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Brief Report

Cartilage evaluation in finger joints in healthy controls and early hand osteoarthritis patients using high-resolution MRI

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SUMMARY

Objective: To compare direct evaluation of cartilage with high resolution MRI (hrMRI) to indirect cartilage evaluation using MRI inter-bone distance in hand OA patients and healthy controls.
Design: 41 hand OA patients and 18 healthy controls underwent hrMRI of the 2nd and 3rd metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. The images were read by two independent readers using OMERACT hand OA MRI inter-bone distance score (0–3 scale) and a new hrMRI cartilage score with direct evaluation of the cartilage (0–3 scale). Inter-reader and intra-reader reliability was calculated using exact and close agreement and kappa values. The prevalence of abnormal scores and agreement between methods was assessed in both hand OA patients and healthy controls.
Results: The intra- and inter-reader reliability of both scores was comparable, with exact agreement in 73–83% and close agreement in 95–100%. In hand OA patients 27% of 161 joints had both cartilage damage and loss of inter-bone distance, cartilage damage by hrMRI only was present in 20% of joints and reduced inter-bone distance only in 4% of joints. In the healthy controls, 1 of 71 joints were scored as abnormal by both hrMRI and inter bone distance scoring, 1 joint was scored as abnormal using the hrMRI cartilage score only, whereas 15% of joints had only reduced inter bone distance.
Conclusions: Direct cartilage evaluation of MCP and PIP joints using hrMRI has a good reliability, and the higher prevalence of hrMRI cartilage damage in hand OA patients and the lower prevalence in healthy controls in comparison to evaluation of inter-bone distance suggests a better validity.
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Introduction

Traditionally conventional radiography has been used for the assessment of hand osteoarthritis (HOA) structural features, and is currently the only imaging method approved by the regulatory agencies for detecting disease modifying effects despite not being able to visualize cartilage directly[1]. Magnetic resonance imaging (MRI) has the advantage that it can depict cartilage directly and is increasingly being used as a structural outcome measure in clinical trials in knee OA[2]. While MRI has contributed to increasing knowledge about the underlying mechanisms in HOA[3], it is difficult to assess the thin cartilage layer in small hand joints using standard clinical MRI coils.

Recently, a HOA MRI scoring system (HOAMRIS) was developed by the OMERACT MRI task force group, for which good reliability was demonstrated in both cross-sectional and longitudinal settings[4]. The system is used to rate bone damage, synovial inflammation, and loss of joint space, but does not include a direct cartilage damage score, as the thin cartilage layer in small hand joints could not be accurately assessed on the MRI images used for the creation and evaluation of the OMERACT HOAMRIS[5]. However, it has been shown that with higher resolution images using dedicated MRI coils the cartilage of MCP joints can be measured

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reliably[6], and it is to be expected that direct evaluation of cartilage is more accurate than indirect measurement of inter-bone distance.

Hence, the aim of this study was to compare direct cartilage evaluation using high resolution MRI (hrMRI) with indirect cartilage evaluation of MRI inter-bone distance, by evaluating their reliability, and prevalence and agreement of cartilage damage in HOA patients and healthy controls.

Method

Participants

We included 50 patients diagnosed with HOA, of whom 19 had previously participated in the Rotterdam Early Arthritis Cohort (REACH)[7], and 31 additional patients from our rheumatology outpatient clinic. A flowchart is provided in Supplemental Fig. 1. To establish the HOA diagnosis, all patients underwent at least a clinical examination by a rheumatologist and multidirectional radiographs of both hands. Patients with OA only in the thumb base or patients with a suspicion or diagnosis of any other rheumatic disease, were excluded. Additionally, 20 healthy female controls between the age of 18 and 35 were invited. Healthy controls were excluded if they had pain, swelling or stiffness in any hand joints or if they had a previous history of joint disease, hand surgery or hand trauma. They did not undergo clinical examination or radiography.

