MRI in imaging of rheumatic diseases: an overview for clinicians

I. Eshed[1], K.G.A. Hermann[2]

[1]*Department of Radiology, Sheba Medical Center, Tel Hashomer, Israel;*
[2]*Department of Radiology, Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Humbolt-Universität zu Berlin, Freie Universität Berlin, Berlin, Germany.*

Iris Eshed, MD
Kay Geert A. Hermann, MD, PhD

Please address correspondence to:
Dr Kay-Geert A. Hermann, Charité, Universitätsmedizin Berlin, Department of Radiology (CCM), Charitéplatz 1, 10117 Berlin, Germany.
E-mail: kghermann@gmail.com

Received on September 11, 2018; accepted in revised form on September 13, 2018.

Clin Exp Rheumatol 2018; 36 (Suppl. 114): S10-S15.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2018.

Key words: whole body MRI, dynamic contrast enhanced MRI, diffusion-weighted imaging, dynamic contrast-enhanced MRI, T2 mapping

Competing interests: none declared.

ABSTRACT

Magnetic resonance imaging (MRI) is a technique that utililises powerful magnets and radiofrequency to produce 3-dimentional images. MRI does not involve ionising radiation and has superb tissue resolution, enabling excellent delineation of anatomy as well as pathology in joints. This article briefly reviews the technical principle of magnetic resonance and discusses advantages and disadvantages of the technique, with particular attention to rheumatologic imaging. New information is summarised concerning the use of contrast media, dynamic, contrast-enhanced MRI, diffusion-weighted imaging, cartilage imaging and whole-body MRI.

Introduction

Magnetic residence imaging (MRI) is a technique that utilises powerful magnets and radiofrequency to produce 3-dimentional images. MRI does not involve ionising radiation and has superb tissue resolution to provide excellent delineation of joint anatomy and pathology. Thus, it is currently considered the optimal non-invasive imaging modality for evaluation of inflammation and its outcomes in joints and their surrounding tissue. With introduction of effective therapies such as TNF-alpha blockers, a need to detect early inflammation was met which led to a surge in its use as a diagnostic and follow-up tool in rheumatic diseases. Refining and improving the MRI units and their techniques is constantly ongoing, leading to shorter scanning times, improved resolution, and enhanced diagnostic capacities. In this review of MRI properties and challenges, contemporary perspectives on developments and advances in the field of MRI in rheumatic diseases will be discussed.

Technical principles

The principle of magnetic resonance is based on the fact that the protons of the atomic nuclei of the object under investigation, *i.e.* generally humans in clinical care, are brought out of their natural, random movement and into a rectilinear movement by an external magnetic field generated by the magnetic resonance scanner. The individual protons are called spins. As a result of an intentionally initiated drop in the external magnetic field, the stimulated spins regain their natural precession direction and speed, releasing electrical energy that can be detected with highly-sensitive coils.

Coils are very important in magnetic resonance imaging, and can be used both to transmit the MR radio frequency pulse and to receive the signals. Not all coils are visible; some are already built into the MR scanner. Thus, in most applications, the body coil forms the tunnel of the magnet and serves to transmit the radio frequency signal. This coil also can be used to receive the signals, but often does not achieve good image quality.

Special receiver array coils are adapted to different body regions. The receiving coil for the spinal column is permanently installed in the table of the MRI device. Other receiving coils can be used for specific applications, *e.g.* the torso coil, the knee coil, the head coil, the shoulder coil, and flexible surface coils. The quality of the coils, as well as the field strength, influence the image quality. Therefore, it is possible to produce high-quality MR images with a 1.5 Tesla magnet with an excellent coil – compared to a 3 Tesla MRI unit with a standard coil.

In addition to the main magnetic field, different gradient fields are generated, which are used for position-coding of individual protons or spins. T1-weighted, proton-weighted and T2-weighted MRI sequences are distinguished according to the time of excitation of the protons and the time between excitation

and readout of the signal. However, many other variants exist which may influence the contrast of MR images, as described in greater detail below.

