7th International Workshop on Osteoarthritis Imaging

"IMAGING IN OA – NOW IS THE TIME TO MOVE AHEAD"

July 9-12, 2014

Reykjavik, Iceland

Welcome to the 7th International Workshop on Osteoarthritis Imaging

The International Workshop on Osteoarthritis Imaging started in 2007 and was held in Ainring, Germany, with 126 registered participants from academia, regulatory and funding agencies, and industry. Since then, the Workshop has been held annually at various locations, historically alternating between the European and North American locations.

This year we have received a record-breaking number of abstracts and 14 countries being represented in attendance.

This workshop is a unique opportunity for scientists, researchers, regulatory agencies, interested members of pharmaceutical companies and others to meet and have an in depth and open minded discussion about the best way to advance the field of osteoarthritis imaging.

For years, we have been trying to understand osteoarthritis from the imaging point of view. We now have a large amount of imaging and clinical data available on osteoarthritis and it is an optimal time to move forward and expand on our understanding of the disease.

Sincerely,

Ali Guermazi, M.D., Ph.D.
Chairman
International Workshop on Osteoarthritis Imaging
Professor of Radiology
Boston University Medical School

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7th International Workshop on Osteoarthritis Imaging

"Imaging in OA – Now is the Time to Move Ahead"

Meeting Chair: Ali Guermazi, MD, PhD

Scientific Program Committee: Richard Frobell, PhD; Martin Englund, MD, PhD; Garry Gold, MD; Thorvaldur Ingvarsson, MD, PhD; Jeffrey Katz, MD, MSc; Kristleifur Kristjansson, MD

July 9-12, 2014 – Askja Venue, Conference room 132, University of Iceland, Reykjavik, Iceland

Tuesday July 8

12:00 PM – 7:00 PM	Visit to Blue Lagoon, a must do and most astonishing natural geothermal spa and one of the most visited attractions in Iceland. The spa is located in a lava field in Grindavík on the Reykjanes Peninsula. Package includes tour and transfers to the Blue Lagoon. (http://www.re.is/DayTours/BlueLagoon/).

Wednesday July 9

9:00 AM – 11:00 PM	**Pre-course – A tour and workshop at Össur - a global leader of non-invasive orthopedics** **Workshop:** Do braces have a role in the treatment of OA of the knee? - Introduction to the Össur Unloader One® brace. **Hosts:** Thorvaldur Ingvarsson (senior VP of R&D), Kristleifur Kristjansson, (Medical Officer) Össur, known as a technical leader in the field of prosthetics and bionic solutions for lower limb amputees is also one of the leading companies in bracing and supports. With increased emphasis on indication based solutions Össur has developed dynamic braces such as the Unloader One® for the relief of pain and improvement of mobility of people with knee OA.
12:30 PM – 2:15 PM	Lunch
2:15 PM – 2:30 PM	**Welcome and Introduction to the Workshop and Social Program** Ali Guermazi
2:30 PM – 4:00 PM	**Module 1: Imaging in Osteoarthritis** Moderator: C. Kent Kwoh
2:30 PM – 3:00 PM	Invited Lecture: What role does imaging play in epidemiological studies and clinical trials of early OA? David T. Felson
3:00 PM – 3:15 PM	Lynch J.A., Liu F., Jungmann P., Lane N., Link T., Nevitt M.C. Quantitative joint space width loss measured in hips with radiographic osteoarthritis from the Osteoarthritis Initiative

3:15 PM – 3:30 PM	Kwoh C.K., Hannon M.J., Fujii T., Guermazi A., Boudreau R., Hunter D.J., Eckstein F., Grago J., Roemer F.W. Recent knee injury or knee surgery is associated with worsening findings on MRI within 12 months prior the development of incident radiographic osteoarthritis: Data from the Osteoarthritis Initiative
3:30 PM – 3:45 PM	Ratzlaff C., Russell R., Duryea J. Quantitatively measured bone marrow lesions in the patellofemoral joint: distribution and association with pain
3:45 PM – 4:00 PM	Roemer F.W., Kwoh C.K., Hannon M.J., Hunter D.J., Boudreau R., Eckstein F., Fujii T., Guermazi A. MRI-based long term prediction of incident radiographic osteoarthritis: Data from the Osteoarthritis Initiative (Best Rated Paper Award)
4:00 PM – 4:30 PM	Break
4:30 PM – 6:00 PM	**Module 2: Imaging and pain in OA** Moderator: Floris Lafeber
4:30 PM – 5:00 PM	Invited Lecture: Pain in OA: What has imaging taught us? C. Kent Kwoh
5:00 PM – 5:15 PM	Cotofana S., Hannon J.M., Eckstein. F., Grago J., Wirth W., Hunter D.J., Kwoh C.K. Are denuded areas of subchondral bone related to localized knee or regional pain as evaluated by the knee pain map? – Data from the Osteoarthritis Initiative
5:15 PM – 5:30 PM	Schiphof D., Oei E.H.G, Waarsing J.H., Bierma-Zeinstra S.M.A. KOOS scores differ with uni- or bilateral knee OA based on MRI
5:30 PM – 5:45 PM	Engelke K., Chappard C., Lowitz T., Museyko O., Laouisset L., Bousson V., Laredo J.-D. Quantitative analysis of subchondral bone structure in knee OA at different levels of spatial resolution using clinical whole body and high resolution peripheral CT scanners
5:45 PM – 6:00 PM	Pedoia V., Lansdown D., Zaid M., Ma C.B., Li X 3D MRI based analysis of the knee shape in patient with ACL injuries
8:00 PM	Dinner at The Grill Market or Grillmarkadurinn. We will enjoy farmed sheep meat, one of the best in the World. (http://www.grillmarkadurinn.is/en/).

Thursday July 10

9:00 AM – 10:30 AM	**Module 3: New Techniques in Imaging** Moderator: Miika Nieminen
9:00 AM – 9:30 AM	Invited Lecture: MRI advances and application in OA assessment (2D vs 3D, high field strength MRI, ultrashort echo (UTE) MRI) John Carrino

9:30 AM – 9:45 AM	Wang A., Abramson E., Pedoia V., Kretzschmar M., Nardo L., Link T.M., Ma C.B., Li X. MR T1ρ & T2 of meniscus after acute anterior cruciate ligament injuries
9:45 AM – 10:00 AM	Segal N.A., Frick E., Nevitt M.C., Torner J.C., Felson D.T., Guermazi A., Anderson D.D. Association between measurements of joint space width on standing CT and WORMS cartilage morphology
10:00 AM – 10:15 AM	Kashyap S., Sonka M. Automated algorithm for 3D MR segmentation and sub-plate detection in 3D MRI: Data from the Osteoarthritis Initiative
10:15 AM – 10:30 AM	Crema M.D., Hunter D.J., Burstein D., Roemer F.W., Li L., Krishnan N., Silva Jr J.R., Marra M.D., Le-Graverand M.-P., Guermazi A. Change in delayed gadolinium-enhanced MRI of tibiofemoral cartilage (dGEMRIC) indices are not associated with cartilage loss over 1 year: A longitudinal 3.0 T MRI study
10:30 AM – 11:00 AM	Break
11:00 AM – 12:00 PM	**5 Top Rated Abstracts from Young Investigators** Moderator: David Wilson
11:00 AM – 11:12 AM	Haugen I.K., Slatkowsky-Christensen B., Sesseng S., van der Heijde D., Kvien T.K. MRI predicts future joint space narrowing and development of erosive disease 5 years later in patients with hand OA. (Young Investigator Award)
11:12 AM – 11:24 AM	Van der Woude J.A.D., Intema F., Wiegant K., Van Roermund P., Maschek, S., Eckstein F., Mastbergen S.C., Lafeber F.P.J.G. Structural survival of the knee joint five years after joint distraction. (Young Investigator Award)
11:24 AM – 11:36 AM	Runhaar J., van Middelkoop M., Reijman M., Oei E.H.G., Bierma-Zeinstra S.M.A. Comparing radiographs and MRI for the prediction of incident knee OA and knee pain in overweight and obese women after 30 months. (Young Investigator Award)
11:36 AM – 11:48 AM	Podlipská J., Koski J.M., Liukkonen E., Tervonen O., Arokoski J.P., Saarakkala S. Association of ultrasonography with radiography and knee pain in knee osteoarthritis
11:48 AM – 12:00 PM	Zhang F., Kumm J., Svensson F., Turkiewicz A., Frobell R., Englund M. Risk factors for meniscal body extrusion on MRI in subjects free of radiographic knee osteoarthritis: Data from the Osteoarthritis Initiative
12:00 PM – 2:00 PM	Lunch
2:00 PM – 3:30 PM	**Module 4: Risk factors and structural**

	Moderator: David J. Hunter
2:00 PM – 2:30 PM	Invited lecture: Challenges in studying risk factors for OA progression. Yuqing Zhang
2:30 PM – 2:45 PM	Ruhdorfer A.S., Dannhauer T., Wirth W., Eckstein F. Longitudinal analysis of thigh muscle, subcutaneous and intermuscular adipose tissue area in knees with chronic pain.
2:45 PM – 3:00 PM	van Meer B.L., Oei E.H.G., Meuffels D.E., van Arkel E.R.A., Verhaar J.A.N., Bierma-Zeinstra S.M.A., Reijman M. Which predictors are related to degenerative changes of the knee following anterior cruciate ligament rupture?
3:00 PM – 3:15 PM	Maschek S., Wirth W., Kwoh C.K., Hunter D.J., Ladel C., Eckstein F. Long term change and measurement variability of cartilage thickness in healthy reference subjects - Data from the Osteoarthritis Initiative
3:15 PM – 3:30 PM	Donoghue C.R., Rao A., Rueckert D., Bull A.M.J. Using manifold learning to discover OA imaging biomarkers for the prediction of joint function with data from the OAI
3:30 PM – 6:00 PM	Poster Session and Social
7:30 PM	Gala Dinner at the Perlan (Pearl), the Reykjavik dome. Visit of the Saga museum of history. The Perlan is a landmark building in Reykjavík. It is 25.7 meters high and is situated on the hill Öskjuhlíð where there had been hot water storage tanks for decades. In 1991 the tanks were updated and a hemispherical structure placed on top. We will have dinner at a rotating restaurant with panoramic view of the city. (http://perlan.is/?lang=en).

Friday July 11

9:00 AM – 10:30 AM	**Module 5: Anti-NGF therapy in the clinical management of OA. The new horizon in pain reduction in osteoarthritis** Moderator: Colin Miller
9:00 AM – 9:20 AM	Invited lecture: Background on aNGF therapy and results from the placebo-controlled clinical trials including the non-serious joint related adverse events. Nancy Lane
9:20 AM – 9:40 AM	Invited Lecture: Adjudication process with results, conclusions and implications for future sponsored trials. Marc Hochberg
9:40 AM – 10:00 AM	Invited Lecture: Clinical Development of Tanezumab for Chronic Pain Christine West
10:00 AM – 10:15 AM	Roemer F.W., Miller C., Hoover K.B., Hayes C.W., Guermazi A. Imaging findings in anti-nerve growth factor (a-NGF) studies: Relevance for eligibility and safety
10:15 AM – 10:30 AM	Guermazi A., Hellio-Le Graverand M.-P., Miller C., Roemer F.W.

	Differences between radiologic assessment in osteoarthritis efficacy studies and nerve growth factor inhibitor programs: Relevance of radiography and MRI
10:30 AM – 12:30 PM	Poster Session and Social.
12:30 PM – 2:00 PM	Lunch
2:00 PM – 4:00 PM	**Module 6: Looking at the same problem from both ends – New insights on the relevance of imaging in joint replacement and incident disease** Moderator: Richard Frobell
2:00 PM – 2:24 PM	Joint replacement from a socio-economic perspective Jeffrey Katz
2:24 PM – 2:48 PM	Morphologic MRI predictors of TKR Frank Roemer
2:48 PM – 3:12 PM	Quantitative MRI predictors of TKR Felix Eckstein
3:12 PM – 3:36 PM	Role of the meniscus in incident OA Martin Englund
3:36 PM – 4:00 PM	Stratification of large OA trials to answer relevant questions: the example of imaging in the OAI Michael C. Nevitt
4:00 PM – 4:30 PM	Break
4:30 PM – 6:30 PM	**Debate – Imaging – Challenges of a slowly progressive disease and implications in making clinical trials more efficient**
4:30 PM – 5:30 PM	Moderator: Michael C. Nevitt Is MRI the next outcome measure to be approved by the FDA-EMEA? Pros: David T. Felson Cons: Jeffrey N. Katz
5:30 PM – 6:30 PM	Moderator: Stefan Lohmander Are we conceptualizing the best OA clinical trials? Pros: Marc Hochberg Cons: David J. Hunter
8:00 PM	Dinner at IDNO which is located in the heart of the city of Reykjavík, beside the City Pond, directly opposite the City Hall. IDNO was built in 1897 and reconstructed in its original form in 1997. It remains as it was in 1897, testament to the grand vision of Iceland's artisans. (http://www.idno.is/english.html).

Saturday July 12

Golden Circle Tour: this is a quite impressive tour and a popular tourist route in South Iceland, covering about 300 km looping from Reykjavík into central Iceland and back. The three primary stops on the route are the national park Thingvellir, the waterfall Gullfoss (meaning "golden falls"), and the geothermally active valley of Haukadalur, which contains the geysers Geysir and Strokkur (http://www.re.is/DayTours/Details/1346).

Conclusion of the 2014 7th International Workshop on Osteoarthritis Imaging

See you in 2015 at the 8th IWOAI in San Francisco!

IWOAI
INTERNATIONAL WORKSHOP ON OSTEOARTHRITIS IMAGING

ORAL PRESENTATIONS

QUANTITIATIVE JOINT SPACE WIDTH LOSS MEASURED IN HIPS WITH RADIOGRAPHIC OSTEOARTHRITIS FROM THE OSTEOARTHRITIS INITIATIVE

*Lynch J.A., *Liu F., *Jungmann P., **Lane N., *Link T., *Nevitt M.C.

*University of California, San Francisco, CA, USA, **University of California, Davis, CA, USA

INTRODUCTION: Although definition of radiographic hip OA (RHOA) depends on multiple features, progression from a normal hip to end-stage disease requires hip joint space width to change from a normal value to bone-on-bone with a joint space width of zero.

OBJECTIVE: In this study, we investigated frequency and rates of change of JSW loss supero-medially and supero-laterally in hips with definite RHOA at baseline visit for participants in the Osteoarthritis Initiative (OAI) using a new semi-automated measurement technique.

METHODS: Paired AP Pelvis radiographs from baseline and 48-month follow-up visits for participants in OAI were read for radiographic features of hip osteoarthritis, including OARSI scores for joint space narrowing osteophytes, sclerosis, cysts. These scores were used to divide hips into those with no RHOA, possible RHOA and definite RHOA at baseline and 48-month follow-up visit. Hip JSW was measured over a 40 degree arc centred on the superior-inferior (SI) direction (defined as the direction perpendicular to a line through the centres of the two femoral heads). The femoral head and acetabular contours were measured by a single reader using livewire algorithm tools. Joint space widths were measured between the femoral head and acetabulum at fixed angles every integer degree up to 20 degrees supero-medially and 20 degrees supero-laterally from the 0 degrees SI direction. The frequency with which supero-medial and/or supero-lateral minimum joint space width (mJSW) decreased by more than 0.7mm was assessed for hips with definite RHOA at baseline and compared to control hips with no RHOA at 48-month follow-up. Rates of change in mJSW from baseline to 48-month follow-up visits in both the supero-lateral and supero-medial arcs as well as overall mJSW were calculated for hips with definite RHOA at baseline and for controls.

RESULTS: From the 128 hips with prevalent definite RHOA, 11 (9%) showed more than 0.7mm mJSW loss in the supero-lateral arc, 11 (9%) showed mJSW loss more than 0.7mm in the superior-medial arc, and 22 (17%) showed mJSW loss more than 0.7mm in both arcs. In the 681 hips with no RHOA at the 48-month visit, 39 (6%) showed more than 0.7mm mJSW loss in the supero-lateral arc, 37 (5%) showed mJSW loss more than 0.7mm in the superior-medial arc, and 23 (3%) showed mJSW loss more than 0.7mm in both arcs. Over the 48-month follow-up period, the hips with definite RHOA at baseline showed a mean (SD) change in mJSW of -0.43 (0.56) mm supero-medially, -0.41 (0.66) mm supero-laterally, more than 2.5 times the mJSW loss seen in the controls. Taking a single outcome of the largest loss of mJSW from the supero-medial and supero-lateral arcs as structural outcome, the mean (SD) change in the hips with definite RHOA was -0.61 (0.61mm), representing an SRM of 1.0, which is relatively high compared to JSW based structural outcomes used in knee OA.

CONCLUSION: Hips with definite RHOA at baseline showed relatively high rates of large (more than 0.7mm) minimum JSW loss, with an average rate of 0.15mm per year loss (with SRM=1.0).

SPONSOR: NIH (HHSN268201000019C “Hip Morphology and Limb-Specific Risk Factors for Radiographic Hip Osteoarthritis”, and the OAI a public–private partnership comprised of 5 contracts (N01-AR-2-2258, N01-AR-2-2259, N01-AR-2-2260, N01-AR-2-2261, N01-AR-2-2262) funded by the NIH. Private funding partners for OAI are Pfizer, Novartis Pharmaceuticals, Merck Research Laboratories, Glaxo-SmithKline. Private sector funding for OAI is managed by FNIH.
DISCLOSURE STATEMENT: none.
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RECENT KNEE INJURY OR KNEE SURGERY IS ASSOCIATED WITH WORSENING FINDINGS ON MRI WITHIN 12 MONTHS PRIOR THE DEVELOPMENT OF INCIDENT RADIOGRAPHIC OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

*,**Kwoh C.K., **Hannon M.J., **Fujii T., ***Guermazi A., **Boudreau R., ****Hunter D.J., *****Eckstein F., **Grago J., ***,******Roemer F.W.

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INTRODUCTION: We have previously reported that recent knee injury or knee surgery increases the risk of developing incident radiographic OA (IncROA) within 12 months of the injury or surgery (OR (95%CI) = 7.66 (3.14-18.69) and 34.81 (5.20-233.07), respectively), but whether there are associated changes on knee MRI is unknown.

OBJECTIVE: We utilized data from the Osteoarthritis Initiative (OAI) to examine the association of new reports of knee injury or knee surgery after the baseline visit with MRI changes in the 12 months prior to the development of IncROA (i.e. defined by the presence of definite osteophytes).

METHODS: The OAI participants in this nested case-control study had risk factors for OA, but did not have definite ROA as yet in the target knee (i.e., baseline KLG of 0 or 1). Participants were assessed by knee radiographs using the OAI protocol. Case knees were those that developed definite ROA (i.e., KLG≥2) on knee radiographs at the 12 months through 48 months annual visits. New knee injury or knee surgery was based on reports of knee injury or knee surgery in the 12 months prior to the development of IncROA. Knee MRIs were read using MOAKS. Logistic regression was used to estimate the odds ratios (OR) of worsening MRI features associated with new injury or surgery over this 12-month period compared to incROA knees with neither injury or surgery. Models were controlled for baseline BMI and history of hand OA as well as the correlation of bilateral knees within an individual, as appropriate.

RESULTS: The table below shows the results for worsening of MRI features associated with new knee injury or surgery in the IncROA cases. The cases had a mean age of 60.7 (SD 8.6), 65% female, mean BMI of 28.9 (SD 4.4), 34 with injury only, and 15 with surgery only.

Variable	Effect	aOR*	LowerCL	UpperCL
BMLs (any increase in grade) N=312	Injury only	2.75	1.33	5.69
	Surgery only	4.26	1.29	14.15
BMLs (any increase in # of subregions) N=309	Injury only	2.38	1.13	5.01
	Surgery only	3.11	1.00	9.65
Effusion-Synovitis (any increase in grade) N=309	Injury only	2.33	1.08	5.06
	Surgery only	2.03	0.68	6.08
Hoffa-Synovitis (any increase in grade) N=308	Injury only	1.79	0.49	6.48
	Surgery only	15.41	4.78	49.73
Meniscal damage N=309	Injury only	2.86	1.37	5.98
	Surgery only	13.27	2.48	70.85
Cartilage damage N=314	Injury only	2.64	1.20	5.78
	Surgery only	7.00	1.63	30.02

*IncROA knees with neither knee injury or knee surgery as referent group.

CONCLUSION: New knee injury or knee surgery is associated with increased risk of worsening of MRI features as well as increased risk of IncROA. The highly increased risk for worsening Hoffa-synovitis and meniscal damage may be attributed at least partially to surgery-induced structural changes. These results indicate potential targets for pharmacologic interventions or secondary prevention to prevent the development of ROA in at-risk populations.

SPONSOR: NIH HHSN2682010000 21C Pivotal OAI MRI Analyses (POMA).
DICLOSURE STATEMENT: see affiliations.
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QUANTITAVELY-MEASURED BONE MARROW LESIONS IN THE PATELLOFEMORAL JOINT: DISTRIBUTION AND ASSOCIATION WITH PAIN

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BACKGROUND**:** Patellofemoral joint (PFJ) OA has received little epidemiologic attention despite accounting for the majority of symptomatic knee OA. It is more likely than the tibiofemoral joint (TFJ) to cause knee OA symptoms, and even isolated PFJ OA can cause considerable symptoms (Crossley et al, 2011). Clinically, medial PFJ pain is common (especially in early to moderate OA) despite the long-held belief that the Q-angle and lateral pull of the IT band/vastus lateralis will preload the lateral PFJ.

OBJECTIVE: To investigate the relationship of BML volume and weight-bearing pain for the TFJ and PFJ separately, and describe the medial-lateral distribution of BML in the PFJ.

METHODS: A cross-sectional study was conducted in 115 subjects from the baseline data of the Osteoarthritis Initiative (OAI) Progression Cohort . Sagittal turbo spin echo fat saturated (TSE FS) (0.357 x 0.357 x 3.0 mm, TR 3200ms, TE 30ms) IW MRI were obtained on a 3T Siemens Trio MR system. A reader used software to segment subchondral BMLs in the patella and anterior femur (trochlea).
Primary outcome: segmented volume of BMLs (mm^3) in the patella, trochlear femoris and in the weight-bearing femur and tibia. For the medial and lateral analysis, division was per the MRI Osteoarthritis Knee Score (MOAKS) (Figure 1).
Pain. We used the WOMAC pain sub-scale and defined the primary outcome of knee pain dichotomously as moderate to severe pain (scores 2-4) on any of the 3 weight-bearing (WB) WOMAC pain questions (pain on walking, climbing stairs, standing). Individual questions and the composite WB pain score were tested for their association with BML volume using the Wilcoxon rank sum test. Chi-square tests were used to compare the medial and lateral PFJ for the number of subjects (%) with BML and BML volume.

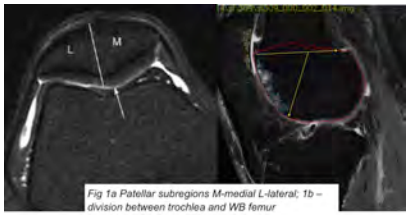

Fig 1a Patellar subregions M-medial L-lateral; 1b – division between trochlea and WB femur

RESULTS: The sample was 84% white, 52% male and were 90% K-L grade 2 and 3. Subjects with weight-bearing knee pain had greater median BML volume than those without for the weight-bearing femur, trochlea femoris and patella, PFJ, but not the tibia. We found an association with greater BML volume and pain during stair-climbing for both the femur, tibia, tibiofemoral and patellofemoral joints, with the difference the greatest in the patellofemoral joint (Table 1). With respect to the distribution of BMLs in the PFJ, prevalence was slightly higher medially, and median BML size was larger (Table 2).

Table 1: Associations of stair-climbing pain[2] with median BML volumes

BML Volume	No Stair Pain (n=58)	Stair Pain (n=57)	p-value[1]
Tibiofemoral	252 mm^3	745 mm^3	0.01
Patellofemoral	44 mm^3	338 mm^3	0.01
Femur (weight-bearing)	0 mm^3	213 mm^3	0.02
Tibia	141 m^3	380 mm^3	0.03

[1] Wilcoxon rank sum test of the differences in medians across pain categories

2 there was no statistically significant relationship with BML volume and walk/stand pain

Table 2 Prevalence and Volume of BML by PFJ compartment

Sub-region	% with BML in sub-region	Median BML size (mm^3)
Medial patella	46	206
Lateral patella	44	285
p-value	0.23	0.41
Medial trochlea	29	424
Lateral trochlea	26	109
p-value	0.01	0.00
Medial PFJ	--	451
Lateral PFJ	--	279
p-value		0.21

CONCLUSION: This cross-sectional study in a sample of baseline OAI subjects provides evidence for a strong relationship between stair-climbing pain and BML volume in knee OA, particularly in the PFJ. Further, PFJ BML volume is least as prevalent medially as lateral. PFJ BML volume may help explain medial PFJ pain, especially in early and moderate disease, have implications for the role of PFJ in OA and be a potential treatment target in early to moderate disease. Further work on the longitudinal relationship between PFJ BML volume and pain is underway.

SPONSOR: None.
DISCLOSURE STATEMENT: None.
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MRI-BASED LONG TERM PREDICITION OF INCIDENT RADIOGRAPHIC OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

[1, 2]Roemer F.W., [3]Kwoh C.K., [4]Hannon M.J., [5]Hunter D.J., [6]Boudreau R., [7]Eckstein F., [4]Fujii T., [2]Guermazi A.

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INTRODUCTION: Pre-radiographic structural damage is likely to increase the risk of incident radiographic osteoarthritis (ROA). It is not known which structural changes allow long-term prediction of incident ROA.

OBJECTIVE: The aim of the study was to assess if presence and severity of structural OA features over up to 4 years prior to the occurrence of incident ROA (time points: P-1 = visit prior reported incidence; P-2 = two visits prior incidence etc.) increase the risk for incident ROA in a nested, matched case-control study in the Osteoarthritis Initiative (OAI) cohort. A secondary aim was if presence at any of these time points increases risk of ROA.

METHODS: Participants were drawn from the OAI including 4796 participants with, or at risk of knee osteoarthritis with visits at regular yearly intervals over 5 years. We studied 355 knees that developed incident ROA before the 60 month visit based on the following definition: either KL 0 in both knees or KL 0 in one knee and KL 1 in the contralateral knee at baseline. They were each matched 1:1 by gender and age within 5 years with a control knee that did not develop incident ROA, with the same KL grade in both knees at baseline. MR images were acquired using 3T scanners. MRIs were read for subchondral bone marrow lesions (BMLs), cartilage status, meniscal integrity (including tears and extrusion), Hoffa- and effusion-synovitis using the MOAKS scoring system. Analyses were performed on a knee and compartmental level considering. Conditional logistic regression was applied to assess the risk of incident ROA in regard to presence of large BMLs (≥2), cartilage lesions (≥ 1.1), meniscal tear or maceration (any), Hoffa- and effusion-synovitis (any) at P-4, P-3, P-2, P-1 or for presence at any of these time points combined.

RESULTS: Subjects were on average 58.6 years old (SD ± 8.5), predominantly female (62.8%) and overweight (mean BMI 28.0 SD ± 4.7). None of the features present at P-4 or P-3 predicted incident ROA. At P-2 only presence of Hoffa-synovitis (OR 2.31 [1.19, 4.48]), and medial meniscal damage (OR 2.44 [1.13, 5.31]), predicted OA incidence 2 year later. At P-1 all features but lateral meniscal damage and any meniscal extrusion predicted incident ROA with odds highest for Hoffa- (OR 2.42 [1.71, 3.42], effusion-synovitis (OR 2.50 [1.76, 3.54] and medial tibiofemoral BMLs (OR 6.50 [2.27, 18.62].
Similar findings were seen for presence of these features at any of the time points with presence of large BMLs (OR 4.62 [2.89, 7.38], effusion-synovitis (OR 3.49 [2.36, 5.15]) and cartilage damage (OR 4.00 [2.20, 7.29] being the strongest predictors.
CONCLUSION: Presence of structural MRI-detected joint damage 3 and 4 years prior incident ROA does not increase risk of ROA. However, one year prior radiographic diagnosis of incident OA presence of almost all joint features increases risk of ROA. When compared to knees that do not show any of the analyzed features during the observational period, knees with presence of MRI features at any of the analyzed time points exhibited an increased risk of ROA. The joint status one-year prior seems to be the most relevant in regard to ROA development.

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ARE DENUDED AREAS OF SUBCHONDRAL BONE RELATED TO LOCALIZED KNEE OR REGIONAL PAIN AS EVALUATED BY THE KNEE PAIN MAP? - DATA FROM THE OSTEOARTHRITIS INITIATIVE

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INTRODUCTION: Denuded areas of subchondral bone (dABs), defined as areas where the subchondral bone was uncovered by cartilage, as visualized on MR imaging have been previously shown to be associated with osteoarthritic (OA) knee pain. Whereas pain intensity or frequency are generally well documented in epidemiological and clinical trials, its precise location around the knee is usually neglected, although potentially informative. The Knee Pain Map (KPM) has been shown to reliably record localized and regional knee pain in individuals with OA, but to date there have been few studies done to relate this tool to structural correlates.

OBJECTIVE: To evaluate the relationship between the presence and size of dABs and locations of pain as indicated on the KPM and thus to provide spatial patterns of structure-pain-correlates in knee OA.

