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Comparing non-enhanced and enhanced sequences in the assessment of effusion and synovitis in knee OA: associations with clinical, macroscopic and microscopic features

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SUMMARY

Objective: The purpose of this study was to evaluate synovial membrane (SM) inflammation and joint effusion scores by semiquantitative magnetic resonance imaging (MRI) assessment with and without enhanced sequences. Gold standards used for comparison were microscopic examination of SM biopsies for SM inflammation and joint volume measurement (JVM) after arthrocentesis for effusion.
Methods: Patients ($n = 30$) fulfilling ACR criteria for knee osteoarthritis (OA) and requiring joint lavage, were evaluated with MRI: (1) SM inflammation was assessed by Whole-Organ Magnetic Resonance Imaging Score (WORMS) on T2 weighted sequences (T2w) a composite score assessing together synovitis and effusion, and the MRI-synovitis score (based on synovitis thickening in five regions of interest) on a T1-weighted fat sat sequence after contrast agent injection (T1wCE). (2) Joint effusion was evaluated by MRI-effusion score (T1wCE) and the WORMS (T2w). JVM was measured after arthrocentesis, and microscopic SM inflammation was determined in SM samples ($n = 86$). Correlations between MRI scores and clinical, biologic and histologic parameters were studied.
Results: Both scores for effusion were well correlated [$r = 0.82$ (0.65–0.91); $P < 0.001$] and presented excellent intraclass correlation coefficient (ICC) for intra- and inter-observer reproducibility. MRI scores for effusion were well correlated with JVM ($r = 0.60$ for WORMS and $r = 0.59$ for MRI-effusion score). Synovitis scores were highly reproducible but moderately correlated ($r = 0.63$; $P < 0.001$). Only MRI-synovitis total score (T1wCE) was correlated with SM microscopic inflammation ($r = 0.46$; $P = 0.01$) and most strongly infiltration ($r = 0.45$; $P < 0.005$).
Conclusions: T2w sequences are adequate in assessing effusion volume in compare to joint volume by arthrocentesis but only T1wCE sequences are able to detect synovitis according to the reference of synovial biopsy.

Introduction

Synovial membrane (SM) inflammation and effusion (Ef) are common in osteoarthritis (OA)[1,2], but their contribution to pain, disability and cartilage breakdown is still debated[3,4] Validated tools are needed to accurately investigate and quantify SM inflammation and joint effusion, and to determine their precise role in clinical symptoms and OA progression.

Magnetic resonance imaging (MRI) has revealed synovial abnormalities in knee OA, but most studies have been performed using fat saturation T2-weighted images (T2w) or T1 images without a contrast agent[5–7]. In that context, SM inflammation may be assessed with good reproducibility using non-injected sequences: T1 sequences for the Knee Osteoarthritis Scoring System (KOSS)[7], and T2 sequences for the Whole-Organ Magnetic Resonance Imaging Score (WORMS)[5], the Boston Leeds Osteoarthritis Knee Score (BLOKS)[8], Pelletier's score[9] and Hill's score[4]. With a non-injected sequence, SM inflammation graded according to an assessment of thickening was found to correlate with mild chronic inflammation (synovial proliferation, mononuclear cell infiltration, and neovascularisation) in 16 SM biopsies[6]. Commonly, signal

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alterations in Hoffa's fat pad are scored as synovitis surrogates, which have shown an association with pain severity, but have proven to represent only a non-specific marker when contrast images are used as gold standard[10]. In fact, inflamed synovium is usually indistinguishable from fatty tissue on these non-injected sequences.

Injected T1-weighted sequences (T1wCE) allow for better characterization of inflamed synovium and better differentiation between synovium[11] and effusion, and were particularly studied in inflammatory diseases such as rheumatoid arthritis and spondyloarthritis and to a lesser degree in OA[12,13]. In OA, SM inflammation has also been scored on injected images. As in inflammatory musculoskeletal diseases, only the enhanced synovial tissue was graded according to its degree of thickening in various regions of interest. All scorings exhibited excellent intra- and inter-observer agreement, but only MRI-synovitis score has been shown to correlate well with histologic parameters obtained on more than 100 SM biopsies[14]. Finally, studies in which drugs were assessed for their local anti-inflammatory effect on synovitis (SM volume or SM enhancement after local knee injection) used only injected sequences[15–18].

The aims of the present study were:

(1) to assess SM inflammation on MRI with two semiquantitative scoring systems, the WORMS (T2w) and the MRI-synovitis score (T1wCE), and to compare the findings to microscopic analysis, considered to be the gold standard; and (2) to assess joint effusion on MRI with two scoring methods, the WORMS (T2w) and the MRI-effusion score (T1wCE) and to compare the findings to the gold standard of joint volume measurement (JVM) quantified by arthrocentesis.

Patients and methods

Patients

MRI was performed on 30 knees of 30 consecutive patients who fulfilled the American College of Rheumatology criteria for knee OA[19] and were scheduled to have joint lavage because the persistence of pain, chronic joint effusion and/or lack of efficacy of general or local treatments (3 months, on average, after corticosteroid or hyaluronate injections). Demographic data and other characteristics were recorded at baseline. Functional disability and pain were assessed using Lequesne's functional index score[20] and a 0–100 pain visual analog scale (VAS). Radiographs were performed in the fully extended position and graded according to the Kellgren and Lawrence classification[21].

