Magnetic Resonance Imaging Is More Sensitive Than Radiographs in Detecting Change in Size of Erosions in Rheumatoid Arthritis

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ABSTRACT: Objective. To evaluate the technological performance of magnetic resonance imaging (MRI) with respect to projection radiography by determining the incidence of changes in the size of individual bone lesions in inflammatory arthritis, using serial high-resolution in-office MRI over short time intervals (8 months average followup), and by comparing the sensitivity of 3-view projection radiography with in-office MRI for detecting changes in size and number of individual erosions.

Methods. MR examinations of the wrists and second and third metacarpophalangeal joints were performed using a portable in-office MR system in a total of 405 patients with inflammatory arthritis, from one rheumatologist’s practice, who were undergoing aggressive disease modifying antirheumatic drug therapy. Of the patients, 156 were imaged at least twice, allowing evaluation of 246 followup examinations (mean followup interval of 8 months over a 2-year period). Baseline and followup plain radiographs were obtained in 165 patient intervals. Patients refused radiographic examination on 81 followup visits.

Results. MRI demonstrated no detectable changes in 124 of the 246 (50%) followup MRI examinations. An increase in the size or number of erosions was demonstrated in 74 (30%) examinations, a decrease in the size or number of erosions in 36 (15%), and both increases and decreases in erosions were seen in 11 (4%). In the 165 studies with followup radiographic comparisons, only one examination (0.8%) showed an erosion not seen on the prior examination and one (0.8%) showed an increase in a previously noted erosion.

Conclusion. We showed that high-resolution in-office MRI with an average followup of 8 months detects changes in bony disease in 50% of compliant patients during aggressive treatment for inflammatory arthritis in a single rheumatologist’s office practice. Plain radiography is insensitive for detecting changes in bone erosions for this patient population in this time frame. (First Release Aug 1 2006; J Rheumatol 2006;33:1957–67)

Key Indexing Terms: RHEUMATOID ARTHRITIS EROSIONS IN-OFFICE MAGNETIC RESONANCE IMAGING DISEASE MODIFYING ANTIRHEUMATIC DRUGS MAGNETIC RESONANCE IMAGING

Rheumatoid arthritis (RA) is a chronic inflammatory arthropathy of unknown etiology that has a worldwide distribution and affects all age groups, although the prevalence increases with age, and the peak incidence in women is between the fourth and sixth decades. The disease affects between 0.3% and 1.5% of the North American population and has a 2.5:1 female-to-male ratio. RA has many visceral manifestations, but it primarily involves the synovium and articular structures of joints where the disease is characterized by synovitis, leading to bone erosions, articular cartilage loss, damage to supporting structures (tendons, ligaments), and potential ankylosis. Because work disability is closely associated with radiographic measures of bone destruction, and its natural course is chronic and unremitting with few patients achieving longterm remission prior to joint destruction, aggressive therapy has been advocated in early disease to prevent joint destruction and accompanying morbidity. The success of disease modifying antirheumatic drugs (DMARD) and more recently biologic response-modifying drugs in arresting and even reversing the bone destruction process, and the high costs of the tumor necrosis factor-alpha inhibitors (TNF-α), have stimulated increased interest in methods for evaluating erosions as objective criteria for instituting more aggressive treatment regimens and monitoring their efficacy.
Clinical and biochemical criteria are important in evaluating patients for diagnosis and disease activity, but bone destruction can progress, even in apparent clinical remission. Imaging, therefore, is a promising adjunct to the evaluation of patients with RA.

Traditionally, conventional radiography has been the gold standard in imaging of RA. Scoring systems such as the Larsen and Sharp systems have been developed and modified in an attempt to standardize evaluation. Ultrasound has been shown to be sensitive in detecting synovial thickening, synovial vascularity, and bone erosions in experienced hands. Multiple studies have measured increased sensitivity of magnetic resonance imaging (MRI) for detecting bone changes characteristic of erosions compared with projection radiography. Lesions detected by MRI may progress to typical radiographic erosions over 2–6 years. Changes in the MR appearance of erosions in patients with established RA are less well described. Our study was designed to compare the sensitivity of MR versus conventional radiography in detecting changes in sizes of erosions over a relatively short timeframe, as detection of changes may be of value in guiding recently advanced pharmacotherapy.

