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MRI IN HAND OSTEOARTHRITIS: VALIDATION OF THE OSLO HAND OSTEOARTHRITIS MRI-SCORE AND ASSOCIATION WITH PAIN, RADIOGRAPHY AND ULTRASOUND

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Submitted

ABSTRACT

Objective

To investigate the reproducibility of the Oslo Hand OA (OHOA)-MRI scoring method and validity against ultrasound (US). To investigate MRI features with pain in patients with hand osteoarthritis (OA).

Methods

In sixteen patients (median age 57 years, 62% female, 13 had erosive OA) with hand OA, 2nd-5th DIPJs/PIPJs of the right hand were included. Pain on palpation was assessed per joint on palpation per joint. Greyscale synovitis and osteophytes were scored with US. 3 Tesla MRI scans with gadolinium were made. MRI-features were scored according to the OHOA-MRI scoring method for synovitis, bone marrow lesions (BMLs) and erosions (grade 0-3). MRIs in six patients were scored twice to calculate the intra-class correlation coefficient (ICC). Correlation of MRI with US-features was assessed with the percentage of exact agreement (PEA). The association between pain and MRI features was examined with Generalized Estimated Equations, adjusted for within-patient effects, age, sex and BMI.

Results

The ICCs ranged from 0.66-1.00 for the MRI-features. Forty-three percent, 27% and 61% of joints had moderate/severe synovitis, BML and erosions on MRI, respectively. Good agreement was reached for moderate/severe synovitis (=grade2/3) on MRI with US greyscale synovitis (PEA 73%) and PDS (PEA 67%). Pain was significantly associated with the presence of moderate/severe synovitis (adjusted OR 2.4 (95% CI 0.1-3.2)), BMLs (3.5 (1.6-7.7)) , bone erosions (4.5 (1.7-11.9)).

Conclusions

The OHOA-MRI scoring method is reproducible. The validity against US is good. The presence of moderate/severe synovitis, BMLs and erosions are associated with pain in the same joint.

INTRODUCTION

Hand osteoarthritis (HOA) is a prevalent musculoskeletal disease that can lead to pain or functional limitations[1,2]. It affects the whole joint, including cartilage, subchondral bone, synovium, capsule and ligaments[3]. HOA is a heterogeneous disorder comprising of different subsets, such as nodal, erosive and thumb base osteoarthritis (OA)[4]. Which underlying pathophysiological processes are involved in structural damage and pain in HOA is unknown.

The clinical presentation of HOA in the interphalangeal joints (IPJs) is characterized by bony enlargements of IPJs in addition to limited mobility and pain[5]. These classical structural features of HOA can be visualized on conventional radiographs as osteophytes and joint space narrowing (JSN)[6]. More recently, ultrasound (US) has been used to visualize soft tissues in HOA. Recent US studies have confirmed that inflammation might play a role in HOA[7-9].

In knee OA, magnetic resonance imaging (MRI) has proven to be a valid imaging modality to visualize not only soft tissues, but also subchondral bone lesions, such as bone marrow lesions (BMLs)[10-12]. For HOA, few studies used MRI to investigate abnormalities in soft tissue and subchondral bone[3,13,14]. Recently, a MRI scoring method supported by an atlas was proposed, which facilitates research with MRI in HOA. The Oslo Hand OA MRI score (OHOA-MRI score) was developed as a reliable method to assess key features in HOA[15]. However, until present, the OHOA-MRI score was not validated in another HOA population and no comparison with other imaging modalities, such as US was performed.

The aim of this paper is to investigate the reproducibility of the OHOA-MRI scoring method in a HOA population from another hospital where the scoring method was developed and to validate it against conventional radiographs and US. Furthermore, we described MRI-findings in HOA patients and investigated the association with pain on palpation and presence of MRI-features in finger joints with and without erosive OA.

METHODS AND MATERIALS

Patient population

Sixteen patients with HOA, fulfilling the criteria of the American College of Rheumatology[5], were recruited from the Rheumatology outpatient clinic from July 2008-October 2010. Patients were involved in an double-blind randomized controlled trial for erosive hand OA, but did not receive any studymedication at the time of clinical, MRI, ultrasound and radiographic assessment. They had at least one (pre) erosive joint in the IPJs on conventional radiographs and pain ≥ 30 mm on the visual analogue scale (VAS). Patients were excluded if they suffered from chronic inflammatory rheumatic disease (e.g. rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, haemochromatosis, gout or chondrocalcinosis) or used prednisolone, hydroxycholoroquine, sulfasalazine or methotrexate within 3 months.

Approval of the study by the medical ethical committee of the Leiden University Medical hospital and signed informed consent was obtained.

