

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/31433> holds various files of this Leiden University dissertation.

**Author:** Kortekaas, Marion Catharina

**Title:** Osteoarthritis: the role of synovitis

**Issue Date:** 2015-01-13

# 9

## **MRI in hand osteoarthritis: validity for osteoarthritis clinical and structural characteristics**

Marion C. Kortekaas, MD<sup>1</sup>

Wing-Yee Kwok, MD, PhD<sup>1</sup>

Monique Reijnierse, MD, PhD<sup>2</sup>

Ron Wolterbeek, PhD<sup>3</sup>

Pernille Boyesen, MD, PhD<sup>4</sup>

Desiree van der Heijde, MD, PhD<sup>1,4</sup>

Johannes L Bloem, MD, PhD<sup>2</sup>

Margreet Kloppenburg, MD, PhD<sup>1</sup>

<sup>1</sup> Leiden University Medical Center, Leiden, the Netherlands, Department of Rheumatology

<sup>2</sup> Leiden University Medical Center, Leiden, the Netherlands, Department of Radiology

<sup>3</sup> Leiden University Medical Center, Leiden, the Netherlands, Department of Medical Statistics.

<sup>4</sup> Diakonhjemmet Hospital, Oslo, Norway, Department of Rheumatology



## ABSTRACT

### Objective

To investigate criterion validity and intraobserver reliability of MRI in hand osteoarthritis (HOA).

### Methods

In sixteen HOA patients (median age 57 years, 62% female, 13 with erosive OA) 3 Tesla MR scans with gadolinium-chelate administration of 2<sup>nd</sup>–5<sup>th</sup> DIPJs/PIPJs of the right hand were obtained and scored according to the Oslo HOA scoring method for synovial thickening, bone marrow lesions (BMLs), osteophytes, joint space narrowing (JSN) and erosions (grade 0-3). Ultrasound was scored for synovial thickening and osteophytes, radiographs for osteophytes and JSN (OARSI score) and anatomical phases (Verbruggen-Veys score). Pain was assessed during physical examination. Correlations of MRI with US and radiographic features were assessed with generalizability theory. With Generalized Estimating Equations MRI features were associated with pain, adjusting for within-patient effects, age, sex and BMI.

### Results

Forty-three percent, 27%, 77% and 61% of joints had synovial thickening (moderate/severe), BML, osteophytes and erosions, on MRI respectively. Intra-observer reliability, assessed in 6 patients, was good (ICCs 0.77-1.00). Correlations between osteophytes, JSN and erosions on radiographs and MRI were moderate, substantial and fair (ICC 0.53, 0.68 and 0.32 respectively), with MRI showing more lesions than radiography. Correlation between synovial thickening and osteophytes on MRI and US was moderate (ICC 0.43 and 0.49 respectively). MRI was more sensitive for synovial thickening, US for osteophytes. Pain was associated with the presence of moderate/severe synovial thickening (adjusted OR 2.4 (95%CI 1.06-5.5)), collateral ligaments (4.2 (2.2-8.3)), BMLs (3.5 (1.6-7.7)), erosions (4.5 (1.7-12.2)) and osteophytes (2.4 (1.1-5.2)).

### Conclusions

MRI is a reliable and valid method to assess inflammatory and structural features in HOA. It gives additional information over radiographs and US.

## INTRODUCTION

Hand osteoarthritis (HOA) is a prevalent musculoskeletal disease that can lead to pain or functional limitations.<sup>1,2</sup> The osteoarthritis (OA) process results in structural involvement of all compartments of the joint, including cartilage, subchondral bone, synovium, capsule and ligaments.<sup>3</sup> In HOA of several subsets can be distinguished, of which nodal and erosive OA preferentially involve the interphalangeal joints (IPJs).<sup>1,4</sup>

Patients with nodal OA in the IPJs present with bony enlargements, deformities and loss of range of motion.<sup>4</sup> These classical structural hallmarks of HOA can be visualized on conventional radiographs as osteophytes, malalignment and joint space narrowing (JSN).<sup>5</sup> In addition in erosive OA, subchondral erosions with widening can be seen.<sup>4</sup> However, radiography is an insensitive imaging modality and a more sensitive method visualizing not only structural changes but also soft tissues is needed. More recently, ultrasound (US) has been introduced to visualize osteophytes and soft tissues in HOA. It has been shown that US is more sensitive than radiography to detect osteophytes, and, moreover, that synovitis is frequently seen in HOA.<sup>1,6-8</sup>

In knee OA, magnetic resonance imaging (MRI) seems to be a valid imaging modality which enables visualization of the subchondral bone, including bone marrow lesions (BMLs) and soft tissues.<sup>9,10</sup> For HOA, few studies used MRI to investigate abnormalities in soft tissue and subchondral bone.<sup>4,11,12,13</sup> 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.<sup>14</sup> To be able to use MRI and a scoring system for HOA, it is however necessary to proof validity, reliability and feasibility.

