

# Magnetic resonance imaging in rheumatoid arthritis

Wilson Campos Tavares Junior<sup>1</sup>, Renata Rolim<sup>2</sup>, Adriana Maria Kakehasi<sup>3</sup>

## ABSTRACT

Rheumatoid arthritis (RA) is a chronic inflammatory polyarthritis that often leads to progressive joint destruction and disability. The treatment and management of RA has been based on early identification of the disease and intervention with disease-modifying antirheumatic drugs (DMARDs). Changes in management have resulted in significant improvements for patients with RA, including reduction of signs and symptoms of disease, joint preservation, and reduction of structural damage progression. In addition, sensitive methods to assess treatment response and predict the course of disease are required. Regarding early diagnosis of RA, longitudinal studies have demonstrated that magnetic resonance imaging (MRI) is more sensitive than X-rays to demonstrate the presence and progression of bone erosions. On the other hand, many factors of poor prognostics have been linked to RA, including demographic, genetic, environmental, clinical, immunological, and radiographic. This paper presents considerations on the use of MRI in RA regarding diagnose, monitoring, and prognostic of disease.

**Keywords:** arthritis, rheumatoid arthritis, magnetic resonance imaging.

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## THE IMPORTANCE OF MAGNETIC RESONANCE IMAGING IN RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a chronic inflammatory polyarthritis, which frequently leads to progressive joint destruction and disability. Regarding early diagnosis of RA, longitudinal studies have demonstrated that magnetic resonance imaging (MRI) is more sensitive than radiography in demonstrating progressive erosive joint damage.<sup>1</sup> MRI is an important imaging technique that provides multiplanar images and is able to visualize a range of joint structures, including synovium, tendons, ligaments, bone, and cartilage. It does not use radiation, so it can be repeated as much as necessary, and allows longitudinal assessment. With the advances in sequence analysis software and lower costs, MRI is likely to become more accessible.

MRI is recognized as the imaging technology of choice for visualization of the inflamed synovial membrane and bone edema.<sup>2</sup> Furthermore, MRI has been shown to be a sensitive, non-invasive method for detection and quantification of bone erosions.<sup>3</sup> Erosions are visible on MRI on average two years before they are visible on radiographs and may become consistently visualized on radiographs of the metacarpophalangeal (MCP) joints only when 20%–30% of the bone is eroded on MRI.<sup>1</sup>

To assess and quantify the disease manifestation in RA, the degree of synovial inflammation (synovitis), bone marrow edema, erosions, and tenosynovitis, several scoring systems have been suggested, and the Outcome Measures in Rheumatoid-Arthritis Clinical Trials (OMERACT) and Rheumatoid Arthritis Magnetic Resonance Image Scoring system (RAMRIS) are the most studied and used in clinical practice.<sup>1,4</sup>

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Hospital das Clínicas of the Universidade Federal de Minas Gerais – HC/UFMG.

1. Physician Assistant of Radiology at the Hospital das Clínicas of the Universidade Federal de Minas Gerais – HC/UFMG; Radiologist Physician of the Ecoar Medicina Diagnóstica

2. Resident Physician at the HC/UFMG

3. Doctor, Professor of Rheumatology at Faculdade de Medicina da UFMG

Correspondence to: Wilson Campos Tavares Junior. Rua Gonçalves Dias, 750/1803 – Funcionários. CEP: 30140-091. Belo Horizonte, MG, Brasil.

E-mail: wilsoncamp2000@yahoo.com.br

Ultrasound (US) is commonly used to assess soft tissue disease or detect articular fluid collection. High-frequency US transducers enable ultrasonographic assessment of small joints. It can also be used to visualize others structures, such as cartilage and bone surface, and can detect cortical defects, extensor tendon sheath thickening and synovial proliferation. However, the diagnostic ultrasound does not provide useful information on intraosseous pathologies. Adequate skill of the sonographers is another requirement for this method.