MATERIALS AND METHODS

Study subjects. Data were based on a total of 405 consecutively seen patients from one rheumatologist’s practice, with a diagnosis of either rheumatoid or psoriatic arthritis (PsA) and no contraindications to MRI, who agreed to be evaluated by MRI. All patients with active disease were aggressively treated with DMARD therapy for inflammatory arthritis over a period of 24 months. Of the patients, 95% met the American College of Rheumatology (ACR) criteria for RA. Five percent satisfied ACR criteria for PsA. Comparisons between the sensitivity of plain radiograph versus MRI findings in detecting periarticular bony lesions in a subgroup of these patients were previously published. That article did not analyze interval changes in erosions. This article documents the incidence of changes in the size and number of bone lesions involving the second and third metacarpophalangeal (MCP) joints and wrists in patients over time intervals ranging from one month to 2 years, as evaluated with in-office MRI versus radiographs. A single rheumatologist (OT) provided clinical management of all study subjects.

MR examination. One hundred fifty-six patients returned for followup examinations, of whom one had 4 followup examinations, 23 had 3 followup examinations, 41 had 2 followup examinations, and 91 had one followup examination. The mean followup interval was 8 months. Followup examinations were compared to the most recent prior examination of the same patient. Each prior examination/followup comparison pair was evaluated independently of any earlier examinations. Two hundred forty-nine patients either did not return for followup or their initial MRI was performed less than 6 months before termination of data acquisition.

MRI examinations were performed using a portable in-office high-resolution scanner (previously distributed in the United States as Applause, GE Medical Systems; manufactured by MagneVu, Carlsbad, California; Figure 1). This portable scanner has a 0.2 Tesla inhomogenous magnetic field and is unique in that it requires no special radio frequency or magnetic shielding, can be plugged into an ordinary 110 V AC wall adapter, and, despite weighing 175 lbs, is mounted on wheels, making it portable. It occupies about 4 m² of floor space. These characteristics make it amenable to in-office placement, and its small size and open configuration enhance patient comfort during the scan.

MR examination of the second and third MCP joints and wrists included 2 sequences in each of the 2 locations: T1 spin echo (3D acquisition, TR/TE, 100/27 ms; flip angle 90°, field of view 50 × 75 × 10 mm; 2 excitations, 1.0 × 1.0 × 1.0 mm isotropic resolution) in the initial one-third of studies and (0.6 mm section thickness and 1.0 mm coronal in-plane resolution, acquisition time 15 min) in the latter two-thirds of studies, and STIR (3D acquisition, TR/TE/TI, 100/24/50 ms; field of view 50 × 75 × 10 mm, 4 excitations, 1.0 mm section thickness, 1.4 mm coronal in-plane resolution) in the initial one-third of studies and (0.6 mm section thickness, 1.4 mm coronal in-plane resolution, acquisition time 13 min) in the latter two-thirds of studies. Other joints were occasionally imaged based on the patient’s clinical symptoms, including the proximal interphalangeal joints and the metatarsophalangeal joints. Although image acquisition was a 3-dimensional technique with isotropic or near isotropic resolution, most interpretations were obtained by displaying the data in the coronal plane.

Radiographic examinations. Baseline standard posteroanterior, lateral, and oblique radiographs of the hands and wrist were obtained in a total of 368 patients. The 3 standard radiographic views were used in this study instead of a single posteroanterior projection, because 3 projections increase the sensitivity for detecting bone lesions and evaluating their sizes and morphologies. One hundred twenty-three patients had a total of 165 followup radiographic examinations. Of these, 224 (78%) were performed on the same day as the MR, and another 21 (7%) examinations were performed within 30 days of the MR. The remaining 41 (14%) examinations were beyond the ± 30 day time frame of the MR examination and were therefore considered invalid for comparison. The projection radiographs were evaluated for the presence of bone erosions before evaluating the MR images and again after interpreting the MR images. On the second viewing of the plain radiographs, the regions associat-
ed with changes in erosions on the MRI studies were reevaluated, and, in order to minimize false-negative radiographic interpretations, the results of the second radiographic interpretations are the results we report. Although the use of the second radiographic interpretation increased the sensitivity for detecting bone erosions in our previous experience\textsuperscript{19}, there were no discrepancies between the first and second radiographic interpretations for erosion changes in the data for this article. The number of followup radiographs is less than the number of MRI due to patients refusing followup radiographs. The most common reason for patient refusal was concern over radiation exposure. The mean followup interval was the same as the MR followup interval (8 months).