METHODS: 440 participants (244 females, 62.5 ± 9 years, 30.1 ± 4.9 kg/m²) from the Osteoarthritis Initiative (OAI) were included in this study and all information used (data release clinical 2.1 and imaging 3.5.0) were publicly available from the OAI webpage: www.oai.ucsf.edu.org. The inclusion criterion was the availability of a complete data set of the Knee Pain Map and complete data on femorotibial cartilage measures, performed on either the FLASH or the DESS sequences of the 24-month MR knee imaging (Chondrometrics GmbH, Ainring, Germany). Participants used the KPM to identify the presence of localized knee pain in medial or lateral superior, joint line or inferior locations, and of regional knee pain in the medial or lateral part of the knee joint. Localized pain was defined as pain where the location was indicated by pointing with one or two fingers, whereas regional pain was identified by using the whole hand. dABs were measured in the external, central, internal medial and lateral central (weight-bearing) femur (cMF, cLF) and in the anterior, posterior, external, central, internal medial and lateral tibia (MT, LT). A mild dAB was defined as being ≤10% denuded of the size of the respective cartilage plate or subregion and a moderate dAB as >10% denuded. Relationships between the location of mild and moderate dABs and the Knee Pain Map were computed using logistic regression models.

RESULTS: 457 knees were included in the statistical analysis, with KLG0=4, 1=12, 2=182, 3=254, 4=5. Localized pain in the medial joint line was significantly associated with moderate dABs in the external cMF OR 2.02 [95% CI 1.26-3.21] and external MT OR 1.69 [95% CI 1.08-2.67] but not with the internal cMF OR 1.03 [95% CI 0.53-2.01] or with internal MT OR 1.29 [95% CI 0.25-6.77] when compared to those without dABs. **Medial** regional pain was significantly associated with moderate dABs in cMF OR 2.03 [95% CI 1.30-3.19] (mild dAB: OR 1.88 [95% CI 1.10-3.23]) and in MT OR 2.46 [95% CI 1.53-3.95] (mild dAB: 1.37 [95% CI 0.82-2.26]) but not associated with dABs in cLF OR 0.47 [95% CI 0.25-0.89] (mild dAB: OR 0.83 [95% CI 0.52-1.32]) or in LT OR 0.60 [95% CI 0.36-1.00] (mild dAB: OR 0.65 [95% CI 0.41-1.03]) when compared to those without any dABs (=0% denuded). No significant relationships were detected between localized or regional **lateral** pain and dABs in the respective cartilage subregions or plates.

CONCLUSION: This cross-sectional analysis reveals a spatial pattern of structure-pain-relationships in knee OA. Localized pain in the medial joint line was associated with externally located dABs whereas internally located dABs were not. Medial regional pain was associated with dABs in the medial central (weight-bearing) femur but not in the lateral one. This study shows that dABs are significantly related to pain in knee OA with the presence of dABs in specific locations being associated with different knee pain locations.

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KOOS SCORES DIFFER WITH UNI- OR BILATERAL KNEE OA BASED ON MRI

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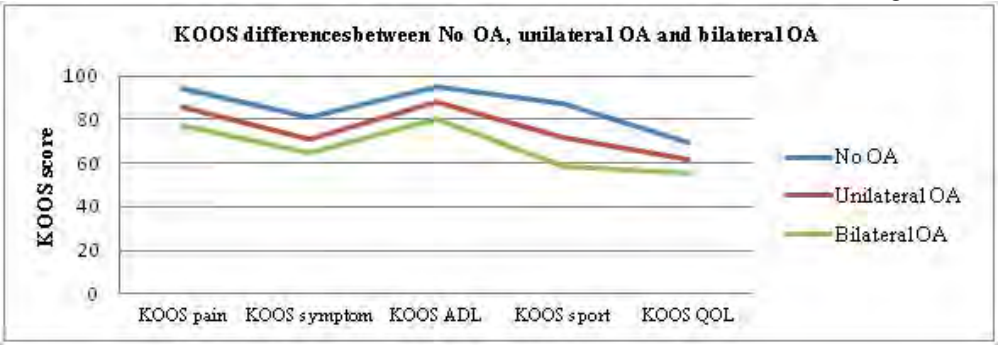
INTRODUCTION: In many OA research with MRIs of the knees analysis are performed on one knee (the most symptomatic knee, the dominant knee or the right knee). OA questionnaires, such as KOOS or WOMAC, are usually recorded on the person level and oftentimes not administered specifically at the knee level.

PURPOSE: To investigate if KOOS scores differ between patients with bilateral knee OA compared to patients with unilateral knee OA and patients without knee OA based on an MRI definition for knee OA.

METHODS: Of 875 females (aged 45-60) from a random subpopulation of the Rotterdam Study, radiographs and MRI of both knees were assessed for knee OA using the Kellgren & Lawrence (KL) classification criteria (0-4) for radiographs and a comprehensive semi-quantitative scoring system (MRI Knee Osteoarthritis Scoring System (MOAKS)) for MRIs. Based on the features scored we applied an MRI definition by Hunter et al. (2011) and distinguished patellofemoral OA (PFOA) from tibiofemoral OA (TFOA). A women had unilateral OA if she had PFOA and/or TFOA in only one knee. Bilateral knee OA was defined as having PFOA and/or TFOA in both knees. All women filled in the KOOS questionnaire. For all subscales of the KOOS (0-100, 100=no symptoms, 0=extreme symptoms) the mean (SD) was calculated separately for women without knee OA, with unilateral knee OA and with bilateral knee OA. With univariate general linear models the differences between the groups was tested for each subscale. All analyses were adjusted for BMI and age. In addition, the analysis were adjusted for KL score (0-4) as a measure for severity of OA.

RESULTS: 696 of the 875 women did not have OA in both knees, 117 women had unilateral OA and 62 women had bilateral OA. The mean (SD) scores for KOOS pain were 94.5 (12.3), 86.0 (19.8) and 76.9 (26.9), respectively. For KOOS symptoms the mean (SD) scores were for women with no OA 81.2 (19.9), for unilateral OA 70.7 (23.0), and 64.7 (20.8) for bilateral OA. The other subscales (KOOS ADL, KOOS sport/rec and KOOS QOL) showed the same trend as can be seen in the Figure. For each subscale the women with no OA scored significantly higher than the women with OA (uni-or bilateral OA). In all subscales, except the KOOS symptoms scale ($p<0.072$), the women with bilateral knee OA had significantly ($p<0.001$) lower scores than the women with unilateral knee OA and women without knee OA. When the analysis was adjusted for OA severity, this lower score was still significant, but the difference between the women without knee OA and unilateral knee OA was not significant anymore.



CONCLUSION: Women with bilateral knee OA have lower KOOS scores for all subscales compared to women with unilateral knee OA and no knee OA. One has to be aware of this when analyzing KOOS questionnaire data obtained for one knee in osteoarthritis research. If we know which factors are related with bilateral knee OA, we can adjust for these factors in the studies with MRIs of only one knee.

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QUANTITATIVE ANALYSIS OF SUBCHONDRAL BONE STRUCTURE IN KNEE OA AT DIFFERENT LEVELS OF SPATIAL RESOLUTION USING CLINICAL WHOLE BODY AND HIGH RESOLUTION PERIPHERAL CT SCANNERS

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INTRODUCTION: Changes of subchondral trabecular architecture may be an important indicator of progress in knee OA, however, the quantification of parameters characterizing trabecular structure in vivo is difficult due to the limited spatial resolution of available CT or MR imaging equipment.

OBJECTIVE: To investigate the use of texture parameters to quantify OA related changes of subchondral trabecular architecture in whole body clinical QCT (wb-QCT) scans and to compare with results obtained from high-resolution peripheral quantitative computed tomography (hr-pQCT).

METHODS: 57 osteoarthritic (OA) human knees from 32 cadavers (18 females (83±8 years), 14 males (79±11 years) were scanned with wb-QCT using a slice thickness of 0.5 mm and an in plane pixel size of 250 µm² (Siemens Sensation 64) and with high resolution peripheral QCT (hr-pQCT) with an isotropic voxel size of 82 µm³ (Scanco XtremeCT). Wb-QCT analysis was performed using MIAF-Knee software [1]. Highly automatic 3D segmentation and registration processes together with automatic positioning of 3D analysis volumes of interest (VOIs) ensured the calculation of BMD and texture parameters at the same anatomical locations in CT and hr-pQCT datasets.

RESULTS: Eight VOIs each were positioned in the epiphysis of the femur and tibia (medial and lateral cortical, subchondral, mid epiphyseal and juxtaphyseal locations). Dice ratios (>0.978) showed that the accuracy of VOI locations between the two CT methods was excellent. As a result BMD in all VOIs did not differ between wb-QCT and hr-pQCT ($p < 0.001$, $R^2 > 0.996$). Absolute values of texture parameters depend on spatial resolution, thus there was a bias between wb-QCT and hr-pQCT analyses. However, in the tibia and femur entropy, global inhomogeneity and anisotropy of the trabecular structure showed significant and highly linear correlations ($p < 0.01$, $R^2 > 0.68$) between wb-QCT and hr-pQCT for all analysis VOIs, i.e. differences among texture values measured with wb-QCT were similar to differences measured with hr-pQCT.

CONCLUSION: The results indicate that texture parameters obtained in vivo from wb-QCT images should be usable to characterize changes of the subchondral trabecular architecture under OA progression. The measurements described above were confirmed by simulations using a digital bone model of trabecular structure (results not shown here) and are currently further evaluated using µCT scans of bone cores obtained from the cadavers of this study.

[1] Zerfass P. et al. (2012). An integrated segmentation and analysis approach for QCT of the knee to determine subchondral bone mineral density and texture. IEEE Trans Biomed Eng 59: 2449-58.

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DISCLOSURE STATEMENT: none.
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3D MRI BASED ANALYSIS OF THE KNEE SHAPE IN PATIENT WITH ACL INJURIES

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INTRODUCTION: Recent literature shows a growing interest in the role that bone shape plays in the development of osteoarthritis. Statistical Shape Modeling (SSM) is a state-of-the-art method for bone shape characterization. The potential of SSM, coupled with the three-dimensional nature of MR imaging, allows for the analysis of the complex shape of the bones of the knee joint.

OBJECTIVE: Anterior cruciate ligament (ACL) injury has been shown to predispose patients to early-onset osteoarthritis. The aim of this work is to apply SSM to MRI in order to analyze the shape of the tibia and femur in patients with ACL injuries to examine for shape differences between control and injured groups.

METHODS: Bilateral knees were scanned using a 3 Tesla MRI scanner (GE Healthcare) with an 8-channel phased array knee coil (Invivo) for: 50 patients with ACL injuries prior to surgical reconstruction (age = 29.6± 8.28 years, 21 female) and 19 control patients with no history of knee injuries (age = 31.33 ± 4.42 years, 7 female). The protocol include T_2 fast spin-echo (FSE) images with TR/TE = 4000/49.3 ms, slice thickness of 1.5 mm, slice spacing of 1.5 mm, pixel size of 0.39 by 0.39 mm. The tibia and femur are segmented semi-automatically. The Statistical Shape Model is extracted individually on the segmentation of tibia and femur to be invariant to the relative position of the joint. Landmarks are defined in a fully automatic fashion with a vertex-to-vertex correspondence algorithm based on the local curvature features. The PCA of the covariance matrix of the landmark 3D coordinates is used to extract a brief signature of the shape. The first 20 modes, which represent more than the 90% of the entire variability, were analyzed. The difference in mode values between injured, control and contralateral knees are considered. Unpaired t-tests were used to compare injured and control knees; paired t-tests were used to compare injured and contralateral knees. Statistical significance was determined at an alpha of 0.05. The physical meaning of the significant modes are investigated by creating new synthetic instances and changing the value of each mode from the mean to mean ± 3 standard deviations (SD).

RESULTS: The 2nd mode for the femur in the control group was 338.26 ± 81.16, which was significantly different compared to both injured (276.94 ± 80.73, P 0.001) and contralateral knee (289.36 ± 80.05, P 0.008) Moreover, significantly difference was found between injured and contralateral knee (P 0.03). The value of this mode is related to internal rotation of the lateral femoral condyle, which results in a relative narrowing of the intercondylar notch. The 3rd mode for the tibia in the control group was 275.53 ± 38.36, which was significantly different compared to both injured (311.51 ± 39.48, P 0.00002) and contralateral knee (315.39 ± 43.15, P 0.00001). There were no significant differences observed between the injured and contralateral knees for this mode. The value of this mode is related to an elevation of the medial tibiae plateau that causes an increase in the posterior tibia slope.

DISCUSSION: Our experiments show that there are significant shape differences between the ACL-injury knees and control knees at baseline, suggesting a common shape feature that may predispose these knees to injury. There are multiple conflicting reports on the narrowing of the intercondylar notch and posterior tibial slope as potential risk factors for ACL injury. These complex shape differences may be clarified using this current methodology with automatic landmark identification.

CONCLUSION: Bone shape quantification has the potential to identify specific risk factors for injuries and to describe novel imaging markers for the development of post-traumatic OA after an acute injury.

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MR T1ρ & T2 OF MENISCUS AFTER ACUTE ANTERIOR CRUCIATE LIGAMENT INJURIES

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INTRODUCTION: Acute anterior cruciate ligament (ACL) injury is a high risk factor for the development of post-traumatic osteoarthritis. Although cartilage changes in such cases have been documented, less research has been conducted on magnetic resonance (MR) quantitative evaluation of meniscal changes following acute ACL injuries.

OBJECTIVE: The goal of this study was to evaluate changes in meniscal T1ρ and T2 quantification in patients with acute ACL injuries and to determine correlations of these changes to MR clinical grading and patient-reported outcomes.

METHODS: Nineteen control subjects (age = 30.9 +/-4.8 years; 6 females) and 53 patients with acute ACL injuries (age = 29.6 +/-8.5 years; 22 females) were scanned using a 3T MR scanner. Injured patients were scanned post-injury and prior to ACL reconstruction. Patients completed the Knee Injury and Osteoarthritis Outcome Score (KOOS), a validated self-assessed questionnaire with five categories: pain, other symptoms, function in sport and recreation, function in daily living (ADL), and knee-related quality of life (QOL). Imaging protocol included sagittal T2-weighted 3D fast spin-echo images (CUBE) and sagittal 3D T1ρ and T2 quantification sequences. Modified whole-organ magnetic resonance imaging scores (WORMS) were determined using CUBE images. Menisci were segmented semi-automatically using CUBE images into four sub-compartments: anterior horn of the lateral/medial meniscus (AHLAT/AHMED) and the posterior horn of the lateral/medial meniscus (PHLAT/PHMED). These regions of interest (ROI) were overlaid onto T1ρ and T2 maps, and mean T1ρ and T2 values were calculated for each ROI. Paired t-tests were performed when comparing injured knees to contralateral (contra) knees; unpaired t-tests were performed when comparing injured knees to the control group; and Spearman correlation coefficients were calculated between meniscal T1ρ/T2 values and WORMS/KOOS. An alpha of less than 0.05 was considered significant.

RESULTS: Mean T2 values were significantly higher in injured knees compared to control knees in all four sub-compartments ($p < 0.003$) and were especially higher in the PHLAT ($p = 8.5e-7$). T2 values were also significantly higher in the AHLAT, PHLAT, and PHMED of injured knees compared to contra knees ($p < 0.02$). Mean T1ρ values were significantly higher in injured knees compared to control knees in the AHLAT, AHMED ($p < 0.02$), and especially in the PHLAT ($p = 0.00009$), as well as significantly higher in injured knees compared to contra knees in the PHLAT ($p = 0.007$). Injured knees without meniscal tears (WORMS = 0 or 1) had significantly higher T2 values compared to control knees in the AHLAT, AHMED ($p < 0.05$), and especially in the PHLAT ($p = 0.013$). Injured knees without meniscal tears also had significantly higher T2 values compared to contra knees in the AHLAT and AHMED ($p < 0.05$). Mean T1ρ values were significantly higher in injured knees without meniscal tears compared to control knees in only the PHMED ($p = 0.02$), but did not reach significance in comparison with contra knees ($p = 0.07$). There was a significant positive association between meniscal WORMS and T1ρ/T2 values of ACL-injured knees in both the PHLAT and PHMED ($p < 0.05$). Significant negative associations were found in the PHLAT between KOOS and T2 for pain and ADL ($\rho = -0.23, -0.35$) and between KOOS and T1ρ for ADL and QOL ($\rho = -0.25, -0.26$).

CONCLUSION: This study found that acute ACL injuries lead to significantly increased T1ρ and T2 values in the meniscus. We observed a particularly significant association between meniscal damage and elevated T1ρ and T2 measurements in the PHLAT. Interestingly, significantly elevated T1ρ and T2 values were also found in ACL-injured knees without meniscal tears compared to controls, indicating that quantitative MR imaging is more sensitive than clinical imaging in detecting composition damage in the meniscus. We also observed that T1ρ and T2 values increase with the severity of meniscal damage (increased WORMS) in acute ACL injuries. A negative association between T1ρ/T2 values and KOOS suggest a notable relationship between meniscal damage and patient reported outcomes following acute injuries. We are currently following up on these patients to evaluate the longitudinal composition changes of meniscus after ACL injury and reconstruction.

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ASSOCIATION BETWEEN MEASUREMENTS OF JOINT SPACE WIDTH ON STANDING CT AND WORMS CARTILAGE MORPHOLOGY

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INTRODUCTION: Because plain radiographs capture a 3D structure in 2D, patient positioning has a large impact on the apparent joint space width (JSW), and the resulting variations can cause substantial measurement imprecision. Nearly half of knees, graded as "completely normal" using radiographs, in fact have at least partial-thickness cartilage loss. In addition, on direct visualization with arthroscopy, many knees graded as "normal" based on radiographs have severe cartilage loss (false negatives), and those with "tibiofemoral JSW loss" frequently have normal articular cartilage (false positives). A more ideal imaging biomarker would correlate more closely with cartilage morphology. While radiographic measurements are limited by overlapping anatomy, 3D imaging enables an unencumbered view of the joint-space, potentially improving reliability and obviating the need for separate image acquisitions at multiple beam angles. If JSW from low dose, standing CT (SCT) validly reflects cartilage morphology, the cost and duration of knee OA clinical trials could be reduced through enabling more reliable baseline grading of disease status.

OBJECTIVE: To assess the association between medial tibiofemoral JSW measured on 3D SCT and WORMS cartilage morphology scores.

METHODS: This study was conducted ancillary to the 84-month visit of the Multicenter Osteoarthritis (MOST) Study, an NIH-funded longitudinal observational study of 3026 community-dwelling men and women age 50-79 with knee OA or known risk factors for knee OA. Participants were eligible if they lived near Iowa City and they had bilateral, standing fixed-flexion knee radiographs in the prior 6 months, knees discordant for KL grade (to include a range of joint space), neither knee with KL grade 4, and distal thigh width on PA radiographs that did not exceed the 38.1cm SCT gantry width. Out of 83 participants who met inclusion criteria, the first 20 volunteers were enrolled. For SCT, a commercial scanner (PedCAT, Curvebeam LLC, Warrington, PA) was modified to enable imaging of knees in a standing fixed-flexion configuration. A custom radiolucent positioning system was used to maintain foot external rotation and fixed knee flexion angles, with participants' thighs and hands contacting the unit for stability and prevention of motion. The scanner produced pulsed cone-beam x-ray (effective dose equivalent 0.1 mSv) on a 30x30 cm amorphous silicon flat-panel detector (194µm pixel size) over a 360° projection angle with a total scan time of 32 seconds. A 3D axial CT dataset with isotropic resolution of 0.37 mm and FOV of 200x350 mm (768x768 matrix) was reconstructed from initial cone-beam projection images. Medial tibiofemoral JSW was assessed on fixed flexion SCT by measuring the shortest distances between points on the tibiofemoral bony articular margins following semi-automated segmentation of 3D SCT image data (Figure 1). Knee MRI was completed using a 1-Tesla ONI OrthOne extremity MRI scanner (GE Healthcare, Waukesha, WI). Experienced radiologist assessed the medial tibiofemoral cartilage morphology on sagittal proton density-w fat-sat and coronal STIR sequences using the WORMS system (0–6).

RESULTS: Lower JSW on SCT corresponded with worse cartilage morphology scores. Figure 2 depicts JSW for 3 examples and the WORMS scores for those medial compartments.

CONCLUSION:
Lower JSW as determined from SCT appears to correspond with the presence and severity of partial and full thickness cartilage lesions in the medial tibiofemoral subregions as determined by semi-quantitative MRI.

Figure 1: Tibiofemoral JSW (mm) 3D Views

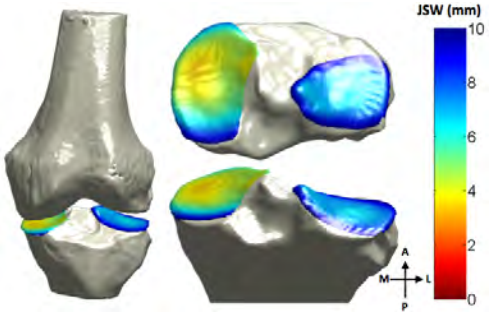
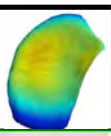
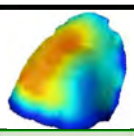
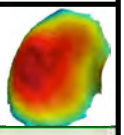


Figure 2: Examples of Medial Tibiofemoral JSW and Medial Compartment WORMS Cartilage Morphology

WORMS Region			
Central Femur	0	3	5
Posterior Femur	0	0	3
Central Tibia	0	3	6
Posterior Tibia	0	0	0

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AUTOMATED ALGORITHM FOR 3D MR SEGMENTATION AND SUB-PLATE DETECTION IN 3D MRI - DATA FROM THE OSTEOARTHRITIS INITIATIVE

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INTRODUCTION: Quantitative 3D analysis of cartilage thickness in specific regions of clinical interest is of utmost interest. With specific cartilage locations showing higher rates of change (e.g., the central weight bearing region), quantitative analysis justifies reducing the numbers of subjects in clinical, drug, and population studies. When performed manually, segmentation and quantitative analysis of knee-joint cartilages requires hours per dataset. Automated segmentation/analysis of knee-joint cartilages is challenging because of their complex anatomy, the presence of osteophytes, tissue thinning, cartilage surface fibrillation, and artifactual or real changes in image intensity.

OBJECTIVE: Our goal is to develop an automated approach for segmentation of bone and cartilage of the knee imaged with 3T MR, providing high analysis accuracy of cartilage sub-plates.

METHODS: Using the OAI progression cohort, OAI-acquired sagittal 3D DESS sequences of 88 knees from baseline (V00) and 12-month follow-up (V01) visits were segmented and analyzed using our graph-based LOGISMOS algorithm with steerable features and used for performance evaluation (total of 176 3D MR datasets). Our fully automated approach consists of two key steps: 1) construction of a graph topologically corresponding to the knee bone/cartilage anatomy, and 2) learning appropriate cost functions for each graph nodes from manually-defined segmentation examples utilizing probability output of a trained random forest classifier. Once applied to previously unseen image data, the resulting segmentation is represented by surface meshes for femur and tibia bones and cartilages, on which MF, 60% cMF, LF, 60% cLF, Tibia Plate, MT, and LT sub-plates are automatically identified. Performance of the reported approach was validated against manually-defined iMorphics independent standard using signed and unsigned surface positioning and cartilage thickness errors.

RESULTS: Segmentation failed in 4 cases. In the remaining 172 datasets, signed and unsigned surface positioning and thickness errors in sub-plates showed minimal bias and sub-voxel per-surface accuracy.

Plate Name	Signed cartilage thickness error [mm]	Signed bone surface positioning error [mm]	Signed cartilage surface positioning error [mm]	Unsigned cartilage thickness error [mm]	Unsigned bone surface positioning error [mm]	Unsigned cartilage surface positioning error [mm]
LF	-0.05 ± 0.15	0.21 ± 0.15	0.10 ± 0.21	0.10 ± 0.21	0.30 ± 0.13	0.43 ± 0.15
MF	-0.15 ± 0.18	0.24 ± 0.23	0.05 ± 0.22	0.19 ± 0.14	0.34 ± 0.19	0.51 ± 0.19
60 % cLF	-0.17 ± 0.14	0.10 ± 0.11	-0.04 ± 0.21	0.19 ± 0.11	0.22 ± 0.07	0.36 ± 0.15
60 % cMF	-0.23 ± 0.18	0.18 ± 0.32	-0.03 ± 0.25	0.25 ± 0.16	0.32 ± 0.27	0.45 ± 0.18
Tibia Plate	-0.13 ± 0.15	0.11 ± 0.23	0.04 ± 0.19	0.16 ± 0.11	0.30 ± 0.18	0.50 ± 0.13
LT	-0.12 ± 0.17	0.09 ± 0.27	0.02 ± 0.21	0.17 ± 0.13	0.29 ± 0.23	0.44 ± 0.13
MT	-0.13 ± 0.18	0.12 ± 0.27	0.05 ± 0.28	0.18 ± 0.14	0.30 ± 0.22	0.55 ± 0.18

CONCLUSION: The results presented above demonstrate that completely automated quantitative knee-joint sub-plate analysis is possible with high accuracy. Analysis of the remaining sub-plates and further improvements of the overall performance of the method are the goal of future work.

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CHANGES IN DELAYED GADOLINIUM-ENHANCED MRI OF TIBIOFEMORAL CARTILAGE (dGEMRIC) INDICES ARE NOT ASSOCIATED WITH CARTILAGE LOSS OVER 1 YEAR: A LONGITUDINAL 3.0T MRI STUDY

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INTRODUCTION: The dGEMRIC technique is capable of detecting early changes in the glycosamoniglycan content of cartilage, which may potentially lead to changes in cartilage morphology. To date, there is no strong evidence that changes in dGEMRIC indices over time are associated with progression of cartilage damage in the knee joint.

OBJECTIVE: To assess the associations of baseline dGEMRIC as well as changes in dGEMRIC indices with cartilage loss in the same region of the knee over one year, in a sample of middle-aged women.

METHODS: A total of 140 women (1 knee per subject) aged ≥ 40 years were prospectively included. 3.0T MRI of the knee was performed at baseline and at one year follow-up. T2-weighted fat-suppressed sequences were used to assess cartilage morphology using the BLOKS scoring system. A 3D inversion recovery-prepared SPGR sequence 90 minutes after i.v. gadolinium injection was acquired for dGEMRIC assessment. Cartilage morphology and dGEMRIC were assessed at baseline and follow-up MRIs in four distinct regions of tibiofemoral compartments: medial femur, medial tibia, lateral femur, and lateral tibia. A decrease in dGEMRIC indices over one year was considered as the predictor of cartilage loss (considered here as any increase of grade in BLOKS – outcome). The association of any decrease in dGEMRIC indices from baseline to follow-up with cartilage loss in the same region was assessed using logistic regression. In addition we used the maximal statistical approach to determine at which cut-off value baseline dGEMRIC would be most predictive for cartilage loss after one year.

RESULTS**:** A total of 433 regions were included in the analyses; 25 (5.8%) had cartilage loss over one year and 408 (92.2%) did not. Furthermore, 153 (35.3%) regions had a decrease in dGEMRIC indices over one year and 280 (64.7%) did not. No significant associations between change in dGEMRIC indices over time and cartilage loss were observed. A cut-off value of dGEMRIC predicting cartilage loss could not be established.

CONCLUSION**:** The predictive effect of changes in dGEMRIC on cartilage loss in the tibiofemoral compartments over one year could not be demonstrated in this sample of middle-aged women.

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MRI PREDICTS FUTURE JOINT SPACE NARROWING AND DEVELOPMENT OF EROSIVE DISEASE 5 YEARS LATER IN PATIENTS WITH HAND OA

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INTRODUCTION: Hand OA is usually a slowly progressing disease. Some patients show more rapid progression and/or development of erosions, leading to considerable pain and disability. Currently, we have limited evidence for predictors for hand OA progression. MRI can visualize the whole joint, providing valuable information about inflammatory and structural features. Due to lack of longitudinal hand OA studies, in which MRI has been obtained, it is unknown whether MRI can predict radiographic progression.

OBJECTIVE: To examine whether MRI features can predict 1) Radiographic progression (defined as narrowing of the joint space) and 2) Development of erosions 5 years later in patients with hand OA.

METHODS: We included 74 patients (67 women) from the Oslo hand OA cohort with a mean (SD) age of 67.9 (5.3) years. They underwent MRI of the 2nd-5th interphalangeal joints of the dominant hand at baseline (2008-09) and hand radiographs at baseline (2008-09) and follow-up (2013). Pre-and post-Gd T1w fat-suppressed images and Short Tau Inversion Recovery (STIR) images were obtained in an 1.0 T extremity scanner. Eight patients had no post-Gd images, and additionally one patient had STIR images only. The MRIs were scored according to the Oslo hand OA MRI score (Haugen. ARD 2011;70:1033), whereas the paired hand radiographs (known time sequence) were scored according to the OARSI atlas for JSN (0-3 scale) and erosions (absent/present). Radiographic progression was defined as increased JSN score during follow-up in joints with JSN grade 0-2 at baseline. Using Generalized Estimating Equations, we evaluated whether MRI features at baseline could predict radiographic progression in the same joint (separate models for each MRI feature). The analyses were adjusted for age, sex, BMI and follow-up time. We repeated the analyses using erosive evolution (incident erosions in joints free of erosions at baseline) as the dependent variable with additional adjustment for the number of other erosive finger joints. Due to erosive evolution in women only, 7 eligible men were excluded.