The purpose of the present study is therefore to test the intraobserver reliability and criterion validity of the MRI in a severe HOA population.

## PATIENTS AND METHODS

### Patient population

Sixteen HOA patients, fulfilling American College of Rheumatology criteria,<sup>15</sup> were recruited from the Rheumatology outpatient clinic from July 2008-October 2010. The patients were all participants of an international placebo-controlled medication study (Clinical Trial Governance reference is: EudraCT 2007-003, 994-18). For this study, baseline data of the participants in the Netherlands were used. Participants had at least one (pre)erosive joint (defined below) in the IPJs on conventional radiographs and pain  $\geq$  30 mm on the visual analogue scale (VAS). Patients were excluded if they suffered from chronic inflammatory rheumatic diseases (e.g. rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, haemochromatosis, gout or chondrocalcinosis).

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

### **Clinical assessment**

Demographic characteristics were collected by standardized questionnaires. All patients completed a 100-mm VAS to assess hand pain over the past 48 hours. Usage of analgesics was allowed during the study. Pain upon palpation, bony and/or soft swelling ('absence'/'presence') for each distal and proximal IPJ (DIPJ, PIPJ) was assessed by a single observer (WYK) during physical examination using the Doyle Index, which has been validated for HOA.<sup>16</sup>

### **MRI examinations**

The 2<sup>nd</sup>-5<sup>th</sup> 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 patient positioned supine with the arm in neutral position parallel to the body. 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-weighted images (ST 3 mm, TR/TE 4013/60 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-gadolinium-chelate (Gd)-DOTA 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: axial 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 axial frequency selective fat-suppressed T2-weighted images (ST 3 mm, TR/TE 4490/60 ms). MRI-examinations were obtained on the same day as clinical assessments and radiographs.

MRI features were scored by a single reader (WYK), after a training session of one week with the developers of the OHOA-MRI score. MRI-features were scored using T1-weighted fat suppressed Gd images for synovial thickening (grade 0-3), flexor tenosynovitis (grade 0-3) and bone cysts (grade 0-1, proximal and distal), using T1 weighted images for collateral ligaments (present or absence: the absence of the collateral ligament was defined as a non-visible or non-continuous collateral ligament) (grade 0-1, radial and ulnar), bone erosions (grade 0-3, proximal and distal), osteophytes (grade 0-3, proximal and distal), JSN (grade 0-3) and malalignment (grade 0-1, sagittal and frontal plane) and using T2 weighted fat suppressed images to detect BMLs at insertion sites of collateral ligaments (grade 0-1, radial, ulnar, proximal and distal), and BMLs (grade 0-3, proximal and distal). For the analyses, collateral ligaments, cysts and erosions were dichotomized as present/ absent. To be able to compare osteophytes on MRI with osteophytes on radiographs and US, the highest score given to either the

distal or proximal part of the joint on MRI images was used. So for instance when a joint had a score 1 at the distal part and score 3 at the proximal part of the joint, score 3 was assigned to that joint.

MRI sequences were adopted according to the original article of the OHOA-MRI score, with the exception of the T1 weighted fat suppressed images, which are normally not used in MR imaging. Instead T1 weighted images without fat suppression were acquired.

Since the study was designed before the OHOA-MRI was published, and the axial planes were not included in the original protocol but sagittal planes were, only the last 4 patients had additional axial planes.

MR images of six patients (three with coronal and sagittal planes only, three with coronal, sagittal and axial planes) were scored twice with an interval of 5 weeks to determine intraobserver reliability.

### **US assessment**

US was performed by one experienced ultrasonographer (WYK) always in the presence of a second ultrasonographer (MCK) scoring together in consensus, using a Toshiba Applio scanner (Toshiba Medical systems, Tustin, California) with a 10-14 MHz linear array transducer. Settings were optimized by the application specialist of the manufacturer of the machine.