Advantages of MRI

- Does not involve exposure to ionising radiation, in contrast to x-ray, CT and scintigraphy. Therefore, it can be used in vulnerable populations such as pregnant women and paediatric patients.
- Images can be acquired in multiple planes (axial, sagittal, coronal, or oblique).
- Produce three-dimensional, cross-section images of the body.
- Demonstrate excellent soft tissue contrast, enabling differentiation between fat, water and muscle, to better characterise of different joint structures such as ligaments, hyaline and fibrocartilage.
- Sensitive to bone marrow changes and can detect bone marrow oedema as in osteitis.
- With contrast material administration, can help in differentiation of synovial inflammation from joint fluid and characterisation of vascular inflammation.
- Advanced techniques such as diffusion, spectroscopy and perfusion allow for precise tissue characterisation.

Limitations of MRI

- Patient inconvenience; enclosed claustrophobic space, loud noises.
- Sensitive to metal and may cause metal heating and movement, therefore specific safety measures are required in patients with metallic and electronic implants and in patients with metallic foreign bodies.
- Requires patient's cooperation including non-movement and breath holding. Thus, anesthesia is needed in infants and non-cooperative patients.
- Relatively low spacial resolution compared to CT, resulting in thicker slices.
- Relatively long examination time of 30 minutes on average, compared to about 10 minutes for CT.
- MRI equipment is expensive to purchase, maintain, and operate.

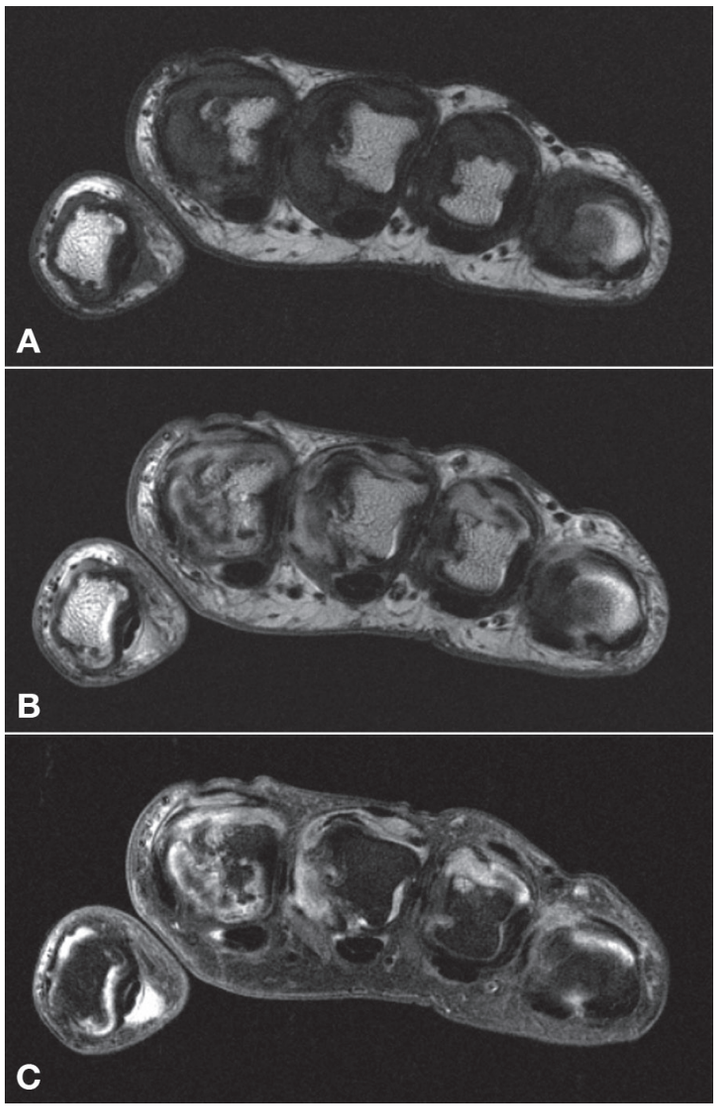

Fig. 1. The MCP joints of a patient with rheumatoid arthritis are shown in transverse slice orientation.
A. The native T1-weighted sequence shows the thickened synovial membrane as well as erosions of the heads of the metacarpal bones.
B. After injection of paramagnetic contrast medium, this synovial membrane appears hyperintense as an expression of active inflammation.
C: With the T1-weighted MRI sequence with fat saturation, both erosive destruction and active inflammation can be visualised and differentiated in one image.