**Interpretation.** Radiographic and MR images were interpreted by a single board-certified radiologist with more than 18 years of musculoskeletal MR reading experience (JC). MR examinations were transferred from the portable scanner in the rheumatologist’s office to the radiologist via a virtual private network on the Internet and were read on soft-copy workstations. All the MR examinations were interpreted prospectively, one time, with the reader aware of the age, sex, and presumptive diagnosis. Conventional radiographs were read as hard-copy films on a standard view box.

On the MR images, the presence of erosions, soft tissue thickening (indicating synovitis), and joint space narrowing were assessed. Erosions were defined as focal areas of marrow signal loss on the T1-weighted images with increased signal intensity on the STIR images in the periarticular regions that extend to the cortical surface. Cortically-based signal changes less than 2 mm in maximum diameter were reported as “cortical irregularity” and not scored as erosions. Lesions were not scored as erosions unless their maximum diameter was 2 mm or greater. Erosion size was documented as a single measurement in the maximum dimension of the erosion as measured on the coronal image extending through the center of the lesion. Typical erosion sizes ranged from 2 mm to 10 mm, although larger erosions were occasionally noted. Changes in erosions were judged to be significant if their measurement varied by 20% or more. This number is a compromise between sensitivity and specificity for lesion growth. This was based upon the image acquisition spatial resolution being at least 1 millimeter in all 3 planes, although most of the followup studies were obtained with 1.0 × 1.0 × 0.6 millimeter spatial resolution. As most lesions were roughly spherical or half-spherical and measured between 3 and 6 mm, many images were obtained through each lesion, minimizing the error due to partial volume artifacts.

**RESULTS**

**MR imaging.** Figure 2 shows a summary of the MR data acquired. No detectable changes were seen in 124 of the 246 (50%) followup MRI examinations. One examination typically included 2 sequences obtained at 4 locations (right and left second and third MCP and right and left wrists). One or more erosions increased in size without any erosions decreasing in size in 74 (30%) study intervals (Figure 3). One or more erosions decreased in size without any erosions increasing in 36 (15%) intervals (Figure 4), and both increases and decreases in erosions were seen in 11 (4%) intervals (Figure 5). Motion artifact obscured images in one (< 1%) study.

When 632 individual locations with erosions were followed, no changes occurred in 481 (76%), increases were seen in 87 (14%), decreases present in 52 (8%), both increases and decreases in 3 (< 1%), and motion artifact obscured 9 (1%). In 178 locations initially without erosions, 150 (84%) showed no changes and 26 (15%) showed new erosions on followup.

Evaluating individual locations of the MR followup exam-
The increased sensitivity of MRI versus projection radiography in detecting focal bone abnormalities in RA is well established\textsuperscript{12,19-22,24,31,33,34}. Consequently, MRI is becoming a valuable tool in staging the extent of erosive disease at the time of diagnosis of inflammatory arthropathy. The sensitivity of MRI in detecting changes in bone injury over time is less well established\textsuperscript{28,29,35}. We attempted to determine how frequently and in what timeframe progression and regression of bone injury could be detected by high-resolution MRI in patients treated with DMARD therapy in a clinical rheumatologist’s practice. With an average followup of 8 months,
50% of patients undergoing aggressive DMARD therapy showed changes in MR findings versus only 1% using projection radiography. In-office, high-resolution MRI is significantly more sensitive in detecting changes in erosions in patients undergoing treatment for RA than projection radiography, supporting MRI as an effective tool for following bone injury in patients with RA treated with DMARD.

When the incidence of bone changes in individual locations was evaluated, the right MCP location was positive more often than any other location at 28% of intervals. Further, comparisons between right-sided versus left-sided changes and MCP versus wrists showed discordant/asymmetric changes. This suggests that imaging a single location will not provide optimal sensitivity for following patients’ response to therapy. However, we were unable to correlate MR changes with patient handedness, with physical examination for inflammation, or with patient symptoms. It is possible that further studies correlating changes in individual locations over time with these parameters might allow more targeted imaging to be performed in following patients, thus increasing the cost-efficacy of MRI.

Other methods of evaluating for bone erosions have been proposed, including ultrasound and computerized tomography (CT). Ultrasound is useful for detection of erosions and can demonstrate pannus formation. But ultrasound is operator dependent, its sensitivity is no better than MRI, and it is insensitive for detection of bone marrow edema or early inflammatory cell infiltration of marrow (osteitis). CT is excellent for demonstrating erosions but is less accurate in evaluating periarticular soft tissues. CT is insensitive for bone marrow edema and early osteitis, and it exposes the patient to ionizing radiation. High-resolution, multi-detector CT also suffers from lack of portability, an advantage of both ultrasound and the in-office MRI. Doppler US and contrast-enhanced MRI can also evaluate disease activity, a function for which contrast-enhanced CT may be less well-suited due to poorer contrast resolution. For these reasons, MRI is the most promising modality for evaluating bony erosive disease.