Few studies have investigated the differential diagnostic value of MRI, with divergent results. The use of MRI for detection of synovitis in hands and wrists have shown some improvement in diagnostic accuracy (94% vs. 83%) in early undifferentiated arthritis patients.<sup>5</sup> In a study of patients with RA, systemic lupus erythematosus, and primary Sjögren’s syndrome with polyarthralgia involving the hand, the presence of bone edema in the MCP joints was much more common in RA patients.<sup>6</sup> Among 41 polyarthrititis patients who were unclassified despite clinical, biochemical and radiographic examinations, the application of the correct MRI classification as RA or non-RA was shown in 39 of 41 patient, when a revision was made after two years using the 1987 American College of Rheumatology (ACR) criteria.<sup>7</sup>

Results from a recent systematic review showed that anti-cyclic citrullinated peptide (anti-CCP2) antibodies in patients with RA for less than two years have almost identical sensitivity to rheumatoid factor (56% vs. 58%), although with considerably higher specificity. In early RA, a positive anti-CCP2 test showed a positive likelihood ratio of 12.7, but sensitivity was higher in studies of established RA. Sensitivity for predicting RA before symptom onset seems lower, although specificity remains high.<sup>8</sup>

## MRI TECHNIQUE

In early RA, wrist and hand involvement are usually bilateral. Some authors perform bilateral MRI of the wrists or hands, but the study of the dominant or more painful wrist is routinely used, assuming that the joint involvement in this wrist will be higher than in the other wrist and hand. The use of MRI in a single hand reduces time, cost and discomfort for the patient. The areas of interest are wrists, MCP joints, and proximal interphalangeal joints. The distal radius and ulna, the carpal bones, and the MCP joints can be visualized together within a Field of View of 120–160 mm.<sup>9</sup>

Usually, MRI studies of RA patients have focused on one or two joint regions – most frequently the wrist – and on the

second through fifth MCP joints. Consequently, MRI may reduce the sample size of joints and follow-up time in exams, due to greater sensitivity in distinguishing between responders and non-responders, as corroborated in clinical trials.<sup>10,11</sup> Basic interpretation of RA changes on MRI among readers is relatively consistent.<sup>12</sup>

The OMERACT group recommends starting with a coronal STIR sequence or a Fat Saturated T2 sequence (only available in high-field scanners > 0.6 T) on the wrist and MCP joints for bone marrow edema detection, followed by a 3D isotropic T1-w gradient echo sequence; or a T1 sequence on the coronal and axial plane before and after gadolinium contrast for detection of bone erosions and synovitis.

Intravenous contrast is necessary to estimate the degree of synovial inflammation and to differentiate the synovial membrane enhancement from the surrounding tissues. Synovitis tends to be overestimated if it is scored based on the STIR or T2 fat-saturated images, because joint effusion cannot be differentiated from synovitis when using T2 sequences.<sup>1,13</sup>

Before the RAMRIS score was developed, manual measurement of the volume of enhancing synovium was used as a measure of treatment response and was recognized as a strong predictor of future disease progression.<sup>1</sup> Table 1 shows the main pattern of MRI in RA.

## MRI FINDINGS

### Synovitis

The thickening of synovial tissue caused by the rheumatoid inflammatory process may be identified on MRI. Synovitis has

**Table 1**  
Main pattern of MRI in RA

Characteristics	Specifications
Joints regions examined	Wrist and second through fifth metacarpophalangeal unilateral, the most painful
MRI damage signs	Edema, synovitis, erosion, tenosynovitis
Equipment-magnetic type	Magnetic field recommendation is 1.5 Tesla
Contrast	Gadolinium
Sequence	Coronal T1, axial T1, coronal T2 with fat saturation, contrast enhanced axial and coronal T1 with fat saturation
Monitoring response therapy (score)	OMERACT/RAMRIS, synovium volume measurement, scoring contrast-enhanced dynamic