Field strengths

MRI requires a magnetic field that is both strong and uniform. The field strength of the magnet is measured in Tesla units. The most commonly used magnets today vary between 1 and 3 Tesla, although the range goes from 0.2 to 7 Tesla for certain applications. The stronger the field strength, the stronger is the produced signal, and a stronger signal results in larger signal-to-noise ratio (SNR). Larger SNR help producing higher image resolution or shorter imaging time. However, stronger field strengths are associated with greater field inhomogeneity; therefore, higher field strengths raise new challenges in addition to its benefits.

Extremity dedicated MRI units allow positioning of only the imaged extremity within the magnet's bore, in contrast to the entire body in the conventional units, and are therefore more convenient to patients. These units are especially useful in patients with rheumatic problems (1). In older extremity dedicated units (0.2–1.0 Tesla), resolution generally was reduced compared to conventional MRI units. However, more advanced, new generation 1.5 Te-

sla extremity dedicated units result in comparable resolution to conventional units (2).

Contrast agents

Although MRI produces superb contrast resolution, some clinical questions require application of contrast agents. The most commonly used agents are gadolinium-based. Gadolinium has strong paramagnetic ions affecting the relaxation times of nuclei within body tissues, enhancing lesions that are highly vascularised such as vessels, tumours or inflamed synovium. Gadolinium based contrast agents generally are considered safe. The use of specific gadolinium chelates in individuals with acute renal disease was linked to the rare but severe complication of nephrogenic systemic fibrosis (3). Deposition of gadolinium in the basal ganglia even after a prolonged period of time also has been reported (4), although it is not known whether these deposits can lead to long-term adverse health effects.

The use of contrast agents in the peripheral joints of patients with inflammatory rheumatic problems generally is recommended (5). Fluid and synovial tissue both lead to high signal on T2 weighted images. Gadolinium administration leads to enhancement of the inflamed synovium, enabling clear characterisation of its thickness and joint involvement and differentiation from joint fluid (Fig. 1).

The use of contrast in the axial skeleton for detection of sacroiliitis and spondylitis is generally not advocated, in contrast to peripheral joints. In the axial skeleton, the cardinal findings of bone marrow oedema (both in the sacroiliac joints and the spinal corners) and structural changes (*e.g.* erosions and fat metaplasia) may be detected directly on T1-weighted and fluid sensitive sequences, and no additive value for gadolinium containing contrast agents was reported (6).

Specific MRI techniques

Dynamic contrast enhanced technique

Dynamic contrast enhanced (DCE) imaging describes the acquisition of baseline images without contrast enhancement, followed by a series of images acquired over time after an intravenous bolus of contrast material. DCE-MRI provides more than just morphological information given in the conventional post contrast technique to detail pathophysiological information regarding the inflammatory processes (Fig. 2), based on the time following injection and the concentration of contrast in the evaluated tissue. A perfusion curve or time intensity curve can be derived, allowing detection and quantification of 'wash-in' and 'wash-out' contrast kinetics.

In practice, the main area in which DCE imaging currently is applicable clinically in rheumatology is synovial activity assessment. Synovial activity can be assessed by measuring the volume of synovial proliferation and its perfusion, both for diagnosis and evaluation of the efficacy of treatment (7). Reduction in synovial perfusion was shown to be a more sensitive indicator of response than synovial volume in patients treated with TNF alpha blockers (8). DCE imaging remains a research tool at this time, but may be helpful in the future in routine care for diagnosis and differentiation between different rheumatic diseases in their earliest stages.