MRI evaluation

Technique

All patients underwent MRI between 1 and 7 days before arthroscopic examination. Imaging was performed using a 1.5 T scanner (General Electric Medical Systems, Milwaukee, WI) with a transmit-receive knee coil to achieve uniform receptivity throughout when the knee was in a neutrally rotated position. Three sequences with fat suppression were performed: axial T2 sequence fast spin echo (repetition time 3000 ms, echo time 66 ms, flip angle 90°, field of view 12 × 12 cm, matrix 256 × 256 pixels, slice thickness 2 mm, slice gap 0.0 mm, and one echo train length); axial T1-weighted gradient echo sequence (2D fast multiplanar spoiled gradient-recalled acquisition in the steady state:repetition time 180 ms, echo time 4.2 ms, flip angle 90°, field of view 12 × 12 cm, matrix 256 × 256 pixels, slice thickness 3 mm, slice gap 0.0 mm, and one acquisition) performed with and without contrast agent. Immediately after contrast agent injection of 0.1 mmol/kg of Gd-DTPA (Guerbet, Aulnay, France) the sequence was repeated and the patient remained in the same position. Total acquisition time for the two last sequences was 6 min and 12 s.

Synovial evaluation

SM inflammation was scored independently by two readers (DL, NS) blinded to the clinical data. They used two validated semi-quantitative scales: (1) the MRI-synovitis score on axial T1-injected images; and (2) the WORMS on an axial T2 sequence[5].

(1) MRI-synovitis score: SM inflammation was scored in five sites of interest and graded on a four-point scale. These sites included three in the suprapatellar recess (lateral recess, medial recess, and just above the trochlear groove) and one each in the lateral and medial femoral gutters (Fig. 1). Thickening of the inflamed SM was determined in each site and graded on a four-point scale according to the Ostergaard's classification: grade 0 lack of enhancement of the synovial tissue (too thin to be seen on MRI, i.e., <100 μm); grade 1 = thickening of the synovial tissue by <2 mm; grade 2 thickening of the synovial tissue varying between 2 mm and 4 mm; grade 3 = synovial tissue >4 mm thick or nodular in pattern[22]. The MRI-synovitis score varied between 0 (normal synovial tissue) and 15 (the most severe and diffuse synovial inflammation)[14].

(2) WORMS: SM and joint effusion were graded together from 0 to 3 in terms of the estimated maximal distension of the synovial cavity: 0 = normal; grade 1 = <33% of maximum potential distension; grade 2 = 33–66% of maximum potential distension; and grade 3 = >66% of maximum potential distension[5].

Effusion evaluation

Synovial fluid effusion was evaluated independently by two readers (DL, NS) blinded to the clinical data. They used two semi-quantitative scales: (1) the WORMS[5] on axial T2w (see above), and (2) the MRI-effusion score on T1wCE. For the MRI-effusion score, only low signal within the intraarticular cavity distinct from the enhancing synovium was scored on an axial T1-injected sequence in the suprapatellar pouch 1 cm above the patella, and in the lateral and medial recesses at the level of the center of the patella. It was graded on a four-point scale: grade 0 = no effusion; grade 1 = minimal effusion; grade 2 = moderate effusion; grade 3 = major effusion defined by capsular distension (Fig. 2). The effusion score was the sum of the scores for the three compartments and varied from 0 = absence of effusion, to 9 = severe effusion.

Effusion volume measurement

Arthrocentesis was conducted for synovial fluid volume measurement before chondroscopic examination by ponction aspiration in the lateral suprapatellar recess.

Chondroscopic examination

Technique

Joint lavage, and SM biopsies were performed during chondroscopic examination with the patient under local anesthesia (lidocaine adrenaline 2%). A standard knee arthroscope (2.7 mm) with a 30° fore oblique lens and a wide field of view was inserted *via* the inferior lateral and medial femorotibial portals. Arthroscopic exploration was combined with joint lavage. All procedures were recorded on VHS videotape (super VHS Panasonic VS 100H; Panasonic, Matsushita Electric Industrial, Osaka, Japan).

Evaluation of the SM

The joint cavity was carefully inspected paying particular attention to the five sites previously described. Where technically possible, SM biopsy specimens were obtained from the five ROIs using 2.7-mm

