Towards a simplified fluid-sensitive MRI protocol in small joints of the hand in early arthritis patients: reliability between modified Dixon and regular Gadolinium enhanced TSE fat saturated MRI-sequences

Boeren, A.M.P.; Niemantsverdriet, E.; Verstappen, M.; Wouters, F.; Bloem, J.L.; Reijnierse, M.; Helm-van Mil, A.H.M. van der

Skeletal Radiology (2023) 52:1193–1202
https://doi.org/10.1007/s00256-022-04238-8

SCIENTIFIC ARTICLE

Towards a simplified fluid-sensitive MRI protocol in small joints of the hand in early arthritis patients: reliability between modified Dixon and regular Gadolinium enhanced TSE fat saturated MRI-sequences

Anna M. P. Boeren[1,2] · Ellis Niemantsverdriet[1] · Marloes Verstappen[1] · Fenne Wouters[1] · Johannes L. Bloem[3] · Monique Reijnierse[3] · Annette H. M. van der Helm-van Mil[1,2]

Received: 31 August 2022 / Revised: 16 November 2022 / Accepted: 16 November 2022 / Published online: 28 November 2022

Abstract

Objective MRI of small joints plays an important role in the early detection and early treatment of rheumatoid arthritis. Despite its sensitivity to demonstrate inflammation, clinical use is hampered by accessibility, long scan time, intravenous contrast, and consequent high costs. To improve the feasibility of MRI implementation in clinical practice, we introduce a modified Dixon sequence, which does not require contrast and reduces total acquisition time to 6 min. Because the reliability in relation to conventional MRI sequences is unknown, we determined this.

Methods In 29 consecutive early arthritis patients, coronal and axial T2-weighted modified Dixon acquisitions on 3.0 T MRI scanner were acquired from metacarpophalangeal 2–5 to the wrist, followed by the standard contrast-enhanced protocol on 1.5 T extremity MRI. Two readers scored osteitis, synovitis and tenosynovitis (summed as total MRI-inflammation), and erosions (all summed as total Rheumatoid Arthritis MRI Score (RAMRIS)). Intraclass correlation coefficients (ICCs) between readers, and comparing the two sequences, were studied. Spearman correlations were determined.

Results Performance between readers was good/excellent. Comparing modified Dixon and conventional sequences revealed good/excellent reliability: ICC for total MRI-inflammation score was 0.84 (95% CI:0.70–0.92), for erosions 0.90 (95% CI:0.79–0.96), and for the total RAMRIS score 0.88 (95% CI:0.77–0.94). The scores of total MRI-inflammation, total erosions, and total RAMRIS were highly correlated ($\rho = 0.80$, $\rho = 0.81$, $\rho = 0.82$, respectively).

Conclusion The modified Dixon protocol is reliable compared to the conventional MRI protocol, suggesting it is accurate to detect MRI inflammation. The good correlation may be the first step towards a patient-friendly, short and affordable MRI protocol, which can facilitate the implementation of MRI for early detection of inflammation in rheumatology practice.

Keywords Magnetic resonance imaging · Dixon technique · Early arthritis · Fat saturation · RAMRIS · Acquisition time · Fluid-sensitive

Introduction

The additional value of magnetic resonance imaging (MRI) of the small joints in the phase of early detection of rheumatoid arthritis (RA) has been established, facilitating early diagnosis and early treatment in order to prevent damage. The European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR) have included MRI in their guidelines for the management of RA [1–3]. Many studies in early (undifferentiated) arthritis and clinically suspect arthralgia have indeed shown the accuracy of imaging in early recognition of

Anna M. P. Boeren and Ellis Niemantsverdriet shared the first authorship.

✉ Anna M. P. Boeren
a.boeren@erasmusmc.nl

[1] Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

[2] Department of Rheumatology, Erasmus Medical Center, Rotterdam, The Netherlands

[3] Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands

(imminent) RA [4–7]. Of all inflammatory features, scored by the Outcome Measures in Rheumatology (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Scoring (RAMRIS) method, tenosynovitis has the highest predictive accuracy for RA [4]. In addition, bone marrow edema is the best predictor for the development of bone erosions [8]. Despite the high accuracy and reproducibility of MRI, it is not in widespread used in daily rheumatology practice, mostly because of practical and financial concerns. Drawbacks of the recommended sequence protocol are long acquisition times, the need for contrast administration and inhomogeneous fat suppression due to magnetic susceptibility differences [9]. If we could overcome these disadvantages, MRI may become affordable, patient-friendly, and feasible.

Until now, in our department, early arthritis patients were scanned on a 1.5 T extremity MR, which has been replaced by a large bore 3.0 T MR. This interval opened the opportunity to implement a 2-point modified-Dixon (mDixon) technique on 3.0 T and scan patients on both MRIs in order to compare this technique to our standard (contrast-enhanced) protocol. This is relevant as a large majority of the evidence on the value of MRI for the detection of joint inflammation is based on MRs made on a 1.5 T extremity MR [10]. Although MRI has been proven useful and its use is recommended and international guidelines, conventional MRI is rarely used in clinical practice because of the mentioned disadvantages. A shorter and cheaper MRI protocol would make MRI feasible for rheumatologists. With this perspective of implementation of evidence obtained on 1.5 T MR in mind, we here sought to compare the conventional protocol at 1.5 T with the mDixon sequence at 3.0 T. We realize that we did not compare these sequences with the conventional protocol at 3.0 T. However, in a separate study, we recently demonstrated an excellent reliability between the conventional contrast-enhanced MRI at 1.5 T and 3.0 T (ICC 0.90 for inflammation score) [11]. This study made clear the standard protocol can be compared between 3.0 T and 1.5 T MR scanners. Other comparison research also reported contrast-agent could not be omitted if our standard protocol is used [12]. Therefore, our aim is to make the next step towards the implementation of Dixon MRI techniques. Advantages of Dixon techniques in general include reconstruction of images with variable fat and water weighting and its insensitivity to magnetic susceptibility differences [13–18]. With little "modification" of the Dixon technique, (mDixon) shorter acquisition times are allowed by using asymmetrical echoes that are used to synthesize images with variable fat and water components, rather than the in- and opposed phase methods of the original Dixon techniques, using symmetrical echoes that are used to generate in or out of phase, fat only and water only images [15]. Our hypothesis is that a time-efficient mDixon-sequence with the option of multiple reconstructions, is as sensitive as the standard-imaging approach, but without the need of contrast and with reduction of scan time. We thus aimed to determine the reliability of these mDixon-sequences on MRI the hand of consecutively referred early arthritis patients.

