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The OMERACT Knee Inflammation MRI Scoring System: Validation of quantitative methodologies and tri-compartmental overlays in osteoarthritis

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ABSTRACT

Objective: To validate a revised version of the KIMRISS method for quantification of BML and synovitis-effusion in the knee by comparison with an established method, MOAKS.
Methods: Novel calibration tools were developed for both methods. We compared reliability for status and change scores of BML and synovitis-effusion on baseline and one-year MRI scans.
Results: Significant increase in both BML and synovitis-effusion was evident using KIMRISS but only for synovitis-effusion using MOAKS. Pre-specified targets for acceptable reliability (≥0.80 and ≥0.70 for status and change scores, respectively) were achieved more frequently for KIMRISS for both BML and synovitis.
Conclusion: Per OFISA criteria, KIMRISS should progress to assessment of discrimination.

Introduction

Bone marrow lesions (BML) and synovitis on MRI are independently associated with the severity and progression of osteoarthritis (OA), [1], and randomized controlled trials have targeted reducing the size of BML and degree of synovitis for the treatment of OA, [2–5]. A variety of semiquantitative knee OA scoring systems have been developed to assess BML and synovitis, the most commonly used including the Whole-Organ MRI Score (WORMS), [6], Boston-Leeds Osteoarthritis Knee Score (BLOKS), [7], and MRI Osteoarthritis Knee Score (MOAKS), [8]. Synovitis has been assessed according to a 0-3 grade on axial images. Each method assesses BML by dividing the knee into subregions and then grading size of BML according to a 0-3 scale. We have developed a novel scoring methodology to assess BML and synovitis, the OMERACT Knee Inflammation MRI Scoring System (KIMRISS), which employs interactive web-based image overlays for each articular surface in the knee on a sagittal fluid sensitive MRI sequence (Short-τ Inversion Recovery (STIR) or fat saturated proton-density-weighted), [9]. The first version of the overlays divided subarticular bone into 763 ~1 × 1 cm regions in the femur, tibia, and patella, each region being scored either 0, by default, or 1 if there is BML after the reader touches or mouse-clicks the BML-containing region which causes it to change color onscreen for feedback. The overlay positions can be automatically adjusted by interpolation to best fit other image slices so that BML is scored on consecutive sagittal slices. We demonstrated that KIMRISS was more reliable and responsive than MOAKS for detection of change in BML in Osteoarthritis Initiative observational data over a 1-year time frame and in a 12-week open label trial of adalimumab for inflammatory OA of the knee, [9]. We also validated a real-time iterative calibration (RETIC) online tool for KIMRISS where readers can improve their scoring proficiency prior to formal scoring exercises, [10]. This tool allows readers to visually observe whether they scored each overlay region in agreement with expert readers by the color-coding of each region, [11]. Intraclass correlation coefficients between the reader and experts are displayed instantly, allowing rapid progressive learning with each new case.

Several limitations of version 1 of these overlays were identified at OMERACT14, primarily pertaining to the aspect of feasibility,

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especially for the femoral overlay. Positioning of the overlays lacked precision for the different contours of the articulating bones and required frequent repositioning. The inclusion of non-articular regions in the overlays raised concerns pertaining to the truth aspect of the OMERACT Filter i.e. non-articular BML may not be relevant to knee OA. Consequently, the overlays were revised to address these concerns and a new RETIC module was created. We also revised the scoring of effusion in 4 pre-defined areas to record the largest diameter perpendicular to the longest axis on all *consecutive* sagittal slices and not just the single slice with the greatest extent of effusion to enhance sensitivity to change. We aimed to validate this revised version of KIMRISS by comparing it with MOAKS for inter-reader agreement for status and change scores, and sensitivity to change.

Materials and methods

Our validation activities conformed to the OMERACT Filter 2.1 Instrument Selection Algorithm (OFISA) [12] and were primarily aimed at addressing sources of variability as described in the report outlining the application of OFISA to the selection of imaging instruments [13] since target domains of BML and synovitis-effusion are well-established for MRI-based instruments in OA [6–8].