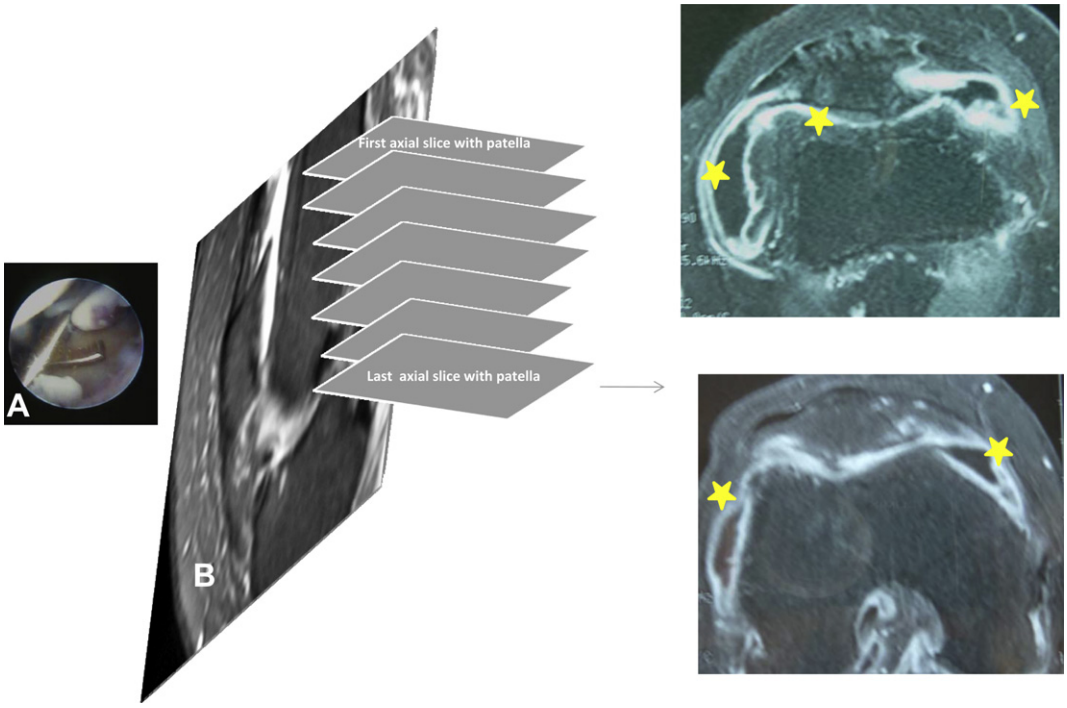


Fig. 1. Synovial biopsies samples were performed during arthroscopy (A) in five sites of interest (three in the suprapatellar recess (lateral central and medial parts) performed just above or laterally to the upper part of the patella and two in the lateral and medial femoral gutters near the inferior part of the patella. MRI-synovitis score assessed synovitis on the same five sites of interest. On the first and the last axial slides where patella is still visible enhanced synovitis is scored according to its degree of thickening (yellow arrow) (C).

biopsy forceps (Arthrex AR 2065; Arthrex, Naples, FL) (Fig. 1). SM biopsy specimens were stored in formaldehyde and embedded in paraffin; 5 μm sections were cut and stained with hematoxylin and eosin for microscopic analysis. Stained sections were coded by an experienced histopathologist who was blinded to all data (MRI findings, stage of the disease). Synovial inflammatory activity was graded separately for each synovial sample. Six parameters were studied on at least five microscopic fields per section. Five of them were microscopy parameters classically used in inflammatory diseases: (1) number of synovial lining cells; (2) subsynovial infiltration by lymphocytes and plasma cells; (3) surface fibrin deposition; (4) congestion related to blood vessel vasodilatation and, to a minor degree, blood vessel proliferation; and (5) fibrosis[14]. The last parameter, the perivascular edema frequently observed in OA biopsy samples but not depicted on normal synovial samples, was also studied. Each parameter was adapted as necessary for OA (changes are qualitatively similar to those seen in RA and SpA, but occur to a lesser degree) and scored as follows: 0 = none; 1 = mild; 2 = moderate; 3 = severe[14]. Grade 0 corresponded to normal synovial tissue and grade 3 to the most severe pattern observed in OA samples (Fig. 3).

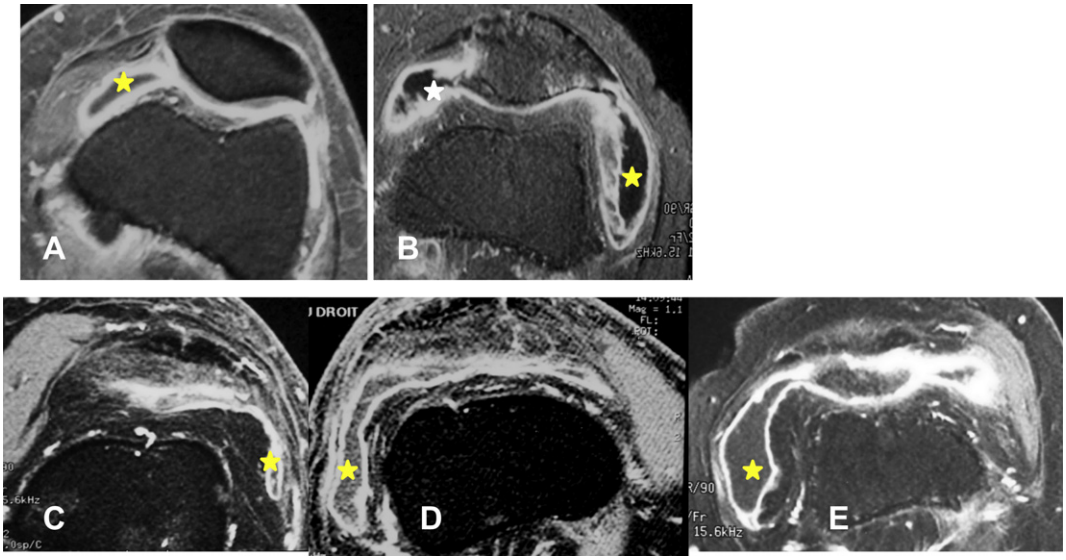


Fig. 2. MRI-effusion score is obtained from axial T1-injected images. On this sequence effusion appeared as a low signal. In the middle part of the patella lateral and medial gutters were graded on a four-point scale: A: grade 1 in the medial gutter and 0 in the lateral recess; B: effusion in graded 2 in the medial recess and 3 in the lateral recess. On the suprapatellar recess, just above the patella, the effusion (yellow star) is graded on axial injected sequence grade 1, 2 and 3 on figure C, D and E respectively.