Participants were excluded if they had any contraindication for MRI or gadolinium contrast. Recruitment started in January 2011 and lasted until December 2012. All participants provided written informed consent prior to the investigation. The study was approved by the local ethics committee.

MRI acquisition

Prior to this study, a custom-built multichannel receive coil for high-resolution finger joint imaging was created in collaboration with Machnet BV (Roden, The Netherlands). This coil allowed us to scan the second and third metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints in one session with high resolution on a clinical 3T MRI scanner (Discovery MR750, GE Healthcare, Milwaukee, WI). Participants were scanned using this coil in a prone superman position and positioned comfortably using torso, head and arm supports to minimize motion artefacts. The scanning protocol consisted of one coronal driven equilibrium fast spin echo proton density (PD) sequence and sagittal fat-suppressed spoiled gradient echo (SPGR) images of each joint separately. For details see Supplemental Table 1.

MRI scoring systems

A face-to-face meeting was organized to demonstrate HOAMRIS[4] to the MRI readers, create the hrMRI cartilage score, and increase reader reliability. Prior to the meeting, JL identified five patients and one healthy control with different amounts of MRI pathology. MSS (radiology resident with 3 years of training in reading musculoskeletal MRI), GSRM (musculoskeletal radiologist for 10 years with previous RAMRIS experience) and IKH (co-developer of HOAMRIS) independently read all images, and the results were discussed to improve reliability.

Inter-bone distance was scored according to the HOAMRIS using the coronal PD images[4]. The hrMRI cartilage score was assessed on the high-resolution SPGR images and is scaled as: 0 = no cartilage damage, 0.5 = single focal cartilage defect <10% of surface area with abrupt edges, 1 = thinning of the cartilage layer >10% of the surface area, without complete thickness loss, 2 = global thinning of the cartilage layers with areas with (near) complete thickness loss, without direct bone–bone contact, 3 = severe cartilage thickness loss with areas of direct bone–bone contact. Example figures of the score are available in the supplemental files. The 0.5 grade has been removed from the tables in the results, as it was never scored. The MRI examinations for final analysis were independently read by both MSS and GSRM. Readings were performed using ClearCanvas Workstation software (Clearcanvas Inc, Toronto, Canada). To determine intra-reader reliability, MSS re-evaluated 10 randomly selected MRI examinations (3 healthy controls and 7 patients) 4 months after the initial reading. A separate reader also measured the cartilage thickness and inter-bone distance of all joints using a ruler tool. These measures were performed in the middle of the joint using the SPGR images.

Statistics

We present the mean values of both readers. Inter-reader and intra-reader reliability were calculated using percentage exact agreement (PEA, the percentage of joints with the exact same value), percentage close agreement (PCA, the percentage of joints with a difference of $\leq$1 between readers), and linear weighted kappa (κ_w). κ_w and confidence intervals were calculated using the irr package in R and a bootstrapping method, and interpreted as proposed by Landis and Koch[8].

Results

Out of the 70 participants, five images sets were excluded and six were used for training and calibration (see Supplemental Fig. 1 for details). The remaining image sets of 18 healthy controls and 41 patients were used for final analysis. Because of artefacts, three joints could not be rated on the PD images and 1 joint not on the SPGR images. Patient characteristics are detailed in Supplemental Table 2.

The inter-reader and intra-reader PEA and PCA values of both scores were comparable (Supplemental Table 3). The inter-reader κ_w of the hrMRI cartilage score was significantly higher than the inter-bone distance κ_w. Readers agreed in 170/233 joints on the inter-bone distance scale. 50 out of the 63 discrepancies in the inter-bone distance score were between grade 0 and grade 1. Reader two scored higher in 38/50 discrepant joints. Readers agreed in 176/234 joints on the hrMRI cartilage score. 23 discrepancies were between grade 0 and grade 1, and 22 between grade 1 and grade 2. Reader one scored higher in 42/45 discrepancies.