Material and methods

Patients and methods

The Leiden Early Arthritis Clinic (EAC) cohort includes patients with clinically confirmed recent-onset arthritis [19]. These patients are Disease-modifying anti-rheumatic drugs (DMARD) naïve. Between 2019 and 2020, consecutive patients ($n=65$) were asked to participate in this "comparison MRI study." Twenty-nine patients agreed and underwent two consecutive hand MRI scans. Characteristics of participating patients are presented in Table 1. All patients gave written informed consent. The study was approved by the local medical ethical committee.

MR-imaging

Unilateral-MRI of the wrist- and metacarpophalangeal (MCP)2–5-joints of the most painful side or dominant side, in case of equally severe symptoms, was performed. As NSAID medication can suppress inflammation, patients were asked not to use any NSAIDs during the 24 h before MRIs.

First, 3.0 T MRI using coronal and axial 2D mDixon sequences was performed, followed by 1.5 T extremity MRI with our standard protocol on the same day.

Table 1 Baseline characteristics of early arthritis patients included in the Early Arthritis Clinic (EAC)-cohort between 2019 and 2020

Included "comparison MRI-study" early arthritis ($n=29$)	
Age, mean (SD)	60.5 (14.9)
Female, *n* (%)	12 (41)
Symptom duration (wks), median (IQR)	10.3 (7.3–15.3)
66-SJC, median (IQR)	3 (1–5.5)
Clinical wrist/MCP arthritis*, *n* (%)	20 (70)
68-TJC, median (IQR)	5 (2–8)
CRP mg/L, median (IQR)	6.9 (4.1–30.7)
ESR mm/h, median (IQR)	25 (7.5–44.5)
RF-positive, *n* (%)	7 (24)
ACPA-positive, *n* (%)	9 (31)

ACPA, anti-citrullinated protein antibodies; *CRP*, C-reactive protein; *ESR*, erythrocyte sedimentation rate; *IQR*, inter quartile range; *MCP*, metacarpophalangeal; *RF*, rheumatoid factor; *SD*, standard deviation; *SJC*, swollen joint count; *TJC*, tender joint count; *wks*, weeks

* as evaluated in the RAMRIS score

mDixon MRI (3.0 T MRI, Philips, Best, the Netherlands). Patients were positioned supine with the hand beside the body, fixed in a dedicated coil with cushions. T2-weighted turbo spin-echo (TSE) 2-point modified (mDixon)-sequences in the coronal plane and axial plane were performed from the wrist to the MCP 2–5 joints. Post-processing included four reconstructions (in-phase, out-phase, water, fat) for each plane. The total acquisition time for the two mDixon sequences was ~ 6 min (Table 2).

*Standard MRI (*1.5 T extremity MRI, GE, Wisconsin, USA). Patients were positioned in a chair beside the scanner, with the hand fixed in a 100 mm coil. Separate acquisitions for MCP2-5 and wrist were made: T1-weighted TSE sequences (T1TSE) in the coronal and axial plane and after intravenous injection of Gd-chelate (gadoteric acid (Dotarem), Guerbet, Paris, France, standard dose of 0.1 mmol/kg), with frequency selective fat-saturation (T1GdFS) in the coronal plane and axial plane (Table 2). Total scan time ~ 30 min.

In this scan protocol, no fluid-sensitive sequences (T2-weighted TSE fat-suppressed or short tau inversion recovery (STIR))are included. Conventionally, this is recommended by the OMERACT RAMRIS study group to assess osteitis (bone marrow edema) [20]. However, based on earlier research in our department and in accordance with the European Society of Musculoskeletal Radiology recommendations (ESSR), we used the T1GdFS sequence to assess osteitis in the wrist and MCP joints [21, 22]. An earlier comparison study from our group showed a high Signal to noise ratio (SNR) and good correlation between T2-weighted TSE fat-suppressed sequences and T1GdFS sequences (agreement ICCs 0.80–0.99), prompting us to omit the fluid sensitive sequence. Similar findings were found by other groups [23–25]. This choice and technical considerations were previously described in detail [26]. Evaluation of osteitis using the T1GdFS sequence already allowed us to reduce the acquisition time of our standard protocol in the past [22]. The other features (synovitis, tenosynovitis, erosions) were scored at the pre- and post-contrast sequences as recommended by the OMERACT RAMRIS protocol [20, 21, 27].

MRI-evaluation

In agreement with the OMERACT trial recommendations, MRIs were scored for erosions and three inflammatory features (osteitis, synovitis, tenosynovitis) according to the RAMRIS and summed as total MRI inflammation [20, 27]. Lesions of the MCP joints were evaluated on a joint-by-joint basis. The carpal region was subdivided into radial, middle, and ulnar components. Tenosynovitis, synovitis, and osteitis were scored in a range of 0–3. For example, tenosynovitis was scored 1 if < 2 mm synovial proliferation/effusion is seen, 2 for ≥ 2– < 5 mm, and 3 for ≥ 5 mm. Synovitis scores

Table 2 MRI parameters of the different sequences used

Field strength (T)	Sequence/orientation	Location (MCP/wrist)	Acquisition time (min)	TR (ms)	TE (ms)	FOV (mm)	Slice thickness/gap (mm)	Number of slices	ETL	matrix
Whole bore MRI 3.0 T	T2 TSE mDixon/cor	Both	4	2818	60	220	2/0.2	22	3	350 × 450
	T2 TSE mDixon/ax	Both	2	5123	60	220	3/0.3	40	2	350 × 450
Extremity MRI 1.5 T	T1W TSE/cor	MCP	5	575	11	100	2/0.2	18	2	388 × 288
	T1W TSE/cor	Wrist	5	575	11	100	2/0.2	18	2	388 × 288
	T1W TSE /ax	MCP	5	570	7	100	3/0.3	16	2	320 × 192
	T1W TSE /ax	Wrist	6	540	7	100	3/0.3	18	2	320 × 192
	T1W TSE FS/cor gadolinium	MCP	5	700	9	100	2/0.2	18	2	364 × 224
	T1W TSE FS/cor gadolinium	Wrist	5	700	9	100	2/0.2	18	2	364 × 224

MCP, metacarpophalangeal joint, *cor*, coronal; *ax*, axial; *TR*, repetition time; *TE*, echo-time; *FOV*, field of view; *ETL*, echo train length

were comparable. Osteitis was scored 0 (no edema), 1 if 1–33% of the bone is involved, 2 if 33–67% is involved and 3 if 68–100% was involved. Erosions were scored from 0 to 10, according to the percentage of involved eroded bone. The erosion score and total inflammation score were summed as total RAMRIS scores [20, 28]. For the mDixon series, the water-only images, coronal, and axial were used to score the three inflammatory MRI features. Fat-only images were used to score erosions. Application of the RAMRIS score was not different for both MRI sequences used.