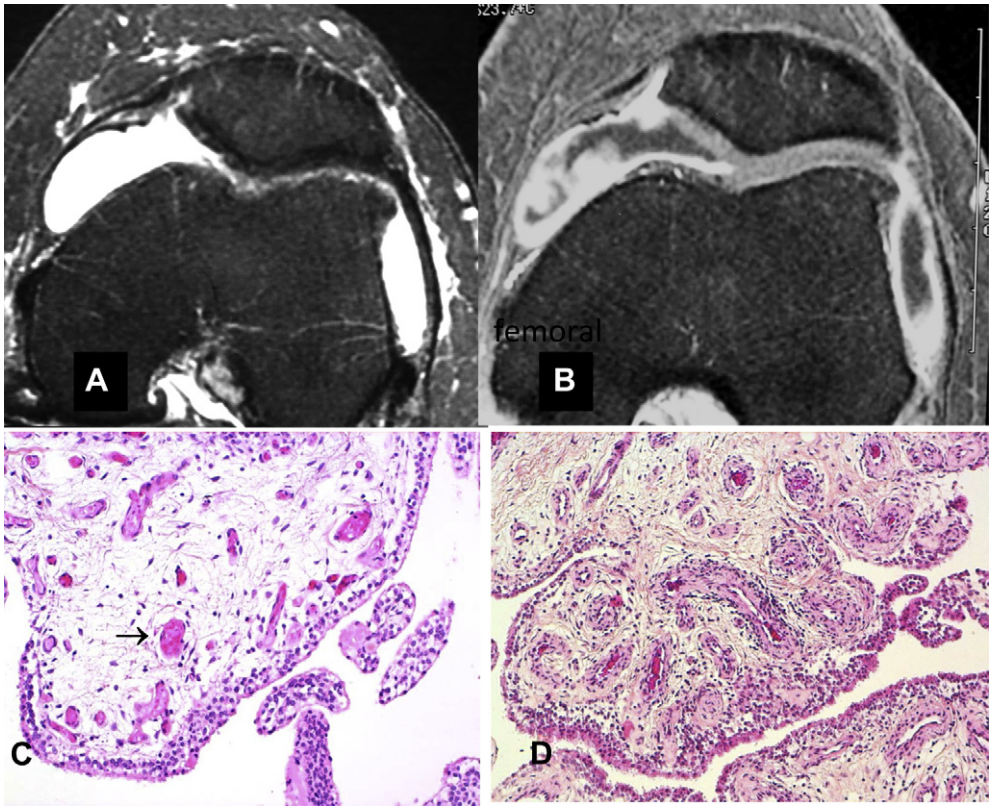


Fig. 3. Distinguishing effusion from synovitis is possible only on injected sequence. A: large effusion in the medial and lateral recesses on axial T2 image. Synovitis appeared in high signal and is undistinguishable from joint effusion also in high signal intensity; B: same location on the injected sequence, only the inflamed SM is enhanced by the contrast agent and scored according to the degree of thickening. The microscopic features of the osteoarthritic (OA) SM are presented on C, "normal" SM composed of 2–3 layers of synovial lining cells (hematoxylin–eosin–safran staining). Beneath them are localized capillaries (arrow) and fat tissue of the subintima. Note that infiltration is moderate; D: severe infiltration associated with an increase of vascularization (congestion) of the subintima without increase in the number of lining cells. (original magnification 200).

Statistical analysis

Inter- and intra-observer reliability of MRI scores was assessed on all exams with intraclass correlation coefficients (ICC) and their 95% confidence intervals (95% CI) derived from a two-way analysis of variance in a random effect model. Inter- and intra-observer reliability of WORMS was assessed with weighted kappa and their 95% CI.

MRI characteristics of SM inflammation were described with medians and ranges. Spearman correlation coefficients (r) and their CI were computed to analyze the correlations between MRI measures and synovial fluid volume, and microscopic characteristics. An r value lower than 0.3 indicates little or no association, between 0.3 and 0.7 the association is moderate, and above 0.7 it is strong. For SM microscopic data, the average grades at the different biopsy sites on the same knee were calculated. Statistical analyses were performed using Statistical Analysis System version 9.1 for Windows (SAS institute, Cary, NC).

Results

Patient characteristics

We assessed 30 subjects (18 females) with a mean age of 58.6 years. Patients presented with high scores for pain [mean VAS 52.3 (4–89)] and disability [mean Lequesne's functional score 11.3 (2–19)]. Concerning structural assessment, patients were classified according to Kellgren and Lawrence as follows: grade 0, $n = 4$; grade 1, $n = 3$; grade 2, $n = 5$; grade 3, $n = 14$; grade 4, $n = 4$.

Test retests reproducibility

The WORMS presented good intra- and inter-observer reproducibility with kappa = 0.78 (95% CI: 0.60–0.92), and kappa = 0.61 (95% CI: 0.41–0.81) respectively. The MRI-effusion and the MRI-synovitis scores presented excellent ICC for intra- and inter-observer reproducibility with ICC = 0.87 (95% CI: 0.75–0.94), ICC = 0.84 (95% CI 0.68–0.91) and ICC = 0.92 (95% CI 0.82–0.96), ICC = 0.90 (95% CI 0.85–0.95) respectively.