RESULTS: Mean (SD) follow-up time was 4.6 (0.4) years. The 74 patients had 507 eligible joints with baseline JSN$\leq$2 (n=85 joints with baseline JSN=3 excluded), of which 86 (17.0%) showed radiographic progression during follow-up. The majority of joints with progression had one grade increase of JSN score. In the crude regression analyses, moderate/severe synovitis, JSN and BM lesions at baseline could predict increasing JSN score during follow-up (data not shown). In the adjusted analyses, the associations remained statistically significant for moderate/severe synovitis (OR=3.52, 95% CI 1.29-9.59), JSN (grade 1: OR=2.70, 95% CI 1.22-5.98, grade 2: OR=4.60, 95% CI 2.02-10.49, grade 3: OR 11.05, 95% CI 3.22-37.90), BM lesions (OR=2.73, 95% CI 1.29-5.78) as well as cysts (OR=2.98, 95% CI 1.04-8.53). A dose-response relationship was found for synovitis and JSN. For synovitis, only moderate/severe synovitis was associated with increasing JSN score. Due to few joints with moderate (n=5) and severe (n=9) BM lesions, a dose-response relationship could not be explored. Erosive evolution appeared in 40 of 438 (9.1%) joints that were non-erosive at baseline. In the crude regression analyses, the majority of MRI features could predict development of erosions (data not shown). In the adjusted analyses, significant associations were found for moderate/severe synovitis (OR 4.83, 95% CI 1.35-17.24), BM lesions (OR 5.61, 95% CI 2.05-15.38) and severe JSN (OR 9.16, 95% CI 3.76-22.32, joints with JSN grade 0-1 as reference). Furthermore, features of bone damage (i.e., erosions and attrition) as well as osteophytes could significantly predict erosive development (data not shown). Malalignment, which was not associated with increasing JSN, was the strongest risk factor for erosive evolution (OR=10.18, 95% CI 2.01-51.64).

CONCLUSION: For the first time, we were able to show that synovitis, BM lesions as well as JSN could significantly predict radiographic progression after 5 years in terms of narrowing of the joint space as well as erosive evolution in the finger joints in patients with hand OA. In addition, malalignment was the strongest risk factor for erosive evolution. Our results suggest that both inflammation, biomechanical factors and bone remodeling are involved in the progression of hand OA. MRI-defined erosions/attrition could predict future radiographic erosions, suggesting that MRI detects bone damage earlier than conventional radiographs.

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STRUCTURAL SURVIVAL OF THE KNEE JOINT FIVE YEARS AFTER JOINT DISTRACTION

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INTRODUCTION: Joint distraction has shown to cause clinical improvement in knee OA, a substantial increase in ThCtAB on MRI and restoration of JSW on weight-bearing x-rays (Intema, 2011, ARD; 70:1441-, Wiegant, 2013, OAC; 21:1660-). The duration of these beneficial effects are yet unclear. The goal of joint distraction is to postpone a total knee prosthesis (TKP).

OBJECTIVE: The aim of the study is to evaluate to what degree this was accomplished 5 years after distraction. Secondary objective was to evaluate whether the initial increase of cartilage thickness on MRI and of JSW on x-ray observed over the first 2 years persist at 5 years follow-up?

METHODS: Twenty patients, eligible for TKP based on symptoms and radiological sign of OA, were treated with 5-millimeter joint distraction by use of an external fixator for 8 weeks. At yearly follow-up, clinical outcome was represented by survival of the knee joint (postponement of TKP) and the WOMAC. ThCtAB was quantified on MRI and change in minimum (min) and mean JSW on standardized semi-flexed x-rays. In a selected group of patients from the OAI, matched for KLG at BL, the 'natural course' in ThCtAB, min and mean JSW were determined (Eckstein, 2012, OAC; 20:1250-; Wirth, 2013, OAC; 21:117-). The linear decrease was extrapolated to 5 years to calculate the expected ThCtAB, min and mean JSW if no joint distraction would have been applied.

RESULTS: Survival of the knee joint in the 20 patients (age 49 ±6; mean ± SD) was 80% at 5 years, 1 patient had received a TKP 4 years after distraction and 3 patients after 5 years. A significantly higher total WOMAC (100 being the best) indicated persistent clinical benefit (mean, 43.9±14.8 at BL to 62.6±26.8 at 5 years; p=0.004). The min JSW of 1.16±1.22mm at BL significantly increased to 1.70±1.38mm at 5 years. The maximum increase in min JSW was reached at 1 year (+0.56±0.93mm) and maintained over time (+0.53±0.77mm at 5 years). The change in min JSW in 560 OAI patients, showed a decrease over 2 years of 3,0 or 9,1%, for KLG 2 and 3, respectively. Extrapolating this, minimal JSW at 5 years of follow-up in case of no treatment would be 1.01±1.07mm, which is significantly different from the registered 1.70±1.38 mm at 5 years (p=0.001). The mean JSW of 2.58 ±1.58mm at BL showed an increase at 1 year up to 3.18 ±0.95mm. This diminished over time, being 2.86±1.48mm at 5 years (p=0.335). The decrease in mean JSW for the OAI patients was over 2 years 3,3 or 7,9% for KLG 2 and 3, respectively (2). Extrapolating these results, a mean JSW of 2.24±1.43mm would be expected, which is statistically different from the observed 2.86±1.48mm (p=0.034). The change in ThCtAB corroborated this. An initial significant increase from 2.32±0.58mm to 3.08±0.73 at 1 year (p=0.003) in the most affected compartment (18 medial, 2 lateral) was at 5 years of follow-up 2.47±0.64mm (p=0.393). The change in ThCtAB in the OAI patients, showed a decrease of 2,8 or 9,1% for medial and lateral compartment, respectively. Extrapolating these results, 2.09±0.56mm would be expected at five years of follow-up, which is significantly different from the observed 2.47±0.64mm (p=0.048).

CONCLUSION: TKP can be postponed for 5 years in 80% of young OA patients. Significant clinical benefits as well as an increase in ThCtAB and JSW were present after 5 years. The effects were not as strong as previously observed 1 and 2 years after treatment, they still represented a significant structural benefit compared with OAI participants who did not receive this type of treatment. Therefore, joint distraction has great potential to effectively postpone TKP in a patient group lacking alternative treatment.

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COMPARING RADIOGRAPHS AND MRI FOR THE PREDICTION OF INCIDENT KNEE OA AND KNEE PAIN IN OVERWEIGHT AND OBESE WOMEN AFTER 30 MONTHS

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INTRODUCTION: Traditionally, knee OA is diagnosed using radiographs. MRI techniques enable visualization of soft tissues in and around the knee joint and hence can show OA changes in the early phase of the disease before changes on radiographs are visible. Therefore, MRI might be more sensitive than radiographs for the identification of subjects at risk of OA development.

OBJECTIVE: To evaluate 1) the presence of tibiofemoral OA on MRI (TF MRI OA)in a high-risk cohort of middle-aged overweight and obese women without clinical and radiological signs of knee OA at baseline, 2) the association between TF MRI OA at baseline and the incidence of clinical and radiological signs of knee OA in this cohort and 3) compare this to the association between baseline KLG1 and incidence knee OA in this cohort.

METHODS: Data of the PROOF study were used. From this preventive RCT among a high-risk group of middle-aged women with a BMI $\geq$ 27 kg/m^2 and without signs of clinical (ACR-criteria) and radiographic (KLG 0 or KLG 1) knee OA, we selected all 620 knees of 329 women with complete follow-up data. At baseline and after 30 months, a standardized semi-flexed AP radiograph and a 1.5 Tesla MRI (coronal and sagittal PD-weighted, coronal T2-weighted SPIR, axial dual spin-echo, and sagittal 3D WATS sequence with fat saturation) were made of both knees of all participants. All participants filled-in a questionnaire regarding knee complaints, and physical activity and underwent a physical examination of both knees. Using Generalized Estimating Equations, the association between the presence of TF MRI OA at baseline (Hunter et al. 2011) and the incidence of KLG$\geq$2, clinical knee OA (ACR-criteria), radiographic JSN $\geq$ 1.0 mm., and presence of chronic pain at follow-up was evaluated. These analyses were repeated using the presence of KLG1 at baseline as independent variable. All analyses were adjusted for significant baseline between-group differences.

RESULTS: Mean age was 55.7 ± 3.2 years and mean BMI was 32.0 ± 3.9 kg/m^2. In total, 70 knees (11%) fulfilled the definition for TF MRI OA at baseline. Knees with TF MRI OA at baseline had significantly higher rates of previous knee injuries, Heberden nodes, KLG1, mild symptoms, and MRI OA in the patellofemoral joint. Compared to knees without TF MRI OA, those with TF MRI OA only had significantly more incident KLG$\geq$2 during follow-up (21% vs. 3%), with an adjusted odds ratio (OR) of 4.7 (95%-CI: 2.0-11.0). Knees with KLG1 at baseline only showed significantly more incident clinical knee OA (10% vs. 1%) and chronic pain (10% vs. 4%), with adjusted OR of 8.0 (95%-CI: 2.7-24.0) and 2.8 (95%-CI: 1.2-6.3) independent of the presence of TF MRI OA at baseline.

CONCLUSIONS: Amongst middle-aged overweight and obese women without clinical and radiographic knee OA, a relatively high number of knees fulfilled the criteria of TF MRI OA (11%). The presence of TF MRI OA at baseline significantly increased the risk for incident radiographic knee OA after 30 months. Contrary to TF MRI OA, the presence of 'doubtful knee OA' on radiographs (KLG1) did predict the incidence of clinical knee OA and chronic pain. For the selection of people at high risk of developing knee OA, for instance for preventive trials, fulfilling the definition of TF MRI OA or KLG1 seems to distinguish different subgroups.

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ASSOCIATION OF ULTRASONOGRAPHY WITH RADIOGRAPHY AND KNEE PAIN IN KNEE OSTEOARTHRITIS

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INTRODUCTION: Knee ultrasonography (US) allows dynamic visualizing of several joint structures involved in knee OA, such as articular cartilage (AC) and marginal osteophytes. Knee pain has multifactorial origin and its association with current gold standard OA imaging modality, i.e. radiography, is highly controversial. Therefore, further studies of relationship between pain and other imaging modalities, such as US, are needed.

OBJECTIVES: 1) To investigate the relationship between semi-quantitative and quantitative US findings and radiographic KLG in symptomatic patient group. 2) To investigate the association between US findings and knee pain in symptomatic patient group and asymptomatic subjects.

METHODS: Patients (n=60, age=59.6±8.4, range=34-70) suffering from knee pain and asymptomatic controls (n=27, age=41.2±13.4, range=24-62) were included into the study. Patients underwent knee radiography evaluated with KLG system. A dynamic US examination of the knee joint was conducted for all subjects. US semi-quantitative grading was used to grade the OA changes in femoral medial, trochlear and lateral AC, and separate grades were summed into the femoral US grade (FUS; range 0-12). Presence and size of medial-femoral, lateral-femoral, medial-tibial and lateral-tibial osteophytes were evaluated by US osteophyte grading, and separate grades were summed into osteophyte US grade (OST US; range 0-12). Finally, the total US grade (Total US; range 0-24) was calculated as a sum of FUS and OST US grades. The AC in MF was manually segmented from ten consecutive video frames, including OA findings, and mean AC thickness was calculated for a patient subgroup (n=33). Knee pain was evaluated by each individual using WOMAC questionnaire. Spearman's correlation and one-way ANOVA LSD post hoc test were used for statistical analysis.

RESULTS: Strong positive correlations were found between semi-quantitative US grades and KLG (Table 1). Moreover, significant differences (p<0.01) in Total US grade were observed between subsequent KLG grades, except between KLG 0&1. Mean AC thickness in MF had a moderate negative association to KLG with differences between KLG 2&3 (p=0.054) and 3&4 (p<0.001). However, no AC thickness changes between KLG 1&2 were found, which were still detected by semi-quantitative medial US grade (1.1±0.7 vs. 2.0±0.6, p=0.006). The WOMAC pain score within all subjects correlated moderately with Total US, FUS and OST US (0.681, p<0.001; 0.685, p<0.001; 0.637, p<0.001). Weak correlations were found when including patient group only (0.341, p=0.008; 0.396, p=0.002; 0.306, p=0.017) as well as in comparison between pain score and KLG (Table 1).

TABLE 1: RELATIONSHIP (MEAN±SD, SPEARMAN'S RHO - R) BETWEEN US GRADES, PAIN SCORE, AC THICKNESS AND KLG.

	KL 0 n=2	**KL 1** n=14	**KL 2** n=14	**KL 3** n=15	**KL 4** n=15	r
Total US grade	3.0±1.4	4.4±2.7	8.8±2.7	12.3±3.7	16.8±2.9	0.854 (p<0.001)
FUS grade	2.0±0.0	3.2±1.5	5.0±1.5	6.2±1.8	7.1±1.6	0.709 (p<0.001)
OST US grade	1.0±1.4	1.2±1.4	3.7±1.9	6.1±2.6	9.7±1.8	0.860 (p<0.001)
WOMAC pain score	63.2±12.8	24.0±19.2	26.5±15.8	42.4±25.2	45.2±25.3	0.278 (p=0.032)
	n=2	n=7	n=10	n=9	n=5	
Mean AC thickness (mm)	1.63±0.06	1.72±0.47	1.72±0.35	1.35±0.46	0.25±0.33	-0.563 (p=0.001)

CONCLUSION: Our preliminary results showed that the novel semi-quantitative US grading, combining evaluation of femoral cartilage degeneration and osteophyte formation, has a strong relationship with radiographic KLG. However, the absolute measure of AC thickness was not able to identify the early local thickness changes from US images. The association between US grades and degree of knee pain was rather weak in the patient group, however when including non-symptomatic subjects clear positive relationship was observed.

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RISK FACTORS FOR MENISCAL BODY EXTRUSION ON MRI IN SUBJECTS FREE OF RADIOGRAPHIC KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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INTRODUCTION**:** Meniscal body extrusion on knee MRI is strongly associated with the development and progression of knee osteoarthritis (OA). However, there is very limited information about risk factors for the onset and development of meniscal extrusion.

OBJECTIVE: To determine risk factors associated with increased meniscal body extrusion using quantitative measurements on knee MRI in subjects free of radiographic OA at baseline. We hypothesized that body mass index (BMI), sex, age, and incident ipsilateral meniscal tear are possible risk factors.

METHODS: Data for these analyses are from the OAI public use data. A cohort of 340 subjects with age between 45 and 55 (mean age 50 years, 51% women, mean BMI 26.7) with bilateral knee MRIs available at the baseline, 24 months, 48 months, and 72 month exam and no radiological signs of knee OA (both knees' KL grade = 0 at baseline) were selected. We assessed mid-coronal IW 3-Tesla MR images from baseline and the 72 month follow-up visit. One observer measured widths of the tibia plateau, both tibia compartments, meniscal body width and meniscal body extrusion to the closest 0.1 mm using Sante DICOM Editor (64-bit) software. (Intraobserver ICC ranging from 0.75 to 0.99). One reader assessed meniscal integrity (presence of tear) at all four time points. To take into account knee size, we calculated an extrusion index as ([meniscal body extrusion]/[tibia width]*100). We evaluated risk factors for increased meniscal body extrusion index from baseline to the 72-month exam by a multivariable linear regression mixed model for medial and lateral compartment, respectively, adjusting for the fact that the same person contributed with two knees and with the covariates: clinical site, age, sex, baseline BMI a, baseline extrusion index, and incident meniscal tear

RESULTS: Mean (SD) medial extrusion index in the right knee at baseline and 72-month follow-up was 3.43 (1.23) and 3.32 (1.30), respectively (similar values in the left knee). The corresponding values for lateral compartment were 1.54 (1.31) and 1.13 (1.52). In the medial compartment we found that female sex (0.35; 95% confidence interval [CI] 0.16-0.53), incident meniscal tear (0.29; 95% CI 0.22-0.55), and the baseline value of the extrusion index (0.63; 95% CI 0.56-0.70) were associated with increased extrusion index by the 72 month follow-up. Results were similar for the lateral compartment (data not shown).

CONCLUSIONS: Female sex, incident meniscal tear, and higher baseline value of extrusion appear to be risk factors for increased meniscal body extrusion in subjects free of radiographic OA.

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LONGITUDINAL ANALYSIS OF THIGH MUSCLE, SUBCUTANEOUS AND INTERMUSCULAR ADIPOSE TISSUE AREA IN KNEES WITH CHRONIC PAIN

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INTRODUCTION: Reduced thigh muscle strength and (anatomical) cross-sectional areas (CSAs) have been associated with increased knee pain. However, longitudinal rates of change in muscle mass in chronically painful (vs. painless) knees have not been reported. Further, adipose tissue is thought to play an endocrine role in the pathophysiology of knee OA and increase in local fat has been associated with reduced limb function. Yet, to what extent longitudinal change in muscle mass in painful limbs is associated with that in adipose tissue content is unknown.

OBJECTIVE: To determine longitudinal 4-year changes in quadriceps, subcutaneous fat (SCF) and intermuscular fat (IMF) CSAs of the thigh in chronically painful limbs vs. matched limbs without pain.

METHODS: We identified OAI participants with a non-acceptable symptom state (≥4 on numeral rating scale [NRS]) and frequent knee pain (most days of a month) for ≥6 months (of the past year) at each of 3 time points: baseline, year 2 and year 4. As controls, we identified OAI participants with NRS≤1 and no or infrequent pain at each of these time points. Matched pairs (painful vs. painless) were formed based on same sex and limb dominance, and similar age (±5 years), body height (±5cm), BMI (±3), and KLG. Quadriceps, SCF, and IMF CSAs were determined by semi-automated segmentation at 33% estimated femoral length (from distal) using axial non-fat-suppressed T1-weighted 3T spin echo MRIs (TR=600ms, TE=10ms). Paired t-tests were used for cross-sectional comparisons (year 2) and longitudinal comparisons of 4-year changes between chronically painful vs. painless knees. Sensitivity analyses were performed stratifying for women and men.

RESULTS: 79 OAI participants had chronic pain based on the above criteria, and 136 had no pain. Of these, 43 participants with chronic pain (23 women, 20 men; 60.7±9.0 years; BMI 28.1±3.5) could be matched 1:1 with painless controls. There only were small cross-sectional differences between painful and painless limbs at year 2 (Table 1). Painful limbs showed a somewhat greater 4-year decrease in quadriceps CSAs than painless limbs, but the difference did not reach statistical significance (Table 1). Whereas the longitudinal gain in IMF CSA was similar, the gain in SCF was significantly greater in painless limbs (Table 1). The PASE score and its 4-year changes did not differ between chronically painful and painless limbs (Table 1). In chronically painful limbs, the correlation between 4-year change in IMF and SCF was r=0.30 and that of SCF and IMF with body weight change was 0.72 and 0.41, respectively. Correlations of 4-year changes in quadriceps with SCF and IMF CSAs, were r=0.45 and 0.10, respectively.

Table 1. Cross-sectional measures at year 2, and 4-year % changes in chronically painful vs painless limbs

* p< 0.05	Cross-sectional (Year 2)		p-value	Longitudinal		p-value
[mean±SD]	Painful (+P)	Painless (-P)	+P vs -P	Painful	Painless	+P vs -P
Quadriceps CSA (cm^2)	50.4 ± 12.8	52.1 ± 11.7	0.56	-3.9 ± 7.7*	-2.4 ± 5.6*	0.34
Subcut. fat CSA(cm2)	65.5 ± 29.4	64.3 ± 36.1	0.88	+8.1 ± 16*	-0.01 ± 14	0.04
Intermusc. fat CSA (cm^2)	11.0 ± 3.5	10.6 ± 2.7	0.60	+4.6 ± 13	+5.7 ± 14	0.72
Body Weight	80.6 ± 12.2	80.6 ± 14.1	0.99	+1.7 ± 6.8	-0.4 ± 5.6	0.18
PASE	166 ± 75.6	158 ± 82.4	0.48	+1.6 ± 54	-7.4 ± 36	0.38

CONCLUSION: Knees with chronic pain show only marginally greater loss in quadriceps CSAs but a significantly greater longitudinal increase in SCF CSAs than painless limbs. The increase in SCF is more strongly associated with that in body weight than with a local loss in muscle mass. As PASE scores did not differ significantly between painful and painless limbs, the effect of pain on SCF may be mediated by other factors, not related to physical activity levels.

SPONSOR: Image acquisition: OAI; image analysis: PMU FFF (R-13/03/049-RUH).
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WHICH PREDICTORS ARE RELATED TO DEGENERATIVE CHANGES OF THE KNEE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RUPTURE?

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INTRODUCTION: ACL rupture is a well-known risk factor for development of knee OA. Recent studies showed that the risk of OA in patients with isolated ACL injuries is low in contrast to patients with concomitant intra-articular lesions. So, not all patients with ACL rupture will ultimately develop knee OA. Better understanding of the pathophysiology of ACL rupture leading to OA and recognition of predictors may aid in preventing the onset or progression of OA.

OBJECTIVE: The aim of our study was to evaluate which predictors are related to early degenerative changes as assessed on MRI after two years of follow-up in patients with a recent ACL rupture.

METHODS: In an observational prospective follow-up study 154 eligible patients were included within 6 months after ACL trauma and evaluated for 2 years. Inclusion criteria were: age between 18 and 45 years and presence of ACL rupture diagnosed by physical examination and MRI. Patients with previous knee trauma or surgery of the involved knee and those with already osteoarthritic changes on X-ray (KLG > 0) were excluded. Patients were treated operatively or non-operatively and were evaluated with the following measurements: administration of questionnaires, standardized physical examination and MRI assessment. MRI scans were evaluated by a trained MD researcher, experienced in assessment of knee MRIs, according to the description of MRI Osteoarthritis Knee Score (MOAKS). Early degenerative changes were defined as progression of cartilage defects in the tibiofemoral medial (TFmedial), lateral (TFlateral) and patellofemoral (PF) compartment and progression of osteophytes in tibiofemoral (TF) and PF compartment. Potential predictors were extracted from baseline characteristics and monitoring during follow-up. Primary analyses were performed with univariable logistic regression analyses using the defined early degenerative changes as the dependent variables. Potential predictors with p-values < 0.15 were used in the multivariable model. MRI data at baseline and two year follow-up were available for 143 patients with the following baseline characteristics: median age 25.2 (IQR 21.4; 32.6) years; 34.3% female; median Tegner activity score pre-trauma 9 (IQR 7; 9); 85% scored ≥2+ on Lachman test and 58% positive (≥ 1+) pivot shift.

RESULTS: Progression of cartilage defect in TFmedial compartment was scored in 12% (17/143) of patients, in TFlateral in 27% (38/143) of patients, progression of osteophytes in TF compartment in 10% (14/143) of patients and progression of cartilage defect and osteophytes in PF compartment in 3% (4/143) and 8% (11/143) of patients. Progression of cartilage defects in TFmedial compartment was significantly associated with the following predictors: cartilage defect at baseline in TFmedial compartment (OR 3.69, 95% CI 1.05; 13.03, p=0.042), BMLs after one-year follow-up in TFmedial compartment (OR 5.21, 95% CI 1.57; 17.29, p=0.007), presence of medial meniscal tear during 2-year follow-up (OR 7.32, 95% CI 1.41; 38.07, p=0.018). The following predictors had a significant relationship with progression of cartilage defects in the TFlateral compartment: female versus male sex (OR 0.25, 95% CI 0.08; 0.77, p=0.016), early versus late ACL reconstruction (OR 0.94, 95% CI 0.90; 0.98, p=0.007), effusion one year after ACL trauma (OR 4.23, 95% CI 1.26; 14.15, p=0.019), presence of medial meniscal tear (OR 4.67, 95% CI 1.02; 21.29, p=0.047) and lateral meniscal tear (OR 11.57, 95% CI 2.89; 46.25, p=0.001) during 2-year follow-up. Potential predictors were not significantly associated with progression of osteophytes in TF and PF compartment.

CONCLUSION: Early degenerative changes are seen especially as a progression of cartilage defects in the TFlateral compartment. Cartilage defects in the TFmedial compartment measured shortly after ACL trauma, and presence of BMLs in the TFmedial compartment and effusion one-year after trauma and concomitant medial and lateral meniscal tears are predictors for early degenerative changes.

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LONG TERM CHANGE AND MEASUREMENT VARIABILITY OF CARTILAGE THICKNESS IN HEALTHY REFERENCE SUBJECTS – DATA FROM THE OSTEOARTHRITIS INITIATIVE

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INTRODUCTION: Reliable detection of structural progression in knee OA in clinical trials is a challenge due to the slow progression of the disease. Although many studies have reported test-retest variability of MRI-based cartilage thickness measurements made on the same day, the aggregate effect of aging and long-term measurement variability has not been studied. Such data are needed to establish thresholds for separating "progression" (knees with definite OA-related cartilage loss) from non-progression (OA knees in whom the observed change cannot be reliably discerned from healthy knees over similar intervals).

OBJECTIVE: To study the long-term (4-year) rates of change in knee cartilage thickness, and measurement variability, in a strictly selected healthy reference cohort from the Osteoarthritis Initiative (OAI).

METHODS: The OAI healthy reference cohort consists of 122 subjects without knee pain, aching or stiffness in the year before inclusion. In addition, neither knee displayed radiographic findings of femorotibial OA (clinical site readings of baseline bilateral fixed flexion radiographs), and there were no risk factors of incident knee OA present (e.g. obesity, history of knee injury, knee surgery, family history of knee replacement, Heberden's nodes, or repetitive knee bending). Of these 122 subjects, we studied those with longitudinal MRI data available who were bilaterally KLG0 based on the central OAI radiographic readings (n=92; 60% female, age 55±8 yrs, BMI 24±3.1 at baseline). Of these, 92 had Y1 (year 1), 88 Y2, and 82 Y4 follow-up measurements with Siemens 3T MRI, using a sagittal DESS sequence. Segmentation of the 4 femorotibial cartilage plates (MT, LT; cMF, cLF) in all right knees was performed with blinding to time point using commercial software (Chondrometrics GmbH). Cartilage thickness was computed in 16 femorotibial subregions over 1-year (BL→Y1, Y1→Y2), 2-year (BL→Y2, Y2→Y4), 3-year (Y1→Y4) and 4-year (BL→Y4) observation periods. A paired t-test was used to explore whether rates of change were significantly different from zero, and the SD of the change was used to describe measurement variability.

RESULTS: The lateral tibia (LT) showed a consistent cartilage thickness loss over 4 years (-26µm, -1.3%; $p<0.001$), whereas thinning in the medial tibia (MT) did not reach statistical significance (-9µm; -0.6%; $p=0.07$). In the medial and lateral femur (cMF; cLF), significant thickening was observed (+20/+21µm; both +1.1%, $p<0.01$). Measurement variability increased slightly with longer observation periods (Table 1).

Table 1: Variability (SD) of knee cartilage thickness measurement over various observation periods

	1 year	2 years	3 years	4 years
Medial compartment (MFTC)	68	73	78	92
Lateral compartment (LFTC)	82	82	99	99
Medial tibia (MT)	39	41	44	47
Lateral tibia (LT)	50	49	62	58
Medial femur (cMF)	52	51	51	66
Lateral femur (cLF)	53	50	56	63

CONCLUSION: We find small, but statistically significant changes in cartilage thickness in healthy reference subjects without any pain, radiographic signs of OA, or OA risk factors. These changes involve thinning in the tibiae, and thickening in the distal femora. A slight increase in measurement variability (≤35%) was observed between 1-year and 4-year observation periods. The results can be used to define thresholds of progression over various observation intervals in different compartments of the knee, with the aim to separate progressors from non-progressors in clinical studies of knee OA.

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USING MANIFOLD LEARNING TO DISCOVER OA IMAGING BIOMARKERS FOR THE PREDICTION OF JOINT FUNCTION WITH DATA FROM THE OAI

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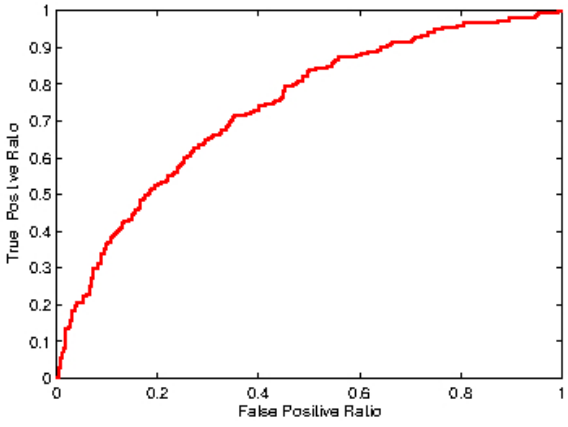
INTRODUCTION: Machine learning algorithms can identify patterns in large datasets with limited or sometimes no human supervision. In this work we use a class of machine learning algorithms called manifold learning to discover novel biomarkers for OA from the appearance of the articular cartilage in knee MRI. We use these new biomarkers to predict joint function.

OBJECTIVE: Our goal is to predict the severity of the WOMAC aggregated total score (provided in the OAI dataset) using novel biomarkers. The biomarkers are discovered using manifold learning algorithms which analyse the appearance of the articular cartilage in MRI.

