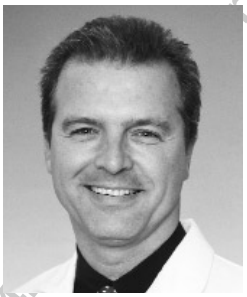
Editorial

Is There a Role for Extremity Magnetic Resonance Imaging in Routine Clinical Management of Rheumatoid Arthritis?



The extraordinary advances of the past few years in structure-modifying therapy have given new hope to patients with rheumatoid arthritis (RA) who previously faced a bleak future of pain and disability from their disease. At the same time, these innovations have raised the bar considerably for medical imaging in rheumatology (Figure 1). In the past, the imaging performance demands of rheumatology were rather minimal. Without any effective therapies to halt the progression of erosive joint damage, there was little need for detailed information about joint structure. Conventional radiography, although intrinsically limited in the information that it could provide in this regard, was adequate for what was needed at the time. Other modalities, particularly magnetic resonance imaging (MRI), offered greater technical performance, but because rheumatologists were satisfied with radiography, they were not willing to pay more for MRI. Indeed, most rheumatologists used even radiography only sparingly, if at all, relying instead on clinical examination and laboratory measures to manage their patients.

However, the introduction of effective structure-modifying therapies for RA has changed these circumstances dramatically. Among other things, it has shifted therapeutic strategy towards early, aggressive treatment before the onset of erosive joint damage in order to prevent irreversible functional disability[1-6]. Additionally, it has made it unethical in clinical research to withhold active therapy and therefore to do true placebo-controlled clinical trials. This has necessitated using active comparator study designs instead, which require more patients, more clinical sites, and longer studies to test the efficacy of putative new therapies. This adds time and cost to drug development, which slows progress and potentially raises the cost of new therapies that do get approved.

Enriching study populations with rapidly progressing patients may offset some of this effect, but this necessitates the availability of prognostic markers that can accurately identify which patients are most likely to develop erosive damage, since as many as half of the patients in early RA cohorts do not progress. Early prognosticators are also needed by clinical practitioners to determine which patients need aggressive treatment before the narrow window of opportunity for containing erosive disease closes. The absence of bone erosions on radiographs reliably identifies non-progressors after 18 months to 2 years, but is only 41% sensitive in early RA[7]. In a study by Machold, *et al*[8], only 13% of patients with RA of less than 3 months' duration had radiographically demonstrable erosions, in contrast to 70–80% prevalence that is typically seen among these patients after 3 years[9]. Clearly, radiography is not adequate for this purpose.

MRI, on the other hand, is unparalleled in its ability to visualize articular tissues, and numerous studies have shown it to be several times more sensitive than radiography[10-21] or ultrasonography[20,21] for detecting bone erosions. In their article in this issue of *The Journal*, Hoving, *et al* report that MRI showed more than twice the sensitivity for bone erosion versus radiography or ultrasonography in 46 patients with early RA (median disease duration was 26 weeks)[21]. In another study, baseline MRI revealed bone erosions in 42% of patients with RA of less than 6 months' duration, whereas radiography detected erosions in only 15% of these patients[10]. Moreover, baseline erosion score was predictive of radiographic erosion score at 2 years ($p = 0.004$)[10]. When synovitis, tendonitis, and bone edema, or more appropriately osteitis[22], were also taken into account, the predictive power — particularly the negative predictive value — of baseline MRI was even greater (86%)[10]. MRI erosions and synovitis, but not osteitis, also were predictive of progression on 6-month followup in the study by Hoving, *et al*[21]. Why osteitis was not as predictive in this study as it was in others[12,17,23] is not known; however, lower prevalence of this feature in the study cohort, combined with limited measurement reproducibility (0.38 kappa) and short followup interval (6 months) are possible explanations. Regardless, the bulk of evidence indicates that MRI is indeed able to identify the aggressively

See Comparison of MRI, sonography, and radiography of the hand in early RA, *page 663 and* Identification of wrist and MCP joint erosions using a portable MR system compared to conventional radiographs, *page 676*