Clinical assessment

Demographic characteristics were collected by standardized questionnaires. All patients completed a 100-mm VAS to assess hand pain ≤ 48 hours. Usage of analgesics was allowed during the study, corticosteroids (oral or intra-articular) were not allowed. Pain upon palpation (grade 0-3) for each distal and proximal interphalangeal and 1st carpometacarpal joint (DIPJs, PIPJs, 1st CMCJs) was assessed by a single observer (WK) during physical examination using the Doyle Index, which has been validated for HOA[16]. Presence of bony/soft tissue swelling and deformity was also assessed. Since grades 2-3 were rarely scored, all features were dichotomized into 'absence'/'presence'.

MRI examinations

The 2nd-5th DIPJs and PIPJs of the right hand were imaged in a 4-channel wrist coil using a 3T MRI Unit (Achieva 3T; Philips Medical Systems), with the hand in the coil along the femur. In all patients, the following sequences were obtained: coronal turbo spin echo (TSE, slice thickness (ST) 2 mm, repetition time/echo time (TR/TE) 1139/20 ms), coronal frequency selective fat-suppressed T2-weigthed images (ST 3 mm, TR/TE 4013/60 ms), coronal 3D water excitation gradient echo images (ST 1 mm, TR/TE 3.3/1.72 ms), sagittal T1-TSE (ST 3 mm, TR/TE 450/20 ms), sagittal frequency selective fat-suppressed T2-weighted images (ST 3.5 mm, TR/TE 7768/60 ms), coronal post-Gd-DOTA (Gadolinium) fat-suppressed images (ST 2 mm, TR/TE 1138/20 ms), sagittal post-Gd-DOTA fat-suppressed images (ST 3 mm, TR/TE 995/20 ms) (0.1 mmol/kg, Dotarem, Guerbet, Netherlands). In 4 patients, additional images were obtained with the following sequences: transversal native T1-weighted images (ST 3 mm, TR/TE 633/20 ms) and post-Gd-DOTA frequency selective fat-suppressed T1- (ST 3 mm, TR/TE 570/20 ms) and transversal frequency selective fat-suppressed T2-weighted images (ST 3 mm, TR/TE 4490/60 ms). The decision to add transversal slices was made after WYK went to Oslo for the training of the MRI scoring method; previous assessments could not be changed. MRI-examinations were obtained at the same day as clinical assessments and radiographs.

MRI-features were scored according to the OHOA-MRI scoring method[15] by one reader (WK), after a training session of one week with the developers of the OHOA-MRI score and training set of MRI images provided by the developers. MRI-features were scored for synovitis (grade 0-3), flexor tenosynovitis (grade 0-3), presence of abnormal collateral ligaments (grade 0-1, instead of absent/non-continuous ligaments in original scoring), BMLs at insertion sites of collateral ligaments (grade 0-1), bone erosions (grade 0-3), bone cysts (grade 0-1), osteophytes (grade 0-3), JSN (grade 0-3), malalignment ≥ 15 degrees (grade 0-1) and subchondral BMLs (grade 0-3). The BMLs scored at the insertion sites of the collateral ligaments were differentiated by location and were not necessarily scored as subchondral BMLs if these lesions were restricted to the insertion sites. The exact definitions of the scoring of the MRI-features are described in detail elsewhere[15].

US assessment

US was performed by two ultrasonographers (MCK, WYK) in consensus using a Toshiba Applio scanner (Toshiba Medical systems, Tustin, California) with a 10-14 MHZ linear

array transducer. MCK (rheumatologist) is certified for musculoskeletal sonography with 4 years of experience, WYK has three years of experience. Power Doppler Signal (PDS) was assessed with a pulse repetition frequency of 13.2 KHz and medium wall filter. Gain was adjusted until background signal was removed. US was performed 3-19 weeks in advance of the MRI and clinical assessment (median 6 weeks) due to logistic/practical reasons.

All hand joints were scanned from the dorsal side only in longitudinal and transverse planes. Features had to be present in both planes. Each joint was scored for osteophytes, PDS and greyscale synovitis, defined as a composite of effusion and synovial thickening[8,17]. All US-features were scored on a four-point scale (0=none, 1=mild, 2=moderate, 3=severe), but were dichotomized into presence/absence for this study. The intra-observer variability was good (kappa= 0.73 for greyscale synovitis)[8].

Conventional radiographs

Radiographs (dorso-volar) were taken of each hand seperately, using a standardized protocol. Osteophytes, JSN and cysts were scored by WK with the OARSI-atlas for osteophytes/JSN (grade 0-3) and cysts (grade 0-1)[6]. Erosive lesions were scored according to the Verbruggen-Veys scoring method, defined as an erosive (E-phase) or remodelled phase (R-phase)[18]. If no joint space is left between the cortex of the joints, were defined as pre-erosive (J-phase). The intraobserver reliability was good for Verbruggen-Veys, OARSI OST and JSN (Intraclass Correlation Coefficient (ICC) 0.91, 95% confidence interval (95%CI) 0.70-0.97, 0.93 (0.81-0.97) and 0.89 (0.76-0.95), respectively).