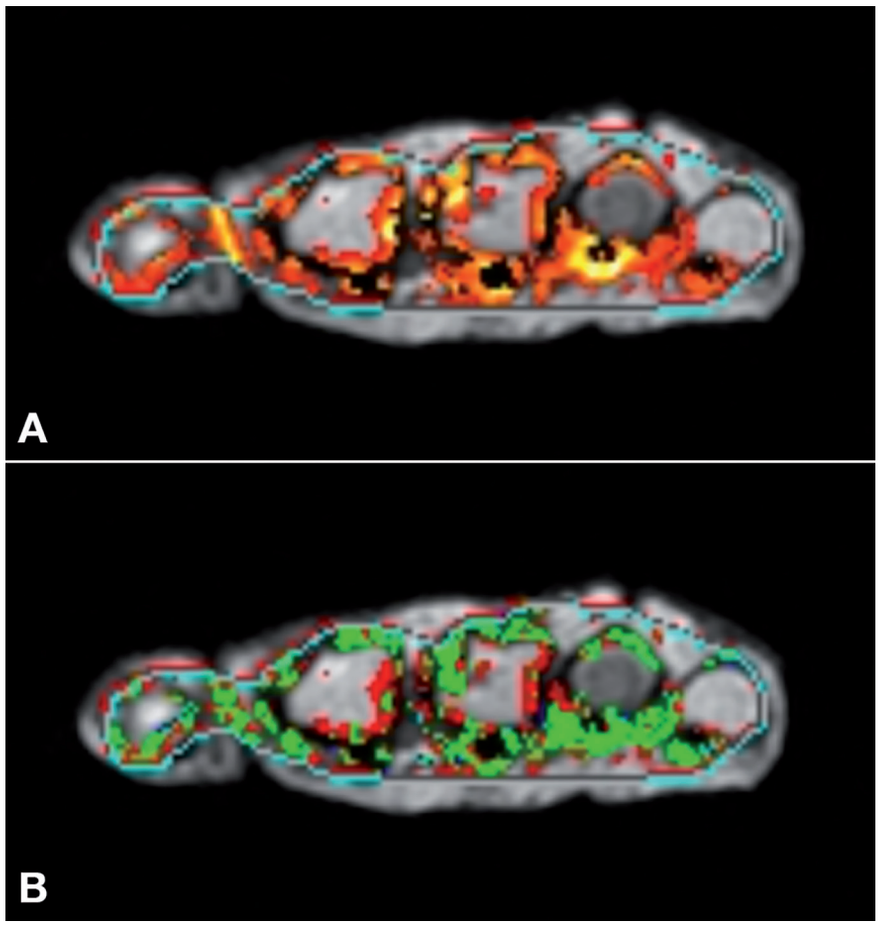

Fig. 2. DCE-MRI of a patient with active rheumatoid arthritis. Using coloured overlay maps, various technical and physiological parameters can be visualised.
A. Representation of inflammatory activity in the form of the maximum Rate of Enhancement (MRE). A very pronounced tenosynovitis of the flexor tendon at the fourth ray as well as moderate synovitis at the MCP joints II and III can be clearly seen.
B. Representation of the curve shape: red with washout phase after steep enhancement, green with plateau phase.

Diffusion weighted MRI

Diffusion-weighted imaging (DWI) is a technique adopted from neuroimaging, in which it is extremely useful in evaluating brain lesions. It is based on the tissue signal attenuation caused by thermal motion of water molecules in the tissue. The diffusion of water inside the tissue is hindered primarily by cell membrane boundaries. The greater the

