PARACELSUS
MEDIZINISCHE PRIVATUNIVERSITÄT

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

5th INTERNATIONAL WORKSHOP ON OSTEOARTHRITIS IMAGING

June 8th to 11th 2011 | Salzburg (Austria)

From Joint Anatomy to Clinical Outcomes in OA and Cartilage Repair

http://oa-imagingworkshop.pmu.ac.at

Final Program

WORKSHOP SPONSORS

We would like to acknowledge the following sponsors for generously supporting this workshop:

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WELCOME

Dear Workshop Participant,

After a successful 1st Workshop in Ainring and Salzburg in 2007, and after three further annual workshops in Boston, York and Vancouver, we are happy and excited to bring the 5th OA Imaging Workshop back to Salzburg, where it all began.

1st OA Imaging Workshop, Ainring/Salzburg, 2007

Since 2007, the field has matured and a "scientific community" of researchers in OA imaging has developed. The OA Initiative continues to produce a wealth of clinical and imaging data that provides a tremendous resource for identifying risk factors for the onset and progression of OA, and for clinically validating imaging biomarkers as surrogates for clinical trials. Continuous discussion is required to exploit this resource in an efficient, collaborative, productive, and targeted manner; therefore, once again, results from the OA Initiative and ideas on how this resource is best used will be a focus of the workshop.

Further, this time we have reached out to the cartilage repair community, because very similar imaging protocols are being used, similar questions about the validation of imaging biomarkers are being discussed, and the same end-stage (joint failure) is to be avoided. The pre-course in synovial joint anatomy aims at giving scientists the opportunity to study synovial joints in small groups. We hope that this will be a highlight to all those, who otherwise have no access to this type of experience.

We are very pleased with the large number of registrations and the high quality of the submitted abstracts. To date we have about 130 registered participants from all over the world. Ten invited key lectures will be given on key topics of OA imaging. A total of 58 abstracts were submitted; 24 will be presented orally and 34 as posters. We hope you will enjoy the focus and the comprehensiveness of the program and will very actively participate in the round table discussion at the end of the program. Our thanks go to the program committee: Gillian Hawker (University of Toronto, Canada), Mika Nieminen (University of Oulu, Finland), Siegfried Trattnig (Medical University of Vienna, Austria), and David Hunter (University of Sydney) for their diligent work on the program and in rating the abstracts despite the short timeframe.

We would also like to thank the many sponsors for their invaluable support, who have made this workshop possible. We are not only grateful for their sponsorship, but for many of them attending the workshop and for actively participating in the scientific discussions on the clinical application and validation of imaging biomarkers.

Special thanks and recognition go to the two organizations supporting the meeting: the Osteoarthritis Research Society International (OARSI) and the Paracelsus Medical University (PMU). PMU was founded in 2003 and is one of very few private medical Universities in Europe. Like their partner, the Mayo Medical School in Rochester (MI), PMU admits only 50 medical students per year who then go through an intense 5 year program. PMU was under reconstruction in 2007 and therefore the workshop was held in Ainring, just across the border in Bavaria (Germany). However, now you will have a chance to visit the campus that was extended in 2007 and be able to enjoy the ambience of a small University, which we hope will be ideally suited for hosting the workshop.

This workshop is meant to be different from larger conferences. It should provide more time for people to listen, think, exchange ideas, explore, discuss, meet and spend time together. It will take place in a relaxed atmosphere at the campus, hopefully with brilliant weather. The dress code is casual: so come without a tie, but with an open mind, and sufficient time to dive and immerse into scientific discussion.

It is our wish that the workshop will provide ample opportunity for building bridges between all with an interest in OA imaging. We also hope that the workshop will provide a good forum to form new collaborations for combating osteoarthritis. Most of all, we hope it will be an opportunity to build or intensify friendships, which has always been the best basis for fruitful scientific collaboration. We look forward to welcoming you to our beautiful part of the world and sharing not only scientific exchange, but also cultural experiences and enjoyable social interactions.

Travel safely, and enjoy!

Felix Eckstein
Institute of Anatomy and Musculoskeletal Research
Paracelsus Medical University, Salzburg, Austria
Workshop Organizer

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PMU Courtyard and Hansjörg Wyss Building

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Photograph on page 21: © Salzkammergutbahn GmbH
Map data page 8: © OpenStreetMap contributors, CC-BY-SA

LOCATIONS AT PMU

Main building:

1st floor, Café Relax: **Registration and Info Point**

2nd floor, Room "Schröcknadel": **Internet Café Kindly Sponsored by** GlaxoSmithKline

3rd floor, Library: **Poster Session Kindly Sponsored by** Pfizer

Hansjörg Wyss Building:

1st floor, Auditorium (HS 1): **Oral Presentations (and Speaker Ready Room)**

PMU Courtyard:

Tent: **Lunch and Conference Dinner**

Open Air: Conference Concert (Claudia Koreck & Band)

TRAVEL INFORMATION

COMING FROM DOWNTOWN BY TAXI

Please tell the taxi driver that you need to go to:

Paracelsus Medical University,
Strubergasse 21

5020 Salzburg, Austria

When you need a taxi from Salzburg, please call:

8111 when calling from within Salzburg

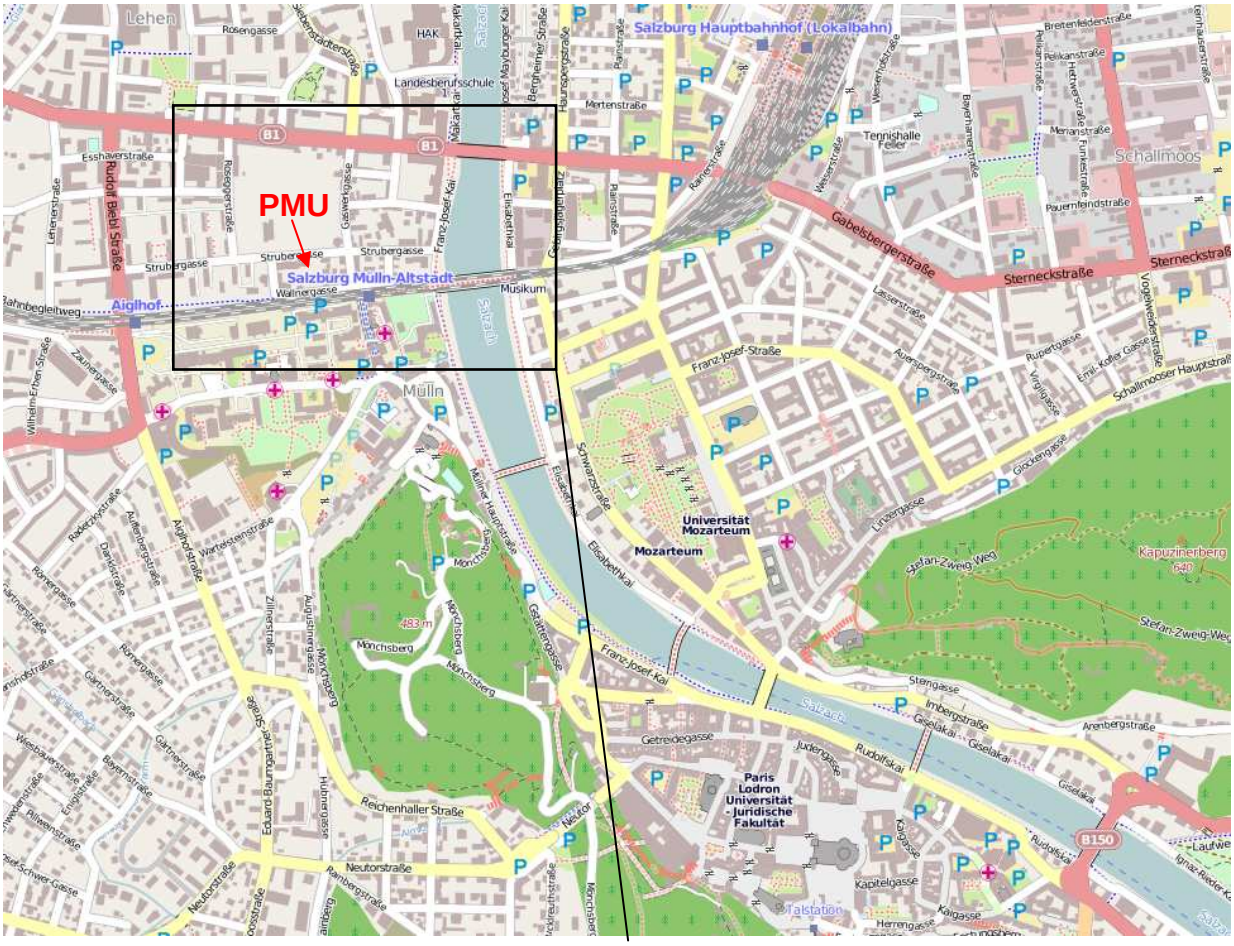
0662 8111 when using a national mobile phone

+ 43 662 8111 when using an international mobile phone

COMING FROM DOWNTOWN BY FOOT

PMU is about 20min walking time from the downtown hotels. Walk down the river on the left bank, pass below the railway bridge, and then turn left into Strubergasse.

Pass Gaswerkgasse and find the PMU building to your left. The registration and info point will be in the ground floor. Turn right, when you have entered, and all your problems will be solved.



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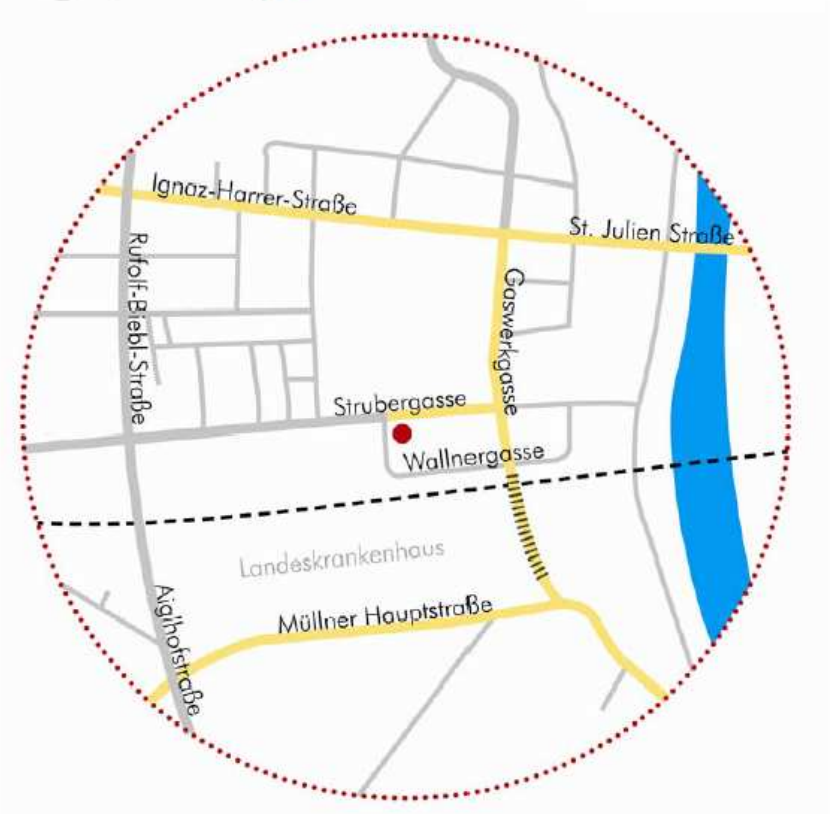

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PROGRAM AT A GLANCE

Wednesday, June 8th, 2011

8.30	Registration Open
9.30 – 12.30	Precourse in Joint Anatomy
13.30 – 14.00	Welcome and Introduction Main Program
14.00 – 15.30	Module 1: Imaging Biomarkers and Clinical Outcomes in Cartilage Repair
16.15 – 17.30	Module 2: 5 Presentations Selected from Abstracts (Cartilage Repair)
17.45	Young Investigator Evening (Braustüberl, Kloster Mülln)
17.45 – 18.30	Corporate Round Table
19.30	Speaker & Sponsor Dinner (M32)

Thursday, June 9th, 2011

9.00 – 10.15	Module 3: 5 Presentations Selected from Abstracts (Osteoarthritis Initiative)
10.45 – 12.30	Module 4: The Osteoarthritis Initiative (OAI)
13.30 – 14.30	Module 5: Young Investigator Session: 4 Top Presentations of Young Investigators Selected from Abstracts.
14.30 – 14.40	Young Investigator Award Session
14.40	Workshop Photograph
14.45 – 17.30	Module 6: Poster Session
18.15	Conference Dinner @ PMU
19.45	Claudia Koreck & Band Live @ PMU

Friday, June 10th, 2011

9.00 – 10.15	Module 7: 5 Presentations Selected from Abstracts (Semi-Quantitative Imaging Outcomes)
10.30 – 12.30	Module 8: Relationships of Imaging Biomarkers with Clinical Outcome.
13.30 – 14.45	Module 9: 5 Presentations Selected from Abstracts (Quantitative Imaging Outcomes)
15.15 – 16.45	Module 10: Round Table Discussion
18.00	Bus Leaves from PMU for Beer Garden Event in Bavaria

Saturday, June 11th, 2011

8.45 – 18.00	Whole Day Break Out Tour to the Salzkammergut, Including a Boat Ride Across Lake Wolfgang and a Stream Train Ride to the Summit of the Spectacular Schafberg
19.30	Chill Out and Informal Get Together at Hangar 7

PROGRAM IN DETAIL | JUNE 8TH, 2011

8.30 **Registration open @ Café Relax, Ground Floor, Main Entrance and Main Building of PMU, Strubergasse 21, Salzburg (Coffee Available)**

9.30 – 12.30 **Precourse in Joint Anatomy***
*pre-registration required. A detailed program has been sent to registered participants

This precourse has been kindly co-sposored by genzyme Biosurgery

12.30 – 13.30 **Lunch on Campus**

13.30 – 14.00 **Welcome and Introduction Main Program**

Felix Eckstein
Institute of Anatomy and Musculoskelettal Research, Paracelsus Medical University, Salzburg, Austria

Rosemarie Forstner
Dean of Student Affairs & Department of Radiology, Paracelsus Medical University, Salzburg, Austria

14.00 – 15.30 **Module 1: Imaging Biomarkers and Clinical Outcomes in Cartilage Repair - Invited Lectures**

Sample guiding question: What clinical outcomes should be used in cartilage repair and which imaging biomarkers predict these most effectively?

Chair: Rosemarie Forstner, Paracelsus Medical University, Salzburg, Austria (20 min presentation + 10 min discussion)

14.00-14.30	**Christoph Erggelet** Educatis University, Altdorf, Switzerland SURGICAL CARTILAGE REPAIR TECHNIQUES AND THEIR APPLICABILITY TO OSTEOARTHRITIS
14.30-15.00	**Siegfried Trattnig** Center of Excellence for High Field MR, Medical University of Vienna, Austria IMAGING TECHNIQUES AND BIOMARKERS FOR MONITORING CARTILAGE REPAIR
15.00-15.30	**Stefan Marlovits** Medical University of Vienna, Austria CLINICAL OUTCOMES AND THEIR RELATIONSHIP WITH IMAGING BIOMARKERS FOR CARTILAGE REPAIR

15.30 – 16.15 **Coffee Break**

16.15 – 17.30 **Module 2: 5 Presentations Selected from Abstracts (Cartilage Repair)**

Chair: Siegfried Trattnig, Medical University Vienna, Austria
(10 min presentation + 5 min discussion)

16.15-16.30	***,**Roemer F.W., ***Felson D.T., ***Wang K., **,****Crema M.D., **,****Marra M.D., *****Nevitt M.C., ***Zhang Y., ******Torner J., *******Lewis C.E., **Guermazi A.** *Department of Radiology, Klinikum Augsburg, Augsburg, Germany, ** Quantitative Imaging Center (QIC), Department of Radiology and ***Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA, ****Institute of Diagnostic Imaging (IDI), Ribeirão Preto, Ribeirão Preto, SP, Brazil, *****Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA, ******Department of Epidemiology, University of Iowa, Iowa City, IA, USA, *******Department of Epidemiology, University of Alabama, Birmingham, AL, USA **FOCAL CARTILAGE DAMAGE OF THE KNEE JOINT AND RISK FOR SUBSEQUENT CARTILAGE LOSS: AN MRI-BASED ANALYSIS FROM THE MOST STUDY**
16.30-16.45	**[1,2]Kulmala K.A.M, [3]Pulkkinen H.J, [1,3]Rieppo L, [3,4]Tiitu V, [5,6]Kiviranta I, [7]Brünott A, [7]Brommer H, [7]van Weeren R, [8]Brama P.A.J, [1]Mikkola M.T, [1]Korhonen R.K, [1]Jurvelin J.S, [1,9]Töyräs J.** [1] Department of Applied Physics, University of Eastern Finland, POB 1627, 70211, Kuopio, Finland, [2] Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland, [3] Department of Biomedicine, Anatomy, University of Eastern Finland, Kuopio, Finland, [4] SIB-labs, University of Eastern Finland, Kuopio, Finland, [5] Department of Orthopaedics and Traumatology, University of Helsinki, Helsinki, Finland, [6] Department of Orthopaedics and Traumatology, Jyväskylä Central Hospital, Jyväskylä, Finland, [7] Department of Equine Sciences, Utrecht University, Utrecht, the Netherlands, [8] Section of Veterinary Clinical Studies, School of Agriculture, Food Science & Veterinary Medicine, University College Dublin, Dublin, Ireland, [9] Department of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland **CONTRAST ENHANCED COMPUTED TOMOGRAPHY IN EVALUATION OF SPONTANEOUS CARTILAGE REPAIR**
16.45-17.00	***,**van Tiel J., **Siebelt M., **Waarsing J.H., *van Straten M., **Verhaar J.A.N., *Krestin G.P., **,***Weinans H., *Oei E.H.G.** *Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands **Department of Orthopedic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands ***Department of Biomechanical Engineering, Delft University of Technology, Delft, The Netherlands **CT ARTHROGRAPHY TO MEASURE CARTILAGE QUALITY: INFLUENCE OF SULPHATED GLYCOSAMINOGLYCAN CONTENT AND STRUCTURAL COMPOSITION OF EXTRACELLULAR MATRIX ON CONTRAST AGENT DIFFUSION INTO CARTILAGE**
17.00-17.15	***,***Tamez-Peña JG, **Trattnig S, ***Totterman S,**Szomolanyi P, *****Shive MS,****Buschmann MD *****Restrepo A.** *Tec de Monterrey, Escuela de Medicina, Monterrey, NL, México; **Medical University of Vienna, Vienna, Austria; ***Qmetrics Technologies, Rochester, NY, USA; ****Ecole Polytechnique, Montreal, Canada, *****Piramal Healthcare (Canada) Ltd. **A QUANTITATIVE METHOD FOR EVALUATING CARTILAGE DEFECT REPAIR: INTRA- AND INTER- READER REPRODUCIBILITY**
17.15-17.30	**Shive, M.S.*, Buschmann, M.B.**, Yaroshinsky, A.***, Tamez-Pena, J.****, Schreyer, E*****, Totterman, S.*****, Trattnig, S.******, Stanish, W.D.*******, Restrepo, A.*** *Piramal Healthcare, Laval, Canada,**Ecole Polytechnique, Montreal, Canada,***San Andreas, USA, ****Tecnologico de Monterrey, Escuela de Medicina, Monterrey, Mexico; *****Qmetrics, Rochester, NY ******Medical University of Vienna, Vienna, Austria; *******Dalhousie University, Halifax, Canada **T2 MRI OF REPAIR CARTILAGE REFLECTS BOTH TISSUE QUALITY AND QUANTITY**

17.45 **Young Investigator Evening (Braustüberl, Kloster Mülln)**
http://www.augustinerbier.at/

Meet in the PMU courtyourd at the tree in front of the lecture theatre. Walk together for about 10 mins to the Mülnnerbräu, or join the group later. Drinks and food can be bought in various food stalls at your own expense.

17.45 – 18.30 **Corporate Round Table**

Chairs:
Gloria Mathews, Genzyme Corp., Cambridge, USA
David Hunter, University of Sydney, Sydney, Australia

This session is targeted at industry sponsors, invited speakers and session chairs to discuss questions of interest that should be addressed during the workshop. However, the session is open to everyone interested in this topic.

19.30 **Speaker & Sponsor Dinner (M32,** http://m32.at/**)**

Take the elevator from Anton Neumayr Platz at the historic city center of Salzburg to the modern art museum and to the M32. A map how to get there can be found at the back of your ticket.

PROGRAM IN DETAIL | JUNE 9TH, 2011

9.00 – 10.15 **Module 3: 5 Presentations Selected from Abstracts (Osteoarthritis Initiative)**

Chair: Michael Nevitt, University of California, San Francisco, USA
(10 min presentation + 5 min discussion)

9.00-9.15	[1,2]Frobell R.B., [3]Nevitt M., [3]McCulloch C., [4]Hochberg M., [5]Duryea J., [2,6]Wirth W., [7]Eaton C., [8]McAlindon T., [3]Maeda J., [3]Lynch J., [2,6]Eckstein F., for the OAI investigators [1]Lund University, Sweden; [2]Paracelsus Medical University, Austria; [3]UCSF & OAI Coordinating Center, CA; [4]University of Maryland, MD; [5]Harvard Medical School, MA; [6]Chondrometrics GmbH, Germany; [7] Memorial Hospital of Rhode Island & Brown Medical School, RI; [8]Tufts University, MA MRI-BASED CARTILAGE THICKNESS LOSS AND JOINT SPACE NARROWING IN AN OAI CORE PROGRESSION SAMPLE, AND THEIR RELATIONSHIP WITH AGE, SEX, AND BMI.
9.15-9.30	*,**Tamez-Peña JG, **González P, **Schreyer E, and **Totterman S. * Tecnológico de Monterrey; Escuela de Medicina; Monterrey, NL, México ** Qmetrics Technologies, Rochester, NY, USA SPATIO-TEMPORAL ANALYSIS OF THE SIGNIFICANT CHANGES IN CARTILAGE MORPHOLOGY: DATA FROM THE OSTEOARTHRITIS INITIATIVE
9.30-9.45	*Wirth W., **Mc Culloch C.E., **Lynch J., **Nevitt M., ***Kwoh C.K., *Maschek S., *Hudelmaier M., ****Sharma L., *Eckstein F., for the OAI investigators * Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany; ** University of California San Francisco, San Francisco, CA; *** Division of Rheum. and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA ****Division of Rheumatology, Feinberg School of Medicine at Northwestern University, IL ARE SHORT-TERM RATES OF MRI-BASED MEASURES OF KNEE CARTILAGE LOSS MARKERS OF LONG-TERM CHANGE? FOUR-YEAR DATA FROM THE OA INITIATIVE
9.45-10.00	*Lammentausta E., *Herronen A., *Ojala R.O. and **Nieminen M.T. *Oulu University Hospital, Oulu, Finland **Oulu University Hospital and University of Oulu, Oulu, Finland T2 REVEALS EARLY CARTILAGE CHANGES DURING TWO YEARS FOLLOW-UP IN SUBJECTS AT RISK FOR OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE
10.00-10.15	*Buck R.J., **Nevitt M, ***Wirth W, ***Eckstein, F – for the OAI investigators * StatAnswers Consulting LLC, Minneapolis, MN; ** University of California and OA Initiative Coordinating Center, San Francisco, CA; *** Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany CORRELATION OF KNEE CARTILAGE THICKNESS CHANGE AT 1 YEAR AND CLINCAL OUTCOME CHANGES AT 3 YEARS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

10.15 – 10.45 **Coffee Break**

10.45 – 12.30 **Module 4: The Osteoarthritis Initiative (OAI) – Invited Lectures**
Sample guiding question: What have we learned from the OAI and where do we go?

Chair: Gillian Hawker, Women's College Hospital, University of Toronto, Canada
(20 min presentation + 10 min discussion / 1st presentation 30 mins + 15 min discussion))

10.45-11.30	**Michael Nevitt and John Lynch** University of California, USA RATES OF STRUCTURAL OA PROGRESSION USING THE OAI IMAGING DATA
11.30-12.00	**Kent Kwoh** University of Pittsburgh, USA RELATING STRUCTURAL OA PROGRESSION (X-RAY AND MRI) TO CLINICAL OUTCOMES IN THE OAI
12.00-12.30	**Gayle Lester** National Institutes of Health (NIH), USA CURRENT STATUS, FUTURE PERSPECTIVES AND FUNDING OPPORTUNITIES FOR THE OAI AND OA RESEARCH

12.30 – 13.30 **Lunch on Campus**

13.30 – 14.30 **Module 5: Young Investigator Session:**
4 Top Presentations of Young Investigators Selected from Abstracts.

Chair: Felix Eckstein, Paracelsus Medical University, Salzburg, Austria
(10 min presentation + 5 min discussion)

13.30-13.45	***Donoghue C.R., **Rao, A., ***Bull, A.M.J., *Rueckert, D.** * Department of Computing, Imperial College London, UK, ** GlaxoSmithKline Research and Development, Clinical Imaging Centre, London, UK *** Department of Bioengineering, Imperial College, London, UK AUTOMATICALLY GENERATED NOVEL DIAGNOSTIC IMAGING BIOMARKERS WITH DATA FROM THE OAI
13.45-14.00	***, **Wiegant K, **Marijnissen A.C.A, *Intema F, *Roermund P.M, ***Eckstein F, ***Cotofana S, **Mastbergen S.C, **Lafeber F.P.J.G.** UMC Utrecht, *dept. of Orthopedics, and **dept. of Rheumatology, the Netherlands; *** Paracelsus Medical University, Institute of Anatomy, Salzburg, Austria STRUCTURAL CARTILAGE PARAMETERS ON MRI AND X-RAY IMPROVE AFTER TREATMENT WITH KNEE JOINT DISTRACTION; A 2 YEAR FOLLOW-UP.

14.00- 14.15	***Haugen IK, *Bøyesen P, *Slatkowsky-Christensen B, *Sesseng S, *** Bijsterbosch J, * ***van der Heijde D, *Kvien TK** * Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway ** Dept. of Radiology, Diakonhjemmet Hospital, Oslo, Norway *** Dept. of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands MRI IS MORE SENSITIVE THAN CONVENTIONAL RADIOGRAPHY IN DETECTION OF EROSIONS IN HAND OSTEOARTHRITIS (OA)
14.15- 14.30	**Laslett L.L., Doré D.A., Quinn S.J., Winzenberg T.M., Boon P., Jones, G.** Menzies Research Institute Tasmania, University of Tasmania, AUSTRALIA. A TWELVE MONTH RANDOMISED CONTROLLED TRIAL OF ZOLEDRONIC ACID FOR KNEE PAIN AND SUBCHONDRAL BONE MARROW LESIONS.

14.30 – 14.40 **Young Investigator awards**

Kindly sponsored by

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14.45 **Workshop Photograph**

Please join for a group photograph in the courtyard on the way to the poster session. The latter is held at the 3rd floor of the main building.

14.45 – 17.30 **Module 6: Poster Session**

15.00 – 16.00 Odd numbered posters (1 to 33)
16.00 – 17.00 Even numbered posters (2 to 34)

Poster presenters, numbers and titles are listed at the end of the program

18.15 Conference Dinner @ PMU

The conference dinner will be a barbeque style buffet from a local, family-run Bavarian caterer with his own free range animals and butchery. Let Ursula & Alois Beer spoil you. Not to worry, vegetarians have not been forgotten!

Dress code casual. Please bring warm clothing depending on weather!

19.45 Claudia Koreck & Band Live @ PMU

This open air concert will take place in the PMU courtyourd. In case of rain, please bring a jacket and/or an umbrella. Claudia Koreck was born in Traunstein, located 30 km west of Salzburg in Bavaria and now lives in Munich. She sings most of her songs in the local Bavarian language and has just produced her third Album (Menschsein). Enjoy an evening with great music.

PROGRAM IN DETAIL | JUNE 10TH, 2011

9.00 – 10.15 **Module 7: 5 Presentations Selected from Abstracts (Semi-Quantitative Imaging Outcomes)**

Chair: David Hunter, University of Sydney, Sydney, Australia
(10 min presentation + 5 min discussion)

9.00-9.15	***Schiphof D., *Klerk B.M. de, **Waarsing J.H., ***Hofman A., ****Ginai A.Z., ****Oei E.H., **Weinans H., *,**Bierma-Zeinstra S.M.A.** * Department of General Practice, Erasmus MC, Rotterdam, The Netherlands ** Department of Orthopeadics, Erasmus MC, Rotterdam, The Netherlands *** Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands **** Department of Radiology, Erasmus MC, Rotterdam, The Netherlands **HOW RISK FACTORS ASSOCIATE TO EARLY OSTEOARTHRITIS SHOWN WITH SEMI-QUANTITATIVE MEASURES ON MRI IN KNEES WITHOUT SIGNS OF RADIOGRAPHIC OA**
9.15-9.30	***Runhaar J MSc, **Steens R MD, **Vroegindeweij D PhD, ***Oei E.H.G, ****Bierma-Zeinstra S.M.A1,4 PhD** *Erasmus MC, Department of General Practice, Rotterdam, the Netherlands ** Maasstad Hospital, Department of Radiology, Rotterdam, the Netherlands *** Erasmus MC, Department of Radiology, Rotterdam, the Netherlands **** Erasmus MC, Department of Orthopedics & Department of General Practice, Rotterdam, the Netherlands **MALALIGNMENT AND THE PRESENCE OF EARLY SIGNS OF KNEE OA IN OBESE WOMEN.**
9.30-9.45	***Guermazi A., *Hayashi D.,*,***Roemer F.W., **Felson D.T., **Wang K.,**** Lynch J., *****Amin S., ****Nevitt M.N.** *Quantitative Imaging Center, Dept. of Radiology, and ** Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, USA ***Department of Radiology, Klinikum Augsburg, Augsburg, Germany ****Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA ***** College of Medicine, Mayo Clinic, Rochester, MN, USA **DOES MRI DEPICT PROGRESSION OF RADIOGRAPHICALLY-DEFINED 'END-STAGE OA (KELLGREN-LAWRENCE GRADE 4)' LONGITUDINALLY? THE MOST STUDY**
9.45-10.00	***,**Englund M., **Felson D.T., **Guermazi A, **,***Roemer F.W., **Wang K., **Crema M.D., ****Lynch J.A. *****Sharma L., ******Segal N., *******Lewis C.E., ****Nevitt M.C.** * Lund University, Lund, Sweden. ** Boston University School of Medicine, Boston, MA, USA. *** Klinikum Augsburg, Augsburg, Germany. **** University of California San Francisco, San Francisco, CA, USA. ***** Northwestern University, Chicago IL, USA. ****** University of Iowa, Iowa City, IA, USA. ******* University of Alabama, Birmingham, AL, USA. **RISK FACTORS FOR MEDIAL MENISCAL LESIONS AND (OR) EXTRUSION ON KNEE MRI IN OLDER U.S. ADULTS: THE MULTICENTER OSTEOARTHRITIS STUDY (MOST)**
10.00-10.15	**Kwoh C.K.*, Hannon M.J.*, Guermazi A.**, Boudreau R.*, Green S.M.*, Roemer F.W.**,***** * University of Pittsburgh, Pittsburgh, PA, United States, ** Boston University School of Medicine, Boston, MA, United States, ***Department of Radiology, Klinikum Augsburg, Augsburg, Germany **IDENTIFICATION OF MRI MORPHOLOGIC FEATURES ASSOCIATED WITH DIFFERENT KNEE PAIN PATTERNS**

10.15 – 10.30 **Coffee Break**

10.30 – 12.30 **Module 8: Relationships of Imaging Biomarkers with Clinical Outcome – Invited Lectures**

Sample guiding question: What clinical outcomes should be used in OA and which imaging biomarkers predict these most effectively?

Chair: Kent Kwoh, University of Pittsburgh, Pittsburgh, USA
(10 min presentation + 5 min discussion)

10.30-11.00	**Gillian Hawker** Women's College Hospital, University of Toronto, Canada CLINICAL OUTCOMES: WHAT IS THE CHOICE IN OA?
11.00-11.30	**Tuhina Neogi** Boston University, USA REVIEW OF THE RELATIONSHIP BETWEEN X-RAY BIOMARKERS AND CLINICAL OUTCOMES IN OA
11.30-12.00	**David Hunter** University of Sydney, Australia REVIEW OF THE RELATIONSHIP BETWEEN MR IMAGING BIOMARKERS AND CLINICAL OUTCOMES IN OA
12.00-12.30	**Gloria Matthews** Genzyme Corp., Cambridge, USA WHAT REQUIREMENTS DOES AN IMAGING BIOMARKER NEED TO SATISFY TO BE USEFUL IN CARTILAGE REPAIR EVALUATION AND DMOAD DEVELOPMENT?

