

# Magnetic Resonance of the Hand in Rheumatoid Arthritis. Review of Methodology and its Use in Diagnosis, Monitoring, and Prognosis

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The ideal aim of treatment in rheumatoid arthritis (RA) is to suppress synovial inflammation and to stop or reduce structural joint damage progression. To evaluate joint damage in RA, radiographic assessment of hands, and feet is the traditional method. Nevertheless, plain film radiography can only evaluate bone damage (erosion) and, indirectly, joint cartilage. Magnetic resonance imaging presents important advantages since allows to study, not only the cortical bone and the marrow, but also the synovial membrane, tendon and ligament structures, and adjacent soft tissue that usually are involved in early disease. Moreover, hand-magnetic resonance (h-MRI) has shown to be more sensitive than plain radiography in detecting early erosions and predicting progression of bone damage, allowing a rapid diagnosis and to start the most efficient therapy as well as to achieve better outcomes for this disease.

**Key words:** Magnetic resonance imaging of the hand. Rheumatoid arthritis. Methodology and diagnosis.

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## Resonancia magnética de la mano en la artritis reumatoide. Revisión de la metodología y la utilidad en el diagnóstico, el seguimiento y el pronóstico

El objetivo ideal del tratamiento en la artritis reumatoide (AR) es la supresión de la inflamación y evitar el daño estructural articular. Para medir la progresión de las lesiones estructurales en la AR disponemos de la radiología de las manos y los pies, que es el método tradicional. Sin embargo, la radiología sólo permite

evaluar la alteración ósea (erosiones) e indirectamente el cartilago articular. Por ello, la resonancia magnética de las manos (RMm) presenta ciertas ventajas al permitir el estudio no sólo de la cortical ósea y el hueso medular, sino también de la membrana sinovial, las estructuras tendinoligamentosas y los tejidos blandos adyacentes, que suelen ser las estructuras que se afectan al inicio de la enfermedad. Además se ha demostrado más sensible que la radiología en la detección precoz de erosiones y en la predicción del daño óseo, lo que permite un rápido diagnóstico, instaurar un tratamiento adecuado y mejorar el pronóstico de los pacientes.

**Palabras clave:** Resonancia magnética de la mano. Artritis reumatoide. Metodología y diagnóstico.

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## Introduction

Rheumatoid arthritis (RA) is an inflammatory disease of the synovial and perithendinous joint tissue that leads to destruction of cartilage and bony erosions, and therefore joint deformity as well as loss of functional capacity. The main objective of treatment in RA is to suppress synovial inflammation and prevent or delay the appearance of structural lesions. In the daily clinical practice, conventional radiology of hands and feet is the standard method used, but other, more sensitive and specific imaging techniques are needed in order to evaluate the alterations in rheumatoid synovium, adjacent soft tissue and even more precisely, cortical, and trabecular bone which permits an early diagnosis of RA.

Magnetic resonance imaging of the hands (MRh) has been shown to have more sensitivity than simple radiographs (Rx) in the early detection of erosions and allows the evaluation and quantification of synovitis, erosions, bone edema, and tendon abnormalities. It is a tool that presents predictive value for structural lesions, allowing the initiation of adequate therapy in early stages of disease, improving the prognosis of patients. Currently its use is not extended to all affected patients due to its elevated cost, low availability and the fact that patients

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find it uncomfortable. The integration of low field MR, dedicated to the examination of the extremities, has shown a similar sensitivity that conventional equipment, which will allow for a greater access to this technique and its application to selected groups of patients.

We present an extensive review of the main publications regarding MRh in RA with relationship to the methodology needed for its realization, the semi quantitative measurement of synovitis, bone edema, and erosions, as recommended by the OMERACT-6 (Outcome Measures in Rheumatoid Arthritis Clinical Trials) task force and its use for early diagnosis and prognosis, as well as the application of this technique as a marker of disease activity and therapeutic response and finally, possible indications and future perspectives in the study of RA.

