

Rheumatoid arthritis

# Imaging of the hand and wrist in RA

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## Interrelationships and comparisons of imaging with clinical disease activity

In the past decade, elucidation of pathophysiological pathways relevant in rheumatoid arthritis (RA) has continued, leading to continuing advances in drug treatment. At the same time, several clinical trials have shown the efficacy of early and aggressive treatment of patients with active disease. Early intervention strategies may reduce functional deterioration and improve long term outcome. Therefore, treatment strategies need to be determined before irreversible damage and functional deterioration occur.

### RADIOGRAPHY

Imaging techniques are useful not only for studying the natural history of the disease but also for assessing the response to disease modifying antirheumatic drugs, and—potentially—for selecting those patients who will benefit most from early aggressive treatment. Conventional or digitised radiography of the hand and wrist is the traditional method used to diagnose, determine the stage, and monitor patients with RA, and to assess treatment efficacy in individual patients. Radiography, using several scoring systems, is also pivotal for the evaluation of disease progression and treatment efficacy in RA clinical trials,<sup>1-3</sup> with excellent intra- and interobserver agreement.<sup>1,4</sup> However, radiography is insensitive in detecting early erosions, and above all, in assessing synovitis.

### MAGNETIC RESONANCE IMAGING AND ULTRASOUND

Recently, more powerful and complex imaging modalities have emerged as alternatives or additions to radiography. These include magnetic resonance imaging (MRI)<sup>5-11</sup> and ultrasound (US).<sup>5,12-18</sup> Several studies have shown the relative usefulness of MRI over radiography in evaluating early RA of the hand and wrist.<sup>5,8,11,19</sup> MRI offers distinct advantages over radiography: in addition to its multiplanar capability, it has the ability to directly image the soft tissues, including the synovial pannus and synovial fluid, as well as bone, cartilage, and tendons. Contrast enhancement with gadolinium (Gd-DTPA) given intravenously allows the visualisation of synovitis based on shortening of the T<sub>1</sub> time, and

the subsequent change in signal intensity. Dynamic enhanced MRI using manual or semi- or fully automated techniques<sup>20-22</sup> can quantitatively assess synovitis. The measurement of synovial volume can be used to monitor the response to treatment, and also to predict those patients more likely to develop erosions at one year.<sup>23</sup> Moreover, semiautomated methods have been developed to measure the volume of bone erosion with MRI, and can be used as surrogate markers of treatment effects in drug trials.<sup>24</sup>

### “Radiography is insensitive in detecting early erosions”

However, the major drawbacks of MRI are its high cost and limited availability, but dedicated low field MRI devices (<1 T) can lower the cost and are an alternative to high field conventional systems.<sup>5,25</sup> Recent studies have shown that US, using either B mode US,<sup>5,12,13,18</sup> Doppler mode without contrast injection,<sup>16,17</sup> or with contrast injection<sup>14,15</sup> is a sensitive method for the detection of erosions, tenosynovitis, synovial pannus, and joint fluid.

### COMPARISON OF MRI AND/OR US WITH RADIOGRAPHY

Although long term follow up using radiography has been reported in several longitudinal studies,<sup>26-28</sup> only a few studies have reported the sensitivity of MRI and/or US compared with radiography in the intermediate (>1 year) and long term follow up of patients with RA.<sup>29,30</sup> In this issue of the *Annals of the Rheumatic Diseases*, Backhaus and colleagues report a two year follow up in 49 patients with different arthritic conditions (including 31 with RA) using multi-imaging modalities, including radiography, US (B mode), low field MRI, and scintigraphy.<sup>31</sup> Paradoxically, despite a decrease in synovitis and tenosynovitis clinically and at imaging (US and MRI), there was an increase in detection of erosions by MRI (and to a lesser extent by US). The authors showed also that at the two year follow up, radiography remained insensitive for the detection of erosions, and that nearly all such erosions were already detected by MRI at

baseline. In addition, many more erosions that were visible at follow up on MRI were not detected by radiography. The study by Backhaus *et al* raises questions about the relationship between synovitis, bone erosions, and clinical activity in patients with RA.<sup>31</sup> McQueen *et al* have previously shown that in early RA, erosions detected by MRI can progress over one year despite clinical improvement and without concomitant significant changes in synovitis.<sup>32</sup> However, their group included patients with early RA, unlike the study by Backhaus *et al*, probably explaining the difference in the time course of synovitis. Existing publications contain conflicting results about the correlation between synovitis at MRI with clinically active disease.<sup>33-36</sup> MRI can detect residual synovitis in patients who apparently are in clinical remission, and the use of quantitative MRI parameters after gadolinium injection can discriminate between patients in “true” versus “apparent” remission.<sup>37</sup>

Although a direct link between synovitis and bone damage is still controversial, there is strong evidence that early bone changes, such as bone oedema, rarely occur in the absence of synovitis, and several authors have suggested a sequence of MRI changes from synovitis to bone oedema to erosions.<sup>7,38</sup> Patients with a pronounced carpal synovitis by MRI at baseline were more likely to develop erosions at one year<sup>23,37</sup> or two years.<sup>30</sup>

### “MRI detects more erosions than radiography at two year follow up”

On the other hand, Kirwan *et al* found only a weak correlation between the changes in the radiographic Larsen scores and the cumulative synovitis scores (evaluated clinically) over a period of two years in the finger joints of patients with RA.<sup>39</sup> They argue against a direct causal relationship between synovitis and erosions. However, the clinical evaluation of synovitis and joint tenderness is known to be relatively subjective with considerable interobserver variability.<sup>40</sup> The study by Backhaus *et al* indicates that even if erosions and synovitis have the same underlying cause, their evolution over time and response to treatment may differ. Long term follow up with MRI and radiography may answer these questions.

### WHICH IMAGING METHOD?

For which patients and when do we need to use MRI and/or US, and what indications remain for radiography? The limitations of radiography in the early stages of disease undermine its ability to select

patients at high risk for joint damage. None the less, radiography still has a prominent role in the basic investigation of RA. Despite its cost and limited availability, we believe that MRI has a potential role in the initial patient management, at least for identifying those patients at risk of developing structural damage. MRI can also add power to drug trials by reducing the length of the studies and the number of patients, and by adding quantitative surrogate end points, as discussed earlier. However, to achieve these goals, there is a strong need for a standardisation and validation of MRI protocols and scoring systems to make it reproducible and reliable. Indeed, the OMERACT has recently reported only low to moderate inter-observer agreement for MRI, especially in the evaluation of joint space narrowing<sup>41</sup> and has proposed some general recommendations.<sup>42</sup> We believe that US can be useful in experienced hands, but is too operator dependent to be used generally. Finally, the sensitivity, specificity, cost effectiveness, and prognostic value of MRI and US in the long term need to be determined.

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