Statistical analysis

Data were analyzed using SPSS, version 17.0 (SPSS Inc, Chicago, Ill).

To determine the reproducibility of the OHOA-MRI scoring method, the intra-reader reliability, displayed as ICCs (95%CI), was based on MRI images of six randomly selected patients (48 joints).

To validate MRI-features against US and radiographs, 2nd-5th DIPJs/PIPJs of the right hand only (128 joints) were compared on all imaging modalities. Chi-square tests were performed to determine significant differences (defined as p-value < 0.05) between MRI-findings versus US or radiographs as dichotomized variables. The correlation of MRI-features with US and radiographic features was assessed with the Spearman's rank correlation coefficient, ρ (p-value) and percentage exact agreement (PEA).

To study the relationship between MRI-features (as independent variables) and pain on the individual joint level, we associated MRI-features with pain upon palpation in hand joints and presence of (pre)erosive phases of the Verbruggen-Veys scoring method (as dependent variables) using generalized estimated equations (GEE) with robust variance estimators and unspecified covariance matrix to account for effects within the same person, age, sex and BMI. Results were presented as odds ratios (OR) with 95%CI.

RESULTS

Study population

Characteristics of 16 patients are shown in table 1 (mean age of 56.7 years, 62% female). The median symptom duration was 6.5 years. Bony swelling was in 61% and soft swelling in 18% of the joints palpable during clinical assessment. Erosive OA was found in 13 patients, defined as having at least one E- or R-phase according to Verbruggen-Veys. The non-erosive hand OA patients had at least one (pre-erosive) J-phase in the interphalangeal joints. This is a severely affected patient population as reflected by a median VAS pain of 70 mm.

Table 1: Demographic characteristics of 16 patients with hand osteoarthritis.

Characteristic	Median (range)
Age, years	56.7 (42.0-70.7)
BMI, kg/m^2	25.7 (20.2-32.4)
Female sex, in no. (%)	10 (62)
Symptom duration, years	6.5 (0-16)
No. of tender joints (DIPJs2-5, PIPJs2-5)	5.0 (1-12)
No. of swollen joints (DIPJs2-5, PIPJs2-5)	2.5 (1-6)
VAS pain, mm (0-100)	70 (35-93)

BMI, Body Mass Index; DIPJs, distal interphalangeal joints; PIPJs, proximal interphalangeal joints; VAS, Visual Analogue Scale.

Reproducibility of OHOA-MRI scoring method

MRI-images of six patients (three with coronal and sagittal planes only, three with coronal, sagittal and axial planes) were scored twice to determine the intra-observer reliability. The reliability, reflected as the ICC, for most features were good to excellent (range 0.75-1.00) (table 2). For one feature, being flexor tenosynovitis, the ICC was lower (0.66).

Table 2: Intra-reader correlation coefficient (ICC, two-way random, absolute agreement), MRIs of 6 patients scored twice.

MRI feature	ICC single measures (95% CI, p-value)
Synovitis	0.94 (0.51 to 0.99, <0.001)
Flexor tenosynovitis	0.66 (-0.11 to 0.95, 0.006)
Collateral ligaments	0.97 (0.84 to 0.99, <0.001)
Bone marrow lesions at insertion site	0.75 (0.11 to 0.96, 0.02)
Bone erosions	0.89 (0.46 to 0.98, 0.002)
Bone cysts	0.91 (0.54 to 0.99, 0.001)
Osteophytes	0.95 (0.66 to 0.99, <0.001)
Joint space narrowing	0.86 (0.37 to 0.98, 0.007)
Malalignment	1.00 (1.00 to 1.00, -)
Bone marrow lesions	0.88 (0.34 to 0.98, 0.002)

Description of OA features on MRI

In one patient, the contrast arrived subcutaneously instead of intravenously. Therefore (teno)synovitis could not be assessed in 8 joints and consequently the number of joints assessed by MRI for the presence of synovitis and structural changes varied. In two DIPJs, correct scoring was not possible for some features due to incorrect positioning of the joint in the coil.

In 117 joints (98%), any sign of synovitis was seen on MRI. If the cut-off for MRI-synovitis is set on grade ≥2 (moderate to severe), 51 joints (43%) have synovitis. Flexor tenosynovitis was seen in 36 (30%), erosions in 77 (61%), bone cysts in 16 (13%) and BMLs in 36 (27%) joints on MRI. Collateral ligaments were seen in 84 (66%) joints and BMLs at the insertion sites of collateral ligaments in 17 (13%) joints. Osteophytes and JSN were seen in 98 (77%) and 116 (91%) joints on MRI, respectively. Malalignment was only seen in 2 DIPJs on MRI. Table 3 shows the distribution of these features stratified for DIPJs/PIPJs.