### **Magnetic Resonance Technique and Methodology for Examination of the Wrist and Hand in Rheumatoid Arthritis**

MR is a multiplanar imaging technique that is non-ionizing and non-invasive imaging technique that, as opposed to simple x-rays, allows not only for the evaluation of bone erosions but to establish the degree of synovial membrane affectation, the state of tendinous and ligamentary structures, and of cartilage. In RA, MRh is recommended because of the analogy with conventional radiographs. Several studies have shown that the presence of erosions and/or the reduction of the joint space present itself, in most of the cases in these joints and in early stages of the disease<sup>1</sup> and that the findings in such localizations are representative of the general alterations of other joints as a whole.<sup>2</sup> Ideally, MR of both hands should be carried out, but in daily clinical practice RM of the dominant extremity is recommended because it is the one that is most likely to be affected due to mechanical effects associated to the joint inflammatory process.<sup>3</sup>

The methodology employed for the realization of MRh recommends obtaining potentiated sequences in T1 and T2 from the radioulnar joint distally to the metacarpophalangeal joints (MCP). The T1 potentiated sequences provide detailed anatomic information of the cortical and trabecular bone, the rheumatoid synovium, and the tendo-ligamentary structures. With the administration of intravenous paramagnetic contrast it is possible to differentiate synovial hypertrophy from synovitis (activity). Gadolinium or gadopentetic dimegluminic sodium (Gd-DTPA) are usually employed as paramagnetic contrast and are administered in the contra lateral arm and show, in the cases of active synovitis or tendinosis/itis, a reinforcement or increase in the signal due to hypervascularization phenomena. In such cases it is possible to carry out fat suppression

in T1, achieving an enhancement in the intensity of synovitis by suppressing the normally hyperintense signal coming from adjacent fatty tissue (Figure 1). Obtaining potentiated images in T2 permits the evaluation of the presence of water and fat present in the bone marrow or subcutaneous tissue as areas with greater signal intensity. Using fat suppression or STIR (Short Tau Inversion Recovery), the hyperintense signal coming from bone marrow and subcutaneous fat is attenuated, allowing for the evaluation of the presence of bone edema, joint and/or peritendinous effusion. The recommended width for each cut is approximately 3 mm, because inferior widths, around 1 mm or less, though more informative regarding small erosions, occasionally can lead to errors in the interpretation of the results, such as mistaking interruptions in cortical bone produced by the entry of nutritious vessels, or ligamentary, or tendinous insertions, with an erosion.

**Figure 1.** Magnetic Resonance of the hand, axial plane, T1 sequence before and after administering paramagnetic contrast with gadolinium. A: synovial hypertrophy of the distal radioulnar joint. B: active synovitis of the distal radioulnar joint.

Widths that are larger than 5-10 mm reduce the sensitivity of the MRh for the detection of small erosions. The recommended planes for examination are coronal and axial, which tend to be sufficient for the study of the hand in RA. It would be possible to include the sagittal planes, but in MRh it does not provide any interesting details for the study of RA.

Most hospitals have high-yield (>1 Tesla) equipment and employ different types of antenna, adapting them to do MRh. In these cases, the patient is usually put in a decubitus position facing upwards with the dominant arm at extension, allowing, after setting up the right antenna, to carry out topograms in 3 planes to localize the corresponding planes, from the radioulnar joint distally to the MCP. An alternative to this method is low-yield extremity-MR (E-MRI) in which the main inconveniences of the conventional equipment, such as uncomfortable position of the patient, claustrophobia and, evidently, the high cost of the traditional method.<sup>4</sup>

The equipment for MRh has been shown to be more sensitive than conventional radiology for the detection of bony erosions (95% for MR vs 59% for Rx)<sup>5</sup> and is comparable to the common high-yield method in the evaluation of synovitis and bony erosions.<sup>6,7</sup> The main inconveniences of this technique are a lower resolution of the images, longer test duration and its current inability to carry out fat-suppression sequences necessary for the evaluation of bone edema.<sup>8</sup> The alternative that is employed in these cases usually is the obtainment of T2 potentiated sequences using STIR though, when comparing both methods, MRh has a lower sensitivity in the evaluation of bone edema.<sup>9</sup>