12.30 – 13.30 **Lunch on Campus**

13.30 - 14.45 **Module 9: 5 Presentations Selected from Abstracts (Quantitative Imaging Outcomes)**

Chair: Miika Nieminen, University of Oulu, Oulo, Finland
(10 min presentation + 5 min discussion)

13.30-13.45	**M. D. Crema*,**, D. J. Hunter***, D. Burstein****, F. W. Roemer*,*****, L. Li******, N. Krishna****, M. D. Marra*,*******, M-P. Hellio Le-Graverand********, A. Guermazi*** *Boston Univ. Sch. of Med., Boston, MA, **Inst. of Diagnostic Imaging (IDI) and Radiology Div., Univ. of São Paulo at Ribeirão Preto, Ribeirão Preto, BRAZIL, ***The Univ. of Sydney, Sydney, AUSTRALIA, ****Harvard Med. Sch., Boston, MA, *****Klinikum Augsburg, Augsburg, GERMANY, ******New England Baptist Hosp., Boston, MA, *******Inst. of Diagnostic Imaging (IDI), Ribeirão Preto, BRAZIL, ********Pfizer Inc., New London, CT. **DELAYED GADOLINIUM-ENHANCED MRI OF MEDIAL TIBIOFEMORAL CARTILAGE (DGEMRIC) AND ITS RELATIONSHIP WITH MEDIAL MENISCAL PATHOLOGY: A 12-MONTH FOLLOW-UP STUDY USING 3.0T MRI.**
13.45-14.00	*** Shiomi T., **Nishii T., ** Tamura S., ***Yamazaki Y., ***Murase K., ****Tanaka H., *Yoshikawa H., **Sugano N.** * Department of Orthoaedic Surgery, ** Department of Orthopaedic Medical Engineering, *** Department of Medical Physics and Engineering, **** Department of Radiology, Osaka University Medical School, Osaka, Japan **THE INFLUENCE OF MEDIAL MENISCECTOMY TO THE STRESS DISTRIBUTION OF FEMORAL CARTILAGE IN PORCINE KNEE -3D RECONSTRUCTED T2 MAPPING STUDY-**
14.00-14.15	***Tamura S., *Nishii T., **Nakata K., **Shiomi T., ***Yamazaki Y., ***Murase K., ****Tanaka H., **Kita K., **Mae T., **Yoshikawa H., *Sugano N.** * Department of Orthopaedic Medical Engineering, Osaka University, Osaka, Japan ** Department of Orthopaedic Surgery, Osaka University, Osaka, Japan *** Department of Medical Physics and Engineering, Osaka University, Japan **** Department of Diagnostic and Interventional Radiology, Osaka University, Japan **ASSESSMENT OF KNEE CARTILAGE IN PATIENTS WITH ACL RUPTURE BY 3D RECONSTRUCTED T2 MAPPING**
14.15-14.30	***Cicconetti, G., *Matheny, C.** * GlaxoSmithKline, Upper Merion, PA, USA **APPLYING A STATISTICAL/GRAPHICAL TOOL TO CHARACTERIZE CHANGES OVER TIME IN MRI-BASED CARTILAGE THICKNESS MEASURES**
14.30-14.45	***Buck R.J.** * StatAnswers Consulting LLC, Minneapolis, MN **SIMULATIONS TO ASSESS BEHAVIOR OF ORDERED VALUES APPROACH IN CLINICAL DRUG TRIALS**

14.45 – 15.15 **Coffee Break**

15.15 – 16.45

Module 10. Round Table Discussion

Sample guiding question: How can we clinically validate and qualify existing imaging biomarkers for cartilage repair and osteoarthritis?

Chairs:
Gloria Mathews, Genzyme Corp., Cambridge, USA
David Hunter, University of Sydney, Sydney, Australia
Frank Roemer, Klinikum Augsburg, Augsburg, Germany
Michael Nevitt, University of California, San Francisco, USA

In this session workshop participants should summarize the lessons that have been learned in context of the clinical validation of imaging biomarkers and should discuss a future research agenda that addresses the most urgent and relevant questions in the field

18.00

Bus Leaves from PMU for Beer Garden Event in Bavaria

Separate registration required. Please bring your ticket.

Choose from a wide menu of typical Bavarian dishes and great beers. For those not familiar with the local terminology: The classic lager is called "Helles" in Bavaria. Wheat beer is called "Weissbier" and you can order the blonde or dark version (helles or dunkles Weissbier). The glass in which Weissbier is served becomes wider at the top and is relatively thin; therefore you should always cheer with the bottom of the glass, and not with its top. During dinner, there will be a musical surprise, featuring Stephan Huber and Sophia Eckstein.

21.30

First Bus Leaves From Beer Garden Back to PMU and Salzburg Downtown

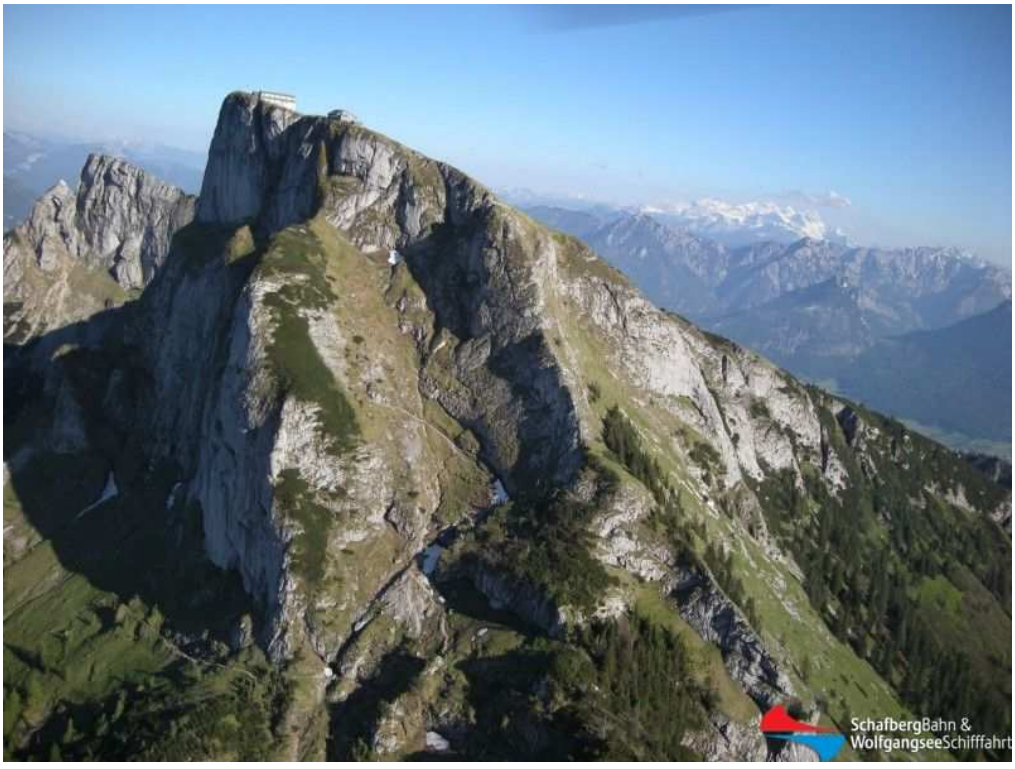
22.30

Last Bus Leaves From Beer Garden Back to PMU and Salzburg Downtown

Taxi transport can be called by those who would like to stay longer. Costs will be approx. 20 € per taxi

PROGRAM IN DETAIL | JUNE 11TH, 2011

8.45 – 18.00	**Whole Day Break Out Tour** Break out tour deepening and continuing discussions initiated at the workshop, to take place during a trip to the Salzkammergut, including a **boat ride** across Lake Wolfgang and a **stream train ride** http.//www.schafbergbahn.at/ to the summit of the spectacular **Schafberg**.
8.45	**Leave with bus from PMU (Salzburg) to St. Gilgen**
10.00	**Leave with boat from St. Gilgen to St. Wolfgang**
11.00	**Take steam train from St. Wolfgang to summit**
11.50	**Arrive at Schafberg summit**
12.45	**Lunch at the Hotel Schafberg** (Kaisersaal)
15.10	**Leave with stream train from summit** (or 10 mins later from middle station)
16.05	**Leave with boat from St. Wolfgang**
17.00	**Bus pick up at St. Gilgen**
18.00	**Return at PMU (Salzburg)**
19.30	**Chill out and Informal get at Hangar-7** (near airport) Hangar-7 is the showcase of Red Bull airplanes, Formula 1 cars, and other fancy toys. We will meet there at approx. 19:30. We have not arranged for transport from Salzburg to Hangar-7, but any taxi will take approx. 10 min from the Salzburg hotels to **Wilhelm-Spazier-Str. 7A** near the airport, where Hangar-7 is located. Let's meet at the ground floor in the exhibition around 19:30. At approx. 20:00 we will then transit to the Members Club in the 4th floor of the right tower to enjoy a selection of drinks. It's an event you do not want to miss! No food will be provided, so if you are hungry after the Schafberg trip, please grab a bite before coming to the Hangar.



POSTER SESSIONS | JUNE 9TH, 2011

Library of Paracelsus Medical University (3rd Floor Main Building)

15.00 – 16.00	Odd Numbered Posters	(1 to 33)
16.00 – 17.00	Even Numbered Posters	(2 to 34)

Poster Presenters, Numbers, and Titles:

1	Lickorish D, Haskell M.M., Wood S.A, Collett A, Goad M.E.P., Schrier D, Flory C. Stryker Regenerative Medicine, North Grafton, USA QUANTIFICATION OF TRABECULAR BONE VASCULARITY IN A RABBIT MODEL OF OSTEOARTHRITIS BY PERFUSION MICRO COMPUTED TOMOGRAPHY
2	*Maschek S., *Eckstein F., *Wirth W., **Gradl G., **Kirchhoff C., ***Wörtler K., **von Eisenhart-Rothe R. *Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany **Clinic for Orthopaedics and Traumatology, Technical University, Munich, Germany ***Clinic for Radiology, Technical University, Munich, Germany DOES ANKLE CARTILAGE ADAPT TO STRONG ALTERATIONS IN LOADING ENVIROMENT AFTER TRANSPLANTATION TO THE KNEE (VAN NEES ROTATIONPLASTY)?
3	*King, A.J., **Deng, C., **Sharp, J. **Tomanek B, *Dunn, J.F. * McCaig Institute & Experimental Imaging Centre & University of Calgary, Calgary, Canada ** National Research Council of Canada – Institute for Biodiagnotics (West), Calgary, Canada (NRC) 3D VISUALIZATION AND MEASUREMENT OF THE POSTERIOR CRUCIATE LIGAMENT IN A FLEXED KNEE USING OPEN-BORE 0.2T MRI
4	*Dam E.B., **Marques J. * BiomedIQ, Copenhagen, Denmark ** BiomedIQ, Copenhagen, Denmark & University of Copenhagen, Denmark AUTOMATIC SEGMENTATION OF BONE AND CARTILAGE FROM KNEE MRI
5	*,**Lammentausta E., **Hawezi Z., ***Tiderius C.J. and **Dahlberg L. *Oulu University Hospital, Oulu, Finland **Lund University, Malmö, Sweden ***Skåne University Hospital, Malmö, Sweden IN VIVO TRANSPORT OF GD-DTPA2- INTO HUMAN KNEE CARTILAGE

6	[1]Eckstein F., [2]Kwoh CK.., [3]Boudreau R., [2]Wang Z., [2]Hannon JM., [1]Cotofana S., [1]Hudelmaier M., [1]Wirth W., [4]Guermazi A., [5]Nevitt M., [6]John M., [7]Hunter D.J., for the OAI investigators [1]Paracelsus Medical University, Salzburg, Austria & Chondrometrics Gmbh, Ainring, Germany [2] Div. of Rheumatology and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA [3]Dept. of Epidemiology, Grad. School of Public Health, Univ. of Pittsburgh, PA; [4]BICL & Boston Univ., Boston, MA; [5]OAI Coordinating Center, UCSF, San Francisco, CA; [6]Novartis Pharma AG, Basel, Switzerland; [7] Royal North Shore Hospital & Northern Clinical School, Univ. Sydney, Australia CARTILAGE THICKNESS, DENUDED AREAS, AND BONE SIZE IN KNEES PRIOR TO TOTAL KNEE REPLACEMENT (TKR) – DATA FROM THE OSTEOARTHRITIS INITIATIVE
7	*Sitoci H., **Hudelmaier M., **Eckstein F. * Institute of Anatomy, Ludwig Maximilians Universität, Munich, Germany ** Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria NOCTURNAL CHANGES IN FEMORO-TIBIAL CARTILAGE THICKNESS IN YOUNG HEALTHY ADULTS
8	*,**Roemer F.W., ***Nevitt M.C, ****Felson D.T., ****Niu J., ***Lynch J.A., **,*****Crema M.D., **,*****Marra M.D.,******Lewis C.E., *******Torner J., **Guermazi A. *Department of Radiology, Klinikum Augsburg, Augsburg, Germany, **Quantitative Imaging Center (QIC), Department of Radiology and ****Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA, ***Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA, *****Institute of Diagnostic Imaging (IDI), Ribeirão Preto, Ribeirão Preto, SP, Brazil, ******Department of Epidemiology, University of Alabama, Birmingham, AL, USA, *******Department of Epidemiology, University of Iowa, Iowa City, IA, USA LONGITUDINAL WITHIN-GRADE SCORING OF CARTILAGE AND BONE MARROW LESIONS: VALIDITY ANALYSES FROM THE MOST STUDY
9	*Cicconetti, G., *Matheny, C. * GlaxoSmithKline, Upper Merion, PA, USA A STATISTICAL/GRAPHICAL TOOL TO IDENTIFY KNEE OA PHENOTYPES BASED ON MRI CARTILAGE THICKNESS MEASURES
10	*Haugen IK, *Bøyesen P, *Slatkowsky-Christensen B, *Sesseng S, * ***van der Heijde D, *Kvien TK * Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway ** Dept. of Radiology, Diakonhjemmet Hospital, Oslo, Norway *** Dept. of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands THE ROLE OF MRI-DEFINED SYNOVITIS IN HAND OSTEOARTHRITIS
11	*Wyman B.T., **Cotofana S., *Zhang Y., ***Souza RB., *Clemmer R., *Hellio Le Graverand M-P, ***Li X., ***Majumdar S., ***Link T.M., ***Eckstein F., ****Vignon E. * Pfizer Inc, Groton, CT, USA; ** Paracelsus Medical University, Salzburg, Austria; *** University of California, San Francisco, CA, USA; **** Claude Bernard University, Lyon, France COMPRESSION OF THE KNEE UPON WEIGHT LOADING IN HEALTHY AND OSTEOARTHRITIS SUBJECTS AS MEASURED BY MRI AND X-RAY
12	Saunders F.R., Barr R.J, Reid D.M., Aspden R.M., Gregory J.S. University of Aberdeen, Aberdeen, Scotland, UK ACTIVE SHAPE MODELLING OF BILATERAL KNEE OSTEOARTHRITIS IN THE OAI

13	*Driban J.B., **Lo G.H., *Price L.L.,*McAlindon T.E. * Tufts Medical Center, Boston, USA ** Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, USA HIP BONE MINERAL DENSITY DOES NOT INFLUENCE TIBIOFEMORAL BONE MARROW LESION SIZE
14	*,**Marques J., **Dam E. * University of Copenhagen, Copenhagen, Denmark ** BiomedIQ, Rødovre, Denmark QUANTIFICATION OF TRABECULAR TIBIA BONE STRUCTURE RELATED TO THE PRESENCE OF OSTEOARTHRITIS
15	*,**Marques J., **Dam E. * University of Copenhagen, Copenhagen, Denmark ** BiomedIQ, Rødovre, Denmark PREDICTION OF CARTILAGE LOSS BY ANALYSIS OF TRABECULAR TIBIA BONE STRUCTURE
16	*Riek, J.K. * VirtualScopics, Inc. Rochester, NY, USA A MULTI-CENTER COMPARISON OF T2 RELAXATION TIMES CALCULATED CENTRALLY VERSUS THOSE GENERATED DIRECTLY BY THE MR SCANNER.
17	Beattie K.A.*, MacIntyre N.J.*, Ramadan K.*, Inglis D.*, Maly M.R.* *McMaster University, Hamilton, ON, Canada LONGITUDINAL CHANGES IN INTERMUSCULAR FAT VOLUME AND QUADRICEPS MUSCLE VOLUME IN THE THIGHS OF FEMALE OAI PARTICIPANTS
18	Rudolphi K, Aigner S, Berg-Scholl I, Bissinger T, Keiffer R, Wunschel, M sanofi-aventis, TSU Aging, Musculoskeletal Cluster, Frankfurt-Main, Germany IMPROVED ASSESSMENT BY QUANTITATIVE DIGITAL HISTOMORPHOMETRY OF HISTOPATHOLOGICAL CHANGES OF ARTICULAR CARTILAGE IN A SURGICAL MODEL OF POST-TRAUMATIC OSTEOARTHRITIS OF THE KNEE JOINT IN RATS
19	*Stok K. S., **Nesic D., ***Zulliger M., *Firminger C.,*Müller R. * Institute for Biomechanics, ETH Zürich, Switzerland ** Department of Clinical Research, University of Bern, Switzerland *** SCANCO Medical AG, Brüttisellen, Switzerland COMPREHENSIVE MORPHOLOGICAL CHARACTERISATION OF ARTHRITIS IN ANIMAL MODELS BY MICRO-COMPUTED TOMOGRAPHY
20	*Stok, K.S., **Glanzmann, M., *Steiner, T., *,** Goldhahn, J., *Müller, R. * Institute for Biomechanics, ETH Zürich, Switzerland ** Schulthess Clinic, Zürich, Switzerland AN INTEGRATIVE IMAGING APPROACH FOR EXAMINING BONE AND CARTILAGE TISSUES IN THE OSTEOARTHRITIC JOINT – A PILOT STUDY
21	*Siorpaes K., *Wenger A., *Bloecker K., **Burgkart R., *Wirth W., *Eckstein F. * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria **Clinic for Orthopaedics and Traumatology, Technical University Munich, Germany INTEROBSERVER VARIATION OF QUANTITATIVE MENISCUS ANALYSIS USING CORONAL MPR DESSWE AND IW TSE MR IMAGING

22	***Bloecker K., *Wirth W., *Hudelmaier M., **Burgkart R., ***Frobell R., *Eckstein F.** * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg , Austria **Clinic for Orthopaedics and Traumatology, Technical University Munich, Germany *** Department of Orthopaedics, Clinical Sciences Lund, Lund University, Lund, Sweden **SIZE AND POSITION OF THE HEALTHY MENISCUS, AND ITS CORRELATION WITH SEX, HEIGHT, WEIGHT, BONE SIZE, AND AGE**
23	***,** Kinds M.B., * Marijnissen A.C.A., ** Vincken K.L., ** Viergever M.A., *** Drossaers-Bakker K.W., * Bijlsma J.W.J., *,**** Welsing P.M.J., * Lafeber F.P.J.G.** * Rheumatology & Clinical Immunology, University Medical Center Utrecht, the Netherlands ** Image Sciences Institute, University Medical Center Utrecht, the Netherlands *** Institute for Behavioral Research, University of Twente and Medisch Spectrum Enschede, the Netherlands **** Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, the Netherlands **ARE SEPARATE QUANTITATIVE RADIOGRAPHIC FEATURES (KIDA) OF KNEE OSTEOARTHRITIS VERY EARLY IN THE DISEASE (CHECK) ASSOCIATED WITH CLINICAL PROGRESSION DURING FOUR-YEAR FOLOW-UP?**
24	***,** Kinds M.B., * Marijnissen A.C.A., ** Vincken K.L., ** Bartels L.W., ** Viergever M.A., *** de Jong H.W.A.M., *Lafeber F.P.J.G.** * Rheumatology & Clinical Immunology, University Medical Center Utrecht, the Netherlands ** Image Sciences Institute, University Medical Center Utrecht, the Netherlands *** Radiology, University Medical Center Utrecht, the Netherlands **FEASIBILITY OF BONE DENSITY EVALUATION USING PLAIN DIGITAL RADIOGRAPHY**
25	*** Hudelmaier M., *Wirth W., *Maschek S., **Nevitt M., *Eckstein F. for the OAI Investigators Group** * Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany ** University of California and OA Initiative Coordinating Center, San Francisco, CA **ONE-YEAR RATE OF CHANGE IN SUBCHONDRAL BONE SIZE IN OSTEOARTHRITIC AND HEALTHY KNEES**
26	***Sattler M., *Dannhauer T., *Hudelmaier M., **Sänger A.M., ***Hunter DJ., ****Kwoh K., *Eckstein F., for the OAI investigators** * Paracelsus Medical University, Salzburg , Austria & Chondrometrics GmbH, Ainring, Germany ** Organismic Biology, Natural Science Faculty, Salzburg University, Salzburg, Austria *** Royal North Shore Hospital & Northern Clinical School, University of Sydney, Sydney, Australia. **** Division of Rheum. and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA **SIDE DIFFERENCES OF THIGH MUSCLE CROSS SECTIONAL AREAS IN KNEES WITH THE SAME RADIOGRAPHIC OA (KL) GRADE, BUT UNILATERAL FREQUENT PAIN**
27	**[1]Cromer M., [1]Bourne R., [2]Fransen M., [1,3]Fulton, R., [4]Wang, S.C.** [1.]Discipline of Medical Radiation Sciences, FHS, University of Sydney, Australia [2.]Clinical and Rehabilitation Sciences Research Group, FHS, University of Sydney, Australia [3.]School of Physics, University of Sydney, Australia [4.]Discipline of Imaging, Sydney Medical School, Australia **QUANTITATIVE ANALYSIS IN THE MEDIAL TIBIO-FEMORAL COMPARTMENT OVER ONE YEAR**

28	*Nishii T., *Tamura S., ** Shiomi T., ***Yamazaki Y., ***Murase K., ****Tanaka H., *Yoshikawa H., **Sugano N. * Department of Orthopaedic Medical Engineering, ** Department of Orthoaedic Surgery, *** Department of Medical Physics and Engineering, and **** Department of Radiology, at Osaka University, Osaka, Japan SIGNIFICANT INFLUENCE ON LOAD RESPONSE OF KNEE CARTILAGE T2 BY MENISCUS DISORDER –A LOADING MRI STUDY
29	*Klocke N.F., **Thedens D.R., *Amendola A., *Pedersen D.R * Orthopaedics and Rehabilitation, University of Iowa, Iowa City, IA, USA ** Radiology, University of Iowa, Iowa City, IA, USA TOWARDS T1RHO IN THE CLINIC: A 3.0T AND 1.5T COMPARISON
30	*Stannus O.P., *Jones,G., * **Ding C. * Menzies Research Institute, University of Tasmania, Hobart, Australia ** Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia CARTILAGE SIGNAL INTENSITY ON MRI: ASSOCIATION WITH BODY MASS INDEX, CARTILAGE DEFECTS AND TYPE II COLLAGEN BREAKDOWN
31	*Buck R.J., **Hellio Le Graverand-Gastineau M-P, ***Nevitt M, ****Wirth W, **** Eckstein, F – for the OAI investigators * StatAnswers Consulting LLC, Minneapolis, MN; ** Pfizer Global Research and Development, Groton, CT; *** University of California and OA Initiative Coordinating Center, San Francisco, CA; **** Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany CLASSIFICATION AND DISTRIBUTION OF CARTILAGE THICKNESS CHANGE IN SUBJECT KNEES: DATA FROM THE OSTEOARTHRITIS INITIATIVE
32	*Tummala S., **Dam E.B., *Nielsen M. * eScience Center, University of Copenhagen, Copenhagen, Denmark ** BiomedIQ, Rødovre, Denmark DIAGNOSIS OF OA BY AUTOMATIC QUANTIFICATION OF INCONGRUITY FROM KNEE MRI
33	*Tamura S., *Nishii T., **Shiomi T., ***Yamazaki Y., ***Murase K., **Yoshikawa H., *Sugano N. * Department of Orthopaedic Medical Engineering, Osaka University, Osaka, Japan ** Department of Orthopaedic Surgery, Osaka University, Osaka, Japan *** Department of Medical Physics and Engineering, Osaka University 3D PATTERNS OF ACETABULAR CARTILAGE DAMAGE IN HIP DYSPLASIA AT PRE- AND EARLY ARTHRITIC STAGES; A HIGH-RESOLUTIONAL CT ARTHROGRAPHY STUDY
34	*Lowitz T., *Zerfaß P., *Engelke K., *Museyko O., **Laredo J.-D., **Bousson V., *Kalender W.A. * Institute of Medical Physics, University of Erlangen-Nürnberg, Germany ** Service de Radiologie Ostéo-Articulaire, Hôpital Lariboisière, Paris, France QUANTITATIVE CT FOR KNEE OSTEOARTHRITIS

Printing of this program has been kindly supported by a grant from

SYNTHES®

ANNOUNEMENTS

6th International Workshop on Osteoarthritis Imaging combined with the
OARSI OA Biomarkers Workshop III - Imaging Biomarker Validation and Qualification

Meeting Chairs: David Hunter, MBBS, PhD, FRACP, Ali Guermazi, MD

Scientific Program Committee: Felix Eckstein, MD, Virginia Byers Kraus, MD, PhD, Elena Losina, PhD

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5th INTERNATIONAL WORKSHOP ON OSTEOARTHRITIS IMAGING

June 8th to 11th 2011 | Salzburg (Austria)

From Joint Anatomy to Clinical Outcomes in OA and Cartilage Repair

http://oa-imagingworkshop.pmu.ac.at

Abstract Book

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MODULE 2: 5 PRESENTATIONS SELECTED FROM ABSTRACTS (CARTILAGE REPAIR)

June 8th, 2011: 16.15 – 17.30

Chair: Siegfried Trattnig, Medical University Vienna, Austria
(10 min presentation + 5 min discussion)

16.15-16.30	*,**Roemer F.W., ***Felson D.T., ***Wang K., **,****Crema M.D., **,****Marra M.D., *****Nevitt M.C., ***Zhang Y., ******Torner J., *******Lewis C.E., **Guermazi A. *Department of Radiology, Klinikum Augsburg, Augsburg, Germany, ** Quantitative Imaging Center (QIC), Department of Radiology and ***Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA, ****Institute of Diagnostic Imaging (IDI), Ribeirão Preto, Ribeirão Preto, SP, Brazil, *****Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA, ******Department of Epidemiology, University of Iowa, Iowa City, IA, USA, *******Department of Epidemiology, University of Alabama, Birmingham, AL, USA **FOCAL CARTILAGE DAMAGE OF THE KNEE JOINT AND RISK FOR SUBSEQUENT CARTILAGE LOSS: AN MRI-BASED ANALYSIS FROM THE MOST STUDY**
16.30-16.45	[1,2]Kulmala K.A.M, [3]Pulkkinen H.J, [1,3]Rieppo L, [3,4]Tiitu V, [5,6]Kiviranta I, [7]Brünott A, [7]Brommer H, [7]van Weeren R, [8]Brama P.A.J, [1]Mikkola M.T, [1]Korhonen R.K, [1]Jurvelin J.S, [1,9]Töyräs J. [1] Department of Applied Physics, University of Eastern Finland, POB 1627, 70211, Kuopio, Finland; [2] Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland; [3] Department of Biomedicine, Anatomy, University of Eastern Finland, Kuopio, Finland; [4] SIB-labs, University of Eastern Finland, Kuopio, Finland; [5] Department of Orthopaedics and Traumatology, University of Helsinki, Helsinki, Finland; [6] Department of Orthopaedics and Traumatology, Jyväskylä Central Hospital, Jyväskylä, Finland; [7] Department of Equine Sciences, Utrecht University, Utrecht, the Netherlands; [8] Section of Veterinary Clinical Studies, School of Agriculture, Food Science & Veterinary Medicine, University College Dublin, Dublin, Ireland; [9] Department of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland **CONTRAST ENHANCED COMPUTED TOMOGRAPHY IN EVALUATION OF SPONTANEOUS CARTILAGE REPAIR**
16.45-17.00	*,**van Tiel J., **Siebelt M., **Waarsing J.H., *van Straten M., **Verhaar J.A.N., *Krestin G.P., **,***Weinans H., *Oei E.H.G. *Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands **Department of Orthopedic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands ***Department of Biomechanical Engineering, Delft University of Technology, Delft, The Netherlands **CT ARTHROGRAPHY TO MEASURE CARTILAGE QUALITY: INFLUENCE OF SULPHATED GLYCOSAMINOGLYCAN CONTENT AND STRUCTURAL COMPOSITION OF EXTRACELLULAR MATRIX ON CONTRAST AGENT DIFFUSION INTO CARTILAGE**
17.00-17.15	*,***Tamez-Peña JG, **Trattnig S, ***Totterman S,**Szomolanyi P, *****Shive MS,****Buschmann MD *****Restrepo A. *Tec de Monterrey, Escuela de Medicina, Monterrey, NL, México; **Medical University of Vienna, Vienna, Austria; ***Qmetrics Technologies, Rochester, NY, USA; ****Ecole Polytechnique, Montreal, Canada, *****Piramal Healthcare (Canada) Ltd. **A QUANTITATIVE METHOD FOR EVALUATING CARTILAGE DEFECT REPAIR: INTRA- AND INTER- READER REPRODUCIBILITY**
17.15-17.30	Shive, M.S.*, Buschmann, M.B.**, Yaroshinsky, A.***, Tamez-Pena, J.****, Schreyer, E*****, Totterman, S.*****, Trattnig, S.******, Stanish, W.D.*******, Restrepo, A.* *Piramal Healthcare, Laval, Canada,**Ecole Polytechnique, Montreal, Canada,***San Andreas, USA, ****Tecnologico de Monterrey, Escuela de Medicina, Monterrey, Mexico; *****Qmetrics, Rochester, NY ******Medical University of Vienna, Vienna, Austria; *******Dalhousie University, Halifax, Canada **T2 MRI OF REPAIR CARTILAGE REFLECTS BOTH TISSUE QUALITY AND QUANTITY**

FOCAL CARTILAGE DAMAGE OF THE KNEE JOINT AND RISK FOR SUBSEQUENT CARTILAGE LOSS: AN MRI-BASED ANALYSIS FROM THE MOST STUDY

*,***Roemer F.W., ***Felson D.T., ***Wang K., **,****Crema M.D., **,****Marra M.D., *****Nevitt M.C., ***Zhang Y., ******Torner J., *******Lewis C.E., **Guermazi A.

*Department of Radiology, Klinikum Augsburg, Augsburg, Germany, ** Quantitative Imaging Center (QIC), Department of Radiology and ***Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA, ****Institute of Diagnostic Imaging (IDI), Ribeirão Preto, Ribeirão Preto, SP, Brazil, *****Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA, ******Department of Epidemiology, University of Iowa, Iowa City, IA, USA, *******Department of Epidemiology, University of Alabama, Birmingham, AL, USA

INTRODUCTION: Several studies suggest that one of the strongest predictors of future cartilage loss is prevalent cartilage damage, which is one of the reasons to treat focal defects surgically in order to prevent further structural deterioration. It is unknown if small superficial focal defects progress at a similar rate as small full-thickness focal defects. Further, the role of adjacent pathology such as meniscal pathology and subchondral bone marrow lesions in regard to progressive cartilage loss is unexplored.

OBJECTIVE: To assess risk of progressive cartilage loss for subregions with small superficial or full-thickness focal cartilage defects in the tibio-femoral and patello-femoral joint, and to analyze possible impact of adjacent articular pathology such as bone marrow lesions, meniscal damage and meniscal extrusion.

METHODS: The MRI protocol included axial and sagittal proton-density weighted fat-suppressed and a coronal STIR sequences (1.0 T extremity system). MRIs were assessed semiquantitatively according to the WORMS scoring system. Included were all knees with available baseline and 30 months MRI. All subregions with baseline scores of 0 or 1 (normal or intrachondral signal alteration = reference group), 2.0 (superficial focal defect) or 2.5 (focal defect extending to bone) were included.
Cartilage loss was defined as an increase of at least within-grade progression in the same subregion at 30 months. We examined the presence of focal cartilage damage (score >1) and other adjacent articular pathology (i.e. bone marrow lesions, meniscal damage and meniscal extrusion) to the risk of cartilage loss at 30 month using logistic regression models. Subregions without any adjacent articular pathology were assessed separately from subregions with adjacent pathology. In the multiple logistic regression model we included baseline effusion, synovitis, BMI, age, gender, radiographic osteoarthritis severity and malalignment.