Table 3: Findings on MRI in the examined right hand in 16 patients with hand OA (total 128 joints), stratified for DIPJs and PIPJs.

Feature (range of scores)	DIPJs, affected/ total no. joints (%)	PIPJs, affected/ total no. joints (%)
Synovitis (grade ≥1)	58/60 (97)	59/60 (98)
Synovitis (grade ≥2)	22/60 (37)	29/60 (48)
Flexor tenosynovitis (grade ≥1)	15/60 (25)	21/60 (35)
Collateral ligaments (normal)	34/63 (54)	50/64 (78)
BML at insertion sites (present)	8/64 (13)	9/64 (14)
Bone erosions (grade ≥1)	45/62 (73)	32/64 (50)
Bone cysts (present)	8/63 (13)	8/64 (13)
Osteophytes (grade ≥1)	54/63 (86)	44/64 (69)
JSN (grade ≥1)	62/63 (98)	54/64 (84)
Malalignment (present)	2/63 (3)	0/64 (0)
BML (grade ≥1)	22/64 (34)	12/64 (19)

DIPJs, distal interphalangeal joints; PIPJs, proximal interphalangeal joints; BML, bone marrow lesions; JSN, joint space narrowing.

Validity of MRI versus ultrasound

Greyscale synovitis was seen in 49 (38%) joints (20 DIPJs, 29 PIPJs). This was significantly less than on MRI (p-value <0.001), where 117 joints (98%) had any sign of synovitis. The US-results were more in line with the percentage of joints showing moderate/severe synovitis on MRI (43%, p<0.001). PDS was seen in 29 joints (23%) (13 DIPJs, 16 in PIPJs), which is significantly less than the percentage of joints with moderate/severe synovitis on MRI (43%, p=0.001). In 23 joints (18%) greyscale synovitis combined with a positive PDS signal was seen. Ultrasonic osteophytes was seen in 127 joints (64 in DIPJs, 63 in PIPJs), which is more than on MRI (77%, p=0.06).

Despite an interval of a median of 6 weeks between US and MRI acquisition, a moderate correlation was found between the presence of moderate/severe synovitis

on MRI and greyscale synovitis on US (Spearman's ρ 0.45, p<0.001, PEA 73%). No correlations were found between the presence of any MRI-synovitis and US-greyscale synovitis (Spearman's ρ 0.02, p=0.79, PEA 42%). Correlation of MRI-synovitis (graded 0-3) with PDS on US (graded 0-3) was Spearman's ρ 0.52, p < 0.001. The PEA between MRI grade 2-3 synovitis and any PDS on US was 67%. Correlation between osteophytes on US (grade 0-3) and MRI (grade 0-6, summed osteophyte score of distal and proximal site) was Spearman's ρ 0.50, p<0.001. The PEA of osteophytes between US and MRI was 78%.

Validity of MRI versus radiographs

One joint is missing due to ankylosing of that joint. Radiographic osteophytes were seen in 53 (41%) and JSN in 97 (76%) joints, significantly less than on MRI (77% (p<0.001) and 91% (p=0.001), respectively). Radiographic erosions were detected in 23 (18%) joints, significantly less than on MRI (61%, p<0.001). Radiographic bone cysts were seen in 25 (20%) joints, significantly more than on MRI (12%, p<0.001). The Spearman's ρ (p-value) for osteophytes, JSN, erosions and cysts were 0.35 (p<0.001, PEA 78%), 0.29 (p=0.001, PEA 79%), 0.33 (p<0.001, PEA 70%) and 0.29 (p=0.001, PEA 81%), respectively, indicating high agreements between the MRI-features versus radiographic features.

Association of MRI-features with pain upon palpation at joint level

Remarkably, a higher grade of synovitis as independent variable was inversely associated with pain upon palpation (as dependent variable, adjusted OR 0.1 (95%CI 0.01-1.0) for grade 1, 0.2 (95%CI 0.03-2.2) for grade 2 and 0.7 (95%CI 0.1-3.2) for grade 3 synovitis). Since only 3 joints were classified as grade 0 synovitis and used for reference category, the same analysis was repeated after dichotomization of synovitis into no/mild (grade 0/1) versus moderate/severe (grade 2/3) synovitis. All other features were dichotomized as presence (grade 1-3) or absence (grade 0).