### **MRh in RA as a Tool for Measurement of Joint Lesions: Synovitis, Bone Edema, Erosion, and Tendon Alterations**

Rheumatoid synovial alterations that can be evaluated using MRh are, among others, hypertrophy and synovitis. Hypertrophy is translated as a widening of the synovium or an increase in its total volume without any signal changes after the administration of paramagnetic contrast; on the contrary, synovitis appears as a hyperintense signal or a reinforcement of T1 sequences after the administration of gadolinium. The first studies carried out in patients with RA and knee arthritis showed that the capture of images in the first 10 minutes following the administration of paramagnetic contrast allows for the differentiation of synovitis from the joint effusion that is frequently associated to it.<sup>10</sup> In healthy patients, the uptake of gadolinium is usually mild and presents itself early on after its application, due to the normal vascularization of the synovium. In the cases of active synovitis, gadolinium hyperuptake is prolonged for the 10 established minutes, allowing it to be

distinguished from healthy patients.<sup>11</sup> There is enough evidence to consider that the intensity of the gadolinium uptake in rheumatoid synovium evaluated through MRh correlates with the vascularization and the degrees of inflammatory activity in the histopathological studies.<sup>12-14</sup>

Quantifying total synovial volume (hypertrophy) and the synovial volume that is reinforced after the administration of gadolinium (synovitis) using manual, semiautomatic and automatic methods is also correlated with inflammatory activity and could be a marker for disease activity.<sup>15-19</sup>

Bone edema, evaluated in T2 sequences with fat-suppression or STIR as an area of increased poorly delineated signal in the yuxta-articular trabecular bone, corresponds to the presence of water and presents itself in an isolated manner or associated to other lesions, in other words adjacent to joint synovitis, peritendinous inflammation, or erosions. Perhaps the most relevant image is the poor definition of the hyperintense trabecular signal, allowing it to be distinguished from other entities such as bone cysts or the normal nutritious vessels. Erosions are seen on MRh as a loss of cortical hyposignal and trabecular subcortical bone hyperintense signal on T1 potentiated sequences, visible on the axial and coronal planes with an interruption of the cortex on at least one plane. Gadolinium uptake by the erosion in some cases indicates active disease due to the presence of an inflammatory pannus (Figure 2). It is possible to measure quantitatively the volume of the erosion, though this requires advanced MR equipment and delays the technique process.<sup>20</sup>

Through MRh, tendons are presented in axial planes as hypointense structures both in T1 and T2 potentiated sequences. The presence of tendinous edema or tendinosis is detected through MRh as an increase in signal from within the tendon in both sequences (T1 with gadolinium and T2). In tendons that have a synovial sheath, peritendinous effusion is seen as halo of increased signal in T2 sequences and tenosynovitis is seen as a hyperintense halo in T1 after gadolinium uptake (Figure 3). Given that all sheathed tendons present, under normal circumstances, a small quantity of T2-hyperintense synovial fluid, some authors recommend that the increased signal halo in T2 be >1 mm to be considered as pathologica.<sup>121</sup> The quantification of damage of the tendons requires protocolized methods, special MR equipment and occasionally needs for a comparison with the contralateral structure to discriminate differences. We currently have very few methods to evaluate and quantify tendinous affection in RA and none of them have been validated. The most commonly employed, described by McQueen et al,<sup>21</sup> includes a total of 9 tendinous groups and evaluates the size of the tendon, tendinosis, and tenosynovitis on the axial plane. Joint cartilage is

**Figure 2.** Magnetic resonance of the hand, coronal, and axial planes, T1 sequence with fat suppression after the administration of paramagnetic contrast with intravenous gadolinium. Active erosion on the radial side of the second metacarpal head.

difficult and, in many cases, structural lesions of RA patients impede its measurement and/or quantification.