RESULTS: 10755 subregions of 1348 knees were included. Of these, 886 (8.2%) showed focal superficial defects and 213 (2.0%) exhibited focal full thickness defects. 2586 (24.0%) subregions exhibited adjacent pathology. Altogether 857 (8.0%) subregions showed progressive cartilage loss at follow-up. Risk of progressive cartilage loss was markedly increased for both subregions with focal superficial defects (adjusted odds ratio [aOR] 9.2, 95% confidence interval [CI] 7.0-12.1) and focal full thickness defects (aOR 4.5, 95% CI 2.5-8.1). Results were comparable for subregions with adjacent bone marrow or meniscal pathology.

CONCLUSION: Risk of cartilage loss is markedly increased for subregions with prevalent focal cartilage defects independently of adjacent pathology, which strongly suggests that prevalent focal cartilage damage is an independent risk factor for future progression of cartilage damage in the same subregion. Treatment of focal cartilage defects to avoid further cartilage loss in the same subregion might be worth consideration regardless of adjacent pathology.

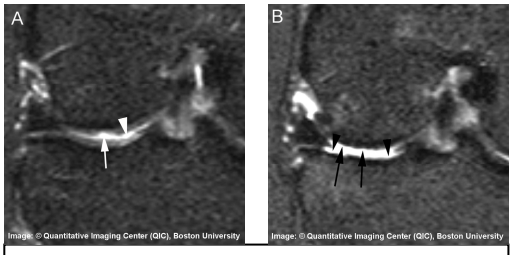

Figure 1: Coronal STIR images. A. Small superficial focal cartilage defects in the central subregions of the lateral femur (arrow) and tibia (arrowhead) are depicted. B. Marked progressive cartilage loss at follow up in the femoral (arrows) and tibial (arrowheads) cartilage surfaces at 30 months follow-up.

SPONSOR: Supported by NIH grants from the National Institute of Aging to Drs. Lewis (U01-AG-18947), Torner (U01-AG-18832), Nevitt (U01-AG-19069), and Felson (U01-AG-18820).
DISCLOSURE STATEMENT: Dr. Guermazi has received consultancies, speaking fees, and/or honoraria from Facet Solutions, Genzyme, Stryker, and from Merck Serono, and is the President of Boston Imaging Core Lab (BICL). He holds a research grant from General Electric Healthcare. Dr. Roemer is Vice President and shareholder of BICL. Dr. Crema and Dr. Marra are shareholders of BICL. None of the other authors have declared any possible conflict of interest.
ACKNOWLEDGMENT: We acknowledge the support of the staff at the Coordinating Center at UCSF, and at the clinical sites in Iowa and Alabama. We further like to thank the participants of the MOST study.
CORRESPONDENCE ADDRESS: froemer@bu.edu

CONTRAST ENHANCED COMPUTED TOMOGRAPHY IN EVALUATION OF SPONTANEOUS CARTILAGE REPAIR

[1,2]Kulmala K.A.M, [3]Pulkkinen H.J, [1,3]Rieppo L, [3,4]Tiitu V, [5,6]Kiviranta I, [7]Brünott A, [7]Brommer H, [7]van Weeren R, [8]Brama P.A.J, [1]Mikkola M.T, [1]Korhonen R.K, [1]Jurvelin J.S, [1,9]Töyräs J.

[1] Department of Applied Physics, University of Eastern Finland, POB 1627, 70211, Kuopio, Finland
[2] Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland
[3] Department of Biomedicine, Anatomy, University of Eastern Finland, Kuopio, Finland
[4] SIB-labs, University of Eastern Finland, Kuopio, Finland
[5] Department of Orthopaedics and Traumatology, University of Helsinki, Helsinki, Finland
[6] Department of Orthopaedics and Traumatology, Jyväskylä Central Hospital, Jyväskylä, Finland
[7] Department of Equine Sciences, Utrecht University, Utrecht, the Netherlands
[8] Section of Veterinary Clinical Studies, School of Agriculture, Food Science & Veterinary Medicine, University College Dublin, Dublin, Ireland
[9] Department of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland

INTRODUCTION: Contrast enhanced computed tomography (CECT) has been introduced for the evaluation of cartilage integrity. Further, CECT enables imaging of the structure and density of subchondral bone.

OBJECTIVE: In this laboratory study, we investigate the ability of CECT to distinguish spontaneously healed osteochondral lesions from adjacent normal tissue in the equine intercarpal joint. More specifically, we analyse the changes in cartilage healing using quantitative CECT parameters (describing cartilage and subchondral bone structure and contrast agent diffusion) and compare them with the changes in the reference parameters (describing histological and mechanical tissue properties).

METHODS: Osteochondral lesions (Ø=6mm) were surgically created on the 4th carpal bone of the equine intercarpal joints (n=7). After spontaneous healing for 12 months, the horses were sacrificed and osteochondral plugs (Ø=14mm) including the repair cartilage and adjacent intact tissue were harvested. The non-fibrillar and fibrillar moduli and the permeability of cartilage were determined using indentation testing combined with the fibril reinforced biphasic modelling. Subsequently, contrast agent diffusion into the samples was imaged for 36h using high resolution CT. Finally, the results from CECT, mechanical testing and microscopic analysis were compared (Wilcoxon signed rank test) and correlated (Spearman's correlation coefficients).

RESULTS: Contrast agent diffusion coefficient and bone structural parameters determined with CECT showed significant (p<0.05) difference between the repair and adjacent intact tissue. Contrast agent diffusion coefficient correlated with the moduli of the non-fibrillar matrix (R=-0.662, p=0.010), collagen fibril parallelism index (R=-0.588, p=0.035) and GAG content (R=-0.503, p=0.067). As revealed by the reference measurements, the repair cartilage was mechanically and structurally different from adjacent intact tissue (p<0.05).

	Reference (n = 7)	Repair (n = 7)
	mean ± SD	
Cartilage		
ThC (mm)	0.57 ± 0.11	1.33 ± 0.40 *
Diffusion coefficient (µm²/s)	29.3 ± 29.2	107.9 ± 61.4 *
Subchondral bone		
Bone volume fraction (%)	87.2 ± 8.05	67.7 ± 16.1 *
Bone surface/volume ratio (1/mm)	5.12 ± 1.64	9.39 ± 3.18 *
Bone mineral density (g/cm^3)	0.84 ± 0.03	0.72 ± 0.03 *
* p < 0.05, Wilcoxon signed rank test		

CONCLUSION: CECT enabled simultaneous quantitative evaluation of subchondral bone and identification of cartilage repair tissue. CECT distinguished quantitatively the repair tissue with inferior quality from the adjacent intact tissue. As a technique capable of simultaneous imaging of cartilage and determination of subchondral bone mineral density and microstructure, CECT could have clinical value.

SPONSOR: Sigrid Jusélius Foundation, Finnish Cultural Foundation North Savo Regional Fund, Kuopio University Hospital (EVO 5041715)
DICLOSURE STATEMENT: None
ACKNOWLEDGMENT: We thank Alpi Linjama for conducting the biomechanical measurements.
CORRESPONDENCE ADDRESS: katariina.kulmala@uef.fi

CT ARTHROGRAPHY TO MEASURE CARTILAGE QUALITY: INFLUENCE OF SULPHATED GLYCOSAMINOGLYCAN CONTENT AND STRUCTURAL COMPOSITION OF EXTRACELLULAR MATRIX ON CONTRAST AGENT DIFFUSION INTO CARTILAGE

*,**van Tiel J., **Siebelt M., **Waarsing J.H., *van Straten M., **Verhaar J.A.N., *Krestin G.P., **,***Weinans H., *Oei E.H.G.

*Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands
**Department of Orthopedic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands
***Department of Biomechanical Engineering, Delft University of Technology, Delft, The Netherlands

INTRODUCTION: Novel imaging techniques which measure cartilage quality in terms of sulphated glycosaminoglycan (sGAG) content are valuable in OA research. An example of such an imaging technique is *in vivo* μCT arthrography in small animals. In humans, CT arthrography (CTa) is an established technique for imaging of knee abnormalities. However, it is usually applied for detection of morphologic derangements and not for the assessment of cartilage quality.

OBJECTIVE: To assess the potential of CTa to evaluate cartilage quality in terms of sGAG content and structural composition of the extracellular matrix (ECM).

METHODS: Eleven human cadaveric knee joints were scanned on a second generation dual source spiral CT scanner before and after intra-articular injection of a negatively charged contrast agent. Mean X-ray attenuation values of both scans were calculated in seven regions of interest (ROIs) of the cartilage (weight-bearing areas of the femoral condyles and tibial plateaus, non weight-bearing areas of the femoral condyles and the mid-portion of the patella). Next, all ROIs were rescanned with contrast-enhanced μCT (CEμCT), which served as reference standard because it accurately measures sGAG content and hence quality of cartilage. Correlation between mean X-ray attenuation values of CTa and CEμCT was analyzed with linear regression. Additionally, residual values from the linear fit between unenhanced CT and CEμCT were used as a covariate measure to identify the influence of structural composition of cartilage ECM, i.e. without influence of sGAG, on contrast diffusion into cartilage.

RESULTS: Mean X-ray attenuation of cartilage was significantly higher for CTa compared to unenhanced CT in all ROIs. Furthermore, CTa attenuation values correlated excellently with reference CEμCT values representing sGAG content of cartilage ($R=0.86$; $R^2=0.73$; $p<0.0001$). When taking into account structural composition of cartilage EMC, this correlation improved substantially ($R=0.95$; $R^2= 0.90$; $p<0.0001$).

CONCLUSION: Contrast diffusion into articular cartilage detected with CTa correlates excellently with sulphated glycosaminoglycan content and to a lesser extent with structural composition of cartilage ECM. Therefore, CTa may be clinically applicable to quantitatively measure the quality of articular cartilage.

SPONSOR: Dutch Arthritis Association (LLP 11) and the Smart Mix Program of the Netherlands Ministry of Economic Affairs and the Netherlands Ministry of Education, Culture and Science
DICLOSURE STATEMENT: All authors indicate that they have nothing to disclose
ACKNOWLEDGMENT: Ronald Booij and Marcel Dijkshoorn are to be thanked for their technical contribution during acquisition of the CT scans
CORRESPONDENCE ADDRESS: j.vantiel@erasmusmc.nl

A QUANTITATIVE METHOD FOR EVALUATING CARTILAGE DEFECT REPAIR: INTRA- AND INTER-READER REPRODUCIBILITY

*,***Tamez-Peña JG, **Trattnig S, ***Totterman S,**Szomolanyi P, *****Shive MS,****Buschmann MD *****Restrepo A.

*Tec de Monterrey, Escuela de Medicina, Monterrey, NL, México; **Medical University of Vienna, Vienna, Austria; ***Qmetrics Technologies, Rochester, NY, USA; ****Ecole Polytechnique, Montreal, Canada, *****Piramal Healthcare (Canada) Ltd.

INTRODUCTION: MRI evaluation of therapies for treating chondral and osteochondral defects has been largely performed by semi-quantitative evaluation of established criteria such as MOCART or WORMS. These methods depend on the expertise and consistency of the radiologists, and variation introduced by subjectivity or inconsistency in evaluation among radiologists reduces the precision of the analysis and presents challenges for applying these methods in clinical studies. To improve the consistency of evaluation, a quantitative approach to assess defect size, degree of repair and quality of repair was developed.

OBJECTIVE: 1) The main purpose of this study was to estimate the intra- and inter- reader precision of the method by and among expert radiologists and 2) To estimate systematic differences among expert radiologists.

METHODS: MRI data obtained during an international, multicenter, randomized clinical trial for cartilage repair (Piramal Healthcare (Canada)) were used for this study. Eighty subjects with Grade 3 or 4 cartilage defects were randomized (1:1) to either micro-fracture or microfracture augmented with the medical device, BST-CarGel. BST-CarGel is a physiological solution of the polyglucosamine, chitosan, which is mixed with freshly drawn autologous and applied to the microfractured lesion to stimulate repair arising from subchondral bone. The standardized trial MRI protocols included GRE, SPGR, Dual Echo Spin Echo and 3D dGEMRIC MRI images of the affected knee taken pre-operatively, at 1 and 12 months post-operative. Ten blinded cases were randomly selected, duplicated and assigned random identifiers to create a set of 20 cases to be analyzed by two expert radiologists. Using the pre-registered SPGR/GRE series, the radiologists manually traced the chondral or osteochondral defect boundaries on the one month post-operative scan. The structural segmentation was then co-registered with follow-up timepoints and the tissue boundaries adjusted by the expert analysts as deemed necessary. Quantitative measurements of defect area at the articular surface, defect volume, fill % and T1/T2 relaxation time of repair tissue were automatically calculated from the edited follow-up segmentations. The cubic roots of the volume measurements and the square roots of the area measurements were computed to linearize the measurements and to mitigate error heteroscedasticity. The inter-reader and intra-reader precision was calculated by comparing the duplicated subject's measurements and by comparing each analyst's set of measurements. Defect surface area, volume, fill % and T2 were compared using a Bland-Altman analysis. The RMS and Pearson Correlations of the repeated measurements were computed. Differences were evaluated using paired t-test.

RESULTS: The intra-and inter-reader analysis indicated that both observers were highly correlated with Pearson correlation coefficients ranging from 0.85, for fill%, to 0.99 for volume measurements. On the other hand, there were systematic differences between the two radiologists when measuring defect area. Those differences were on the order of 1.4 mm ($p<0.001$). These systematic differences in defect interpretation did not affect the estimation of fill%. On average, the two radiologists agreed with near zero systematic differences in fill% estimation ($p=0.83$). The estimated T2 values resulting from both analysts also agreed and no systematic differences between observers were statistically detected. T1 measurements, on the other hand, showed high correlation (Pearson $r=0.98$) and systematic differences between observers on the order of 15.1 ms ($p=0.013$).

CONCLUSION: The analyses of intra- and inter-reader results indicate that the quantitative MRI method used in this trial is capable of providing precise and consistent results independent of the particular radiologists. The design of future cartilage repair trials using quantitative MRI imaging may benefit from this information in planning imaging sequence parameters. Overall, a quantitative approach to evaluating cartilage repair therapies may provide improved objectivity and precision compared to more subjective methods.

SPONSOR: Piramal Healthcare (Canada) Ltd,.
DICLOSURE STATEMENT: Tamez-Peña, and Totterman have ownership interest in Qmetrics Technologies. Trattnig provides consulting services to Piramal.
ACKNOWLEDGMENT: Patricia González and Ed Schreyer to be thanked for technical assistance.
CORRESPONDENCE ADDRESS: jose.tamezpena@itesm.mx

T2 MRI OF REPAIR CARTILAGE REFLECTS BOTH TISSUE QUALITY AND QUANTITY

Shive, M.S.*, Buschmann, M.B.**, Yaroshinsky, A.***, Tamez-Pena, J.****, Schreyer, E*****, Totterman, S.*****, Trattnig, S.******, Stanish, W.D.*******, Restrepo, A.*

*Piramal Healthcare, Laval, Canada,**Ecole Polytechnique, Montreal, Canada,***San Andreas, USA, ****Tecnologico de Monterrey, Escuela de Medicina, Monterrey, Mexico; *****Qmetrics, Rochester, NY ******Medical University of Vienna, Vienna, Austria; *******Dalhousie University, Halifax, Canada

INTRODUCTION: It is believed that improved repair cartilage structure will lead to longer durability and sustained clinical benefit. Since the collagen network is the primary determinant of cartilage mechanical properties and durability, its architecture represents an important potential biomarker of structural quality of repair tissue and thus a valuable endpoint in cartilage repair studies. Microscopic methods, including polarized light microscopy, have been previously used in determining the collagen organization in cartilage histological sections; the need for surgical biopsies complicates its use at a large clinical scale. Recently, T2 MRI has been used to assess the quality of repair cartilage since it reflects cartilage collagen macromolecular concentration, orientation and hydration, and permits non-invasive study of cartilage repair. Nonetheless T2-based parameters have yet to be firmly correlated to established structural assessment techniques (MRI or microscopy-based) in the context of cartilage repair studies.
OBJECTIVE: To determine which characteristics of cartilage repair tissue determined by microscopic methods correlate with T2 MRI.
METHODS: MRI scans (n=78) and repair tissue biopsies (n=38) were obtained during an international, multicenter, randomized clinical trial for cartilage repair (Piramal Healthcare (Canada)). Eighty subjects with Grade 3 or 4 condylar cartilage defects were randomized (1:1) to either microfracture or microfracture augmented with BST-CarGel, a chitosan-based medical device that is mixed with autologous blood prior to application. The standardized MRI protocols included GRE, SPGR, and Dual Echo Spin Echo MRI images of the index knee taken pre-operatively, and at 1 and 12 months postoperative. Specific quantitative MRI analyses were applied to native cartilage, baseline lesions and new repair tissue to provide several parameters reflecting quantity and quality of repair tissue including % Fill and T2. Average T2 values were calculated from the entire 3D repair tissue volume. Elective osteochondral biopsies were arthroscopically obtained from the central region of treated lesions at 13 months postoperative. Histological sections underwent scoring using a published PLM score that grades collagen architecture and zonal stratification. Additional histological analyses were carried out using ICRS I & II scores and immunohistochemical staining for collagen type I and II. Pre-specified linear and non-linear statistical models were evaluated to establish associations of T2 with histological and MRI structural data.
RESULTS: Average T2 was 77.1±29.0 ms for repair tissue, and 50.3±7.6 ms for native cartilage. Average T2 correlated moderately with PLM score and %Fill individually (r=0.42, 0.51 respectively). Furthermore, ANCOVA assessed the association of T2 with both PLM and %Fill. Both were found to be significant co-factors in explaining the T2 response (p=0.013 and p=0.003 respectively), revealing a multiple correlation coefficient of R=0.62. Importantly, this correlation was confirmed to be independent of treatment.
CONCLUSIONS: Average T2 MRI is an intrinsic multifactorial measure of repair tissue quality which may depend on both repair tissue quality (collagen organization as assessed by PLM) and quantity (%Fill).

SPONSOR: Piramal Healthcare (Canada), Laval, Canada
DICLOSURE STATEMENT: Shive, Buschmann, Yaroshinsky and Trattnig are consultants to Sponsor. Schreyer, Tamez and Totterman have ownership interest in Qmetrics.
ACKNOWLEDGMENTS: ***Biomaterials and Cartilage Laboratory, Montreal, QC***
CORRESPONDENCE ADDRESS: Alberto Restrepo, alberto.restrepo@piramal.com, 1-450-686-2437x303

MODULE 3: 5 PRESENTATIONS SELECTED FROM ABSTRACTS (OSTEOARTHRITIS INITIATIVE)

June 9th, 2011: 9.00 – 10.15

Chair: Michael Nevitt, University of California, San Francisco, USA
(10 min presentation + 5 min discussion)

9.00-9.15	[1,2]Frobell R.B., [3]Nevitt M., [3]McCulloch C., [4]Hochberg M., [5]Duryea J., [2,6]Wirth W., [7]Eaton C., [8]McAlindon T., [3]Maeda J., [3]Lynch J., [2,6]Eckstein F., for the OAI investigators [1]Lund University, Sweden; [2]Paracelsus Medical University, Austria; [3]UCSF & OAI Coordinating Center, CA; [4]University of Maryland, MD; [5]Harvard Medical School, MA; [6]Chondrometrics GmbH, Germany; [7] Memorial Hospital of Rhode Island & Brown Medical School, RI; [8]Tufts University, MA MRI-BASED CARTILAGE THICKNESS LOSS AND JOINT SPACE NARROWING IN AN OAI CORE PROGRESSION SAMPLE, AND THEIR RELATIONSHIP WITH AGE, SEX, AND BMI.
9.15-9.30	*,**Tamez-Peña JG, **González P, **Schreyer E, and **Totterman S. * Tecnológico de Monterrey; Escuela de Medicina; Monterrey, NL, México ** Qmetrics Technologies, Rochester, NY, USA SPATIO-TEMPORAL ANALYSIS OF THE SIGNIFICANT CHANGES IN CARTILAGE MORPHOLOGY: DATA FROM THE OSTEOARTHRITIS INITIATIVE
9.30-9.45	*Wirth W., **Mc Culloch C.E., **Lynch J., **Nevitt M., ***Kwoh C.K., *Maschek S., *Hudelmaier M., ****Sharma L., *Eckstein F., for the OAI investigators * Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany; ** University of California San Francisco, San Francisco, CA; *** Division of Rheum. and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA ****Division of Rheumatology, Feinberg School of Medicine at Northwestern University, IL ARE SHORT-TERM RATES OF MRI-BASED MEASURES OF KNEE CARTILAGE LOSS MARKERS OF LONG-TERM CHANGE? FOUR-YEAR DATA FROM THE OA INITIATIVE
9.45-10.00	*Lammentausta E., *Herronen A., *Ojala R.O. and **Nieminen M.T. *Oulu University Hospital, Oulu, Finland **Oulu University Hospital and University of Oulu, Oulu, Finland T2 REVEALS EARLY CARTILAGE CHANGES DURING TWO YEARS FOLLOW-UP IN SUBJECTS AT RISK FOR OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE
10.00-10.15	*Buck R.J., **Nevitt M, ***Wirth W, ***Eckstein, F – for the OAI investigators * StatAnswers Consulting LLC, Minneapolis, MN; ** University of California and OA Initiative Coordinating Center, San Francisco, CA; *** Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany CORRELATION OF KNEE CARTILAGE THICKNESS CHANGE AT 1 YEAR AND CLINCAL OUTCOME CHANGES AT 3 YEARS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

MRI-BASED CARTILAGE THICKNESS LOSS AND JOINT SPACE NARROWING IN AN OAI CORE PROGRESSION SAMPLE, AND THEIR RELATIONSHIP WITH AGE, SEX, AND BMI.

[1,2]Frobell R.B., [3]Nevitt M., [3]McCulloch C., [4]Hochberg M., [5]Duryea J., [2,6]Wirth W., [7]Eaton C., [8]McAlindon T., [3]Maeda J., [3]Lynch J., [2,6]Eckstein F., for the OAI investigators

[1]Lund University, Sweden; [2]Paracelsus Medical University, Austria; [3]UCSF & OAI Coordinating Center, CA; [4]University of Maryland, MD; [5]Harvard Medical School, MA; [6]Chondrometrics GmbH, Germany; [7] Memorial Hospital of Rhode Island & Brown Medical School, RI; [8]Tufts University, MA

INTRODUCTION: High age, BMI, and female sex are established risk factors for the *onset* of knee OA. However, evidence to support these as risk factors for *structural progression* of knee OA is conflicting. Radiography is the accepted standard for measuring structural progression, but it is unclear whether MRI permits identification of risk factor-progression relationships with greater sensitivity than X-rays.

OBJECTIVE: 1) To determine the most sensitive measurement location in fixed flexion radiographs (JSW) and MRI (cartilage thickness; ThC), over 2 years, in a core sample of the OAI progression cohort; 2) To evaluate age, sex, and BMI as independent risk factors of structural progression at these locations.

METHOD: One knee in each of 541 (224 men) OAI participants enrolled in the progression cohort was studied (all had frequent knee pain; 249 had KL Grade 2; 292 had KL Grade 3). Change in medial femorotibial JSW was measured automatically at 7 locations (fixed distances, FD) from PA fixed flexion radiographs, and change in ThC was measured in 16 femorotibial subregions after manually segmenting sagittal DESS images. The standardized response means (SRM) were used to determine the most sensitive measurement locations. Results were compared between men and women, and between the highest vs. lowest tertiles of age and BMI using t-tests, and general linear models with adjustment for the other variables. Beta coefficients (with 95% CI) and standardized beta (Z-scores) are presented.

RESULTS: In this OAI core sample, the FD 0.225 JSW location was the most sensitive X-ray measure (SRM = 0.40), and the central medial femoro-tibial compartment subregion (cMFTC.ThC) the most sensitive MRI measure for structural progression over two years (SRM = 0.48). Age tertiles studied were 66-79 yrs, vs. 45-56 yrs, and BMI tertiles 31.8-47.7 kg/m^2 vs.18.2-27.7. Age, sex, and BMI explained only 2.6% of the variation in structural progression (R^2 of adjusted model) in X-ray and 3.9% in MRI. With X-ray, BMI (β=-0.198mm, 95% CI -0.333, -0.064, standard β=-0.308) had a significant relationship with progression (Fig. 1), but neither age (adjusted p=0.587) nor sex (p=0.099) did. With MRI, high BMI (β= -0.092mm, 95% CI -0.161, -0.023, standard β=-0.278), high age (β= -0.090mm, 95% CI -0.159, -0.021, standard β=-0.270) and male sex (β= -0.099mm, 95% CI -0.156, -0.042, standard β=-0.299) were all identified as significant risk factors for structural progression (Fig. 1).

CONCLUSION: Measurement locations in the central aspect of the medial femorotibial compartment were most sensitive to structural progression for both imaging methodologies, with MRI providing slightly greater sensitivity to change than fixed flexion radiographs over 2 years. Age, sex, and BMI explained <4% of the variation in structural progression with both methodologies. All were significantly associated with progression as measured with MRI (where men surprisingly showed greater progression than women) while only BMI was associated with progression as measured by X-ray. Our data suggest that MRI may be more sensitive for identifying progression of medial compartment knee OA than plain radiographs.

SPONSOR: Image acquisition: The OAI; Image analysis: NIH vendor contract N01-AR-2-2258 (UCSF)
DISCLOSURE STATEMENT: see affiliation.
CORRESPONDENCE ADDRESS: richard.frobell@med.lu.se

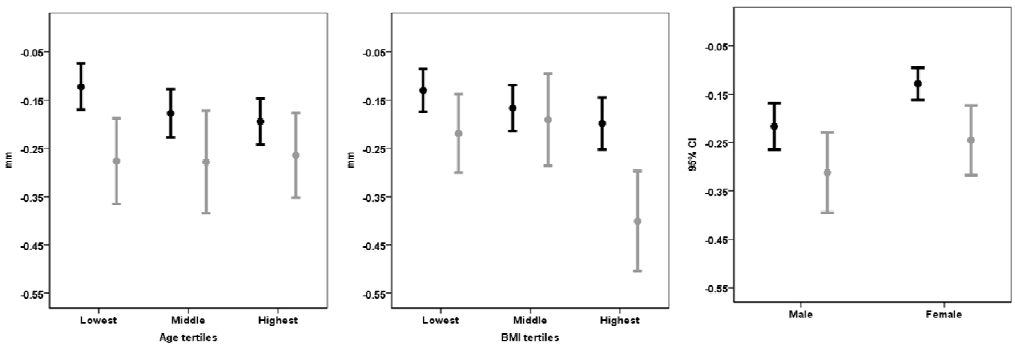

Figure 1. Mean change (mm) of the most sensitive X-ray location (grey) and MRI (black) for tertiles of age (left) and BMI tertiles (middle) and sex (right). Error bars display the 95% confidence intervals.

SPATIO-TEMPORAL ANALYSIS OF THE SIGNIFICANT CHANGES IN CARTILAGE MORPHOLOGY: DATA FROM THE OSTEOARTHRITIS INITIATIVE

*,**Tamez-Peña JG, **González P, **Schreyer E, and **Totterman S.

* Tecnológico de Monterrey; Escuela de Medicina; Monterrey, NL, México
** Qmetrics Technologies, Rochester, NY, USA

INTRODUCTION: Changes in cartilage morphology are important features associated with the progression of OA. Average cartilage thickness and cartilage volume are some the most common structural features that have been used to monitor the changes in cartilage morphology, but those measurements have shown small and heterogeneous responsiveness. To better understand the disease heterogeneity we applied an advanced image analysis methodology to detect, to map and to study the spatial location and time evolution of the formation of significant changes in cartilage thickness.

OBJECTIVE: 1) To study the spatio-temporal presentation of the changes in cartilage morphology using significant change detection from standardized thickness maps. 2) To report the rate of progression of significant changes in cartilage thickness.

METHODS: OAI MRI data sets releases: 0.3C.2 (Baseline), 1.C.2 (12 month) and 3.C.1 (24 month) were used in this study. The most diseased knee per subject and with the three complete MRI observations were selected and analyzed (138 subjects, 3 Timepoints). The baseline-image analysis data extracted from the OAI site was used to stratify knees into three groups: Non-denuded: Knees without full cartilage thickness defects (n=52)
Low-Denuded: Subjects with small full thickness defects (n=43). Top-Denuded: Subjects with large full thickness defects (n=43). All the 414 DESS MRI images were independently segmented using a fully automated multi-atlas segmentation algorithm that created atlas-referenced thickness maps of the tibia and the femur cartilage. The segmentation quality was visually inspected. The Pilot OAI scan-rescan data was used to estimate the paired-measurement noise of the method in creating atlas-referenced thickness maps. The 12-month and 24-month cartilage thickness maps were compared to the baseline observation and standardized thickness change maps were created by subtracting the two time points and then dividing the point-by-point changes by the standard deviation of the paired-measurement noise. The standardized thickness points with z-values lower than 1.96 ($p<0.05$) were marked and counted as points with significant cartilage loss. The proportion of marked points was reported as the percentage of significant cartilage loss at the femur cartilage and the tibia cartilage. Finally, all the 12-month and 24-month change maps were aggregated into a single standardized change map. The significant cartilage loss maps were aggregated into a single heat-map that showed the prevalence and localization of the significant changes in cartilage thickness. The difference between 24-month changes and 12-month changes were used to estimate the standardized response of the mean (SRM) of the methodology.

RESULTS: One knee observation was dropped due to poor segmentation quality. The heat maps showed different patterns of loss among the no-denuded, the low-denuded and the high-denuded groups. The entire femur showed an average significant 12-month loss on 6.9% of its surface. The loss progressed towards an 8.9% loss with a SRM of 0.48 (0.31 to 0.65). The tibia progressed from a 7.0% loss to an 8.6% loss with a SRM of 0.25 (0.08 to 0.42). The knees with no-denuded areas showed cartilage loss at 5.4% of their femoral cartilage and progressed towards a 7.8% loss with a SRM of 0.73 (0.45 to 1.01) and 74.5% (60.1% to 85.2%) of the knees worsening the affected area. The tibia progressed from a 5.9% loss towards a 7.9% loss with a SRM of 0.39 (0.11 to 0.67). Subjects with small denuded areas showed a 12-month, 24-month loss of 7.1%, 8.6% respectively with a 0.36 SRM in the entire femur. Subjects with large denuded areas showed a 12-month, 24-month loss of 9.1%, 11.0% respectively with a 0.36 SRM.

CONCLUSION: The image analysis technology used in this study provided quantitative and statistical maps that showed the prevalence and location of changes in cartilage thickness. The spatial localization and the prevalence of those changes were different in the different OA groups studied in this work, indicating the degree of heterogeneity of the disease presentation and progression. Furthermore, the methodology showed that early stage OA (Bone free of denuded areas) is very dynamic with cartilage loss progressing at the annual rate of 2.2% ($0.45<SRM<1.01$). Future work will compare the rate and localization of the changes among the non-exposed OAI cohort, a symptomatic worsening OAI group, and an age matched symptom stable OAI group.

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ACKNOWLEDGMENT: OAI. Santiago González to be thanked for technical assistance.
CORRESPONDENCE ADDRESS: jose.tamezpena@itesm.mx

ARE SHORT-TERM RATES OF MRI-BASED MEASURES OF KNEE CARTILAGE LOSS MARKERS OF LONG-TERM CHANGE? FOUR-YEAR DATA FROM THE OA INITIATIVE

*Wirth W., **Mc Culloch C.E., **Lynch J., **Nevitt M., ***Kwoh C.K., *Maschek S., *Hudelmaier M., ****Sharma L., *Eckstein F., for the OAI investigators

* Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany;
** University of California San Francisco, San Francisco, CA;
*** Division of Rheum. and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA
****Division of Rheumatology, Feinberg School of Medicine at Northwestern University, IL

INTRODUCTION: Most MRI studies on structural progression of knee OA have relied on relatively short observation periods (e.g. 1 year). Although the rate of change is expected to increase linearly with the length of the observation period, it is currently unclear to what extent the sensitivity to change increases, and whether short-term cartilage loss predicts cartilage loss over longer observation periods in individual knees. It is important to note that an analysis of different observations periods should not rely on common baseline or intermediate time points, because precision errors occurring at these time points distort association among the observed correlations (in positive direction when using a common timepoint [e.g. baseline], and in negative direction when using a common intermediate time point).