With the hrMRI cartilage score 64/81 PIP and 21/81MCP joints had cartilage damage, including 27 PIP and five MCP joints with areas of full-thickness loss (Table I). Normal inter-bone distance was found in 41 PIP and 69 MCP joints in HOA patients. Of these, 24 PIP and 9 MCP showed cartilage thinning with hrMRI, of which 12 PIP and two MCP showed areas with full thickness cartilage loss (Supplemental Table 4 and Fig. 1). three PIP and 4 MCP joints in HOA patients showed no cartilage damage with hrMRI, but were scored as abnormal using the inter-bone distance. In healthy controls, reduced inter-bone distance was found in 10 PIP and one MCP joints, of which 9 did not show cartilage loss with hrMRI.

Normal cartilage thickness showed a large variation in healthy controls (Supplemental Fig. 2). In MCP joints thickness varied between 0.3 and 0.9 mm (mean 0.6 mm (sd 0.1)), and in PIP joints thickness varied between 0.2 and 0.7 mm (mean 0.4 mm (sd 0.1)). These values showed a large overlap with HOA patients, as cartilage thickness for MCP joints in HOA patients varied between 0.0 and 1.0 mm (mean 0.5 mm (sd 0.2)) and thickness in PIP joints varied between 0.0 and 0.9 mm mean (0.4 mm (sd 0.1)).

Table I
Reclassification table of inter bone distance to the high-resolution cartilage score

	No cartilage damage	Thinning of cartilage layer >10% of surface area, without complete loss	Thinning of cartilage with areas with complete cartilage loss Without bone–bone contact	Severe cartilage loss including areas with direct bone–bone contact
Joints of hand OA patients (n=161)				
Normal inter-bone distance	77	19	14	0
Loss of cartilage space without bone–bone contact	7	19	15	2
Focal complete loss with bone–bone contact	0	1	4	2
Bone–bone contact >50%	0	0	0	0
Joints of healthy controls (n=71)				
Normal inter-bone distance	59	1	0	0
Loss of cartilage space without bone–bone contact	9	1	0	0
Focal complete loss with bone–bone contact	1	0	0	0
Bone–bone contact >50%	0	0	0	0

n = number of assessed joints. Presented values are means of the two readers (rounded down).The rows represent the HOAMRIS inter bone distance score. The columns represent the hrMRI cartilage score.

Discussion

Using the hrMRI cartilage score the readers identified more joints with cartilage damage than with inter-bone distance scoring in the OA group, and identified less joints with cartilage damage in healthy controls. Reliability of both scores were comparable. The differences can mostly be explained because inter-bone distance is scored on thicker slices, and therefore more prone to partial volume averaging.

Large variations of cartilage thickness and cartilage shape were present in both HOA patients and controls. For example, some healthy controls had considerably thinner cartilage centrally on the metacarpal head than on the rest of the metacarpal head. It is unlikely that this thinner cartilage in some healthy controls was caused by early HOA, or any other cartilage damaging disease, because the controls were young, healthy and screened against any history of joint disease or trauma. Furthermore, similar variations in cartilage thickness of MCP joints in healthy controls were found with MRI[9], with US and on cadaveric specimens[10]. These variations between persons make it challenging to distinguish between normal cartilage and minor cartilage loss in cross sectional imaging studies in early HOA, especially without a reference for the individual patient.

The observed pattern of cartilage loss in our patients was overall diffuse loss of cartilage thickness over large areas of the joint. Small focal cartilage lesions with abrupt edges which have been observed in the knee[11] were not detected in our study. Our results may suggest that either the normal pattern of cartilage loss in HOA consists of more gradual and continual cartilage loss, or we are unable to see small focal lesions, even with our hrMRI images.

We used a special MRI coil, as a normal wrist coil will not be able to acquire comparable high resolution scans of finger joints. Our coil was designed to image 4 joints within one imaging session, without the need to adjust coil placement between image acquisitions. The used coil is not commercially available from major vendors, but the knowledge on how to create the coil for different vendor machines is. However single small loop coils, which are standard commercially available from most MRI vendors (e.g., microscopy coil from Philips, small loop coil from Siemens) can be used to acquire the same image quality, but need to be repositioned for each scanned joint, and are more prone to motion artifacts, so good stabilization is necessary.