The mDixon and conventional MRIs were scored by two readers (MV, FW) independently, blinded for clinical data, at different time points. Both readers were unaware of the scores that were applied when scoring the conventional protocol when evaluating the mDixon sequence and vice versa. The readers were unaware on the clinical rheumatological diagnosis and whether or not the participants had a clinical arthritis in the joints that were imaged. Both readers are experienced and scored > 400 conventional MRIs prior to evaluate MRIs that are part of this study. In earlier research, the interreader ICC was 0.96, and intrareader ICCs, all determined before the start of this study, were 0.98 (reader 1) and 0.94 (reader 2) [11]. In addition, to improve the two readers' knowledge about the interpretation of the reconstructed images of the mDixon sequence, musculoskeletal radiologists (MR, JB) trained the readers for several weeks.

Analyses

Intraclass correlation coefficient (ICCs) estimates and their 95% confident intervals (95%CI) were calculated (2-way mixed-effects model, absolute agreement; average measures of both readers for performance between readers, single measures (mean score of 2 readers) for comparing two sequences) [29]. ICCs < 0.5, 0.5–0.75, 0.75–0.9, and > 0.9 indicate poor, moderate, good, and excellent reliability, respectively [29]. Bland–Altman- and correlation plots were drawn, and Spearman correlation coefficients were determined [30]. Statistical analyses were made with SPSS Statistics V25, and GraphPad Prism V8 was used for the figures.

Results

Patient characteristics

Patients had a mean age of 61, median symptom duration of 10 weeks, (median) 5 swollen joints, 31% was ACPA-positive and 20 patients had an arthritis in one of the scanned joints (Table 1).

Reliability between readers

ICCs between readers were determined by conventional MRI (Table 3) and were excellent, 0.94 for total RAMRIS, 0.92 for erosion, and 0.91 for total MRI-inflammation score.

Between-readers performance for mDixon-MRI was also excellent, ICC 0.96, 0.95, and 0.92 for total RAMRIS, erosions, and total MRI-inflammation score, respectively.

Reliability between mDixon-MRI and conventional-MRI sequences

Then, we compared the mDixon with the conventional sequences by comparing the average scores of both readers; ICCs were good/excellent, 0.88 for total RAMRIS, 0.90 for erosions, and 0.84 for the total MRI-inflammation score (Table 3). For the individual MRI-inflammation scores, ICCs were 0.95, 0.78, and 0.57 for osteitis, tenosynovitis, and synovitis, respectively. Figure 1 presents Bland–Altman plots, measuring agreement between two (semi-) quantative methods (average of the two readers). Figure 2 depicts correlation plots. Spearman correlation coefficients were calculated for total RAMRIS ($\rho = 0.82$), erosions ($\rho = 0.81$), total inflammation score ($\rho = 0.80$), osteitis ($\rho = 0.95$), tenosynovitis ($\rho = 0.64$), and synovitis ($\rho = 0.36$). Examples of both used sequences in the axial plane for the wrist and MCP

Table 3 Reliability between readers for scoring each of two MRI sequences, and for comparing mDixon-MRI with conventional-MRI

	Reader 1 versus 2		mDixon-MRI versus conventional-MRI
	Conventional-MRI	mDixon-MRI	Average readers 1&2
Total RAMRIS, ICC (95% CI)	0.94 (0.61–0.98)	0.96 (0.90–0.98)	0.88 (0.77–0.94)
Erosions, ICC (95%CI)	0.92 (083–0.96)	0.95 (0.89–0.98)	0.90 (0.79–0.96)
Total- inflammation, ICC (95%CI)	0.91 (0.56–0.97)	0.92 (0.83–0.96)	0.84 (0.70–0.92)
Osteitis, ICC (95%CI)	0.90 (0.80–0.96)	0.96 (0.92–0.98)	0.95 (0.91–0.98)
Synovitis, ICC (95%CI)	0.93 (0.54–0.98)	0.76 (0.50–0.89)	0.57 (0.26–0.77)
Tenosynovitis, ICC (95%CI)	0.88 (0.25–0.96)	0.89 (0.76–0.95)	0.78 (0.58–0.89)

CI, confidence interval; *ICC*, intraclass correlation coefficients; *MRI*, magnetic resonance imaging; *RAMRIS*, rheumatoid arthritis magnetic resonance imaging score