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, power Doppler signal (PDS) and synovial thickening.<sup>7,17</sup> All US-features were scored on a four-point scale (0=none, 1=mild, 2=moderate, 3=severe). The intra-observer reliability was good to excellent (ICC= 0.62-0.91).<sup>7</sup>

### **Conventional radiographs**

Radiographs (dorso-volar) of the right hand, using a standardized protocol, were read by WYK, and scored for osteophytes (grade 0-3), JSN (grade 0-3) and cysts (grade 0-1) using the OARSI-atlas.<sup>18</sup> Erosions were scored according to the Verbruggen-Veys scoring method, defined as an erosive (E-phase) or remodelled phase (R-phase).<sup>19</sup> A pre-erosive joint was defined as a joint with complete joint space loss in part or the whole joint (J-phase). The intraobserver reliability was good to excellent (ICC 0.62-0.94) for all radiographic features.

### Statistical analysis

Data were analyzed using SPSS, version 20.0 (IBM SPSS statistics, New York, USA).

Reliability was determined by estimating intra-class correlation coefficients (ICC) using generalizability theory, a random factor model ANOVA approach that estimates the components of variance within each model. Using this method was more suitable compared to the traditional ICC analyses due to the separate outcomes on joint level, with unique joints clustered within a patient. The ICC calculated in this study is not similar to the classical definition of ICC, and are called G-coefficients as defined by Streiner and Norman.<sup>20</sup> We retained the term ICC to indicate that the results are comparable to the classical ICC. Interpretation of the correlations are: 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial and 0.81-1.00 almost perfect.

Elementary sources of variance in data are called facets in generalizability theory. For intra-observer reliability relevant facets in this study are: patients (0-16) and hand joints (0-8). Dependent variables were the separate features of each imaging modality.

In generalizability theory, a distinction is made between fixed and random facets. The facets 'patient' and 'hand joints' were defined as random facets. The facet 'hand joints' was nested within the facet 'patient' since each patient has a unique set of hand joints.

In order to study criterion validity of MRI features, concurrent validity was evaluated by comparing MRI with radiograph and US features in the 2<sup>nd</sup>-5<sup>th</sup> DIPJs/PIPJs of the right hand only (128 joints). Subsequently, generalizability theory was used to determine correlations between MRI and US or radiographic features, since for these analyses separate outcome per joint are of relevance, in a situation where in a patient 8 unique joints are clustered. Generalizability theory is a statistical method that is capable of analyzing this nested model.

For the different imaging modalities the facets were defined as 'patient' (0-16), 'hand joints' (0-8) and 'method' (MRI, US, CR). The dependent variables being imaging features. The facets 'patient' and 'hand joints' were defined as random facets, the imaging modality as fixed facet. The facet 'hand joints' was again nested within the facet 'patient'.

Since we expected, based on results from earlier studies,<sup>21-23</sup> that radiographs are less sensitive in detecting features compared to MRI, we expected to find correlations between the imaging modalities, but these correlations were expected not to be 1, but ranging between about 0.4 and 0.8.

We expected to find higher correlations between MRI and US since they are both considered to be more sensitive imaging modalities when compared to radiographs.

Mann-Whitney U test was used to compare affected joints between the different imaging modalities.  $P < 0.05$  was considered significant.

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 using Generalized Estimating Equations (GEE) with robust variance estimators to account for the correlation of observations within the same person. Adjustments were made for age, sex and BMI. Results were presented as odds ratios (OR) with 95% confidence intervals (CI).

## RESULTS

### Study population

Sixteen patients (median (range) age 56.7 (42.0-70.7) years, 62% female, median (range) BMI 25.7 (20.2-32.4)  $\text{kg}/\text{m}^2$ ) were included. The median symptom duration was 6.5 years. Erosive OA was found in 13 patients and median (range) VAS pain was 70 (35-93) mm. The median (range) number of swollen and tender joints was 2.5 (1-6) and 5 (1-12), respectively. Bony swelling was present in 61% and soft swelling in 18% of the joints palpable during clinical assessment.

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 synovial thickening 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.

MRI detected synovial thickening was present in 117 joints (98%). If the cut-off for MRI synovitis is set on grade  $\geq 2$  (moderate to severe), 51 joints (43%) had synovial thickening. 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 present 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 the 2 DIPJs on MRI. Table 9.1 shows the distribution of these features stratified for DIPJs/PIPJs.



