FULL-GRADE AND WITHIN-GRADE CARTILAGE CHANGE OVER TWO YEARS AS ASSESSED USING THE MOAKS SCORING INSTRUMENT AND CONCURRENT QUANTITATIVE CARTILAGE THICKNESS LOSS:

DATA FROM THE OAI FNIH BIOMARKERS CONSORTIUM STUDY

[1,2]Frank W. Roemer, [3]Susanne Maschek, [4]Anna Wisser, [1,4]Ali Guermazi, [5]David J. Hunter, [3]Wolfgang Wirth

[1]Quantitative Imaging Center, Department of Radiology, Boston University School of Medicine, Boston, MA; [2]Department of Radiology, Universitätsklinikum Erlangen & Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany;
[2]Paracelsus Medical University & Chondrometrics GmbH, Salzburg, Austria & Freilassing, Germany, Austria [4]Department of Radiology, VA Boston Healthcare System, West Roxbury, MA, USA, [5]Department of Rheumatology, University of Sydney, Australia

BACKGROUND AND PURPOSE

- Semi-quantitative (SQ) MOAKS [1] cartilage scores and quantitative (Q) cartilage thickness measurements are used as outcome measures in observational studies and interventional knee OA trials
- Both methods considered complementary
- SQ scoring by experts is considered less sensitive to change compared to Q approaches based on cartilage segmentation
- On the other hand, change in focal defects commonly is not detectable by Q approaches
- In order to increase sensitivity to change of SQ instruments so-called within-grade changes not fulfilling criteria of a full-grade change have been introduced [2]
- While the validity of these changes has been shown, the association between longitudinal change of SQ-defined within-grade and full-grade changes and longitudinal Q cartilage loss has not been established
- Our aim was to study the association between full-grade only changes, within-grade only changes and full-grade plus within-grade change in MOAKS cartilage scores and concurrent change in quantitative cartilage thickness measurements over 24 months within the FNIH Biomarker Consortium study

METHODS

- Of the 600 participants from the OAI FNIH study, 599 had MOAKS cartilage assessments and quantitative cartilage thickness measurements (age: 62y, BMI: 31kg/m², 59% female)
- MOAKS assesses cartilage in a two-digit fashion taking into account the area extent and the extent that is full thickness loss (possible grades: 0.0, 1.0, 1.1, 2.0, 2.1, 2.2, 3.0, 3.1, 3.2 and 3.3)
- The maximum MOAKS area extent score(MOAKSext, 1st component of MOAKS cartilage scale), and the maximum MOAKS cartilage damage full-thickness score (MOAKSft, 2nd MOAKS cartilage component) in each 3 tibial and 1 central femoral MOAKS subregion were determined at baseline and two-year follow-up for the medial and lateral compartment
- Medial and lateral compartment cartilage thickness (MFTC/LFTC) change over the subsequent two years were stratified by ipsi-compartmental change in MOAKSext, and MOAKSft score
- Within-grade changes were assessed in knees without full-grade change in comparison to knees without any change
- Knees with full grade changes only, with within-grade changes only and with any (either full-grade change, within-grade change or both) change in MOAKSext and MOAKS ft were considered separately and compared
- A number of subregion-approach considering subregions that show change was used in addition
- Between-group comparisons were performed using ANCOVA with adjustment for age, sex, and BMI. Results were presented as mean adjusted difference (MAD) and 95% confidence intervals