The current study proposes hrMRI to improve semi-quantitative cartilage scoring. However, hrMRI can also be used for quantitative cartilage measurements. Full quantitative measurements have the advantage of being less reader dependent and may be able to pinpoint smaller changes[12]. Previously, quantitative cartilage volume measurements has been demonstrated to work in MCP joints[6], and hrMRI was also used once for quantitative measures of cartilage composition[9], which can detect beginning cartilage degradation before cartilage thickness loss is apparent[13].

A limitation of our study is the absence of a true gold standard. Comparison with histology is hard to obtain in our study population. In a previous study we found that comparable hrMRI of the

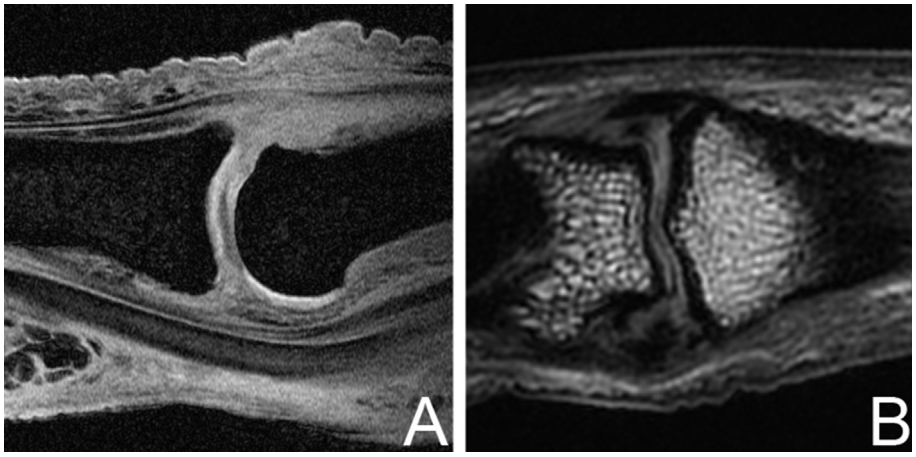

Fig. 1. Cartilage thinning, only detected with direct cartilage imaging. A: Sagittal spoiled gradient echo (SPGR) image of the proximal interphalangeal (PIP) joint of a hand osteoarthritis (HOA) patient. There is loss of cartilage on the head of the proximal phalanx. B: Coronal proton density (PD) image of the same joint at the level of the cartilage defect, which was scored by both readers as a joint without loss of inter-bone distance.

CMC one joint in patients scheduled for trapeziectomy detected cartilage damage with high sensitivity in comparison with histology, but might underestimate the amount of full-thickness loss in areas with severe cartilage loss[14]. As no patients with severe cartilage loss were present the current study, we expect that the detected cartilage loss corresponds to real cartilage loss. Another limitation is the inclusion of the second and third MCP and PIP joints only. The used MRI coil was built for imaging two MCP and two PIP joints. The second and third digits were chosen as these are the most affected MCP and PIP joints in HOA[15]. However, HOA is more often occurring in the DIP joints than in PIP and MCP joints. We expect hrMRI to also be better than inter-bone distance detection in DIP joints, despite the smaller size of these joints.

In conclusion, we have demonstrated that cartilage can be detected directly with good reliability using hrMRI. As compared to evaluation of inter-bone distance, which is the current standard, direct evaluation of the cartilage using hrMRI identified more joints with pathology in OA patients and less joints with pathology in healthy controls, suggesting better sensitivity and specificity.

Author contributions

All authors contributed to the conception and/or the design.

MS and GM read all the images. MS performed most of the analysis and drafted the first manuscript. All authors revised the manuscript for important intellectual content, and read and approved the final version of the manuscript. MS takes the responsibility for the integrity of the work as a whole.

Conflict of interest

The author(s) declare that they have no conflicting interests.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2019.05.003.

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