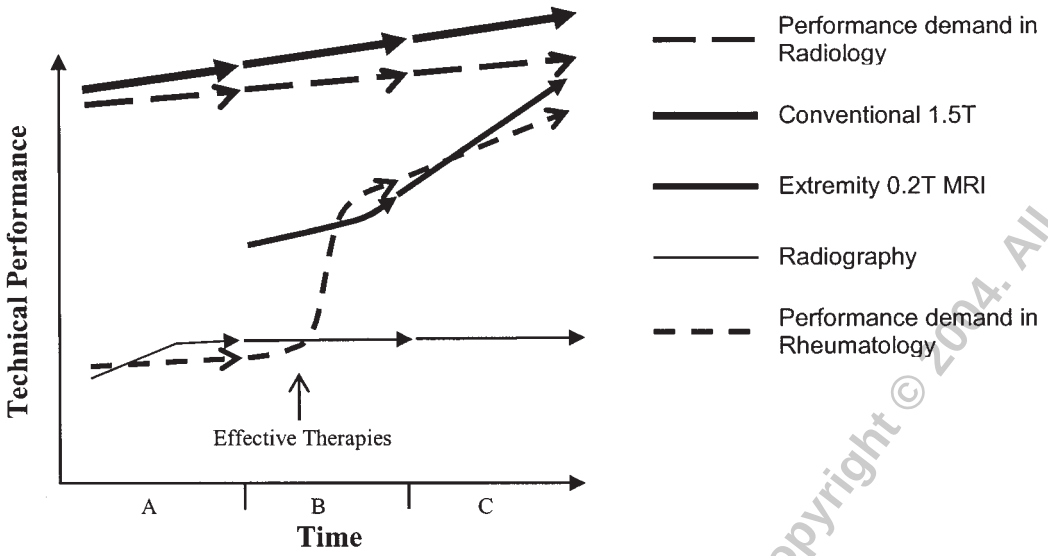


Figure 1. Technical demand-performance relationships for radiography and MRI in RA. A. Before the availability of effective structure-modifying therapy, clinical rheumatology's demand for technical performance in imaging (broken line) was modest and flat, increasing only slightly over time. Radiography (thin line) met these technical demands, and was the dominant imaging method used. Radiography improved initially with the introduction of better film-screen designs, but has remained relatively flat since. Conventional 1.5-T MRI (thick solid line) was technically superior to radiography, but rheumatologists were satisfied with radiography's performance, and therefore not willing to accept additional cost and inconvenience for MRI. Because of this performance surplus, MRI was not used. B. When small, low-field extremity MRI systems (intermediate solid line) were introduced, although they also outperformed radiography but were less expensive and more convenient than conventional MRI, they still were not adopted by rheumatologists initially because their extra performance was considered unnecessary at the time. The basis for competition among the various imaging modalities was, at this point, convenience and cost, rather than functionality and reliability. With the introduction of effective therapies for RA (arrow), rheumatology's technical requirements for imaging have increased beyond what radiography can deliver, creating a new demand for MRI. Conventional MRI is still believed to provide excess performance, and accordingly, it is not used in most cases. Low-field extremity MRI offers adequate performance, but less expensively and with greater patient comfort and convenience. This will drive increased use of MRI by rheumatologists. C. Over time, rheumatologists' demand for imaging performance will steadily increase. Fueled by the increasing use, extremity MRI will innovate and improve its performance to keep pace with and possibly exceed the demand from rheumatology. Eventually, it may become competitive with high-field MRI in mainstream radiological applications. Adapted from Peterfy CG. Semin Arthritis Rheum 2001;30:375-96.

erosive phenotype of RA in early disease, and may therefore offer a valuable tool for early patient management.

While MRI is a relatively expensive procedure, its use in RA may prove cost-efficient if it can reduce unnecessary treatment of patients with costly biological therapies. As noted above, this may apply to more than 30% of RA patients on initial presentation. Nevertheless, conventional whole-body MRI is still relatively expensive and inconvenient, and although it is free of ionizing radiation, it is contraindicated in patients with pacemakers, aneurism clips, and certain other metal objects. Additionally, some patients find the experience unpleasant, and about 5% are unable to complete the examination because of claustrophobia. Recently, low field-strength extremity MRI systems were introduced as lower-cost alternatives in such circumstances[24,25]. Because these systems operate at lower magnetic field strength, typically 0.2 Tesla, they can be made much smaller and operated less expensively. Also, whereas conventional 1.5-Tesla magnets require placing the entire body into the magnet bore, imaging with extremity MRI systems requires patients to insert only their limb into the magnet while sitting or lying next to the unit (Figure 2). This eliminates claustrophobia, and reduces risks associated with metal in the body or in the examination room. Because of the small fringe-field, low weight, and small footprint of these systems, they can operate in environments that were previously inaccessible to MRI, such as medical offices. The smallest extremity MRI system that is currently available commercially is described by Crues, *et al* in this issue[24] (Figure 2B). This system can operate in as little as 4 square meters of space, and is actually portable.