### **Methodology for Evaluation and Quantification: Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS)**

It is possible to use MRh to quantify inflammatory lesions (current disease activity): joint synovitis, peritendinous swelling, tendinosis, bone edema, and as a method to evaluate the degree of structural lesion (erosions). Currently, the RA committee experts of the OMERACT consensus have proposed a series of general recommendations concerning the realization and standardized evaluation of the main alterations in RA as seen by MRh. Using the RAMRIS grading system proposed by OMERACT, it is possible to evaluate in a semi quantitative manner the erosions, bone edema, and synovitis in RA<sup>22-26</sup> and an atlas has been developed to facilitate its interpretation and lecture<sup>27-30</sup> (Table 1).

Every measurement tool is considered valid when it has an interclass agreement coefficient (IAC), interobserver, and intraobserver higher than 75%. An IAC for synovitis, bone edema, and erosion of 78%, 93%, and 92%, intraobserver agreement respectively has been found, and the interobserver agreement is approximately 77% for the different scores of the RAMRIS system. The

**Figure 3.** Magnetic resonance of the hand, axial plane, T2 sequence of the distal radioulnar joint. Hyperintense peritendinous halo >1 cm, that corresponds to common flexor finger tendon package tenosynovitis.

a structure that presents an intermediate signal in T1 and T2 potentiated sequences, in other words, it is isointense when compared to the adjacent muscle. The best sequence for its evaluation is T2 with proton density, fat suppression and carried out on an axial plane. When cartilage is altered, it is seen as irregular and discreetly more hyperintense than the surrounding muscle. Measuring cartilage width or volume is possible, but in the hand it is minimal, making its evaluation

**TABLE 1. Definition, Basic Sequences, Anatomic Planes and Areas, and RAMRIS System Scores as Proposed by the OMERACT Task Force\***

	Definition	Sequence/Planes	Anatomical Areas	Score/Total
Synovitis	Area of the synovial compartment that shows hyperintensity before gadolinium	T1 before and after axial contrast	2nd to 5th distal radioulnar, radiocarpal, intercarpal	Score: 0-3 thirds of the maximum synovial volume that uptakes contrast. Total 0-21.
Bone edema	Poorly limited trabecular bone lesion that shows T2 hypersignal with fat suppression/STIR/or T1 hypointensity	2 fat suppression T or STIR, coronal	2nd to 5th MCPL heads, base of P1, 8 carpal bones, bases of 1st to 5th MCP, distal radius and ulna†	Score: 0-3, 0: no bone edema, 1: bone edema that occupies 1%-33% of bone, 2: bone edema that occupies 34%-66% of bone, 3: bone edema that occupies 67% to 100% of bone. Total 0-69
Erosion	Well-limited juxtaarticular erosion that shows loss of normal hyposignal of cortical bone and hypersignal of trabecular bone on T1 visible on 2 planes with loss of cortical bone signal visible at least on 1 plane	T1†/axial and coronal	2nd to 5th MCPL heads, base of P1, 8 carpal bones, bases of 1st to 5th MCP, distal radius and ulna†	Score 0-10 (% of volume that the erosion occupies on the bone, 0: no erosion, 1: erosion occupying 1%-10% of bone, 2: erosion occupying 11%-20% of bone. Total 0-230

\*In the case of long bones, it is measured from the joint surface to 1 cm depth; carpal bones are evaluated as a whole.

†The administration of contrast with gadolinium allows for the evaluation of erosion activity due to the presence of inflammatory pannus. MCP indicates metacarpophalangeal; MCPL, metacarpal; 1P, first phalanx.

trustworthiness of this method is therefore optimal and it has a satisfactory sensitivity to change.<sup>26,31</sup> The OMERACT task force does not include quantification of tendinous lesions in RA, though recent studies consider that the interobserver and intraobserver agreement is acceptable, with ICC values ranging from 73% to 85% and could constitute a criterion to consider in the RAMRIS scoring system.<sup>32</sup> The presence of erosions and bone deformity in RA make the evaluation of the cartilage volume difficult in these patients, leading to low intra and interobserver agreement and its incorporation into RAMRIS is not currently contemplated. RAMRIS is currently the most used validated method in recent biologic therapy studies in RA patients.