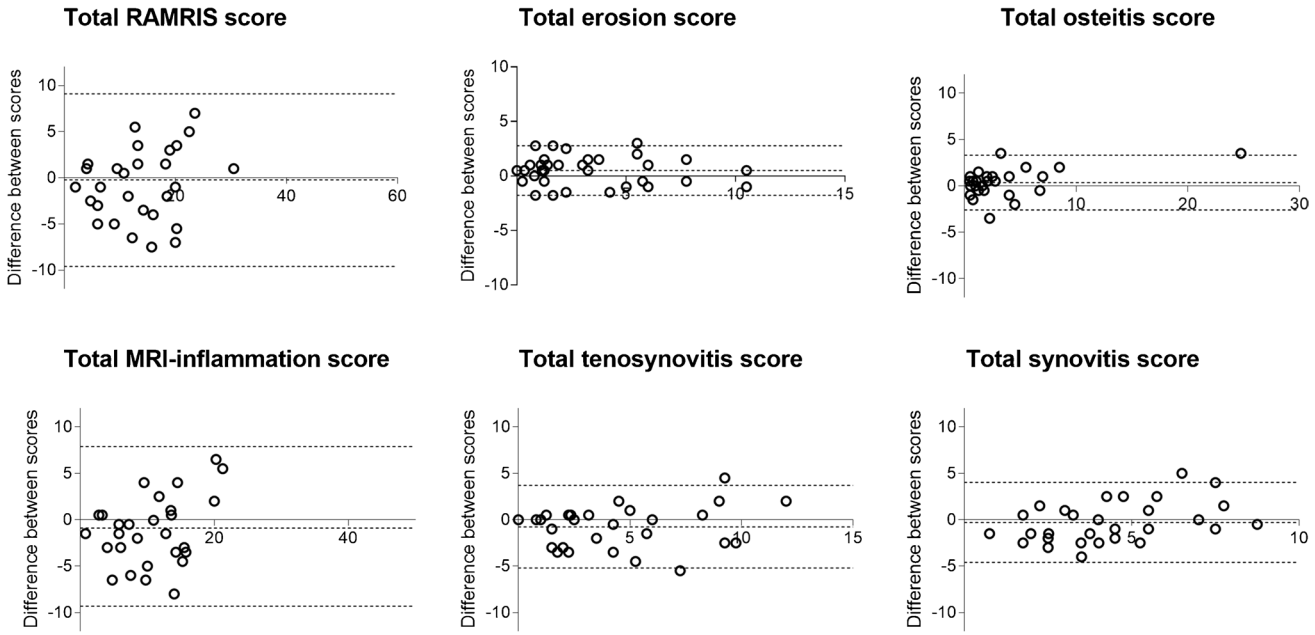

Fig. 1 Bland–Altman plots depicting reliability for comparison of mDixon- with conventional MRI. Legend: Bland–Altman plots of the average score of both readers. The *Y*-axes demonstrate the absolute difference between contrast-enhanced fat-suppressed sequences minus the mDixon-sequence. The *X*-axes denote the average value between the two techniques ((conventional-MRI minus mDixon-MRI)/2)

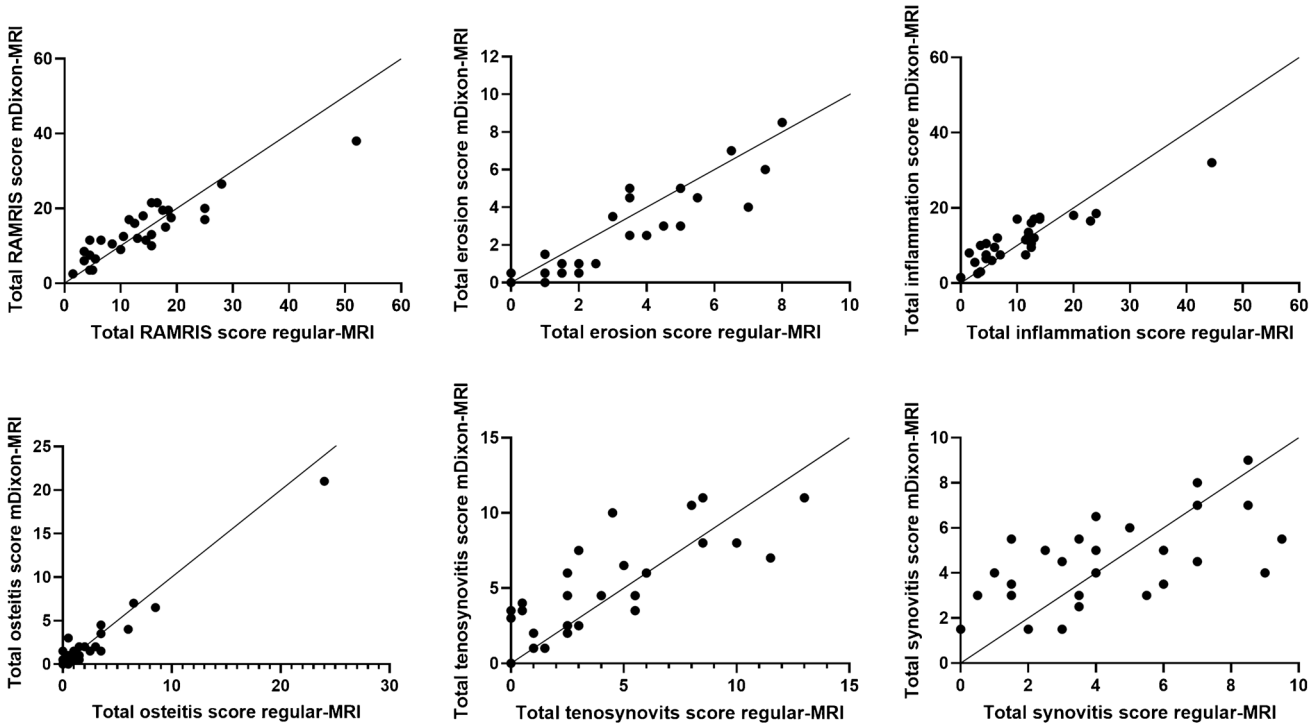

Fig. 2 Correlation plots. Legend: Spearman correlation coefficients for total RAMRIS ($\rho = 0.82$), erosions ($\rho = 0.81$), total inflammation score ($\rho = 0.80$), osteitis ($\rho = 0.95$), tenosynovitis ($\rho = 0.64$), and synovitis ($\rho = 0.36$)