After dichotomization, the presence of moderate/severe synovitis, BMLs, bone erosions, osteophytes and abnormal collateral ligaments (as independent variables) was significantly associated with more pain upon palpation (as dependent variable) after adjustments for age, sex, BMI and within-patient effect (table 4). A positive trend was seen with BMLs at the insertion sites of collateral ligaments, cysts and JSN. A dose-response relationship is seen with JSN; a higher grade of JSN is more often associated with pain (adjusted OR 2.3 (95%CI 0.3-20.9) for grade 1, 9.9 (95%CI 1.4-67.9) for grade 2 and 13.2 (95%CI 1.8-97.9) for grade 3).

OA processes in joints of different stages of HOA

The MRI findings stratified for the anatomical phases according to Verbruggen-Veys were shown in table 5. Presence of subchondral BML (as independent variable) was significantly associated with J- or E-phase presence (as dependent variables, reference category N-phase/S-phase) with adjusted ORs of 8.5 (95%CI 3.5-20.2) and 60.3 (95% CI 9.0-404.2), respectively (table 6). BMLs at the insertion sites of collateral

Table 4: Association of MRI features and pain upon palpation in 16 patients (total 128 joints) with hand osteoarthritis.

MRI feature score	No. of normal joints		No. of abnormal joints		Adjusted OR* (95%CI)
	DIPs	PIPs	DIPs	PIPs	
Synovitis (grade 2-3)	38	31	22	29	2.4 (1.1-5.5)
Flexor tenosynovitis	45	39	15	21	0.5 (0.2-1.2)
Collateral ligaments	34	50	29	14	4.3 (2.2-8.4)
BML at insertion sites	56	55	8	9	3.3 (0.9-10.3)
Bone erosions	17	32	45	32	4.5 (1.7-11.9)
Bone cysts	55	56	8	8	2.0 (0.5-7.0)
Osteophytes	9	20	54	44	2.4 (1.1-5.3)
Joint space narrowing	1	10	62	54	5.6 (0.8-42.2)
Malalignment	61	64	2	0	2.3 (0.2-32.9)
Bone marrow lesions	42	52	22	12	3.5 (1.6-7.7)

OR, odds ratio; 95%CI, 95% confidence interval; DIPJ, distal interphalangeal joint; PIPJ, proximal interphalangeal joint; *adjustments for age, sex and body mass index.
Normal joints = scored as grade 0, abnormal joints = scored as grade 1-3 (except synovitis, grade 0 and 1 is normal, grade 2 and 3 is abnormal).
Eight joints not available for (teno)synovitis.
One DIPJ not available for collateral ligaments, bone cysts, osteophytes, joint space narrowing, malalignment.
Two DIPJs not available for bone erosions.

Table 5: MRI-findings in 16 patients with hand OA stratified for the anatomical phases of the Verbruggen-Veys scoring method (total 128 joints, 1 missing).

MRI feature, in no. (%)	N phase N=30	S phase N=63	J phase N=11	E phase N=11	R phase N=12
Synovitis (grade 1-3)	27 (90)	59 (94)	11 (100)	9 (82)	10 (83)
Synovitis (grade 2-3)	11 (37)	28 (44)	6 (54)	5 (45)	0 (0)
Flexor tenosynovitis	11 (37)	17 (27)	3 (27)	3 (27)	2 (17)
Abnormal coll. ligaments	3 (10)	12 (19)	7 (64)	10 (91)	11 (92)
BML at insertion sites	2 (7)	6 (9)	6 (55)	2 (18)	1 (8)
Subchondral erosions	12 (40)	33 (52)	9 (82)	11 (100)	11 (92)
Subchondral BML	2 (7)	11 (17)	7 (64)	10 (91)	4 (33)
Cysts	4 (13)	3 (5)	3 (27)	5 (45)	0 (0)
Osteophytes	19 (63)	45 (71)	10 (91)	11 (100)	12 (100)
JSN	23 (77)	58 (92)	11 (100)	11 (100)	12 (100)

Coll., collateral ligaments; BML, bone marrow lesions; JSN, joint space narrowing; N phase, normal phase, no signs of osteoarthritis; S phase, stationary phase, signs of osteoarthritis; J phase, joint space loss; E phase, erosive phases, underbreaking of cortex in subchondral bone (centrally); R phase, remodelled phase, remodelled cortex of subchondral bone.

ligaments as independent variable was also associated with more often J-phase presence (adjusted OR 11.4 (95%CI 2.7-47.5), which was not the case for E- and R-phases. Cysts were more associated with a joint in E-phase (dependent variable, adjusted OR 8.0 (95%CI 2.9-29.5). Presence of abnormal collateral ligaments were associated with all phases (table 6).

Table 6: Association of MRI-findings with presence of pre-erosive (J phase) and erosive phase (E phase) and remodelled phase (R phase) versus normal and non-erosive OA phases (N- and S phase) according to the Verbruggen-Veys scoring method.