METHODS: This work uses N=1131 right knee MRI acquired using the sagittal 3D DESS sequence from the OAI at baseline. The structural diagnostic distribution described by K&L grades is 0=30%, 1=11%, 2=24%, 3=16%, 4=3%, no data=16%. MR images are very high dimensional data, with as many dimensions as there are voxels. Manifold learning finds a low dimensional representation of the data by ensuring subjects with similar articular cartilage appearances are close together in this new representation. We use the low dimensional representations of the images as biomarkers. Initially our algorithm automatically roughly segments the articular cartilage for all subjects using an atlas-based approach [1]. This segmentation is then subdivided into small articular cartilage ROIs as described by Wirth and Eckstein [2]. For each of these subregions we construct low dimensional representations of the data using a manifold learning algorithm. The co-ordinates of these new representations are combined and their dimensionality is further reduced using principle component analysis (PCA) to create the final biomarkers. Further details of the methodology can be found [1] where it has been shown that this technique can be used to predict diagnostic K&L grades with very high accuracy.

With these novel biomarkers extracted from the imaging data, we use linear discriminant analysis (LDA) to classify WOMAC. We summarise the classifier performance using the area under the receiver operator curve (AUC) with a 95% confidence interval.

RESULTS: The AUC is 0.737 with a 95% confidence interval of 0.700-0.775. We also present the receiver operator curve (ROC) in figure 1.



CONCLUSION: The techniques we present are fully automated, which enables the experiments to scale to larger cohorts and increase result reproducibility. The experiments show promising results for prediction of joint function from MRI. However, for useful clinical applications it would be more significant to predict future joint function. We plan to explore whether this method could be used to predict pain in the future as a prognostic tool. We intend to extend this work by providing a comparison with existing biomarkers.

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DICLOSURE STATEMENT: None.
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[1] C R Donoghue, A Rao, AMJ Bull, D Rueckert, ISBI 2014
[2] W Wirth, F Eckstein, TMI 2008

IMAGING FINDINGS IN ANTI NERVE GROWTH FACTOR (a-NGF) STUDIES: RELEVANCE FOR ELIGIBITILIY AND SAFETY

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INTRODUCTION: Monoclonal antibodies that bind and inhibit nerve growth factor (NGF) have demonstrated both, good analgesic efficacy and improvement in function in patients with OA. Despite initial promising data, trials in OA had been suspended due to concerns over accelerated rates of OA progression to total joint replacement. However, since anti(a)-NGF therapies offer potential as the first new class of analgesics for many years, future studies of a-NGF drugs will require more rigorous safety criteria. Imaging plays a crucial role in clinical trials to define eligibility of potential participants and monitor safety during the course of these studies. This will identify subjects at risk for rapidly progressive OA (RPOA) prior to inclusion and identify subjects on study with adverse events such as RPOA Type I (i.e. rapid progression of joint space narrowing >1mm/year) or II (i.e. abnormal loss of bone or bone destruction that does not normally occur in end-stage osteoarthritis) so treatment can be discontinued. Several pathologic entities have been identified that are relevant for patient eligibility and safety. These will be reviewed in this presentation based on experience with tanezumab, one of the a-NGF compounds currently under investigation.

OBJECTIVE: To describe and illustrate imaging findings on radiography and MRI that are relevant for patient eligibility and safety monitoring in studies investigating a-NGF compounds based on experiences with the tanezumab program.

METHODS: This presentation is based on repetitive meetings of four experienced musculoskeletal radiologists to define potential eligibility and safety findings relevant for a-NGF clinical trials. 400+ image examples were reviewed in-consensus to define the most relevant and present characteristic imaging findings. Diagnoses of exclusion for eligibility that potentially increase risk of RPOA Type I or II were pre-existing RPOA, subchondral insufficiency fractures and atrophic OA. In addition, severe malalignment of the knee in the anterior-posterior direction may also increase the risk of RPOA. Additional diagnoses of exclusion were considered that do not predispose subjects for increased risk for RPOA per se such as tumors or other arthropathies, but these will not be covered in this presentation. Diagnoses relevant for safety after enrolment (i.e. joint safety findings) are RPOA Types I and II, subchondral insufficiency fractures, osteonecrosis and pathologic fractures, which will be covered in detail. Several of these diagnoses have non-specific findings on the radiograph or cannot be detected radiographically in early stages. Thus, in cases of inconclusive or suspicious radiography an additional MRI examination will commonly be acquired to rule out or confirm some of these diagnoses especially in early stages and thus, MRI findings will be presented in addition.

RESULTS: Early and late signs of diagnoses relevant for eligibility will be presented.

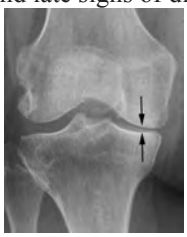
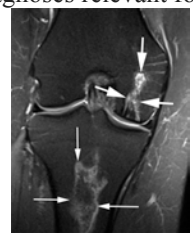


Fig 1.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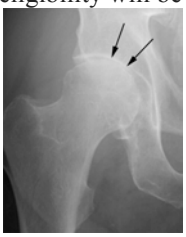
Fig. 3A

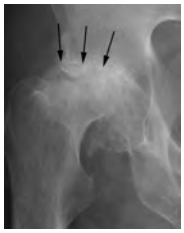
Fig. 3B

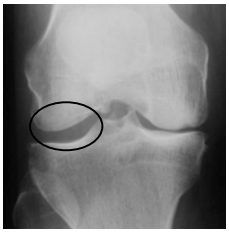
Fig.4

Fig. 1. Atrophic OA. Marked medial joint space narrowing with minimal osteophytes formation (arrows).
Fig 2. Typical MRI findings of osteonecrosis in the medial femur and the metaphyseal tibial plateau (arrows).
Fig 3. A. Atrophic OA at baseline with marked joint space narrowing superior-medial (arrows). B. At follow-up there is destruction of the femoral head consistent with RPOA Type II (arrows).
Fig 4. Subchondral insufficiency fracture (also termed SONK) at the medial femur (oval).

CONCLUSION: Expert readers in a-NGF programs need to be aware of relevant imaging findings in a-NGF studies including early signs of diagnoses relevant for RPOA Type I and II on radiography and potential X-ray and MRI diagnoses relevant for eligibility and safety during a-NGF studies.

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DIFFERENCES BETWEEN RADIOLOGIC ASSESSMENT IN OSTEOARTHRITIS EFFICACY STUDIES AND NERVE GROWTH FACTOR INHIBITOR PROGRAMS: RELEVANCE OF RADIOGRAPHY AND MRI

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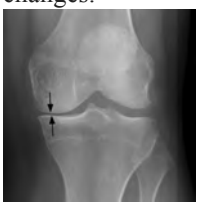
INTRODUCTION: The osteoarthritis (OA) research community has long-standing experience with studies assessing therapeutic efficacy for disease modifying intervention, which is commonly defined as slowing of joint space narrowing (JSN) on anterior-posterior radiographs. Paramount for longitudinal radiologic evaluation of radiographs is high precision, which requires optimized image acquisition in a reliable fashion commonly using fixed-flexion protocols in order to guarantee comparability between time points. Recently nerve growth factor inhibitors (NGFi) have been introduced for treatment of OA symptoms, and have shown good analgesic efficacy and improvement in function in patients with OA. However, NGFi trials in OA had been suspended due to concerns over accelerated rates of OA progression to total joint replacement. Since NGFi therapies offer potential as the first new class of analgesics for many years, future studies assessing NGFi compounds will have to include stringent eligibility criteria and will require a rigorous safety monitoring. While disease-modifying effects are not expected in NGFi treatment, imaging is paramount to identify potential negative outcomes as early as possible. These imaging findings include atrophic OA, osteonecrosis and others at eligibility and especially rapid progressive OA (RPOA) Type I (i.e. rapid progression of JSN >1mm/year) and RPOA II (i.e. abnormal loss of bone or bone destruction that does not normally occur in end-stage OA) during the course of treatment.

OBJECTIVE: To describe the core differences in regard to image acquisition and radiologic assessment in OA efficacy studies and studies assessing NGFi compounds.

METHODS: The current standards in image acquisition and assessment in OA efficacy studies will be reviewed based on the authors' long-standing involvement in OA trials and the available literature. In particular, the complementary role of radiography and MRI will be briefly reviewed. These findings will be contrasted to past and future NGFi studies applying radiography and MRI for patient eligibility and safety monitoring. Differences between expected JSN in OA vs. rapid progression will be discussed. In addition, the role of MRI as an adjunct instrument to detect early findings of relevance will be emphasized.

RESULTS: In regard to eligibility OA efficacy studies require semiquantitative assessment of screening radiographs to define disease severity based on the Kellgren-Lawrence or OARSI scales. In a-NGF studies, subjects may similarly be included based on screening radiographs. In addition to standard semiquantitative assessment, additional pre-defined diagnoses of exclusion have to be considered such as atrophic OA that potentially indicate increased risk of more rapid progression. In regard to on-study radiologic assessment, the focus in OA efficacy studies is on maximized precision or sensitivity to detect change over time in JSN, while in NGFi studies the focus lies on maximized sensitivity to detect early adverse findings that potentially result in withdrawal from treatment. Especially in cases of discrepant clinical and radiographic findings additional MRI examinations are needed to increase sensitivity to detect early changes.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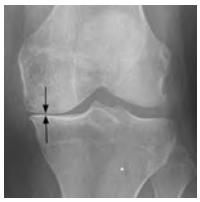


Fig. 1B

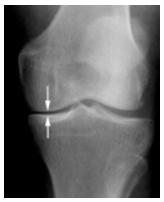
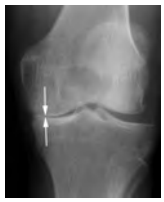


Fig. 2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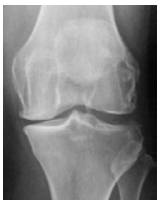
Fig. 3A

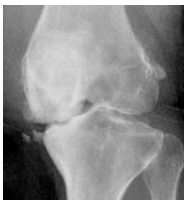
Fig. 3B

Fig. 1. Osteoarthritis efficacy study. A baseline image shows medial joint space narrowing (JSN) (arrows). B. At 2-year follow-up there is an increase in JSN that is definite but does not suggest rapid progression,
Fig 2. NGFi study. A. Baseline image shows definite medial JSN (arrows) and no osteophytes consistent with atrophic OA. B. At 9-month follow-up rapid progression in JSN is seen with now bone-to-bone appearance (arrows). Finding is consistent with RPOA Type I.
Fig 3. NGFi study. A. Baseline image shows definite osteoarthritis Kellgren-Lawrence grade 3 with presence of osteophytes and medial JSN. B. At 12-month follow-up severe disintegration of the medial compartment including collapse of the tibial plateau is observed. Finding is consistent with RPOA Type II.

CONCLUSION: The role of radiologic assessment differs in efficacy and NGFi studies. While in efficacy studies image acquisition and evaluation is optimized for sensitivity to detect minor changes between treated and non-treated subjects, in NGFi studies the focus is on early detection of diagnoses that either put a subject at increased risk for an adverse outcome (eligibility) or may result in withdrawal from treatment (safety).

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POSTER PRESENTATIONS

HOW MUCH PAIN REDUCES ISOMETRIC MUSCLE STRENGTH BY HOW MUCH? – A CROSS-SECTIONAL ANALYSIS OF ALL OSTEOARTHRITIS INITIATIVE PARTICIPANTS

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INTRODUCTION: We have previously demonstrated that knees with moderate to severe levels of pain (WOMAC≥5) display significantly lower isometric muscle strength than painless knees, independent of their radiographic OA (KLG) status. However, it is unclear a) whether mild pain also is associated with a reduction in muscle strength, b) whether the relationship between pain and reduction in muscle strength is "linear" across the spectrum of the WOMAC scale, and c) whether pain-strength relationships are similar between men and women.

OBJECTIVE: To cross-sectionally determine the magnitude of reduction in age-adjusted isometric knee extensor and flexor strength per unit of WOMAC knee pain in men and women, across a wide spectrum of observed WOMAC pain scores in a large cohort.

METHODS: Of the 4796 OAI participants, 4553 had demographic and WOMAC knee pain data (range 0-20; 20=worst) and isometric measurements of knee extensor and flexor muscle strength ("Good Strength Chair", Metitur Oy, Finland). Strength data of all dominant (or right) limbs were used either from baseline or from 1-year follow-up. Since muscle strength is known to decline with age, independent of radiographic OA (KLG) status, muscle strength was adjusted to the mean age of 61.3 years. The reduction in age-adjusted extensor and flexor strength (and strength/body weight) per unit increase on the WOMAC knee pain scale was then estimated from linear regression analysis. Further, sex-specific and age-adjusted strength in strata encompassing 2 WOMAC units each (i.e. the minimal clinically perceptible improvement) was related to strength measured in fully painless knees (WOMAC=0) (Table 1).

RESULTS: The 4553 participants (2651 women, 1902 men) were 61.3±9.2 y old (BMI 28.7±4.8 kg/m^2). Based on linear regression, the reduction in age-adjusted isometric extensor strength for each unit of WOMAC pain was 1.9% (5.8N) in women and 1.6% (7.3N) in men. Reduction in flexor strength was 2.5% (2.9N) and 1.8% (3.3N), respectively. Reductions in strength/weight for each unit of WOMAC pain ranged from 2.2 to 3.4%. Age-adjusted extensor strength values across WOMAC strata are shown in Table 1: There was no indication of a non-linear relationship between pain and strength across the range of observed WOMAC values, nor obvious differences in the pain-strength relationship between men and women.

Table 1. Isometric extensor strength (mean±SD) and %-differences for WOMAC strata vs WOMAC=0

	WOMEN (*unpaired t-test; p<0.05)				MEN (*unpaired t-test; p<0.05)			
WOMAC Strata	n= limbs	Extensor Strength	%Difference vs WOMAC0	Cohen d	n= limbs	Extensor Strength	%Difference vs WOMAC0	Cohen d
0	1018	303±81.2	ref.	ref.	851	458±124	ref.	ref.
1-2	624	291±84.9	-4.1*	-0.15	450	431±116	-5.9*	-0.22
3-4	379	273±81.0	-10*	-0.37	284	423±121	-7.7*	-0.29
5-6	252	267±82.8	-12*	-0.44	155	412±115	-10*	-0.38
7-8	158	256±87.0	-16*	-0.58	73	411±115	-10*	-0.39
9-10	113	261±88.6	-14*	-0.51	50	377±117	-18*	-0.65
11-12	64	223±89.3	-27*	-0.98	26	375±129	-18*	-0.67
>12	43	231±106	-24*	-0.88	13	372±142	-19*	-0.69

CONCLUSION: A reduction of approximately 2% in age-adjusted isometric extensor and flexor strength is related to each 1-unit increase on the WOMAC knee pain scale, both in men and women. Comparing WOMAC pain strata across the full-observed spectrum did not indicate that the reduction in age-adjusted isometric muscle strength follows a non-linear relationship.

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DICLOSURE STATEMENT: FE and WW are employees and co-owners of Chondrometrics GmbH.
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THE ASSOCIATION OF KNEE SHAPE WITH SEX: THE OSTEOARTHRITIS INITIATIVE

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INTRODUCTION: Incidence of knee osteoarthritis (OA) is much higher in women than in men. Previous studies have shown that bone shape is a risk factor for knee OA. To date no study has examined whether knee shape differs between men and women. The findings on bone shape in men and women may shed light on the etiology of knee OA.

OBJECTIVE: To determine if there are sex differences in knee shape.

METHODS: We used information from the NIH-funded Osteoarthritis Initiative (OAI), a cohort of persons aged 45-79 at baseline who either had symptomatic knee OA or were at high risk of it. Among participants aged between 45 and 60 years, we randomly sampled 339 knees without radiographic OA (i.e., Kellgren/Lawrence grade of 0 in central readings on baseline radiograph). We characterized distal femur and proximal tibia shape of these selected radiographs using Active Shape Modeling (ASM). ASM generates independent modes that together explain the shape of the bones. We performed linear regression to examine the association between sex and proximal tibia and distal femur shape, adjusting for age, race, body mass index (BMI) and clinic site. Beta coefficients and 95% confidence intervals were estimated to represent the difference in bone shape between women and men.

RESULTS: Mean age was 52.7 years (±4.3 SD) for both men and women. There were 192 female and 147 male knees for the distal femur analysis. Thirteen modes were derived for femoral shape, accounting for 95.5% of the total variance. Distal femur Mode 1 had the greatest effect size for association with sex (adjusted beta estimate 1.04; 95%CI 0.85-1.23; p<0.0001). For tibial shape, 191 female knees and 149 male knees were used for the analysis. Ten modes explained 95.5% of shape variance. Of them Mode 2 had the greatest effect size for the association with sex (adjusted beta estimate -0.3; 95%CI -0.51—0.08; p=0.009).

CONCLUSIONS: Bone shapes that make up the knee joint (distal femur and proximal tibia) differ by sex. Further analyses to assess to what extent sex difference in risk of knee OA is mediated by the bone shape are warranted.

Distal Femur Shape with Sex

Mode	**Adjusted Beta (95%CI)**	**Mode Description – primary alteration of shape with increased SD weighting**
1	1.044 (0.85 to 1.23)	Increased shaft width relative to epicondylar width, and deepening of patellar notch.
2	0.022 (-0.18 to 0.23)	Epicondylar head is shifted laterally in relation to the shaft. The patellar groove is less concave and shifted medially with respect to the rest of head.
3	0.23 (0.03 to 0.43)	Decreased inferior projection of medial and lateral condylar heads with respect to the patellar groove.

Proximal Tibia Shape with Sex

Mode	**Adjusted Beta (95%CI)**	**Mode Description – primary alteration of shape with increased SD weighting**
1	-0.19 (-0.41 to 0.04)	Decreased concavity, elevation of lateral compartment plateau, and decreased shaft width.
2	-0.30 (-0.51 to -0.08)	Tibial head shifted laterally in relation to the shaft, and head width increased. The lateral tibial plateau is more concave.
3	-0.22 (-0.43 to -0.01)	Slightly increased tibial width, depression of medial plateau and elevation of lateral plateau.

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DISCLOSURE STATEMENT: BLW has received research contract with Pfizer, Inc.
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LOCATION-SPECIFIC HIP JOINT SPACE WIDTH FOR HIP OSTEOARTHRITIS: PREDICTIVE VALIDITY AND RESPONSIVENESS OF A NEW COMPUTERIZED MEASURE

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INTRODUCTION: Responsive measures of radiographic JSW in hip OA are important for the evaluation of treatment interventions but current measures lack responsiveness and predictive validity. One problem may be reliance on identification on the site of mJSW, which can vary within and between readers and be at different locations on serial radiographs. At the knee, location-specific JSW has overcome these problems and can outperform mJSW. A similar method is now evaluated at the hip.

OBJECTIVE: To evaluate predictive validity and responsiveness for hip JSW measured at 3 fixed locations in the superior hip joint by a semi-automated quantitative software tool and to examine the association between JSW change and pain.

METHODS: A nested case-control study (n=158) was conducted in the OAI. OAI subjects had standing AP pelvis radiographs at baseline and 48 month visits using a standardized protocol.
Case group 1: subjects with a THR after the 48-month visit (at 60 and 72 months) (n=27).
Case group 2: contralateral (CL) hip of subjects who had a THR at any point (12-72 months) after baseline (n=79). In both groups, subjects were matched (1:1) on age and gender with subjects who did not receive a THR, reported no hip pain, and had no self-reported diagnosis of hip OA.
Pain and JSW analysis: the CL hips to a THR (n=79) were stratified on the presence of hip pain.
Measurements of hip JSW were made at 3 fixed locations, per Figure 1. Location 1 was in the superior-lateral hip joint space and was 10° from a reference line (from the femoral head centre to the outer edge of the acetabular roof), lateral line in Figure 1). Location 2 was 30° and location 3 was 50° from the reference line. Measurement was facilitated by software that delineated the femoral head and found the acetabular margin along each of the 3 lines. A reader used software to correct the output if needed.
Statistical analysis: Sensitivity to change was estimated by the standardized response mean for 4-year change. Paired t-tests were used to test difference for cases and controls.

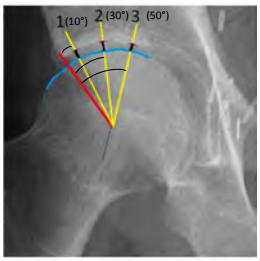

Figure 1 Example of hip JSW measurement

RESULTS: The overall sample was 47% male, 91% Caucasian had a mean age of 64.2 and BMI of 27.9. Significant differences in responsiveness were observed between cases and controls in both case-control groups. Location 3 (sup-med) was the most responsive to change in JSW (Table 1). Reading time was approximately 1 minute per hip. Those with pain had significantly greater 48-month change in JSW and responsiveness at locations 1 and 3 than those without pain (Table 2).

Table 1. Mean (sd) 4-year change (mm) in hip JSW and SRM's in THR hips (and controls) and in contralateral hips

Group 1 (THR)	ΔmJSW	ΔJSW 1 (sup-lat)	ΔJSW 2 (sup)	ΔJSW 3 (sup-med)	SRM mJSW	SRM 1	SRM 2	SRM 3
THR Cases (n=27)	-1.18 (1.18)	-1.51 (1.42)	-1.25 (1.60)	-1.29 (1.24)	-1.00	-1.06	-0.78	-1.04
Controls (n=27)	0.06 (0.71)	-0.03 (0.53)	-0.08 (0.54)	0.01 (0.50)	0.08	-0.06	-0.15	0.02
p-value [1]	**0.000**	**0.000**	**0.001**	**0.000**				
Group 2 (contra)								
Cases (n=79)	-0.29 (0.81)	-0.23 (0.68)	-0.24 (0.63)	-0.40 (0.75)	-0.36	-0.34	-0.37	-0.53
Controls (n=79)	-0.02 (0.59)	-0.03 (0.46)	-0.03 (0.81)	-0.13 (0.60)	-0.03	-0.07	-0.04	-0.21
p-value [1]	**0.01**	**0.03**	0.07	**0.01**				

Table 2. 4-year change in JSW and SRM, by location, in contralatearl hips (from THR) by hip pain

Anterior hip or groin pain	ΔmJSW	ΔJSW 1	ΔJSW 2	ΔJSW 3	SRM mJSW	SRM 1	SRM 2	SRM 3
Pain at ≥1 or more follow-ups (n=17)	-0.40 (0.63)	-0.58 (1.06)	-0.32 (1.06)	-0.90 (1.23)	0.63	-0.55	-0.30	-0.74
No hip pain 0-48 months (n=62)	-0.31 (0.75)	-0.14 (0.59)	-0.21 (0.46)	-0.26 (0.49)	0.42	-0.24	-0.46	-0.54
p-value[+]	0.67	**0.02**	0.55	**0.00**				

CONCLUSION: A new computer-assisted rapid measure of hip JSW has good predictive validity and responsiveness at various stages of disease, better than mJSW. Location 3 was most responsive.

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DISCLOSURE STATEMENT: None.
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NATURAL ANKLE CONDITION 8-10 YEARS AFTER FIXATOR DISTRACTION FOR OA

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INTRODUCTION: Patients under 50 years of age present a particularly difficult population to treat for post-traumatic osteoarthritis (PTOA). Ankle arthrodesis is an accepted definitive treatment in the young PTOA population, but there is a significant incidence of adjacent joint arthritis and functional limitations, without any subsequent options should failure occur. Alternatively, results and survivorship of total ankle arthroplasty (TAA) are not as predictable as for hip and knee replacement. Therefore this young active population is at risk for early revision of the implant, which is fraught with complications at repeat surgery and subsequent performance falling short of primary total joint reconstruction results. A desirable alternative is natural joint preservation by restoring the joint space with joint distraction arthroplasty using external fixation.

OBJECTIVE: Results of this controlled trial follow-up, 10 years after surgery, demonstrate the potential of ankle distraction in reversing the painful disease process of OA and in prolonging natural joint function.

METHODS: Thirty-six patients were enrolled who underwent ankle distraction surgery between December 2002 and October 2006. Inclusion criteria included: (1) symptomatic isolated, unilateral Kellgren-Lawrence grade 3-4 ankle OA; (2) skeletally mature to age 60 years old; (3) failure of non-surgical treatment for more than a year, including 3 months of continuous treatment with nonsteroidal anti-inflammatory drugs and 3 months of unloading treatment ; (4) ability to maintain extremity non-weight-bearing using ambulatory aids. Excluded were patients with serious co-morbidities, those with contralateral OA, and those with significant hindfoot or tibial misalignment, or with a current history of alcohol or drug abuse. IRB approved consent was obtained. Patients were evaluated by an independent clinical investigator and were asked to complete the Ankle Osteoarthritis Scale (AOS) and the SF-36 surveys. Radiological evaluations included pre-op, post-op and 2-year follow-up plain radiographs and CT arthrography. Radiographs, CT scans, diagnostic MRI and qMRI $T1\varrho$ were acquired at 8-10 year follow-up visits. Patients who were not able to return for a clinic visit were offered a survey evaluation including the AOS, SF-36 and basic health questions designed to replace the clinical interviews.

RESULTS: From a total of 36 patients, data is available on 27 patients (77%) and one passed away. Fourteen patients still have their native ankle while 13 were fused or converted to TAA. Patients who ultimately required ankle fusion or TAA showed early signs of distraction failure. At 2 year follow up, they demonstrated lower functional scores (average AOS of 49±17, $p<0.05$) compared to patients with native joints at the same time point (average AOS of 33±25). Even in distraction failure cases when patients elected to proceed with ankle fusion or ankle replacement, they still experienced the clinical benefit of the conversion surgeries and demonstrated significant improvement of the SF-36 Physical Component Scale (39±3.8 compared to 36±8.9 at baseline $p<0.05$). Imaging results show cartilage and subchondral bone inhomogeneities have returned to differing degrees in native ankles at 10-year follow-up, ranging from well-defined articular cartilage to focal eburnation and early stages of subchondral erosion and auto-fusion.

CONCLUSION: Ankle distraction surgery offers an effective alternative treatment for end stage OA, which allows young patients to preserve their native joints throughout the most productive years of their lives. These results indicate that ankle distraction surgery does not complicate later conversion surgeries or in any way limit patients' physical improvement. By delaying the need for joint sacrificing surgeries for over a decade, ankle distraction not only minimizes complications of joint sacrificing surgeries such as adjacent joint arthritis following ankle arthrodesis but also increases implant longevity to later revision TAA.

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A PRELIMINARY REPORT ON A MULTI-CENTER FEASIBILITY TRIAL ESTABLIHSING IMAGING TECHNOLOGIES AS MEASURES OF KNEE CARTILAGE COMPOSITION FOLLOWING ACL INJURY

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INTRODUCTION: Anterior cruciate ligament (ACL) injuries place patients at an increased risk of developing early-onset post-traumatic osteoarthritis. The current gold-standard for evaluating for degenerative changes is through radiographs, though degenerative changes take 10 to 15 years before becoming detectable on radiographs. Quantitative MRI with $T_1\rho$ and T_2 offers the potential to non-invasively assess the biochemical and structural properties of cartilage earlier in the disease course, and previous smaller studies have shown the capabilities of these technologies.

OBJECTIVE: The purpose of this study is to evaluate $T_1\rho$ and T_2 MR imaging of cartilage in healthy volunteers, to assess reproducibility, and in patients with ACL injury, to detect acute cartilage changes, in a multi-center trial.

METHODS: Quantitative cartilage imaging was performed in 4 volunteers (2 female, 30.8 ± 1.7 years) with no prior history of knee injury. Scan/re-scan data for two volunteers were acquired at 3 sites, while two volunteers were imaged at one site. Fourteen patients (9 female, 35.5 ± 10.1 years) underwent imaging of both the injured and contralateral knees within 1 month following ACL injury. All imaging studies were performed on 3T MR systems (GE Healthcare) with a concatenated $T_1\rho$ and T_2 sequence.[1] Cartilage segmentation was performed semi-automatically, and $T_1\rho$ and T_2 relaxation times were calculated with a pixel-by-pixel, mono-exponential fit. Cartilage values were analyzed for the lateral and medial femoral condyles (LFC/MFC), lateral and medial tibial plateaus (LT/MT), patella and femoral trochlea. The mean absolute differences in relaxation times between scans for each volunteer were calculated, as well as the mean difference for scans across the three different sites. For patients, the mean values in each compartment for the injured knee were compared to each patient's contralateral knee with a paired Student's t-tests with significance defined as $p < 0.05$.

RESULTS: The mean scan-rescan difference was 1.65 ms for $T_1\rho$ and 1.67 ms for T_2. For the volunteers scanned at all 3 sites, the scan-rescan difference was 1.85 ms for $T_1\rho$ and 1.97 ms for T_2. The mean difference in each sub-compartment ranged from 0.93 ms in the LT (CV = 1.75%) to 2.28 ms in the MT (CV = 4.22%) for $T_1\rho$ and from 1.00 ms in the LT (CV = 2.58%) to 2.30 ms in the MT (CV = 6.01%) for T_2. Coefficients of variation were 2.72% for $T_1\rho$ and 3.93% for T_2 across all sites. In patients with acute ACL injuries, the mean relaxation times were significantly higher in the LFC for $T_1\rho$ (43.9 ± 2.8 ms vs. 42.0 ± 2.4 ms; $p = 0.008$) and the MFC for T_2 (33.3 ± 2.5 ms vs. 31.6 ± 2.4 ms; $p = 0.02$) relative to the patient's uninjured knee. The posterior LT had significantly higher T_2 values (34.6 ± 4.9 ms vs 30.5 ± 3.1 ms; $p = 0.035$) and increased, though not statistically significant, $T_1\rho$ values (45.8 ± 6.7 ms vs. 42.6 ± 4.1 ms; $p = 0.11$).