Effusion

Arthrocentesis was successfully performed in 18 patients (60%) with a median JVM calculated at 3 ml (0–29). For MRI-effusion score, the median score was 4.5 (range: 0–8) one knee presented no joint effusion (3.3%), two knees (6.7%) presented effusion in only one region, 12 (40%) in two regions and 15 (50%) in the three regions. For the WORMS, the distribution was two (6.6%), 16 (53.3%), nine (30.0%) and three (10.5%) patients for scores 0, 1, 2 and 3 respectively. JVM correlated with Lequesne's functional index ($r = 0.39$; $P < 0.05$) but not with pain-VAS. On MRI, joint effusion was not associated with pain or disability.

JVM was moderately correlated with the WORMS and MRI-effusion score (Table I). Distributions of the MRI scores according to JVM are presented on graph. JVM MRI-effusion score and WORMS were not associated with microscopic patterns of SM inflammation (Table I). Correlations between MRI-effusion score, WORMS and JVM are presented in Table I. Both MRI scores were well correlated [$r = 0.6868$ (0.42–0.91); $P < 0.001$] (Graph 1 and Table I).

Table I
Correlations between clinical, MRI and microscopic data (correlation coefficients and 95% CI)

		WORMS (0–3)	MRI-synovitis score (0–15)	MRI-effusion score (0–9)
Clinical data	VAS-pain (0–100)	−0.02 (−0.41–0.37)	0.18 (−0.22–0.53)	−0.25 (−0.58–0.15)
	Lequesne functional index (0–24)	0.03 (−0.34–0.39)	0.10 (−0.27–0.45)	−0.04 (−0.4–0.33)
	JVM (ml)	0.60 (0.30–0.79)*	0.47 (0.14–0.71)*	0.59 (0.29–0.78)*
SM biopsies	Microscopic evaluation			
	Infiltration (0–3)	0.31 (−0.7–0.61)	0.45 (0.10–0.77)*	0.15 (−0.22–0.49)
	Synovial lining cells (0–3)	0.08 (−0.30–0.43)	0.25 (−0.13–0.56)	−0.15 (−0.48–0.22)
	Fibrosis (0–3)	0.12 (−0.26–0.47)	0.30 (−0.07–0.60)	−0.09 (−0.44–0.28)
	Fibrin (0–3)	−0.08 (−0.44–0.29)	0.34 (−0.03–0.63)	0.01 (−0.35–0.37)
	Edema (0–3)	0.19 (−0.19–0.52)	0.25 (−0.13–0.56)	−0.03 (−0.39–0.33)
	Congestion (0–3)	0.22 (−0.16–0.54)	0.34 (−0.03–0.63)	0.14 (−0.23–0.48)
MRI scores	WORMS (0–3)		0.63 (0.35–081)*	0.68 (0.42–0.83)*
	MRI-synovitis score (0–12)			0.51 (0.18–0.73)*

VAS-pain: pain Visual Analog Scale; * = $P < 0.05$.

