

In-office magnetic resonance imaging to monitor responses to therapy in rheumatoid arthritis

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Abstract Low-field extremity magnetic resonance imaging (MRI) has been developed as an alternative method for detecting inflammatory changes and structural damage associated with rheumatoid arthritis (RA). Studies have shown that extremity MRI is able to predict future joint damage in patients with early RA and is more sensitive than conventional radiography at detecting joint erosions. This report uses four different cases to illustrate how extremity MRI can be used to monitor disease activity and inform treatment decisions during the management of RA in the routine clinical practice setting.

Keywords MRI · Functional · Infliximab · Rheumatoid arthritis · Rituximab · Disease management · Drug therapy management

Introduction

Magnetic resonance imaging (MRI) is a highly sensitive method for the early detection of inflammatory changes and structural damage associated with rheumatoid arthritis (RA). The development of low-field extremity MRI, designed specifically for assessing the peripheral

joints, has provided a low-cost, convenient MRI tool with potential suitability for daily practice. Small clinical trials have demonstrated the utility of extremity MRI in predicting future joint damage in patients with early RA [1–3], while other studies have shown that high-resolution in-office MRI can be more sensitive than conventional radiography for detecting changes in the number and/or size of joint erosions [4, 5]. This report uses four cases to illustrate how extremity MRI can be used in routine clinical practice to monitor joint damage and response to therapy and to inform RA treatment decisions.

Patients and methods

Imaging methods

Imaging was performed using a dedicated portable MagneVu (MagneVu, Carlsbad, California) or C-Scan (Hologic Inc, Bedford, Massachusetts) extremity MRI system. Images were acquired using 3D volume T1-weighted (T1W) and short TI inversion recovery (STIR) sequences or coronal 3D T1 and STIR and axial T1.