CONCLUSION: The preliminary results presented here suggest that quantitative MR imaging of cartilage through T1ρ and T2 mapping is a reproducible measurement that can be applied across multiple institutions. Previous work has shown that early degenerative changes result in a 6.5 ms increase in T1ρ, greater than the variability observed in our volunteer subjects.[2] Additionally, we have observed acute cartilage changes in the patients following ACL injury, primarily in the lateral compartment. Through continued and longitudinal evaluation, we will further investigate the feasibility of these promising imaging techniques to detect and monitor degenerative changes after ACL injury.

SPONSOR: This study was supported by funding from the Arthritis Foundation.
DISCLOSURE: None.
REFERENCES: (1) Li, et al. J Magn Reson, 2013. (2) Li, et al. Osteoarthr and Cartilage, 2007.
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CAN BONE SHAPE PREDICT OA PROGRESSION? - DATA FROM THE OAI

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INTRODUCTION: Osteoarthritis (OA) is a whole-joint disease effecting changes in bone and soft tissue. The gross shape of articulating bone surfaces has been shown to differ between osteoarthritic and normal subjects. Tibiofemoral joint space measured from plain film x-rays is reduced due to factors including loss of cartilage, meniscal deterioration, subluxation and bone shape changes.

OBJECTIVE: To investigate the association of bone shape and tibiofemoral joint space geometry with incident and end-stage OA.

METHODS: Case and control pairs were selected from 4,796 participants from the Osteoarthritis Initiative (OAI), a multicenter population-based cohort study designed to identify biomarkers of knee OA development and/or progression. Incident cases (n = 289) were defined by a change from KL0/1 to KL >=2. End-stage cases (n = 119) were participants who received a Total Knee Replacement (TKR), confirmed by radiography and/or review of hospital records. Matched controls were selected with same KL (and contralateral knee KL for the incident cases), sex, and age within 5 years. Timepoints included the defining event (T0), where the case reported a TKR or where incident OA was found, and available preceding timepoints. Quantitative measurements of bone curvature for total and sub-regional articulating bone surfaces were obtained from sagittal 3D WE DESS MRI images acquired at each time point using CiPAS atlas-based segmentation software (Qmetrics, Rochester, NY). Tibiofemoral joint space measurements were derived from opposing subchondral bone surfaces of femur and tibia. Mean and standard deviation of curvature and joint space longitudinal measurements for case and control cohorts were analyzed using a Generalized Estimating Equation model (SAS: GENMOD, Cary, NC) to account for the interdependence between longitudinal outcomes.

RESULTS: There were statistically significant differences between case and control pairs for incident cohort for whole femur and central (weight-bearing) medial and lateral femur curvature measurements, and for medial and lateral joint-space width measurements. Table 1 summarizes the OA factors. Incident OA knees generally had lower curvature at baseline and flattened at a greater rate over time than control knees. For late-stage OA, as determined by TKR, there were statistically significant differences between cases and controls only for whole femur curvature and central medial femur curvature standard deviation when the mixed model analysis was applied. Complete results are presented in Table 1.

CONCLUSIONS: In this study bone curvature measurements were significantly different between both early stage subjects who developed radiographic OA and late stage subjects who received a TKR vs. corresponding control subjects who did not develop radiographic OA or receive a TKR. Cases had flatter femur bone surfaces than controls and higher rates of change (flattening) than controls for incident OA and TKR, suggesting that femoral bone shape changes throughout the knee OA disease process. Standard deviation (SD) of the curvature, which indicates variability of the measurements, was significantly different for femur at incident OA only for central lateral and central medial femur. At TKR, the SD was significant only for central medial femur. This may suggest that OA-related structural changes are not concentrated solely in the weight-bearing regions, and that the femur may exhibit greater plasticity during the OA process than the tibia.

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Table 1: Longitudinal Analyses for Incident OA and TKR Using Generalized Estimating Equation Model

GENMOD (GEE)	Longitudinal (AR1) Analysis (Beta and P-value)					
	Control Slope		Case vs Control (Intercept) *		Case vs Control (Slope)	
	Incident OA	TKR	Incident OA	TKR	Incident OA	TKR
F_c_std	0.0002 (<.0001)	0.0004 (<.0001)	0.0005 (0.1099)	0.0022 (0.0005)	0.0002 (0.0037)	0.0002 (0.0325)
F_c_mean	0.0000 (0.0539)	-0.0003 (<.0001)	-0.0010 (0.0001)	-0.0016 (0.0012)	-0.0002 (<.0001)	-0.0003 (<.0001)
LT_c_std	0.0001 (0.6031)	0.0006 (0.0251)	0.0005 (0.6004)	0.0029 (0.0709)	0.0001 (0.6115)	0.0006 (0.1296)
LT_c_mean	-0.0001 (0.3074)	0.0000 (0.9394)	-0.0007 (0.3469)	-0.0017 (0.1090)	-0.0001 (0.5128)	-0.0002 (0.4569)
MT_c_std	0.0004 (0.0633)	0.0004 (0.1859)	-0.0001 (0.9089)	-0.0028 (0.0683)	-0.0004 (0.1895)	-0.0001 (0.8670)
MT_c_mean	0.0002 (0.2384)	-0.0002 (0.4144)	-0.0008 (0.2803)	0.0035 (0.0039)	-0.0002 (0.4522)	0.0008 (0.0179)
cLF_c_std	0.0002 (0.1008)	0.0007 (0.0015)	-0.0003 (0.6067)	0.0001 (0.9322)	-0.0001 (0.6232)	0.0001 (0.8224)
cLF_c_mean	0.0001 (0.2399)	-0.0001 (0.5211)	-0.0010 (0.0014)	-0.0009 (0.0964)	-0.0002 (0.0003)	-0.0001 (0.2788)
cMF_c_std	0.0000 (0.7835)	0.0003 (0.1145)	0.0008 (0.1878)	0.0039 (0.0022)	0.0004 (0.0079)	0.0006 (0.0336)
cMF_c_mean	-0.0001 (0.0518)	-0.0001 (0.0335)	-0.0001 (0.7796)	-0.0002 (0.6584)	-0.0001 (0.3552)	0.0001 (0.6321)

*Difference at time of incident knee OA or TKR, respectively

VOLUMETRIC ANALYSIS OF THE INFRA-PATELLAR FAT PAT (IPFP) – COMPARISON BETWEEN FAT-SUPRRESSED AND NON-FAT-SUPRRRESED IMAGING; AND PRELIMINARY FINDINGS IN SUBJECTS WITH UNILATERAL KNEE PAIN

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INTRODUCTION: The infra-patellar fat pat (IPFP) represents an accumulation of intra-articular adipose tissue and has been shown to be a source and mediator of intra-articular inflammation. One study specifically showed that leptin secretion from the IPFP was found sufficient to induce matrix metalloproteinase (MMP) gene expression. A pilot study examined IPFP volume with MRI in a small sample of women with knee OA vs. controls and found some relationships with age, but did not have sufficient statistical power to detect associations with BMI and OA status.

OBJECTIVE: a) To study inter-observer variability of MRI-based volumetric measurement of the IPFP in humans, b) to compare analyses based on fat-suppressed vs. non-fat-suppressed MRI, and c) to explore side differences in OAI participants with the same grade of bilateral radiographic knee OA, but with frequent pain in one and no pain in the contra-lateral knee.

METHODS: After initial training on three randomly selected data sets, two observers segmented the IPFP in 10 subjects from the OAI healthy reference cohort (4 men, 6 women), using a sagittal fat-suppressed fs (IW) TSE (TR=3200ms, TE=30ms, slice thickness 3.00mm) and a sagittal non-fat-suppressed (nfs) SE MRI sequence (TR= 2700ms, TE=30ms, slice thickness 3.48mm). All slices clearly depicting the IPFP were analyzed, and its volume, anterior surface (towards the lig. patellae) and mean thickness (depth) were then computed using custom software (Chondrometrics GmbH). Results were compared between both observers and between fat-suppressed and non-fat-suppressed images using paired t-tests and Pearson correlation coefficients. In a next step, subjects in whom both knees displayed the same radiographic status (KLG2 or 3), but in whom one knee was frequently painful (most days of at least one month within the past 12 months) and the other knee was painless within the past year, were drawn from 4,796 OAI participants. In the latter participants, the IPFP was measured in both knees using the sagittal fat-suppressed IW TSE.

RESULTS: In both the fs and nfs SE MRIs, there was a systematic, statistically significant offset in IPFP volume measures between both observers; however, the measurements were highly correlated between them (r=0.94 for fs and 0.95 for nfs SE). IPFP volume measurements obtained from nfs SE were slightly greater (7-11%) than for fs SE, but again, volume (and other) measures between both imaging sequences were highly correlated (r=0.90 in one and 0.97 in the other observer). 48 subjects (31 women; 17 men; age 63±10 years) fulfilled the selection criterion of unilateral (frequent) pain but identical radiographic status (KLG) in both knees. Of those, 10 were segmented to date (9 women, 1 man; age 62±11 years; BMI 29.9±4.01). At this stage, there did not appear to be systematic difference in quantitative IPFP parameters between painful vs. painless knees (Table 1).

Table 1: Quantitative measures of the IPFP in frequently painful vs. painless knees (within-person comparison)

	Painful knees Mean±SD	Painless knees Mean±SD	Pairwise Diff. [%] Mean±SD	T-test paired
IPFP Volume (cm^3)	16.2±3.62	16.2±1.96	-1.19±11.6	0.911
IPFP Anterior surface (cm^2)	13.6±1.83	13.9±1.89	-0.85±12.3	0.694
IPFP Mean thickness (mm)	11.8±1.26	11.8±1.62	0.27±10.3	0.871

CONCLUSION: This is one of the first studies to explore quantitative measures of the IPFP. Although the IPFP is more clearly depicted in non-fat-suppressed (nfs) images, these were only acquired in one (of both) knee(s) in the OAI, whereas fat-suppressed (fs) images are available for both knees. For this reason we examined the agreement between segmentations from both sequences. Despite small systematic offsets, there was a high linear relationship between both. The systematic offsets between two observers, after initial training on 3 data sets, suggests that central quality control by an expert reader will be needed if data from different observers are pooled, and this process will be implemented throughout further study. The preliminary data on the effect of pain did not indicate a systematic difference in quantitative IPFP parameters between painful vs. painless knees.

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FEASIBILITY OF PLANAR DGEMRIC MAPS IN AIDING THE RADIOLOGICAL ASSESSMENT OF ACETABULAR HIP CARTILAGE

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INTRODUCTION: 3D dGEMRIC has been shown to have potential for the quantitative assessment of biochemical changes associated with early-stage OA. However, clinical analysis using the dGEMRIC index is still being done in a slice-by-slice manner, thus limiting the usefulness of 3D data in providing an overall impression of cartilage quality. Recently, our group has developed a method for automating the segmentation of 3D 1.5T hip dGEMRIC data and subsequent production of an unfolded, planar map of the dGEMRIC index for the acetabular AC. Since implementation, though, the method has not yet been tested for its potential in improving radiological evaluation.

OBJECTIVE: We sought to test whether planar dGEMRIC maps of acetabular cartilage could improve the correlation between radiological and intraoperative assessment of acetabular chondromalacia in patients diagnosed with femoroacetabular impingement, or FAI.

METHODS: We performed a retrospective analysis of 47 hips with symptomatic FAI that obtained a 1.5T dGEMRIC scan within six months prior to intra-articular surgery. The cohort came from 24 male and 21 female subjects, with the mean age at surgery being 28.5 +/- 11.4 (SD) years and the range from 14.2 to 56.5 years. 3D TrueFISP, dGEMRIC, and T1 map sequences acquired in the sagittal oblique plane at 0.8^3 mm^3 (TrueFISP) or 0.6^3 mm^3 (dGEMRIC) voxel sizes were automatically segmented and unfolded according to previously-published methods. Using the generated planar dGEMRIC maps and the de-identified studies, a musculoskeletal radiologist performed both morphological grading and dGEMRIC index measurement on the original sequences as follows: Six sub-regions of the acetabulum (anterior-peripheral, AP; anterior-central, AC; superior-peripheral, SP; superior-central, SC; posterior-peripheral, PP; posterior-central, PC) were separately graded on the radially reformatted morphological sequences using the modified Outerbridge scale. Region-of-interest (ROI) T1 averages were also taken for each sub-region using the radially reformatted T1 map. Each hip was evaluated both without reference to the planar dGEMRIC map and with the map guiding manual radial reformatting and selection of slices with the worst-looking chondromalacia for each sub-region. All repeated grading and measurement on each study was done at least three weeks apart. Beck's intraoperative chondromalacia scores (likewise, recorded per sub-region) served as the gold standard for comparison.

RESULTS: For comparing Outerbridge grades to Beck's grades by sub-region (AP, AC, SP, SC, PP, PC), the Spearman's rho without the planar dGEMRIC map is 0.40 ($p<0.01$), 0.14 ($p=0.36$), 0.54 ($p<0.001$), 0.41 ($p<0.01$), 0.15 ($p=0.34$), and 0.30 ($p<0.05$) respectively. With the map, it is 0.39 ($p<0.02$), 0.34 ($p<0.03$), 0.52 ($p<0.001$), 0.42 ($p<0.01$), 0.22 ($p=0.16$), and 0.26 ($p=0.09$) respectively. For comparing ROI T1 averages to Beck's grades by sub-region, the Spearman's rho without the map is -0.35 ($p<0.03$), -0.03 ($p=0.87$), -0.65 ($p<0.0001$), -0.32 ($p<0.04$), -0.10 ($p=0.54$), and -0.29 ($p=0.06$) respectively. With the map, it is -0.28 ($p=0.07$), -0.20 ($p=0.19$), -0.60 ($p<0.0001$), -0.32 ($p<0.04$), -0.16 ($p=0.31$), and -0.04 ($p=0.78$) respectively. For comparing Outerbridge grades to ROI T1 averages by sub-region, the Spearman's rho without the map is -0.53 ($p<0.001$), -0.35 ($p<0.02$), -0.71 ($p<0.0001$), -0.74 ($p<0.0001$), -0.56 ($p<0.001$), and -0.26 ($p=0.10$) respectively. With the map, it is -0.69 ($p<0.0001$), -0.78 ($p<0.0001$), -0.77 ($p<0.0001$), -0.70 ($p<0.0001$), -0.54 ($p<0.001$), and -0.50 ($p<0.001$) respectively. Receiver-operator analysis for dichotomizing normal and abnormal cartilage (Beck's = 1 and >1, respectively) in sub-regions AP and SP yields an area-under-curve of 0.72 without the map and 0.70 with the map.

CONCLUSION: While planar dGEMRIC maps do not appear to significantly improve the radiologist's ability to predict surgical evaluation of chondromalacia in the areas of the acetabulum that are typically the most damaged in FAI cases (AP and SP), improvement is noted elsewhere (in AC and PP). Map-dependent improvement in the correlation of Outerbridge scores and ROI T1 averages is noted for most sub-regions (AP, AC, SP, and PC). This suggests the potential of planar dGEMRIC maps to increase the consistency of radiological assessment of chondromalacia. Future work will aim to refine how the planar maps are processed and displayed so as to further benefit radiological evaluation.

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AUTOMATED LANDMARK PLACEMENT FOR RADIOGRAPHIC FEMORAL HIP ACTIVE SHAPE MODELING

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INTRODUCTION: Active shape modeling (ASM) is one method of investigating femoral hip shape differences in OA. Pre-specified measures of interest are not required, but landmarks used must represent equivalent anatomic locations across patients. Radiographic hip shapes are often open contours which further complicates landmark placement. Reliable and meaningful placement of equivalent landmarks is needed to accurately compare hips between subjects or over time.

OBJECTIVE: To compare the reproducibility of automated and manual landmark placement methods for hip ASM, and to validate the models on associations with race and gender.

METHODS: AP pelvis radiographs were selected from the OAI study. Two readers (R1 and R2) segmented 1096 hips using software developed in-house (MATLAB, The MathWorks). Fifty-four hips were read for inter-reader reproducibility and 106 hips were read for intra-reader reproducibility. Sixty-point hip shapes were derived from the segmentations using 4 landmarks: (1) inferior margin of the lesser trochanter protuberance, (2) point on the lateral femoral shaft on a line perpendicular to the femoral shaft axis and originating from (1), (3) inferior and (4) superior points of the narrowest femoral neck width perpendicular to the femoral neck axis. Contours were reduced to equally spaced points (10/30/20 points) between landmarks 1, 3, 4, and 2. Landmarks were defined by (a) manual placement and (b) automatic placement calculated from segmentations. Active shape models were constructed for both methods. Reliability was reported as percentage of points with inter-point differences < 2mm, and ICCs for ASM modes. Associations of the resulting modes of variation to race and gender were analyzed using binary logistic regression with GEE to correct for 2 hips per person.

RESULTS: Inter-point differences < 2 mm were 23% (R1) and 37% (R2), and 34% (R1 vs R2) in the manual landmark model; and 87% (R1), 82% (R2), and 83% (R1 vs R2) in the automated landmark model. ICCs were 0.32-0.92 (R1), 0.72-0.96 (R2), and 0.53-0.92 (R1 vs R2) in the 13 manual ASM modes; and 0.87- 0.97, 0.73-0.96, and 0.65-0.96 in the 13 automated ASM modes. In the manual ASM, 3 modes had significant associations with race in men, and 3 modes with race in women ($p<0.05$); in the automated ASM, 5 were significant with race in men and 6 with race in women ($p<0.05$).

CONCLUSION: The associations between ASM modes to race agree with previously reported associations and more significant modes were found in the automatic ASM model. The automated method described presents a more reliable method for placing meaningful landmarks for hip ASM than using manual placement of the 4 landmarks.

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RELIABILITY AND DIAGNOSTIC PERFORMANCE OF SEMIQUANTITATIVE OSTEOARTHRITIS ASSESSMENT USING A NOVEL DEDICATED 1.5 T EXTREMITY MRI SYSTEM COMPARED TO ESTABLISHED 1.0 T EXTREMITY MRI: DATA FROM THE MOST STUDY

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INTRODUCTION: Commonly, semiquantitative (SQ) MRI assessment in osteoarthritis (OA) studies is performed using image data acquired using large bore 1.5 T or 3 T systems. The exception is the MOST study, which has employed 1.0T extremity MRI for SQ OA assessment for cost savings and improved participant comfort during the examination. Comparability with 1.5T large bore systems has been shown previously. Recently a novel 1.5 T extremity system has been introduced that is based on an identical design as the previous 1.0 T system with the advantage of superior image quality due to improved signal to noise and field homogeneity. Comparability of SQ scoring from 1.5T extremity MRI image data and 1.0T in OA assessment has not been shown.

OBJECTIVE: To compare SQ OA scoring on 1.5 T extremity MRI using the established 1.0 T system as the reference.

METHODS: The Multicenter Osteoarthritis (MOST) Study is a longitudinal observational study of individuals who have or are at high risk for knee OA. In a sample of 17 subjects who volunteered to undergo both, 1.0 and 1.5 T extremity MRI fat-suppressed proton-density weighted sequences in the sagittal and axial planes and a STIR sequence in the coronal plane were acquired. MRIs were read according to the Whole Organ Magnetic Resonance Imaging Score (WORMS). Agreement was determined using kappa statistics and overall percent agreement. Sensitivity, specificity, and accuracy were determined using the readings of the 1.0 T system as the reference standard and vice versa (using 1.5T as the reference). Reason for this reciprocal approach was the fact the 1.5 T system is superior to the old system, however the new system needs testing using the established one as the reference as common practice in medicine when new diagnostic tests are introduced. In addition, percentage of non-readable features for both systems was determined.

RESULTS: Percent agreement between 1.0 T and 1.5 T MRI was good to excellent and ranged between 58.8% (joint effusion) and 96.4% (bone marrow lesions). Non-readable features were observed only for the 1.0 T MRI system with 9 of 272 (3.3%) osteophyte locations being the most frequent. Weighted kappas ranged between 0.26 (joint effusion) and 0.89 (meniscal extrusion). Sensitivity of 1.5 T MRI using 1.0 T as the reference ranged between 0.63 (effusion-synovitis) and 0.90 (cartilage morphology). Specificity ranged between 0.67 (effusion-synovitis) and 1.00 (meniscal extrusion). The details on diagnostic performance are presented in **Table 1**.

feature	TP	TN	FP	FN	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)
Cartilage morphology	36 (15.5%)	174 (75.0%	18 (7.8%)	4 (1.7%)	0.90 (0.81,0.99)	0.91 (0.87,0.95)	0.91 (0.87,0.94)
Bone Marrow Lesions	11 (4.5%)	227 (91.9%	5 (2.0%)	4 (1.6%)	0.73 (0.51,0.96)	0.98 (0.96,0.99)	0.96(0.94,0.99)
Osteophytes	57 (21.7%)	160 (60.8%	35 (13.1%)	11 (4.2%)	0.84 (0.75,0.93)	0.82 (0.77,0.87)	0.83 (0.78,0.87)
Meniscal extrusion	6 (17.4%)	26 (76.5%)	0	2 (5.9%)	0.75 (0.45,1.00)	1.00	0.94 (0.86,1.00)
Meniscal tear	8 (7.8%)	65 (63.7%)	28 (27.4%)	1 (1.0%)	0.89 (0.68,1.00)	0.70 (0.61,0.79)	0.72 (0.63,0.80)
Hoffa-synovitis	8 (26.7%)	17 (5.7%)	3 (10.0%)	2 (6.7%)	0.80 (0.55,1.00)	0.85 (0.69,1.00)	0.83 (0.70,0.97)
Effusion-synovitis	5 (29.4%)	6 (35.3%)	3 (10.0%)	3 (10.0%)	0.63 (0.29,0.96)	0.67 (0.36,0.97)	0.65 (0.42,0.87)

CONCLUSION: The newly introduced 1.5 T extremity MRI shows good to excellent agreement and good diagnostic performance when compared to the established 1.0 T MRI system. The lower agreement for effusion-synovitis needs further exploration. The higher frequency of non-readable features using 1.0 T MRI is explained by the inferior field inhomogeneity of the 1.0 T system.

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RELIABILITY OF SEMIQUANTITATIVE OSTEOARTHRITIS MRI SCORING: MULTI-READER CROSS-SECTIONAL AND LONGITUDINAL DATA FROM THE MOST STUDY

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INTRODUCTION: Several large epidemiologic osteoarthritis (OA) studies including magnetic resonance imaging (MRI) are currently ongoing. A large proportion of these MRI datasets is being assessed in semiquantitative (SQ) fashion by teams of expert radiologist readers using validated scoring instruments. For meaningful data interpretation it is paramount to ensure both, cross-sectional and longitudinal reliability between all readers. While cross-sectional reliability results between two trained and calibrated readers have been presented for all MRI scoring systems, data on longitudinal reliability of detection of change over time and agreement among more than two readers has not been presented to date.

OBJECTIVE: The aim of this study was to determine reliability among four different readers in cross-sectional and longitudinal fashion in the MOST study.

METHODS: The Multicenter Osteoarthritis (MOST) study is a longitudinal cohort study of subjects with or at high risk of knee OA. MRI was performed at a 1.0 T extremity system using axial and sagittal proton-density weighted sequences and a coronal STIR sequence. 10 randomly selected subjects were included in substudy A that had 60 months and 84 months MRIs available. Another 10 participants were included is substudy B that had baseline, 60 and 84 months MRIs. Cases were selected to represent a spectrum of disease severity and longitudinal change. MRIs were read by four radiologists separately with the chronological sequence known to the readers. MRIs were assessed semiquantitatively using a modified WORMS system. For substudy B, readers were aware of the baseline images and scores, which they could change when needed. Assessed were cartilage, osteophytes, bone marrow lesions (BMLs), subchondral cysts, bone attrition, meniscus damage, meniscal extrusion, Hoffa-synovitis, effusion-synovitis, cruciate and collateral ligaments, popliteal cysts, tibio-fibular cysts, loose intra-articular bodies and anserine and pre-patellar bursitis. Weighted kappa statistics were applied to determine reliability between readers.

RESULTS: Subjects were on average 65.4 years old (SD ± 7.4) with 12 (60%) women and mean BMI of 29.8 (SD ± 5.0). Two, 7, 6 and 5 knees had baseline Kellgren-Lawrence grades of 0, 1, 2 and 3 respectively. For substudy A, the ranges for inter-reader weighted kappas for cross-sectional and longitudinal reliability, respectively, were 0.77 to 0.87 and 0.62 to 0.78 for cartilage, 0.80 to 0.89 and 0.75 to 0.88 for BMLs, 0.92 to 0.96 and 0.75 to 0.92 for meniscal tears, and 0.47 to 0.80 and 0.43 to 0.76 for osteophytes. For substudy B weighted kappa ranges were from 0.85 to 0.96 (cross-sectional) and 0.50 to 0.82 (longitudinal) for cartilage, from 0.86 to 0.93 (cross-sectional) and 0.71 to 0.88 (longitudinal) for BMLs, from 0.89 to 0.97 (cross-sectional) and 0.71 to 0.88 (longitudinal) for meniscal tears, and from 0.92 to 0.95 (cross-sectional) and 0.49 to 0.71 (longitudinal) for osteophytes.

CONCLUSION: Semiquantitative OA assessment on MRI shows good reliability for up to four trained and calibrated readers. Cross-sectional reliability seems to be slightly superior compared to scoring of change. Reliability did not differ for readings of three time points with baseline known to the readers or for two time points without knowledge of baseline scores, although direct comparability was not possible due to the different reading design of the two substudies.

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INCREASED RISK FOR RADIOGRAPHIC OSTEOARTHRITIS FEATURES IN YOUNG ACTIVE ATHLETES: A CROSS-SECTIONAL MATCHED CASE-CONTROL STUDY

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INTRODUCTION: Sports injury to the knee joint may lead to accelerated joint degeneration and has been observed especially as a long term sequelae of anterior cruciate ligament tears. Data on osteophyte presence and pre-ROA features prevalence in the general population are available for the elderly population but has not been reported for a young at-risk group such as soccer payers. Given exposure to high loads to the knee joint and to minor repetitive trauma, increased subchondral and peripheral bone remodeling may be expected. These changes may be physiologic adaptations to stress or may represent signs of early OA.

OBJECTIVE: Aim was to compare frequencies of OA features on the weight-bearing radiograph in active athletes between 18 and 36 years of age and compare these findings with a reference group of age matched non-athletes. Further, we wished to evaluate whether athlete status, gender, previous ACL surgery and age increase risk for ROA.

METHODS: 135 non-selected consecutive athletes (82% soccer players) 18 to 36 years old and 550 non-athlete aged-matched controls had radiography (Lyon-Schuss protocol) for assessment of subacute or chronic knee complaints. Patients with acute trauma or fractures were excluded. Radiographs were graded according to the Kellgren-Lawrence (KL) (from 0 to 4) and OARSI scales taking into account osteophytes and joint space narrowing (JSN). In addition, medial and lateral intercondylar notch osteophytes were scored. Risk of ROA was assessed using logistic regression models taking into account athlete status, prior ACL surgery, gender and age after adjustment for the same parameters as confounders. In addition maximum osteophyte size according to location was considered.

RESULTS: Included were 685 patients of which 135 were athletes. 556 (81.2%) were male and 129 (18.8%) female. 60 (8.8%) patients had previous ACL surgery. 133 (19.4%) patients were in the age group 18-22 years, 181 (26.4%) in the range of 23-27, 155 (22.6%) in the range of 28-32 and 216 (31.5%) were between 33 and 36 years old. Mean age was 28.5 years (SD ± 6.5). Marginal osteophytes were observed in 3.8% (medial femur), 5.4% (medial tibia), 3.9% (lateral femur) and 6.5% (lateral tibia) of the knees. Joint space narrowing was seen in 2.5% medially and 3.1% laterally, while 8.5% of the patients had radiographic tibiofemoral OA. Risk of tibiofemoral marginal osteophytes was markedly increased for athletes compared to non-athletes for all maximum grades: (aOR 2.9 (1.6;5.4) for grade 1 osteophytes, aOR 4.7 (1.7;13.3) for grade 2 osteophytes and aOR 4.8 (1.0;21.9) for grade 3 osteophytes). Female gender was a protective factor for all osteoarthritis features. Prior ACL surgery highly increased risk for presence of osteophytes. Being in the highest age group increased risk for marginal and notch osteophytes but not for joint space narrowing.

CONCLUSION: Athlete status and higher age increased risk of ROA with previous ACL surgery being the strongest risk factor. No differences in regard to risk of JSN were observed suggesting that osteophytes are earlier manifestations of disease emphasizing the validity of the KL grading scale. Preventive measures are paramount to protect this young active population from premature OA and subsequent joint replacement.

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RECENT MENISCAL SURGERY INCREASES RISK FOR INCIDENT RADIOGRAPHIC OSTEOARTHRITIS AND CARTILAGE LOSS IN THE FOLLOWING YEAR: DATA FROM THE OAI

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INTRODUCTION: Meniscal damage and extrusion are risk factors for the development of radiographic OA and structural progression in OA knees. Meniscal surgery, especially partial meniscectomy, is a very common procedure to alleviate knee pain and functional impairment. However, it is not known if meniscal surgery increases risk for structural joint degeneration in the short term following the surgical procedure.

OBJECTIVE: To assess if meniscal surgery increases risk for incident radiographic osteoarthritis (OA) and cartilage loss in the following year compared to knees that did not undergo surgery and did not show any signs of meniscal damage.