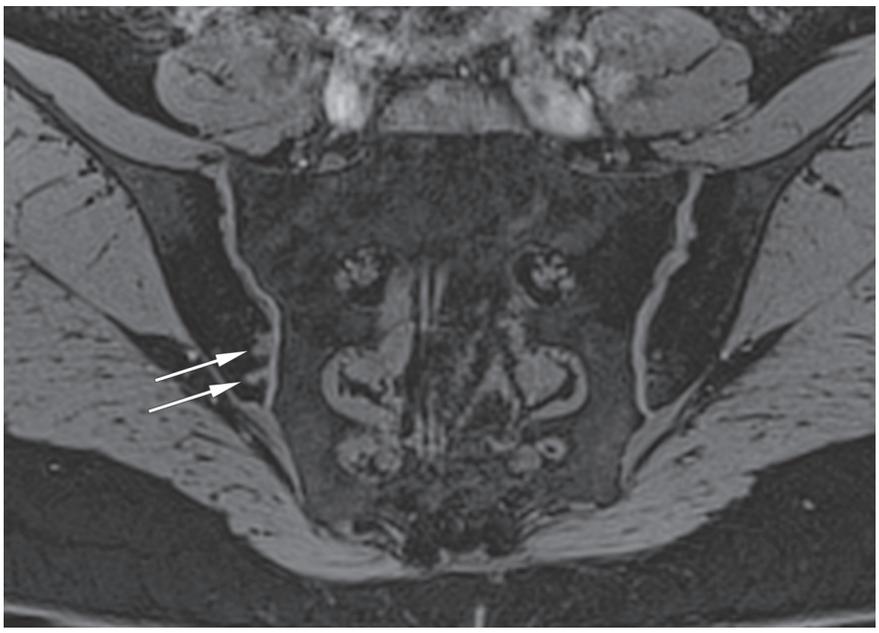

Fig. 3. Patient with early axial spondyloarthritis. The VIBE sequence shows a high signal intensity of the articular cartilage and depicts osseous erosions in high detail (arrows) due to the saturated fat signal. These erosions would have escaped detection in conventional T1-weighted images.

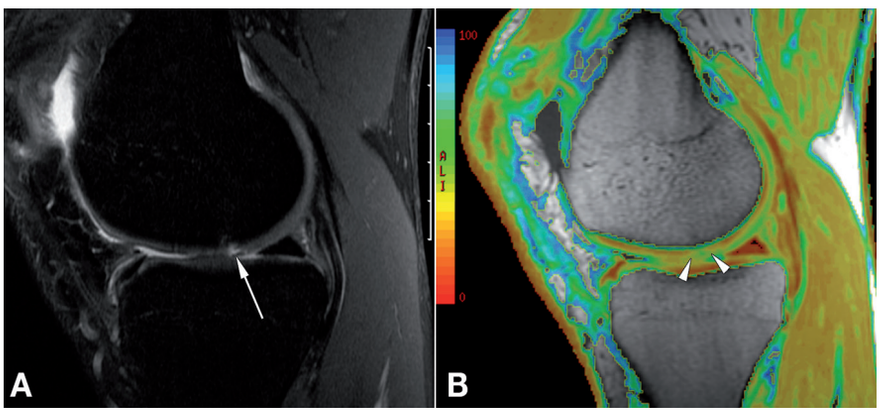

Fig. 4. A. Circumscribed cartilage defect in the medial femoral condyle of a hobby soccer player (arrow). **B.** The T2 mapping sequence clearly shows signal alteration in the corresponding area (arrowheads) as an indication of disintegrity of the extracellular matrix, especially the collagen fibres.

mean free path of water molecules, the greater the signal loss; in other words, the greater the cellularity, the more restricted is the diffusion. Thus, water molecule diffusion patterns can reveal microscopic details about tissue architecture, either normal or in a diseased state. Using diffusion, extracellular water has low signal whereas
intracellular water has high DWI signal. Inflammatory lesions are expected to have an altered ratio of intra- to extra-cellular water and thus an altered signal. Currently, improvements in resolution appear needed before the technique can be used more widely. However, with improvement, the technique may prove to be beneficial in detection of early inflammatory activity (9, 10).

Cartilage imaging

Hyaline cartilage tissue is an extremely organised structure sustained by structured type-II collagen fibre architecture, in which abundant water molecules and proteoglycans and few chondrocytes are distributed. Contemporary high-resolution MRI allows for a comprehensive evaluation articular hyaline cartilage in the joint. For example, it has recently been shown that cartilage-sensitive sequences are more effective to detect erosions of the sacroiliac joints compared to conventional T1-weighted sequences (11) (Fig. 3). Advanced MRI sequences are being applied successfully not only for evaluation of morphological cartilage, but also for evaluation of histological component evaluation, providing qualitative and quantitative information on early detection of cartilage damage, and value in monitoring treatment. Multiple types of sequences are used to this end, of which T2 mapping and delayed gadolinium enhanced sequences are the most commonly used.

T2 mapping

T2 mapping sequences aim to detect the content and integrity of the joint's hyaline cartilage collagen fibres and water distribution, based on fast spin echo technology. Using a high resolution, 3 Tesla MRI unit and an advanced knee coil, a multiple-echo sequence is performed. Each echo of the echo train produces a separate image, with different time-to-echo (TE) properties. Using a post processing workstation, a T2 value is calculated for each pixel in the image and a colour map is displayed.
T2 relaxation time depends on the amount of water and the integrity of the extracellular matrix, mainly secondary to collagen fibre density. The chemical interaction of collagen fibres with water protons results in a shortening of T2 relaxation time of the normal cartilage. A direct correlation is seen between T2 values and water content, and an inverse correlation with collagen concentration (12). In this manner, areas of injured cartilage show a decrease in extracellular matrix (mainly collagen and proteoglycans) and increased water content. By increasing the TE, T2 mapping can detect these areas of early injury (13).