RESULTS

- 331 knees had no change in cartilage SQ scores, 41 knees had only within-grade changes, 170 knees had only full-grade changes, and 57 knees had both within-grade and full-grade changes
- Knees with any increase in MOAKS cartilage scores (MOAKSext and/or MOAKSft) in the MFTC (n=268) showed more MFTC cartilage loss than knees that remained stable (mean adjusted difference (MAD) -0.16 mm,95% CI: [-0.19, -0.13] mm)
- Cartilage thickness loss increased with higher grade MOAKSext cartilage change (change by 1 grade: MAD 0.13 mm, 95% CI: [-0.18, -0.08] mm; change by 2 grades: MAD -0.22 mm, 95% CI:[-0.27, -0.17] mm)
- Similar findings were observed for increase in MOAKSft dimension: (change by 1 grade: MAD -0.12 mm, 95% CI: [-0.16, -0.08] mm; by 2 grades: MAD -0.28 mm, 95% CI: [-0.32, -0.23] mm)
- While knees with within-grade-only changes showed markedly less cartilage thickness loss compared to knees with full grade-only changes, the amount of loss was still three times higher than for those without any change
- The number of knees with any change in MOAKS cartilage (full-grade, within-grade or both) was markedly higher, including within grade changes (n=268) compared to knees with full grade changes only (n= 170) while the MAD of cartilage loss was similar
- The MAD increased linearly with increase in number of subregions showing any change (1 subregion: MAD -0.07 mm, 95% CI: [-0.10, -0.03] mm; 2 subregions: MAD -0.20 mm, 95% CI: [-0.24, -0.16] mm; 3 subregions: MAD -0.37 mm, 95% CI: [-0.42 -0.32] mm). **Table 1** shows these results in detail

Table 1. Change of cartilage damage (MOAKS) over 24 months and concurrent mean change in cartilage thickness in the medial femoro-tibial compartment

Δ	N	Mean	SD	95% CI	Mean adj. diff	95% CI
Mean change in MFTC cartilage thickness in knees with vs. without any[1] change in MFTC cartilage damage scores						
No	331	-0.02	0.12	(-0.04, -0.01)	(Reference)	
Yes	268	-0.19	0.25	(-0.22, -0.16)	-0.16	(-0.19, -0.13)
Any[2] increase in area dimension MOAKSext cartilage scores						
0	470	-0.06	0.16	(-0.08, -0.05)	(Reference)	
1	60	-0.19	0.25	(-0.26, -0.12)	-0.13	(-0.18, -0.08)
2	68	-0.28	0.29	(-0.35, -0.21)	-0.22	(-0.27, -0.17)
3	1	n/a (too few knees)				
Any[2] increase in full thickness dimension MOAKSft MFTC cartilage damage scores						
0	435	-0.05	0.14	(-0.06, -0.03)	(Reference)	
1	91	-0.18	0.23	(-0.22, -0.13)	-0.12	(-0.16, -0.08)
2	73	-0.33	0.32	(-0.40, -0.25)	-0.28	(-0.32, -0.23)
Full-grade only increase in any (MOAKSext and MOAKSft) MFTC MOAKS cartilage scores [3]						
No	331	-0.02	0.12	(-0.04, -0.01)	(Reference)	
Yes	170	-0.20	0.26	(-0.24, -0.17)	-0.17	(-0.21, -0.14)
Half-grade only increase in any (MOAKSext and MOAKSft) MFTC MOAKS cartilage scores [4]						
No	331	-0.02	0.12	(-0.04, -0.01)	(Reference)	
Yes	41	-0.06	0.12	(-0.09, -0.02)	-0.03	(-0.07, 0.01)
Number of subregions with any (full-grade, within-grade, both) increase in any (MOAKSext/MOAKSft) MOAKS cartilage damage scores						
0	331	-0.02	0.12	(-0.04, -0.01)	(Reference)	
1	135	-0.10	0.17	(-0.13, -0.07)	-0.07	(-0.10, -0.03)
,	86	-0.23	0.24	(-0.28, -0.18)	-0.20	(-0.24, -0.16)
3	47	-0.40	0.31	(-0.50, -0.31)	-0.37	(-0.42, -0.32)
Number of subregions with full-grade only increase in any MOAKS cartilage damage scores						
0	331	-0.02	0.12	(-0.04, -0.01)	(Reference)	
1	87	-0.12	0.19	(-0.16, -0.08)	-0.09	(-0.12, -0.05)
2	59	-0.22	0.24	(-0.28, -0.16)	-0.19	(-0.24, -0.15)
3	24	-0.48	0.31	(-0.61, -0.36)	-0.45	(-0.52, -0.38)
Number of subregions with within-grade only increase in any MOAKS cartilage damage scores						
0	332	-0.02	0.12	(-0.04, -0.01)	(Reference)	
1	37	-0.05	0.12	(-0.09, -0.01)	-0.02	(-0.06, 0.02)
2	4	n/a (too few knees)				