METHODS: Participants were drawn from the Osteoarthritis Initiative (OAI) including 4796 participants with, or at risk of knee osteoarthritis. We studied 355 knees that developed incident ROA before the OAI 48 month visit that were each matched with a control knee that did not develop incident ROA. Matching was done by baseline KL grade, collateral knee KL grade, gender and age within 5 years. MR images were acquired at four OAI clinical centers using Siemens Trio 3 T scanners. MRIs were read for medial and lateral meniscal and for cartilage morphology using the semiquantitative MOAKS system at the time point prior and at the case defining visit. Conditional logistic regression was applied to assess risk of incident ROA while risk of cartilage loss was assessed using logistic regression adjusted for the case/control matching factors. We looked at risk of OA/cartilage loss for knees that had surgery in the year prior developing incident ROA and for knees with prevalent meniscal tears and/or substance loss using knees without prevalent meniscal damage as the reference.

RESULTS: Subjects were on average 60.2 years old (SD ± 8.6), predominantly female (66.5%) and overweight (mean BMI 28.3 SD ± 4.5). Thirty one (4.4%) knees underwent meniscal surgery during the year prior the case defining visit. 238 (34.9%) knees had prevalent meniscal tears and 42 (6.2%) knees showed any meniscal maceration at the time point prior the case-defining visit not including the knees that had surgery. All (100%) knees that had meniscal surgery 58.9% of the knees with prevalent meniscal damage developed incident ROA. 30% of knees with mensical damage and 81.0% of knees with surgery showed cartilage loss, compared to only 23.2% overall. Risk of cartilage loss was significantly increased for knees exhibiting any prevalent meniscal damage without surgery (OR=1.5 95% confidence interval [CI] [1.1,2.2]) but markedly further increased for knees that had surgery (OR=13.1 95% confidence interval [CI] [4.7,36.3]) when compared to knees with normal meniscal morphology as the reference.

CONCLUSION: All knees undergoing meniscal surgery developed incident ROA. Further risk for cartilage loss is much higher for knees undergoing surgery compared to knees with prevalent meniscal damage. Meniscal surgery has deleterious effects on joint structure in knees without ROA. The decision for meniscal surgery needs to be carefully considered in order to avoid accelerated joint degeneration.

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EFFECT OF POSTURE ON FEMORACETABULAR IMPINGEMENT

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INTRODUCTION: Cam-type femoroacetabular impingement (FAI) is associated with abnormal concavity at the femoral head/neck junction. The cam deformity is thought to damage the acetabular labrum and cartilage during some hip movements, which leads to hip pain and ultimately to hip osteoarthritis. The alpha angle describes the location of the cam deformity but does not describe its interaction with the acetabulum. Determining which postures cause impingement between the femoral deformity and the acetabulum is a key step in determining the mechanism of joint damage in FAI, assessing the effectiveness of surgery, and designing effective physical therapy and activity modification programs.

OBJECTIVE: Determine how posture affects direct impingement in patients with cam deformity.

METHODS: We assessed impingement between the cam deformity and the acetabulum in 11 participants imaged in four different postures within a vertical open MR scanner. We recruited 6 males and 5 females (mean age 45 (range 29-52)) with cam FAI from a larger, population-based sample of subjects with hip pain. Each participant was scanned within the 58cm gap of a 0.5T vertical open MRI scanner (MROpen, Paramed, Genoa, Italy). The postures included supine as well as combined hip flexion, adduction and internal rotation (FADIR) in standing, seated and supine postures. Images were taken in the plane passing through the femoral neck axis and perpendicular to the coronal plane of the femur with a slice thickness of 5mm and a gap of 1mm using a 2-channel RF send-receive flex coil and the following pulse sequence: T1 weighted GFE with TR/TE=333/12ms, FA=60°, FOV 220 × 220 mm^2, matrix = 256 × 256, imaging time 133s. We measured the beta angle (Wyss, Clin Orth Rel Res 2007;460:152-8) to describe clearance between the first asphericity on the femur and the most prominent part of the acetabulum (Figure 1). We tested the hypothesis that posture affects beta angle using a repeated measures ANOVA and Tukey's HSD test. We also assessed inter- and intra-reader variability for 3 trials each of 2 readers.

Posture	Beta Angle (degrees) mean (std)	Inter ICC	Intra ICC
Supine	64 (25)	0.98	0.99
Supine FADIR	18 (15)	0.90	0.99
Standing FADIR	36 (20)	0.87	0.97
Sitting FADIR	6 (10)	0.89	0.98

Table 1: Beta angles and inter and intra reader ICCs

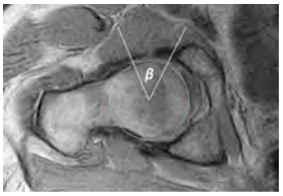

Figure 1: Measurement of beta angle

RESULTS: Beta angles for the four postures were all significantly different from each other ($p<0.05$) (Table 1). The sitting FADIR posture moved the deformity closest to the acetabular rim (lowest beta angle). Inter and intra-reader ICCs were above 0.87 for all measures.

CONCLUSIONS: All FADIR positions move the cam deformity closer to the acetabular rim than the supine position, as reflected by a reduced beta angle. Hips with cam deformities have reduced range of motion in the FADIR position, and our finding of small beta angles at limits of motion in the FADIR position suggests the posture causes interaction between the cam deformity and acetabulum. Sitting FADIR is the posture that moved the deformity closest to the acetabulum, which suggests that this posture may be useful for future imaging studies assessing the risk and mechanism of impingement.

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REPRODUCIBILITY OF A SEMI-AUTOMATIC KNEE JOINT ANALYSIS TOOL

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BACKGROUND: Minimal Joint Space Width (mJSW, defined as the narrowest point of the tibio-femoral joint), and anatomical axis angle (AAA, the angle formed by the lines bisecting the femur and the tibia as they intersect at the center of the tibial spine tips on plain radiographs of the knee can be used to evaluate the severity and progression of knee osteoarthritis. These measurements are therefore useful in determining subject eligibility and safety in clinical trials for osteoarthritis treatment. To be practical for clinical trials, an efficient, accurate and precise measurement system is required which also features the QC tool for Inter-margin-distance (IMD).

OBJECTIVE: To evaluate a new semi-automated knee joint analysis tool to measure mJSW, AAA and IMD for use in clinical trials.

METHODS: Both mJSW and AAA were automatically calculated with minimal user interactions (Figure 1 and 2), while IMD was measured using a built-in caliper. Both mJSW and AAA were measured on AP knee radiographs from 30 subjects or 60 knees, by two experienced users, to assess inter- and intra-observer reproducibility. The Mean (and SD) value of absolute difference in each measurement was computed. IMD precision was not evaluated in this study.

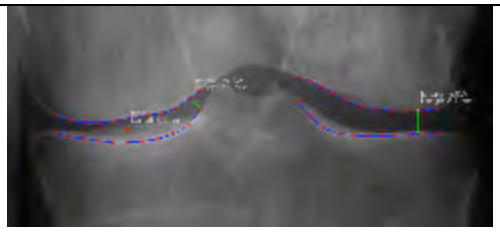

Figure 1. Semi-automatic detection of lateral and medial mJSW

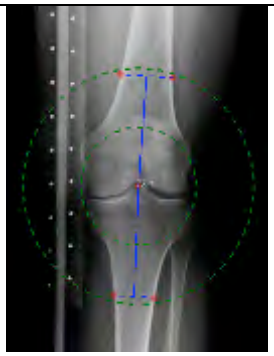

Figure 2. Semi-automatic AAA measurement using the 5 points angle tool

RESULTS: mJSW: The intra-observer ICC values for medial mJSW were 0.991 (0.358, 1.00) and 0.985 (0.362, 1.00), for observers 1 and 2 respectively. The inter-observer ICC for medial mJSW, for read sessions 1 and 2 using the semi-automated method were 0.926 (0.136, 1.00) and 0.910 (0.152, 0.999), respectively. The mean differences (SD) between observers for medial and lateral measurements were 0.477 (0.300) and 0.520 (0.358). AAA: The intra-observer ICC value, for observers 1 and 2 were 0.966 (0.361, 1.00) and 0.944 (0.34, 0.999), respectively. The inter-observer ICC values for read sessions 1 and 2 were 0.824 (0.316, 0.992) and 0.908 (0.335, 0.998) respectively. The absolute difference is less than 1°.

CONCLUSION: The analysis tool presented here provided good intra- and inter-observer reproducibility. The constraints aided in the user a rapid identification of location and reproducible landmarks. This comprehensive semi-automated analysis tool and is suitable for the assessment of knee joints in clinical trials. Further confirmation awaits comparison to manual measurement and application to a larger sample size.

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A SEMI-AUTOMATED SOFTWARE FOR MINIMAL JOINT SPACE WIDTH DETECTION IN HIP RADIOGRAPHS

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BACKGROUND: Joint space width (JSW) and joint space narrowing on plain radiographs are used to evaluate the severity and progression of osteoarthritis and for monitoring the impact of osteoarthritis therapies in clinical trials. The minimal joint space width (mJSW) is defined as the narrowest point between the cortical surface of the acetabulum and the femoral head. The use of manual calipers is prone to operator error for reasons including manual selection of the narrowest point, ensuring measurement is perpendicular to the cortical edge and that measurement does not overlap with cortical bone.

OBJECTIVE: A semi-automated software to evaluate mJSW was developed for improved precision and higher throughput analysis in clinical trials and is presented here.

METHODS: The mJSW in millimeters (mm) was measured on both right and left hips by 2 techniques: 1) manually using a caliper tool and 2) using the semi-automated software. Measurements were made by 2 experienced observers on AP pelvis radiographs from 30 subjects. Each observer measured the mJSW using both techniques, twice over a minimum interval of 15 days. The mJSW values from both methods were compared and presented as mean +/- SD. Intra- and inter-observer reproducibility was assessed using the intra-class correlation coefficient (ICC) and the Bland-Altman plotting method.

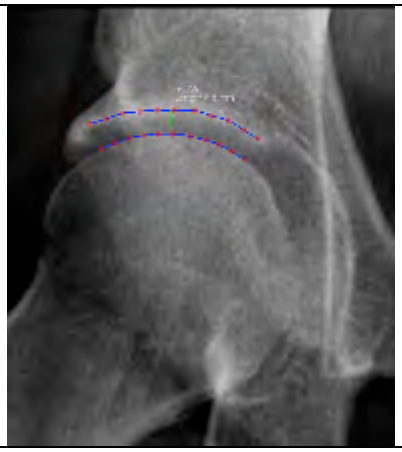

Figure 1. Semi-automatic detection of hip mJSW

RESULTS: The intra-observer ICC values, for observers 1 and 2 using the semi-automated method were 0.96 and 0.99, respectively, whereas the overall ICC from manual measurement was 0.80. The inter-observer ICC values, for read sessions 1 and 2 using the semi-automated method were 0.85 and 0.88, respectively, whereas the overall ICC from manual measurement was 0.62. The Inter-observer bias (mean difference, [SD]) was higher for manually measured mJSW (-0.77 mm, [0.78]) compared to semi-automated measured mJSW (-0.38 mm, [0.07]).

CONCLUSION: This technique provided good intra- and inter-observer reproducibility and provided superior precision from mJSW obtained from manual measurements. This new technique for mJSW measurement is suitable for use in clinical trials where assessment of the hip joint maybe required.

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TISSUE QUANTIFICATION THIGH MRI IN OSTEOARTHRITIS

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INTRODUCTION: Inter-muscular and intra-muscular adipose tissues are defined as the adipose tissue visible between muscle groups and muscle fibers, respectively. The quantities of inter-muscular adipose tissue (inter-MAT), intra-muscular adipose tissue (intra-MAT) and muscle in the thigh reflect adverse metabolic effects and muscle function. Traditional manual analysis is time-consuming and operator-dependent, especially towards 3D datasets, thus not best suited for use in clinical trials.

OBJECTIVE: Here we propose a robust and semi-automatic algorithm for the quantitative assessment of volume and cross-sectional area (CSA) of thigh muscle, inter- and intra-muscular fat. Furthermore, this technique has been applied to the Osteoarthritis Initiative (OAI) MRI data to explore differences of such metrics between those with radiographic osteoarthritis (ROA) and those without ROA (non-ROA).

METHODS: The OAI database was queried for subjects with the KLG scores and mid-thigh axial T1-weighted MRIs (15 contiguous slices, 5 mm slice thickness) at baseline. 103 subjects out of 4,796 participants were drawn, and 88 subjects (51 male, 37 female; age: 45-79) were processed after image QC. The left leg of each subject was processed and were visually inspected and corrected for segmentation errors. The legs with KLG score 0 or 1 were labeled as non-ROA; those with KLG score 2, 3 or 4 were labeled as ROA. An semi-automatic quantification algorithm was applied, which includes 5 major steps: 1) intensity inhomogeneity correction; 2) subcutaneous adipose tissue removal; 3) tissue labeling for bone, marrow, fat and muscle; 4) inter- and intra-MAT classification; 5) tissue assessment. Total volume (15 slices) and CSA at the 14^{th} slice were calculated and quantification differences of tissue between groups (1. ROA vs non-ROA, 2. Male vs Female) were explored using t-tests. Correlations were examined between subject demographic, KLG status and tissue volumes and CSAs.

RESULTS: There was no significant difference between ROA and non-ROA legs for inter-MAT volume presented as mean ± SD (90.42±55.21 cm^3 vs 102.11±55.42 cm^3, $p = 0.27$), intra-MAT volume (64.73±41.89 cm^3 vs 63.99±37.44 cm^3, $p = 0.84$), and total muscle volume (746.44±299.54 cm^3 vs 708.35±344.99 cm^3, $p = 0.47$). Gender differences were found for inter-MAT volume (105.85±53.91 cm^3 vs 88.20±52.98 cm^3, $p < 0.01$), intra-MAT volume (72.79±40.63 cm^3 vs 53.00±30.16 cm^3, $p < 0.01$), and total muscle volume (809.80±391.54 cm^3 vs 604.55±241.20 cm^3, $p < 0.01$), where male has higher volumes than female, with no significant gender differences for KLG status and total thigh volume. These tissue assessments were also significantly correlated to BMI (r-values ranging from 0.46 to 0.66, $p < 0.01$), with no age dependency. Results were consistent for CSA analyses.

CONCLUSION: Preliminary results showed gender differences in adipose tissue and muscle content in thigh tissue quantification but according to KLG status. The proposed algorithm provides a semi-automated approach for quantitative thigh tissue assessment, which has a potential for clinical and clinical trial applications. Further validation is required and there are ongoing development efforts which include comparison to manual segmentation, enhancement of clustering and contouring accuracy and precision for fatty infiltration, and individual muscle group segmentation.

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ACKNOWLEDGMENT: None.
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SIX WEEKS OF KNEE JOINT DISTRACTION: SUFFICIENT FOR CARTILAGE TISSUE REPAIR

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INTRODUCTION: We previously reported on the prospective evaluation of knee joint distraction (KJD) treatment in case of end stage knee OA considered for a prosthesis. In 20 patients significant cartilage repair at 1 year and beyond accompanied by clinical benefit could be demonstrated. During the 8-week distraction period these patients visited every 2 weeks (three times) day care practice. After temporarily removal of the distraction frame, the knee was passively bent in a continuous passive motion (CPM) device. Patients might perceive the 8 weeks of intermittent KJD with frequent hospital visits as a burden.

OBJECTIVE: The aim of this study was to evaluate whether 6 weeks of continuous KJD gives the same tissue structure repair and clinical benefit as eight weeks of KJD at 1-year follow-up.

METHODS: The 8-week KJD group consisted of 20 patients (age 49 ± 6; mean ± SD), eligible for total knee prosthesis (TKP) based on symptoms and radiological signs of knee OA (KLG 2.6 ± 0.9 at baseline). The 6-week KJD group consisted of 20 patients (age 55 ± 8, KLG 3.0 ± 0.9 at baseline (BL)), who were included in an ongoing randomized controlled trial in the Sint Maartenskliniek Woerden. Both groups were treated with 5 mm joint distraction by use of an external fixator for 8 weeks (average 59 days ± 4) with every 2 weeks CPM or 6 weeks (average 42 days ± 2) continuously. At the different outpatients visits (BL, 3, 6 and 12 months) a WOMAC (100 being the best condition) questionnaire and the VAS for pain (0 meaning no pain) were assessed, representing the clinical outcome. Structural outcome was quantified as the change in minimum (min) JSW and mean JSW on standardized semi-flexed x-rays at BL and 1 year of follow-up using KIDA software (Marijnissen et al. OAC 2008;16:234-). T-tests were applied to analyze change over time for different parameters. To compare both groups general linear modeling (GLM) was applied.

RESULTS: The 6-week group showed an comparable increase from 53 ± 17 points at BL to 76 ± 17 points at one-year follow up ($p<0.001$) as the 8-week group (from BL 45 ± 16 points to 77 ± 21 points at the 1-year follow-up; $p<0.001$). Similar results were found for the individual components of the WOMAC index (pain, stiffness and function). Akin, similar responses were found for the VAS pain score (6-weeks: from 60 ± 20 mm to 37 ± 24 mm; $p=0.002$ vs. 8-weeks 73 ± 9 mm to 31 ± 26 mm; $p<0.001$). GLM showed no statistical significant difference between the two groups ($p=0.591$), as over time ($p=0.420$) for the WOMAC index score. Most importantly, the structural parameters revealed similar improvements between both groups. The mean JSW of the most affected compartment (MAC) of the 6-week group increased from 1.80 ± 1.61mm at BL to 2.86 ± 1.59mm at 1 year ($p=0.001$) vs. 2.63 ± 1.62mm at BL to 3.55 ± 0.99mm at 1 year ($p=0.006$) for the 8-week group. The min JSW of the MAC shows a similar trend in both groups (6-week: 0.54 ± 1.06mm to 1.39 ± 1.03mm; $p=0.002$ vs. 8-week: 1.03 ± 1.27mm to 2.12 ± 1.30mm; $p<0.001$). Both the increase of the mean and min JSW showed no significant statistical difference between the two groups ($p= 0.729$ and $p=0.463$). Interestingly, despite the smaller JSW in the 6-weeks KJD treatment as compared to the 8-weeks KJD (1.8 vs. 2.63mm resp.), the increase in both groups was similar (+1.06 ± 1.19mm for 6-week vs. +0.92 ± 1.33mm for 8 week).

CONCLUSION: 6 weeks continuous KJD gives significant clinical improvement and a significant increase in radiographic JSW suggesting functional cartilage tissue repair. Moreover, 6 weeks of continuous distraction treatment does not lead to a stiffer knee in comparison with the 'intermittent' 8-week treatment. The higher age and slightly higher K&L grade, supported by the smaller JSW at base line did not influence the cartilage tissue structure repair, suggesting that cartilage tissue repair is even possible by KJD in severely damaged joints.

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MRI OSTEOARTHRITIS SOFTWARE SCORE (MOSS): A COMPUTERIZED METHOD FOR QUANTITATIVE ASSESSMENT MORPHOLOGIC FEATURES OF KNEE OSTEOARTHRITIS

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INTRODUCTION: Magnetic resonance imaging (MRI) is an ideal modality for assessing the progression of knee OA since the soft tissue structures relevant to the disease are easily visualized. Research studies use semi-quantitative scoring systems such as the Whole-Organ MRI Score (WORMS), Boston Leeds OA Knee Score (BLOKS), and MRI OA Knee Score (MOAKS) to assess knee MRI data sets. Fully quantitative software-based methods have also been developed and validated by various groups to provide individual measures of morphological change. However, there exists no comprehensive quantitative software scoring system analogous to WORMS, BLOKS, or MOAKS.

OBJECTIVE: The goal of this study is to report progress on developing the MRI Osteoarthritis Software Score (MOSS), a fully quantitative tool to assess morphologic features such as cartilage, bone marrow lesions (BMLs), osteophytes, effusion-synovitis, Hoffa's synovitis, and meniscal changes on knee MRI data sets.

METHODS: Our group has developed and validated several automated software tools to measure individual structures of knee OA on MRI images. For cartilage morphometry we have developed the Local-Area Cartilage Segmentation (LACS) technique, which can be used to measure cartilage volume and thickness in localized regions of the femur. The regions are established with respect to a mathematically robust coordinate system defined with respect to anatomical landmarks. BML volume is measured using a semi-automated threshold-based software tool that allows the reader to select relevant hyper intense regions corresponding to OA-related BMLs. A similar technique is used to segment areas of effusion-synovitis. The tool uses an edge detection algorithm to determine osteophyte volume in the central weight-bearing region on sagittal scans. Hoffa's synovitis is evaluated by applying a software algorithm to regions of interest on the image that provides an output that relates to gray scale patterns associated with Hoffa's fat pad edema.

RESULTS: The computerized methods have been validated in several studies using data from the Osteoarthritis Initiative (OAI). Longitudinal studies of OAI subjects demonstrated that measures of cartilage and osteophyte volume were reproducible and responsive. The BML volume measurement was shown to be reproducible, have criterion validity through a comparison to WORMS scores and clinical validation through association with weight-bearing knee pain. A comparison to MOAKS scoring was used to establish the criterion validity of the effusion-synovitis and Hoffa's synovitis components of MOSS. A software method to characterize the structural changes associated with meniscal damage is under development.

CONCLUSION: We report substantial progress on the development of MOSS, a software-based quantitative OA scoring method for knee OA. Future work will include adding the tibia and patella to the LACS method, further refinement and validation of the osteophyte and synovitis components, and developing a tool to characterize meniscal changes. Once completed, we expect MOSS to provide quantitative assessments of each of the individual OA-related structures as well as a single "global" score that integrates all measures.

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DISCLOSURE STATEMENT: None.
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A NEW COMPUTERIZED MEASURE OF CAM FAI FROM AP PELVIS RADIOGRAPHS

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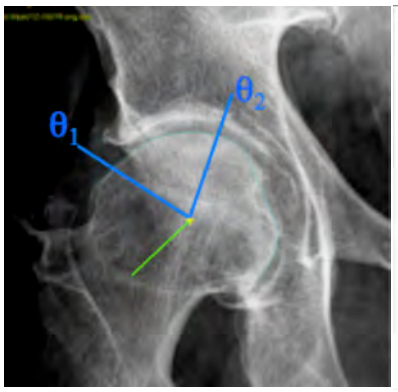
INTRODUCTION: Femoral-acetabular impingement (FAI) of the hip was first formally described in 1999 and has subsequently been proposed as an explanation for the majority of primary hip OA. CAM-type FAI is caused by a bony 'bump' at the superior-lateral femoral head-neck junction ('pistol grip' deformity) and has been associated with subsequent development of hip OA (Nichols 2011, Thomas 2012). The best current radiographic measure is the alpha angle on an AP pelvis or specialized oblique lateral views (e.g., Dunn view). While the AP pelvis view is most often available clinically and for large research cohorts (e.g, OAI), alpha angle measured from this view may miss some CAM deformity. Furthermore the angle is based on just a single point and does not reflect the full shape and size of the CAM deformity.

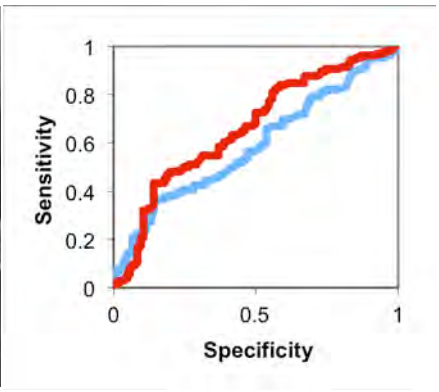
HYPOTHESIS: We hypothesize that a new metric based on the shape of the superior-lateral portion of the femoral head and neck will be a better diagnostic preditor (as measured by the AUC) for subsequent symptomatic hip OA than the alpha angle alone.

METHODS: A case-control study (n=158) was conducted among subjects from the OAI, a longitudinal cohort study of knee OA. OAI participants had standing AP pelvis radiographs at baseline and 48 month visits using a standardized AP protocol. We identified subjects who had a THR at any point after baseline but before 48 months (n=79). These subjects were matched (1:1) on age and gender with subjects who did not receive a THR, reported no hip pain, and had no self-reported diagnosis of hip OA.

Measurement: The method was facilitated by our automated software, developed to measure JSW, which automatically delineated the margins of the femoral head and neck. Using the center point of the head and the axis of the femoral neck (Figure 1) we converted the delineated margins to polar coordinates, where r was the distance from the center point to the delineated margin, and q was the angle with respect to the neck axis (green line). A second order polynomial ($r = C_0+C_1q + C_2q^2$) was fit to the portion of the curve between two angles: q_1 and q_2. A new metric (ξ) was defined as a linear weighed sum of the coefficients ($\xi = w_0C_0 + w_1C_1 + w_2C_2$). ξ was optimized as a function of q_1, q_2, w_0, w_1, and w_2.

Analysis: Receiver operating characteristic (ROC) analysis to distinguish between cases and controls and a threshold on ξ defined true positives (TPs), false positives (FPs), true negatives (TNs) and false negatives (FNs). Varying the threshold allow us to map out the ROC curve and calculate the area under the curve (AUC) for both measures.





RESULTS: The ROC curves for the alpha angle (blue) and x (red) are shown in Figure 2. The AUC was 0.587 and 0.661 for alpha angle and x respectively.

CONCLUSION: The new metric x is promising and may mitigate some of the problems associated with measuring alpha angle on standard AP hip radiographs.

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DISCLOSURE STATEMENT: None.

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MECHANICAL AND ANATOMIC MALALIGNMENT INDEPENDENTLY PREDICT COMPARTMENT SPECIFIC KNEE JOINT SPACE NARROWING LONGITUDINALLY

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INTRODUCTION: Lower limb malalignment assessed from the mechanical axis from hip-knee-ankle angle (HKA from full limb radiographs) correlates with an anatomic femorotibial axis (FTA from knee radiographs) but there are often knees in which there are disagreements on malalignment.

OBJECTIVE: We investigated the associations between both HKA and FTA and longitudinal joint space narrowing (JSN), in knees from the Osteoarthritis Initiative (OAI)

METHODS: Measurements of HKA and FTA and OARSI scores for JSN from the OAI publically released datasets were used. Knees were categorised based on 2 outcomes of JSN worsening (medial or lateral) between baseline and 48-month follow-up visits. Knees showing no JSN worsening were the reference group. Malalignment was classified as neutral, varus or valgus using each of HKA and FTA. Neutral HKA was -2 to +2 degrees, and neutral FTA was -7.3 to -3.3 degrees. Logistic regression with GEE (since more than 1 knee per person) was used to investigate whether HKA and FTA predicted JSN outcomes. Covariates were age, sex, BMI, baseline OA severity (Kellgren and Lawrence grade).

RESULTS: The table below shows odd-ratios for both medial and lateral JSN outcomes for knees for the different categories of malalignment predictors. Knee varus on both HKA and FTA have highly increased odds of medial JSN worsening and highly decreased odds of lateral JSN worsening. Similarly knees valgus on both methods have highly increased odds of lateral JSN worsening and highly decreased odds of medial JSN worsening. When one of the methods categorised the knee as neutral, those odds were diminished. When the 2 methods disagreed (ie: varus on one method but valgus on the other), odds of lateral JSN worsening increased compared to knees neutral by both methods.

Table 1. Odds-ratios (OR) for categories of malalignment predicting JSN worsening.

Malalignment			Medial JSN Worsening				Lateral JSN Worsening			
HKA	FTA	N	OR	95% CI		p	OR	95% CI		p
Neutral	Neutral	1243	REF				REF			
Neutral	Varus	188	2.00	1.31	3.05	0.0012	0.15	0.02	1.18	0.0714
Varus	Neutral	972	2.60	1.98	3.41	<.0001	0.21	0.09	0.52	0.0007
Varus	Varus	765	3.20	2.38	4.30	<.0001	0.04	0.01	0.32	0.0020
Neutral	Valgus	258	0.84	0.46	1.53	0.5694	6.27	3.77	10.42	<.0001
Valgus	Neutral	341	0.40	0.22	0.74	0.0037	3.43	2.01	5.84	<.0001
Valgus	Valgus	382	0.20	0.08	0.49	0.0005	12.46	8.08	19.22	<.0001
Varus	Valgus	81	0.9	0.37	2.18	0.8191	3.12	1.33	7.34	0.0090
Valgus	Varus	20	0.73	0.1	5.04	0.7468	6.51	1.01	41.99	0.0489

CONCLUSION: HKA and FTA appear to be independently associated with longitudinal worsening of joint space. Further work, including assessing longitudinal changes in alignment is needed.

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IMAGING FOR MULTI-CENTER OA CLINICAL TRIALS

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INTRODUCTION: The OAI has more or less defined what level of imaging is expected in an osteoarthritis clinical trial. Although the OAI utilized three MR imaging sites, all of the sites had the same scanner, with the same hardware, software and coils. When considering running a multi-center clinical trial, it is very unlikely to achieve that level of homogeneity in the MRI scanners at the imaging sites. In this paper, we present some of the challenges and considerations when attempting to standardize the imaging across multiple vendors with different hardware and software configurations.

OBJECTIVE: The objective of this paper is to educate the audience of the issues that may arise when implementing the imaging portion of a multi-center OA clinical trial. Things to consider include the imaging endpoints, the magnet strength, the sequences that are available on the different vendors' scanners, and what packages/coils are required to implement the required protocol.