OMERACT/RAMRIS: Outcome Measurement Rheumatoid Arthritis Clinical Trials/Rheumatoid Arthritis Magnetic Resonance Imaging Scoring System.

an intermediate to low signal intensity on T1-weighted images and, due to the increased water content, high signal intensity on T2-weighted images.<sup>2</sup> MRI signs of synovitis include increased synovial volume, increased water content, contrast enhancement (increased signal intensity after the intravenous injection of gadolinium-based contrast material) (Figure 1).<sup>2</sup>

MRI is more sensitive than clinical examination in detecting synovitis in inflammatory arthritis and shows synovial inflammation in early RA.<sup>14,15</sup> On RA, the hypertrophic active synovium can invade and erode contiguous bone and cartilage.

Contrast-enhanced T1-weighted image is considered very sensitive and specific for assessment of acute synovitis, as reported in an article of Ostendorf et al.<sup>16</sup> When examined the second MCP joint using miniarthroscopy and MRI, it shows enhancement postcontrast in 86% of synovitis patients.<sup>16</sup> McQueen et al.<sup>17</sup> found that 93% of a cohort of 42 RA patients had evidence of MRI synovitis at the wrist within 6 months of the onset of symptoms. Acute synovitis has been shown to enhance rapidly and intensely after the intravenous administration of gadolinium-based contrast material, unlike joint effusion, which does not enhance in the early phase. This early phase lasts approximately 5 minutes after injection. Images obtained from 10 minutes after injection may not accurately delineate the extent of the synovitis, since gadolinium may be excreted into the synovial joint fluid.

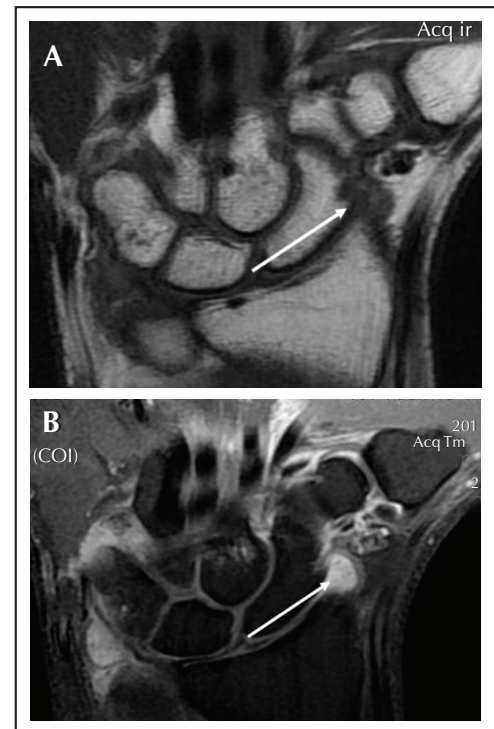
Fibrotic pannus, which is usually present in end-stage of RA, appears relatively hypovascular after the intravenous administration of gadolinium. Moreover, with T2-weighted sequences, fibrous pannus with intermediate to low signal intensity can be distinguished from acute synovitis and joint fluid.<sup>2,18,19</sup>

### Bone marrow edema

Although bone marrow edema is nonspecific and has been well documented in traumatic, neoplastic, and degenerative bone processes, it is reported to be an important MRI finding in patients with RA, especially in the earlier phases of the disease.

Bone edema refers to a unique MRI-detected abnormality with high signal intensity on fat-suppressed MRI sequences and could enhance after contrast administration (Figure 2).

Bone edema is defined by OMERACT as a lesion within the trabecular bone with ill-defined margins and signal characteristics of increased water content.<sup>20</sup> When present, it correlates with the severity of adjacent synovitis and it seems to be an independent predictor of erosion development.<sup>21</sup> An image study of the wrist in early RA found that bone edema is a strong predictive aspect of the development of conventional radiography erosions and also predicts functional outcome six years later.<sup>22</sup>



**Figure 1** Synovitis in a 36-year-old man with early RA of the wrist (eight months duration) and normal radiographic finding. **(A)** Coronal T1-weighted MRI shows radio carpal synovitis as low signal intensity (arrow). **(B)** Coronal gadolinium-enhanced fat suppressed T1-weighted MRI shows intense enhancement of the radio carpal synovitis.