**Table 9.1** Findings on MRI in the examined right hand in 16 patients with hand osteoarthritis (total 128 joints), stratified for DIPJs and PIPJs

Feature (range of scores)	DIPJs, affected/total no. joints (%)	PIPJs, affected/total no. joints (%)
Synovial thickening (grade $\geq 1$ )	58/60 (97)	59/60 (98)
Synovial thickening (grade $\geq 2$ )	22/60 (37)	29/60 (48)
Flexor tenosynovitis (grade $\geq 1$ )	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 $\geq 1$ )	45/62 (73)	32/64 (50)
Bone cysts (present)	8/63 (13)	8/64 (13)
Osteophytes (grade $\geq 1$ )	54/63 (86)	44/64 (69)
JSN (grade $\geq 1$ )	62/63 (98)	54/64 (84)
Malalignment (present)	2/63 (3)	0/64 (0)
BML (grade $\geq 1$ )	22/64 (34)	12/64 (19)

DIPJs = Distal interphalangeal joints

PIPJs = Proximal interphalangeal joints

BML = Bone marrow lesions

JSN = Joint space narrowing

**Table 9.2** Intra-observer reliability depicted by intraclass correlation coefficient for MRI features of 48 joints of erosive hand osteoarthritis patients.

MRI feature	ICC
<b>Synovial thickening</b>	0.94
<b>Flexor tenosynovitis</b>	0.77
<b>Collateral ligaments</b>	0.79
<b>Bone marrow lesions at insertion site</b>	0.72
<b>Bone erosions</b>	
Distal	0.91
Proximal	0.87
<b>Bone cysts</b>	0.93
<b>Osteophytes</b>	
Distal	0.92
Proximal	0.86
<b>Joint space narrowing</b>	0.88
<b>Malalignment</b>	1
<b>Bone marrow lesions</b>	
Distal	0.89
Proximal	0.87

MRI=magnetic resonance imaging, ICC= intraclass correlation coefficient, estimated using generalizability theory.

### Reliability

The intra-observer reliability of MRI features as determined in 6 patients with 48 hand joints was substantial to almost perfect, as depicted in table 9.2.

### Validity of MRI versus ultrasound

US detected synovial thickenings (grade  $\geq 1$ ) in 54 (42%) of 128 joints (20 DIPJs, 34 PIPJs), PDS in 29 joints (23%) (13 DIPJs, 16 in PIPJs), and osteophytes in 127 joints (64 in DIPJs, 63 in PIPJs). MRI was significantly more sensitive for the detection of synovial thickening compared to US ( $p < 0.0001$ ), while MRI was less sensitive for osteophytes ( $p < 0.0001$ ).

A moderate correlation coefficient of 0.43 was found between synovial thickening on MRI (graded 0-3) and on US (graded 0-3). When presence of MRI synovial thickening was defined as grade  $> 1$ , an ICC of 0.54 was found.

Correlation coefficient between osteophytes on US (grade 0-3) and MRI (grade 0-3) was 0.49.

### Validity of MRI versus radiography

Radiographic osteophytes (grade  $\geq 1$ ) were present in 53 (41%) and JSN (grade  $\geq 1$ ) 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%),  $p < 0.001$ . Twenty-two joints with radiographic erosions were erosive on MRI as well. Radiographic bone cysts were seen in 25 (20%) joints, significantly more than on MRI (12%,  $p < 0.001$ ) (table 9.3).

**Table 9.3** Overview of MRI, ultrasonographic and radiographic features in distal and proximal interphalangeal joints (total 128 joints, but 1 missing) of the right hand of 16 patients with hand osteoarthritis.

Feature	MRI	Ultrasound	Radiographs
Synovial thickening	117 (98)*	49 (38)	NA
Synovial thickening**	51 (43)	48 (38)	NA
Osteophytes	98 (77)	127 (99)	52 (41)
Joint space narrowing	116 (91)	NA	97 (76)
Erosions	76 (60)	NA	23 (18)
Cysts	16 (12)	NA	25 (20)

\* Depicted are numbers (%) \*\*Synovial thickening in MRI defined as  $\geq$  grade 2.