Materials

The KIMRISS web-based overlays were revised to reduce the number of non-articular regions so that the total number of regions decreased from 763 to an even 500 (supplementary figure 1), [11]. The 0-500 scoring range for KIMRISS BML is comprised of the following scoring ranges and number of designated slices for the different regions of the knee: 0-200 for tibia (20 slices), 0-24 for patella (6 slices), 0-24 for intercondylar region of femur (4 slices), 0-140 for lateral condyle of femur (10 slices), 0-112 for medial femoral condyle (8 slices). The 0-100 scoring range for KIMRISS synovitis-effusion is based on the scoring of 25 slices and a 0-4 grading scheme per slice. Since slice thickness may vary, scores for each region are prorated separately according to the actual number of slices that include each anatomical area. We programmed a series of overlay anchors to superimpose the border of the overlay over the articular bone to minimize the requirement for repositioning of the overlay when scrolling through sagittal slices. A powerpoint module and Youtube video were developed illustrating the KIMRISS method and the approach to the setting of anchors, [11]. A new RETIC module was developed which comprised 20 cases with knee OA, each with baseline and 1-year scans scored by the 3 developers of KIMRISS, [11]. Readers had to score cases in the RETIC module and achieve scoring proficiency targets according to the intra-class correlation coefficient (ICC) ($\geq$0.80 for status score, $\geq$0.70 for change score, for both BML and synovitis-effusion) that were comparable to those achieved by the developers (0.90 and 0.88 for status and change scores, respectively) before embarking on the formal scoring exercise.

The knowledge transfer tools detailing the methodology for scoring MOAKS are comprised of two manuscripts (personal communication from MOAKS developer, Dr. Frank Roemer), [8,14]. A new powerpoint module was designed based on these manuscripts as well as new web-based overlays and a new scoring interface to enable direct online data entry for recording BML in the different anatomical regions stipulated in MOAKS [11, 15].

The MRI scans for the reading exercise were extracted from the OAI database (http://www.oai.ucsf.edu/) and included baseline and 1-year scans from 38 cases with MOAKS BML score $\geq$1, which were read in pairs blinded-to-timepoint.

MRI readers included 3 rheumatologists and one musculoskeletal radiologist with >10-years of experience in development and validation of MRI-based scoring instruments and prior participation in several OMERACT meetings and scoring exercises. An additional reader was a radiology fellow, the designated OMERACT fellow, with no prior knowledge of or experience in using such instruments. Acceptable targets for reader reliability were pre-specified as an ICC of $\geq$0.80 for status scores and $\geq$0.70 for change scores for each of BML and synovitis-effusion.

Statistics

Descriptive statistics were reported as mean±SD. Given the large scoring ranges of both MOAKS and KIMRISS BML scores, we treated each as a quasi-continuous variable for analysis, and for simplicity, considered the whole-joint total BML score for most analyses. For assessment of interobserver reliability, we used the single measure intraclass correlation coefficient (ICC), absolute agreement definition, [16]. We also generated Bland-Altman plots comparing expert reader scores and computed smallest detectable change (SDC) based on the 95% CI of interobserver variability of change scores. The use of combinations of these methods to assess agreement has been recommended in a previous OMERACT publication [17]. For responsiveness, we computed standardised response means (SRM) and performed paired Student's t-tests.

Results

The baseline characteristics of cases whose scans were evaluated in this exercise were as follows: mean (SD) age of 61.7(9.1) years, 21 (55.3%) males, WOMAC pain (mean(SD)) 3.57 (3.63), WOMAC function (mean(SD)) 11.73 (11.70), Kellgren-Lawrence grades 0 (10.5%), 1 (10.5%), 2 (18.4%), 3 (34.2%), 4 (26.3%). Mean time to read a case was 23 minutes for KIMRISS and 13 minutes for MOAKS. The increase in BML score after one year was small though significant when assessed using KIMRISS but change in MOAKS BML was non-significant (Table 1). There was a significant increase in synovitis-effusion at 1

Table 1
Bone marrow lesion and synovitis-effusion scores at baseline and one year in cases with OA assessed using the OMERACT KIMRISS and MOAKS methods.