METHODS: Many of the MRI endpoints that would be recommended for an OA clinical trial are the ones that have been utilized in the FNIH Osteoarthritis Biomarker Project. Quantitative MRI biomarkers to consider are morphological measurements of bone, cartilage and meniscus, T2 relaxation time, bone marrow lesion volume, synovitis and effusion volume, and osteophyte volume. Semi-quantitative MRI scoring such as MOAKS (MRI OsteoArthritis Knee Score) may also be considered. Certain advanced imaging techniques that provide compositional cartilage measurement, such as sodium imaging and T1-rho are not suitable for most multi-center clinical trials as the required sequences are not available on clinical magnets. T2 mapping may be useful, but on GE, it requires the purchase of their CartiGram package. Obtaining multiple sequences to perform all of the possible measurements may prove too time-consuming, and patient burden is a serious consideration in clinical trials. Many of the required MRI sequences are not what most sites would consider "standard of care", requiring detailed training for the imaging sites. In addition, the longer the patient lies in the magnet, the more likely the patient is to move. Motion artifacts will lead to additional scanning time, and possibly rescanning of the patient, or increased variability in the measurements made from those images.

CONCLUSIONS: Several factors should be considered while designing the imaging portion of an OA clinical trial. These decisions will affect the imaging sites that can be utilized, the patient burden, the endpoints and the variability in those endpoints, which ultimately affects the power of the study.

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MULTIVARIATE ANALYSIS OF OAI IMAGE ASSESSMENTS: A WIDE ASSOCIATION STUDY FOR PROGRESSION INDICES

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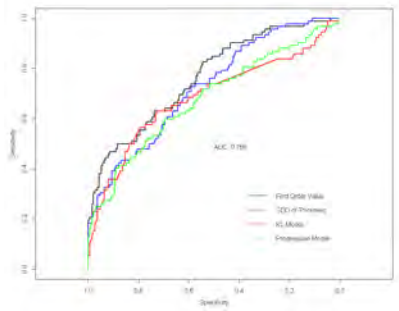
INTRODUCTION: Kellgren-Lawrence (KL) grades, which are based on several plain film findings, present a composite index for Osteoarthritis (OA). Several scoring systems and quantitative analyses exist for MRI-based OA findings, however there is no method for a comparable MRI OA index.

OBJECTIVE: (1) To evaluate which quantitative MRI parameters comprise the best OA index for staging and evaluating OA and (2) to compare the performance of the MRI OA index to KL and to ordered statistics.

METHODS: Publicly-available OAI MRI assessments (Project 9A, F. Eckstein) and X-ray (Project 15, BU) for 565 subjects (236 Male, 329 Female) were selected. 72 Baseline, 12M and 24M MRI variables, except denuded variables and baseline and 24M central X-ray reads of KL, medial and lateral JSN were adjusted for gender, age and height. Subjects with no denuded areas and JSN=0 were used to estimate the adjusting equation. Adjusted measurements were normal-rank-inverse standardized according to the distribution of subjects with JSN=1 and no denuded areas, then split into two equal sets; one for training and biomarker discovery and one for testing and reporting. Baseline KL scores were insufficiently populated with KL 4 cases, therefore the 24M observation of the training set was used to model the KL scores yielding a split of KL 2 cases into KL 1.5 cases with JSN=0 and KL 2 cases with JSN = 1. A Wilcoxon test on residual improvement was used to find the best linear model (R v3.0.3, www.r-project.org). 250 bootstraps were performed on the training set to determine the optimal MRI factor index to mimic the BU KL scores. OA progression was modeled using time as the dependent factor in the linear model $t=b_0+\ldots+b_ix_i$ using 200 bootstraps on the training set to determine the optimal factors. The KL and progression models were applied to the testing set using subjects with worsening KL or JSN scores at 24M as cases. AUC was used to evaluate the predictive ability of the multivariate models to predict x-ray progression. ROC curves of the models were compared to ordered MRI features, including the first order value, last order value, standard deviation of the differences (SDD) in mean thickness and the range between first and last ordered value. Finally, standard response mean (SRM) was calculated for the models.

RESULTS: The optimal KL and Progression models ROC curves are presented in Fig. 1 compared to ordered statistics (first ordered value and SDD of thickness). AUCs for the models were .686, .680, .766 and .726, respectively. The multivariate index predictive ability at 24M yielded SRMs of .864 (cases) and .537 (controls).

ROC Comparisons:



KL Index:

EMTMTH	Mean cartilage thickness - medial tibia (external) (eMT.ThCtAB) [mm]
CBMFMTH	Mean cartilage thickness - central medial femur (center) (ccMF.ThCtAB) [mm]
CMTMTH	Mean cartilage thickness - medial tibia (center) (cMT.ThCtAB) [mm]
WMTFVCL	Cartilage volume - medial tib-fem compartment (MFTC.VC) [mm^3]
EBMFMTH	Mean cartilage thickness - central medial femur (external) (ecMF.ThCtAB) [mm]
WLTACS	Area of cartilage surface - lateral tibia (LT.AC) [cm^2]

Progression Index:

BMTFMTH	Mean cartilage thickness - central medial tib-fem compartment (weight bearing) (cMFTC.ThCtAB) [mm]
BLFCTS	SD of cartilage thickness - central lateral femur (cLF.ThCtAB) [mm]
WLTSBA	Total area of subchondral bone - lateral tibia (LT.tAB) [cm^2]
WMTSBA	Total area of subchondral bone - medial tibia (MT.tAB) [cm^2]
BMFACS	Area of cartilage surface - central medial femur (cMF.AC) [cm^2]
BLTFMTH	Mean cartilage thickness - central lateral tib-fem compartment (weight bearing) (cLFTC.ThCtAB) [mm]
EBMFMTH	Mean cartilage thickness - central medial femur (external) (ecMF.ThCtAB) [mm]

Figure 1. ROC comparisons of KL and Progression multivariate models with ordered statistics (first order value and standard deviation of the differences in thickness).

CONCLUSIONS: The multivariate index predicted KL scores with good sensitivity to longitudinal change. The predictive performance of the index was equivalent to ordered value statistics of individual features, however, the indices do not have bias, therefore they supported computation of SRM as well as the ability to use a minimum detection limit to set a threshold for progression. Ordered value statistics, e.g. first order value and standard deviation of differences are biased statistics; therefore it is not possible to compute SRM. Therefore, use of a multivariate MRI index may provide practical benefits in clinical trial settings.

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TWO YEAR LONGITUDINAL CHANGE IN SIZE AND POSITION OF THE MEDIAL AND LATERAL MENISCI IN KNEES WITH MEDIAL RADIOGRAPHIC JOINT SPACE NARROWING (JSN)

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INTRODUCTION: Quantitative, MRI-based 3D technology for measuring meniscus size and position has been developed. Baseline measures have been related to pain, radiographic OA stage, and subsequent cartilage loss. However, longitudinal changes of 3D meniscus size and position have not been reported.

OBJECTIVE: To study longitudinal rates and sensitivity to change of size and position measures of the medial and lateral meniscus over 2 years (Y) in knees with medial radiographic joint space narrowing (JSN). To explore whether the rate of change depends on age, sex, BMI, baseline radiographic JSN grades, and /or baseline semi-quantitative MOAKS (MRI Osteoarthritis Knee Score) meniscus lesion or extrusion scores.

METHODS: We studied 60 participants with bilateral painful knees, with unilateral medial (but not lateral) OARSI JSN grade 1-3 [contralateral knee OARSI JSN grade 0] from the OAI (38 women, 22 men; age 61.3±9.2 years, BMI 31.3±3.9). Of these, 47 had MRI follow-up 2 years (Y) later (37 JSN grade1, 10 JSN 2/3). The menisci were evaluated semi-quantitatively (IW-TSE fs) by an expert radiologist (AG) using the MOAKS system. Manual segmentation of the medial and lateral meniscus and tibial plateau surface was performed on coronal MPRs of baseline and 2Y DESSwe images. The %-coverage of the tibia by the meniscus, total extrusion area, extrusion distance (central slice), and the volume, width, and height throughout the total medial and lateral meniscus were computed using custom software (Chondrometrics GmbH). Differences between baseline and 2Y follow-up are reported as absolute and percent changes, and the standardized response mean (SRM =mean/SD change) as a measure of sensitivity to change. General linear models and one-factorial ANOVA were used to evaluate the impact of age, sex, BMI, JSN, MOAKS lesions and extrusion scores on longitudinal changes.

RESULTS: Over 2 years, meniscus coverage of the tibia decreased from 34.8% (mean) to 29.9% medially (SRM -0.82), and from 58.0% to 54.4% (SRM -0.96) laterally (both $p<0.001$). The relative area of the meniscus extruding the tibia increased 28.7% to 33.9% medially (SRM 0.56; $p<0.001$), but did not show a significant change laterally (3.9% to 4.2%; SRM 0.13; $p=0.39$). Longitudinal changes of other measures are shown in Table 1. Volume loss in the central part of the medial meniscus (-7.5%; SRM -0.39) was similar to that of the total meniscus (-9.5%; SRM -0.56), but was stronger in the posterior (-13.3%; SRM -0.51) than in the anterior horn (2.8%; SRM -0.15). 2-year change in medial tibial coverage, extrusion area, and meniscus volume was not significantly associated with age, sex or BMI ($p>0.29$). Although loss of %-tibial coverage and meniscus volume, and gain in extrusion tended to be greater in JSN 2/3 than in JSN1 knees, the difference did not reach statistical significance ($p=0.08$-0.31). The changes did not show a significant relationship with baseline MOAKS lesion or extrusions scores, but the increase in extrusion area showed a borderline significant relationship with greater lesions scores ($p=0.06$).

Table 1: Two-year change in quantitative measures of meniscus size and position

	Medial meniscus		Lateral meniscus	
	% change (p)	SRM	% change (p)	SRM
Extrusion distance (mm)	+7.2% (0.21)	0.18	(no extrusion at baseline)	
Meniscus volume (mm3)	-9.5% (<0.001)	-0.56	-1.7% (0.29)	-0.16
Meniscus width (mm)	-7.3% (<0.001)	-0.72	-4.4% (<0.001)	-0.69
Meniscus height (mm)	-1.8% (<0.08)	-0.26	3.1% (0.001)	-0.50

CONCLUSION: To our knowledge, this is the first study to report the longitudinal rate of change in medial and lateral meniscus position and size using 3D MRI measurement technology. The study confirms that, at least in knees with medial radiographic JSN, 2-year changes in the medial meniscus can be captured with reasonable sensitivity to change. A substantial loss of tibial coverage and increase in extrusion area was noted, and meniscus volume loss was greatest in the posterior, and least in the anterior horn.

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INDICES OF PARASPINAL MUSCLE DEGENERATION: RELIABILITY AND ASSOCIATION WITH FACET JOINT OSTEOARTHRITIS

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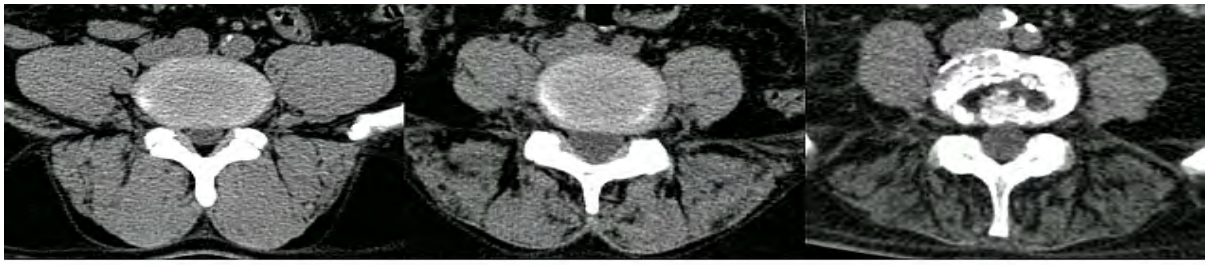
INTRODUCTION: Current evidence suggests that the paraspinal muscles degeneration is associated with low back pain, facet joint osteoarthritis, spondylolisthesis and degenerative disc disease. However, the evaluation of paraspinal muscles on CT is not radiological routine, probably because of absence of simple and reliable indices of paraspinal degeneration.

OBJECTIVE*:* to introduce a scoring system for visible fat infiltration in paraspinal muscles; to evaluate inter- and intra-tester reliability of this system and its relationship with indices of muscle density; to evaluate the association between indices of paraspinal muscle degeneration and facet joint osteoarthritis.

METHODS: A reliability and cross-sectional observational study. 150 consecutive CT scans of the lower back (N=75) or abdomen (N=75) were evaluated. Mean radiographic density (in Hounsfield units) and standard deviation (STD) of the density of multifidus and erector spinae were evaluated at the L4-5 spinal level. A new index of muscle degeneration, radiographic density ratio (RDR) = muscle density/STD of density, was calculated. To evaluate the visible fat infiltration in paraspinal muscles, we proposed a 3-graded scoring system (Figure 1). The prevalence of facet joint osteoarthritis was also evaluated. ICC and Kappa statistics were used to evaluate inter- and intra-rater reliability. Logistic regression examined the association between paraspinal muscle indices and facet joint osteoarthritis.

Figure 1. Examples of different grades of paraspinal muscle degeneration.



RESULTS*:* Intra-rater reliability for fat infiltration score (kappa) ranged between 0.87-0.92; inter-rater reliability between 0.70-0.81. Intra-rater reliability (ICC) for mean density of paraspinal muscles ranged between 0.96-0.99, inter-rater reliability between 0.95-0.99; STD intra-rater reliability ranged between 0.82-0.91, inter-rater reliability between 0.80 -0.89. Significant associations ($p<0.01$) were found between facet joint osteoarthritis, fat infiltration score and RDR.

CONCLUSION: Two suggested indices of paraspinal muscle degeneration showed excellent reliability and were significantly associated with facet joint osteoarthritis. Additional studies are needed to evaluate the associations with other spinal degeneration features and low back pain.

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T2 VALUE OF THE TALAR TROCHLEAR ARTICUALR CARTILAGE: COMPARISON BETWEEN LATERAL INSTABILTITY PATIENTS AND HEALTHY VOLUNTEERS

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INTRODUCTION: Although posttraumatic osteoarthritis of the ankle after fracture is well established, It has not been well known whether the lateral ankle instability without gross cartilage injury can cause talar cartilage damage or not.

PURPOSE: To evaluate the difference in T2 value of talar trochelar cartilage (TTC) between lateral instability patients and healthy volunteers.

METHODS: The study was approved by our institutional review board and informed consent was waived for patients and taken from all volunteers. Retrospectively enrolled patients received preoperative MR and surgery from April 2011 to January 2013. Thirteen ankle MRIs including T2 mapping in 12 patients (10 male, 2 female, mean age of 34.8) who underwent Broestrôm operation for lateral instability with arthroscopically proven normal TTC were enrolled. Then 13 ankle MRIs in age, sex matched 12 healthy volunteers were obtained prospectively. T2 mapping using the multi-echo sequence (TR; 2756ms, TE; 15, 30, 45, 60, 75, 90ms) was obtained in sagittal plane. Two radiologists measured T2 value of TTC [two layers (superficial and deep) and 6 compartments (medial anterior, M1; medial middle, M2; medial posterior, M3; lateral anterior, L1; lateral middle, L2; lateral posterior, L3)] using commercial software independently. They measured in three consecutive T2 maps for medial or lateral TTC, and the mean of values were regarded as representative T2 value of each compartments. Mann Whitney U test was used to evaluate the difference of T2 values between patients and healthy volunteers, and ICC was performed to evaluate the intra- and inter-observer reliabilities.

RESULTS: For reviewer 1, the mean T2 value of TTC in 5 compartments of superficial layer excluding M1 was significantly higher in patients group (M2 superficial; p=0.0008, M3 superficial; p=0.001, L1 superficial; p=0.045, L2 superficial; p=0.0004, L3 superficial; p=0.0008). The rest of compartments excluding L1 deep layer show higher T2 value in patients but there were no statistical difference. For reviewer 2, the mean T2 value of TTC was significantly higher in patients group in all 6 compartments of superficial layer and M2 of deep layer (M1 superficial; p=0.008, M2 superficial; p=0.0004, M3 superficial; p=0.005, L1 superficial; p=0.013, L2 superficial; p=0.0029, L3 superficial; p=0.021, M2 deep; p=0.008). The rest of 5 compartments of deep layer show higher T2 value in patients but there was no statistical difference. All the intra- and inter-observer reliabilities were excellent.

CONCLUSION: T2 value of arthroscopically proven normal TTC in lateral instability patient was higher than that of normal volunteer.

DICLOSURE STATEMENT: none.
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COMPARISON OF MEASUREMENTS OF TIBIOFEMORAL JOINT SPACE WIDTH FROM STANDING CT AND FIXED FLEXION RADIOGRAPHY

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INTRODUCTION: Because plain radiographs capture a 3D structure in 2D, patient positioning has a large impact on the apparent tibiofemoral joint space width (JSW) on radiographs. In addition to methods for standardizing positioning, multiple techniques (e.g. fluoroscopic positioning or radiographic exposures at multiple beam angles) are used in an effort to achieve superimposition of the anterior and posterior margins of the medial tibial plateau, a key criterion for the reproducible measurement of JSW. Low dose, standing CT (SCT) could enable the optimal assessment of JSW on every acquisition by assuring consistent measurement of the distance between the bony margins without the interference of overlapping anatomy.

OBJECTIVE: To determine the correspondence between the mean medial tibiofemoral JSW(x) obtained from fixed flexion radiographs and the distribution of JSW at each of corresponding locations on 3D SCT.

METHODS: This study was conducted ancillary to the 84-month visit of the Multicenter Osteoarthritis Study (MOST). We recruited 20 participants (50% women; mean (SD) age 66.8 (5.7) years and BMI 29.6 (5.0) kg/m^2). Participants were eligible if they lived in proximity, had bilateral standing fixed-flexion PA knee radiographs (using Synaflexer frame) in the prior 6 months, knees discordant for KL grade (to include a range of JSW), neither knee was KL grade 4, and distal thigh width < 38.1cm (SCT gantry width). For SCT, a commercial scanner (PedCAT, Curvebeam LLC, Warrington, PA) was modified to enable imaging of bilateral knees while standing in a custom positioning system that maintained foot external rotation and fixed knee flexion. The scanner produced pulsed cone-beam x-ray (effective dose equivalent 0.1 mSv) on a 30x30 cm amorphous silicon flat-panel detector over a 360° projection angle with total scan time of 32 seconds. A 3D CT dataset with isotropic resolution of 0.37 mm and FOV of 200x350 mm was reconstructed from initial cone-beam projections. Medial tibiofemoral JSW at 7 locations (from 15% to 30% of the femoral condylar width) was assessed on fixed flexion radiographs using a software method (Duryea et al) and on SCT images by measuring the shortest distances between the tibiofemoral bony articular margins, following semi-automated segmentation of 3D SCT data. The articular locations where radiographic JSW(x) measurements were equivalent to those from SCT were plotted within each joint and within the anteroposterior distribution of JSW for each knee. Paired t-tests assessed differences between JSW measurements.

RESULTS: There were statistically significant differences between the radiographic and SCT JSW distribution at each mediolateral location except for: the 60th percentile from x=0.150–0.225, the 75th percentile for x=0.250–0.275 and the 80th percentile for x=0.300. The locations where radiographic JSW(x) measurements were approximately equal to SCT are circled in an example knee in Figure 1, and the means for radiographic JSW(x) compared to the distribution of 3D JSW(x) percentiles are plotted in Figure 2.

Figure 1: Anatomic Locations of Approximate Equivalency Between Radiographic and 3D JSW(x)

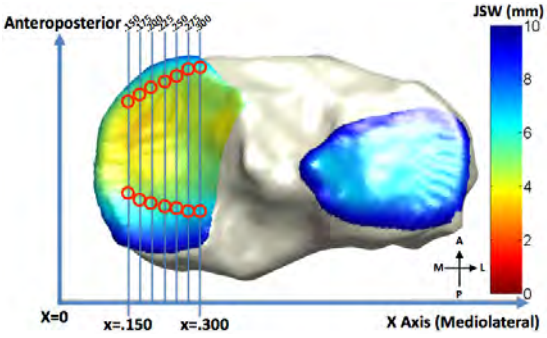
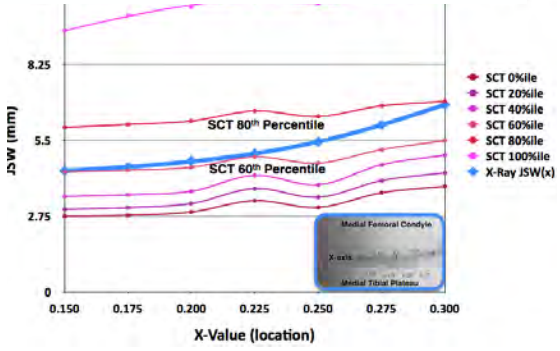


Figure 2: Comparison of Radiographic Medial Tibiofemoral JSW(x) and SCT JSW at Each X-Value



CONCLUSION: For the knees studied, rather than the minimum JSW, on average, radiographic JSW(x) values represent areas of the joint in the 60th–80th percentiles of the 3D JSW at each mediolateral location. This is likely due to the overlap of anatomy obscuring portions of the joint on radiographic projections.

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OPTICAL SPECTRAL TRANSMISSION MEASUREMENTS (OST) FOR ASSESSMENT OF SYNOVITIS MIGHT BE USEFUL FOR HAND OA

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INTRODUCTION: In OA, joint inflammation is increasingly considered an important target for treatment to prevent tissue damage. (e.g. Wang Q, et al. Nature Medicine 2011). However, inflammation is in general secondary and mild as compared to rheumatoid arthritis. Therefore, increasingly imaging modalities like MRI and US are used in clinical practice and research to detect (subclinical) inflammation. In contrast to MRI and ultrasound (US), optical spectral transmission (OST) measurements are non-invasive, fast, and operator independent. In order to identify and follow inflammation in hand and wrist joints an objective and simple tool to assess inflammation in the hand joints has been developed, the HandScan. Hemics BV (www.hemics.com) has originally developed the HandScan to assess disease activity in rheumatoid arthritis (RA) patients. The system has been presented fully operational at the recent EULAR conference 2013. The technology is based on quantifying the inflammation related hemodynamic response to an applied stimulus (Meier AJ, et al. J Biomed Opt. 2012). An assistant without medical background can operate the device. The patient places both hands in the scanner and within 1.5 min the outcome provides a direct measure for inflammation of all hand joints.

OBJECTIVE: To compare (sub)clinical hand joint inflammation detection between the HandScan, US and MRI.

METHODS: HandScan measurements were performed on 69 RA patients. The same joints were evaluated by US. Synovitis on Grey-scale ultrasonography (GSUS) was measured using OMERACT definitions, graded according to Skudlarek's (0-3). Power Doppler ultrasonography (PDUS) was scored as well (0-3). Synovitis was defined as GSUS > 0 and/or PDUS> 0. Twenty-seven subjects underwent MRI of wrist and MCP joints 1-5 of the right hand as well. These images were scored according to OMERACT Rheumatoid Arthritis MRI Scoring (RAMRIS) method, evaluating synovitis in MCP2-5 and the wrists. Clinical examination comprises joint swelling and joint tenderness according to the disease activity score (DAS28).

RESULT: At the joint level, there was good agreement between HandScan and US in PIP-joints (AUC of 0.85, $p<0.0001$) and MCP-joints (AUC 0.77, $p<0.0001$) and moderate agreement on wrist-level (AUC 0.64, $p=0.006$). On patient level, OST correlated with clinical examination (DAS28 $r=0.40$, $p=0.001$), and US scores ($r=0.63$, $p<0.0001$). In patients with RA, median (IQR) OST was different between patients with and without ACR/EULAR remission: 4.3 (2.6-4.4) vs. 5.3 (4.1-7.4, respectively, $p=0.02$) and with and without DAS28 remission: 4.5 (3.5-5.5) vs. 6.3 (4.2-9.0, respectively, $p=0.01$. Importantly, in patients with subclinical disease activity, there was a correlation between HandScan and MRI synovitis score (RAMRIS synovitis), $r=0.57$, $p=0.008$).

CONCLUSION: Inflammation measured with the HandScan demonstrated a good agreement with ultrasound (US) measurements of inflammation and superior performance compared to clinical examination, assuming US as a more sensitive (gold) standard for joint inflammation. As such this technology may support the rheumatologist in daily practice, saving time and with improved sensitivity, in determining the level of inflammation in case of hand arthritis. There is clear evidence that (subclinical) low-grade inflammation is common in hand OA, even in the absence of acute inflammatory flares. (Bonnet CS et al, Rheumatology 2005) The data on RA warrants evaluation of the HandScan in hand OA as a diagnostic tool to assess inflammation in hand OA and with that stratification for anti-inflammatory therapy.

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A LONGITUDINAL STUDY OF INDIVIDUAL REGIONAL KNEE CARTILAGE THICKNESS CHANGE IN PATIENTS WITH OSTEOARTHRITIS

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INTRODUCTION: Large differences (>10%/y or <-10%/y) in knee cartilage thickness of OA patients have been seen in distinct femorotibial subregions in as little as six months follow-up, indicating that subregions may undergo large thickness increases or decreases (rapid thickening or thinning) over time. These insights were gained from paired readings of different follow-up visits with baseline, but the pattern of change over time in individuals has not been studied directly. Identifying regions as rapidly progressing at a particular visit provides estimates of the frequency, but estimates of change at that visit will be biased due to the selection process. Estimates from the closest preceding or succeeding visits may provide fairly accurate unbiased estimates of change.

OBJECTIVE: The goal of this study is to explore the longitudinal pattern of knee cartilage thickness change over 24 months in patients with medial radiographic knee OA (ROA).

METHODS: Coronal MR images (3T) were acquired in 145 women (71 with ROA, 74 without symptoms or ROA) at baseline, 3, 6, 12 and 24 months. Femorotibial cartilage thickness was determined for 16 subregions across the medial/lateral compartments at each visit. Segmentation was done in visit pairs (follow-up and baseline) with readers blinded to visit. Generally 3, 6, and 12 month segmentations (paired with baseline) of a subject were provided by different readers, while their 12 and 24 month segmentations were done by the same reader. For each visit, subject-regions were placed into nine progression classes depending on the magnitude of their normalized thickness change, c, at that (classification) visit. The rates of change of the regions for a given progression class were examined at their preceding and succeeding visits to provide unbiased estimates and assess trends in thickness change over the course of the study.

RESULTS: Figure 1 shows that when rapid progression occurred at early visits, T= 0 for month 3 (orange +) or 6 (red ×), the closest visits also had large changes. Over the course of the study, however, the large early rates diminished by 24 months, indicating periods of status or reversal after brief periods of rapid progression. When rapid progression was seen at 12 (black ■) or 24 (blue □) months, earlier visits generally had progressively higher rates of change.

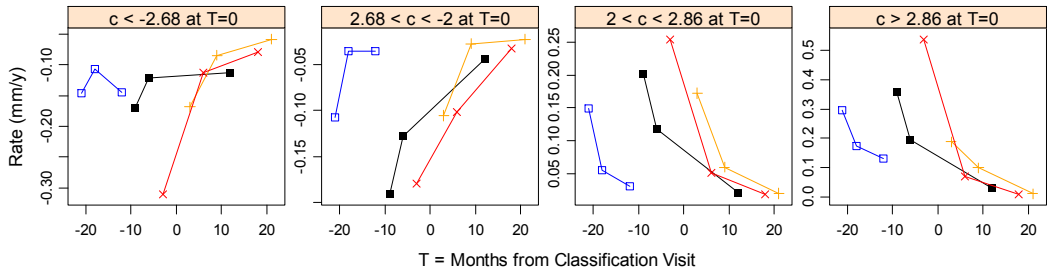

Fig 1. Rate of change at different visits when rapid progression occurred at classification visit (T=0). Color (shape) = rate at different visits in regions with the same classification visit.

CONCLUSION: The above results indicate that observations of rapid progression are confirmed by high rates of progression at visits immediately preceding or succeeding the visit with rapid progression. When rapid progression occurred at early visits, the overall rate tended to slow considerably by 24 months, indicating that rapid progression rates are not maintained over the full course of the study.

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SUBREGIONAL FEMOROTIBIAL CARTILAGE THICKNESS CHANGE IN A MODEL OF EARLY, PRE-RADIOGRAPHIC HUMAN KNEE OSTEOARTHRITIS

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INTRODUCTION: MRI is commonly used to measure cartilage change quantitatively in radiographic OA (ROA), but the specific early (pre-radiographic) changes remain unknown. We propose a model of early, pre-radiographic human knee OA, to examine early structural changes in cartilage.

OBJECTIVE: To study knees without radiographic OA (ROA) in subjects with moderate to advanced ROA (but no trauma history) in the contralateral knee. This approach was based on the notion that idiopathic OA is a bilateral disease, and that in subjects with unilateral (idiopathic) ROA, the contralateral KLG0 knee is at increased risk of incident ROA. We tested the specific hypotheses that such KLG0 (case) knees display greater subregional cartilage thickening (e.g. in the external medial femur [ecMF]), and greater thinning (e.g. in the internal and posterior lateral tibia [iLT, pLT]) than healthy reference subjects.

METHODS: Using central reading KLG from fixed flexion radiographs, we identified 554 (of 4796) OAI participants without radiographic OA (ROA) in one knee (KLG0), and with definite ROA in the other knee (KLG≥2). Of these, 293 did not have a trauma history in the KLG ≥2 knee, and 211 had 3T MRI data in the KLG0 (case) knee at baseline and 2-year follow-up. Segmentation of the 4 femorotibial cartilage plates of the case knee was performed with blinding to time point. Cartilage thickness change in subregions was compared with that in the 88 participants from the OAI healthy reference subcohort (no pain in either knee, bilateral KLG0, no risk factors) using an unpaired t-test. The number of "progressor knees" was identified based on a 2.5 SD threshold of variability in longitudinal change in the 88 healthy reference knees.