### Usefulness of Hand and Wrist MR in Early Arthritis: Diagnostic and Prognostic Value

MRh is more sensitive than a conventional hand x-ray for the detection of erosions in RA, though its specificity is less well established. A recent study that evaluates the specificity of MRh estimates a prevalence of changes that may suggest synovitis among healthy patients of approximately 9% of joints and 2% for erosions. In the case of synovitis, a discreet elevation in C-reactive protein (CRP) and/or seropositivity for rheumatoid factor (RF) was associated to the possibility of subclinical arthritis. Lesions suggesting erosions in healthy patients are usually small, single and do not present gadolinium

uptake and could be excluded for scoring by the RAMRIS system.<sup>33</sup> There is enough evidence that confirms that MRh is more sensitive than radiology in the detection of early erosions.<sup>34,35</sup> McQueen et al<sup>36</sup> demonstrated early erosions in 42 RA patients using MRh, compared to 15% shown by conventional radiology, and in many cases these lesions appeared in the first months of the disease. Because the criteria proposed in 1987 by the American College of Rheumatology (ACR) for the classification of RA lack specificity at the beginning of the disease, some authors propose the question of whether the detection of altered joints through MRh could be included as an ACR criteria for RA. Sugimoto et al<sup>37</sup> have shown that the "bilateral joint hyperuptake" criteria, evaluated through MRh after the infusion of paramagnetic contrast (Gd-DTPA) increases the sensitivity of the ACR criteria for RA from 77% to 96%. The combination of this with positive biologic markers such as anti-citrullinated peptide antibodies or RF, with the MRh parameters (symmetric synovitis, bone edema, erosions) has a sensitivity and a specificity for the detection of early RA of 82.5% and 84.8% respectively.<sup>38</sup> It is possible that the detailed study of anatomical alterations and their localization through MRh, especially at early stages of disease, allow for the differentiation of RA from other inflammatory arthropathies. X-rays have shown that erosions in RA are preferentially located on the radioulnar joint (radial styloid process, ulnar styloid process, Mannerfelt crypt) and on the radial side of the

second and third MCP joint and, in contrast lack the sensitivity for the study of the carpal bones in early stages of disease. MRh confirms such findings and allows for a more precise evaluation of carpal erosions; capitate, triquetrum and lunate bones are those mainly affected at the beginning of the disease.<sup>36,39,40</sup> Little is known of the prevalence of tendon alteration in early RA and occasionally can be the first and only manifestation of disease. A recent study using MRh estimates a prevalence of 75%-80% in tendons of the fingers of patients with early RA.<sup>41</sup> Previous studies on carpus MR show similar prevalence values.<sup>34,36</sup> Though it has been demonstrated that in RA flexor tendons of the hand and carpal are affected more frequently than the extensors, some researchers have shown a more prevalent affection of extensor tendons in early RA, especially the ulnar extensor tendon of the carpus.<sup>21,42</sup> The inflammatory process of the bone insertions of ligaments and tendons, known as enthesitis, is shown in MR as a hyperintense T2 and STIR sequence signal in the tendon and ligament insertion zone, associated to adjacent bone edema. This finding is a sign that MR could differentiate, in initial stages of the disease, spondyloarthropathies from RA.<sup>43,44</sup>

Currently, the few studies that employ MR for the differential diagnosis of RA with SLE, Sjögrens Syndrome,<sup>45</sup> or psoriatic arthritis<sup>46</sup> don't find statistically significant differences regarding synovitis, erosions, or tendinous alterations. The different parameters evaluated by MRh are employed as predictive markers of erosions, allowing the clinician to select patients with a worse prognosis and establish a rapid and aggressive therapeutic strategy. Numerous studies show that synovitis, bone edema, and erosions evaluated through MRh predict the appearance and/or progression of radiologically evident erosions. Therefore, the general scoring of MRh (erosion, bone edema, synovitis, and tendinitis) at baseline seems to be predictive of radiologically evident erosions after 2 years of follow-up, with a sensitivity and specificity of approximately 80%,<sup>47</sup> and 78%, and with erosions evident in patients with RA after a 5 year follow-up through MRh up to 2 years earlier.<sup>48</sup>