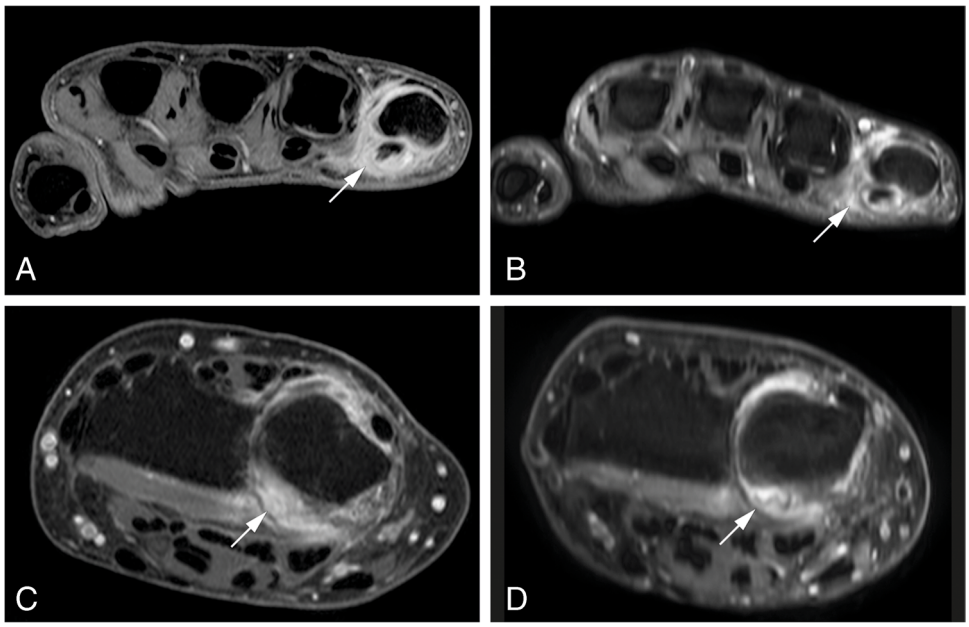

Fig. 3 Example of inflammation seen in axial T1-weighted TSE fat-saturated post-gadolinium images (**A**, **C**) and corresponding axial water-only mDixon images (**B**, **D**). Legend: Image **A** and **C** are axial T1-weighted post-gadolinium with fat suppression obtained with the conventional MRI sequences and **B** and **D** are the corresponding axial water-only T2-weighted spin echo acquired with the modified Dixon sequence. In the upper part of the figure (**A**, **B**) are the metacarpophalangeal joints (MCPs) of one patient, of which MCP5 is scored for synovitis and tenosynovitis of the flexor tendon at both sequences (indicated with white arrows). The lower part (**C**, **D**) shows high-intensity signals of synovitis in the distal radioulnar-joint at both sequences (indicated with white arrows). Both fluid and inflamed synovium are high on mDixon, whereas only the synovium enhances after gadolinium administration

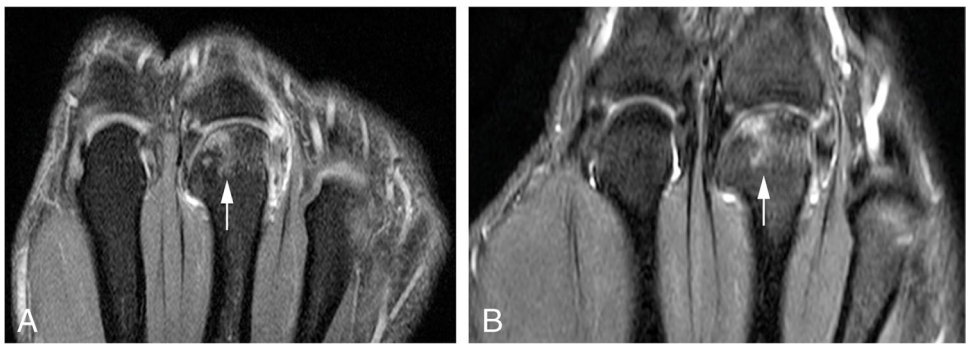

Fig. 4 Example of osteitis in distal metacarpal bone of finger three in coronal T1-weighted TSE fat-saturated post gadolinium image (**A**) and corresponding coronal water-only mDixon images (**B**). Legend: Image **A** is a coronal image of the T1-weighted post-gadolinium TSE sequence with fat- suppression obtained with conventional MRI sequences and image **B** a T2-weighted spin echo sequence acquired with the modified Dixon technique. Both sequences show osteitis in the upper part of the metacarpal bone of finger three (indicated with white arrows)

joints are depicted in Fig. 3. Figure 4 depicts an example in the coronal plane for osteitis in the MCP joint.

Sub analyses

The reliability between both sequences was investigated for each reader individually. The results were similar (Supplementary Table 1).

Discussion

In this comparison study, we evaluated the reliability between mDixon sequences on whole bore 3.0 T and standard contrast-enhanced sequences on 1.5 T extremity MR scanners for the detection of MR inflammation in patients with early arthritis. MRI is in widespread used in RA patients and is of added clinical value [7, 31]. Overall, the agreement was good to excellent.

mDixon-MRI performed good/excellent for all summed measures and for all individual MRI features, except for synovitis where it performed moderate. This can be explained by underlying differences in technology, resulting in differences in the obtained images by conventional- and mDixon-MRI. Conventional contrast-enhanced-MRI initially shows a high T1 signal of synovial tissue and a low signal of synovial fluid. As diffusion of contrast-agent into the synovial fluid takes time, enhancing synovium is easy to detect. In mDixon-MRI hypertrophic synovium and its conjoined effusion, both have high signal intensity on water reconstructions and cannot be separated, in earlier research [12]. Examples of dissimilarities in the enhancement of the synovial fluid are shown in Fig. 5.

Also, subtle effusion, which may be physiologically present, is seen on mDixon-MRI but not at conventional-contrast enhanced-MRI. This difference in technique, and resulting images, imply that a reference of normality should be created for mDixon-MRI, to prevent that normal variants are considered pathologic, and to ensure a high specificity [26, 32]. To this end, symptom-free persons from the general population and from different age categories need to be scanned, similar to what was done for contrast-enhanced images [32–34]. This work is ongoing and supported by a grant from the International Skeletal Society (ISS).

The consequence of the moderate reliability of synovitis for early detection of RA may be limited, as in clinical practice, MRI results are evaluated on patient level, being normal/abnormal or negative/positive and several inflammatory features are generally simultaneously present, thus the total evaluation is not dependent on synovitis alone. Interestingly, tenosynovitis is the best predictive/discriminative feature in enabling earlier diagnoses of RA [4–6, 35–37]. Our data showed that the reliability of mDixon for both total MRI inflammation and tenosynovitis was high. Thus the moderate reliability of synovitis may have limited impact on the accuracy when assessed at patient level.