NA= not applicable

The correlation coefficient for osteophytes (0-3), JSN (0-3) erosions (0-1), and cysts (0-1) were 0.53, 0.68, 0.32 and 0.43, respectively, indicating fair to substantial correlations between the MRI versus radiographic features.

### Validity of MRI features with pain upon palpation at joint level

We hypothesized that joints with osteoarthritic MRI features would be painful more often. Therefore, associations between pain upon palpation and synovial thickening were calculated.

Only 3 joints were classified as grade 0 for synovial thickening and could not be used as reference category. Therefore synovial thickening was dichotomized into no/mild (grade 0/1) versus moderate/severe (grade 2/3) for the analyses. All other features were dichotomized as presence (grade 1-3) or absence (grade 0).

Pain upon palpation was significantly associated with the presence of moderate/severe synovial thickening, BMLs, erosions, and abnormal collateral ligaments after adjustments for age, sex, and BMI (table 9.4). A positive trend was seen with BMLs at the insertion sites of collateral ligaments and JSN.

**Table 9.4** Association of MRI features and pain upon palpation in distal and proximal interphalangeal joints of the right hand in 16 patients (total 128 joints) with hand osteoarthritis

MRI feature score	No. of normal joints without feature		No. of abnormal joints with feature		Adjusted OR* (95%CI)
	DIPJs	PIPJs	DIPJs	PIPJs	
Syn. thick (grade 2-3)	38	31	22	29	2.4 (1.06-5.5)
Collateral ligaments	34	50	29	14	4.2 (2.2-8.3)
BML at insertion sites	56	55	8	9	3.1 (0.95-10.1)
Bone erosions	17	32	45	32	4.5 (1.7-12.2)
Bone cysts	55	56	8	8	2.0 (0.6-7.1)
Osteophytes	9	20	54	44	2.4 (1.1-5.2)
Joint space narrowing	1	10	62	54	5.6 (0.8-41.4)
Malalignment	61	64	2	0	2.2 (0.2-26.2)
Bone marrow lesions	42	52	22	12	3.5 (1.6-7.7)

No.=number, DIPJs= distal interphalangeal joints, PIPJs=proximal interphalangeal joints, OR=odds ratio, 95%CI = 95% confidence interval, syn. thick= synovial thickening, BML=bone marrow lesion

\*= Adjustments for age, sex, body mass index and within patient effects.

8 joints not available for (teno)synovitis

1 DIPJ not available for collateral ligaments, bone cysts, osteophytes, JSN, malalignment

2 DIPJs not available for bone erosions

## DISCUSSION

In this severe, (pre)erosive, HOA population MRI was found to be a reliable method to investigate OA characteristics in HOA, as shown by substantial to almost perfect intraobserver reliability of all MRI features.

MRI criterion validity was confirmed by comparing MRI with ultrasonography, radiography and clinical features showing substantial correlations.

Comparison with physical examination showed that MRI abnormalities such as synovial thickening, osteophytes, but also abnormal collateral ligaments, BMLs, and bone erosions, were associated with pain upon palpation in individual joints.

Up till now, radiographs are used as golden standard for detection of HOA features for diagnosis and research purposes. Unfortunately, this imaging modality has limitations since it is unable to show soft tissue. Recently, US has been used not only for visualization of structural, but also inflammatory features. A drawback of this imaging modality is however the inability of the US beam to penetrate through bone, making it more difficult to visualize subchondral abnormalities, such as BMLs. MRI has the possibility to identify both soft tissue, structural abnormalities and abnormalities in subchondral bone, and is therefore potentially a better alternative to radiographs as golden standard.

In order to test this hypothesis, concurrent validity was assessed by comparing features detected on radiographs and US with those found on MRI. As expected correlations found were between 0.40 and 0.80 for all features, except for erosions. MRI is therefore a valid method.

Erosions detected on MRI versus radiographs showed a lower correlation than expected (0.32). This might be explained by the fact that erosions on MRI were not always identified as erosions on radiographs, but were classified as cysts. The latter became obvious when comparing the presence of cysts and/or erosions on MRI and radiographs on joint level. The observation that cysts found on radiographs appear to be erosions on MRI was also made by Haugen et al.<sup>21</sup>

In the present study, MRI showed far more joints with synovial thickening compared to US. Only few studies compared synovial thickening on MRI and US earlier.