Several studies consider that the intensity of gadolinium uptake, that is, the synovial volume reinforced after paramagnetic contrast infusion (synovitis) and total synovial volume (hypertrophy), are predictors of erosions at the beginning of disease. Conaghan et al<sup>49</sup> demonstrated in 40 patients with early RA that the appearance of erosions after 1 year of follow-up was only present in patients with synovitis seen by MRh and not when it was absent. Additionally, the quantitative measurement of the synovial volume that is responsible for the uptake of gadolinium in MRh of the manual measurement of the total volume (hypertrophy) seem to be disease activity markers and are correlated with progression of the erosions.<sup>50,51</sup>

Some authors point out that the most precocious bone alterations, such as bone edema, rarely occur when synovitis is absent<sup>52</sup> and in RA have been shown to possess a predictive value for erosive disease.<sup>51,53</sup>

McQueen et al<sup>54</sup> deserves special notice because they have shown that in 31 patients with early RA, baseline bone edema of the carpus is a predictive marker of future radiologically evident erosions ( $P=.01$ ) in a follow up period of up to 6 years.

Quantification through MRh of tendon affection at the beginning of RA can, in some cases, predict future tendinous ruptures in follow-up periods of up to 6 years.<sup>21</sup> Also, a recent study in 28 early RA patients with a follow-up of 8 years evidenced that erosions or bone edema at the beginning of the disease predict future tendon disfunction.<sup>55</sup> Due to this and in spite of not having conclusive data, it has been indicated that in RA there is a temporal sequence concerning lesions, from synovitis to bone edema and ultimately erosion.

### Use of MR as a Marker of Response to Therapy, Activity, and Remission in RA

Clinical and biological parameters as well as compound scores as well as traditional techniques such as x-rays are employed to measure disease activity and treatment efficacy in patients with RA. In spite of the fact that conventional radiology is still the standard to document structural damage and evaluate response to treatment, other, more sensitive, and specific imaging techniques are necessary to allow for fast and effective therapeutic decisions. The joint destructive process that is most relevant is bone erosion and this constitutes the lesion that determines the capacity of the different treatments to delay or prevent structural lesions. Few studies have evaluated efficacy of DMARDS through MR concerning the reduction in structural defects. Reece et al<sup>56</sup> have shown, through quantitative analysis of the gadolinium signal, that leflunomide significantly reduced synovial inflammation when compared to methotrexate after 4 months of follow-up in 39 patients with RA and knee synovitis. Ejbjerg et al,<sup>57</sup> in contrast, did not find a beneficial effect on the reduction in synovitis and the progression to erosions through MR when examining the association of cyclosporin A with methotrexate and intra-articular steroids in patients with RA.

Recent publications have used MRh to evaluate the efficacy of biologic treatment in the reduction of erosions and synovitis<sup>58-66</sup> (Table 2). These studies allow the affirmation that monitoring response to treatment through MRh offers certain advantages with respect to x-rays, allowing a fast and objective evaluation of the evolution of structural damage, which is the main objective of any therapy for RA. Maybe the main advantage is that in a short period (6 weeks) of biologic therapy it is possible to show, using

MRh, a statistically significant reduction in synovitis ( $P=.036$ ).<sup>65</sup>

Though some studies have correlated the different parameters of MRh (synovitis, bone edema, erosion, Tendon alterations) with clinical and biological activity markers in patients with RA, no conclusive data is available. Goupille et al<sup>67</sup> have shown that in approximately 60% of patients with RA there is a lack of agreement between MRh and painful and/or swollen joints detectable through examination of the patient, with statistically significant differences (synovitis in 162 joints detected through MRh vs 59 through examination;  $P=.0002$ ).