MRI feature	J phase, adj. OR* (95% CI)	E phase, adj. OR* (95% CI)	R phase, adj. OR* (95% CI)
Synovitis (gr 0-1/ gr 2-3)	1.7 (0.5-5.6)	1.7 (0.4-7.5)	**
BML (yes/no)	8.5 (3.5-20.2)	60.3 (9.0-404.2)	3.0 (0.8-11.5)
BML at insertion sites (yes/no)	11.4 (2.7-47.5)	1.1 (0.1-19.6)	0.4 (0.02-11.8)
Coll. ligaments (abn./normal)	7.2 (2.5-20.5)	76.3 (25.1-231.4)	61.3 (8.6-434.5)
Cysts (yes/no)	3.8 (0.6-25.0)	8.0 (2.2-29.5)	**

Adj. OR*, adjusted Odds ratio, adjustments for age, sex, body mass index and within-patient effect; **, no good estimation possible, no R-phases with synovitis grade 2-3 or cysts, BML, bone marrow lesions; coll., collateral ligaments; abn., abnormal.

DISCUSSION

The OHOA-MRI scoring method is reproducible method to study OA features on MRI. The validation of MRI features against ultrasound was good. In this severe, predominantly erosive, HOA population many MRI abnormalities were present; synovitis, abnormal collateral ligaments, BMLs, bone erosions and osteophytes were associated with pain upon palpation in individual joints. BMLs at the insertion sites of collateral ligaments were more often present in pre-erosive joints and subchondral BMLs, erosions and cysts more often in active erosive joints.

The reproducibility of the OHOA-MRI score was assessed in a severe HOA population from another hospital, which did not develop the scoring method. Our 3.0T MRI-images (supplementary figure S1A-E) were of good quality and gave the opportunity to assess the images in a clear way, compared to the 1.0T images of the atlas. Also, fat-suppressed T2-images were used to determine BMLs instead of short T1 inversion recovery (STIR) images from the OHOA-MRI atlas[15]. The scoring method is reproducible, as reflected by a good to excellent intra-reader reliability for most features, except for flexor tenosynovitis. Two explanations could be given for this finding. Firstly, it was difficult to distinguish flexor tenosynovitis from synovitis, even on 3.0T images. Secondly, variation in normal subjects is difficult to differentiate from pathology, as confirmed with US where a thin regular hypoechoic rim < 0.1 mm thick can be seen surrounding the flexor tendons in the palm or fingers[19].

The validity of MRI features in the OHOA-MRI scoring method was investigated by comparing the MRI with ultrasound and radiography, which was good for moderate/ severe synovitis, osteophytes, JSN, erosions and cysts, as showed by the high percentages of agreement despite the relatively long interval between US and MRI assessment. Since the different imaging modalities are not measuring the features in the same way (possibly one method more sensitive than another method), it is not likely that the Spearman's ρ would be high. Also the definition of synovitis scored on a 4-point scale (grade 0=normal, grade 1, 2 and 3 are mild, moderate and severe synovitis, respectively) was questioned. In our population nearly no joints were without synovitis. When MRI synovitis was compared with US greyscale synovitis, no correlation

was found. However, normal synovial tissue usually enhances after administration of Gd-DOTA. The question arises whether grade 1 enhancement indicate pathology or enhancement of normal synovium. In that case, synovitis grade 1 is an overestimation leading to false-positive findings and illustrating that the MRI scoring for synovitis is too sensitive. We therefore suggest that both grade 0 and 1 should be regarded as normal and grade 2-3 as abnormal. Another explanation for the discrepancy between the frequency of synovitis detected in US and MRI could be that the US and MRI assessment was not performed at the same day and interfered with the validity.

Furthermore, we would suggest some changes to optimize the OHOA-MRI score. The present scoring method scores collateral ligaments as 'absence' or 'presence', suggesting that the absence of collateral ligaments is a rupture of these ligaments. However, if abnormal collateral ligaments are scored, more signal will be visualized on MRI (e.g. effusion), mimicking the 'absence' of the ligament as illustrated in the MRI-atlas and therefore suggesting to score collateral ligaments as 'normal'/'abnormal'. Since the scoring of MRI-images was time consuming (approximately 75-90 minutes per patient), a simplification or dichotomization for scoring some features would be more convenient, without loss of sensitivity. Finally, it remains unclear how 1st IPJs and/or 1st CMCJs should be scored, since OHOA-MRI score was designed to score DIPJs and PIPJs. However, the current knowledge from the scoring method can be used to develop scoring methods for these joints in the future.