Vlychou et al studied MCP, PIP and DIP joints of one hand of erosive HOA (N=13) and non-erosive HOA (N=7) patients. In this study population, means of affected joints appeared higher in US compared to MRI, but results have to be interpreted with caution due to the small sample sizes since analyses were done on patient level.<sup>22</sup>

Wittoek et al<sup>8</sup> studied 8 interphalangeal joints of 14 patients (9 erosive HOA, 5 non-erosive HOA) and found more synovitis using 3 Tesla MRI (20% of all joints) compared to US (15% of joints) with a percentage exact agreement of 87%. The authors used recommendations for hand joint pathology in RA. In these recommendations synovitis on contrast enhanced MRI is defined as an area in the synovial compartment that shows above normal post-gadolinium enhancement of a thickness greater than the width of the normal synovium.

After contrast administration, normal synovial tissue enhances as well as abnormal and thickened synovial tissue. The threshold for abnormal synovial thickening is most likely set too low in the present study. A reason for this might be that more detail could be visualized on the high resolution images of the 3 Tesla MRI machine. Thin synovial tissue is seen in these images while this is less visible on the atlas used as a reference, which is based on images derived from a 1 Tesla MRI machine. Moreover, sequences used were not obtained directly but were constructed afterwards, which results in a lower resolution of images.

When in the present study MRI synovial thickening score 0 and 1 were considered both within the normal limits, MRI and US demonstrated synovial thickening in 43 and 42% of hand joints respectively, and correlation between the two modalities increased.

It was expected that US and MRI showed more osteophytes compared to radiographs, since these two imaging modalities are capable of scanning in different planes enabling osteophytes on locations other than on the sides to be detected. US however detected more osteophytes compared to MRI. This is in concordance with earlier studies.<sup>8, 21</sup> The reason for this higher sensitivity might be the ability to scan around the joint in a continuum using ultrasound, while MRI is performed in coronal and sagittal slices. Maybe this is making it more difficult to discern osteophytes that are for instance in between two images.

MRI features of OA were frequently seen in the hand joints of our HOA population. The prevalence of MRI-abnormalities are comparable with those described earlier. In the present study 61% erosions, 77% osteophytes and 27% BMLs were found. Wittoek et al.<sup>8</sup> studied 9 erosive HOA patients using 3.0T MRI and found 63% erosions, 57% osteophytes and 52% BMLs. In another study in HOA patients, done by the developers of the OHOA-MRI score,<sup>11</sup> osteophytes were found in 89%, erosions in 51% and BML in 13% of joints.

The association between MRI features with pain was also investigated to increase the understanding of causes of pain in HOA and validate MRI with clinical features. We showed that presence of moderate/severe synovitis and BMLs were positively associated with pain, suggesting that inflammation is an underlying cause of pain in

HOA. This is in line with an earlier study in HOA,<sup>11</sup> and an US study in HOA showing that synovial thickening and PDS are associated with more pain per joint.<sup>7</sup>

The MRI images were scored by the recently developed OHOA-MRI score.<sup>14</sup> Our 3.0T MRI-images (supplementary figure S9.1-9.4) were of good quality with higher spatial resolution compared to the 1.0T images of the atlas that was made by the developers of the OHOA-MRI score.

After implementing and using the scoring method, we experienced some items that need consideration.

First of all, it is not common practice to use T1 weighted fat suppressed images as the OHOA-MRI developers recommend. In T1 sequences all water containing structures appear black in the image, leaving good visualisation of fat containing structures. After suppression of the latter, it is difficult to discern any structure. Therefore, T1 weighted images were used instead.

Also, 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 abnormalities around collateral ligaments are present, more signal will be visualized on MRI, mimicking the 'absence' of the ligament as illustrated in the MRI-atlas and therefore we suggest scoring collateral ligaments as 'normal'/'abnormal'.

Although the objective of this study didn't allow investigation of feasibility, it was noticed during scoring of MRI-images that a considerable amount of time was needed for the assessment of one patient (approximately 75-90 minutes). This should be an objective for further studies.

Several limitations can be addressed in this study. MR-images were obtained in a highly selected population with severe complaints. The sample size was small. This could influence the results especially on patient level. All analyses were however performed on joint level, taking into account patient effect. Therefore, we believe that results are of importance.

No finger joints of a control group were imaged with MRI, since this study focusses on the validity of MRI in patients with HOA.