Several studies have shown CRP to be the biologic marker that better correlates with activity detected as MRh synovitis. Klarlund et al<sup>68</sup> established a positive and statistically significant ( $P<.006$ ) between CRP and synovial volume quantification in 37 Ra patients

compared to a control group. Also, in a 1-year follow-up, baseline CRP seems to be a predictive marker for the presence of erosions detected through MRh.<sup>69</sup> The total score obtained through the RAMRIS system, synovitis, and the intensity of gadolinium uptake by synovial tissue are MRh parameters that correlate with an increased activity evaluated using DAS.<sup>19,36,67</sup>

Synovial membrane gadolinium reinforcement (synovitis) is statistically correlated ( $P=.0002$  to  $P=.0007$ ) with the Health Assessment Questionnaire (HAQ)<sup>19</sup> and patients with a higher MRh score of the tendon affection are those with a worse functional capacity.<sup>21</sup> Occasionally, patients with apparent clinical and biologic remission present with progression of the radiologically evident lesions. The Ejbjerg et al<sup>70</sup> study in 132 patients with RA initially showed, after a follow-up of one year, that erosions and synovitis had progressed, even in

**TABLE 2. Response to Biologic Therapy Using Magnetic Resonance (MR) in Patients With Rheumatoid Arthritis. Main Studies**

Author/Year	N	Biologic Therapy	MR	Follow-Up, Months	Main Variable	Results
Scheel AK/2004*	16	Adalimumab ±MTX	MCP and PIP	3	Synovitis (OMERACT)	Reduction of synovitis of 11.8 to 10 in the first 3 months ( $P<.05$ )
Zikou AK/2005*	13	Adalimumab	Hand*	12	Synovitis (VUST)	Reduction of VUST in 84.6% of patients
Quinn MA/2005*	20	Infliximab ±MTX	MCP	12	Synovitis, bone edema, and erosion (OMERACT)	Statistically significant reduction in synovitis and bone edema at 14 weeks of follow-up. Less erosions in the infliximab treated group ( $P=.0125$ )
Gaylis NB/2005*	41	Infliximab	Hand*	12	Erosion (size and signal on T1)	Stability of erosions in 75% of patients and regression in 20%
Haavardsholm EA/2005*	27	Infliximab 48.2%; etanercept 18.5%; adalimumab 33.3%	Carpus	12	Erosion (OMERACT)	MR has similar sensitivity to change than x-rays of both hands
Haavardsholm EA/2005*	19	Infliximab 47.4%; etanercept 21.1%; adalimumab 31.5%	Carpo	12	Synovitis, bone edema, and erosion (OMERACT)	Rapid reduction in MR parameters in the first 6 months of biologic therapy
Dohn UM/2005*	5	Etanercept	Hand*	4	Erosion (OMERACT)	No erosions in spite of synovitis and bone edema
Lisbona MP/2005*	9	Etanercept ±DMARD	Hand*	1.5	Synovitis and bone edema (OMERACT)	Reduction of synovitis from 12.5 to 9.5 in only 6 weeks ( $P=.036$ )
Ostergaard M/2005*	17	Anakinra +MTX	Hand*	9	Synovitis, bone edema and erosion (OMERACT)	Basal score of synovitis and erosion in MRh correlates with progression of radiological erosions at 36 weeks. Progression of erosions with no statistically significant reduction of synovitis in spite of the association to anakinra

\*Includes carpus and metacarpophalangeal joints.

PIP indicates proximal interphalangeal joints; DMARD, disease modifying anti-rheumatic drug; MCP, metacarpophalangeal joints; MTX, methotrexate.

those cases with clinical remission (as defined by a DAS score of <2.6). Other authors have shown that patients in remission by ACR criteria still had synovitis as measured by MRh.<sup>71</sup> These discrepancies between remission by clinical-biological criteria and the MRh parameters are confirmed in a recent study with 107 patients with RA. 55%-57% of them had remission as defined by ACR and/or DAS<sup>28</sup> but only 6.5% as defined by MRh.<sup>72</sup>

Current criteria for remission do not include radiologic variables because of the limitations that are inherent to this technique, making the application of other techniques, such as MRh, of the utmost importance.