Delayed gadolinium-enhanced MRI of cartilage

Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) is a sequence aimed to estimate the content of glycosaminoglycan within the hyaline cartilage in the joint. Glycosaminoglycans (GAG) are negatively charged side-chains of the cartilage proteoglycans. Gadolinium-based contrast agents also are negatively

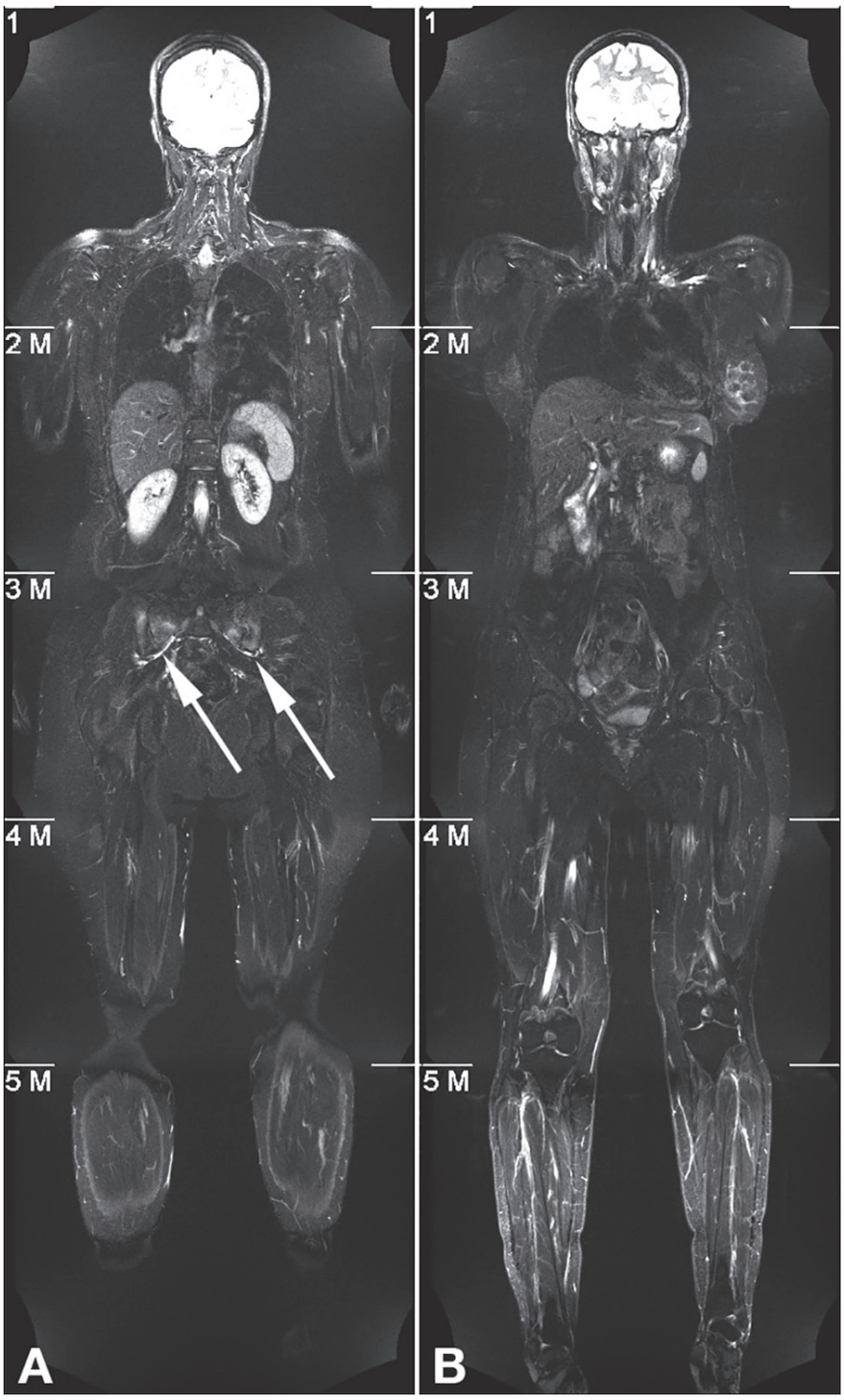

Fig. 5. A. Coronal whole-body STIR sequence of a patient with axial spondyloarthritis and active sacroiliitis (arrows). **B.** In the same session, the shoulder joints, hip joints, knee joints, and ankle joints are also acquired, although these were normal in this patient.