RESULTS: There were 211 case knees with contra-lateral (CL) idiopathic ROA (161 CL KLG2; 50 CL KLG 3/4). The subjects were 64±9 yrs. old (60% women; BMI 28±4.2). There was no indication of greater cartilage thickening in case knees in ecMF or across all subregions (SR Thick Score) (Table 1); however there was greater cartilage thinning in iLT (p=0.05) and across all subregions (SR Thinn Score; p=0.02) in (KLG0) case knees compared with the healthy reference knees. Greater thinning in case knees also was observed in the total femorotibial joint (FTJ) and in the central medial compartment (cMFTC), but the differences did not reach statistical significance (p=0.09 and 0.06). Sensitivity analyses indicated stronger effects in case knees with contra-lateral KLG 3/4 than KLG2 (Table 1). Based on the 2.5SD threshold, 5.2% of the unilateral case knees showed progression (thinning) in FTJ (4.3% with CL KLG2 and 8.0% with CL KLG 3/4), and 2.8% in cMFTC (1.2% with CL KLG2 and 8.0% with CL KLG 3/4).

Table 1. Mean change (mean) and standard deviation (SD) in cartilage thickness in femorotibial regions/subregions (*= p≤0.05; **=p≤0.01)

	Healthy (n=88)		**All Cases (n=211)**		**CL KLG2**		**CL KLG3/4**	
Change in µm	Mean	SD	Mean	SD	Mean	SD	Mean	SD
ecMF	18	82	10	84	13	83	-1	87
iLT	-12	104	-44*	135	-41	139	-55*	122
pLT	-33	68	-36	104	-32	92	-48	135
SR Thinn Score	-506	307	-679*	680	-643	644	-796**	783
SR Thick Score	485	301	481	322	495	327	435	305
FTJ	1	133	-42	215	-28	205	-88	241
cMFTC	11	123	-25	166	-21	151	-38	210

CONCLUSION: In this model of early, pre-radiographic human knee OA (unilateral KLG0), we find evidence of larger rates of subregional cartilage thinning compared with healthy reference knees. Such a model may be useful to test the effect of preventive disease modification in clinical trials.

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P30

SINGLE SLICE MR AREA OF ANTERIOR THIGH COMPARTMENT MUSCLES PREDICT KNEE REPLACEMENT SURGERY IN MEN

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INTRODUCTION: Total knee replacement (TKR) is the final effective treatment of OA after other treatment attempts fails to provide pain relief. Anterior compartment of thigh muscles are the major stabilizer of knee joint.

OBJECTIVE: Our purpose was to evaluate the relationship between having TKR in patients with OA and their quantitative measurements of single slice areas (SSA) of thigh muscles and fat as well as muscle quality (MQ).

METHODS: Cases were defined as OAI participants who had a TKR between enrollment and the 60 months visit. Controls were matched by age (within 5 years), sex, and baseline KLG. Participants who had available mid-thigh MR imaging scans (15 contiguous slices, 5mm slice thickness) at baseline and full-limb X-rays were evaluated. To obtain a comparable measure from legs of different sizes, we measured and compared the femur length (FL), distance of epiphyseal line (DEL) to the most distal point of femur and the DEL to the first imaging slice of all participants. The slice at the 33rd percentile of femur length was selected for SSA of muscle and fat measurements. Segmentation was done by a radiologist who was blinded to TKR status. A second radiologist segmented 20 legs for reliability measurements. MQ was defined as the peak muscle strength divided by SSA of muscle compartment. Conditional logistic regression analysis was used for statistical evaluation. All measures of volume and muscle quality were standardized.

RESULTS: There were 135 case-control pairs (n=60 male, n=75 female) of thighs from OAI database that were included in this case-control study. Regarding volume measurement reliability, inter-observer and intra-observer interclass correlation coefficient was 0.997 and 0.999 respectively. Overall, when adjusted for only body composition (Body surface area [BSA] and FL), the odds of not having a TKR was higher in patients with larger SSA of total thigh muscles (TTM), anterior thigh compartment muscles (ATCM), ATCM to intermuscular fat (IMF) ratio and, TTM to IMF ratio (Odds Ratio [OR]: 1.61, CI: 1.05-2.48; OR: 1.60, CI: 1.05-2.45; OR: 1.42, CI: 1.05-1.91; OR: 1.41, CI: 1.05-1.90, respectively). We further tested this model in men and women pairs separately. Only larger SSA of ATCM and TTM remained and showed a link of higher odds of not having a TKR in men with OA (OR: 2.23, CI: 1.14-4.38; OR: 2.17, CI: 1.10-4.27, respectively). After adjusting for BSA, FL, race, collateral knee KLG, and WOMAC, only SSA of ATCM in men with OA remained significant in terms of predicting not having a TKR (aOR: 2.54, CI:1.09-5.93). MQ didn't show any statistical significance.

CONCLUSION: The odds of not having future TKR is higher with a larger SSA of ATCM in men with OA. We think that SSA of ATCM has a potential of being a biomarker for predicting future TKR candidates. Future studies may address the importance of increasing SSA of ATCM by life style modifications and its effects on progression of disease.

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3D PROJECTION MAP OF QUANTITATIVE T_2 RELAXATION TIMES: DEVELOPMENT AND EVALUATION IN THE FEMORAL CONDYLAR CARTILAGE OF HEALTHY AND ACL-INJURED SUBJECTS

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INTRODUCTION: 3D MRI acquisition techniques have been developed to assess cartilage molecular composition that may facilitate the early detection of degenerative OA changes (Gold 2009). Despite the acquisition of 3D quantitative data (such as T_2 relaxation times), most MRI studies evaluate just a single slice from the medial and lateral compartments of the knee (Bolbos 2008, Li 2011). This single-slice assessment may not fully describe the cartilage variation across the cartilage plate and may obscure longitudinal changes.

OBJECTIVE: To develop and evaluate a method for visualizing 3D quantitative femoral articular cartilage data.

METHODS: *MRI Acquisition:* Sagittal MRI scans were acquired in 5 healthy volunteers (mean age 29.6±4.9 years; at baseline, day 1 and 1 year) and 5 ACL-injured patients (mean age 31±8.6 years; at baseline and 1 year) using an MR750 3.0T scanner (GE Healthcare, Waukesha, WI) and a transmit-receive 8-channel knee coil (Invivo Inc. Gainesville, FL). Two quantitative double-echo in steady-state (qDESS) image sets with 3mm slice thickness, 16cm FOV, 256x256 matrix and a scan time of 9.40 min were acquired and used for T2 relaxation time mapping (Staroswiecki 2012).
Projection Map: Cartilage was segmented manually from the qDESS images in a slice-by-slice manner and the segmented regions were superimposed on the T_2 relaxation time maps using custom software developed in Matlab. The segmented femoral cartilage was fit to a best-fit cylinder. Radial projections from the cylinder center at fixed 1^o increments (from 0^o to 245^o) were superimposed on each slice and the quantitative T_2 values were averaged depth-wise per angular bin to form a projection map (Fig 1A).
Reproducibility: Radial pixel-wise root mean square coefficient of variation (CV_{RMS}) and global CV_{RMS} (averaged over entire cartilage plate) of the projection maps were calculated for five healthy volunteers between day 1 and day 2.
Longitudinal Analysis: Difference maps between the baseline and the 1-year scans for both populations were calculated (Fig. 1). A difference threshold of 5ms was selected based on reported OA T_2 changes (Li 2007) and used to determine the percentage of pixels above this threshold in both the healthy and ACL-injured groups.

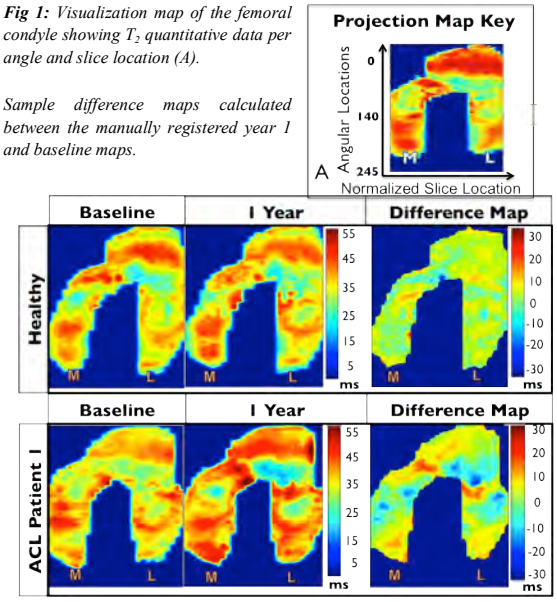

Fig 1: *Visualization map of the femoral condyle showing T_2 quantitative data per angle and slice location (A).*

Sample difference maps calculated between the manually registered year 1 and baseline maps.

RESULTS: The radial pixel-wise CV_{RMS} for all five healthy volunteers was 13.2%; the global CV_{RMS} was 7.9%. On average, 33±9.2% of the pixels in the healthy volunteer population and 47±10% of the pixels in the ACL-injured population were above the 5ms threshold in the difference maps.

CONCLUSION: With this technique it is possible to visualize and assess differences across the entire femoral cartilage plate, fully utilizing 3D MRI data. The global CV_{RMS} found here is similar to those of single slice analysis techniques reported previously (Mosher 2011). While the radial-pixel-wise CV_{RMS} was greater, this was not surprising of a pixel-wise versus global comparison. For the patient comparison, the use of a threshold helped to quantify visible changes in the projection maps. An advantage of this technique is not constrained to T_2 relaxation time mapping; it can be used with any 3D quantitative MRI data. This technique may be particularly useful for quantifying focal defects and carrying out longitudinal comparisons, which may ultimately improve our understanding of the pathophysiology of OA.

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K-MEANS CLUSTERING OF MULTIPARAMETRIC MRI DATA FOR IMPROVED CLASSIFICATION OF ARTICULAR ARTICULAR CARTILAGE DEGENERATION

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INTRODUCTION: Several qMRI techniques have shown to be sensitive to pre-radiographic pathological changes in articular cartilage (AC).

OBJECTIVE: To employ k-means clustering (KMC) of multiparametric MRI data for improved classification of AC degeneration.

METHODS: Bovine osteochondral samples were prepared from intact bovine patellae (n = 6), each samples was cut into three sections: one was used as control, one digested for 44 hours in collagenase (30 U/ml) and one in chondroitinase ABC (0.1 U/ml) to induce collagen or GAG depletion, respectively. Human tibial plateaus were harvested from total knee arthroplasty surgeries (n = 17) with permission from the local ethical committee. Multiparametric MR experiments were performed at 9.4 T and 8 different parameters were measured by modifying a preparation block followed by a FSE readout (ETL = 4, TR = 5 s, TE_{eff} = 5 ms, matrix = 256x128, slice thickness 1 mm, FOV = 16 x 16 mm^2): adiabatic $T_{1\rho}$ (γB_{1max} = 2.5 kHz), adiabatic $T_{2\rho}$ (γB_{1max} = 2.5 kHz), continuous waves (CW) T1ρ (γB_1 = 1 kHz), relaxation along a fictitious field (RAFF), T_1 during off resonance saturation (δ = +10 kHz, γB_1 = 250 Hz, T_1 sat); T_2 was measured with FSE; T_1 relaxation time was measured by varying the TR saturation recovery with 7 TRs from 80 to 5120 ms; MTR was defined as $1\text{-}M_{sat}/M_0$. Human samples were divided in two groups: early and advanced OA (OARSI grade >1.5). For all samples, three ROI were considered: 5%, 25% and 100% of thickness. KMC was performed separately for human and bovine data set using all possible combinations of doublets and triplets of MRI parameter.

RESULTS: For the human data set, the best classifications were achieved considering the whole AC thickness. Several doublets were able to classify all the early OA samples in the same cluster in all ROIs. Compact and well-separated clusters were obtained in the 25% thickness ROI with decreased sensitivity. In bovine samples similar accuracies were attained in the three ROIs, although cluster separations were higher in the most superficial ROIs. The doublets {CW $T_{1\rho}$, T_{1sat}} and {AD $T_{2\rho}$, T_{1sat}} were the best combination in both 5% and 25% thickness ROIs. A combination of three parameters did not bring further improvements.

CONCLUSION: Best discrimination of AC status was obtained when employing KMC of two MR parameters, particularly when rotating-frame techniques were used. Different results for the two data sets may be explained by the classification method: enzymatic digestion is depth dependent and more efficient in the superficial layers; on the other hand, the classification of human samples was based on the OARSI grading, which evaluates the whole AC and thus offered the best result with the full thickness ROI.

SPONSOR: none.
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MRI OF ARTICULAR CARTILAGE AT MICROSCOPIC RESOLUTION

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INTRODUCTION: MRI is the only non-invasive imaging tool with excellent soft-tissue contrast. However, its resolution across the thin thickness of articular cartilage is limited in clinical MRI. Based on the same physics principles and engineering architecture, microscopic MRI (μMRI) can have fine resolution in tens of microns and serve as the logical bridge that translates the findings between invasive procedures (e.g., light microscopy or biochemical assay) and human MRI diagnostics.

OBJECTIVE: The non-trivial effects of imaging resolution on the outcomes of the MRI experiment will be discussed, based on some high-resolution studies of articular cartilage in the animal models.

METHODS: The Pond-Nuki model of anterior cruciate ligament transection in canine knee has been the gold standard in OA research. In addition, canine humeral cartilage has often been used as a model system. μMRI experiments of cartilage-bone blocks were performed on a Bruker AVANCE Ⅱ 300 system. All imaging experiments used the magnetization-prepared protocols that were previously documented. T1 was measured by an IR sequence together with gadolinium contrast agent to determine the PG concentration. T2 was measured by a CPMG sequence to determine the relaxation anisotropy (the magic angle effect). T1rho was measured by a spin-lock sequence to determine the charged macromolecules in cartilage.

RESULTS: The goal in any MRI experiment is to tailor the dimensions and orientation of the image voxel to maximize the homogeneity of the molecular environment in each voxel, consequently reducing any artifacts due to partial volume averaging among different molecular populations or different tissue structures within the same voxel (e.g., small lesion and large background tissue). A resolution scaling law in MRI of cartilage was formulated several years ago, which used the percentage tissue per pixel instead of microns per pixel in the discussion. It concluded that the transverse resolution in MRI of cartilage should ideally be 2% of the relative tissue depth per image pixel, which translates to about 40μm for a 2-mm thick tissue (~ human knee or hip). This ideal resolution, at the present time, still poses momentous challenge to any whole-body MRI scanner. However, the societal importance of managing joint diseases, which is the number one cause of disabilities in the population, is a sufficient motivation for all of us to work together to design higher-resolution MRI systems (e.g., extremity MRI) around our problem and to develop novel MRI protocols (e.g., short echo-time protocols) that are exquisitely sensitive to the unique events in the early degradation of cartilage. In addition to improve the imaging resolution, many experimental and image-analysis details should also be considered carefully. For example, not all cartilage can be visualized in an MRI experiment. Since the echo time (TE) in common MRI sequence is finite, it is difficult to image the portion of the tissue that has a T2 relaxation time much shorter than the min TE. (In cartilage MRI, the finite-width dark band between the soft tissue and bone might contain the invisible tissue.) Finally, not all cartilage is created equal. This is certainly true for cartilage from different joints or different species. Even cartilage from different sampling sites of the same joint, a number of topographical variations in the chemical, physical, optical, and mechanical properties have been observed; these topographical variations are also age-dependent which are probably the consequence of the load-bearing history and motional patterns for a particular joint and animal.

CONCLUSION: The use of μMRI to study animal models of osteoarthritis bypasses the fundamental limiting factors in clinical MRI of human (e.g., resolution, imaging time, orientation), permitting a thorough understanding of the complex mechanisms in the early disease process. The use of μMRI for an animal model also ensures a translational pathway for any new knowledge directly to clinical MRI, since both share the same principles and architectures. Finally, by using several complementary micro-imaging tools to map the same tissue system, the physical, chemical, and mechanical properties of cartilage during its early degradation can be unequivocally determined.

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AUTOMATIC QUANTIFICATION OF JOINT SPACE WIDTH IN HAND RADIOGRAPHS: THE FIRST RESULTS

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INTRODUCTION: The assessment of joint space width in hand X-ray images of patients suffering from rheumatoid arthritis (RA) and osteoarthritis (OA) is a time-consuming task. The manual assessment is semi-quantitative and is highly observer-dependent which hinders an accurate evaluation of joint damage, particularly in the early stages. Automatic analysis of the joint space width (JSW) could be a step forward since it is a true quantitative and sensitive measurement of the JSW, observer independent, and is time efficient.

OBJECTIVE: Automatically quantify the JSW of hand joints in hand radiographs to aid RA and OA progression assessment.

METHODS: Thirty hand radiographs pre-scored according to the Sharp/van der Heijde method were assessed in the experiment, of which 22 hands had joint space narrowing (JSN) in at least one joint. The assessment included all distal interphalangeals (DIPs), proximal interphalangeals (PIPs), metacarpophalangeals (MCPs), and 3 joints in the wrist (M-NAV, CAPNLun, and RadCar). We fully automatically detected the joint locations, delineated the joint margins, and calculated the corresponding JSW. The performance of the method was evaluated in comparison to manual delineations. Next, the relative JSWs of the abnormal joints (score > 0) compared to the mean JSW of the normal joints (score = 0) of the same joint type was calculated for each joint. Since no JSN was observed in the wrist joints, this proportion calculation was performed only for the DIP, PIP and MCP joints per finger. In the end, all JSW proportions of the joints with JSN score 1, 2 and 3 were aggregated respectively, and were compared with the ordinal JSN scores.

RESULTS: All finger joint locations were automatically detected within a radius of 3 mm around the manually indicated positions. The percentage of the correctly delineated margins−which was examined by a medical expert−was 93.8%. For the wrist, 3 joint locations (3.3%) were incorrectly detected owing to the bone overlapping problem. The margins from 2 joints (2.2%) with low contrast region were incorrectly delineated. In the remaining joints, subtle manual adaption was needed for 12 cases (14.1%) owing to the complex morphology of the wrist. For the comparison with the ordinal scores, the mean relative JSW of the joints with JSN score 1, 2 and 3 as compared to the JSW of normal joints (=100%) were 83.6% (±15.9%), 67.4% (±11.4%), and 57.2% (±11.3%), respectively, showing a clear JSW decline tendency and a close correlation with the conventional JSN scores.

CONCLUSION: Fully automated JSW assessment is a true quantitative measurement of joint damage, and reflects the JSN levels of the conventional scoring method. Hence, the automatic JSW evaluation method could be beneficial to the medical expert for the RA and OA progression assessment. The joint of the thumb base has not been included in this work, but present results warrant investigation on the feasibility of JSW assessment for that joint as well. Clearly, acquisition of the radiographic images is essential, which is influenced by hand rotation and may lead to unpredictable results. Including a hand positioning mold during acquisition (ongoing experiments) might further improve automated JSW assessment for RA and OA.

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LATE BREAKING POSTER PRESENTATIONS

IS COMPLETE SEGMENTATION OF THE OAI KNEE MRI FEASIBLE?

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INTRODUCTION: Complete analysis of the Osteoarthritis Initiative (OAI) data has been limited by the task of quantifying the approximately 50,000 knee MRI in the multi-visit study with 4,769 participants.

OBJECTIVE: To investigate the feasibility of fully automatic, computer-based cartilage segmentation on a large OAI sub-population, and to validate the volume quantifications against independent measurements from Chondrometrics and VirtualScopics provided by the OAI.

METHODS: The knee MRI were acquired on a Siemens 3T Trio scanner using a sagittal 3D DESS WE sequence (25º flip angle, 16ms RT, 4.7ms ET, 0.36 x 0.36 x 0.7mm voxels, scan time 10min). The analysis population of 1436 knees was selected as those with publicly available year 0 cartilage volume scores from Chondrometrics including all OAI projects (excluding two with missing laterality). They had age 61±9 years, BMI 29±5, with 41% women. 78% of the knees were right knees. Their Kellgren and Lawrence grades (KL) were distributed with 16%, 10%, 39%, 30%, and 5% at KL0-4. The KneeIQ segmentation framework from Biomediq combining multi-atlas registration with a multi-structure voxel classifier was trained and validated on baseline MRI with cartilage segmentations provided by OAI courtesy of iMorphics (44 for training and 44 for validation). For each knee, cartilage volumes were quantified for five compartments: patellar and medial/lateral tibial/femoral cartilages. The quantifications were validated against volume (VC) scores provided by OAI courtesy of Chondrometrics (Eckstein, Wirth) for tibial compartments (where all agreed on compartment definitions). The volume scores agreement were evaluated by the linear correlation coefficient (r) and the median of the deviation from the median on the relative differences (MM).

RESULTS: On the iMorphics validation set (n=44), the segmentation accuracy given as Dice volume overlap was 0.74 for patellar cartilage and between 0.81 and 0.87 for the four tibiofemoral compartments. The linear correlations were between r=0.90 and r=0.96. The tibiofemoral compartments had MM between 5% and 6% and the patellar compartment had MM 9%. The correlations r and MM for the medial and lateral tibial cartilage volume scores were as in the table. For each comparison five numbers are given: number of knees included, r medial/lateral, MM medial/lateral.

	Biomediq (fully automatic)			iMorphics (semi-automated)			Chondrometrics (manual)		
	N	r	MM	n	r	MM	n	r	MM
Biomediq				58	.95/.96	5/5	1436	.91/.90	8/9
iMorphics	58	.95/.96	5/5				58	.92/.96	6/7
Chondrometrics	1436	.91/.90	8/9	58	.92/.96	6/7			

CONCLUSION: We presented results including fully automatic segmentation of 1436 OAI knee MRI. The results confirmed previous studies showing high correlations between different segmentation methods. However, the typical volume deviations between 5-9% also demonstrated that measurements from different methods should not be pooled. Therefore, the feasibility of complete segmentation of all OAI knee MRI relies on a single, fully automatic method (and a large computer).

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SEX-DIFFERENCES OF QUANTITATIVE IMAGING MEASURES OF THE INFRAPATELLAR FAT PAD (IPFP) IN HEALTHY REFERENCE SUBJECTS – DATA FROM THE OA INITIATIVE (OAI)

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INTRODUCTION: The infra-patellar fat pad (IPFP) or "Hoffa" consists of adipose tissue that is located intra-articularly, inferior to the patella and posterior to the lig. patellae. It is well known that the distribution of adipose tissue differs vastly between men and women, with women showing greater amounts of subcutaneous, and men greater amounts of abdominal adipose tissue. The IPFP has been shown to be a relevant source of intra-articular adipokines (e.g. leptin and adiponectin), which have been associated with inflammatory processes and knee OA. However, it has not been studied whether the amount of intra-articular IPFP adipose tissue differs between (healthy) men and women.

OBJECTIVE: a) To provide normal values for quantitative imaging measures of the IPFP in healthy men and women without knee pain, radiographic knee OA, or risk factors of incident knee OA; b) to describe sex differences in the IPFP, c) to explore the correlation of IPFP volume with body weight, and d) to test whether the ratio of between IPFP volume versus body weight is similar in healthy men and women.

METHODS: We studied the healthy (non-exposed) reference cohort of the Osteoarthritis initiative (OAI), consisting of 122 healthy men and women without knee pain, aching or stiffness in the year before inclusion. Further, these knees did not display radiographic femorotibial OA (clinical site readings of baseline bilateral fixed flexion radiographs) and no risk factors of incident knee OA (e.g. obesity, history of knee injury, knee surgery, family history of knee replacement, Heberden's nodes, or repetitive knee bending) were present. Of the 122 subjects, 92 were bilaterally normal (KLG0) based also on the central OAI radiographic readings, and had MR images available (60% female, baseline age 54±6 y [range 46 to 69], BMI 23±2.5 [range 17.7 to 29.3]). The IPFP was analyzed by a single reader (JD), using sagittal fat-suppressed IW TSE MR Images (TR=3200ms, TE=30ms, slice thickness 3.0mm; in plane resolution 0.36mm; 3T Magnetom Trio), segmenting all slices that clearly depicted the IPFP. The IPFP volume, anterior surface area (towards the lig. patellae) and mean thickness (depth) was computed using custom software (Chondrometrics GmbH). Sex differences were evaluated using an unpaired t-test, with the primary analytic focus being the ratio of IPFP volume versus body weight.

RESULTS: Healthy men displayed a 28% greater anterior surface area, a 12% greater thickness (depth) and a 43% greater volume of the IPFP than healthy women ($p<0.001$; Table 1). Men also had a significantly ($p=0.01$) greater ratio of IPFP volume versus body weight then women (Table 1). There was a weak to moderate correlation of IPFP volume with body weight ($r=0.29$ in men and $r=0.51$ in women), but no relevant correlation of the IPFP volume with age in either men ($r=0.03$) or women ($r=-0.06$).

Table 1. Sex differences of quantitative measures of the IPFP in healthy women and men

	Women Mean± SD	Men Mean± SD	Percent difference (M vs. W)	p value M vs. W (unpaired t-test)
Body weight (BW)	61.8 ± 8.1	79.6 ± 8.3	+29%	<0.001
IPFP ant. surface (cm^2)	19.3 ± 3.1	24.2 ± 4.1	+28%	<0.001
IPFP thickness (mm)	10.71 ± 1.3	12.02 ± 1.3	+12%	<0.001
IPFP volume (cm^3)	20.7 ± 3.5	29.1 ± 4.5	+43%	<0.001
IPFP volume/BW	0.34 ± 0.05	0.40 ± 0.1	+11%	<0.01

CONCLUSION: This is the first study to explore quantitative measures of the IPFP in healthy men and women. It is well known that women have a greater accumulation of subcutaneous adipose tissue than men, whereas men have more abdominal fat than women. Interestingly, we find the ratio of intra-articular adipose tissue (IPFP) vs. body weight to be significantly greater in men than women, and to be only weakly to moderatly correlated with body weight. These data provide a basis for further systematic study of the impact of BMI and knee OA status (pain and/or radiographic change) on the size and shape of the IPFP.

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KNEE JOINT SUBCHONDRAL BONE STRUCTURE ALTERATIONS IN ACTIVE ATHLETES: A CROSS SECTIONAL MATCHED CASE-CONTROL STUDY

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INTRODUCTION: It has been shown that trabecular bone structure parameters extracted from radiographs known as fractal signature or bone texture analysis (FSA) is able to predict structural outcomes such as radiographic osteoarthritis progression or clinical endpoints such as total joint replacement. To date most studies investigating bone structure using FSA have focused on osteoarthritic joints in older subjects. Little is known about early disease or about differences between subjects exposed to increased joint loading such as young active athletes compared to non-athletes. Given the repetitive impact of loads to the knee joint in sports like soccer it should be expected that subchondral bone adaptations as measured by FSA are to be observed. Further it is not known if previous surgery, gender or age has a similar impact on subchondral bone structure.

OBJECTIVE: Aim was to compare horizontal and vertical dimensions of bone texture considering athlete status, gender, previous anterior cruciate ligament surgery and age after combining these features into one single model.

METHODS: 135 consecutive athletes (82% soccer players) 18 to 36 years old and 550 non-athletes aged-matched controls had knee radiography (Lyon-Schuss protocol) for assessment of subacute or chronic knee complaints. Patients with acute trauma or fractures were excluded. Regions of interest were placed in the subchondral medial and lateral tibial plateaus. The landmarks used were the tibial borders, tibial spine, fibula head and cortical plates. Fractal signatures were calculated in the horizontal and vertical dimensions. 19 trabecular images sizes (radii) were applied ranging from 0.9 mm to 2.9 mm. The statistical model used was $Yijk = u + athlete + gender + ACLR + agecat + r_k + r_k^2 + r_k * athlete + r_k^2 * athlete + r_k * gender + r_k^2 * gender + r_k * ACLR + r_k^2 * ACLR + r_k * agecat + r_k^2 * agecat + P_{ij} + e_{ijk}$ with: r_k: radius, P_{ij}: the random effect associated with the subject in group, and e_{ijk}: the random error with the subject in group. Curve fitting algorithms were applied taking into account all four risk factors in the same model adjusting for each other to assess differences between athletes vs. non athletes, gender, previous ACL surgery and age assessing ROIs in medial and lateral compartments separately.

RESULTS: Included were 685 patients of which 135 were athletes. 556 (81.2%) were male and 60 (8.8%) patients had previous ACL surgery. 133 (19.4%) patients were in the age group 18-22 years, 181 (26.4%) in the range of 23-27, 155 (22.6%) in the range of 28-32 and 216 (31.5%) were between 33 and 36 years old. Mean age was 28.5 years (SD ± 6.5). For the horizontal dimensions significant differences were observed for gender (estimate (E) 0.098 standard error (SE) 0.004, p<.0001), previous ACL surgery (E -0.031, SE 0.006, p<.0001) and the highest age group (E -0.039, SE 0.005, p<.0001). For vertical dimensions, significant differences were shown for athletes (E -0.012, SE 0.004, p<.0001), gender (E 0.056, SE 0.004, p<.0001), and age range from 28-32 years (E -0.028, SE 0.005, p<.0001).

CONCLUSION: Trabecular bone structure differs between athletes and non-athletes, in regard to previous ACL surgery, for gender and for higher age. Specific differences observed for horizontal and vertical dimensions of FSA warrant further exploration. FSA is a promising tool to define early subchondral bone alterations in young active subjects. The role of early subchondral bone changes defined by FSA in regard to longitudinal assessment and risk of premature joint degeneration needs to be evaluated further.

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