synovial compartments or in the followup of treated patients. In spite of this limitation, we demonstrated a different pattern of synovitis in the 2 diseases, supporting the view that DCE-MRI and its interpretation by Dynamika could represent a valid tool to investigate various types of arthritis. Second, patients with RA had more active disease than patients with PsA, as is commonly encountered in clinical practice. The absence of comparability of the 2 groups stresses differences revealed by DCE-MRI. Third, it is difficult to understand the complete significance of the findings of our pilot study in the absence of followup evaluation and correlations with different disease features. Finally, the grouping of tendons in 5 compartments was somewhat arbitrary and based on the feasibility of ROI positioning. In spite of these limititations, we feel that DCE-MRI can reveal useful and potentially clinically important information about the characteristics of arthritis.

We have shown that synovitis studied by sensitive imaging methods is similar in the wrist joint and in the synovial sheaths in both PsA and RA. This technique could also be useful to investigate different aspects of inflammation that are not easily differentiated by clinical and laboratory studies.

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