OBJECTIVES: To determine 1) the mean change and the sensitivity to change of cartilage thickness (ThCtAB) loss over one-, two-, three-, and four years; 2) the consistency of the subregion with the greatest rate of change in each knee over different follow-up periods; 3) the relationship between short- and long-term changes and specifically whether short-term changes predict loss over longer periods

METHODS: Clinical and 3T sagittal DESS MRI data of 331 OAI participants (one knee each, 159 KLG2; 172 KLG3) were analyzed. Images were grouped by knee, but blinded to acquisition order for manual segmentation of femorotibial cartilage at baseline (BL), year one (Y1), year two (Y2), and year four (Y4). Mean change (MC) in ThCtAB and the standardized response mean (SRM=MC/SD of change) were computed over 1-year (BL→Y1, Y1→Y2), 2-year (BL→Y2, Y2→Y4), 3-year (Y1→Y4) and 4-year time periods (BL→Y4). The ordered values (OV) approach was applied to determine the subregion showing the highest rate of change (OV1). Short- and long-term changes without common baseline/intermediate time points (Y1→Y2 vs. BL→Y4 / BL→Y1 vs. Y2→Y4) were compared using Spearman rank correlation coefficients as well as the smallest detectable change (SDC) approach, classifying knees as (non-) progressors. The receiver operating characteristics (ROC) curve was determined using a fixed long-term (226µm) and a variable short-term threshold and the area under the ROC curve was calculated to assess the predictive value of short-term loss for long-term changes.

RESULTS: In the total femorotibial joint (FTJ), the MC% was -1.1%/-0.8% over one (BL→Y1/ Y1→Y2), -1.9%/-2.4% over two (BL→Y2/ Y2→Y4), -3.2% over three (Y1→Y4), and -4.3% over four years (BL→Y4). The SRMs were -0.38/-0.27 over one, -0.52/-0.51 over two, -0.58 over three, and -0.71 over four years. The location of OV 1 was consistent between short- and long-term changes in 23%/14% of the knees (Y1→Y2 vs BL→Y4 / BL→Y1 vs Y2→Y4). The correlation between short- and long-term change was r=0.35 (Y1→Y2 vs. BL→Y4) and r=0.16 (BL→Y1 vs. Y2→Y4). Of 62 knees classified as progressors by SDC at Y1→Y2, 47 (76%) also showed progression at BL→Y4, while 39 (49%) of the 80 knees progressing between BL→Y1 also progressed between Y2→Y4. The area under the ROC curve was 0.65 for Y1→Y2 vs. BL→Y4 and 0.64 for BL →Y1 vs. Y2→Y4.

CONCLUSION: On a cohort-level, the rate of change in ThCtAB increased almost linearly with the length of the observation period, while the SRM increased from -0.38/-0.27 to -0.71 for a one- vs. four year observation period. When not including a common time points in the analysis, correlations of short- and long-term changes were weak to moderate. The application of the SDC approach showed a moderate consistency between the knees identified as progressors over short- and long-term periods. Longer observation periods may therefore be preferable to achieve robust results in individual knees.

SPONSOR: Image acquisition: Osteoarthritis Initiative; Image analysis: NIH vendor contract N01-AR-2-2258 (UCSF) and OAI ancillary study R01 AR52918 (Northwestern University)
DISCLOSURE STATEMENT: see affiliation.
CORRESPONDENCE ADDRESS: wolfgang.wirth@pmu.ac.at

T2 REVEALS EARLY CARTILAGE CHANGES DURING TWO YEARS FOLLOW-UP IN SUBJECTS AT RISK FOR OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE.

*Lammentausta E., *Herronen A., *Ojala R.O. and **Nieminen M.T.

*Oulu University Hospital, Oulu, Finland
**Oulu University Hospital and University of Oulu, Oulu, Finland

INTRODUCTION:
Several factors increase the risk of OA, including age, overweight, knee injury, race, sex, and genome [1]. Currently OA is diagnosed based on clinical symptoms and JSN. Unfortunately, at the point of detectable JSN, the development of the disease is already at an advanced, irreversible stage. T2 provides indirect information about the integrity of the collagen network and water content of cartilage, and an elevation of T2 has been associated with cartilage degeneration [2, 3].

OBJECTIVE:
To investigate the longitudinal change in T2 in femoral cartilage of subjects without radiographic changes but at risk for OA.

METHODS:
From the OAI incidence cohort, caucasian subjects with available MRI data were selected. This totaled to forty-one subjects (17 male, 24 female; mean age 58±9 years; body mass index (BMI) 25.7±3.7 kg/m^2). By definition, the subjects of the incidence cohort did not have radiographic changes (KLG=0) or regular knee pain at baseline, and had one or more of the risk factors for knee OA defined at the OAI protocol [4]. KLG was confirmed to remain zero at all time points, leading to the exclusion of two subjects. T2 measurements were conducted according to the OAI protocol [4] at baseline, 1-year follow-up and 2-years follow-up. T2 maps were computed and further analyzed with an in-house Matlab application. Three regions from the primary weight-bearing cartilage and surrounding areas at the slice covering the center of each condyle of the right knee were manually segmented. The regions were further divided into deep and superficial ROIs, and mean values for each ROI were calculated. The non-parametric Wilcoxon-test was used to compare T2 values at different time points.

RESULTS:
Compared to baseline, a statistically significant elongation of T2 was observed at 1-year and 2-year follow-up in both lateral and medial condyles. In particular, T2 was elevated at the primary weight-bearing cartilage (pCF, Figure 1). An increasing trend of elevated T2 was observed at most ROIs, although the change was not statistically significant at all ROIs. The most pronounced changes occurred from baseline to 1-year follow-up.

CONCLUSION:
For the first time, the present results show an increase in T2 in subjects without radiographic joint changes but with known risks for OA development. Particularly in the primary weight-bearing region of the femur, T2 increased significantly in all ROIs. The present results suggest that T2 can serve as a sensitive tool to detect early osteoarthritic cartilage changes that occur prior to the onset of the clinical symptoms. Since the KLG of study subjects remained unchanged, T2 appears more sensitive than radiography to reveal changes in cartilage status. Furthermore, T2 provides information on the biochemical status of articular cartilage while radiography or MR morphometry are merely measures of cartilage quantity. The present results are very promising in view of predicting OA in subjects at risk for the disease.

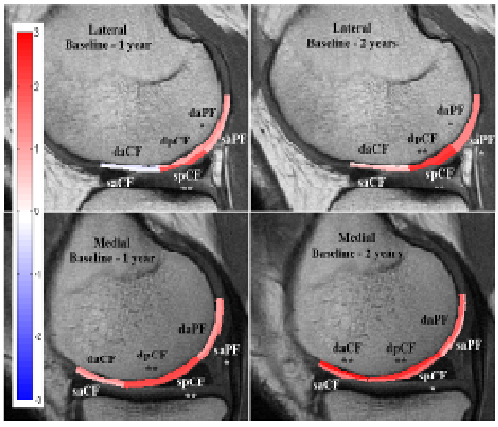

Fig.1. Change in T2 (ms) from baseline to one/two-year follow-up at various ROIs. **p<0.01, *p<0.05.

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[1] Felson DT et al. Ann Intern Med 2000; 133:635-646. [2] Nieminen MT et al. Magn Reson Med 2000;43:676.–681. [3] Fragonas E et al. Osteoarthritis Cartilage 1998;6:24-32. [4] Peterfy CG et al. Osteoarthritis Cartilage 2008;16:1433-1441.

CORRESPONDENCE ADDRESS:
eveliina.lammentausta@oulu.fi

CORRELATION OF KNEE CARTILAGE THICKNESS CHANGE AT 1 YEAR AND CLINCAL OUTCOME CHANGES AT 3 YEARS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

*Buck R.J., **Nevitt M, ***Wirth W, ***Eckstein, F – for the OAI investigators

* StatAnswers Consulting LLC, Minneapolis, MN;
** University of California and OA Initiative Coordinating Center, San Francisco, CA;
*** Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany

INTRODUCTION: An important characteristic of any biomarker is that it be able to predict future outcomes. Change in knee cartilage thickness is an important characteristic of osteoarthritis and is believed to impact clinical outcomes such as pain assessments which are key to disease management. Hence small short-term changes in knee cartilage thickness may predict changes in future clinical outcomes. The OAI study provides an opportunity to examine the relationship between short (1 year) changes in knee cartilage thickness and longer (3 years) term changes in clinical outcomes.

OBJECTIVE: To examine the association between changes in subregion cartilage knee thickness (ΔThCtAB) at one year and change in different clinical outcomes (ΔOutcome) at three years.

METHODS: Measurements of change in mean subregional cartilage thickness (ΔThCtAB) over 12 months were available from coronal FLASH MR images for one knee of 795 OAI subjects, 185 men and 242 women from the Progression cohort and 135 men and 233 women from the Incidence cohort. The Progression cohort was split to consider signal (osteophytes and pain present) and non-signal knees (either osteophytes or pain not present) separately. See Table for sample sizes. Baseline and follow-up scans were read in pairs with readers blinded to visit. Change in ThCtAB was measured in 16 femorotibial subregions [2]. Linear models considering all subregion ΔThCtAB were constructed to predict change in clinical outcomes over 3 years (ΔOutcome). Clinical outcomes examined were WOMAC (Total, Pain, Stiffness, Disability) or KOOS (Pain, Symptom) individual knee scores. Ordered values (OV) of ΔThCtAB were also considered as predictors [1]. Ordered values were considered for medial and lateral subregions separately and combined (All). Coefficient of determination, R^2, was used to measure association between multivariate Predictors and ΔOutcomes.

RESULTS: The (min, mean, max) of coefficients of determination, R^2, across clinical outcomes for different cohorts and predictors based on stepwise regression are shown. R^2 was relatively consistent across clinical outcomes. R^2 was typically low (< 0.07) when predicting ΔOutcome using all subjects, Incidence or Progression cohorts. R^2 increased when signal and non-signal knees of Progression cohort are considered separately, particularly for non-signal knee with OV as predictors ($R^2 > 0.09$).

Cohort	N	ThCtAB	med + lat OV	All OV
All	795	(0.01,0.02,0.04)	(0.02,0.02,0.04)	(0.01,0.02,0.03)
Incidence	368	(0.00,0.01,0.02)	(0.02,0.05,0.13)	(0.03,0.05,0.08)
Progression	427	(0.03,0.05,0.07)	(0.04,0.05,0.06)	(0.02,0.04,0.07)
Signal	317	(0.05,0.08,0.12)	(0.05,0.07,0.09)	(0.05,0.07,0.10)
No Signal	110	(0.03,0.07,0.11)	(0.13,0.20,0.25)	(0.09,0.15,0.29)

Of the 150 correlations examined 83% had p-values < 0.05, with most (18 of 26) non-significant correlations observed with All subjects or Incidence cohort.

CONCLUSION: The The use of ordered values (OV) as predictors produced larger R^2 than use of subregion ΔThCtAB Results. Non-signal knees of Progression cohort had larger R^2 than signal knees.

REFERENCES: [1] Buck RJ, et al (2009) : ACR, 61:917-924
[2] Wirth W, Eckstein F (2008): IEEE Trans.Med.Imaging. 27: 737-44

SPONSOR: Image acquisition: the OAI; Image analysis: a consortium of Pfizer, EliLilly, Merck- Serono, Glaxo Smith Kline, UCSF, Wyeth, Centocor, Novartis; Statstical Analysis. MerckSerono
DISCLOSURE STATEMENT: see affiliations.
ACKNOWLEDGMENT: The OAI investigators and technicians; the Chondrometrics readers
CORRESPONDENCE ADDRESS: robert.j.buck@gmail.com

MODULE 5: YOUNG INVESTIGATOR SESSION: 4 TOP PRESENTATIONS OF YOUNG INVESTIGATORS SELECTED FROM ABSTRACTS.

June 9th, 2011: 13.30 – 14.30

Chair: Felix Eckstein, Paracelsus Medical University, Salzburg, Austria
(10 min presentation + 5 min discussion)

13.30-13.45	***Donoghue C.R., **Rao, A., ***Bull, A.M.J., *Rueckert, D.** * Department of Computing, Imperial College London, UK, ** GlaxoSmithKline Research and Development, Clinical Imaging Centre, London, UK *** Department of Bioengineering, Imperial College, London, UK **AUTOMATICALLY GENERATED NOVEL DIAGNOSTIC IMAGING BIOMARKERS WITH DATA FROM THE OAI**
13.45-14.00	***, **Wiegant K, **Marijnissen A.C.A, *Intema F, *Roermund P.M, ***Eckstein F, ***Cotofana S, **Mastbergen S.C, **Lafeber F.P.J.G.** UMC Utrecht, *dept. of Orthopedics, and **dept. of Rheumatology, the Netherlands; *** Paracelsus Medical University, Institute of Anatomy, Salzburg, Austria **STRUCTURAL CARTILAGE PARAMETERS ON MRI AND X-RAY IMPROVE AFTER TREATMENT WITH KNEE JOINT DISTRACTION; A 2 YEAR FOLLOW-UP.**
14.00-14.15	***Haugen IK, *Bøyesen P, *Slatkowsky-Christensen B, *Sesseng S, *** Bijsterbosch J, * ***van der Heijde D, *Kvien TK** * Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway ** Dept. of Radiology, Diakonhjemmet Hospital, Oslo, Norway *** Dept. of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands **MRI IS MORE SENSITIVE THAN CONVENTIONAL RADIOGRAPHY IN DETECTION OF EROSIONS IN HAND OSTEOARTHRITIS (OA)**
14.15-14.30	**Laslett L.L., Doré D.A., Quinn S.J., Winzenberg T.M., Boon P., Jones, G.** Menzies Research Institute Tasmania, University of Tasmania, AUSTRALIA. **A TWELVE MONTH RANDOMISED CONTROLLED TRIAL OF ZOLEDRONIC ACID FOR KNEE PAIN AND SUBCHONDRAL BONE MARROW LESIONS.**

AUTOMATICALLY GENERATED NOVEL DIAGNOSTIC IMAGING BIOMARKERS WITH DATA FROM THE OAI

*Donoghue C.R., **Rao, A., ***Bull, A.M.J., *Rueckert, D.

* Department of Computing, Imperial College London, UK,
** GlaxoSmithKline Research and Development, Clinical Imaging Centre, London, UK
*** Department of Bioengineering, Imperial College, London, UK

INTRODUCTION: We present novel automatically generated imaging biomarkers which are designed to diagnose OA status using a technique called manifold learning. We validate our biomarkers using KLG. Current state of the art MRI biomarkers typically require an accurate segmentation of the articular cartilage and then morphemetric measurements are extracted, such as thickness or volume. Segmentations can be time-consuming to acquire manually and can lack in accuracy when performed automatically. We propose an alternative methodology to extract meaningful biomarkers from MRI.

OBJECTIVE: To automatically generate novel diagnostic regional biomarkers from MRI with the aim to demonstrate their ability to predict KLG as provided by OAI.

METHODS: We propose a data-driven approach which aims to model a large population of knee SAG 3D DESS MRI (n=918) provided by OAI . This is validated using KLG for which there are 181 corresponding values. Initially we register or align our sample of images to single selected subject. The articular cartilage of this selected subject is segmented, the segmentation is dilated so that it can be used as a rough ROI for every image in the sample. We then use an entropy based similarity measure to compute how "similar" each pair of images are, this allows us to represent the population as a complex network or web in a high dimensional space. Typically biological data forms strong non-linear patterns and thus is thought to lie on or near a surface (or manifold) within this high dimensional space. We use machine learning techniques to learn the the structure of the manifold of knee MRI images. Specifically, we compute a laplacian eigenmap embedding which reduces the dimensionality of the data non-linearly. The co-ordinates of images in the manifold embedding tells us where the subject lies within the population of images and these co-ordinates are proposed as our novel biomarkers and are generated fully automatically. These biomarkers or co-ordinates of the manifold embedding can be used to predict classification of radiographic outcomes, such as KLG. We present binary classification results using LDA. A separate manifold embedding is computed for each of the 16 ROI described by Wirth et al, 2008 (TMI) and 9 further composites of those ROIs. The biomarkers from each of these regional manifolds can be consolidated in to a single manifold to enable a global classification of the entire knee in terms of OA status

RESULTS: Typically the manifold for this application can be described using approximately 10-dimensions, however a visualisation can be constructed in 2-dimensions to show the distribution of the subjects. Each point on the scatter graph represents a subject and the colour corresponds to their KLG. Binary classification accuracy for KLG<1 is 70.2%, KLG<2 is 82.3% , KLG<3 is 88.4% and KLG<4 is 85.1%. When binary classification KLG<2 for each region was computed and ordered; it was found that the top 3 regions best able to classify OA status in descending order were; cMF, cLF and cMF combined and cLT.

CONCLUSION: These novel biomarkers are able to predict KLG automatically, despite the limitations with KLG diagnosis. Weight-bearing regions; cMF, cLF and cLT appear to provide greatest diagnostic information with the methodoloy presented.

SPONSOR: BBSRC, GSK
CORRESPONDENCE ADDRESS: cdonoghu@doc.ic.ac.uk

STRUCTURAL CARTILAGE PARAMETERS ON MRI AND X-RAY IMPROVE AFTER TREATMENT WITH KNEE JOINT DISTRACTION; A 2 YEAR FOLLOW-UP.

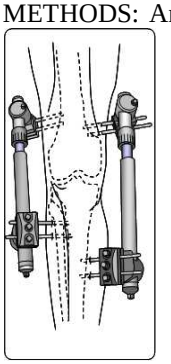
*, **Wiegant K, **Marijnissen A.C.A, *Intema F, *Roermund P.M, ***Eckstein F, ***Cotofana S, **Mastbergen S.C, **Lafeber F.P.J.G.

UMC Utrecht, *dept. of Orthopedics, and **dept. of Rheumatology, the Netherlands;
*** Paracelsus Medical University, Institute of Anatomy, Salzburg, Austria

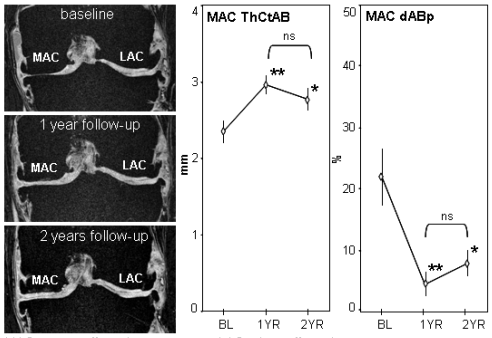
INTRODUCTION: Knee joint distraction (KJD) is an experimental treatment for severe knee osteoarthritis (OA), that temporarily unloads the femorotibial cartilage and subchondral bone by the use of an external fixation frame. This technique was previously shown to improve significantly the clinical outcome as well as cartilage status when evaluated by MRI, X-ray, and collagen type II biomarker analyses after one year follow-up. This study provides the two years data of the first study on KJD.

OBJECTIVE: Does KJD induce prolonged structural cartilage improvement, i.e. over 2 years?

METHODS: An open, uncontrolled study was performed, including 20 patients (mean age 49±6 years, 11 females) with end-stage knee OA, considered for total knee replacement (in accordance with a Kellgren and Lawrence score of > 2 and a visual analogue pain score of > 60mm). Patients were treated with KJD for 2 months. The study was approved by the medical ethical committee (METC) of the University of Utrecht. All patients gave written informed consent. Two monotubes with internal coil springs were placed bridging the knee joint and distracted for 5 mm, confirmed by X-ray. Patients were encouraged to load the knee during distraction, in order to achieve intermittent intra-articular fluid pressures. Structural outcome parameters were assessed by using quantitative cartilage MRI parameters (unloaded images), and minimal and mean joint space width (JSW) on plain standardized weight bearing X-rays. Clinical parameters were assessed by using the WOMAC (Western Ontario McMasters University index) questionnaire and by the visual analogue pain scale. Additionally, biochemical markers, for collagen type II, were evaluated.

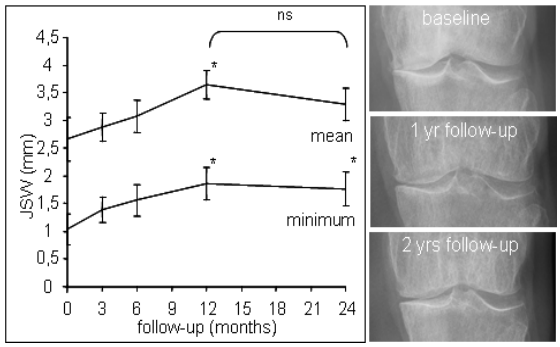


RESULTS: MRI analysis demonstrated an increase in cartilage thickness of the most affected compartment from 2.4±0.1 to 2.8±0.1 mm (p<0.05). Denuded subchondral bone areas decreased from 22±5 to 8±2 % (p<0.004). X-ray analysis depicted an increased minimum JSW from 1.0±0.3 to 1.8±0.3 mm (p<0.03). MRI and X-ray changes were moderately correlated (r=0.67 p<0.000).
From 6 months to 2 years follow-up, the average change in the ratio of PIIANP / CTXII was in favor of collgen type II synthesis (p<0.003). Clinical parameters at 2 years after KJD treatment demonstrated an increase in the total WOMAC score from 45±3.6 to 78±4.8 % (p<0.000) and a decrease in pain score from 73±2.1 to 28±6.0 mm (p<0.000).



MAC = most affected compartment; LAC = less affected compartment.

CONCLUSION: Joint distraction results in significant improvement in cartilage status in end-stage knee OA, demonstrated by quantitative MRI and X-ray. The mechanical competence of the newly formed tissue is suggested by an increase in JSW on weight bearing X-rays. The hyaline nature of the cartilage-like tissue is suggested by collagen type II biomarker analyses. Structural improvement, however, was less than that observed at 1 year follow-up[1] therefore longer follow-up has to demonstrate to what extent therapeutic effects are maintained.



REFERENCES: [1]Intema F, et al. Ann. Rheum. Dis 2011
SPONSOR: none
DISCLOSURE STATEMENT: F.E. is co-owner and CEO of Chrondrometics GmbH
CORRESPONDENCE ADDRESS: f.lafeber@umcutrecht.nl, telno: +31 88 755 8521

MRI IS MORE SENSITIVE THAN CONVENTIONAL RADIOGRAPHY IN DETECTION OF EROSIONS IN HAND OSTEOARTHRITIS (OA)

*Haugen IK, *Bøyesen P, *Slatkowsky-Christensen B, *Sesseng S, *** Bijsterbosch J, * ***van der Heijde D, *Kvien TK

* Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway
** Dept. of Radiology, Diakonhjemmet Hospital, Oslo, Norway
*** Dept. of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

INTRODUCTION: Erosive hand OA is traditionally assessed with conventional radiography (CR).

OBJECTIVE: To compare the sensitivity of MRI and CR in detection of erosions in hand OA.

METHODS: We included 106 patients from the Oslo hand OA cohort (97 women, mean (SD) age 68.9 (5.6) years) with posteroanterior CR and MRI (coronal/sagittal/axial T1w fat-suppressed images) of the dominant hand. One investigator (IKH) scored the distal (DIP) and proximal interphalangeal (PIP) joints for presence of subchondral central erosions (grade 0-1) according to the OARSI atlas. JB rescored 30 radiographs, and both intra-reader (IKH) and inter-reader (IKH, JB) reliability were very good (kappa≥0.81). One investigator (IKH) scored the same DIP/PIP joints according to the Oslo hand OA score for MRI blinded for the CR readings (1). Erosions (grade 0-3; distal/proximal) and subchondral collapse of the joint plate (grade 0-1; distal/proximal) were scored separately, in contrast to the proposed combined definition and grading. Erosion was defined as "a sharply marginated bone lesion, which is visible in 2 planes with a cortical break seen in at least one plane", while subchondral collapse was scored if there was typical depression of the joint plate ("seagull-wing"). We used the highest value of the distal and proximal score for that joint in the analyses. Intra-reader reliability (IKH) was good for both erosions (weighted kappa=0.84) and subchondral collapse (kappa=0.78). We compared the median (interquartile range; IQR) number of radiographic erosive joints and joints with MRI-defined erosions and subchondral collapse with Wilcoxon signed-rank test, and examined the agreement at individual joint level. In order to compare MRI-defined erosions against radiographic erosions, which were scored as absent/present, we dichotomised the MRI-defined erosion scores (grade 0=absent, grade 1-3=present). We calculated the percentage exact agreement (PEA) between radiographic erosions and MRI-defined erosions and between radiographic erosions and MRI-defined subchondral collapse. Agreement between the two modalities was further assessed by calculation of kappa and sensitivity/specificity of MRI with CR used as reference.

RESULTS: The median (IQR) numbers of joints with MRI-defined erosions and subchondral collapse were 4 (2-6) and 1 (0-3), respectively. The median (IQR) number of radiographic erosions was 0 (0-3). The difference between MRI-defined erosions and radiographic erosions was statistically significant ($p<0.001$), while the difference between MRI-defined subchondral collapse and radiographic erosions was non-significant for ($p=0.32$). In those with no radiographic erosions in the joints that were imaged by MRI (n=54), MRI detected ≥1 joints with erosions in 51 patients (94.4%) and ≥1 joints with subchondral collapse in 9 patients (16.7%). The sensitivity of MRI (with CR as reference) was very high for erosions, while the specificity was lower (table). The majority of MRI-defined erosions in radiographic non-erosive joints were classified as small. The agreement between MRI-defined subchondral collapse and radiographic erosions was good (table).

Table: Agreement between MRI and conventional radiography (CR).

	PEA	**Kappa**	**Sensitivity***	**Specificity***
MRI erosions vs. radiographic erosions	67.3	0.34	0.92	0.61
MRI subchondral collapse vs. radiographic erosions	91.8	0.75	0.83	0.94

PEA=percentage exact agreement, * CR used as reference

CONCLUSIONS: MRI detects more erosions than conventional radiography, suggesting that erosive OA may be more common than indicated by CR. Whether MRI-defined erosions reflect another pathology than radiographic central erosions needs to be further examined.

1. Haugen. Ann Rheum Dis 2011 [Epub ehead of print]

DISCLOSURES: No competing interests
SPONSOR: South-Eastern Norway Regional Health Authority
CORRESPONDENCE ADDRESS: haugen_ida@hotmail.com

A TWELVE MONTH RANDOMISED CONTROLLED TRIAL OF ZOLEDRONIC ACID FOR KNEE PAIN AND SUBCHONDRAL BONE MARROW LESIONS.

Laslett L.L., Doré D.A., Quinn S.J., Winzenberg T.M., Boon P., Jones, G.

Menzies Research Institute Tasmania, University of Tasmania, AUSTRALIA.

INTRODUCTION: Knee osteoarthritis (OA) is a leading cause of chronic disability. Bone marrow lesions (BMLs) are regions of increased signal intensity seen on MR images. Knee BMLs are associated with knee pain,[1-3] joint space loss,[4] cartilage defect progression,[5] cartilage volume loss and joint replacement.[5-7] This suggests that knee BMLs are a potential target for therapy. Bisphosphonates may modify the progression of BMLs as they are less common in persons taking bisphosphonates,[8] and an open label study of IV ibandronate showed resolution of hip BMLs.[9]

OBJECTIVE: To assess the efficacy of one infusion of intravenous (IV) zoledronic acid (ZA) (5mg/100ml) or placebo on BMLs, knee pain and function over twelve months.

METHODS: Single centre placebo controlled double blind randomised controlled trial of a single intravenous (IV) infusion of ZA (5mg/100ml) in adults aged 50-80 years (n=59) with knee pain (visual analogue scale (VAS) $\geq$ 40mm), clinical knee OA and a knee BML on MRI. BML area was assessed on MR images of the whole knee, using a T2-weighted fat saturation 2-dimensional (2-D) fast spin echo sequence in the sagittal plane (repetition time 3875 ms, echo time 42 ms, slice thickness 3.3 mm, interslice gap 0.3 mm, field of view 16 cm, 224 x 448–pixel matrix, number of excitations 2). The "least significant criterion" (LSC) [10] was also used to assess improvement in BMLs. Pain and function were measured using a VAS and the Knee Injury and Osteoarthritis Outcome Score (KOOS) scale (measured at baseline, 3, 6 and 12 months). Treatment effect (change in BML size or VAS score) was assessed using multivariate linear regression and difference in the outcome between time points, after adjustment for age, sex, pain score and use of pain medications at baseline.

RESULTS: In adjusted analysis, total BML area was significantly reduced in the group who received ZA compared to the group who received placebo after 6 months (difference -170.3 mm^2, p= 0.03) with a consistent trend after 12 months (difference -141.1 mm^2, p= 0.08). Using the LSC, there was a trend to a greater proportion reducing BML size in the group receiving ZA compared to placebo after 6 months (71 vs 54%; p=0.09) which was significant by 12 months (77% vs 54%, p=0.02). Similarly, VAS pain scores were significantly reduced in the ZA group compared to placebo after six months (difference -14.5 mm, p=0.04) but not after twelve months (difference -7.7 mm, p=0.30). Improvements in the pain and symptom scales of the KOOS did not reach statistical significance after either 6 (6.2, p= 0.16 for pain; 3.3, p= 0.50 for symptoms) or 12 months (2.6, p= 0.65; 6.3, p= 0.26).

CONCLUSION: A single infusion of IV ZA reduces both knee pain and areal BML size over 6 months and increases the proportion of participants having reduced BML size over 12 months This proof of concept trial suggests that ZA may modify BML natural history and associated knee pain although more frequent infusions may be required to achieve greater resolution.

SPONSOR: This is an investigator initiated trial, with Prof G. Jones as the chief investigator.
DICLOSURE STATEMENT: Novartis Pharmaceuticals provided the study medication but had no involvement in analysis or abstract preparation.
CORRESPONDENCE ADDRESS: llaslett@utas.edu.au

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MODULE 7: 5 PRESENTATIONS SELECTED FROM ABSTRACTS (SEMI-QUANTITATIVE IMAGING OUTCOMES)

June 10th, 2011: 9.00 – 10.15

Chair: David Hunter,University of Sydney, Sydney, Australia
(10 min presentation + 5 min discussion)

9.00- 9.15	***Schiphof D., *Klerk B.M. de, **Waarsing J.H., ***Hofman A., ****Ginai A.Z., ****Oei E.H., **Weinans H., *,**Bierma-Zeinstra S.M.A.** * Department of General Practice, Erasmus MC, Rotterdam, The Netherlands ** Department of Orthopeadics, Erasmus MC, Rotterdam, The Netherlands *** Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands **** Department of Radiology, Erasmus MC, Rotterdam, The Netherlands **HOW RISK FACTORS ASSOCIATE TO EARLY OSTEOARTHRITIS SHOWN WITH SEMI-QUANTITATIVE MEASURES ON MRI IN KNEES WITHOUT SIGNS OF RADIOGRAPHIC OA**
9.15- 9.30	***Runhaar J MSc, **Steens R MD, **Vroegindeweij D PhD, ***Oei E.H.G, ****Bierma-Zeinstra S.M.A1,4 PhD** *Erasmus MC, Department of General Practice, Rotterdam, the Netherlands ** Maasstad Hospital, Department of Radiology, Rotterdam, the Netherlands *** Erasmus MC, Department of Radiology, Rotterdam, the Netherlands **** Erasmus MC, Department of Orthopedics & Department of General Practice, Rotterdam, the Netherlands **MALALIGNMENT AND THE PRESENCE OF EARLY SIGNS OF KNEE OA IN OBESE WOMEN.**
9.30- 9.45	***Guermazi A., *Hayashi D.,*,***Roemer F.W., **Felson D.T., **Wang K.,**** Lynch J., *****Amin S., ****Nevitt M.N.** *Quantitative Imaging Center, Dept. of Radiology, and ** Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, USA ***Department of Radiology, Klinikum Augsburg, Augsburg, Germany ****Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA ***** College of Medicine, Mayo Clinic, Rochester, MN, USA **DOES MRI DEPICT PROGRESSION OF RADIOGRAPHICALLY-DEFINED 'END-STAGE OA (KELLGREN-LAWRENCE GRADE 4)' LONGITUDINALLY? THE MOST STUDY**
9.45- 10.00	***,**Englund M., **Felson D.T., **Guermazi A, **,***Roemer F.W., **Wang K., **Crema M.D., ****Lynch J.A. *****Sharma L., ******Segal N., *******Lewis C.E., ****Nevitt M.C.** * Lund University, Lund, Sweden. ** Boston University School of Medicine, Boston, MA, USA. *** Klinikum Augsburg, Augsburg, Germany. **** University of California San Francisco, San Francisco, CA, USA. ***** Northwestern University, Chicago IL, USA. ****** University of Iowa, Iowa City, IA, USA. ******* University of Alabama, Birmingham, AL, USA. **RISK FACTORS FOR MEDIAL MENISCAL LESIONS AND (OR) EXTRUSION ON KNEE MRI IN OLDER U.S. ADULTS: THE MULTICENTER OSTEOARTHRITIS STUDY (MOST)**
10.00- 10.15	**Kwoh C.K.*, Hannon M.J.*, Guermazi A.**, Boudreau R.*, Green S.M.*, Roemer F.W.**,***** * University of Pittsburgh, Pittsburgh, PA, United States, ** Boston University School of Medicine, Boston, MA, United States, ***Department of Radiology, Klinikum Augsburg, Augsburg, Germany **IDENTIFICATION OF MRI MORPHOLOGIC FEATURES ASSOCIATED WITH DIFFERENT KNEE PAIN PATTERNS**

HOW RISK FACTORS ASSOCIATE TO EARLY OSTEOARTHRITIS SHOWN WITH SEMI-QUANTITATIVE MEASURES ON MRI IN KNEES WITHOUT SIGNS OF RADIOGRAPHIC OA

*Schiphof D., *Klerk B.M. de, **Waarsing J.H., ***Hofman A., ****Ginai A.Z., ****Oei E.H., **Weinans H., *,**Bierma-Zeinstra S.M.A.