[1] any: either MOAKSext, MOAKSft or both, full grade change, within grade change or both in either dimension
[2] any: full grade change, within grade change or both
[3] within-grade change knees counted as no change
[4] 41 knees with within-grade change only. 170 knees with full-grade-only changes and 57 knees with both within-grade and full-grade changes not considered

CONCLUSION

- Both full-grade and within-grade changes in MOAKS cartilage scores corresponded with ipsicompartmental Q cartilage thickness loss confirming the validity of within-grade assessment
- In the medial compartment, concurrent change in cartilage thickness was comparable for change in the MOAKSext and MOAKSft change dimensions
- The effect was less pronounced for MOAKS within-grade changes
- However, sensitivity to change is markedly improved, including within-grade change-only knees, with knees showing any change increasing by 24% compared to using full grade change-only - emphasizing the benefit of including within grade scoring when applying the MOAKS ordinal scoring instrument
- SQ assessment seems a potential alternative as an outcome measure when Q evaluation is not feasible or available.

REFERENCES

[1] Hunter DJ, Guermazi A, Lo GH, Grainger AJ, Conaghan PG, Boudreau RM, et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). Osteoarthritis Cartilage. 2011;19(8):990-1002

[2] Roemer FW, Nevitt MC, Felson DT, Niu J, Lynch JA, Crema MD, et al. Predictive validity of within-grade scoring of longitudinal changes of MRI-based cartilage morphology and bone marrow lesion assessment in the tibio-femoral joint--the MOST study. Osteoarthritis Cartilage. 2012;20(11):1391-8.

FUNDING AND DISCLOSURES

Funding: Scientific and financial support for the Foundation for the National Institutes of Health (FNIH) Osteoarthritis (OA) Biomarkers Consortium and for this study has been made possible through grants as well as direct and indirect in-kind contributions from AbbVie, Amgen Inc., the Arthritis Foundation, Bioiberica SA, DePuy Mitek, Inc., Flexion Therapeutics, Inc., GlaxoSmithKline, Merck Serono, Rottapharm | Madaus, Sanofi, Stryker, and the Pivotal Osteoarthritis Initiative Magnetic Resonance Imaging Analyses (POMA) Study (NIH/National Heart, Lung, and Blood Institute grant HHSN- 2682010000). The Osteoarthritis Initiative (OAI) is a public–private partnership between the NIH (contracts N01-AR-2-2258, N01-AR-2- 2259, N01-AR-2-2260, N01-AR-2-2261, and N01-AR-2-2262) and private funding partners (Merck Research Laboratories, Novartis Pharmaceuticals, GlaxoSmithKline, and Pfizer, Inc.) and is conducted by the OAI Study Investigators. Private sector funding for the Biomarkers Consortium and the OAI is managed by the FNIH.

Disclosures: AG has received consultancies, speaking fees, and/or honoraria from Pfizer, Novartis, AstraZeneca, Merck Serono, and TissueGene and is President and shareholder of Boston Imaging Core Lab (BICL), LLC a company providing image assessment services. FWR is Chief Medical Officer and shareholder of BICL, LLC. and has received consultancies, speaking fees, and/or honoraria from Calibr –California Institute of Biomedical Research and Grünenthal, GmbH

ACKNOWLEDGMENTS

•We thank the Osteoarthritis Research Society International (OARSI) for their leadership and expertise on the FNIH OA Biomarker Consortium project.