charged. The dGEMRIC sequence is based on these repelling properties between the two negatively charged molecules. After injection of the negatively charged contrast medium, it diffuses into the cartilage in an inverse relationship to GAG content-charged density, so that gadolinium enhancement will be seen in GAG reduced areas of the cartilage (14), providing an indirect quantitative outcome measure for cartilage GAG content. dGEMRIC has been shown to be a highly reproducible outcome measure of cartilage GAG content over time in early-stage OA of the knee, and is a used for standard assessment of articular cartilage GAG content in OA research (15, 16), but not to date not in routine clinical care.

Whole body MRI

MRI of the entire body can now be performed within 30–45 minutes using multichannel technology with the concurrent use of several coils. T1-weighted and short inversion time recovery (STIR) sequences can be performed with either of two goals, to image the entire body including the spine, shoulders and arms, anterior chest wall, and pelvis including the SIJ and the lower extremities applying specific planes for specific joints (17, 18) (designated true wbMRI, figure 6), or dedicated to the entire spine with additional semicoronal orientation for the SIJ (designated whole-spine MRI). wbMRI allows simultaneous assessment of peripheral and axial joints. In rheumatology, whole spine MRI has been applied to evaluation of spondyloarthritis, while true wbMRI is used to evaluate extent and localisation of paediatric patients with chronic recurrent multifocal osteomyelitis. wbMRI has been used in clinical studies to evaluate inflammatory involvement and treatment response in several rheumatic conditions, including spondyloarthritis, rheumatoid arthritis and psoriatic arthritis (19-22).

Conclusion

Magnetic resonance imaging (MRI) has advanced in rheumatology from a research tool to a routine imaging option for the musculoskeletal system, and thus supplements radiography and ultrasonography." The Magnetic resonance imaging (MRI) has become a reliable problem-solving option for imaging of the musculoskeletal system, in addition to radiography and ultrasonography. MRI has facilitated documentation of the efficacy of new pharmacological agents, with greater sensitivity in fewer subjects that had been available previously. In the future, functional MRI methods that describe the microstructure of joints and entheses more precisely may become increasingly important in routine clinical care.