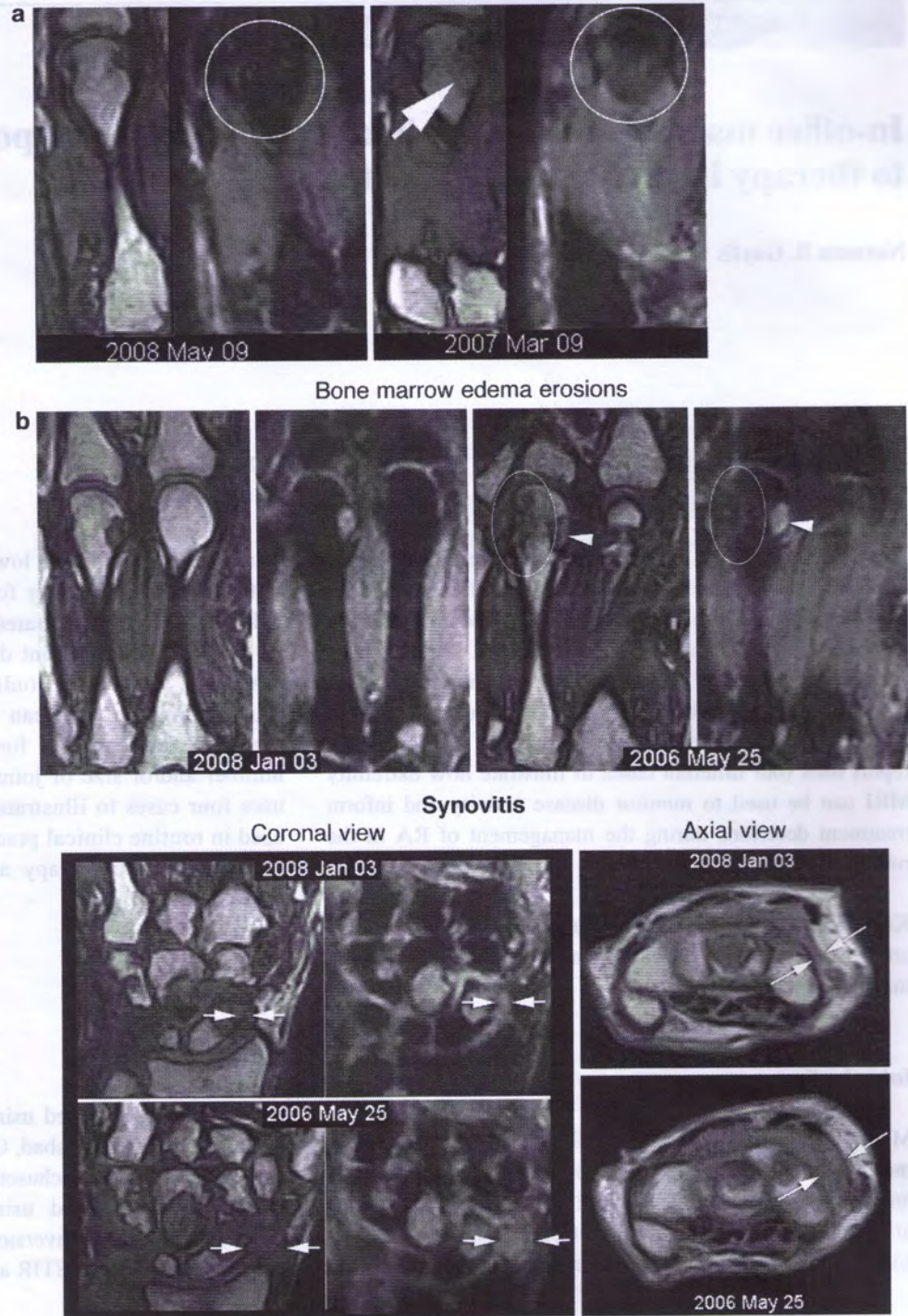
Patient 1

A 50-year-old male with a history of gout presented with swollen metacarpophalangeal (MCP) joints. An MRI scan of the left wrist (March 2007) showed synovitis and bone marrow edema osteitis of the fourth MCP (Fig. 1a). Despite the absence of other signs of RA, the patient was started on methotrexate (MTX) 17.5 mg/week and prednisone 10 mg/day. Within a few months, the patient's symptoms were well controlled and he was able to stop

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Fig. 1 Magnetic resonance imaging scans of the left wrist (patient 1) and of the hands and wrists (patient 2). **a** (patient 1): The baseline examination (March 2007; right-hand images) shows bone marrow edema/osteitis as poorly defined, low T1 signal (*arrow*) and patchy, bright, short T1 inversion recovery signal (*circle*) in the fourth metacarpal head. The follow-up examinations (May 2008; left-hand images) show resolution of these signal changes. **b** (patient 2): Bone marrow edema and erosions (*upper panels*): The baseline examination (May 2006; right-hand images) shows poorly defined erosions associated with bone marrow edema/osteitis (*circles*) of the fourth metacarpal head. The follow-up examination (January 2008; left-hand images) shows complete resolution of these changes. Note also a well-defined erosion (*arrow-heads*) that remained stable between the two examinations. *Synovitis* (*lower panels*): The baseline examination (May 2006; bottom images) showed significant synovitis adjacent to the distal pole of the scaphoid bone (*arrows*). The follow-up examination (January 2008; top images) shows regression of these changes. Erosions noted throughout the carpal bones were intervally unchanged between the two examinations. Images captured in the coronal and axial planes are shown



the prednisone, continuing on MTX 15 mg/week. Approximately 14 months later (May 2008), a follow-up MRI scan of the left wrist revealed intervally regressed osteitis and synovitis of the fourth metacarpal heads, intervally stable chronic erosions of the third and fourth metacarpal heads, and no other active marginal erosions (Fig. 1a). As a result, treatment with weekly MTX was deemed sufficient to maintain the patient's low disease activity status.

Patient 2

An 85-year-old female first presented with multiple joint pain, including swelling of the MCPs in both hands. X-ray imaging showed no frank erosive changes and her symptoms were controlled with daily prednisone. Follow-up laboratory measurements indicated significant disease activity and it was decided to commence treatment with infliximab (3 mg/kg every 8 weeks). MRI scans (May 2003) revealed

subacute erosions in the hamate and capitate bones of both wrists and in the lunate bone of the left wrist. Follow-up scans indicated no progression of these erosions over the subsequent 3 years (Fig. 1b). The patient remained on infliximab, although MTX 15 mg/week was added due to intermittent disease flaring. Symptoms became well controlled, with laboratory measures suggesting low disease activity. These observations were supported by MRI scans (January 2008; Fig. 1b). Compared with earlier scans, interval resolution of the bone marrow edema with associated erosions of the third and fourth metacarpal heads and interally regressed synovitis of the carpal bone could be seen. All other erosions noted previously were stable. The favorable MRI results supported the decision to step down maintenance therapy to infliximab alone.

Patient 3

A 55-year-old female presented in May 2005 with joint pain, fatigue, morning stiffness, and difficulty walking. Radiographic examination revealed destruction of the first and second MCP joints, fusion of the carpal bones, and synovitis in the right ankle. Initial therapy was infliximab 3 mg/kg plus MTX 15 mg/week and prednisone 10 mg/day. Following a good initial response, it was necessary to increase the infliximab dose (to 5 mg/kg) after approximately 6 months. MRI scans carried out at this time showed diffuse carpal erosions, extensive erosive changes of the first and second MCP joints, and a small erosion of the third metacarpal head in both the left and right hands (Fig. 2A). Over the next 6–12 months, the patient gradually lost responsiveness to infliximab and it was decided to switch biologic therapy to the anti-CD20 monoclonal antibody rituximab. The first course of rituximab (2 × 1,000 mg infusions given 2 weeks apart) was administered in May 2006; premedications were acetaminophen 1,000 mg, diphenhydramine 50 mg, and intravenous methylprednisone 100 mg. The patient remained on MTX. Disease activity improved and she subsequently received two further courses of rituximab at intervals of approximately 6–8 months. Follow-up MRI scans revealed no significant interval change compared with the scans conducted while the patient was receiving infliximab, with diffuse erosive changes and deformity, bony coalescence, and chronic erosive changes at the second and third metacarpal heads (Fig. 2a). In February 2008, the patient received her fourth course of rituximab and, at the time of writing, her disease is well controlled.