* Department of General Practice, Erasmus MC, Rotterdam, The Netherlands
** Department of Orthopeadics, Erasmus MC, Rotterdam, The Netherlands
*** Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands
**** Department of Radiology, Erasmus MC, Rotterdam, The Netherlands

INTRODUCTION: Little is known about the association of the different risk factors with early signs of OA at MRI; whether the risk factors lead to different initial damage and therefore to different MRI features or start in different compartments of the joint. In addition, pain is sometimes an early sign/symptom of OA, but which early MRI-signs of OA relate to the presence of pain is not yet clear.

OBJECTIVE: To assess 1) how the different risk factors associate with early OA features detectable on MRI in women without evident radiographic knee OA, and 2) to investigate how these MRI-features associates with pain in the knee.

METHODS: Of 891women, aged 45 to 60, from an open population cohort, a subcohort of the Rotterdam Study, radiographs and MRI's of the knees were made. Data based a questionnaire, were used for demographic information. Radiographs were scored for OA with Kellgren and Lawrence classification criteria (K&L) and 1404 knees with K&L=0 were included in analysis (n=771, mean age is 53.5 years, mean BMI is 26.8). On MR-images semi-quantitative scores for OA of the knees were done with KOSS (Knee Osteoarthritis Scoring System). With Generalized Estimating Equations (univariate and multivariate) we analysed the association between the OA risk factors and the features of knee OA from the KOSS in medial and lateral FT joint (MFTJ, LFTJ) and patello-femoral joint (PFJ), and between pain and the early features of knee OA.

RESULTS: Age and overweight are in all three jointcompartments significant risk factors for having osteophytes (OR_{MFTJ}=1.04, p<0.001; OR_{LFTJ}=1.04, p<0.001; OR_{PFJ}= 1.05, p<0.001) and in almost all joint compartments for diffuse cartilage defects (OR_{MFTJ}= 1.01, p=0.02; OR_{PFJ}=1.058, p<0.001). Overweight is also associated with joint effusion(OR=1.10, p=0.01). An injury of the knee in history shows a significant association with BM lesions in the lateral FTJ(OR=1.18, p<0.01). The presence of Heberden's nodes is significantly associated with diffuse cartilage lesions, osteophytes and cysts in medial FTJ (OR=1.17, p<0.01; OR=1.20, p=0.03; OR=1.06, p=0.03 respectively). Current knee pain was significantly associated with joint effusion (OR=1.07, p=0.01). If knee pain was persisting for more than 4 days a week or most days of the last month, it was significantly associated with bone marrow lesions in PFJ (OR=1.06, p=0.05).

CONCLUSION: In conclusion, none of the risk factors is discriminative for one MRI feature, age and overweight are also not discriminative risk factors for compartment of the knee. In all three compartments age and overweight are risk factors for osteophytes, in almost all for diffuse cartilage defects. A potential discriminative risk factor for lateral knee OA is an injury of the knee in history. Having Heberden's nodes seems a discriminative risk factor for medial knee OA. The knowledge generated in this study might assist in the development and testing of preventive strategies on early treatment in knee OA.

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CORRESPONDENCE ADDRESS: d.schiphof@erasmusmc.nl

MALALIGNMENT AND THE PRESENCE OF EARLY SIGNS OF KNEE OA IN OBESE WOMEN.

*Runhaar J MSc, **Steens R MD, **Vroegindeweij D PhD, ***Oei E.H.G, ****Bierma-Zeinstra S.M.A[1,4] PhD

*Erasmus MC, Department of General Practice, Rotterdam, the Netherlands
** Maasstad Hospital, Department of Radiology, Rotterdam, the Netherlands
*** Erasmus MC, Department of Radiology, Rotterdam, the Netherlands
**** Erasmus MC, Department of Orthopedics & Department of General Practice, Rotterdam, the Netherlands

INTRODUCTION: Whether malalignment is a risk factor for development of knee OA or a risk factor for progression of knee OA is subject of debate. Prospective studies among healthy subjects showed contradicting results on the relationship between malalignment and incident knee OA. However, all these studies were among healthy, normal body weight or overweight subjects. Brouwer et al. showed that in overweight and especially obese individuals, malalignment significantly increased the risk on development of knee OA (odds ratio 2.0 for varus alignment in subjects with BMI = 25 and <30 and 3.3 and 5.1 for valgus and varus alignment in subjects with BMI = 30). In subjects with a normal body weight, no association between malalignment and incident knee OA was found (odds ratio 1.1 and 1.3 for valgus and varus alignment in subjects with BMI < 25).

OBJECTIVE: Purpose of the preset study was to investigate the association of alignment to the presence of early knee OA signs as seen on MRI in obese individuals free of clinical and radiological signs of knee OA.

METHODS: All participants were recruited through their general practitioner (GP). 50 GP's in the area of Rotterdam, The Netherlands, invited all registered women between 50 and 60 years to participate. All willing women with a BMI ≥ 30 and without clinical knee OA according to the ACR-criteria, or radiological signs of knee OA (K&L ≥ 2), or contra-indication to MRI were included. X-rays and MRI of both knees and body weight and height were obtained among 270 women. On MRI, presence of diffuse and focal cartilage defects and bone marrow lesions were scored on the medial and lateral tibiofemoral joint. Besides, presence of degeneration, tears and subluxation of the medial and lateral meniscus was scored. Knee alignment was defined as in Brouwer et al. to enhance comparison (after correction of 4 degrees, angles between 178 and 180 degrees were defined as normal alignment, >180 as valgus and <178 as varus). Using Generalized Estimated Equations, which takes the correlation between knees within subjects into account, relations between varus and valgus alignment and the presence of early signs of knee OA, corrected for age, BMI and K&L-grade, were investigated.

RESULTS: Associations between varus alignment and presence of bone marrow lesions in the medial tibiofemoral joint (OR 2.2, p = 0.002) and between valgus alignment and presence of diffuse cartilage defects in the medial tibiofemoral joint (OR 2.0, p = 0.038) appeared to be significant. However, presences of both scores were highly associated to subluxation of the medial meniscus (p ≤ 0.001). Additionally correcting for the presence of subluxation of the medial meniscus neutralized the effects of varus and valgus alignment. By itself, the association between varus alignment and the presence of subluxation of the medial meniscus was borderline significant (OR 3.1, p = 0.062).

CONCLUSION: In obese women without clinical and radiological signs of knee OA, malalignment was associated to early signs of knee OA. These associations seemed to be based on the presence of subluxation of the medial meniscus. This confirms that meniscal subluxation can be seen as precursor of knee OA. Follow-up data will be needed to confirm that the presence of varus alignment and meniscal subluxation will lead to the development on knee OA in these obese middle-aged women. If so, a possible intervention on prevention of knee OA should be tested, since varus alignment can partly be opposed by the use of wedged insoles and braces.

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DISCLOSURE STATEMENT: none
ACKNOWLEDGMENT: none
CORRESPONDENCE ADDRESS: j.runhaar@erasmusmc.nl

DOES MRI DEPICT PROGRESSION OF RADIOGRAPHICALLY-DEFINED 'END-STAGE OA (KELLGREN-LAWRENCE GRADE 4)' LONGITUDINALLY? THE MOST STUDY

*Guermazi A., *Hayashi D.,*,***Roemer F.W., **Felson D.T., **Wang K.,**** Lynch J., *****Amin S., ****Nevitt M.N.

*Quantitative Imaging Center, Dept. of Radiology, and ** Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, USA
***Department of Radiology, Klinikum Augsburg, Augsburg, Germany
****Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA
***** College of Medicine, Mayo Clinic, Rochester, MN, USA

INTRODUCTION: Kellgren-Lawrence grade 4 (KL4) knees are currently considered 'end-stage' knee OA (bone-on-bone appearance) which theoretically cannot progress further.

OBJECTIVE: To examine what proportion of KL 4 knees at baseline demonstrate further progression longitudinally in regard to features only detectable by MRI, i.e. cartilage, bone marrow lesion (BML), meniscus, Hoffa-synovitis, and effusion-synovitis.

METHODS: We studied subjects from the Multicenter Osteoarthritis Study (MOST) who had KL4 knee at baseline and had baseline and 30-month MRI. Cartilage, BML, meniscus, Hoffa-synovitis, and effusion-synovitis were semiquantitatively scored using the WORMS system in the 5 subregions of the medial and lateral tibiofemoral (TF) compartments of the knee: central and posterior femoral, anterior, central and posterior tibial subregions. Analysis was performed for the compartment showing bone-on-bone appearance ("index") on radiograph and also for the other TF compartment of the same knee. Hoffa-synovitis and effusion-synovitis were assessed for the whole knee. Changes in scores at follow-up were noted for each feature. For cartilage and BML, within-grade changes were also recorded.

RESULTS: 67 knees from 63 subjects were included (51% women, 84% White, mean age 65.1±8.6 years, mean BMI 30.2±5.2 kg/m^2). At baseline, in the index TF compartment, all knees showed severe cartilage loss (max WORMS score from 5 subregions was 5 in 1 knee and 6 in 66 knees), 54 knees (80%) showed moderate to severe BML (max WORMS score 2 or 3), and 62 knees (94%) had severe meniscal lesions (i.e. displaced tear or maceration). In the other TF compartment, 12 knees (18%) had severe cartilage loss, but 47 (71%) had no BML and 57 (97%) had no meniscal damage. 39 knees (58%) had moderate to severe effusion-synovitis, 56 knees (86%) had mild or moderate Hoffa-synovitis. Longitudinally, 22 index compartments (35%) showed increase in the sum of cartilage scores from all subregions, while only 2 (3%) showed increase in the max cartilage score. In the other TF compartment, 22% showed an increase in the sum score for cartilage damage, while 15% showed increase in max score. For BML, 19 knees (31%) showed increase in max score and 11 (18%) showed decrease in the index TF compartment. Fluctuation of BML was also seen in the other TF compartment, but to a lesser extent. Meniscal status mostly remained the same in the index (98%) and other TF (95%) compartments. Effusion-synovitis worsened in 15 knees (27%) and improved in 2 knees (4%). Hoffa-synovitis worsened in 6 knees (11%) and improved in 2 knees (4%).

CONCLUSION: MRI revealed progression of cartilage loss in the TF compartment showing 'bone-on-bone' appearance, and also in the other TF compartment in ~20%. However, BMLs showed fluctuation in size in both directions in both TF compartments even in KL4 knees. Menisci in the index TF compartment were severely damaged but those in the other TF compartment were mostly not damaged at both time points. Hoffa-synovitis did not show much longitudinal change, while effusion-synovitis worsened in about a quarter of knees. Our findings support the idea that inflammatory processes in KL4 knees are still active and may play a role in regard to structural progression and symptoms.

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ACKNOWLEDGEMENT: We thank the participants and the staff of the MOST Study.
CORRESPONDENCE ADDRESS: guermazi@bu.edu

RISK FACTORS FOR MEDIAL MENISCAL LESIONS AND (OR) EXTRUSION ON KNEE MRI IN OLDER U.S. ADULTS: THE MULTICENTER OSTEOARTHRITIS STUDY (MOST)

*,***Englund M., **Felson D.T., **Guermazi A, **,***Roemer F.W., **Wang K., **Crema M.D., ****Lynch J.A. *****Sharma L., ******Segal N., *******Lewis C.E., ****Nevitt M.C.

* Lund University, Lund, Sweden.
** Boston University School of Medicine, Boston, MA, USA.
*** Klinikum Augsburg, Augsburg, Germany.
**** University of California San Francisco, San Francisco, CA, USA.
***** Northwestern University, Chicago IL, USA.
****** University of Iowa, Iowa City, IA, USA.
******* University of Alabama, Birmingham, AL, USA.

INTRODUCTION: Knee trauma is a known cause of meniscal tear. However, meniscal pathology where the etiology is often unclear is a frequent finding on knee MRI.

OBJECTIVE: To investigate potential risk factors that may be casually associated with medial meniscal lesions or extrusion in middle-aged and elderly persons.

METHODS: Prospective cohort study using population-based subjects from Birmingham, Alabama and Iowa City, Iowa, United States. We studied 644 men and women aged 50 to 79 years with or at high risk of knee osteoarthritis (Kellgren and Lawrence grade 0 to 2) but with normal medial meniscal status at baseline. We scored paired baseline and 30- month 1.0T knee MRIs for meniscal lesions and extrusion (pathology) and evaluated the following systemic, knee-specific, and compartment-specific potential risk factors: age, sex, body mass index, bony enlargement of finger joints, knee trauma, leg-length inequality, and knee alignment.

RESULTS: Of 791 knees, 77 (9.7%) had medial meniscal pathology at 30-months follow-up. Sixty-one of these 77 knees (81%) had no report of trauma during follow-up. Including all potential risk factors in the multivariable model, the adjusted odds ratio (OR) for medial meniscal pathology was 4.14 (95% confidence interval 2.06, 8.31) for knee trauma during follow-up, 1.64 (1.00, 2.70) for ≥5 bony enlargements of finger joints (vs. ≤4 [median]), and 2.00 (1.18, 3.40) for varus alignment (vs. not varus) at baseline exam. Further, obesity was a risk factor for the development of meniscal extrusion, OR 3.04 (1.04, 8.93) but not for meniscal lesions, OR 1.15 (0.52, 2.54).

CONCLUSION: Apart from knee trauma, possible generalized osteoarthritis, expressed as multiple bony enlargements of finger joints, varus alignment, and obesity are risk factors for medial meniscal pathology.

SPONSOR: The Multicenter Osteoarthritis (MOST) Study is a cooperative epidemiological study of knee OA funded by the National Institute on Aging (NIA): Felson – 1 U01 AG18820; Torner – 1 U01 AG18832; Lewis – 1 U01 AG18947; Nevitt – 1 U01 AG19069. Dr Englund is supported by the Swedish Research Council, and the Faculty of Medicine, Lund University, Sweden.
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CORRESPONDENCE ADDRESS: martin.englund@med.lu.se

IDENTIFICATION OF MRI MORPHOLOGIC FEATURES ASSOCIATED WITH DIFFERENT KNEE PAIN PATTERNS

Kwoh C.K.*, Hannon M.J.*, Guermazi A.**, Boudreau R.*, Green S.M.*, Roemer F.W.[**,***]

[*] University of Pittsburgh, Pittsburgh, PA, United States, ** Boston University School of Medicine, Boston, MA, United States, [***]Department of Radiology, Klinikum Augsburg, Augsburg, Germany

INTRODUCTION: Knee pain is the main reason for patients to seek care for knee osteoarthritis, but the cause for knee pain is unclear. The Knee Pain Map is a validated measure to assess different knee pain patterns in regard to specific joint locations.

OBJECTIVE: The aim of the study was to examine the association of joint morphologic features on MRI with knee pain in specific locations, regions or global pain patterns.

METHODS: The JOG study includes 177 subjects aged 35-65 (95 men and 82 women) with chronic, frequent knee pain in at least one knee. 3T MRI of both knees was performed at baseline on a Siemens Trio using the same pulse sequence protocol as in the OAI. All MRI features were scored semi-quantitatively using a modified WORMS system. Cartilage damage was scored on a scale from 0-6 and bone marrow (BM) lesions were scored on a scale from 0-3 using all 5 sequences in 15 articular subregions. Meniscal damage was assessed in 6 locations, meniscal extrusion was evaluated on the coronal plane from 0-2, and the presence of synovitis and effusion was scored from 0-3. All MR features were divided into two categories: present (score ≥1) and absent (score=0). Knees were characterized into localized, regional or global pain patterns using the Knee Pain Map, an interviewer-administered assessment of location-specific knee pain patterns based on the presence of pain in the past 30 days. Associations of MRI abnormalities in any subregion of the medial and lateral compartments with pain localized in that joint line and with regional or global pain patterns in each respective compartment were evaluated. Multinomial logistic regression was used to compare the knee pain patterns controlling for clustering by person.

RESULTS: A total of 46 knees had no knee pain, 83 had localized medial joint line pain, 36 had medial regional pain, 68 had localized lateral joint line pain, 31 had lateral regional pain, and 27 had global knee pain. The medial and lateral joint lines were the most common localized pain patterns. The association of pain pattern with each separate MRI abnormality is shown in the table below.

	Local Joint line Pain (n = 83)			Regional Pain (n = 36)			Global Pain (n = 27)		
MEDIAL*	RRR**	[95%CI]		RRR	[95% CI]		RRR	[95% CI]	
Cartilage damage	2.52	1.07	5.92	3.97	1.28	12.35	4.65	1.37	15.81
BM lesions	9.89	2.04	47.99	12.10	2.27	64.60	12.44	2.24	69.05
Synovitis/effusion	0.99	0.46	2.14	1.62	0.61	4.28	0.94	0.31	2.79
Meniscal damage	1.46	0.56	3.77	3.72	1.10	12.60	2.65	0.77	9.11
Meniscal extrusion	1.08	0.47	2.49	8.77	2.18	35.23	3.46	1.00	12.05

*adjusted for age, sex and BMI and compared to knees with pain in the past 30 days; ** relative risk ratio

In addition, MRI features from the medial compartment were combined into a single multivariable, multinomial model predicting each of the three patterns of knee pain." For the multivariate analyses, BM lesions were significantly associated with local joint line pain, regional pain and global pain when compared to no pain. RRRs and 95% CIs were 7.97 (1.48, 43.01), 8.56 (1.45, 50.4), and 8.04 (1.35, 48.0), respectively. Meniscal extrusion was significantly associated with regional pain, with an RRR of 6.76 (1.574, 29.05).

CONCLUSIONS: The presence of MRI-detected pathology was associated with localized joint line pain, regional pain and global pain patterns. Of note, meniscal extrusion and meniscal damage were associated with the regional knee pain pattern. These findings may help to identify more homogenous populations for targeted interventions.

SPONSOR: The Beverage Institute for Health and Wellness/ The Coca-Cola Company
DISCLOSURE STATEMENT: Dr. Guermazi has received consultancies, speaking fees, and/or honoraria from Facet Solutions, Genzyme, Stryker, and from Merck Serono, and is the President of Boston Imaging Core Lab (BICL). He holds a research grant from General Electric Healthcare. Dr. Roemer is Vice President and shareholder of BICL.
ACKNOWLEDGMENT: NIH/NIAMS P60AR054731
CORRESPONDENCE ADDRESS: kwoh@pitt.edu, 412-383-8100

MODULE 9: 5 PRESENTATIONS SELECTED FROM ABSTRACTS (QUANTITATIVE IMAGING OUTCOMES)

June 10th, 2011: 13.30 – 14.45

Chair: Miika Nieminen,University of Oulu, Oulo, Finland
(10 min presentation + 5 min discussion)

13.30-13.45	M. D. Crema*,**, D. J. Hunter***, D. Burstein****, F. W. Roemer*,*****, L. Li******, N. Krishna****, M. D. Marra*,*******, M-P. Hellio Le-Graverand********, A. Guermazi* *Boston Univ. Sch. of Med., Boston, MA, **Inst. of Diagnostic Imaging (IDI) and Radiology Div., Univ. of São Paulo at Ribeirão Preto, Ribeirão Preto, BRAZIL, ***The Univ. of Sydney, Sydney, AUSTRALIA, ****Harvard Med. Sch., Boston, MA, *****Klinikum Augsburg, Augsburg, GERMANY, ******New England Baptist Hosp., Boston, MA, *******Inst. of Diagnostic Imaging (IDI), Ribeirão Preto, BRAZIL, ********Pfizer Inc., New London, CT. DELAYED GADOLINIUM-ENHANCED MRI OF MEDIAL TIBIOFEMORAL CARTILAGE (DGEMRIC) AND ITS RELATIONSHIP WITH MEDIAL MENISCAL PATHOLOGY: A 12-MONTH FOLLOW-UP STUDY USING 3.0T MRI.
13.45-14.00	* Shiomi T., **Nishii T., ** Tamura S., ***Yamazaki Y., ***Murase K., ****Tanaka H., *Yoshikawa H., **Sugano N. * Department of Orthoaedic Surgery, ** Department of Orthopaedic Medical Engineering, *** Department of Medical Physics and Engineering, **** Department of Radiology, Osaka University Medical School, Osaka, Japan THE INFLUENCE OF MEDIAL MENISCECTOMY TO THE STRESS DISTRIBUTION OF FEMORAL CARTILAGE IN PORCINE KNEE -3D RECONSTRUCTED T2 MAPPING STUDY-
14.00-14.15	*Tamura S., *Nishii T., **Nakata K., **Shiomi T., ***Yamazaki Y., ***Murase K., ****Tanaka H., **Kita K., **Mae T., **Yoshikawa H., *Sugano N. * Department of Orthopaedic Medical Engineering, Osaka University, Osaka, Japan ** Department of Orthopaedic Surgery, Osaka University, Osaka, Japan *** Department of Medical Physics and Engineering, Osaka University, Japan **** Department of Diagnostic and Interventional Radiology, Osaka University, Japan ASSESSMENT OF KNEE CARTILAGE IN PATIENTS WITH ACL RUPTURE BY 3D RECONSTRUCTED T2 MAPPING
14.15-14.30	*Cicconetti, G., *Matheny, C. * GlaxoSmithKline, Upper Merion, PA, USA APPLYING A STATISTICAL/GRAPHICAL TOOL TO CHARACTERIZE CHANGES OVER TIME IN MRI-BASED CARTILAGE THICKNESS MEASURES
14.30-14.45	*Buck R.J. * StatAnswers Consulting LLC, Minneapolis, MN SIMULATIONS TO ASSESS BEHAVIOR OF ORDERED VALUES APPROACH IN CLINICAL DRUG TRIALS

DELAYED GADOLINIUM-ENHANCED MRI OF MEDIAL TIBIOFEMORAL CARTILAGE (DGEMRIC) AND ITS RELATIONSHIP WITH MEDIAL MENISCAL PATHOLOGY: A 12-MONTH FOLLOW-UP STUDY USING 3.0T MRI.

M. D. Crema[*,**], D. J. Hunter[***], D. Burstein[****], F. W. Roemer[*,*****], L. Li[******], N. Krishna[****], M. D. Marra[*,*******], M-P. Hellio Le-Graverand[********], A. Guermazi[*]

[*]Boston Univ. Sch. of Med., Boston, MA, [**]Inst. of Diagnostic Imaging (IDI) and Radiology Div., Univ. of São Paulo at Ribeirão Preto, Ribeirão Preto, BRAZIL, [***]The Univ. of Sydney, Sydney, AUSTRALIA, [****]Harvard Med. Sch., Boston, MA, [*****]Klinikum Augsburg, Augsburg, GERMANY, [******]New England Baptist Hosp., Boston, MA, [*******]Inst. of Diagnostic Imaging (IDI), Ribeirão Preto, BRAZIL, [********]Pfizer Inc., New London, CT.

INTRODUCTION: Meniscal tears are known factors associated with progression of cartilage loss in the tibiofemoral compartments. Several studies demonstrated that early degeneration of cartilage matrix may be depicted using delayed gadolinium-enhanced MRI. The usefulness of dGEMRIC in monitoring cartilage composition regarding meniscal pathology has been little explored.

OBJECTIVE: To assess the relationship between cartilage matrix changes by applying dGEMRIC of medial tibiofemoral cartilage and medial meniscal pathology in a sample of middle-aged women, over a 1-year period using 3.0T MRI.

METHODS: A total of 148 women aged ≥ 40 years were included in this longitudinal and observational study of knee osteoarthritis. Knees were assessed by MRI at baseline (BL) and 12 months follow-up (FU). T2-weighted fat-suppressed sequences (meniscal assessment) and three-dimensional inversion recovery-prepared spoiled gradient recalled echo sequences 90 minutes after injecting gadolinium ($Gd\text{-}DTPA^{2-}$) (dGEMRIC assessment) were performed. BL medial meniscal pathology was scored as follows: 0 (normal), 1 (intra-substance meniscal signal changes), 2 (single tears), and 3 (complex tears/maceration). Assessment of dGEMRIC was performed at BL and FU in the central medial femur (cMF), the medial tibial plateau (MT) and the posterior medial femur (pMF) regions of the medial tibiofemoral compartment. Analysis of covariance was used to examine if BL and FU dGEMRIC values in matched regions were different regarding BL medial meniscal damage severity. BL normal medial menisci were considered the reference group for the analysis.

RESULTS: At BL, 62 (41.9%) medial menisci were normal (grade 0), 59 (39.9%) had grade 1 changes, 12 (8.1%) had grade 2 lesions, and 15 (10.1%) had grade 3 lesions. The mean dGEMRIC values in medial regions assessed varied from 563.1 milliseconds (ms) (MT) to 606.5 ms (pMF) at BL, and from 599.5 ms at cMF to 618.5 ms (pMF) at FU. Medial tibiofemoral compartments with grade 3 meniscal lesions showed significantly decreased dGEMRIC values (less proteoglycan content) at the cMF region compared with values of compartments with normal menisci. Differences in dGEMRIC values between grade 3 vs. grade 0 menisci were -119.1 ± 34.2 ms at BL ($p=0.03$) and -120.3 ± 35.2 ms at FU ($p=0.04$). There were no significant differences in dGEMRIC values regarding medial compartments with grade 1 meniscal changes or grade 2 meniscal lesions when compared with the reference group.

CONCLUSION: In this sample of middle-aged women, alterations in cartilage composition (proteoglycan content) as assessed by dGEMRIC had a significant relationship with high grade damage of the medial meniscus at both BL and FU assessments. No significant changes in cartilage composition were observed on compartments with only intra-substance meniscal signal changes or meniscal single tears.

SPONSOR: Pfizer Inc.

DISCLOSURE STATEMENT: Dr. Guermazi has received consultancies, speaking fees, and/or honoraria from Facet Solutions, Genzyme, Stryker, and from Merck Serono, and is the President of Boston Imaging Core Lab (BICL). He holds a research grant from General Electric Healthcare. Dr. Roemer is Vice President and shareholder of BICL. Dr. Crema and Dr. Marra are shareholders of BICL. None of the other authors have declared any possible conflict of interest.

ACKNOWLEDGMENT: We would like to thank the participants and staff of the Pfizer A9001140 Osteoarthritis Study.

CORRESPONDENCE ADDRESS: micrema@bu.edu

THE INFLUENCE OF MEDIAL MENISCECTOMY TO THE STRESS DISTRIBUTION OF FEMORAL CARTILAGE IN PORCINE KNEE -3D RECONSTRUCTED T2 MAPPING STUDY-

* Shiomi T., **Nishii T., ** Tamura S., ***Yamazaki Y., ***Murase K., ****Tanaka H., *Yoshikawa H., **Sugano N.

* Department of Orthoaedic Surgery, ** Department of Orthopaedic Medical Engineering,
*** Department of Medical Physics and Engineering, **** Department of Radiology, Osaka University Medical School, Osaka, Japan

INTRODUCTION: Previous cadaveric studies showed meniscectomy results in significant increase of local load transmission and may leads to degeneration of the articular cartilage in the knee joint. However there has been no reliable methods which allows in vivo 3D assessment of load distribution in the knee articular cartilage after menisectomy or meniscal injuries.

OBJECTIVE: The purpose of this study is to assess influence of medial meniscectomy on 3D reconstructed T2 mapping of the femoral cartilage in the knee joint, using a custom-made non-metallic pressure device under different loading or knee alignments.

METHODS: Five normal porcine knee joints, harvested en bloc with intact capsules and surrounding muscles, were imaged using the custom-made pressure device and 3.0T MR imaging system. First, sagittal 3D-FIESTA-C images (TR/TE:12.7/6.3ms; slice thickness: 1.0mm; FOV: 12 cm) and sagittal T2 map images (TR: 1500 ms; TE: 8 echoes between 10- 80 ms; slice thickness: 3.0 mm; FOV: 12 cm). were obtained in the neutral alignment without loading (Condition N), under mechanical compression of 300 N (Condition L), and under compression of 300N with the knee at 10° varus alignment (Condition V). After medial meniscectomy, the two series of MR images under the aforementioned three conditions were obtained. T2 color map was overlaid on the 3D cartilage and meniscus morphology model reconstructed from the FIESTA-C by using custom-made software. The region of interest (ROI) was manually defined on the femoral cartilage covered by the medial and lateral meniscus, which was divided into 12 ROIs (Fig.1). The decrease of mean T2 value at each ROI under each condition was calculated as (values in Condition N - values in each condition) / values in Condition N. The decrease of T2 before and after meniscectomy was compared at each condition.

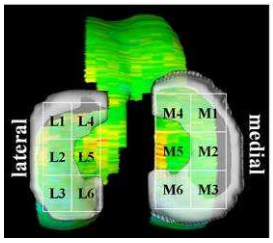


Fig 1. Definition of ROIs

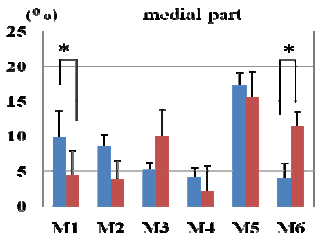


Fig 2. Decrease of T2 value before/after meniscectomy in Condition L

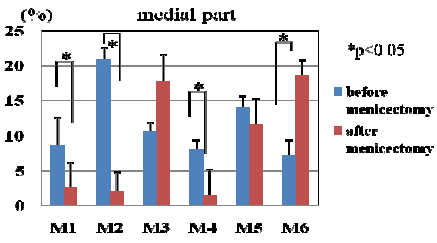


Fig 3. Decrease of T2 value before/after meniscectomy in Condition V

RESULTS: At medial part in Condition L, large decreases of T2 were seen at M1, M2, and M5 before meniscectomy, and at M3, M5, and M6 after meniscectomy (Fig.2). There were significant differences at M1 and M6 (before/after; M1:9.8%/4.3%, M6:4.0%/11.4%) ($p<0.05$). There was no significant difference at the lateral parts. At medial part in Condition V, large decreases of T2 were seen at M2 and M5 before meniscectomy, and at M3 and M6 after meniscectomy (Fig.3). and there were significant differences at M1, M2, M4, and M6 (before/after; M1:8.7%/2.5%, M2:20.8%/2.1%, M4:8.0%/1.5%, M6:7.2%/18.7%) ($p<0.05$). At the lateral part, after meniscectomy the decrease rate was significantly smaller at L3 and L6 (before/after; L3:8.2%/-3.6%, L6:8.1%/2.8%) ($p<0.05$).

CONCLUSION: Assuming that decrease of T2 value by loading was correlated with applied pressure value onto the cartilage, deficiency of medial meniscus might result in shift of stress concentration to the posterior part of medial condyle, especially at varus alignment which was often seen in OA. The results may allow non-invasive assessment of biomechanical disorder in patients with traumatic meniscus disorder and with knee OA associated with meniscus deficiency.

SPONSOR: none
DICLOSURE STATEMENT: none
CORRESPONDENCE ADDRESS: t-shiomi@ka2.so-net.ne.jp

ASSESSMENT OF KNEE CARTILAGE IN PATIENTS WITH ACL RUPTURE BY 3D RECONSTRUCTED T2 MAPPING

*Tamura S., *Nishii T., **Nakata K., **Shiomi T., ***Yamazaki Y., ***Murase K., ****Tanaka H., **Kita K., **Mae T., **Yoshikawa H., *Sugano N.