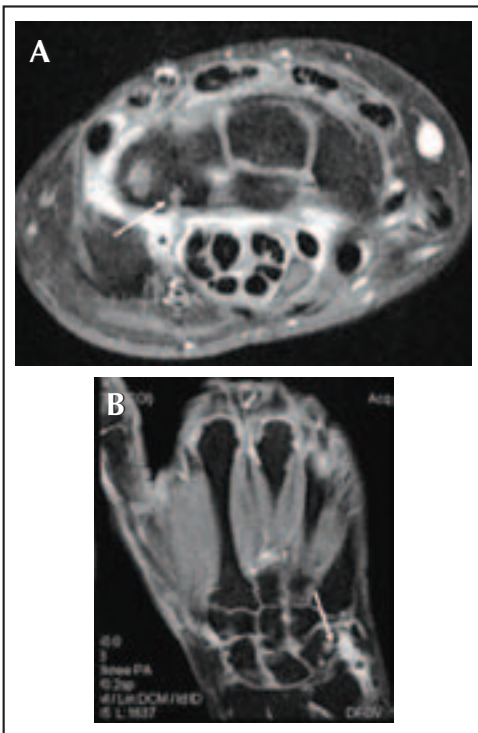
**Figure 2** Bone marrow edema in a 37-year-old man with early RA of the wrist. Coronal T2-weighted MRI shows pyramidal bone edema represented by high signal intensity (arrow).

### Erosions

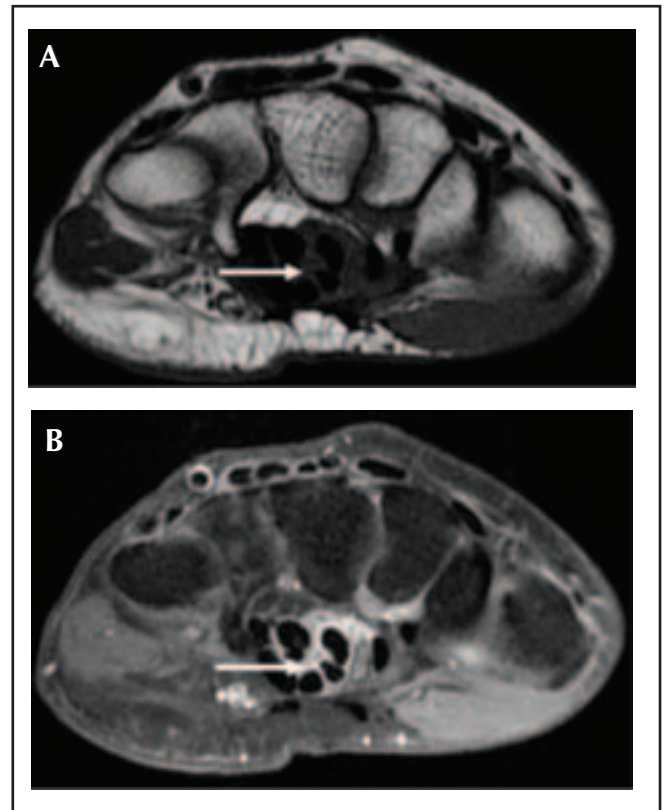
The detection of erosions on MRI is important because it contributes for diagnosis and prognosis in RA patients.<sup>23</sup> MRI could provide an early diagnosis of RA by revealing erosions, whose presence constitutes one of the ACR 1987 diagnostic criteria. MRI erosions have been shown to be predictive of later progression in cohorts followed for up to six years.<sup>24</sup>