This comparison study has limitations. Firstly, the compared sequences were obtained with two different MR machines. Ideally, the mDixon sequence is compared to the standard MR protocol at both 1.5 T and the same large bore 3.0 T MR. Having three scans at the same day was not possible. Moreover, we recently already compared the standard sequences at 1.5 T and 3.0 T (thus using the same MRI

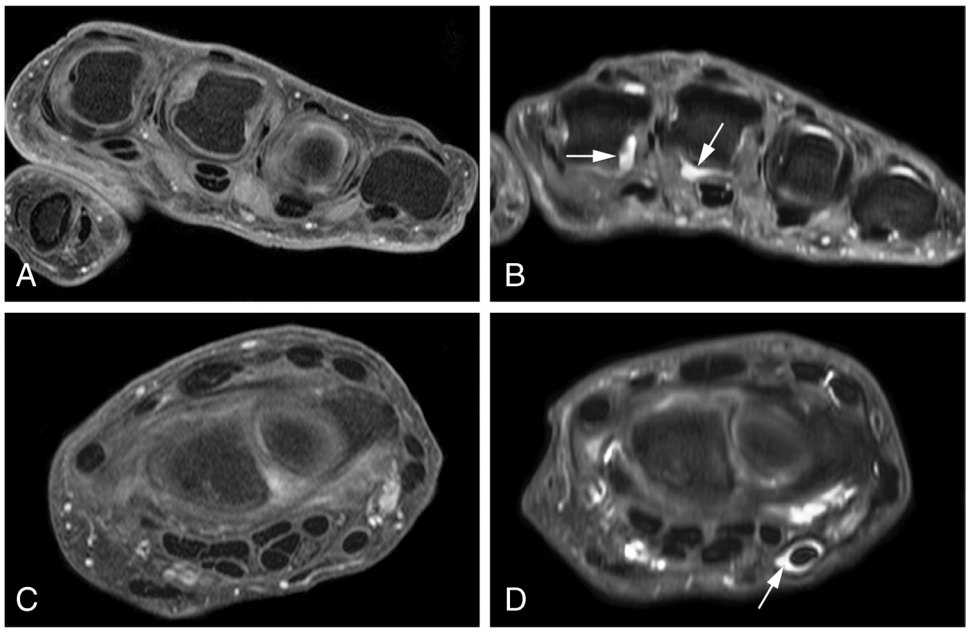

Fig. 5 Examples of discrepancy in synovitis and tenosynovitis score between conventional axial T1-weighted TSE fat-saturated post-gadolinium images (**A**, **C**) and corresponding axial water-only mDixon images (**B**, **D**). Legend: Image **A** is an axial T1-weighted post-gadolinium TSE sequence with a fat-suppression image and the **B** the corresponding water-only axial image obtained with the T2-weighted spin-echo mDixon image of the metacarpophalangeal (MCP) joints. Joint fluid in the MCP joints results in a high signal on mDixon (indicated with white arrows) without enhancement on the post-gadolinium images. At the level of the MCP joints, no enhancing thickened synovium is seen, no (teno) synovitis is present (**A**). A physiologic amount of fluid at MCP 2 and 3 can be misinterpreted as synovitis on mDixon (**B**) (white arrows). Image **C** is an axial T1-weighted post-gadolinium TSE sequence with a fat-suppression image and the **D** the corresponding water-only axial image obtained with the T2-weighted spin-echo mDixon image of the wrist. At the level of the wrist, no (teno)synovitis is present (**C**). Fluid is encircling the flexor carpi ulnaris tendon on mDixon (**D**)(white arrow). A small amount of fluid, which can be physiologic, is present in the 2nd extensor compartment. These findings underline the need for a mDixon atlas as a reference of normality. In addition, there is a ganglion cyst at the ulnar side of the carpus

scanners, hospital, setting, and comparable patient population as used in the current study) showing excellent reliability (ICC 0.90 for total inflammation score) [11]. Also, in other musculoskeletal literature the performance of high-end scanners is comparable [38–41]. In addition, for implementation in rheumatology practice, the comparison between 1.5 T with mDixon at 3.0 T is most relevant, since a large majority of relevant research is done at 1.5 T while mDixon would be implanted in clinical practice [4, 5, 42, 43]. A second limitation is that mDixon-sequences were evaluated using the RAMRIS system, while this system was not developed to apply to Dixon-sequences. However, it is the only validated and standardized MRI-scoring system [27]. Lastly, limitations of the mDixon technique could be blurring artifacts and local swapping of water and fat signal [15]; however, these were not detected in our study.

With the application of the mDixon sequence, total scanning time is shortened. However, the acquisition time would have already been reduced by the shift to the whole bore system. The extremity scanner has a small field of view of 100 mm, consequently, the MCP and wrist were scanned separately, resulting in 6 consecutive sequences (Table 2). Total acquisition time is therefore about 30 min. In a whole-body MRI scanner, MCP and wrist can be scanned in one field of view with high SNR, decreasing the total acquisition time to approximately 15 min. With respect to pulse sequences, the mDixon sequence allows further reduction of total acquisition time to approximately 6 min.

The increase in health care costs is an important motivation to address the cost-effectiveness of imaging. MRI is more sensitive in the detection of joint inflammation than ultrasound, which is commonly used in daily rheumatological practice. MRI is especially more sensitive for the detection of tenosynovitis, which has the highest accuracy for early detection of RA and is missed with the US in up to 81% of patients [44]. Long scan time contributes to the high costs of MRI and has negative impact on the accessibility. Our data suggest that mDixon can become cheaper than standard MRI as contrast-agent administration is no longer needed and scan time is reduced. However, actual prices for MRI scans are nationally or regionally negotiated, and to our knowledge, this is not yet done for a short protocol limited to mDixon sequences. Formal cost-effectiveness studies (comparing mDixon to conventional MRI) remain to be done and might facilitate achieving lower prices for clinical practice.

With respect to implementation, the Dixon technique in general, and also the mDixon sequence, can be applied on different whole-bore MRI scanners (3.0 T and 1.5 T) in countries/settings with regular software updates [16, 45–47]. Therefore, the combined generalizability and reduction in scan time mDixon could increase the accessibility of MRI. Thus, mDixon-MRI can combine the accuracy and reproducibility of conventional MRI with accessibility in a patient-friendly and affordable manner and become a future-proof way of imaging.

Further research should include large observational study cohorts in the diagnostic phase of RA, including patients with early arthritis and arthralgia, with the ultimate goal to allow the implementation of mDixon-MRI for early detection of joint inflammation and RA in daily clinical practice. Likewise, and as discussed, the specificity remains to be determined by also using mDixon sequences in symptom-free persons from the general population. In addition, it will be relevant to evaluate if this short non-invasive MRI may be helpful in facilitating triaging patients referred from primary care.

In conclusion, our results suggest that the mDixon-sequence is a promising technique, which reliably detects MR inflammation and structural damage, in a patient-friendly manner with cost reduction. This is the first step towards an abbreviated MRI protocol in small hand joints for early detection of inflammation and early diagnosis of RA.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00256-022-04238-8.

Funding This work was supported by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Starting grant, agreement No 714312), the Dutch Arthritis Society, and the 2021 International Skeletal Society Seed Grant.