Patient 4

A 49-year-old female presented in October 2003 with fatigue, morning stiffness, and multiple joint pain. Initial

treatment consisted of MTX 15 mg/week, prednisone 10 mg/day, and hydroxychloroquine 200 mg twice daily. Infliximab was added 6 months later. MRI scans conducted at this time revealed carpal erosions and a small chronic erosion in the third metacarpal of the left hand, and a small dot erosion in the dorsal margin of the lunate bone of the right hand. The patient's good response to infliximab was confirmed by a second series of MRI scans, which revealed no significant changes from those seen previously. During 2005, the patient experienced intermittent disease flaring and gradually lost responsiveness to infliximab. MRI scans conducted in February 2006 showed a stable erosion in the third MCP of the left hand, which was unchanged from previous scans, and no active marginal erosions evident in either hand (Fig. 2b). In October 2006, the patient was started on rituximab (schedule and premedications as for patient 3). MRI scans performed around the time of the patient's second course of rituximab revealed no progression, with the previously noted dot erosion in the dorsal margin of the lunate bone in the right hand not easily visible on the scan images (Fig. 2b). At the time of writing, the patient has received three courses of rituximab and her RA symptoms are well controlled.

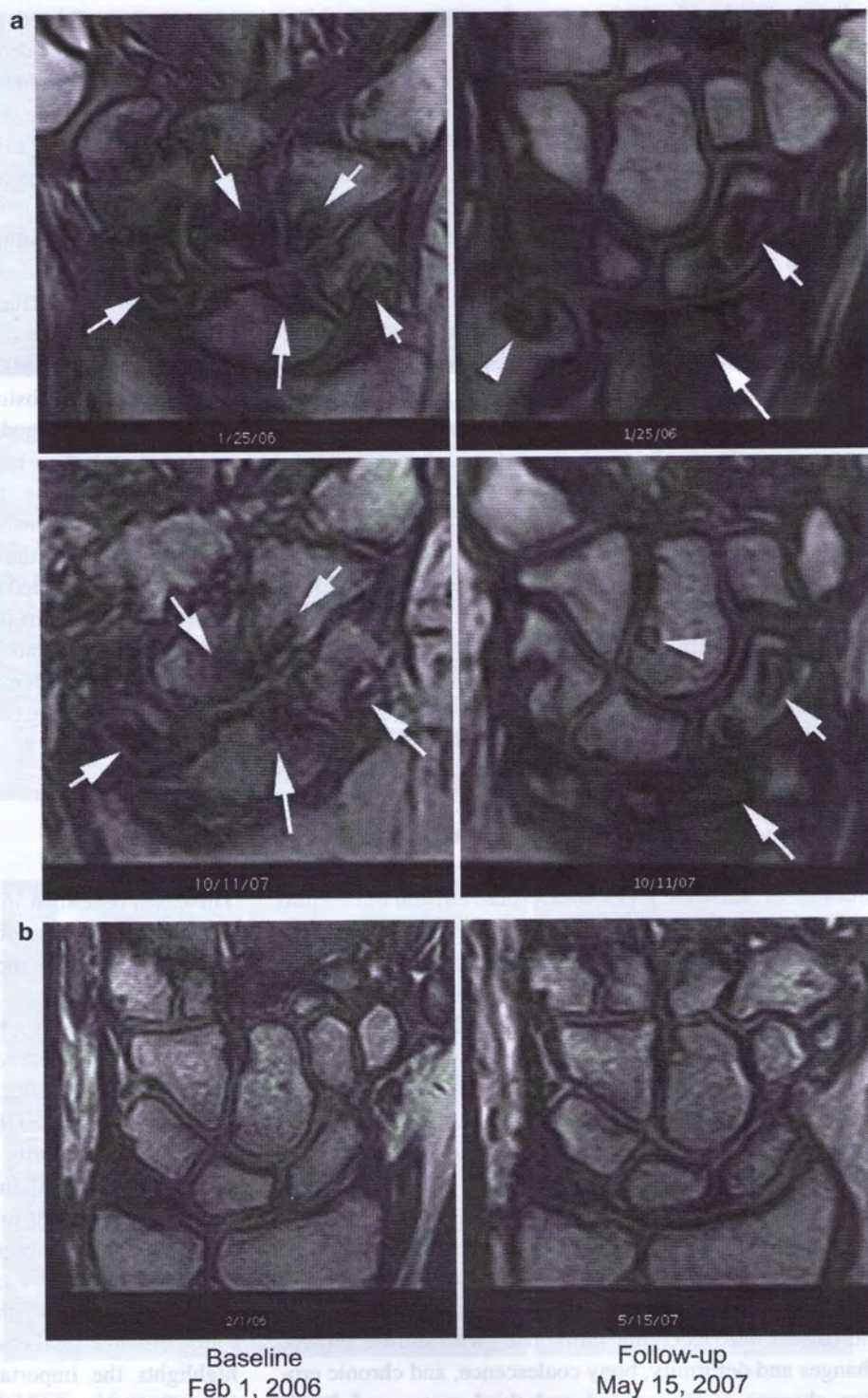
Discussion

The cases described in this report illustrate how extremity MRI imaging can be utilized in the routine in-office setting as a sensitive tool to monitor response to therapy in patients with RA.

Case 1 illustrates a typical example of a patient who, as is common practice, received non-biologic disease-modifying antirheumatic drug therapy (MTX) due to poor disease control with conventional standard of care treatment. Although the majority of patients ultimately lose responsiveness to MTX [6], the decision about whether or when to add a biologic agent to the treatment regimen can be difficult. In this particular case, the lack of joint damage progression revealed by in-office MRI provided reassurance (in conjunction with the patient's stable signs and symptoms) that step-up therapy was not necessary. The case also highlights the importance of monitoring progression of joint changes, even in the absence of other signs and symptoms of RA.

A similar scenario is illustrated by Case 2, where, instead of MTX, the patient had started biologic therapy around the time MRI monitoring began. The lack of progression of joint damage shown by MRI provided the necessary backup evidence to support the clinical and laboratory findings indicating that the disease was well controlled. Consequently, there was no requirement in this case