The main disadvantage of extremity MRI systems is that their low magnetic field strength cannot support as much image resolution or as many image contrast mechanisms as conventional whole-body 1.5-Tesla systems[26]. Additionally, the small size of these systems precludes imaging other body parts, such as the shoulders, hips, spine, chest, abdomen, and

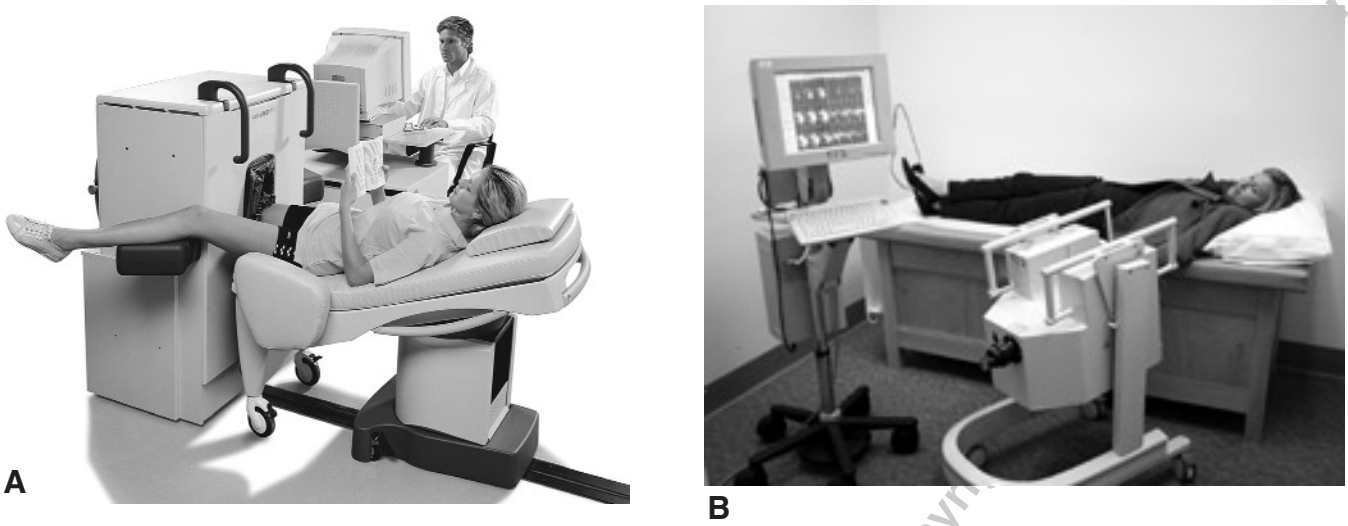


Figure 2. Low-field extremity MRI. A. Lunar (GE/Esaote) 0.2-Tesla extremity MRI system. B. MagneVu 0.2-Tesla portable extremity MRI system.

pelvis, which is a capability that most radiology services require. Because of these limitations, extremity MRI systems were not initially felt by mainstream radiology to provide sufficient performance for their needs. Higher field strength (1.0 Tesla) extremity systems that can support higher spatial resolution and broader contrast mechanisms, as well as larger