Data availability The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Ethics approval EAC Leiden was approved by the Local Medical Ethics Committee, named 'Commissie Medische Ethiek'. Informed consent was obtained from all patients. The study complies with the Declaration of Helsinki.

Conflict of interest The authors declare no competing interests.

References

1. Combe B, Landewe R, Daien CI, Hua C, Aletaha D, Alvaro-Gracia JM, et al. 2016 update of the EULAR recommendations for the management of early arthritis. Ann Rheum Dis. 2017;76(6):948–59.
2. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62(9):2569–81.
3. Colebatch AN, Edwards CJ, Østergaard M, van der Heijde D, Balint PV, D'Agostino M-A, et al. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Ann Rheum Dis. 2013;72(6):804–14.

4. Matthijssen XME, Wouters F, Boeters DM, Boer AC, Dakkak YJ, Niemantsverdriet E, et al. A search to the target tissue in which RA-specific inflammation starts: a detailed MRI study to improve identification of RA-specific features in the phase of clinically suspect arthralgia. Arthritis Res Ther. 2019;21(1):249.
5. Nieuwenhuis WP, van Steenbergen HW, Mangnus L, Newsum EC, Bloem JL, Huizinga TWJ, et al. Evaluation of the diagnostic accuracy of hand and foot MRI for early Rheumatoid Arthritis. Rheumatology (Oxford). 2017;56(8):1367–77.
6. van Steenbergen HW, Mangnus L, Reijnierse M, Huizinga TW, van der Helm-van Mil AH. Clinical factors, anticitrullinated peptide antibodies and MRI-detected subclinical inflammation in relation to progression from clinically suspect arthralgia to arthritis. Ann Rheum Dis. 2016;75(10):1824–30.
7. Rubin DA. MR and ultrasound of the hands and wrists in rheumatoid arthritis. Part II. Added clinical value. Skeletal Radiol. 2019;48(6):837–57.
8. Nieuwenhuis WP, van Steenbergen HW, Stomp W, Stijnen T, Huizinga TW, Bloem JL, et al. The course of bone marrow edema in early undifferentiated arthritis and rheumatoid arthritis: a longitudinal magnetic resonance imaging study at bone level. Arthritis Rheumatol. 2016;68(5):1080–8.
9. Del Grande F, Santini F, Herzka DA, Aro MR, Dean CW, Gold GE, et al. Fat-suppression techniques for 3-T MR imaging of the musculoskeletal system. Radiographics : Rev Publ Radiol Soc North Am, Inc. 2014;34(1):217–33.
10. Boeren AMP, Oei EHG, van der Helm - van Mil AHM. The value of MRI for detecting subclinical joint inflammation in clinically suspect arthralgia. RMD Open. 2022;8(2):e002128.
11. Krijbolder DI, Verstappen M, Wouters F, Lard LR, de Buck P, Veris-van Dieren JJ, Bloem JL, Reijnierse M, van der Helm-van Mil A. Comparison between 1.5T and 3.0T MRI: both field strengths sensitively detect subclinical inflammation of hand and forefoot in patients with arthralgia. Scand J Rheumatol. 2022;51(4):284–90. https://doi.org/10.1080/03009742.2021.1935313.
12. Stomp W, Krabben A, van der Heijde D, Huizinga TW, Bloem JL, Østergaard M, et al. Aiming for a simpler early arthritis MRI protocol: can Gd contrast administration be eliminated? Eur Radiol. 2015;25(5):1520–7.
13. Dixon WT. Simple proton spectroscopic imaging. Radiol. 1984;153(1):189–94.
14. Eggers H, Brendel B, Duijndam A, Herigault G. Dual-echo Dixon imaging with flexible choice of echo times. Magn Reson Med. 2011;65(1):96–107.
15. Eggers H, Bornert P. Chemical shift encoding-based water-fat separation methods. J Magn Reson Imaging : JMRI. 2014;40(2):251–68.
16. Kirchgesner T, Stoenoiu M, Michoux N, Durez P, Vande BB. Comparison between 3-point Dixon- and CHESS-based OMERACT-recommended MRI protocols in hands of patients with suspicion of early rheumatoid arthritis. Eur J Radiol. 2021;134:109412.
17. Park HJ, Lee SY, Rho MH, Chung EC, Ahn JH, Park JH, et al. Usefulness of the fast spin-echo three-point Dixon (mDixon) image of the knee joint on 3.0-T MRI: comparison with conventional fast spin-echo T2 weighted image. Br J Radiol. 2016;89(1062):20151074.
18. Brandao S, Seixas D, Ayres-Basto M, Castro S, Neto J, Martins C, et al. Comparing T1-weighted and T2-weighted three-point Dixon technique with conventional T1-weighted fat-saturation and short-tau inversion recovery (STIR) techniques for the study of the lumbar spine in a short-bore MRI machine. Clin Radiol. 2013;68(11):e617–623.
19. de Rooy DP, van der Linden MP, Knevel R, Huizinga TW, van der Helm-van Mil AH. Predicting arthritis outcomes–what can be learned from the Leiden Early Arthritis Clinic? Rheumatol (Oxford). 2011;50(1):93–100.
20. Ostergaard M, Peterfy C, Conaghan P, McQueen F, Bird P, Ejbjerg B, et al. OMERACT Rheumatoid arthritis magnetic resonance imaging studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system. The J Rheumatol. 2003;30(6):1385–6.
21. Sudol-Szopinska I, Jurik AG, Eshed I, Lennart J, Grainger A, Ostergaard M, et al. Recommendations of the ESSR arthritis subcommittee for the use of magnetic resonance imaging in musculoskeletal rheumatic diseases. Sem Musculoskelet Radiol. 2015;19(4):396–411.
22. Stomp W, Krabben A, van der Heijde D, Huizinga TW, Bloem JL, van der Helm-van Mil AH, et al. Aiming for a shorter rheumatoid arthritis MRI protocol: can contrast-enhanced MRI replace T2 for the detection of bone marrow oedema? Eur Radiol. 2014;24(10):2614–22.
23. Mayerhoefer ME, Breitenseher MJ, Kramer J, Aigner N, Norden C, Hofmann S. STIR vs T1-weighted fat-suppressed gadolinium-enhanced MRI of bone marrow edema of the knee: computer-assisted quantitative comparison and influence of injected contrast media volume and acquisition parameters. J Magn Reson Imaging : JMRI. 2005;22(6):788–93.
24. Schmid MR, Hodler J, Vienne P, Binkert CA, Zanetti M. Bone marrow abnormalities of foot and ankle: STIR versus T1-weighted contrast-enhanced fat-suppressed spin-echo MR imaging. Radiol. 2002;224(2):463–9.
25. Tamai M, Kawakami A, Uetani M, Fukushima A, Arima K, Fujikawa K, et al. Magnetic resonance imaging (MRI) detection of synovitis and bone lesions of the wrists and finger joints in early-stage rheumatoid arthritis: comparison of the accuracy of plain MRI-based findings and gadolinium-diethylenetriamine pentaacetic acid-enhanced MRI-based findings. Mod Rheumatol. 2012;22(5):654–8.
26. Bloem JL, Reijnierse M, Huizinga TWJ, van der Helm-van Mil AHM. MR signal intensity: staying on the bright side in MR image interpretation. RMD Open. 2018;4(1):e000728.
27. Østergaard M, Peterfy CG, Bird P, Gandjbakhch F, Glinatsi D, Eshed I, et al. The OMERACT rheumatoid arthritis magnetic resonance imaging (MRI) scoring system: updated recommendations by the OMERACT MRI in arthritis working group. J Rheumatol. 2017;44(11):1706–12.
28. Haavardsholm EA, Ostergaard M, Ejbjerg BJ, Kvan NP, Kvien TK. Introduction of a novel magnetic resonance imaging tenosynovitis score for rheumatoid arthritis: reliability in a multireader longitudinal study. Ann Rheum Dis. 2007;66(9):1216–20.
29. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155–63.
30. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1(8476):307–10.
31. Rubin DA. MRI and ultrasound of the hands and wrists in rheumatoid arthritis. I Imaging findings Skeletal Radiol. 2019;48(5):677–95.
32. Boer AC, Burgers LE, Mangnus L, Ten Brinck RM, Nieuwenhuis WP, van Steenbergen HW, et al. Using a reference when defining an abnormal MRI reduces false-positive MRI results-a longitudinal study in two cohorts at risk for rheumatoid arthritis. Rheumatol (Oxford). 2017;56(10):1700–6.
33. Mangnus L, van Steenbergen HW, Reijnierse M, van der Helm-van Mil AH. Magnetic resonance imaging-detected features of inflammation and erosions in symptom-free persons from the general population. Arthritis Rheumatol. 2016;68(11):2593–602.