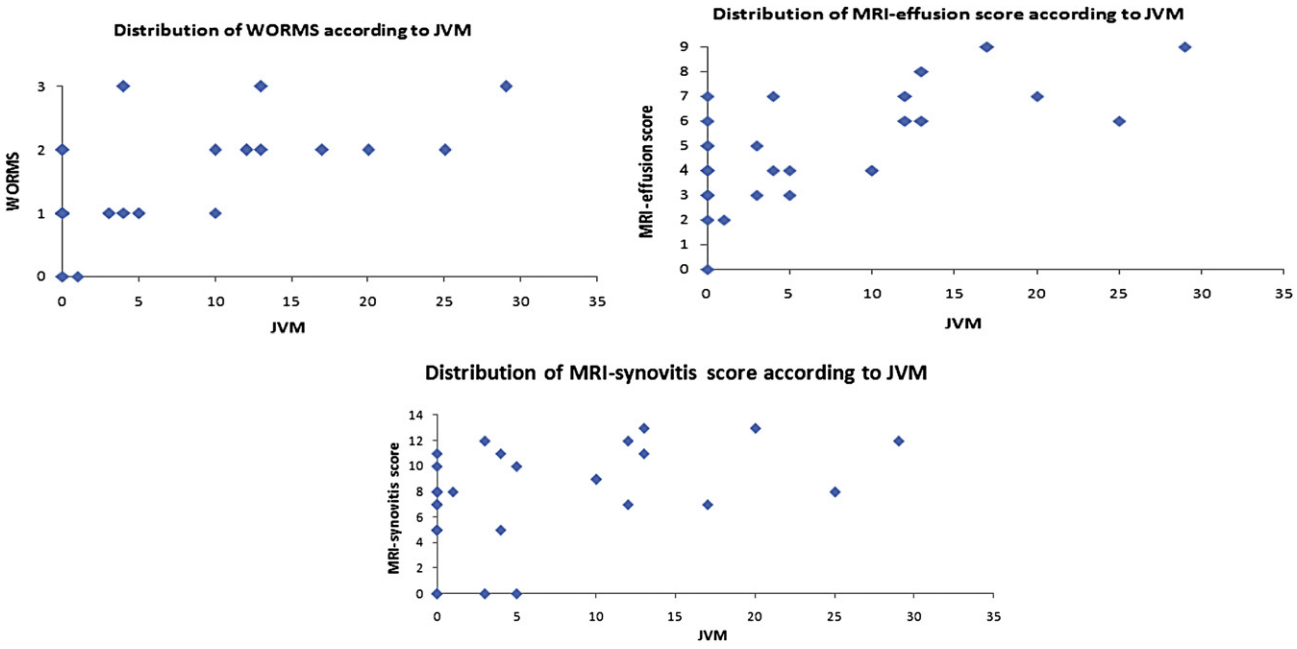
Synovitis

With regard to microscopic evaluation, 86 synovial biopsies were scored (Fig. 3). The median scores (0–3) for synovial lining cells, fibrin, fibrosis, vascular congestion, edema, and infiltration were 2.0, 1.8, 1.6, 1 and 1.3 respectively. For MRI-synovitis score, four knees presented no SM inflammation and the median MRI-synovitis score in inflamed knees was 8 (0–13). For the WORMS, see the distribution above (effusion paragraph) since synovitis and effusion were scored together. Pain and disability did not correlate with microscopic analysis in our population. MRI-synovitis score was not associated with pain or disability. This score was moderately correlated with JVM (graph) MRI-effusion score and WORMS (Table I). The MRI-synovitis score was moderately correlated with infiltration ($r = 0.45$; $P < 0.05$). None of the microscopic parameters were correlated with WORMS (Table I).

Discussion

This study demonstrates, a moderate correlation between JVM as measured by arthrocentesis ($r = 0.57–0.60$; $P < 0.05$) and MRI scores. We demonstrated a high frequency of effusion on MRI (93.3–96.6%) while the frequency of positive arthrocentesis is relatively low (60%). This moderate correlation may be explained on one hand by the lack of effusion volume measurements on MRI, and on the other hand by the fact that arthrocentesis, performed to remove all synovial fluid from the articular cavity, may be uncompleted, leaving a small quantity of effusion in the joint especially when synovial fluid is localized in one of the two femoral gutters; or impossible when a direct aspiration is performed in a compartment without effusion. In this study, MR-effusion score showed an inhomogeneous distribution of joint effusion. In 50% of our population, no joint fluid was depicted in one of the three regions of interest. Recently Li *et al.* quantified knee effusion according to a volumetric approach and demonstrated excellent correlation ($r = 0.88$) with a direct aspiration performed in the lateral suprapatellar recess[23].

Nevertheless, joint effusion assessed by arthrocentesis was associated with disability but not with pain. Surprisingly, if JVM and effusion assessed by MRI (the WORMS and the MRI-effusion score) were well correlated, no relationship, were found between MRI-effusion score, WORMS and pain or disability. So the results should be interpreted with caution as the cross-sectional nature of the study does not allow conclusions to be drawn about the causal relationships between effusion and patient symptoms. Moreover the low frequency of patient without effusion or with low score for MRI-effusion and WORMS did not permit to demonstrate any



Graph 1. Distribution of MRI scores according to JVM.

relationship between effusion in MRI and pain. The results of this study cannot be generalized to all subjects with knee OA as our sample included patients scheduled to have joint lavage because of the persistence of pain and effusion and lack of efficacy of other treatments. Thus, compared to the recent study presented by Roemer *et al.*, we found a higher frequency of joint effusion 93.3–96.6% vs 73% by MRI[24].

Concerning joint effusion on MRI, no difference was noted between non-injected images (the WORMS) and injected images (the MRI-effusion score); excellent correlation was noted between both scores, and both methods exhibited good intra- and inter-observer reproducibility (ICC = 0.73–0.89). Both MRI scores presented good correlations with JVM and depicted effusion with the same range of severity. But this study presented some limits: (1) the aspiration of synovial fluid by artrocentesis, usually used as gold standard, can be incomplete and as results criticized; (2) the semiquantitative approach in MRI is less accurate to determine joint than volumetric measurement and both methods should be compared. To finish recent studies have shown that T2 images may overestimate joint effusion measurement according to volume measurement in comparison to T1wCE, suggesting that both synovitis and joint effusion are taken together on T2w images[25].

About the relationship between joint effusion and SM inflammation, we observed on MRI, a good correlation between MRI scores for effusion (MRI-effusion score and WORMS) and MRI-synovitis score ($r = 0.56$; $P < 0.009$) whereas we found no association between JVM and SM assessed on microscopic analysis. This result suggested that microscopic inflammatory synovial patterns are dissociated from mechanisms leading to joint effusion while in MRI, mechanisms leading to joint effusion and synovitis seem more related. Recently, Roemer *et al.* showed similar results on MRI with a high frequency of synovitis associated with effusion[24]. Previously, Østergaard *et al.* found a weak correlation between the volume of joint effusion assessed by MRI (but not by arthrocentesis) on injected sequences and SM microscopic data on a smaller sample of OA patients ($n = 25$)[12]. All these results should be interpreted with caution because these studies were performed on a small sample of patients.