Due to logistical reasons, US was performed some weeks before the MRI. This might have influenced the results on the correlation between MR and US detected synovial thickening, since synovial thickening can fluctuate over time.<sup>24</sup> Therefore, it is possible that the correlation is underestimated.

Since the OHOA-MRI scoring method was published during the course of the present study, axial sequences were not performed by all patients. Therefore, features

such as synovitis could not be scored optimally in the patients where these sequences were lacking. This might have underestimated correlations.

Regarding the scoring of MRI, only one observer reviewed all MRI-images since the scoring was time consuming. However, the intraobserver reliability is substantial to almost perfect and the reader was trained by the developers of the OHOA-MRI scoring method. In the future, MRI-studies in less selected HOA population with follow-up data are needed to confirm these findings. In addition, further investigation in a longitudinal study is recommended to study other metric properties of the scoring method, being longitudinal inter and intraobserver reliability and sensitivity to change. In addition, also the influence of variation in the acquisition of the MR images should be studied.

### **Acknowledgements**

The authors would like to acknowledge Ida Haugen for her effort in teaching the OHOA-MRI scoring method.

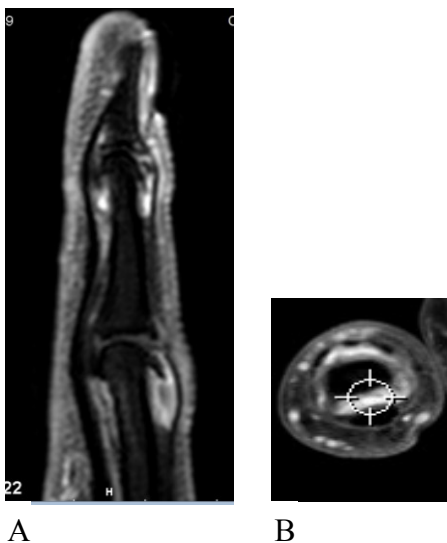
**REFERENCE LIST**

- 1 Kloppenburg M, Kwok WY. Hand osteoarthritis - a heterogeneous disorder. *Nat Rev Rheumatol* 2011;8:22-31.
- 2 Zhang Y, Jordan JM. Epidemiology of osteoarthritis. *Rheum Dis Clin North Am* 2008;34:515-29.
- 3 Tan AL, Grainger AJ, Tanner SF, Shelley DM, Pease C, Emery P, et al. High-resolution magnetic resonance imaging for the assessment of hand osteoarthritis. *Arthritis Rheum* 2005;52:2355-65.
- 4 Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. *Ann Rheum Dis* 2009;68:8-17.
- 5 Visser AW, Bøyesen P, Haugen IK, Schoones JW, van der Heijde DM, Rosendaal FR, Kloppenburg M. Radiographic scoring methods in hand osteoarthritis--a systematic literature search and descriptive review. *Osteoarthritis Cartilage* 2014;22:1710-23.
- 6 Keen HI, Wakefield RJ, Grainger AJ, Hensor EM, Emery P, Conaghan PG. An ultrasonographic study of osteoarthritis of the hand: synovitis and its relationship to structural pathology and symptoms. *Arthritis Rheum* 2008;59:1756-63.
- 7 Kortekaas MC, Kwok WY, Reijnen M, Watt I, Huizinga TW, Kloppenburg M. Pain in hand osteoarthritis is associated with inflammation: the value of ultrasound. *Ann Rheum Dis* 2010;69:1367-9.
- 8 Wittoek R, Carron P, Verbruggen G. Structural and inflammatory sonographic findings in erosive and non-erosive osteoarthritis of the interphalangeal finger joints. *Ann Rheum Dis* 2010;69:2173-6.
- 9 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.
- 10 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.
- 11 Haugen IK, Boyesen P, Slatkowsky-Christensen B, Sesseng S, van der Heijde D, Kvien TK. Associations between MRI-defined synovitis, bone marrow lesions and structural features and measures of pain and physical function in hand osteoarthritis. *Ann Rheum Dis* 2012;71:899-904.
- 12 Jans L, De CT, Wittoek R, Lambrecht V, Huisse W, Verbruggen G, et al. 3 T DCE-MRI assessment of synovitis of the interphalangeal joints in patients with erosive osteoarthritis for treatment response monitoring. *Skeletal Radiol* 2013;42:255-60.
- 13 Tan AL, Toumi H, Benjamin M, Grainger AJ, Tanner SF, Emery P, et al. Combined high-resolution magnetic resonance imaging and histologic examination to explore the role of ligaments and tendons in the phenotypic expression of early hand osteoarthritis. *Ann Rheum Dis* 2006;65:1267-72.
- 14 Haugen IK, Lillegraven S, Slatkowsky-Christensen B, Haavardsholm EA, Sesseng S, Kvien TK, et al. Hand osteoarthritis and MRI: development and first validation step of the proposed Oslo Hand Osteoarthritis MRI score. *Ann Rheum Dis* 2011;70:1033-8.
- 15 Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum* 1990;33:1601-10.
- 16 Bijsterbosch J, Wassenaar MJ, le CS, Slagboom PE, Rosendaal FR, Huizinga TW, et al. Doyle Index is a valuable additional pain measure in osteoarthritis. *Osteoarthritis Cartilage* 2010;18:1046-50.