The MRI definitions of erosions on T1-weighted images are loss of normal low signal intensity of cortical bone and loss of normal high signal intensity of the bone marrow cavity, with enhancement after the administration of gadolinium-based contrast material; and high signal intensity on T2-weighted and STIR images (Figure 3).<sup>13</sup>

The contrast enhancement of erosions implies the presence of inflamed synovium and is useful differentiating them from fluid-filled cystic lesions.<sup>2</sup> In the carpal bones the nutrient foramina may be shown in some sequences and could be mistaken for small erosions. Similarly, interosseous ligament insertions at the volar aspect of the carpal bones can simulate erosions.



**Figure 3**  
Erosions in a 54-year-old woman with early RA of the wrist (12 months duration). (A) Coronal T1-weighted MR unenhanced and gadolinium enhance fat suppressed T1-weighted MRI in axial and coronal. (B) The erosion in the pyramidal bone that is enhanced after gadolinium (arrow). Synovitis is seen in wrist (\*).



**Figure 4**  
Tenosynovitis in a 53-year-old woman with early RA of the wrist (16 months duration) and normal radiographic finding. (A) Coronal T1-weighted MR. (B) Coronal gadolinium-enhanced fat suppressed T1 MRI shows extensive flexor tenosynovitis with intense enhancement (arrow) and minimal extensor tenosynovitis with mild enhancement (arrow head).

Some attention is required since small erosion-like lesions were identified in two planes in about 2% of metacarpal and wrist bones in healthy subjects, but these lesions did not enhance after the administration of gadolinium-based contrast material and were not associated with bone edema.<sup>25</sup>

### Tenosynovitis

MRI signs of tenosynovitis include fluid in the tendon sheath, increased thickness and contrast enhancement of the tendon sheath synovium (Figure 4). Small amounts of fluid are usually seen in the tendon sheaths of the wrist in healthy subjects, especially in the extensor compartments. When the diameter of the fluid in the tendon sheath is less than the diameter of the corresponding tendon, the fluid could be considered normal.

Contrast enhancement of the tendon sheath synovium is considered a specific sign of tenosynovitis.

Tenosynovitis is clinically significant in early RA because joint synovitis and tenosynovitis represent the same process, and in some patients with early RA, tenosynovitis could predominate over joint synovitis.<sup>26</sup> Dorsal tenosynovitis of the wrist is associated with tendon rupture, which has been described as the invasion of the tendon by the sheath synovitis and fraying of the tendon against eroded bone margins.<sup>27</sup>

### Predictors of imaging progression

Substantial efforts have been exerted to identify patients with poor prognosis at the time of diagnosis and several promising prognostic markers have been identified.<sup>13,27</sup>

MRI erosion score and MRI bone marrow edema score were significantly and independently associated with radiographic progression after two years. The main finding was that MRI bone marrow edema at presentation was the strongest predictor of radiographic progression two years later in patients with early RA.<sup>1</sup>

Bone marrow edema is considered an early marker of inflammation, given that its presence is correlated with increased levels of acute phase reactants (erythrocyte sedimentation rate and C-reactive protein) and scales for the clinical evaluation of disease activity.<sup>28,29</sup>

MRI bone marrow edema may represent inflammatory infiltrate in the bone marrow of RA patient, and these lesions affect a higher percent of bones in established disease than in early disease.<sup>30</sup> In contrast to radiographic erosions, which reflect bone damage that has already occurred, bone marrow edema thus may represent an important part of the early immunopathological development in RA, and it could be reversed if recommended treatment is introduced.<sup>31,32</sup>

Methodological studies have reported that the sensitivity for detecting bone marrow edema may vary within different types of MRI units.<sup>7</sup> Regional MRI could be a predictor of radiographic progression in other anatomical regions according to previous studies.<sup>33</sup>