* Department of Orthopaedic Medical Engineering, Osaka University, Osaka, Japan
** Department of Orthopaedic Surgery, Osaka University, Osaka, Japan
*** Department of Medical Physics and Engineering, Osaka University, Japan
**** Department of Diagnostic and Interventional Radiology, Osaka University, Japan

INTRODUCTION: Patients with ACL rupture have high likelihood of subsequent progression of knee OA. Patients often sustain ACL injury combined with meniscal tears. Since meniscal tears are likely to change load transmission and instability of knee joint, presence of meniscal tears may be a significant influential factor on cartilage degeneration and osteoarthritis involvement in patients with ACL rupture.

OBJECTIVE: The objectives of this study was to evaluate influence of combined lateral meniscal tear on cartilage damage in patients with ACL rupture by using 3D reconstructed cartilage T2 mapping.

METHODS: Twenty-three patients with ACL rupture scheduled for ACL reconstruction surgery (ACLR) and twelve volunteers who had no pain and no previous surgery in the knee were included. MR imaging of patients with ACL rupture were performed one day before ACLR. Sagittal 3D-FIESTA-C image (TR/TE:12.7/6.3ms; slice thickness: 1.5mm; FOV: 12 cm; acquiring time: 10min27sec.) and 2D sagittal T2 map image (TR: 1500 ms; TE: 8 echoes between 10- 80 ms; slice thickness: 3 mm; FOV: 12 cm; acquiring time: 12min54sec.) were obtained using 3.0-T MRI system (GE Healthcare). After the 3D cartilage model and meniscus model was reconstructed from the images of FIESTA-C, T2 color map was laid on the 3D model using custom-made software (Baum, Osaka Univ.). The region of interest (ROI) was manually defined on the femoral condyle cartilage, as weight bearing area covered by meniscus (Z2), anterior area (Z1) and posterior area (Z3) (Fig.1). T2 value at each ROI was calculated with cartilage at full thickness, superficial layer and deep layer. Twenty-three patients with ACL rupture were divided into ACL rupture combined with lateral meniscal tear (10 patients; mean age: 22.1±6.0 years; male/female: 5/5; Group L) and ACL rupture without lateral meniscal tear (13 patients; mean age: 26.0±7.9 years; male/female: 8/5; Group S). T2 value at each ROI was compared among Group L, Group S and volunteer (12 volunteer; mean age: 25.0±5.2 years; male/female: 6/6;Group C) by using unpaired t test. There were no significant difference in age and gender among Group L, S and C.

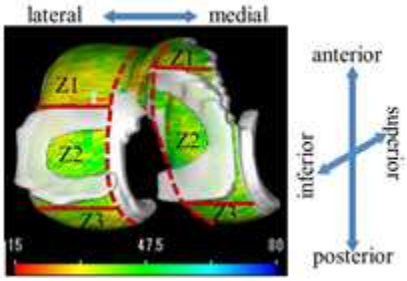


Fig.1

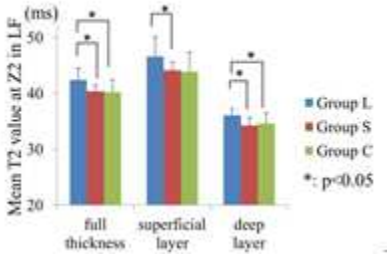


Fig.2

RESULTS: At Z2 of LF, T2 values of Group L were significantly higher than those of Group C (full thickness; Group L/C: 42.4±2.2/40.2±2.2ms, p =0.03, deep layer; Group L/C: 36.1±1.2/34.6±1.9ms, p=0.02), and higher than those of Group S (full thickness; Group L/S: 42.4±2.2/40.3±1.1ms, p =0.01, superficial; Group L/S: 46.6± 3.5/44.1±1.5 ms, p=0.03, deep; Group L/S: 36.1±1.2/34.2±1.5ms, p<0.01) (Fig.2). However, there were no significant differences of T2 values between Group S and C.

CONCLUSION: Using 3D reconstruction images of T2 mapping, whole femoral condyle can be evaluated generally and locally. Patients with ACL rupture combined lateral meniscal tear may have more severe damage of cartilage than patients with pure ACL rupture and may have higher requirements of early surgical treatment.

SPONSOR: None
DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: tamura-osk@umin.net

APPLYING A STATISTICAL/GRAPHICAL TOOL TO CHARACTERIZE CHANGES OVER TIME IN MRI-BASED CARTILAGE THICKNESS MEASURES

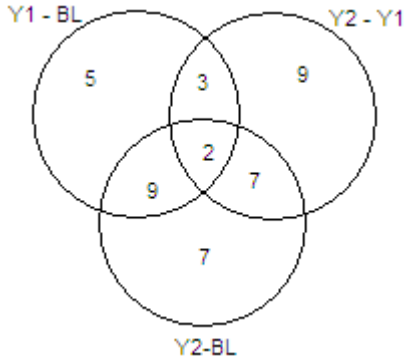
*Cicconetti, G., *Matheny, C.
* GlaxoSmithKline, Upper Merion, PA, USA

INTRODUCTION: Fundamental questions to assist development of DMOADs include 'Can knee OA phenotypes be defined based on MRI features?' and if so, 'Do these knee OA phenotypes associate with progression and/or response to intervention?' To address the second question, Buck et al (2011) considered ordered subregional cartilage thickness changes as a means of increasing sensitivity in detecting knee OA disease progression. Here, we explore the merits of statistical and graphical approaches that utilize multi-dimensional distance measures to identify subjects experiencing atypical changes in subregional cartilage distribution relative to the cohort. An inherent advantage of this approach is that it accounts for correlation among thicknesses measured in the various subregions

OBJECTIVE: The objective is to determine if assigning multi-dimensional distance measures to changes in subregional cartilage thickness can identify those knees with the greatest amount of change and assist in characterizing knee OA 'progressors'.

METHODS: Cartilage thickness measures were obtained from 238 subjects from the Osteoarthritis Initiative study with Baseline (BL), Y1 and Y2 MRI data available to sponsors participating in the OAI Consortium. MRIs were acquired using the FLASH sequence on the right knee; for brevity focus here is on LFTC. Y1 - BL differences in thickness measures from eight subregions associated with the LFTC (eLT, iLT, aLT, pLT, cLT, icLF, ccLF, ecLF) were vectorized as follows: Let x be the 1x8 vector associated with the first subject's 8 Y1 - BL subregional cartilage thickness measures. Further, let S be the 8 x 8 sample covariance matrix and let y be the 8-dimensional vector of subregional cartilage thickness means associated with these difference among the sample of 238 knees. The first subject's Squared Mahalanobis Distance: is MD2(x) = (x – y)inv(S)tr(x – y), where tr( ) is the transpose function, and inv(S) is the inverse of the covariance matrix. Under the assumption of multivariate normality, MD2(x) is distributed as a Chi-Square with 8 degrees of freedom (df, ChiSq(8)). Repeat this to obtain distance measures for all knees. This process is repeated for Y1 – Y2 and Y2 – BL. Subjects are flagged when their distances measures fall beyond the 95th percentile of ChiSq(8).

RESULTS: 19, 21, and 25 subjects were flagged as having Y1-BL, Y2-Y1, Y2-BL changes, respectively, in subregional cartilage thickness leading to distance measures falling beyond the 95th percentile of ChiSq(8). A Venn diagram suggests some patients slowly change over 2 years, others have marked changes over a single year, while others experience significant changes over a single year but these changes are muted relative to changes over 2 years. Novel graphics have also been developed to assist in interrogating how the individual subregional cartilage thickness changes contributed to a knee being flagged with a large multidimensional distance.



CONCLUSION: Characterization of osteoarthritis disease progression remains elusive. Applying a multi-dimensional measures of distance allowed us to identify patients with the largest changes over 1-year and 2-year periods. Applying to the tool to 3 time intervals, suggested a novel way to retrospectively classify subjects as those experiencing with slow and fast changes in subregional cartilage thicknesses. Further insight is gained by further interrogating the subregions that contributed most distance measures. It is important to note that this method identifyied subjests whose changes are extreme relative to the mean subregional changes among the knees in this cohort. By replacing the sample mean vector with a vector 0's, one can consider how individual knees compare to a hypothetical non-progressor cohort (that still shares the inherent correlation structure of the sample).

SPONSOR: GlaxoSmithKline
DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: greg.2.cicconetti@gsk.com

Reference: Buck, R., Wyman, B., Hellio Le Graverand, M., Hunter, D., Vignon,Wirthm, W., Eckstein, F. Using ordered values of subregional cartilage thickness change increases sensitivity in detecting risk factors for osteoarthritis progression. Osteoarthritis and Cartilage 19 (2011) 302-308.

SIMULATIONS TO ASSESS BEHAVIOR OF ORDERED VALUES APPROACH IN CLINICAL DRUG TRIALS

*Buck R.J.

* StatAnswers Consulting LLC, Minneapolis, MN

INTRODUCTION: Change in cartilage thickness is an important aspect of osteoarthritis progression and is considered a possible alternative to joint space narrowing as a proof of concept efficacy endpoint. Detecting differences in population change between two or more cohorts is the fundamental hypothesis in clinical trials for assessing new treatments. Ordered values of change in cartilage have been shown to be more sensitive in detecting differences in thickness change between two cohorts, but the properties of this new metric have not been examined under conditions that mimic efficacy trials.

OBJECTIVE: To identify the best (most sensitive in detecting differences between drug and placebo treatments) cartilage morphology biomarkers through the use of simulation models.

METHODS: Simulation models were based on parametric models, i.e., they were based on theoretical distributions and estimates of population characteristics, or resampling of study data with adjustments to reflect beliefs about drug effects in a clinical trial. Three general classes of simulation were examined:
1) Null scenarios had no differences between drug and placebo group and were used to assess whether tests using different metrics show test bias, i.e., whether observed rate of statistical significance under the null hypothesis is different from the chosen rate of Type I error for each individual simulated test.
2) Experimental models examined the effect of population characteristics on testing methods by assessing the sensitivity (power) for t test and Wilcoxon rank-sum test for fixed location regions and ordered values. Simulation model parameter values were selected in these scenarios more to exercise various population characteristics rather than simulate "realistic" scenarios.
3) Observational models were constructed to describe anticipated drug effects. Simulation model parameter values were selected to reflect three characteristics of drug effect: a reduction in proportion and/or magnitude change in fast progressors in the study population, and a general reduction in the magnitude of change (decline) in all subjects. Observational models were either resampling of OAI data at baseline and Year 2 or used parameters based on this data.

The scenarios cover conditions where differences exist in: fixed or random location for change in basic subpopulation; a fixed or random location for a fast progressors subpopulation; more than one random location for change in a fast progressor subpopulation.

RESULTS: Results for the null scenarios indicate that both *t* and Wilcoxon rank-sum tests are negligibly biased. The fixed location method was more powerful than the ordered values approach if change was restricted to the basic subpopulation. The ordered values approach was more powerful, however, when fast progressors (decliners only) were present and change varied in location between individuals in the study, regardless whether fast progression was limited to one location per individual or not. The two methods were equally sensitive when change was at fixed location and fast progressors were present. Test sensitivity was generally comparable for *t* and Wilcoxon rank-sum tests, but *t* tests were more powerful in some cases.

CONCLUSION: Testing based on ordered values method appears to be unbiased and is more sensitive than fixed location approach only when a fast progressors subpopulation is present. It appears that both ordered values and fixed region methods should be employed to cover either scenario.

SPONSOR: Merck Serono.
DISCLOSURE STATEMENT: Merck Serono has reviewed and that the views and opinions described in each publication do not necessarily reflect those of Merck Serono.
ACKNOWLEDGMENT: Don Dreher, Sylvain Larroque, and Scarlet Hellot of Merck Serono; the OAI investigators and technicians; the Chondrometrics readers.
CORRESPONDENCE ADDRESS: robert.j.buck@gmail.com

POSTER SESSION

June 9th, 2011: 15.00 – 16:00 - Odd numbered posters (No. 1 to 33)

1	Lickorish D, Haskell M.M., Wood S.A, Collett A, Goad M.E.P., Schrier D, Flory C. Stryker Regenerative Medicine, North Grafton, USA QUANTIFICATION OF TRABECULAR BONE VASCULARITY IN A RABBIT MODEL OF OSTEOARTHRITIS BY PERFUSION MICRO COMPUTED TOMOGRAPHY
3	*King, A.J., **Deng, C., **Sharp, J. **Tomanek B, *Dunn, J.F. * McCaig Institute & Experimental Imaging Centre & University of Calgary, Calgary, Canada ** National Research Council of Canada – Institute for Biodiagnotics (West), Calgary, Canada (NRC) 3D VISUALIZATION AND MEASUREMENT OF THE POSTERIOR CRUCIATE LIGAMENT IN A FLEXED KNEE USING OPEN-BORE 0.2T MRI
5	*,**Lammentausta E., **Hawezi Z., ***Tiderius C.J. and **Dahlberg L. *Oulu University Hospital, Oulu, Finland **Lund University, Malmö, Sweden ***Skåne University Hospital, Malmö, Sweden IN VIVO TRANSPORT OF GD-DTPA2- INTO HUMAN KNEE CARTILAGE
7	*Sitoci H., **Hudelmaier M., **Eckstein F. * Institute of Anatomy, Ludwig Maximilians Universität, Munich, Germany ** Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria NOCTURNAL CHANGES IN FEMORO-TIBIAL CARTILAGE THICKNESS IN YOUNG HEALTHY ADULTS
9	*Cicconetti, G., *Matheny, C. * GlaxoSmithKline, Upper Merion, PA, USA A STATISTICAL/GRAPHICAL TOOL TO IDENTIFY KNEE OA PHENOTYPES BASED ON MRI CARTILAGE THICKNESS MEASURES
11	*Wyman BT., **Cotofana S., *Zhang Y., ***Souza RB., *Clemmer R., *Hellio Le Graverand M-P, ***Li X., ***Majumdar S., ***Link TM., ***Eckstein F., ****Vignon E. * Pfizer Inc, Groton, CT, USA; ** Paracelsus Medical University, Salzburg, Austria; *** University of California, San Francisco, CA, USA; **** Claude Bernard University, Lyon, France COMPRESSION OF THE KNEE UPON WEIGHT LOADING IN HEALTHY AND OSTEOARTHRITIS SUBJECTS AS MEASURED BY MRI AND X-RAY
13	*Driban J.B., **Lo G.H., *Price L.L.,*McAlindon T.E. * Tufts Medical Center, Boston, USA ** Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, USA HIP BONE MINERAL DENSITY DOES NOT INFLUENCE TIBIOFEMORAL BONE MARROW LESION SIZE
15	*,**Marques J., **Dam E. * University of Copenhagen, Copenhagen, Denmark ** BiomedIQ, Rødovre, Denmark PREDICTION OF CARTILAGE LOSS BY ANALYSIS OF TRABECULAR TIBIA BONE STRUCTURE
17	Beattie K.A.*, MacIntyre N.J.*, Ramadan K.*, Inglis D.*, Maly M.R.* *McMaster University, Hamilton, ON, Canada LONGITUDINAL CHANGES IN INTERMUSCULAR FAT VOLUME AND QUADRICEPS MUSCLE VOLUME IN THE THIGHS OF FEMALE OAI PARTICIPANTS
19	*Stok K. S., **Nesic D., ***Zulliger M., *Firminger C.,*Müller R. * Institute for Biomechanics, ETH Zürich, Switzerland ** Department of Clinical Research, University of Bern, Switzerland *** SCANCO Medical AG, Brüttisellen, Switzerland COMPREHENSIVE MORPHOLOGICAL CHARACTERISATION OF ARTHRITIS IN ANIMAL MODELS BY MICRO-COMPUTED TOMOGRAPHY

21	*Siorpaes K., *Wenger A., *Bloecker K., **Burgkart R., *Wirth W., *Eckstein F. * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria **Clinic for Orthopaedics and Traumatology, Technical University Munich, Germany INTEROBSERVER VARIATION OF QUANTITATIVE MENISCUS ANALYSIS USING CORONAL MPR DESSWE AND IW TSE MR IMAGING
23	* , ** Kinds M.B., * Marijnissen A.C.A., ** Vincken K.L., ** Viergever M.A., *** Drossaers-Bakker K.W., * Bijlsma J.W.J., * , **** Welsing P.M.J., * Lafeber F.P.J.G. * Rheumatology & Clinical Immunology, University Medical Center Utrecht, the Netherlands ** Image Sciences Institute, University Medical Center Utrecht, the Netherlands *** Institute for Behavioral Research, University of Twente and Medisch Spectrum Enschede, the Netherlands **** Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, the Netherlands ARE SEPARATE QUANTITATIVE RADIOGRAPHIC FEATURES (KIDA) OF KNEE OSTEOARTHRITIS VERY EARLY IN THE DISEASE (CHECK) ASSOCIATED WITH CLINICAL PROGRESSION DURING FOUR-YEAR FOLOW-UP?
25	* Hudelmaier M, *Wirth W, *Maschek S, **Nevitt M, *Eckstein F for the OAI Investigators Group * Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany ** University of California and OA Initiative Coordinating Center, San Francisco, CA ONE-YEAR RATE OF CHANGE IN SUBCHONDRAL BONE SIZE IN OSTEOARTHRITIC AND HEALTHY KNEES
27	[1.]Cromer M, [1.]Bourne R, [2.]Fransen M, [1,3.]Fulton, R, [4.]Wang, SC. [1.]Discipline of Medical Radiation Sciences, FHS, University of Sydney, Australia [2.]Clinical and Rehabilitation Sciences Research Group, FHS, University of Sydney, Australia [3.]School of Physics, University of Sydney, Australia [4.]Discipline of Imaging, Sydney Medical School, Australia QUANTITATIVE ANALYSIS IN THE MEDIAL TIBIO-FEMORAL COMPARTMENT OVER ONE YEAR
29	*Klocke N.F., **Thedens D.R., *Amendola A., *Pedersen D.R * Orthopaedics and Rehabilitation, University of Iowa, Iowa City, IA, USA ** Radiology, University of Iowa, Iowa City, IA, USA TOWARDS T1RHO IN THE CLINIC: A 3.0T AND 1.5T COMPARISON
31	*Buck R.J., **Hellio Le Graverand-Gastineau M-P, ***Nevitt M, ****Wirth W, **** Eckstein, F – for the OAI investigators * StatAnswers Consulting LLC, Minneapolis, MN; ** Pfizer Global Research and Development, Groton, CT; *** University of California and OA Initiative Coordinating Center, San Francisco, CA; **** Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany CLASSIFICATION AND DISTRIBUTION OF CARTILAGE THICKNESS CHANGE IN SUBJECT KNEES: DATA FROM THE OSTEOARTHRITIS INITIATIVE
33	*Tamura S., *Nishii T., **Shiomi T., ***Yamazaki Y., ***Murase K., **Yoshikawa H., *Sugano N. * Department of Orthopaedic Medical Engineering, Osaka University, Osaka, Japan ** Department of Orthopaedic Surgery, Osaka University, Osaka, Japan *** Department of Medical Physics and Engineering, Osaka University 3D PATTERNS OF ACETABULAR CARTILAGE DAMAGE IN HIP DYSPLASIA AT PRE- AND EARLY ARTHRITIC STAGES; A HIGH-RESOLUTIONAL CT ARTHROGRAPHY STUDY

QUANTIFICATION OF TRABECULAR BONE VASCULARITY IN A RABBIT MODEL OF OSTEOARTHRITIS BY PERFUSION MICRO COMPUTED TOMOGRAPHY

Lickorish D, Haskell M.M., Wood S.A, Collett A, Goad M.E.P., Schrier D, Flory C.

Stryker Regenerative Medicine, North Grafton, USA

INTRODUCTION: MicroCT following intravascular perfusion of heavy metal preparations has found increasing use as a non-destructive analytical method of vascular architecture in a wide range of preclinical models. Intraosseous vascular analysis by contrast microCT is confounded by the difficulty in separating osseous tissues from intravascular contrast agent. The rabbit ACLT/MMT model is a common model of post-traumatic OA, however, no microCT data is available on the 3D vascularity within the femoral subchondral trabecular space in this model. Characterization of the trabecular bone vascularity in the ACLT/MMT model of OA may shed light on vascular changes that occur following ACLT trauma and provide an additional analytical endpoint for pharmaceutical interventional studies.

OBJECTIVE: To determine if a barium/gelatin perfusion protocol can yield a reproducible method of quantifying blood vessel architecture in the distal femur of a rabbit following ACLT/MMT.

METHODS:
Female NZW rabbits (n=5) underwent ACLT/MMT surgery in the left stifle. At 8 weeks post-surgery animals were given an intramuscular injection of acepromazine (0.5mg/kg) prior to induction of isofluorane general anesthesia by mask. A vascular perfusion protocol reported by Sider et al (2010) in the rat was modified to apply to the rabbit. Animals were given 1000U of heparin by ear vein 5 mins prior to a midline laparotomy. Following blunt dissection of the abdominal aorta and inferior vena cava (IVC), 2 silk sutures were placed around each vessel approximately 1cm apart. Sutures were loosely tied and the free ends secured with a hemostat to allow for ease of tying following perfusion. A 16G catheter was introduced into the abdominal aorta in a caudal direction between the 2 sutures and securely tied in place with the distal suture. Immediately prior to perfusion, the IVC was partially lacerated between the sutures to allow outflow. 300mls of warmed PBS with papaverine hydrochloride (0.02mg/mL) was perfused at a rate of approximately 50mls/min followed by 250mls of warmed 2% gelatin solution containing 30% (w/v) of micronized barium sulfate. All ligatures were then tied and the catheter removed. Animals were placed at 4 degrees overnight to allow gelatin to set. Disarticulated femurs were scanned at 18µm resolution using a Skyscan 1076 Invivo microCT (88kv, 112mA, Al. filter, Step 0.6º, 180 degree, 15min scan time). Regions of interest in the medial and lateral trabecular compartments of the distal femur were manually drawn using CTAn and vasculature threshold segmented using a constant threshold level. Percent vessel volume/tissue volume (%VV/TV) was calculated for both ACLT/MMT and contralateral control femurs. Data were analyzed using paired t test.

RESULTS: All animals were successfully perfused using this protocol. Complete perfusion of the distal vasculature with the barium/gelatin preparation was confirmed by white venous outflow. ACLT femora had markedly increased VV/TV (0.16 ± 0.04) when compared to unoperated contralateral femurs (0.07 ± 0.01, $p=0.0509$).

CONCLUSION: Preliminary data confirms that the intraosseous vascular anatomy of the distal femur following ACLT/MMT in the rabbit can be quantitatively assessed using a barium/gelatin perfusion protocol. Pilot studies in rats and rabbits demonstrate that the use of heparin and papaverine (vasodilator) greatly improved the perfusion. A limitation of the current study is the resolution of the microCT. Vessels smaller than 40µm in diameter could not be resolved. The use of higher resolution synchrotron source microCT could, however, overcome this limitation. An advantage of the barium vascular perfusion method is that it does not interfere with traditional measurements of structural parameters such as macroscopic assessments of cartilage damage by india ink, microCT analysis of trabecular/subchondral bone architecture and subsequent histology.

REFERENCE: Sider et al (2010) A new bone vascular perfusion compound for the simultaneous analysis of bone and vasculature, Microsc Res Tech. 73(7):665-72
SPONSOR: Stryker Regenerative Medicine
DISCLOSURE STATEMENT: All authors are employees of Stryker Regenerative Medicine
CORRESPONDENCE ADDRESS: david.lickorish@stryker.com; (+1) 203 745 7559

3D VISUALIZATION AND MEASUREMENT OF THE POSTERIOR CRUCIATE LIGAMENT IN A FLEXED KNEE USING OPEN-BORE 0.2T MRI

*King, A.J., **Deng, C., **Sharp, J. **Tomanek B, *Dunn, J.F.

* McCaig Institute & Experimental Imaging Centre & University of Calgary, Calgary, Canada
** National Research Council of Canada – Institute for Biodiagnotics (West), Calgary, Canada (NRC)

INTRODUCTION: Cruciate ligament biodynamics in the flexing knee are particularly complex because these ligaments change shape and orientation in 3 dimensions. Such biodynamics make single 2D slices unreliable for measuring cruciate ligament length. Crucite ligament dysfunction (trauma, rupture and laxity) is associated with OA. However, we do not have metrics on the biodynamics of healthy cruciate ligaments. This limits our understanding of how OA changes the inner workings of the knee and limits our ability to surgically restore ruptured ligaments to their natural state.

OBJECTIVE: To determine if we can measure length changes in the posterior cruciate ligament as the knee moves from extended to flexed using an open-bore low-field magnet and 3D rendering software.

METHODS: One knee each of 8 healthy subjects (mean age±standard deviation: 44.4±10.3 years) was imaged using an open-bore 0.2T MRI scanner and a single turn coil. Each knee was imaged while maximally passivley extended (mean±standard deviation: 12°±4° flexion) and while maximally passively flexed (mean±standard deviation: 117°±5°). Pulse sequence and parameters were: 3D SSFP-FID, sagittal section, TE/TR=10/20ms, matrix=128x128x32, FOV=18.0x18.0x9.6cm^3, voxel=1.41x1.41x 3.0mm^3, FA=80°, NEX=4, acquisition time=5min38s. Flip angles of less than 80° yielded poorer contrast. The PCL was manually segmented and reconstructed in 3D using Amira software (Visage Imaging). The longest distance between the attachments of the ligament was measured ALONG THE SURFACE of the anterior and posterior sides of the PCL. Using a paired t-test, the length of one side of the PCL in the extended knee was compared to the same side when the knee was flexed.

RESULTS: The PCL was located, reconstructed in 3D and measured in 7/8 subjects. The anterior aspect of the PCL increased 26.1±4.4% (mean ± standard deviation) in length after flexion ($p<0.001$, t=27.023, n=7, $t_{0.05}$=2.447). The posterior side, however, did not change length significantly (3.8±7.0%, p=n.s., t=1.467, n=7, $t_{0.05}$ =2.447)(Fig).

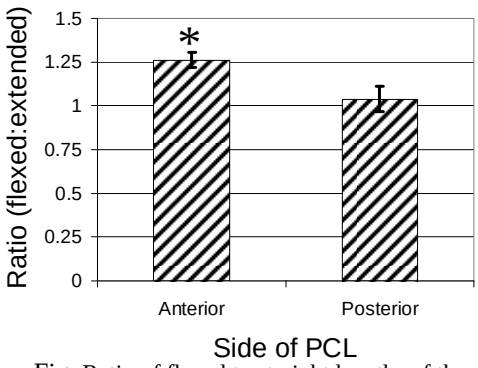


Fig. Ratio of flexed to straight lengths of the anterior and posterior sides of the PCL (mean±S.D). Ratio of 1 = no change. *flexed length significantly different from extended length, $p<0.001$, n=7.

CONCLUSION: Low-field MRI and a 3D SSFP pulse squence are sufficient to image the posterior cruciate ligament in healthy volunteers. By reconstructing the PCL in 3D using visualization software, we were able to use the shape of the PCL's attachments to measure a similar path along the PCL in both extended and flexed knees. Our measurements were accurate enough to detect length changes in the PCL during knee flexion. Ours are the first direct measurements of the length of the surface of the PCL. Previous studies have used indirect methods and produced conflicing results. Our results suggest that the PCL length change depends on where it is measured; our mesaurements reveal that the anterior and posterior sides of the PCL change in length differently during knee flexion. This position-dependence suggests that there is a difference between the biomechanical environment and/or the biomechanical properties of the anterior and posterior sides of the PCL. Future studies in our lab will investigate whether this difference also exists in OA patients and patients who have had their PCL surgically reconstructed.

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CORRESPONDENCE ADDRESS: dunnj@ucalgary.ca, +1-403-210-3886.

IN VIVO TRANSPORT OF Gd-DTPA^{2-} INTO HUMAN KNEE CARTILAGE

*&**Lammentausta E., **Hawezi Z., ***Tiderius C.J. and **Dahlberg L.

*Oulu University Hospital, Oulu, Finland
**Lund University, Malmö, Sweden
***Skåne University Hospital, Malmö, Sweden

INTRODUCTION:
dGEMRIC is a quantitative MRI method utilizing anionic contrast agent Gd-DTPA^{2-}. The fixed charge density of cartilage, induced by GAG, is suggested to determine the contrast agent distribution in cartilage [1]. However, very little is known about temporal and spatial transport patterns in vivo. This knowledge would help interpreting dGEMRIC with respect to cartilage molecular structure.
OBJECTIVE:
To investigate the transport of Gd-DTPA^{2-} into human knee cartilage.
METHODS:
Asymptomatic volunteers (n=5, age 20-45 years) were examined using a 1.5 T scanner (Siemens, Erlangen, Germany). T_1 was measured using inversion recovery fast spin echo sequence (TR=2000 ms, 6 TI's between 50 and 1600 ms, FOV 12 cm, matrix 256*256, slice thickness 3 mm). Single sagittal slice was localized into the middle of lateral condyle of the left knee. Before triple dose (3 mM/kg) of Gd-DTPA^{2-} (Magnevist, Bayer Schering, Germany) injection, T_1 was measured. Subsequently, the volunteers walked up and down stairs. T_1 measurement was repeated every 12 minutes until two hours. Between measurements the volunteers walked the stairs. Regions of interest were segmented into femoral (central, anterior and posterior) and tibial (central) cartilage. The change of relaxation rate (ΔR_1) was calculated.
RESULTS:
ΔR_1 increased faster in the superficial than the deep cartilage layer at all regions (Figure 1). ΔR_1 kept increasing at all regions throughout the entire measurement period. There was a significant difference between deep and superficial ΔR_1 at all time points, except for anterior femur (Kruskal-Wallis test).
DISCUSSION:
The current results indicate that no transport of Gd-DTPA^{2-} into cartilage occurs from the subchondral bone, because in the deep cartilage regions of central femur and tibia at the earliest time points ΔR_1 could be considered to be zero in the limits of the reproducibility of dGEMRIC [2]. The amount of contrast agent and the speed of the transport vary considerably between different regions, with lower amounts and slower transport with more weight bearing regions, which is in agreement with previous results about the relation between loading conditions and dGEMRIC [3]. With transport only from the synovial side, a T_1 analysis of bulk cartilage regions will be influenced by cartilage thickness.
REFERENCES:
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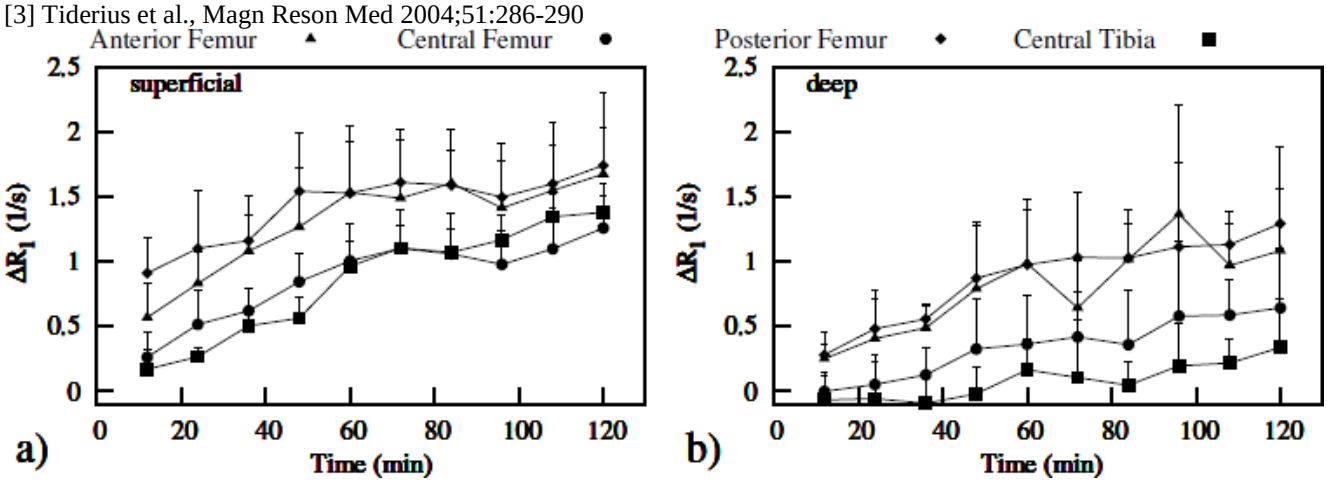


Figure 1. The change of relaxation rate (ΔR_1) representing the contrast agent concentration as a function of time after Gd-DTPA^{2-} injection in different cartilage regions for a) superficial and b) deep regions.

CORRESPONDENCE ADDRESS: eveliina.lammentausta@oulu.fi

NOCTURNAL CHANGES IN FEMORO-TIBIAL CARTILAGE THICKNESS IN YOUNG HEALTHY ADULTS

*Sitoci H., **Hudelmaier M., **Eckstein F.