### Comparison Between Imaging Diagnostic Techniques in RA: MR, Echography, and Computed Tomography

Ultrasound or echography is an innocuous, well-tolerated, easy and rapid imaging method when done by experts and its low cost is perhaps the greatest advantage that allows for the realization of a dynamic study of the locomotor apparatus. Its main inconvenient is the impossibility to visualize the subchondral bone and the fact that its accuracy depends on the person carrying out the study. The application of color Doppler and power Doppler permit the study of blood flow with a good correlation to synovial vasculature in histological studies.<sup>73,74</sup> Inflammatory activity of the rheumatoid synovium evaluated through color Doppler and power Doppler have been shown to be similar to dynamic MR using paramagnetic contrast, allowing for the study of the same vascular phenomena.<sup>75,76</sup> Echography and MR both have a superior sensitivity than conventional x-rays for the early detection of erosions<sup>77</sup> and are similar for the evaluation of synovitis and other soft tissue lesions.<sup>78-80</sup>

Computerized tomography (CT) is a procedure with no clear advantages over MR because it produces ionizing radiation and is uncomfortable for the patient. Its main limitation for the study of RA is a reduced sensitivity for the visualization of synovial and soft tissue, though it provides maximum definition of cortical bone and, therefore, of erosions. A recent study that compares both techniques and using CT as a reference point shows MRh to be less sensitive (67%) though more specific (91%-96%) to detect erosions.<sup>81,82</sup> CT of certain anatomical areas (ie, the base of the metacarpal bones) and in cases of small erosions allow for a better delimitation of cortical bone,<sup>83</sup> but when it comes to evaluation of disease activity, MR offers certain advantages over CT, allowing the clinician to determine if the erosion is active or not due to the hyperintense signal that comes from gadolinium-enhanced T1 sequences that show pannus in the erosion.<sup>19</sup>

### Indications for MRh in Daily Clinical Practice. Future Perspectives

The capacity of MRh to detect early changes in soft and synovial tissue, bone and extraarticular makes this technique a useful tool in the study of RA. It is therefore necessary to establish, according to the evidence at hand, possible indications for MRh in RA as well as to evaluate early structural alterations that are otherwise not susceptible to exploration by other means such as radiology and the study of structural damage in anatomically inaccessible sites, such as the wrist.

Numerous studies have shown the predictive value of MRh, allowing us to know the prognosis at the beginning of the disease and to make fast and effective therapeutic decisions to delay or prevent structural damage. MR is an acceptable method in terms of confidence and has enough sensitivity to change to make it applicable as a tool for disease activity and therapeutic response monitoring, mainly in patients undergoing biologic therapy, because of its rapid effect. It has been demonstrated that cases of clinical and biological remission present a radiological evident erosion progression. MRh allows for a real evaluation of disease activity of the disease in all patients with apparent remission and, in consequence, an adequate therapeutic decision.

Possible future applications of MRh would be to examine the capacity of this technique to allow for the diagnosis of different inflammatory arthropathies based on anatomical localization of the structural lesions or the type of lesion, such as enthesitis in the case of spondyloarthropathies. On the other hand, knowing the sensitivity and specificity of MRh as a diagnostic or classification criteria at the beginning of the disease, and lastly, the capacity of this modality to help in the selection of patients with worse or better prognosis or even as responders to therapy or not.

The technical advances in the development of equipment of dedicated MRh, with a larger resolution for imaging and even portability, as well as the adequate training to interpret results, are hopeful proposals for the application of MRh in the diagnosis, follow-up and prognosis in patients with RA. Nonetheless, there are still many questions and more studies are needed to allow for some answers to these and other questions.

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