Fig. 2 Magnetic resonance imaging scans of the left and right wrists (patient 3) and of the left hand and wrist (patient 4). **a** (patient 3): Multiple carpal erosions of the left wrist seen at the baseline examination (January 2006) are denoted by the arrows (*top left*). These erosions were unchanged in size and number at the follow-up examination (October 2007; *bottom left*). Also shown are erosions of the scaphoid and distal radius in the right wrist at the baseline examination (*arrows, top right*), unchanged in the follow-up scan examination (*bottom right*). Erosions in the distal ulna and capitate bone (*arrowheads, top right*) were unchanged compared with other images from the same examinations (not shown). **b** (patient 4): Images of the left hand and wrist from the baseline (February 2006; *left-hand image*) and follow-up (May 2007; *right-hand image*) examinations



to switch treatment, for example to a second-line biologic agent.

Cases 3 and 4 illustrate another commonly encountered clinical situation of inadequate disease control following a period of first-line biologic therapy. Although the decision to switch to another class of biologic (rituximab, in these cases) was taken primarily in view of the patients' clinical

symptoms and laboratory findings, the use of MRI in these cases allowed precise monitoring of the joint damage that had already occurred before and during infliximab treatment. The lack of further progression on rituximab therapy and, in one case, apparent reversal of damage, revealed by the follow-up MRI, provided invaluable complementary backup to the standard monitoring of disease activity.

Previous studies have demonstrated the sensitivity of MRI compared with both conventional radiographic methods and high-field whole-body MRI in the detection of joint erosions in patients with RA [1–3]. One recent study showed in-office MRI to be approximately twice as sensitive as conventional radiography [7], while other comparative studies indicate that extremity MRI exhibits higher sensitivity in the detection of erosions in metacarpal heads and carpal bones compared with conventional radiographs [8].

The advantages of extremity MRI over other available imaging techniques include its low cost, convenience to the patient and high sensitivity. Although more expensive than conventional X-ray radiography, the superior sensitivity of MRI to detect erosive changes may prove cost-effective in the long term. As illustrated here, MRI results can provide reassurance regarding decisions to maintain treatment with non-biologic therapies earlier in the typical RA treatment algorithm, as well as guide decisions about the timing of biologic therapy. Extremity MRI should therefore be considered as a routine tool for monitoring disease activity and response to therapy in patients with RA.

Competing interests

Dr. Gaylis participates on speaker boards for Centocor, Genentech, and Eli Lilly and is, or has been, a primary investigator in clinical trials funded by Centocor, Genentech, Bristol-Myers Squibb, Rigol, Wyeth, UCB, Roche, Merrimack, and Human Genome Sciences. Dr Needell has no financial disclosures relevant to this manuscript.

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