* Institute of Anatomy, Ludwig Maximilians Universität, Munich, Germany
** Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria

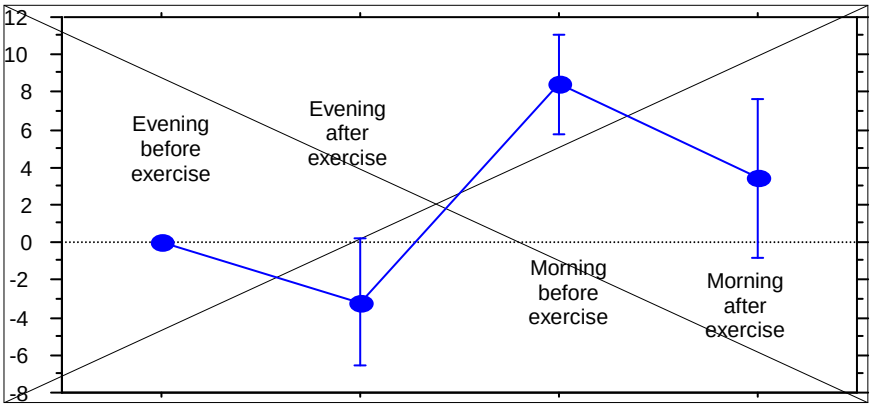
INTRODUCTION: Magnetic resonance imaging is a promising tool for analyzing cartilage physiology and function in vivo. This can be used also to characterize the mechanical target environment of prospective cartilage transplants. Cartilage deforms during loading, but little is known about its actual in situ deformation during physiological loading and its recovery after deformation.

OBJECTIVE: To study "nocturnal" changes in knee cartilage thickness in the femorotibial and in the femoropatellar joint, and to explore whether post-exercise deformation is greater in the morning (after nocturnal rest) than in the evening.

METHODS: Coronal magnetic resonance images (fast low angle shot = FLASH sequence) of the right femoro-tibial joint were acquired in 8 young healthy volunteers (4 men, 4 women; age 20 to 26 yrs.), and axial images of the right patella in 17 volunteers (9 men, 8 women; age 20 to 28 yrs). Images were acquired after a normal day, and then after 30 deep knee bends (axial images) and after statically loading one leg for 2mins with 150% body weight (coronal images). The volunteers then remained unloaded overnight and the same protocol and exercise was repeated in the morning. The mean cartilage thickness was determined in the medial (MT) and lateral tibia (LT) [coronal images], and in the patella (P) [axial images], after segmenting the total bone areas (tAB) and cartilage surfaces (AC).

RESULTS: A significant increase ($p<0.01$) in cartilage thickness was observed between evening (pre-exercise) and morning (pre-exercise): +8.4% in the MT (Fig. 1), +6.2% in the LT and +2.4% in the P. Deformation in the morning (-4.6% in MT/-5.1% in LT/-6.8% in P) tended to be greater than that in the evening (-3.2% in MT/-3.7%in LT/-5.4% in P). No differences in nocturnal thickness increase or in post-exercise deformation were observed between men and women.

Figure 1: Percent (%) changes in mean cartilage thickness in the medial tibia (MT) between evening and morning (before and after exercise [knee bends and static loading])



CONCLUSION: Healthy knee cartilage is physiologically compressed during a normal work day. This effect is stronger in the femoro-tibial than in the femoro-patellar joint, likely because the femoro-tibial joint is loaded more strongly (and continuously) during a normal day. Similar to the intervertebral disc, knee cartilage (thickness) recovers over night under physiological rest. After nocturnal periods of unloading, morning post-exercise deformation of the cartilage has a greater magnitude than evening post-exercise deformation. The findings have potential implications for standardizing the day time of acquisition in clinical trials, in which cartilage loss is measured longitudinally.

SPONSOR: The German Research Foundation (DFG).
DISCLOSURE STATEMENT: see affiliations
CORRESPONDENCE ADDRESS: felix.eckstein@pmu.ac.at

A STATISTICAL/GRAPHICAL TOOL TO IDENTIFY KNEE OA PHENOTYPES BASED ON MRI CARTILAGE THICKNESS MEASURES

*Cicconetti, G., *Matheny, C.
* GlaxoSmithKline, Upper Merion, PA, USA

INTRODUCTION: Fundamental questions to assist development of DMOADs include 'Can knee OA phenotypes be defined based on MRI features?' and if so, 'Do these knee OA phenotypes associate with progression and/or response to intervention?' Buck et al (2011) considered subregional cartilage thickness changes as to address questions related to disease progression. Here, we explore the merits of statistical and graphical tools that utilize a multi-dimensional distance measure to characterize individual knees relative to the 'typical' knee in the cohort. An inherent advantage of this approach is that it accounts for correlation among thicknesses measured in the various subregions. Since this method also provides a way to rank individual knees relative to 'typical' knee, this method can serve as a tool to assist in establishing knee OA phenotypes.

OBJECTIVE: The objective is to determine if applying multi-dimensional distance measures to subregional cartilage can be used to discriminate knee OA phenotypes.

METHODS: Regional knee cartilage thickness measures were obtained from 238 subjects from the OAI study with Baseline, Yr 1 and Yr 2 MRI data available to sponsors participating in the OAI Consortium. MRIs were acquired using the FLASH sequence on the right knee; for brevity focus here is on left femoral tibial compartment (LFTC). Subregional cartilage thicknesses are treated as vectors originating from a multi-dimensional normal distribution, and a statistical method for computing distance in multi-dimensional space is applied to baseline cartilage thickness measures. Under the assumption of multivariate normality, these distance measures follow a chi-square distribution. The baseline thickness measures obtained from the eight subregions associated with the LFTC were vectorized as follows: Let x be the 1x8 vector associated with the first subject's 8 baseline subregional cartilage thickness measures. Further, let S be the 8 x 8 sample covariance matrix and let y be the 8-dimensional vector of baseling subregional cartilage thickness means associated with the sample of 238 knees. Then, the first subject's Squared Mahalanobis Distance is $MD2(x) = (x - y)inv(S)tr(x - y)$, where tr( ) is the transpose function, and inv(S) is the inverse of the covariance matrix. MD2(x) is distributed as a Chi-Square with 8 degrees of freedom (df, ChiSq(8)). Repeat this to obtain distance measures for all knees. With adjustments to df, this approach extends naturally to LT, cLF, MTFC, etc.

RESULTS: Those with distance measures falling below the 25th percentile of ChiSq(8) were relatively similar to the typical knee (as characterized by averaging the subregional cartilage thicknesses). However, in focusing on knees with more extreme distance measures, the number of knees identified decreases sharply, cartilage distribution is decidedly more atypical, and it becomes easier to discriminate phenotypes. For example, the 47 knees associated with distance measures beyond the 75th percentile of ChiSq(8) can readily be bucketed into groups: Knees may have consistently large (or small) thickness measures across many subregions, or buck the mean trend, having larger than typical thicknesses in some subregions, and smaller than typcial thicknesses in others. Graphical displays further facilitate intepretation and discrimination.

CONCLUSION: This methodology facilitated knee OA phenotype identification by identifying subjects with measurements that deviate from the typical knee. This approach is similar to the t-score used for osteoporosis: the t-score provides a standardized distance measure that relates an indivdual's bone minearl density to a healthy population. With only one variable of interest, the (positive/negative) sign of the t-score readily informs if one is better or worse than the population mean. In the current setting, since the distance measure is non-negative and only serves as a first sieve: it is necessary to interrogate the subregional thicknesses of outliers further to complete the process of phenotype identification. In this exercise the cohort under study characterized the 'typical' knee. However, the analogy with t-score can be further extended by replacing the vector of mean cartilage thicknesses and covariance matrices obtained from these 238 knees, with comparable measures obtained from a healthy cohort.

SPONSOR: GlaxoSmithKline
DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: greg.2.cicconetti@gsk.com

Reference: Buck, R., Wyman, B., Hellio Le Graverand, M., Hunter, D., Vignon,Wirthm, W., Eckstein, F. Using ordered values of subregional cartilage thickness change increases sensitivity in detecting risk factors for osteoarthritis progression. Osteoarthritis and Cartilage 19 (2011) 302-308.

COMPRESSION OF THE KNEE UPON WEIGHT LOADING IN HEALTHY AND OSTEOARTHRITIS SUBJECTS AS MEASURED BY MRI AND X-RAY

*Wyman BT., **Cotofana S., *Zhang Y., ***Souza RB., *Clemmer R., *Hellio Le Graverand M-P, ***Li X., ***Majumdar S., ***Link TM., ***Eckstein F., ****Vignon E.

* Pfizer Inc, Groton, CT, USA; ** Paracelsus Medical University, Salzburg, Austria; *** University of California, San Francisco, CA, USA; **** Claude Bernard University, Lyon, France

INTRODUCTION: Measurements of cartilage morphology with MRI have not been shown to be considerably more sensitive to disease progression than joint space width (JSW) measured from x-ray [1]. This may be partially a result of knee x-rays being acquired in standing position with the cartilage loaded by body weight while MRI is acquired supine with no load being applied to the knee. This study aims to investigate the impact of loading on JSW measured from x-ray and cartilage thickness measured from MRI and whether participants with knee OA encounter greater compression of knee cartilage under loading compared with healthy subjects.

METHODS: Thirty-one women age 55 (±6.0) years and BMI 28 (±2.4) had x-rays and MRI of the knee in weight bearing (WB) and non weight-bearing (NWB) positions. Eleven subjects had no OA, Kellgren Lawrence grade (KLG) of 0. The other subjects had mild or moderate radiographic OA KLG 2 (n=10) and KLG 3 (n=10). Lyon-schuss x-rays were acquired using a Synaflexer (Synarc, San Francisco, USA) Plexiglas positioning frame. The WB x-ray was acquired with the subjects standing while the NWB x-ray was acquired with the subjects lying prone. Care was taken to insure the medial-tibial margins were aligned and the knee positioning was consistent between WB and NWB. The minimum medial JSW was measured using automated software (HOLYs, Lyon France) by an experienced reader blinded by subject and loading. Subjects were positioned supine in the scanner on a custom-made MRI compatible loading device. The knee was positioned with 15º of flexion and 10º of external foot rotation approximating the positioning of the Synaflexer used for x-rays. Coronal, 3D water-excite SPGR images, were acquired on a 3.0T GE scanner using an 8-channel knee coil with TR = 23 ms, TE = 6.88 ms, flip angle = 18º, BW = 31.25 KHz, FOV = 14 cm, slice thickness = 1.5 mm, and matrix = 512x512. The sequence was first acquired with no loading (NWB) and then repeated with the leg pressing against a weight equal to half of the subjects body weight. The cartilage was manually segmented using proprietary software (Chondrometrics GmbH, Ainring, Germany) and the average thickness of the medial femoral tibial cartilage (MFTC_ThCtAB) was calculated. Values were reported as the % difference calculated as (WB – NWB)/NWB x 100%. Negative values indicate compression under loading. A linear model was fitted to assess the effect of KLG on the percent change from NWB in the endpoint and significance was determined, without multiplicity adjustment, at the $p < 0.05$ level (two sided).

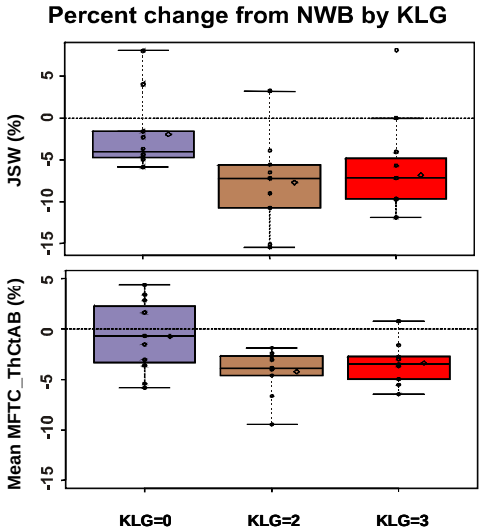


Figure 1 Box plots showing individual data (o), median values (middle bar) 25%-75% quartiles (colored box), mean (◊), whiskers show data range excluding identified outliers. **Top**: %change in JSW from non-WB measured by x-ray. **Bottom:**, %change in mean MFTC_ThCTAB measured by MRI.

RESULTS: The mean change for KLG 0 was -2.0% and -0.76% for JSW and MFTC_ThCtAB respectively (p=NS). For KLG 2 the mean change was -7.7% and -4.2% (p=0.0003 and 0.0048, respectively) for JSW and MFTC_ThCtAB and for KLG 3 the mean change was -6.9% and -3.4% (p=0.0002 and 0.0012, respectively) for JSW and MFTC_ThCtAB.

DISCUSSION: Compared to healthy subjects, there was a significant decrease in JSW and mean cartilage thickness in MRI in the knees of subjects with OA under WB conditions. It is possible that the increased compression in the joint space and cartilage seen in OA subjects may be a result of compositional and mechanical tissue degradation which is not apparent from morphological measurements made during NWB conditions.

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ACKNOWLEDGMENT: Karen Huerta for skillful x-ray acquisition, Choogsoo Shin for data acquisition assistance and Thelma Munoz for study coordination.
CORRESPONDENCE ADDRESS: helliomp@pfizer.com
REFERENCES: [1] Hellio Le Graverand, ARD 2008. [2]http://en.wikipedia.org/wiki/Studentized_residual

HIP BONE MINERAL DENSITY DOES NOT INFLUENCE TIBIOFEMORAL BONE MARROW LESION SIZE

*Driban J.B., **Lo G.H., *Price L.L.,*McAlindon T.E.

* Tufts Medical Center, Boston, USA
** Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, USA

INTRODUCTION: High hip bone mineral density (BMD) has been recognized as a potential risk factor for incident knee OA but the relation between hip BMD and knee OA progression remains unclear. If hip BMD influences OA progression then the greatest influence may be on a bone-related OA lesion. Subschondral bone marrow lesions (BMLs), common OA-related MRI findings, can get larger and smaller over time and are associated with OA progression. No study has evaluated the relationship between hip BMD and knee BML size.

OBJECTIVE: To evaluate the cross-sectional and longitudinal associations between hip (total hip and femoral neck) BMD and knee BML size.

METHODS: The sample comprised 103 OA knees (KLG $\geq$ 2) from participants in a randomized-clinical trial of vitamin D who had sagittal and coronal IM fat-suppressed (FS) 1.5-tesla MRIs and dual-energy x-ray absorptiometry (DXA) scans at baseline and 2-years. The IM FS sequences had a time to recovery (TR) of 2950 ms, time to echo (TE) of 31 ms, slice thickness of 3 mm, space thickness of 0.5 mm, and field of view (FOV) of 140 mm. We defined BMLs as regions of high-signal intensity on IM FS images located within 1.0 cm of hyaline cartilage and present on $\geq$2 sagittal or coronal images and classified them within 4 regions: index femur, index tibia, nonindex femur, and nonindex tibia. Two rheumatologists defined the index compartment as the compartment (medial or lateral) with greater pathology based on radiograph and MRI findings. We measured the maximal anterior-posterior, medial-lateral, and vertical dimensions of each BML. Their product represented the approximate volume of each BML (intra-tester ICC = .96). When multiple BMLs were present in a region their volumes were summed to calculate regional volume. Total knee BML size was calculated by summing all of the BML volumes in a knee. Total hip and femoral neck BMD were assessed with DXAs (GE Lunar Prodigy Advance Bone Densitometry scanner). We assessed cross-sectional and longitudinal correlations between BMD and BML size using Spearman rank correlation coefficients. All analyses were performed in SAS 9.2 and statistically significant correlations were defined by $p \leq 0.05$.

RESULTS: Participants were 63.4±8.6 years of age, body mass index 29.8±5.3 kg/m^2, 64% female, and had definite radiographic knee OA (52% KLG=2, 30% KLG=3, and 17% KLG=4). Baseline total hip and femoral neck BMD was not correlated to baseline BML size or longitudinal change (see table). Longitudinal change in total hip and femoral neck BMD was not associated with longitudinal changes in BML size (r = -0.11 to -0.03).

Table. Spearman Correlation Coefficients (95% CI) Between Baseline Total Hip and Femoral Neck Bone Mineral Density (BMD) as well as Knee Bone Marrow Lesion (BML) size

		Total Hip BMD: Baseline	Femoral Neck BMD: Baseline
Baseline:	Total Knee BML Size (n = 104)	0.05 (-0.14 to 0.24)	0.08 (-0.12 to 0.27)
	Index Femur BML Size (n = 73)	0.07 (-0.16 to 0.30)	0.11 (-0.13 to 0.33)
	Index Tibia BML Size (n = 74)	0.15 (-0.08 to 0.37)	0.23 (0.00 to 0.44)
24-month Change:	Total Knee BML Size (n =104)	0.01 (-0.18 to 0.21)	-0.05 (-0.24 to 0.15)
	Index Femur BML Size (n = 79)	0.13 (-0.10 to 0.34)	0.11 (-0.11 to 0.32)
	Index Tibia BML Size (n =76)	0.01 (-0.22 to 0.23)	-0.03 (-0.26 to 0.20)

CI= Confidence Interval. No correlation coefficients were statistically significant ($p > 0.05$).

CONCLUSION: Among patients with knee OA, hip BMD was not related to knee BML size. These findings support a recent epidemiological study that reported no association between femoral neck BMD and JSN progression among patients with knee OA.

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CORRESPONDENCE ADDRESS: jdriban@tuftsmedicalcenter.org

PREDICTION OF CARTILAGE LOSS BY ANALYSIS OF TRABECULAR TIBIA BONE STRUCTURE

*,***Marques J., **Dam E.

* University of Copenhagen, Copenhagen, Denmark
** BiomedIQ, Rødovre, Denmark

INTRODUCTION: Degradation of the articular cartilage and overall bone remodeling are the main effects of OA progression. MRI has helped experts to diagnose OA by providing methods for quantification the multiple components of the knee joint and detecting early tissue changes. Recently, the automatic quantification of the cartilage volume using MRI scans was reported have good agreement with manual segmentations.

OBJECTIVE: We analyzed MRI scans to investigate the feasibility of predict the rapid/slow progressors of tibial volume cartilage loss by a fully automatic quantification the trabecular tibia bone structure.

METHODS: The longitudinal study included 159 subjects from a community-based, non-treatment study. The dataset consisted of 268 knees MRI, after exclusion of scans due to the subjects that dropped out in the follow-up or to acquisition errors. The population characteristics were: age 56±16, BMI 26±4, 47% female, and 19% with radiographic OA (KLG>1). The KLG was determined from load-bearing radiographs in semi-flexed position using the SynaFlex (Synarc). MRI scans were acquired using a Turbo 3D T1 sequence from a 0.18T Esaote scanner (40° FA, TR 50ms, TE 16ms, scan time 10 minutes, resolution 0.7mm x 0.7mm x 0.8mm).
MRI was performed at baseline and 21 months later to assess cartilage volume changes over time. The cartilage volume was estimated by a process of segmentation.
To quantify the bone structure, initially a voxel classification method determines a region-of-interest (ROI) by segmenting the tibia bone. From the ROI, a generic set of 534 features is extracted by applying Gaussian derivatives at multiple scales. At next step, a machine learning approach applies partial least square feature extraction to identify the linear combination of the features that best relate the tibia structure with the volume cartilage loss. The features extracted are employed to train the linear discriminant analysis (LDA) classifier using cross-validation. The outcome is the probability of rapid cartilage volume loss progression.

RESULTS: By quantifying the bone structure, the framework predicted the rapid/slow progressors with odds ratio of 2.38 ($p<0.05$). The figure shows the cartilage volume loss separated out by 2 and 3-quantiles of the bone marker. The median of the subjects classified as slow and rapid progressors was 1.6% and 4.4% per year respectively.

CONCLUSION: The investigation revealed that is possible to predict the cartilage volume loss by analyzing the tibia bone structure. In practical terms, the developed quantification can be applied to support experts in selecting patients in longitudinal studies. The advantages of this approach are the use of low cost MRI equipments and a fully automatic computer-based framework, which allows scalability to large, multi-center studies.

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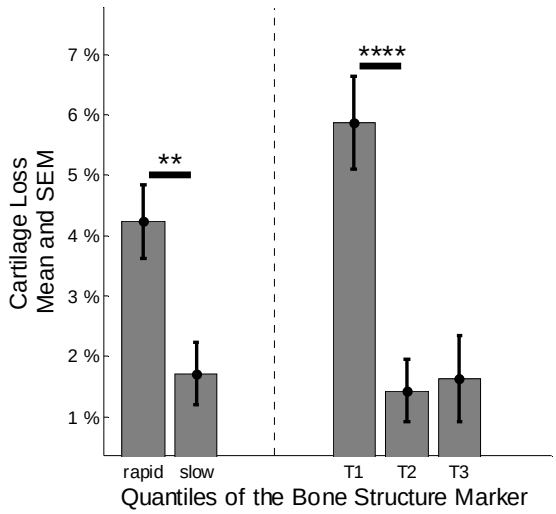
CORRESPONDENCE ADDRESS: jm@nordicbioscience.com



LONGITUDINAL CHANGES IN INTERMUSCULAR FAT VOLUME AND QUADRICEPS MUSCLE VOLUME IN THE THIGHS OF FEMALE OAI PARTICIPANTS

Beattie K.A.*, MacIntyre N.J.*, Ramadan K.*, Inglis D.*, Maly M.R.*
*McMaster University, Hamilton, ON, Canada

INTRODUCTION: Obesity and muscle weakness are risk factors for both incident and progressive knee OA. However, longitudinal changes in these tissues have not been investigated. While changes in thigh fat and muscle cross-sectional area can be measured through analyses of CT and MR images, changes in tissue volume are more robust and less sensitive to error due to inconsistencies in scanning regions of interest between time points. Given that longitudinal volume changes in muscle and fat have not been quantified, the clinical relevance of these changes are also unknown.
OBJECTIVES: To quantify rates of change in quadriceps muscle (QM) and intermuscular fat (IMF) volumes over two years in the thighs of women in the incident and progression cohorts of the OAI study and examine group differences.

METHODS: The online OAI database was queried for women ≥50 years old in the incident or progression cohorts with baseline and two-year thigh images available. Eligible women with mid-thigh T1-weighted axial MRI scans consisting of 15 contiguous slices (5 mm slice thickness) were randomly selected. Anonymized baseline and follow-up were registered, using Analyze 8.1 (AnalyzeDirect, Inc., Overland Park, KS, USA) and segmented using SliceOmatic 4.3 (Tomovision, Magog, QC, Canada). Baseline and follow-up scans were segmented in pairs (N=100) with the segmenter blinded to image acquisition time point. Image pairs were excluded if there was a) inconsistent spatial resolution between baseline and follow-up scans, b) compressed or flattened thighs on either one of the two scans or c) less than 12 of the 15 slices matched between baseline and follow-up. Scans were segmented on a slice-by-slice basis to quantify QM and IMF volume in the 12 most proximal matching slices. Descriptive statistics were calculated for each group and differences in tissue volume changes between cohorts were tested using ANCOVA with age considered a covariate.

RESULTS: Image pairs were segmented for 49 women in the incident cohort (mean (SD) age 61.4 (7.5) yrs; mean BMI 26.8 (4.6) kg/m^2) and 51 women in the progression cohort (mean (SD) age 64.3 (7.0) yrs; mean BMI 29.3 (5.1) kg/m^2). The mean (SD) baseline QM and IMF volumes in the incident cohort were 259.6 (53.3) cm^3 and 101.4 (26.2) cm^3, respectively. Corresponding baseline QM and IMF volumes in the progression cohort were 251.7 (50.3) cm^3 and 111.5 (37.7) cm^3, respectively. The mean QM volume increased by 0.4 (5.1)% in the incident cohort compared to a decrease of 1.8 (5.9)% in the progression cohort. Concurrently, the mean IMF volume increased by 2.7 (7.4)% in the incident cohort as compared to 3.8 (7.4)% in the progression cohort. The group difference in change in QM volume when adjusted for age was statistically significant [ANCOVA: $F(1,97)=4.029$, $p=0.048$)]. However, a significant difference between the groups was not observed for the age-adjusted change in IMF volume [ANCOVA: $F(1,97)=0.825$, $p=0.366$)].

CONCLUSIONS: Longitudinal changes in QM and IMF volumes appeared larger in women with established knee OA compared to women at risk for knee OA, although only the loss in QM volume was statistically significant. Women with established knee OA lost muscle mass and gained fat mass, results consistent with muscle disuse or atrophy. An investigation of the clinical relevance of these changes is warranted.

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CORRESPONDENCE ADDRESS: Dr. Karen Beattie, 501-25 Charlton Ave. East, Hamilton, ON, L8N 1Y2, Canada; karen.beattie@camris.ca

COMPREHENSIVE MORPHOLOGICAL CHARACTERISATION OF ARTHRITIS IN ANIMAL MODELS BY MICRO-COMPUTED TOMOGRAPHY

*Stok K. S., **Nesic D., ***Zulliger M., *Firminger C.,*Müller R.

* Institute for Biomechanics, ETH Zürich, Switzerland
** Department of Clinical Research, University of Bern, Switzerland
*** SCANCO Medical AG, Brüttisellen, Switzerland

INTRODUCTION: Understanding the development of osteoarthritis (OA) and the subsequent establishment of efficacious treatment strategies have been confounded by the inability to visualise the condition of the cartilage and quantitatively assess and monitor pathological changes in time. Previous studies have demonstrated the potential of combining a contrast agent Hexabrix^{TM} with micro-computed tomography (micro-CT) imaging in animal and human cartilage explants or disrupted joints. Hexabrix^{TM} is a negatively-charged iodinated dimer which inversely correlates to the proteoglycan content of articular cartilage allowing quantitative assessment of cartilage quality [1].

OBJECTIVE: Develop a quantitative 3D imaging methodology for the measurement and analysis of intact knee joint tissues in a commonly-used animal model of OA by combining Hexabrix^{TM} with micro-CT imaging.

METHODS: The tibio-femoral right-leg joints from 11 rats were employed in the first stage to establish the SOP for the scans that would distinguish between joint space, soft tissue and bone. Various contrast agents were explored by either direct injection into the knee joint, to encourage diffusion into the cartilage or to fill the joint space, or by immersing the sample and staining the surrounding joint structures. Additionally, sample preparation and handling methods, including warming, massaging, flexion and ultrasonic vibration were explored to enhance flow through the joint space and improve distribution. Subsequently, the knee joints were scanned with micro-CT (μCT 80, Scanco Medical, CH) at an isotropic voxel size of 10 μm. The outcome criterion was the clear distinction of structures inside the joint (i.e. cartilage, joint space and bone) within our images. These structures should be clearly manually segmented from each other, with the option of automated segmentation in the best case. Secondary exclusion criteria for any agent, based on visual examination of the images, included the absence of any contrast or unequal filling of the joint space. Preparation and handling methods were further optimised according to the success of the output images.

RESULTS: An SOP was established for optimal sample preparation, handling, stain and scan quality. The injected silicon-based contrast agent was able to fill the joint space and distinguish the synovial spaces separately from the cartilage and surrounding tissues. Using massage and flexion of the joint after injection, a reproducible and even stain could be achieved. Following this, immersion of the sample overnight in Hexabrix^{TM} and re-scanning enabled not only the discrimination of the cartilage tissue for morphometric analysis, but also demonstrated the potential to correlate GAG content with the gradation of grey content in the stained tissue. All structures of interest could be both manually and automatically segmented, providing a way forward for the project.

CONCLUSION: The established protocol has great potential to provide a sensitive and reproducible technique for gathering 3D image data on both healthy and diseased animal models. The method is currently being tested against the histological gold standard. In a next step this novel technique will be reproduced in rabbit and goat models with the goal of providing a preclinical tool for assessment of commonly-used animal models of OA. Additionally, more quantitative outcome criteria based on preclinical and clinical interests will be defined for a more comprehensive overview of the OA joint. These quantitative outcomes will include cartilage measures such as GAG content, volume, surface, surface roughness; joint measures such as curvature and morphometry, alignment angles and translation, joint space volume and thickness; bone measures such as subchondral cortical and trabecular bone morphometry, and number of osteophytes.

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CORRESPONDENCE ADDRESS: kas@ethz.ch

INTEROBSERVER VARIATION OF QUANTITATIVE MENISCUS ANALYSIS USING CORONAL MPR DESSwe and IW TSE MR IMAGING

*Siorpaes K., *Wenger A., *Bloecker K., **Burgkart R., *Wirth W., *Eckstein F.

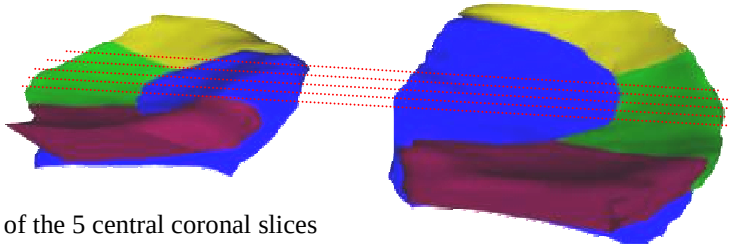
* Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg, Austria
**Clinic for Orthopaedics and Traumatology, Technical University Munich, Germany

INTRODUCTION: The meniscus plays an important role in the onset, progression and clinical management of knee OA. 3D morphometric analysis [1] can reveal quantitative relationships of meniscus size, shape, and extrusion that are not apparent at subjective evaluation.

OBJECTIVE: 1) To determine the inter-observer reproducibility of the quantitative analysis of the medial and lateral meniscus; 2) To compare the inter-observer reproducibility in different subregions of the meniscus, specifically the anterior horn, pars intermedia, and posterior horn (when relying on a coronal protocol); 3) To compare the inter-observer reproducibility, the agreement and the correlation of MPR DESSwe gradient echo with intermediately weighted (IW) turbo spin echo (TSE) imaging.

METHODS: 8 knees (4 healthy, 4 with definite radiographic knee OA) were drawn from the Osteoarthritis Initiative (public-use 0.F.1 and 0.E.1. data sets). Segmentation of the tibial plateau area (ACdAB) and the tibial (TA), femoral (FA), and external (EA) meniscus area (Fig. 1) were performed by 3 observers (KS, AW, KB). Coronal MPR DESSwe images (resolution 1.5x 0.36x 0.36 mm) and IW TSE images (resolution 3.0x 0.36x 0.36 mm, interpolated to 1.5mm) were used, and quantitative measures of meniscus size and position computed in 3D [1] for the entire meniscus and subregions (Fig. 1). The inter-observer reproducibility was determined by calculating the root mean square (RMS) standard deviation (SD) for measures of extrusion, and the RMS coefficient of variation (CV%) for measures of size. These values were compared with the inter-subject variability across the 8 knees.

Fig. 1: 3D reconstruction of the medial (right) and lateral (left) tibial plateau (ACdAB), and the medial and lateral meniscus:
- ✓ Anterior horn = yellow
- ✓ Pars intermedia = green
- ✓ Posterior horn = dark red



* the 5 red lines indicate the position of the 5 central coronal slices

RESULTS: Inter-observer reproducibility errors were (considerably) smaller than the inter-subject variability for all parameters (ratio 1:2 to 1:6). This was true for the MPR DESSwe and the IW TSE. Generally, larger inter-observer errors were observed for the lateral than for the medial meniscus. Inter-observer errors were similar for the MPR DESSwe and the IW TSE. With regard to mean extrusion, (Ex.Me) inter-observer errors were much smaller for the central 5 (coronal) slices (Fig. 1) than for entire meniscus (DESSwe: 0.25 vs. 0.53 mm in the medial and 0.28 vs. 0.65 mm in the lateral meniscus; IW TSE: 0.27 vs. 0.48 mm in the medial and 0.17 vs. 0.73 mm in the lateral meniscus). Generally, the inter-observer reproducibility was higher in the meniscus body than in the anterior and posterior horns. Absolute (mean) values for surface areas (but not thickness and extrusion) were somewhat smaller in IW TSE than in MPR DESS, but high correlations were observed between both sequences (r=0.99 for medial ACdAB; r=0.83 for medial (tibial) meniscus area; r=0.98 for mean meniscus thickness; r=0.89 for mean meniscus extrusion).

CONCLUSION: Meniscus morphometry has acceptable inter-observer reproducibility, with inter-observer deviations being considerably smaller than the inter-subject variability. Although minor systematic offsets were observed between DESS and IW TSE, 3D measures of meniscus size and position were highly correlated when being derived from these imaging protocols.