References

1. SCHIRMER C, SCHEEL AK, ALTHOFF CE *et al*.: Diagnostic quality and scoring of synovitis, tenosynovitis and erosions in low-field MRI of patients with rheumatoid arthritis: a comparison with conventional MRI. *Ann Rheum Dis* 2007; 66: 522-9.
2. SUTTER R, TRESCH F, BUCK FM, PFIRRMANN CW: Is dedicated extremity 1.5-T MRI equivalent to standard large-bore 1.5-T MRI for foot and knee examinations? *AJR Am J Roentgenol* 2014; 203: 1293-302.
3. MARCKMANN P, SKOV L, ROSSEN K *et al*.: Nephrogenic systemic fibrosis: suspected causative role of gadodiamide used for contrast-enhanced magnetic resonance imaging. *J Am Soc Nephrol* 2006; 17: 2359-62.
4. STOJANOV D, ARACKI-TRENKIC A, BENEDETO-STOJANOV D: Gadolinium deposition within the dentate nucleus and globus pallidus after repeated administrations of gadolinium-based contrast agents-current status. *Neuroradiology* 2016; 58: 433-41.
5. SUDOL-SZOPINSKA I, JURIK AG, ESHED I *et al*.: Recommendations of the ESSR Arthritis Subcommittee for the use of magnetic resonance imaging in musculoskeletal rheumatic diseases. *Semin Musculoskelet Radiol* 2015; 19: 396-411.
6. ALTHOFF CE, FEIST E, BUROVA E *et al*.: Magnetic resonance imaging of active sacroiliitis: do we really need gadolinium? *Eur J Radiol* 2009; 71: 232-6.
7. MEIER R, THUERMEL K, NOEL PB *et al*.: Synovitis in patients with early inflammatory arthritis monitored with quantitative analysis of dynamic contrast-enhanced optical imaging and MR imaging. *Radiology* 2014; 270: 176-85.
8. TAM LS, GRIFFITH JF, YU AB, LI TK, LI EK: Rapid improvement in rheumatoid arthritis patients on combination of methotrexate and infliximab: clinical and magnetic resonance imaging evaluation. *Clin Rheumatol* 2007; 26: 941-6.
9. BOZGEYIK Z, OZGOCMEN S, KOCAKOC E: Role of diffusion-weighted MRI in the detection of early active sacroiliitis. *AJR Am J Roentgenol* 2008; 191: 980-6.
10. GEZMIS E, DONMEZ FY, AGILDERE M: Diagnosis of early sacroiliitis in seronegative spondyloarthropathies by DWI and correlation of clinical and laboratory findings with ADC values. *Eur J Radiol* 2013; 82: 2316-21.
11. DIEKHOFF T, GREESE J, SIEPER J, PODDUBNYY D, HAMM B, HERMANN KGA: Improved detection of erosions in the sacroiliac joints on MRI with volumetric interpolated breathhold examination (VIBE): results from the SIMACT study. *Ann Rheum Dis* 2018.
12. MOSHER TJ, LIU Y, TOROK CM: Functional cartilage MRI T2 mapping: evaluating the effect of age and training on knee cartilage response to running. *Osteoarthritis Cartilage* 2010; 18: 358-64.
13. GRIFFITH JF: Functional imaging of the musculoskeletal system. *Quant Imaging Med Surg* 2015; 5: 323-31.
14. TIDERIUS CJ, SVENSSON J, LEANDER P, OLA T, DAHLBERG L: dGEMRIC (delayed gadolinium-enhanced MRI of cartilage) indicates adaptive capacity of human knee cartilage. *Magn Reson Med* 2004; 51: 286-90.
15. VAN TIEL J, BRON EE, TIDERIUS CJ *et al*.: Reproducibility of 3D delayed gadolinium enhanced MRI of cartilage (dGEMRIC) of the knee at 3.0 T in patients with early stage osteoarthritis. *Eur Radiol* 2013; 23: 496-504.
16. VAN TIEL J, REIJMAN M, BOS PK *et al*.: Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) shows no change in cartilage structural composition after viscosupplementation in patients with early-stage knee osteoarthritis. *PLoS One* 2013; 8: e79785.
17. OSTERGAARD M, ESHED I, ALTHOFF CE *et al*.: Whole-body magnetic resonance imaging in inflammatory arthritis: systematic literature review and first steps toward standardization and an OMERACT scoring system. *J Rheumatol* 2017; 44: 1699-705.
18. ALTHOFF CE, SIEPER J, SONG IH *et al*.: Active inflammation and structural change in early active axial spondyloarthritis as detected by whole-body MRI. *Ann Rheum Dis* 2013; 72: 967-73.
19. ALTHOFF CE, SIEPER J, SONG IH *et al*.: Comparison of clinical examination versus whole-body magnetic resonance imaging of enthesitis in patients with early axial spondyloarthritis during 3 years of continuous etanercept treatment. *J Rheumatol* 2016; 43: 618-24.
20. AXELSEN MB, ESHED I, OSTERGAARD M *et al*.: Monitoring total-body inflammation and damage in joints and entheses: the first follow-up study of whole-body magnetic resonance imaging in rheumatoid arthritis. *Scand J Rheumatol* 2017; 46: 253-62.
21. DE MARCO G, HELLIWELL P, MCGONAGLE D *et al*.: The GOLMePsA study protocol: an investigator-initiated, double-blind, parallel-group, randomised, controlled trial of GOLimumab and methotrexate versus methotrexate in early diagnosed psoriatic arthritis using clinical and whole body MRI outcomes. *BMC Musculoskelet Disord* 2017; 18: 303.
22. KRABBE S, OSTERGAARD M, ESHED I *et al*.: Whole-body magnetic resonance imaging in axial spondyloarthritis: reduction of sacroiliac, spinal, and entheseal inflammation in a placebo-controlled trial of adalimumab. *J Rheumatol* 2018.