Microscopic analysis is usually considered the gold standard for assessment of SM inflammation in OA[26]. As previously shown, this study failed to detect a relationship between that and pain or disability, so microscopic features in knee OA reflecting more chronic than acute modifications[26]. We confirmed the good correlations previously demonstrated between SM inflammation assessment performed on T1-injected sequences, and infiltration ($r = 0.45$; $P < 0.05$)[14] while no correlation was observed on the WORMS (T2w). Moreover, Loeuille *et al.* demonstrated that SM volume with high speed of enhancement ($>1\%/s^{-1}$) measured 186 s after contrast agent injection, was highly correlated with vascular congestion in knee OA ($r = 0.79$; $P < 0.01$)[26]. However, evaluation performed on T2 axial images (the WORMS) did not correlate with microscopic parameters. In non-injected sequences, especially T2 sequences with fat suppression, inflamed SM appears in high signal intensity indistinguishable from synovial fluid, and fibrotic SM has a low signal intensity indistinguishable from that of fat tissue or capsule on fat suppressed sequences (Fig. 3). Thus, use of a contrast agent is the only way to accurately visualize inflamed SM (see the example in Fig. 3) as only the inflamed SM, not synovial fluid or fat tissue, is enhanced by the contrast agent. Gadolinium is entrapped in the synovial tissue before diffusing throughout the synovial fluid[27–29]. In order to perform in optimal conditions T1-injected images, contrast agent has to be intravenously injected just before the sequence to avoid any underestimation or any overestimation of synovitis in MRI. In clinical practice, use of contrast agents should be discussed since induction of nephrogenic systemic fibrosis has been observed in patients with renal dysfunction[30]. Thus, T2 sequences are still recommended to visualize articular disorders in knee OA (menisci lesions, bone marrow edema, abarticular lesions), but in our opinion and from a clinical research standpoint, only injected sequences seem relevant to accurately assess synovial inflammation and to assess local anti-inflammatory effects of therapeutic agents on synovitis. Most of the studies performed on T1-injected sequences result in evidence of an anti-inflammatory effect after intraarticular injections of triamcinolone hexacetonide[18] or methylprednisolone[16] and after oral administration of NSAID or acetaminophen[31]. All these treatments reduce SM volume. In contrast, intraarticular injection of samarium combined with triamcinolone hexacetonide[18], or intraarticular injection of kineret[17] at a dose of 50 or 150 mg has no effect on SM volume, MRI-synovitis or MRI-effusion scores.

This study suggests that joint effusion can be assessed with the same level of performance on T1wCE and T2w images on MRI. However, T1-injected images are more accurate in assessing the impact of synovial inflammation and especially infiltration. This kind of sequence could be recommended in a clinical research context to assess the role of synovitis on cartilage breakdown and/or evaluate therapeutic response to drugs administered for SM inflammation in knee OA.

Author contribution

Concerning contributions to the article:

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Collection and assembly data: Damien Loeuille, Norbert Saulière.

Conflict of interest

No conflict of interest.

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References

1. Hill CL, Gale DG, Chaisson CE, Skinner K, Kazis L, Gale, *et al.* Knee effusions, popliteal cysts, and synovial thickening: association with knee pain in osteoarthritis. J Rheumatol 2001;28:1330–7.
2. Tarhan S, Unlu Z. Magnetic resonance imaging and ultrasonographic evaluation of the patients with knee osteoarthritis: a comparative study. Clin Rheumatol 2003;22:181–8.
3. Roemer FW, Zhang Y, Niu J, Lynch JA, Crema MD, Marra MD, *et al.* Multicenter Osteoarthritis Study Investigators. Tibiofemoral joint osteoarthritis: risk factors for MR-depicted fast