MRI-features of OA were frequently seen in the hand joints of our HOA population. There is a discrepancy in prevalence of MRI-abnormalities between our findings and those of Wittoek *et al.*[13] Both studies used 3.0T MRI and included severely affected patients with HOA with signs of erosive disease. We found 61% erosions, 77% osteophytes and 27% BMLs in our study versus 29% erosions, 34% osteophytes and 39% BMLs in the Belgian study. Explanations for the difference could be the different study populations or that our study used the OHOA-MRI score, especially developed for HOA and possibly too sensitive, whereas the Belgian study used the OMERACT definitions for rheumatoid arthritis[20].

The association between MRI-features with pain was also investigated to increase the understanding of causes of pain in HOA. We showed that presence of moderate/severe synovitis and BMLs were positively associated with pain, suggesting that inflammation is an underlying cause for pain in HOA. No earlier MRI-studies in HOA reported this association, but this finding is in line with an US-study in HOA[8], showing that greyscale synovitis and PDS are associated with more pain per joint, and with MRI-studies in knee OA[21]. Presence of abnormal collateral ligaments was associated with pain. Tan *et al*. showed previously that complete disruptions of collateral ligaments and bone marrow edema on 1.5T MRI are present in HOA, however no data about the association of collateral ligaments and pain was reported[3,22]. The finding that (pre) erosive and remodelled phases of hand OA were associated with the presence of abnormal collateral ligaments, are also in line with the studies of Tan *et al*.[3,23].

Presence of BMLs is associated with a higher chance to be in a radiographic pre-erosive (J-phase) or erosive phase (E-phase), but not in remodelled phases (R-phase) after the erosive process of the joint. Also cysts are more associated with the presence of an

radiographic erosive phase. Since the present study did not included longitudinal data, we cannot suggest that erosive OA is could be a disease starting from the subchondral bone with possible inflammatory signs. However, this finding may give lead to future studies that gives more insight in understanding processes in OA pathogenesis.

Several limitations can be addressed in this study. MRI-images were obtained in a highly selected population with severe complaints. Although the US and MRI were not assessed at the same day, the validity is good as reflected by the PEA. Furthermore, no finger joints of a control group were imaged with MRI. Since MRI in HOA is not often performed, the cross-sectional information derived in this study is still valuable to present as a proof-of-concept. Regarding the scoring, one observer reviewed all MRI-images but this observer was well trained by the developers of the original OHOA-MRI scoring method. In summary, this proof-of-concept study supports that the OHOA-MRI scoring method is useful for research in hand OA. In the future, MRI-studies in less selected HOA population with follow-up data are needed to confirm the findings of the present study and what the clinical value of the MRI hand OA will be.

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Supplementary Figure S1: Examples of 3T images of a 56-year old woman with signs of synovial thickening, erosion and BMLs in PIPJ3 right.

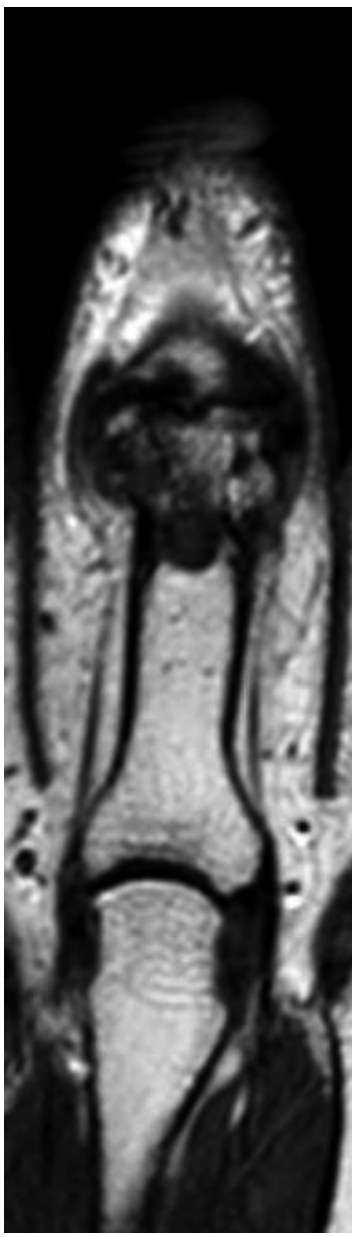

Figure S1A: Coronal, pre-gadolinium.