A “window of opportunity” hypothesis has been proposed suggesting that early DMARD treatment may be critical in stabilizing or reversing disease progression. This hypothesis states that patients treated early in their disease course with disease modifying therapy will fare better than those with delayed treatment. This is in part due to evidence that irreversible bone destruction occurs early in the course of RA in....
many patients and the possibility that the mechanism of disease in RA may be ameliorated if checked early. Further, bone destruction can occur even in the absence of clinical and biochemical changes, thus highlighting the need for imaging. Current recommendations that patients should be followed with periodic radiographs should be reconsidered, since radiographic detection of erosions will not occur until significant damage has occurred, precluding the benefits of early treatment. Prior data showing the increased sensitivity of MRI over plain radiography in detecting bone injury supports a role for MRI in determining when advanced therapy to modify bone injury should be introduced into the treatment decision algorithm for patients with RA. Our study shows that in-office MRI is significantly more sensitive than projection radiography in detecting changes in bone erosions on the average of 8-month intervals, strongly suggesting that MRI is a better tool than projection radiography in following bone injury response to treatment. Well-defined studies using MRI to follow patients on specific treatment protocols are warranted to confirm this finding.

Criticisms of using MRI instead of plain radiography center on the issues of cost and access, the lack of specificity of MRI in diagnosing RA, and high interobserver variability. Standard MRI is more costly than radiography. However, the cost-effectiveness of MRI must be evaluated considering the difference in total costs of treatment and disability between patients managed with and managed without access to MRI information. When this has been evaluated in other areas of the musculoskeletal system, the cost-efficacy of MRI has been favorable. Considering the costs of both advanced treatment and disability in RA, it seems likely that similar studies could prove significant cost-efficacy for MRI in RA. Access to MRI is also a concern, especially in areas with relatively low numbers of MRI scanners per population. This problem can be alleviated by the use of portable in-office scanners, which are relatively inexpensive and provide a level of comfort and convenience that traditional scanners cannot. In-office MRI scanners do raise significant issues of self-referral, quality control, and professional expertise that need to be addressed to ensure widespread acceptance.
Lastly, there are critics who state that there are no firm guidelines or set criteria for interpreting rheumatologic MRI, leading to high interobserver variability. This is a universal problem with any new imaging modality, including rheumatologic ultrasound\(^5\). Current recommendations for standardization of RA MRI interpretation using standard scanners have been published, but modifications may be necessary to be applicable to small field-of-view in-office scanners\(^2\)-\(^8\). One particular problem we encountered using the Applause in-office scanner in interpreting studies is that the acquisition field of view was only 1 cm in the anterior-posterior direction, often incompletely visualizing the dorsal and volar aspects of the bones. An advantage of this in-office scanner is that it images at significantly higher through-plane resolution than performed in most published studies using whole-body scanners. Through-plane resolution is the spatial resolution in the dimension perpendicular to the plane of the displayed images. This is typically 2.5–3.0 mm in standard high-field imaging. In-plane resolution is the spatial resolution along the 2 dimensions within the plane of imaging, typically 0.4 mm. For spherical lesions, like small erosions, the ability to accurately resolve spatial detail of the lesion is largely dependent on the spatial resolution in the dimension with the lowest resolution, and the importance of high through-plane resolution has been shown to be significant when quantifying volume of pathology, such as articular cartilage in osteoarthritis\(^3\). Thus, we believe that isotropic or near isotropic imaging is highly advantageous for imaging of inflammatory arthropathies.

However, with isotropic resolution equal to or better than 1 mm in all 3 planes, normal undulations in the bone cortex associated with ligamentous and tendinous insertions, vascular channels, and subchondral cysts that extend to the cortex can simulate small erosions not detectable with lower resolution imaging. This may increase the false-positive findings, since not all erosion-like lesions are related to inflammatory arthritis\(^4\). Between 3% and 15% false-positive studies have been described using standard MR imaging. Many of these lesions may be posttraumatic in etiology. Demonstrating changes in erosions in 50% of our examination intervals supports the assumption that many of the bone lesions we have followed in patients with RA are associated with an active inflammatory process. Also, most patients with RA in our study presented with synovial thickening on MRI, consistent with synovitis, whereas the patients without clinical RA that we have evaluated with MRI in workers’ compensation injuries rarely present with synovial thickening (unpublished data).