### Monitoring disease activity and damage

Several prospective follow-up imaging studies performed to compare radiography, US, and MRI findings demonstrate that US and MRI are more sensitive for visualization of inflammatory and destructive changes in joints and have major potential for improved examination compared to X-ray. Both US and MRI are in good agreement with clinical findings.<sup>34,35</sup> Traditional scoring systems developed for X-ray are not directly designed for MRI and US; they are predominantly qualitative and based on visual assessment of data with further

grading according to a given scale. Extraction of quantitative measurements is not trivial. Several scoring systems for MRI and US have been suggested over the years. The aim of the new systems is to counteract the limits of traditional evaluation, which is prone to high personnel costs and human errors.

Several authors have used quantitative and semiquantitative analyses of synovial volume, more or less effectively linking it to disease activity.<sup>36</sup> Volume measurement are often performed directly by manually outlining the inflamed synovium or erosions, which is a very time-consuming operation.<sup>37</sup>

The OMERACT 2001 test the interreader agreement of synovitis on RA joints using MRI demonstrated a moderate level of agreement.<sup>38</sup> The OMERACT 6 group (2003) found high intrareader agreement for a trained reader.<sup>39</sup> A longitudinal study assessed intra- and interreader reliability shows good intrareader correlation.<sup>40</sup>

Synovitis, bone edema, and erosions on MRI have been defined by the Outcome Measures in Rheumatology (OMERACT) MRI Task Force and a scoring system, termed the RA MRI score (RAMRIS), and has been validated and evaluated for sensitivity to change in a longitudinal setting. The RAMRIS system does not, however, include a scoring system for tendons or a score for cartilage loss; this relates to non adequate image resolution of cartilage in small joints.

Recently, Haarvardsholm et al.<sup>41</sup> have published a scoring system for tenosynovitis based on semiquantitative scoring (0–3) of flexor and extensor tenosynovitis at the wrist in 10 anatomical areas. The maximum width of postcontrast enhancement within each anatomical area on axial T1-weighted images was scored, producing a potential maximum score of 30. This system was also tested for reliability in a longitudinal setting and provides a useful adjunct for the conventional RAMRIS. The evaluation of cartilage changes on MRI, however, remains an important research goal.

The OMERACT synovitis score is sensitive to change of inflamed synovium over weeks as well as months.<sup>2</sup> MRI is being increasingly used when the treatment is associated with biological agents to measure changes in synovitis. MRI is more sensitive than X-ray for monitoring erosive progression in individual joint regions.<sup>42</sup>

The score of each synovitis, bone erosions, and bone marrow edema is made from individual joints; synovitis is scored 0–3 in each of the distal radioulnar, radiocarpal, intercarpal-carpometacarpal, and second through fifth MCP joints. Bone changes are scored in each of the carpal bones, distal radius, distal ulna, and metacarpal bases. Erosions are scored 0–10 and edema 0–3, as a fraction of the bone involved within 1 cm of the joint line.<sup>4,6,43</sup>

Although the RAMRIS system is specific for wrist and MCP joints, it has been modified for use in the feet, and there is some

evidence to suggest that, as with X-rays, MRI of the feet may be more sensitive, revealing changes in the feet even if the hands are not involved. Scoring of the feet may therefore be of use in early disease, and the parameters are the same used for the hands.

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## CONCLUSION

The classification criteria for RA published by the ACR in 1987 are useful to ensure a uniform patient population when comparing experience and clinical treatment results between countries, but is not useful for early diagnosis of RA. In

2010, a new classification criteria were introduced with the aim to facilitate the study of patients at earlier stages of the disease.<sup>26</sup> MRI has the importance of detecting bone damage, particularly when radiographs are normal, contributing with this emerging tool for the diagnosis. With the advent of more powerful treatment strategies, the accurate diagnosis is the central topic related to the ability to select and initiate treatment programs, as is the ability to differentiate between responders and non-responders patients. Surely, the MRI characteristics can provide support in many of these aspects of RA management.

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