Method	MRI feature	Scores (Mean(SD))			SDC (% of maximum)	P value	SRM
		Baseline	1-year	Change			
MOAKS (0-45)	**BML**	3.6 (2.9)	3.4 (2.3)	-0.2 (1.9)	1.0 (2.2%)	0.72	-0.11
KIMRISS (0-500)	**BML**	15.7 (13.3)	21.2 (22.5)	5.5 (15.3)	5.6 (1.1%)	0.02	0.36
MOAKS (0-3)	**Synovitis-effusion**	1.3 (0.8)	1.5 (0.8)	0.2 (0.4)	0.4 (13.3%)	0.02	0.50
KIMRISS (0-100)	**Synovitis-effusion**	21.8 (12.0)	24.3 (11.9)	2.5 (7.4)	2.8 (2.8%)	0.04	0.34

Table 2
Inter-reader reliability for status (baseline scan) and baseline to 1-year change score in BML using the OMERACT KIMRISS and MOAKS scoring platforms in 38 cases selected from the Osteoarthritis Initiative database. Values in the table reflect pair-wise intraclass correlation coefficients (95% confidence intervals) and bolded values are those which attain the pre-specified targets for acceptable reliability (≥0.80 and ≥0.70 for status and change scores, respectively).

OMERACT KIMRISS BML Status Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	**0.94 (0.90-0.97)**	**0.87 (0.77-0.93)**	**0.86 (0.75-0.93)**	0.61 (0.12-0.82)
Reader 2*		**0.89 (0.80-0.94)**	**0.83 (0.70-0.91)**	0.58 (0.09-0.80)
Reader 3			0.77 (0.60-0.87)	0.48 (0.10-0.72)
Reader 4				0.62 (0.01-0.85)
MOAKS BML Status Score Reliability				
	Reader 2	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1	**0.81 (0.67-0.90)**	0.72 (0.39-0.87)	0.71 (0.18-0.88)	0.75 (0.51-0.87)
Reader 2		0.74 (0.29-0.89)	0.76 (0.29-0.91)	0.72 (0.43-0.86)
Reader 3			0.58 (-0.08-0.85)	**0.90 (0.82-0.95)**
Reader 4				0.59 (-0.04-0.84)
OMERACT KIMRISS BML Change Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	**0.92 (0.86-0.96)**	**0.87 (0.76-0.93)**	**0.88 (0.78-0.93)**	**0.76 (0.58-0.87)**
Reader 2*		**0.92 (0.86-0.96)**	**0.88 (0.79-0.94)**	**0.78 (0.62-0.88)**
Reader 3			**0.77 (0.59-0.87)**	0.62 (0.37-0.78)
Reader 4				**0.88 (0.79-0.94)**
MOAKS BML Change Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	**0.81 (0.67-0.89)**	0.67 (0.45-0.82)	**0.73 (0.54-0.85)**	0.69 (0.48-0.83)
Reader 2*		**0.76 (0.58-0.87)**	**0.81 (0.67-0.90)**	0.63 (0.40-0.79)
Reader 3			**0.80 (0.64-0.89)**	**0.73 (0.54-0.85)**
Reader 4				0.66 (0.44-0.81)

* Developers of KIMRISS scoring method

year according to both methods. Acceptable reliability for status score was achieved for almost all pairs of experienced readers (5/6) using KIMRISS for both BML and synovitis-effusion but only 1 reader pair using MOAKS BML and synovitis-effusion (Tables 2 and 3). The OMERACT fellow achieved acceptable reliability for only one reader pair combination for BML but for all reader pairs for KIMRISS synovitis-effusion. Acceptable reliability for change score of BML and synovitis-effusion was achieved for all pairs of experienced readers using KIMRISS and also for most of the pair-wise comparisons that included the OMERACT fellow. For MOAKS BML, acceptable reliability for change score was achieved for almost all pairs of experienced readers (5/6) but only for one reader pair that included the OMERACT fellow. For MOAKS synovitis-effusion only 1 reader pair achieved acceptable reliability for change score. Supplementary figure 2 illustrates the reliability of scores across the whole range of change scores according to individual reader data using cumulative probability plots. Bland-Altman plots for both methods are shown in supplementary figure 3 and indicate no evidence of systematic reader bias.

Discussion

KIMRISS BML performed favourably compared to MOAKS BML, especially for the reliable detection of change scores, as evident by the higher ICC and lower SDC as a percentage of the maximum score, despite the small degree of change in BML over one year. Moreover, the KIMRISS method was readily adopted and scoring proficiency attained by a naïve reader. Similar conclusions can be drawn for synovitis-effusion.