**Limitations.** Partial-volume artifacts could artificially create the illusion of changes in lesion size if the thickness of the image slice is larger than or on the order of the size of the lesion being evaluated. Since most of the lesions in this study measured from 3 to 6 mm in diameter, through-plane resolution of the order of 2.5 to 4.5 mm used with most traditional large scanners using 2-dimensional Fourier-transform reconstruction techniques (2–4 mm thick slices with 0.5 mm skip) could create artifacts due to geometrical limitations of the scanning technique. In order to minimize this effect, we used 3-dimensional Fourier-transform imaging. With this technique the slice thickness was 1.0 mm at the beginning of the study and 0.625 mm for the latter two-thirds of the study. Unlike the 2-dimensional Fourier-transform technique, there is no skip between slices using a 3-dimensional technique. Consequently, multiple images were obtained through most lesions, so partial volume artifacts are substantially less with this technique than with traditional MRI. Only lesions greater than 2 mm were considered erosions, with most lesions showing changes being larger lesions, where partial-volume artifacts are less problematic. Consequently, we believe that the 20% change in diameter threshold used to signify biologic activity is above measurement variations based on geometric arguments from partial-volume artifacts for most lesions, but this technique is insensitive to 20% changes in lesions less than 5 mm and underreports changes in small erosions. However, repeated measurements of the same patients on the same day were not performed to measure the reproducibility of detection and size measurements of lesions. So some of the interval changes we reported could be variability of measurement inherent in the technique used rather than biologic changes. We believe that these measurement variabilities were minimized due to the use of near isotropic voxel sizes, limiting erosions to lesions greater than 2 mm in size, and requiring that a greater than 20% change in maximum diameter be measured before scoring the change as significant. Further studies are warranted to confirm this assumption.

The overall followup length of our study (2 years) is rather short considering the chronic course of the disease being studied. Longer-term studies would help to confirm the benefits of integrating MRI into the management of these patients. Another limitation of the study is that patient treatment regimen was not controlled. Different treatment protocols and algorithms influence the likelihood of changes in bone erosions. Although all of our patients were taking DMARD therapy, no conclusions can be drawn as to the efficacy of the different therapeutic agents used. Our data are also based on a single observer’s interpretations and therefore interobserver variability for interval changes was not measured.

Extrapolation of our findings as representative of a rheumatologist’s practice must be done cautiously, as only 405 patients with the diagnosis of RA or PsA seen over a 2-

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**Figure 6 (Opposite page).** New erosion detected by radiograph and MRI. A. PA radiograph obtained on March 27, 2003, showed no erosions of the left second and third MCP. B. The T1-weighted MRI obtained on the same date also showed no erosions. C. The PA radiograph obtained on September 8, 2003, showed a new marginal erosion involving the radial aspect of the second proximal phalanx (arrow). Other new erosions were also present. D. The T1-weighted MRI also shows the new erosion (arrow). Radial-side second MCP erosions are also present, but incompletely seen on this single tomographic slice.
In conclusion, with the increased recognition of the association of structural bone damage with disability in patients with RA and the efficacy of methotrexate (MTX) and TNF-α inhibitors in controlling the progression of bone injury, accurate measures of erosive disease have garnered increased interest. Both MRI and ultrasound have shown increased sensitivity for detection of erosions and are promising modalities for staging disease burden. We showed that for patients with RA taking DMARD therapy in a single rheumatologist’s practice, 50% of compliant patients showed changes in the size of at least one erosion using in-office MRI in an 8-month follow-up period, as opposed to 1% with 3-view projection radiography. This supports MRI as a promising modality for following patients’ structural damage while being treated with DMARD. But further studies are needed to more accurately define the sensitivity and specificity of in-office MRI in evaluating erosive changes in defined patient populations, and to establish a possible role for MRI in patient management.

REFERENCES

28. Bird P, Kirkham B, Portek I, et al. Documenting damage because of rheumatoid arthritis? Results of five years’ follow up period agreed to undergo MR examination. Of these, only 156 patients returned for at least 2 MRI examinations so that an interval comparison could be made. This may have introduced an uncontrolled selection bias in the data.