cartilage loss over a 30-month period in the multicenter osteoarthritis study. Radiology 2009;252:772–80.
4. Hill CL, Hunter DJ, Niu J, Clancy M, Guermazi A, Genant H, *et al*. Synovitis detected on magnetic resonance imaging and its relation to pain and cartilage loss in knee osteoarthritis. Ann Rheum Dis 2007;66:1599–603.
5. Peterfy CG, Guermazi A, Zaim S, Tirman PF, Miaux Y, White D, *et al*. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage 2004;12:177–90.
6. Fernandez-Madrid F, Karvonen RL, Teitge RA, Miller PR, An T, Negendank WG. Synovial thickening detected by MR imaging in osteoarthritis of the knee confirmed by biopsy as synovitis. Magn Reson Imaging 1995;13:177–83.
7. Kornaat PR, Ceulemans RY, Kroon HM, Riyazi N, Kloppenburg M, Carter WO, *et al*. MRI assessment of knee osteoarthritis: Knee Osteoarthritis Scoring System (KOSS) inter-observer and intra-observer reproducibility of a compartment-based scoring system. Skeletal Radiol 2005;34:95–102.
8. Hunter DJ, Lo GH, Gale D, Grainger AJ, Guermazi A, Conaghan PG. The reliability of a new scoring system for knee osteoarthritis MRI and the validity of bone marrow lesion assessment: BLOKS (Boston Leeds Osteoarthritis Knee Score). Ann Rheum Dis 2008;67:206–11.
9. Pelletier JP, Raynauld JP, Abram F, Haraoui B, Choquette D, Martel-Pelletier J. A new non-invasive method to assess synovitis severity in relation to symptoms and cartilage volume loss in knee osteoarthritis patients using MRI. Osteoarthritis Cartilage 2008;16(Suppl 3):S8–S13.
10. Roemer FW, Guermazi A, Zhang Y, Yang M, Hunter DJ, Crema MD, *et al*. Hoffa's fat pad: evaluation on unenhanced MR images as a measures of patella femoral synovitis in OA. AJR 2009;192:1696–700.
11. Baker K, Grainger A, Niu J, Clancy M, Guermazi A, Crema M, *et al*. Relation of synovitis to knee pain using contrast-enhanced MRIs. Ann Rheum Dis 2010 May 14.
12. Ostergaard M, Stoltenberg M, Lovgreen-Nielsen P, Volck B, Jensen CH, Lorenzen I. Magnetic resonance imaging-determined synovial membrane and joint effusion volumes in rheumatoid arthritis and osteoarthritis: comparison with the macroscopic and microscopic appearance of the synovium. Arthritis Rheum 1997;40:1856–67.
13. Hoenen-Clavert V, Rat AC, Loeuille D, Bettembourg-Brault I, Michel-Batot C, Blum A, *et al*. Inflammatory and structural evaluation in spondyloarthritis: magnetic resonance imaging analysis of axial and peripheral involvement. J Rheumatol 2007;34:762–8.
14. Loeuille D, Chary-Valckenaere I, Champigneulle J, Rat AC, Toussaint F, Pinzano-Watrin A, *et al*. Macroscopic and microscopic features of synovial membrane inflammation in the osteoarthritic knee: correlating magnetic resonance imaging findings with disease severity. Arthritis Rheum 2005;52:3492–501.
15. Ostergaard M, Stoltenberg M, Gideon P, Wieslander S, Sonne-Holm S, Kryger P, *et al*. Effect of intraarticular osmic acid on synovial membrane volume and inflammation, determined by magnetic resonance imaging. Scand J Rheumatol 1995;24:5–12. Erratum in: Scand J Rheumatol 1995;24:127.
16. Ostergaard M, Stoltenberg M, Gideon P, Sørensen K, Henriksen O, Lorenzen I. Changes in synovial membrane and joint effusion volumes after intraarticular methylprednisolone. Quantitative assessment of inflammatory and destructive changes in arthritis by MRI. J Rheumatol 1996;23:1151–61.
17. Loeuille D, Chary-Valckenaere I, Goebel JC, Rat AC, Blum A, Kiefer P, *et al*. MRI evaluation of the synovial membrane after a single intraarticular (IA) injection of Anakinra in 7 patients with osteoarthritis of the knee suggests antiinflammatory effect. Arthritis Rheum 2005;52(Suppl 9). S70.
18. Clunie GP, Wilkinson ID, Lui D, Hall-Craggs MA, Paley MN, Edwards JC, *et al*. Changes in articular synovial lining volume measured by magnetic resonance in a randomized, double-blind, controlled trial of intra-articular samarium-153 particulate hydroxyapatite for chronic knee synovitis. Rheumatology 1999;38:113–7.
19. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, *et al*. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 1986;29:1039–49.
20. Lequesne MG, Mery C, Samson M, Gerard P. Indexes of severity for osteoarthritis of the hip and knee. Validation–value in comparison with other assessment tests. Scand J Rheumatol (Suppl) 1987;65:85–9.
21. Kellgren JH, Lawrence DM. Radiological assessment of osteo-arthritis. Ann Rheum Dis 1957;16:494–502.
22. Ostergaard M, Hansen M, Stoltenberg M, Gideon P, Klarlund M, Jensen KE, *et al*. Magnetic resonance imaging-determined synovial membrane volume as a marker of disease activity and a predictor of progressive joint destruction in the wrists of patients with rheumatoid arthritis. Arthritis Rheum 1999;42:918–29.
23. Li W, Abram F, Pelletier JP, Raynaud JP, Dorais M, D'Anjou MA, *et al*. Fully automated system for the quantification of human osteoarthritic knee joint effusion volume using magnetic resonance imaging. Arthritis Res Ther 2010:R12–R173.
24. Roemer FW, Kassim Javaid M, Guermazi A, Thomas M, Kiran A, Keen R, *et al*. Anatomical distribution of synovitis in knee osteoarthritis and its association with joint effusion assessed on non-enhanced and contrast-enhanced MRI. Osteoarthritis Cartilage 2010;18:1269–74.
25. Habib S, Guermazi A, Ozonoff A, Hayashi D, Crema MD, Roemer FW. MRI-based volumetric assessment of joint effusion in knee osteoarthritis using proton density-weighted fat-suppressed and T1-weighted contrast-enhanced fat-suppressed sequences. Skeletal Radiol 2011 May 20 [Epub ahead of print].
26. Loeuille D, Rat AC, Goebel JC, Champigneulle J, Blum A, Netter P, *et al*. Magnetic resonance imaging in osteoarthritis: which method best reflects synovial membrane inflammation? Correlations with clinical, macroscopic and microscopic features. Osteoarthritis Cartilage 2009 Mar 24.
27. Drapé JL, Thelen P, Gay-Depassier P, Silbermann O, Benacerraf R. Intraarticular diffusion of Gd-DOTA after intravenous injection in the knee: MR imaging evaluation. Radiology 1993;188:227–34.
28. Watrin-Pinzano A, Loeuille D, Goebel JC, Lapicque F, Walter F, Robert P, *et al*. Quantitative dynamic contrast enhanced MRI of experimental synovitis in the rabbit knee: comparison of macromolecular blood pool agents vs. Gadolinium-DOTA. Biomed Mater Eng 2008;18:261–72.
29. Winalski CS, Aliabadi P, Wright RJ, Shortkroff S, Sledge CB, Weissman BN. Enhancement of joint fluid with intravenously administered gadopentetate dimeglumine: technique, rationale, and implications. Radiology 1993;187:179–85.
30. Thomsen HS. Nephrogenic systemic fibrosis: history and epidemiology. Radiol Clin North Am 2009;47:827–31. vi. Review.
31. Brandt KD, Mazzuca SA, Buckwalter KA. Acetaminophen, like conventional NSAIDs, may reduce synovitis in osteoarthritic knees. Rheumatology 2006;45:1389–94.