34. Kroon FPB, Peterfy CG, Conaghan PG, Foltz V, Gandjbakhch F, Eshed I, et al. Atlas for the OMERACT thumb base osteoarthritis MRI scoring system (TOMS). RMD Open. 2018;4(1):e000583.
35. Rogier C, Hayer S, van der Helm-van MA. Not only synovitis but also tenosynovitis needs to be considered: why it is time to update textbook images of rheumatoid arthritis. Ann Rheum Dis. 2020;79(4):546–7.
36. Niemantsverdriet E, van der Helm-van Mil AHM. Imaging detected tenosynovitis of metacarpophalangeal and wrist joints: an increasingly recognised characteristic of rheumatoid arthritis. Clin Exp Rheumatol. 2018;114(5):131–8.
37. Dakkak YJ, van Dijk BT, Jansen FP, Wisse LJ, Reijnierse M, van der Helm-van Mil AHM, et al. Evidence for the presence of synovial sheaths surrounding the extensor tendons at the metacarpophalangeal joints: a microscopy study. Arthritis Res Ther. 2022;24(1):154.
38. Van Dyck P. MR imaging of the knee at 3T–diagnostic performance and comparison with 1.5T. JBR-BTR. 2014;97(2):126–7.
39. Krabbe S, Eshed I, Pedersen SJ, Bøyesen P, Møller JM, Therkildsen F, et al. Bone marrow oedema assessment by magnetic resonance imaging in rheumatoid arthritis wrist and metacarpophalangeal joints: the importance of field strength, coil type and image resolution. Rheumatol. 2014;53(8):1446–51.
40. Sormaala MJ, Ruohola JP, Mattila VM, Koskinen SK, Pihlajamaki HK. Comparison of 1.5T and 3T MRI scanners in evaluation of acute bone stress in the foot. BMC Musculoskelet Disord. 2011;12:128.
41. Liebl H, Heilmeier U, Lee S, Nardo L, Patsch J, Schuppert C, et al. In vitro assessment of knee MRI in the presence of metal implants comparing MAVRIC-SL and conventional fast spin echo sequences at 1.5 and 3 T field strength. J Magn Reson Imaging : JMRI. 2015;41(5):1291–9.
42. Krijbolder DI, Wouters F, van Mulligen E, van der Helm-van Mil AHM. Morning stiffness precedes the development of rheumatoid arthritis and associates with systemic and subclinical joint inflammation in arthralgia patients. Rheumatology (Oxford). 2022;61(5):2113–8. https://doi.org/10.1093/rheumatology/keab651.
43. van Dijk BT, Dakkak YJ, Matthijssen XME, Niemantsverdriet E, Reijnierse M, van der Helm-van Mil AHM. Intermetatarsal Bursitis, a novel feature of Juxtaarticular inflammation in early rheumatoid arthritis related to clinical signs: Results of a longitudinal magnetic resonance imaging study. Arthritis Care Res (Hoboken). 2022;74(10):1713–22. https://doi.org/10.1002/acr.24640.
44. Ohrndorf S, Boer AC, Boeters DM, Ten Brinck RM, Burmester GR, Kortekaas MC, et al. Do musculoskeletal ultrasound and magnetic resonance imaging identify synovitis and tenosynovitis at the same joints and tendons? a comparative study in early inflammatory arthritis and clinically suspect arthralgia. Arthritis Res Ther. 2019;21(1):59.
45. Huijgen WHF, van Rijswijk CSP, Bloem JL. Is fat suppression in T1 and T2 FSE with mDixon superior to the frequency selection-based SPAIR technique in musculoskeletal tumor imaging? Skeletal Radiol. 2019;48(12):1905–14.
46. Dogan BE, Ma J, Hwang K, Liu P, Yang WT. T1-weighted 3D dynamic contrast-enhanced MRI of the breast using a dual-echo Dixon technique at 3 T. J Magn Reson Imaging : JMRI. 2011;34(4):842–51.
47. Lins CF, Salmon CEG, Nogueira-Barbosa MH. Applications of the Dixon technique in the evaluation of the musculoskeletal system. Radiol Bras. 2021;54(1):33–42.