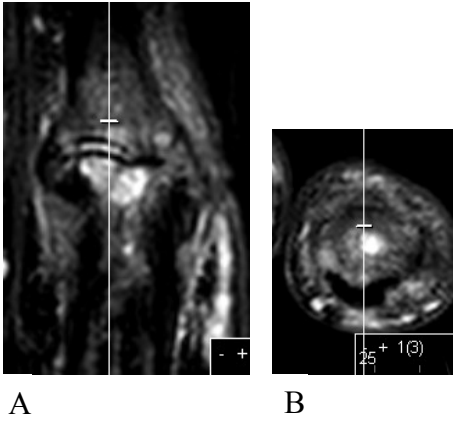


- 17 Keen HI, Lavie F, Wakefield RJ, D'Agostino MA, Hammer HB, Hensor E, et al. The development of a preliminary ultrasonographic scoring system for features of hand osteoarthritis. *Ann Rheum Dis* 2008;67:651-5.
- 18 Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthritis Cartilage* 2007;15 Suppl A:A1-56.
- 19 Verbruggen G, Veys EM. Numerical scoring systems for the anatomic evolution of osteoarthritis of the finger joints. *Arthritis Rheum* 1996;39:308-20.
- 20 Streiner DL, Norman GR. Health measurement scales. A practical guide to their development and use. Fourth ed. Oxford University Press; 2008.
- 21 Haugen IK, Boyesen P, Slatkowsky-Christensen B, Sesseng S, Bijsterbosch J, van der Heijde D, et al. Comparison of features by MRI and radiographs of the interphalangeal finger joints in patients with hand osteoarthritis. *Ann Rheum Dis* 2012;71:345-50.
- 22 Vlychou M, Koutroumpas A, Alexiou I, Fezoulidis I, Sakkas LI. High-resolution ultrasonography and 3.0 T magnetic resonance imaging in erosive and nodal hand osteoarthritis: high frequency of erosions in nodal osteoarthritis. *Clin Rheumatol* 2013;32:755-62.
- 23 Mathiessen A, Haugen IK, Slatkowsky-Christensen B, Bøyesen P, Kvien TK, Hammer HB. Ultrasonographic assessment of osteophytes in 127 patients with hand osteoarthritis: exploring reliability and associations with MRI, radiographs and clinical joint findings. *Ann Rheum Dis* 2013;72:51-6.
- 24 Kortekaas MC, Kwok WY, Reijnierse M, Huizinga TW, Kloppenburg M. Follow-up study of inflammatory ultrasound features in hand osteoarthritis over a period of 3 months: variable as well as constant. *Osteoarthritis Cartilage* 2014;22:40-3.

Supplement: Images of 3T MRI of osteoarthritis features in interphalangeal joints.



**Figure S9.1** A: Sagittal and B: post-gd-DOTA fat suppressed image. 2<sup>th</sup> DIP and PIP joint of the right hand showing synovial thickening. B: Axial post-gd-DOTA fat suppressed image. 5<sup>th</sup> PIP joint of the right hand showing synovial thickening.



**Figure S9.2** A: Coronal and B: axial frequency selective fat suppressed T2 weighted image. Second PIP joint of the right hand with bone marrow lesions.



**Figure S9.3** Coronal T1 weighted image. 4<sup>th</sup> DIP joint with erosion (arrow).



**Figure S9.4** Coronal T1 weighted image. Second DIP and PIP joint with osteophyte (arrow)