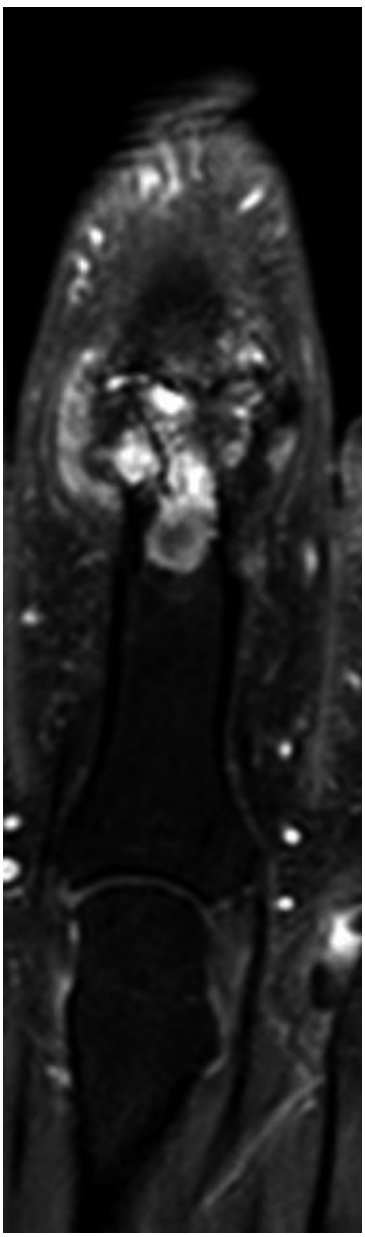

Figure S1B: Coronal, post-T1 image, example of erosion gadolinium T1-image, with fat-suppression, example of erosion and enhancement of gadolinium, indication of synovitis.

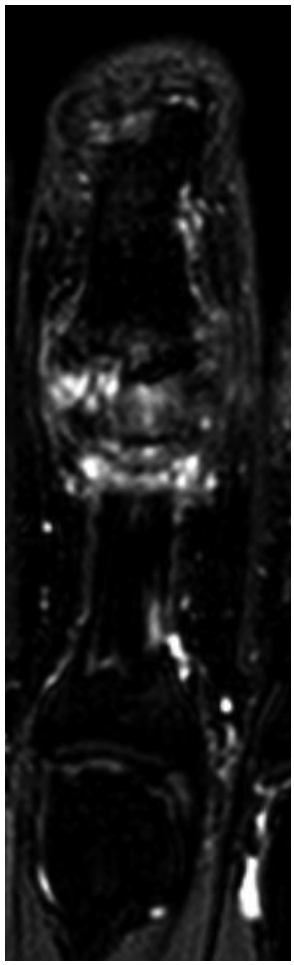

Figure S1C: Coronal T2-image, SPAIR.

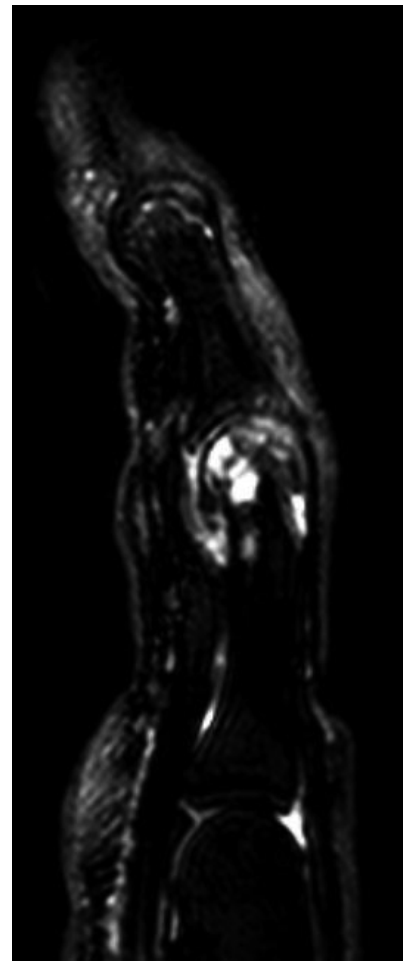

Figure S1D: Sagittal T2-image, SPAIR, example of BML.

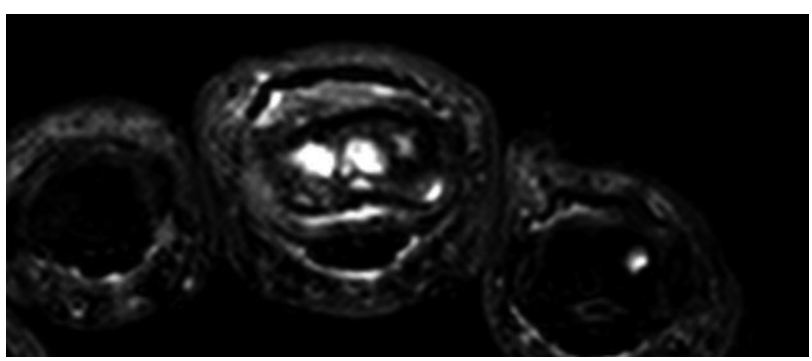

Figure S1E: Axial T2-image, SPAIR, example of BML.

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