There are several study limitations. Sensitivity to change and discrimination cannot be readily assessed because of the lack of interventions that influence these lesions in OA, especially in the time frame of placebo-controlled trials. The KIMRISS and MOAKS methods have markedly different scoring ranges precluding comparisons of reliability using a relative measure such as the ICC statistic. However, additional measures (SDC, Limits of Agreement) support our study conclusions. A RETIC module, or a similar knowledge transfer tool, has not been made available by the developers of MOAKS. In fact, to our knowledge, there is a paucity of such tools for all the additional methods developed to score BML and synovitis in OA. We developed *de novo* web-based overlays and a scoring interface for direct online data entry for MOAKS but did not consider it our prerogative to develop a RETIC module as we are not the developers of this tool.

In conclusion, we have demonstrated that the KIMRISS method compares favourably to a more established scoring instrument for detection of BML and synovitis-effusion in OA. Fully automated methodologies for linkage of overlays to articular bone contours and absolute quantitation of synovitis-effusion constitute the next phase of development of the KIMRISS method.

Declaration of Competing Interest

None.

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Table 3
Inter-reader reliability for status (baseline scan) and baseline to 1-year change score in synovitis-effusion using the OMERACT KIMRISS and MOAKS scoring platforms in 38 cases selected from the Osteoarthritis Initiative database. Values in the table reflect pair-wise intraclass correlation coefficients (95% confidence intervals) and bolded values are those which attain the pre-specified targets for acceptable reliability (≥0.80 and ≥0.70 for status and change scores, respectively).

OMERACT KIMRISS Synovitis-effusion Status Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	**0.97 (0.87-0.99)**	**0.97 (0.94-0.99)**	**0.82 (0.67-0.90)**	**0.90 (0.47-0.96)**
Reader 2*		**0.95 (0.56-0.99)**	0.78 (0.57-0.89)	**0.85 (0.09-0.95)**
Reader 3			**0.83 (0.70-0.91)**	**0.91 (0.73-0.96)**
Reader 4				**0.82 (0.67-0.90)**
MOAKS Synovitis-effusion Status Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	0.56 (0.14-0.78)	0.62 (0.18-0.82)	0.66 (0.43-0.81)	0.77 (0.60-0.88)
Reader 2*		**0.82 (0.67-0.90)**	0.67 (0.30-0.84)	0.52 (0.15-0.74)
Reader 3			0.62 (0.32-0.80)	0.67 (0.22-0.85)
Reader 4				0.56 (0.30-0.75)
OMERACT KIMRISS Synovitis=-effusion Change Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	**0.95 (0.91-0.97)**	**0.90 (0.81-0.95)**	**0.80 (0.64-0.89)**	**0.87 (0.76-0.93)**
Reader 2*		**0.92 (0.85-0.96)**	**0.79 (0.64-0.89)**	**0.88 (0.79-0.94)**
Reader 3			**0.84 (0.71-0.91)**	**0.88 (0.78-0.94)**
Reader 4				**0.81 (0.66-0.90)**
MOAKS Synovitis-effusion Change Score Reliability				
	Reader 2*	Reader 3	Reader 4	Reader 5 OMERACT Fellow
Reader 1*	0.50 (022-0.70)	0.45 (0.17-0.67)	0.30 (-0.02-0.56)	0.39 (0.09-0.62)
Reader 2*		**0.76 (0.58-0.87)**	0.46 (0.17-0.68)	0.54 (0.27-0.73)
Reader 3			0.49 (0.21-0.70)	0.59 (0.33-0.76)
Reader 4				0.62 (0.38-0.78)

* Developers of KIMRISS scoring method

Disclosures

WPM is Chief Medical Officer CARE Arthritis Limited and has acted as a paid consultant/participated in advisory boards for AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer and UCB; received research and/or educational grants from AbbVie, Novartis, Pfizer and UCB; and received speaker fees from AbbVie, Janssen, Novartis, Pfizer and UCB. SJP has been an advisory board member for AbbVie and Novartis; and received research support from AbbVie, MSD, and Novartis; received speaker fees from MSD, Pfizer, AbbVie, Novartis and UCB. RGL has received consulting fees from CARE Arthritis Limited, Parexel and Pfizer.

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Supplementary materials

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