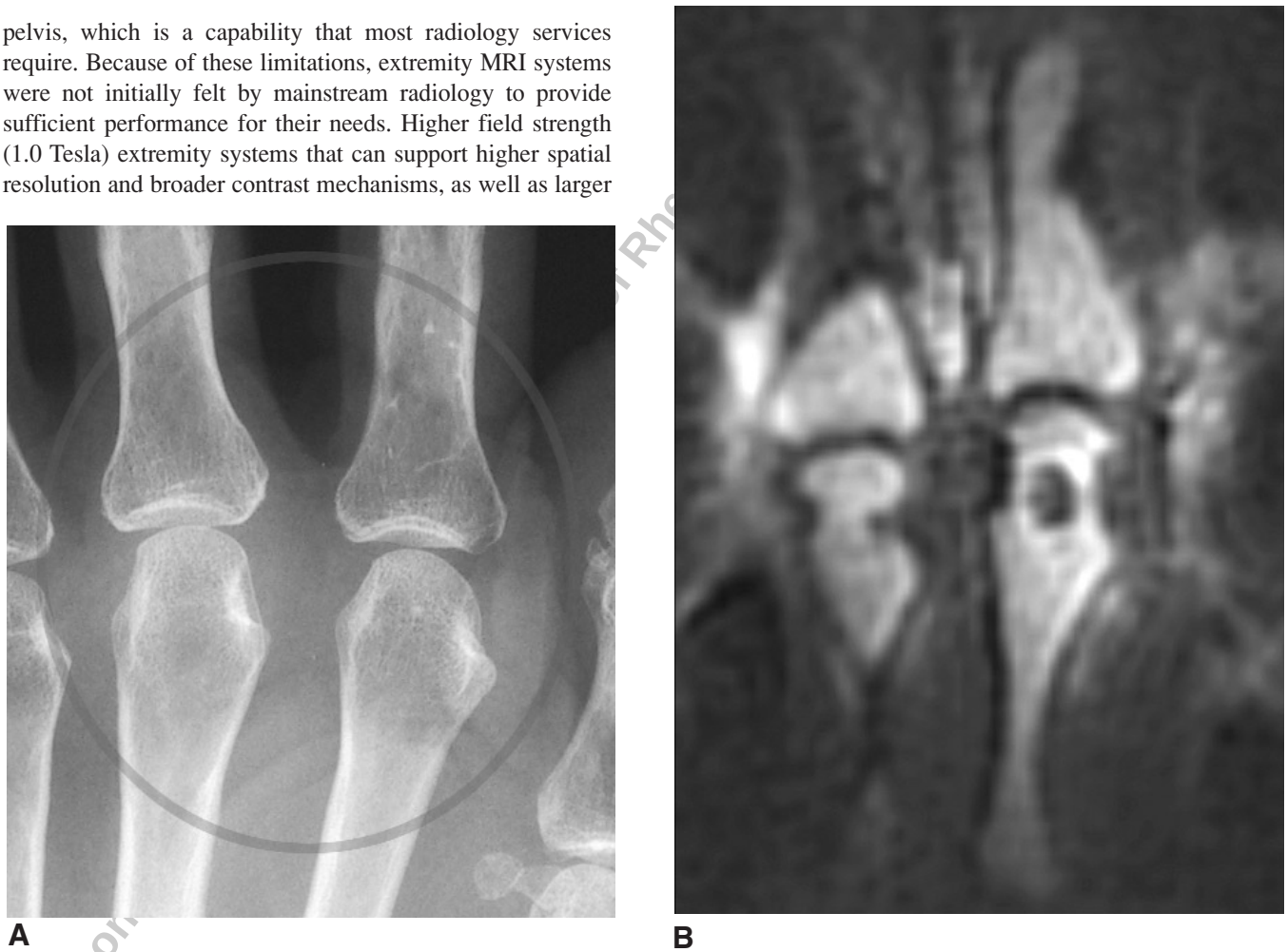


Figure 3. Low-field extremity MRI is more sensitive for bone erosion than radiography. A. Radiograph of the second and third metacarpophalangeal joints shows no evidence of bone erosions. B. Coronal extremity MRI image of the same region acquired with the portable extremity MRI system illustrated in Figure 1B shows a large intramedullary bone erosion in the distal end of the second metacarpal that is completely occult on radiographs. Courtesy of N. Gaylis, Arthritis and Rheumatic Disease Specialties, Miami, Florida.

low-field systems that can accommodate additional anatomical sites, such as the shoulders, have since become available, but at the expense of larger space requirements and greater cost, and even these systems still offer some performance deficit in the eyes of many radiologists.

It is important to bear in mind, however, that the needs of radiology are not the same as those of mainstream rheumatology. The circumstances and therefore the technical performance requirements for MRI in these 2 disciplines are very different. Rheumatologists do not need to image multiple body parts — at least, not in patients with RA. Imaging the hands, wrists, and feet is usually sufficient. They do not need, at this stage, highly sophisticated pulse sequences and contrast mechanisms. The ability to detect radiographically occult bone erosions, synovitis, and possibly osteitis and tendonitis would be good enough.

A number of studies have already demonstrated that low-field MRI systems are technically capable of doing this[20,25-29]. In a study of 227 wrists of 132 patients with inflammatory arthritis, 95% of which had RA, Crues, *et al*[24] were able to identify roughly twice as many erosions using a small, portable 0.2-Tesla MRI system than they could with radiography (Figure 3). Østergaard, *et al* described similar findings in a different cohort of patients using a different low-field extremity system[29]. In a study of 103 patients with inflammatory arthritis (78) or noninflammatory arthralgia (25), Savnik, *et al* found no significant difference in synovial volume measured by 0.2-Tesla extremity MRI and that measured by 1.5-Tesla conventional whole-body MRI[27]. Cimmino, *et al* found that the rate of synovial enhancement with gadolinium-containing contrast medium in 36 patients with RA and 5 healthy controls measured with 0.2-Tesla extremity MRI correlated with clinical and laboratory markers of inflammation[28].

Accordingly, low-field extremity MRI provides a promising solution for rheumatologists looking for sufficient diagnostic power to detect inflammation and erosive damage in early RA without the cost and inconvenience associated with conventional whole-body MRI. As experience with the use of MRI in RA increases among rheumatologists, their demand for technical performance can be expected to increase. Fueled by increasing utilization, extremity MRI systems can in turn be expected to continuously improve their technical performance in order to keep pace. If the trajectory of this improvement is steeper than that of mainstream radiology's demand for increasing technical performance in MRI, then at some point low-cost extremity MRI's performance may even satisfy some of mainstream radiology's needs, and thus begin displacing conventional MRI for certain applications. How quickly this process will play out is difficult to say. However, MRI is certainly expected to play an increasingly important role in day-to-day rheumatological practice over the next several years.

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