REFERENCES: [1] Wirth W et al. Magn Reson Med 2010; 63 1162-71
SPONSOR: Image acquisition: the OAI. Image analysis: PMU Forschungsförderungsfond (FFF).
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CORRESPONDENCE ADDRESS: felix.eckstein@pmu.ac.at

ARE SEPARATE QUANTITATIVE RADIOGRAPHIC FEATURES (KIDA) OF KNEE OSTEOARTHRITIS VERY EARLY IN THE DISEASE (CHECK) ASSOCIATED WITH CLINICAL PROGRESSION DURING FOUR-YEAR FOLOW-UP?

* [&] ** Kinds M.B., * Marijnissen A.C.A., ** Vincken K.L., ** Viergever M.A., *** Drossaers-Bakker K.W., * Bijlsma J.W.J., * [&] **** Welsing P.M.J., * Lafeber F.P.J.G.

* Rheumatology & Clinical Immunology, University Medical Center Utrecht, the Netherlands
** Image Sciences Institute, University Medical Center Utrecht, the Netherlands
*** Institute for Behavioral Research, University of Twente and Medisch Spectrum Enschede, the Netherlands
**** Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, the Netherlands

INTRODUCTION: The inconsistent association between radiographic and clinical features of OA hampers definition, diagnosis, and evaluation of progression. Separate quantitative radiographic features of OA might be associated with clinical progression of disease. In clinical practice progression of clinical and radiographic features will be determined by comparison with clinical and radiographic features at the previous visit.

OBJECTIVE: To evaluate whether separate quantitative radiographic features at baseline are associated with clinical progression during four-year follow-up in a cohort of participants with early knee OA.

METHODS: From the early OA study Cohort Hip & Cohort Knee (CHECK), participants with knee pain only were selected. Clinical progression was evaluated by use of the pain and function scale of the WOMAC index (0-100 scale; 100 is worst). To account for variation the baseline WOMAC score was calculated as the mean of the first two years (0 and 1) and compared to follow-up score, calculated as the mean of the last two years (3 and 4). Clinical progression was classified by the quintile approach (proposed by Sharma) as ‘good’ (move to lower quintile or remain in lowest two quintiles) or ‘poor’ (move to higher quintile or remain in highest three quintiles) outcome. Standardized posteroanterior semiflexed knee radiographs were evaluated with Knee Images Digital Analysis (KIDA) for quantitative measurement of JSW, osteophyte area (OPA) and bone density (BD) in the lateral and medial compartment of femur and tibia. Using logistic regression it was evaluated which KIDA parameters at baseline were associated with clinical progression, in addition to baseline WOMAC score and patient characteristics.

RESULTS: Of 266 participants the baseline mean WOMAC pain score was 21 and 23 for ‘good’ and ‘poor’ outcome respectively, and mean function score was 18 and 23 for ‘good’ and ‘poor’ outcome. In the ‘poor’ outcome group, pain and function values increased to 30 at follow-up. OPA at the lateral and medial compartment were significantly ($p=0.003$ and $p=0.010$) associated with WOMAC pain outcome, in addition to baseline pain and patient characteristics. Predicted probability (mean ± SD [range]) for ‘poor’ pain outcome was 0.53±0.15 [0.17-0.92]. For WOMAC function outcome a significant association was found for JSW minimum, OPA lateral, and OPA medial ($p=0.028$, 0.002, and 0.004) in addition to baseline characteristics. Predicted probability for ‘poor’ function outcome was 0.56±0.17 [0.15-0.95]. In contrast, the commonly used KLG was not statistically significantly associated with pain and function outcome.

CONCLUSION: In individuals with early complaints of knee OA, pain and function scores are relatively low at baseline, and are slightly increased at follow-up in the ‘poor’ outcome groups. Separate quantitative radiographic features measured by KIDA at baseline are statistically significantly (although weakly) associated with clinical progression of pain and functional limitations during four-year follow-up in a cohort of participants with early knee OA, an association not found with KLG.

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DICLOSURE STATEMENT: No conflict of interest.
CORRESPONDENCE ADDRESS: M.B.Kinds@umcutrecht.nl.

ONE-YEAR RATE OF CHANGE IN SUBCHONDRAL BONE SIZE IN OSTEOARTHRITIC AND HEALTHY KNEES

* Hudelmaier M, *Wirth W, *Maschek S, **Nevitt M, *Eckstein F for the OAI Investigators Group

* Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany
** University of California and OA Initiative Coordinating Center, San Francisco, CA

INTRODUCTION: An increase in the size of the subchondral bone area (tAB) in knee OA has been reported in several studies, but it is unclear whether this is specific to OA progression or an expression of the biomechanical environment. We investigated the rate of change in tAB of the knee over one year in healthy subjects and those with different grades of radiographic OA (rOA).

OBJECTIVE: To test the hypotheses that 1) knees with definite rOA (KLG≥2) show a significant increase in the tAB over 12 months; 2) the rate of change in tAB is greater in knees with definite rOA than in control knees without rOA; 3) the rate of change in tAB is greater on the JSN affected side in knees with unilateral rOA.

METHODS: Coronal FLASHwe MR images of 900 right knees from OA Initiative participants (540 women, 360 men; age 61.6±9.5; BMI 28.9±4.8) were acquired at baseline and 12 months (public use data 0/1.F.1; 0/1.E.1). There were 112 healthy controls without symptoms, radiographic signs, and risk factors of knee OA and 788 knees with various rOA grades (Table 1; KLG 2b=knees with definite JSN but without osteophytes). The tAB of the medial and lateral tibia (MT/LT) and central femoral condyles (cMF/cLF) were segmented by experienced readers, by matching numbers of slices processed per plate in scan pairs, but with blinding to acquisition order. The size of the tAB was calculated in 3D. Because an increase in tAB was expected, particularly in rOA, the following tests were employed: hypotheses 1&3) 1-sided paired-t-test, hypothesis 2) 1-sided non-paired t-test.

RESULTS: tAB changes were less than 1% in all strata and were not significant in control knees (Table 1). rOA knees (KLG≥2) showed a significant tAB increase in MT (0.09%±1.08%; p=0.011), cMF (0.29±1.69%; p<0.0001), and cLF (0.15±1.44%; p=0.004). However, tAB changes were not significantly greater than those in control knees. Medial JSN knees showed significantly greater changes in MT than LT (p=0.002), but lateral JSN knees showed no significant differences between lateral vs. medial changes (Table 1).

Table 1: Change in the subchondral bone area (tAB [%]) over 12 months in OAI knees

		MT	LT	cMF	cLF
Controls	n= 112	-0.08±1.05	-0.06±1.25	0.28±1.97	0.03±1.50
KLG0&1	n= 66	-0.13±0.98	0.09±0.97	0.14±1.77	0.06±1.48
KLG2a	n= 308	0.04±0.96	0.08±1.17	0.25±1.49	0.06±1.45
KLG2b	n= 6	0.57±1.50	0.08±0.69	0.36±1.40	0.97±1.47
KLG3	n= 299	0.11±1.13	0.04±1.28	0.32±1.74	0.17±1.40
KLG4	n= 109	0.29±1.20	-0.05±1.24	0.38±1.79	0.32±1.47
No JSN	n= 356	0.00±0.97	0.11±1.14	0.24±1.54	0.03±1.44
Lateral JSN	n= 123	0.17±1.09	0.29±1.30	0.44±1.41	0.44±1.36
Medial JSN	n= 250	0.22±1.20	-0.10±1.24	0.20±1.75	0.18±1.46
Bilateral JSN	n= 59	-0.11±1.02	-0.18±1.10	0.60±2.23	0.07±1.42

CONCLUSION: tABs increases in rOA knees are small, and predominantly occur in the medial compartment, particularly in knees with medial JSN. These findings may be explained as a reaction to the increased loading of the medial compartment in medial JSN knees, potentially due to varus malalignment. A general metabolic bone reaction in rOA appears less plausible, as knees with bilateral JSN did not show a significant increase in tAB over 12 months.

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DICLOSURE STATEMENT: see affiliations
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CORRESPONDENCE ADDRESS: martin.hudelmaier@pmu.ac.at

QUANTITATIVE ANALYSIS IN THE MEDIAL TIBIO-FEMORAL COMPARTMENT OVER ONE YEAR

1.Cromer M, 1.Bourne R, 2.Fransen M, 1,3.Fulton, R, 4.Wang, SC.
1.Discipline of Medical Radiation Sciences, FHS, University of Sydney, Australia 2.Clinical and Rehabilitation Sciences Research Group, FHS, University of Sydney, Australia 3.School of Physics, University of Sydney, Australia 4.Discipline of Imaging, Sydney Medical School, Australia

INTRODUCTION: qMRI has proven to be an important and reliable tool for cartilage evaluation in OA patients. However, cartilage plate thickness measurements and quantitative total cartilage volume analysis may be insensitive to clinically important changes in regional volume or thickness changes within cartilage plates. Cartilage is not homogenously lost over the cartilage plates(1). Regional analysis can monitor changes in specific anatomic subregions(2). Regional analysis or the utilization of an ordered value(2) approach may prove to be more sensitive to change between imaging time points than radiographic measures of JSN or global qMRI.

OBJECTIVE: To assess whether JSN measured by radiography, global qMRI or regional analysis with MRI is the most responsive indicator of natural disease progression in the medial compartment of the knee over a one year period.

METHOD: A cohort of 23 patients, (65% Female; ages 64 ± 8 years) with radiographically defined medial compartment knee OA were imaged (MRI and weight-bearing radiographs) at baseline and one-year time points. Sagittal FLASHwe datasets were acquired on a 3T Siemens Magnetom Trio (Erlangen, Germany) with a quadrature transmit-receive coil (TR-18ms, TE- 8ms, flip angle–25, in-plane resolution 0.3125/0.3125, 1 mm slice thickness, FOV–16cm). Knee radiographs were obtained using a semi-flexed non-fluoroscopically-controlled view (MTP view)(3). Footmaps were drawn to standardise positioning between assessments. Manual segmentation of the MT and the cMF was performed by one author (MC) blinded to time-point, using Chondrometrics software (Chondrometrics GmbH, Ainring, Germany). Minimum medial JSW (mJSW) was measured by one author (MF) using Holy's software (Lyon, France).

RESULTS: Measures are mean ± standard deviation; SRM – Standardize Response Mean

Quantitative Measure	Baseline	One Year	SRM	P value
mJSW (mm)	3.6 ± 1.0	3.5 ± 1.1	-0.388	0.118
Global				
cMF75.ThCtAB (mm)	1.69 ± 0.39	1.60 ± 0.42	-0.609	0.008
MT.ThCtAB (mm)	1.44 ± 0.25	1.40 ± 0.27	-0.562	0.016
MT.VCtAB (mm)	1.51 ± 0.26	1.47 ± 0.28	-0.639	0.008
cMF.75VCtAB (mm)	1.75 ± 0.40	1.66 ± 0.44	-0.591	0.011
Regional Analysis*				
cMT.ThCtAB (mm)	1.75 ± 0.38	1.71 ± 0.41	-0.342	0.115
eMT.ThCtAB (mm)	1.20 ± 0.20	1.16 ± 0.21	-0.251	0.031
iMT.ThCtAB (mm)	1.94 ± 0.44	1.88 ± 0.49	-0.460	0.038
aMT.ThCtAB (mm)	1.31 ± 0.28	1.34 ± 0.31	0.291	0.177
pMT.ThCtAB (mm)	1.27 ± 0.18	1.20 ± 0.18	-0.785	0.001
ccMF.75ThCtAB (mm)	1.96 ± 0.5	1.83 ± 0.56	-0.580	0.011
ecMF.75ThCtAB (mm)	1.44 ± 0.30	1.34 ± 0.30	-0.838	0.001
icMF.75ThCtAB (mm)	1.71 ± 0.15	1.68 ± 0.53	-0.267	0.214
Ordered Value Analysis	Results	to	come	

*ThCtAB – mean thickness measure; c-central, e–external, i–internal, a–anterior, p-posterior

DISCUSSION: Regional analysis revealed cartilage thickness changes were greater in the medial femur in the external and central weight bearing regions (ecMF.75ThCtAB,ccMF.75ThCtAB) and in the posterior subregion of the medial tibia (pMT.ThCtAB). Global measures revealed significant cartilage loss in the MT and cMF (both normalised to total area of subchondral bone).

CONCLUSION: TO BE CONFIRMED

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CORRESPONDENCE ADDRESS: megan.cromer@swahs.health.nsw.gov.au

TOWARDS T1RHO IN THE CLINIC: A 3.0T AND 1.5T COMPARISON

*Klocke N.F., **Thedens D.R., *Amendola A., *Pedersen D.R

* Orthopaedics and Rehabilitation, University of Iowa, Iowa City, IA, USA
** Radiology, University of Iowa, Iowa City, IA, USA

INTRODUCTION: T1ρ MRI has shown to be sensitive to changes in water proton-PG interactions in articular cartilage. For this technique to fulfill its promise as a clinical measure of cartilage composition in OA onset and progression, T1ρ relaxation times–compositional relationships documented on 3.0T systems must be reproducible at 1.5T as used in 60-75% of private practices in the United States.

OBJECTIVE: 1) To compare cartilage T1ρ relaxation times and image quality of a healthy subject on same-day data collected from 1.5T and 3.0T MRI scanners using identical pulse sequences; 2) To document the effects of reducing the number of spin-lock times to acquire full 3-D joint coverage.

METHODS: With appropriate Institutional Review Board approval and subject consent, one healthy 23 year-old female was the subject for this study. Same day scans eliminated day-to-day variability within the T1ρ FSE-based acquisition on a 3T Siemens TIM Trio scanner and an Avanto 1.5T scanner; both used a quadrature knee coil. Twelve spin-lock (SL) times at 400Hz were chosen (SL=0.5,5,10,15,20, 25,30,40,50,60,70,80 ms) in a 2D oblique sagittal slice through the LFC midline. Other imaging parameters were slice thickness=4mm, TR/TE=3000/10 ms (3.0T), 3000/12ms (1.5T), echo train length=13, FOV=140mm×140mm, in-plane resolution=0.55mm. All possible (4017) SL permutations of three or more SL relaxation times generated relaxation maps after automated registration of the SL images using a non-linear least squares, mono-exponential fit with a bilinear squares robustness measure applied on a voxel-by-voxel basis using Matlab. An objective, Canny-based line profile analysis was used to assess T1ρ relaxation times through the cLT for nominally deep (DZ), radial (RZ), and superficial (SZ) cartilage zones. The LFC coordinate system identified similar regions of cartilage, infrapatellar fat pad, gastrocnemius muscle, and femoral bone from both datasets for ROI analysis. Signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR), signal-difference-to-noise ratio (SDNR), and relative-contrast (RC) ratio comparisons between the 3.0T and 1.5T image sets were derived from image signal and noise statistics. Student's two-tailed t-test with equal variance determined statistical significance (p=0.05) for each of the tests to elucidate equivalency across systems.

RESULTS: The 1.5T average (±SD) relaxation times were DZ:49.6 (±2.7) ms, RZ:52.0 (±4.7) ms, SZ:48.4 (±6.0) ms, whereas the average 3.0T relaxation times were DZ:38.3 (±2.1) ms, RZ:44.2 (±2.4) ms, and SZ: 49.4 (±2.3) ms. T1ρ relaxation times from the 3.0T scan were generally lower than those at1.5T (percent difference, DZ:-22.5% (±4.9%), RZ:-14.2% (±10.9%), SZ:4.0% (±16.8%)). The relaxation times for the DZ and RZ proved to be significantly different when comparing the 1.5T to the 3.0T values, but the SZ's relaxation times were not (p=0.27). All three layers had statistically distinct relaxation behavior for the 3.0T dataset, while only the DZ compared to the SZ was not significant (p=0.22) for 1.5T. As SL time increased, the overall cartilage signal intensity diminished nearly monotonically for both 1.5T and 3.0T datasets. The images between MR scanners for each SL image which had cartilage signal intensities with $p \leq 0.05$ were SL= 0.5, 5, 10, 15, 50, 70 ms. The average SNR increase from a 1.5T scanner to a 3.0T scanner for cartilage was 2.02 (±0.26), with bone, fat, and muscle having an average SNR increase of 2.32 (± 1.43), 1.81 (±0.69), and 1.75 (±0.29), respectively. Most other tissue comparisons were approximately a two-fold increase in 3.0T compared to 1.5T. Reduced sets of spin-lock times increased the magnitude and spread of T1ρ relaxation times.

CONCLUSION: 3.0T T1ρ images demonstrated improved SNR and other parameters over 1.5T. However, overall clarity of the1.5T T1ρ images remained useful and relaxation times between cartilage layers were still distinct, showing T1ρ's diagnostic potential at 1.5T. Although the ROI data and line profile data had many samples, a limitation is the small subject size (n=1). This study showed the comparable data quality; additional standardized phantoms and more *in vivo* data are needed to determine optimal SL time sets to produce T1ρ relaxation times indicative of normal and traumatized cartilage, and to acquire consistent absolute and comparable values across magnet strengths.

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CORRESPONDENCE ADDRESS: noelle-klocke@uiowa.edu

CLASSIFICATION AND DISTRIBUTION OF CARTILAGE THICKNESS CHANGE IN SUBJECT KNEES: DATA FROM THE OSTEOARTHRITIS INITIATIVE

*Buck R.J., **Hellio Le Graverand-Gastineau M-P, ***Nevitt M, ****Wirth W, **** Eckstein, F – for the OAI investigators

* StatAnswers Consulting LLC, Minneapolis, MN; ** Pfizer Global Research and Development, Groton, CT; *** University of California and OA Initiative Coordinating Center, San Francisco, CA;
**** Paracelsus Medical University, Salzburg, Austria & Chondrometrics, Ainring, Germany

INTRODUCTION: The clinical management of knee OA and the recruitment for clinical trials requires in depth knowledge on which OA knees will structurally progress and which will not. A recently proposed method showed success in classifying subjects by OA-related change in subregional cartilage thickness based on a reference distribution of asymptomatic subjects and revealed that not only cartilage thinning but also thickening may be part of the OA process. However, this study was limited to the medial femorotibial compartment, to women, and to knees with KL grades 2 and 3 [1].

OBJECTIVE: To estimate the relative frequency and spatial location of progression (cartilage thinning or thickening) in men and women from the OAI with different structural disease (e.g. KL) grades.

METHODS: Measurements of change in mean subregional cartilage thickness (ThCtAB) over 12 months were available from coronal FLASH MR images of one knee of 907 subjects. Subjects were from the Progression, Incidence, and asymptomatic Control (all cKLG0, no pain, and no risk factors) Cohorts. The Progression cohort was split to consider signal (osteophytes and pain present) and non-signal knees (either osteophytes or pain not present) separately. See Table for sample sizes. Baseline and follow-up scans were read in pairs with readers blinded to visit. Change in ThCtAB was measured in 16 femorotibial subregions [2]. Classification of progression was done by comparing individual rates of change in each subregion against the distribution of change found in the Control cohort [1]. Standard deviations of change for each subregion and sex in the Control cohort were used to normalize individual subregion cartilage change. Logistic regression was used to assess differences in frequency of thinning or thickening for cohort covariates e.g., sex, or cKLG.

RESULTS: Only 161 (25.4%) of the 795 Progression and Incidence cohort knees showed progression (i.e. cartilage thinning or thickening). The table provides number of total knees and percent of knees classified as thinning or thickening for each cKLG and OAI subcohort.

	Incidence Cohort			Progression non-signal knee			Progression signal knee		
cKLG	N	%Thin	%Thick	N	%Thin	%Thick	N	%Thin	%Thick
Normal	23	0.0	0.0	9	0.0	0.0	0	NA	NA
Possible	15	15.4	0.0	23	21.1	9.5	0	NA	NA
Mild	157	9.0	1.3	40	21.2	0.0	119	10.2	5.3
Moderate	137	23.4	2.2	38	22.6	5.6	125	37.4	5.9
Severe	36	24.1	2.9	0	NA	NA	73	58.7	10.6
Total	368	15.6	1.7	110	19.9	3.9	317	32.1	6.8

Odds of thinning was 26% higher when compare all knees with cKLG≥2 against cKLG1 ($p = 0.64$) and 143% higher when compare cKLG3+4 with cKLG1+2 ($p<0.0001$). Differences in relative frequency were not found between men and women (p value > 0.2), but was significantly different between subcohorts ($p=0.013$). The ecMF and ccMF were the most common subregions to be identified with progression (36.0% and 33.5% of knees), respectively) followed by eMT (22.4%) and cMT (14.3%).

CONCLUSION: Results extend published work [1] and shows that the relative frequency of progression increases with OA grade and appears higher in the Progression cohort signal knees compared to the Incidence cohort and Progression non-signal knees, but is independent of gender.

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[2] Wirth W, Eckstein F (2008): IEEE Trans.Med.Imaging. 27: 737-44

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DISCLOSURE STATEMENT: see affiliations.
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CORRESPONDENCE ADDRESS: robert.j.buck@gmail.com

3D PATTERNS OF ACETABULAR CARTILAGE DAMAGE IN HIP DYSPLASIA AT PRE- AND EARLY ARTHRITIC STAGES; A HIGH-RESOLUTIONAL CT ARTHROGRAPHY STUDY

*Tamura S., *Nishii T., **Shiomi T., ***Yamazaki Y., ***Murase K., **Yoshikawa H., *Sugano N.

* Department of Orthopaedic Medical Engineering, Osaka University, Osaka, Japan
** Department of Orthopaedic Surgery, Osaka University, Osaka, Japan
*** Department of Medical Physics and Engineering, Osaka University

INTRODUCTION: Even at pre-arthritc stage in hip dysplasia, high frequency of aceatabular cartilage damage was shown in arthroscopic studies. However, there were no reliable imaging methods to assess early localized cartilage lesions. MR imaging was useful to assess articular cartilage due to a good contrast between articular cartilage and adjacent subchondral bone or articular fluid, but there remains a concern for limited spatial resolution and decrease in signal to noise ratio of MR imaging to achieve accurate morphological assessments. CT arthrography has great advantage in superior spatial resolution and high signal contrast.

OBJECTIVE: The objectives of this study were to investigate 3D distribution of acetabular cartilage thickness in patients with hip dysplasia by semi-automatic computer analysis of high-resolutional isotrophic CT arthrography, and to explore 3D progression patterns of early damage in the aceataublar cartilage of hip dysplasia at pre- and early arthritic stage.

METHODS: Twenty six females with twenty one dysplasitc hips at radiologically pre-arthritic stage and eleven dysplastic hips at radiologically early arthritic stage were analyzed. Each patient received isotropic, high-resolutional CT arthrography (Aquilion ONE; Toshiba) under a leg traction system using following parameters: collimation, 120 kVp; tube charge, 300mAs; helical scan. Axial images were reconstructed with an in-plane resolution of 0.5x 0.5mm with longitudunal resolution of 0.5mm. 3D distribution of acetabular cartilage thickness model was generated by Baum globe (Osaka Univ.) and cartilage thickness distribution at 12 zones partitioning the weight-bearing area along radial and lateral /medial directions was evaluated (Figure 1). Cartilage thickness at each direction was compared between lateral and adjacent medial zone in each arthritic stage by Wilcoxon test and between hips at pre- and early arthritic stage by Mann-Whitney U test. LM ratio (thickness at lateral zone/ at adjacent medial zone) was compared between hips at pre and early arthritic stage by Mann-Whitney U test.

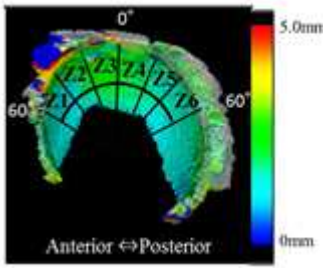

Figure 1

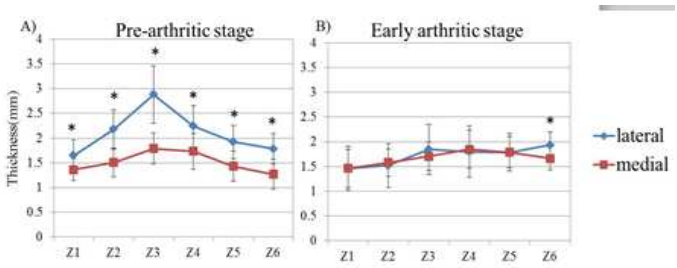

Figure 2

RESULTS: Comparing between lateral zone and medial zone, there were significant differences in cartilage thickness at all radial directions, most prominent at the antero-superior zones, in pre-arthritic stage (Figure 2A), while there was no significant difference except most posterior zones in early arthritic stage (Figure 2B). At lateral part, there were significant difference in cartilage thickness between hips at pre- and early arthritic stage in Z2, Z3 and Z4 (Z2: $p=0.002$, Z3: $p<0.001$, Z4: $p=0.03$). LM ratio at each zone was significantly higher in pre-arthritic stage than early arthritic stage and the largest change between pre and early arthritic stage was seen at Z3 (pre/early: $1.65\pm0.44/1.09\pm0.26$, $p<0.001$). Hips with LM ratio less than 1.4 had more extensive involvement of labral tears than others.

CONCLUSION: Damage of acetabular cartilage was most likely to occur at the antero-superior lateral area in hip dysplasia, and LM ratio may be a potent index to quantify early osteoarthric involvement.

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DICLOSURE STATEMENT: None
CORRESPONDENCE ADDRESS: tamura-osk@umin.net

POSTER SESSION

June 9th, 2011: 16.00 – 17:00 - Even numbered posters (No. 2 to 34)

2	*Maschek S., *Eckstein F., *Wirth W., **Gradl G., **Kirchhoff C., ***Wörtler K., **von Eisenhart-Rothe R. *Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany ; **Clinic for Orthopaedics and Traumatology, Technical University, Munich, Germany; ***Clinic for Radiology, Technical University, Munich, Germany DOES ANKLE CARTILAGE ADAPT TO STRONG ALTERATIONS IN LOADING ENVIROMENT AFTER TRANSPLANTATION TO THE KNEE (VAN NEES ROTATIONPLASTY)?
4	*Dam E.B., **Marques J. * BiomedIQ, Copenhagen, Denmark ** BiomedIQ, Copenhagen, Denmark & University of Copenhagen, Denmark AUTOMATIC SEGMENTATION OF BONE AND CARTILAGE FROM KNEE MRI
6	[1]Eckstein F., [2]Kwoh CK.., [3]Boudreau R., [2]Wang Z., [2]Hannon JM., [1]Cotofana S., [1]Hudelmaier M., [1]Wirth., [4]Guermazi A., [5]Nevitt M., [6]John M., [7]Hunter DJ., for the OAI investigators [1]Paracelsus Medical University, Salzburg, Austria & Chondrometrics Gmbh, Ainring, Germany [2] Div. of Rheumatology and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA [3]Dept. of Epidemiology, Grad. School of Public Health, Univ. of Pittsburgh, PA; [4]BICL & Boston Univ., Boston, MA; [5]OAI Coordinating Center, UCSF, San Francisco, CA; [6]Novartis Pharma AG, Basel, Switzerland; [7] Royal North Shore Hospital & Northern Clinical School, Univ. Sydney, Australia CARTILAGE THICKNESS, DENUDED AREAS, AND BONE SIZE IN KNEES PRIOR TO TOTAL KNEE REPLACEMENT (TKR) – DATA FROM THE OSTEOARTHRITIS INITIATIVE
8	*,**Roemer F.W., ***Nevitt M.C, ****Felson D.T., ****Niu J., ***Lynch J.A., **,*****Crema M.D., **,*****Marra M.D.,******Lewis C.E., *******Torner J., **Guermazi A. *Department of Radiology, Klinikum Augsburg, Augsburg, Germany, **Quantitative Imaging Center (QIC), Department of Radiology and ****Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA, ***Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA, *****Institute of Diagnostic Imaging (IDI), Ribeirão Preto, Ribeirão Preto, SP, Brazil, ******Department of Epidemiology, University of Alabama, Birmingham, AL, USA, *******Department of Epidemiology, University of Iowa, Iowa City, IA, USA LONGITUDINAL WITHIN-GRADE SCORING OF CARTILAGE AND BONE MARROW LESIONS: VALIDITY ANALYSES FROM THE MOST STUDY
10	*Haugen IK, *Bøyesen P, *Slatkowsky-Christensen B, *Sesseng S, * ***van der Heijde D, *Kvien TK * Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway ** Dept. of Radiology, Diakonhjemmet Hospital, Oslo, Norway *** Dept. of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands THE ROLE OF MRI-DEFINED SYNOVITIS IN HAND OSTEOARTHRITIS
12	Saunders F.R., Barr R.J, Reid D.M., Aspden R.M., Gregory J.S. University of Aberdeen, Aberdeen, Scotland, UK ACTIVE SHAPE MODELLING OF BILATERAL KNEE OSTEOARTHRITIS IN THE OAI
14	*,**Marques J., **Dam E. * University of Copenhagen, Copenhagen, Denmark ** BiomedIQ, Rødovre, Denmark QUANTIFICATION OF TRABECULAR TIBIA BONE STRUCTURE RELATED TO THE PRESENCE OF OSTEOARTHRITIS
16	*Riek, J.K. * VirtualScopics, Inc. Rochester, NY, USA A MULTI-CENTER COMPARISON OF T2 RELAXATION TIMES CALCULATED CENTRALLY VERSUS THOSE GENERATED DIRECTLY BY THE MR SCANNER.
18	Rudolphi K, Aigner S, Berg-Scholl I, Bissinger T, Keiffer R, Wunschel, M

	sanofi-aventis, TSU Aging, Musculoskeletal Cluster, Frankfurt-Main, Germany IMPROVED ASSESSMENT BY QUANTITATIVE DIGITAL HISTOMORPHOMETRY OF HISTOPATHOLOGICAL CHANGES OF ARTICULAR CARTILAGE IN A SURGICAL MODEL OF POST-TRAUMATIC OSTEOARTHRITIS OF THE KNEE JOINT IN RATS
20	*Stok, K.S., **Glanzmann, M., *Steiner, T., *,** Goldhahn, J., *Müller, R. * Institute for Biomechanics, ETH Zürich, Switzerland ** Schulthess Clinic, Zürich, Switzerland AN INTEGRATIVE IMAGING APPROACH FOR EXAMINING BONE AND CARTILAGE TISSUES IN THE OSTEOARTHRITIC JOINT – A PILOT STUDY
22	*Bloecker K., *Wirth W., *Hudelmaier M., **Burgkart R., ***Frobell R., *Eckstein F. * Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg , Austria **Clinic for Orthopaedics and Traumatology, Technical University Munich, Germany *** Department of Orthopaedics, Clinical Sciences Lund, Lund University, Lund, Sweden SIZE AND POSITION OF THE HEALTHY MENISCUS, AND ITS CORRELATION WITH SEX, HEIGHT, WEIGHT, BONE SIZE, AND AGE
24	* , ** Kinds M.B., * Marijnissen A.C.A., ** Vincken K.L., ** Bartels L.W., ** Viergever M.A., *** de Jong H.W.A.M., *Lafeber F.P.J.G. * Rheumatology & Clinical Immunology, University Medical Center Utrecht, the Netherlands ** Image Sciences Institute, University Medical Center Utrecht, the Netherlands *** Radiology, University Medical Center Utrecht, the Netherlands FEASIBILITY OF BONE DENSITY EVALUATION USING PLAIN DIGITAL RADIOGRAPHY
26	*Sattler M., *Dannhauer T., *Hudelmaier M., **Sänger A.M., ***Hunter DJ., ****Kwoh K., *Eckstein F., for the OAI investigators * Paracelsus Medical University, Salzburg , Austria & Chondrometrics GmbH, Ainring, Germany ** Organismic Biology, Natural Science Faculty, Salzburg University, Salzburg, Austria *** Royal North Shore Hospital & Northern Clinical School, University of Sydney, Sydney, Australia. **** Division of Rheum. and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA SIDE DIFFERENCES OF THIGH MUSCLE CROSS SECTIONAL AREAS IN KNEES WITH THE SAME RADIOGRAPHIC OA (KL) GRADE, BUT UNILATERAL FREQUENT PAIN
28	*Nishii T., *Tamura S., ** Shiomi T., ***Yamazaki Y., ***Murase K., ****Tanaka H., *Yoshikawa H., **Sugano N. * Department of Orthopaedic Medical Engineering, ** Department of Orthoaedic Surgery, *** Department of Medical Physics and Engineering, and **** Department of Radiology, at Osaka University, Osaka, Japan SIGNIFICANT INFLUENCE ON LOAD RESPONSE OF KNEE CARTILAGE T2 BY MENISCUS DISORDER –A LOADING MRI STUDY
30	*Stannus O.P., *Jones,G., * **Ding C. * Menzies Research Institute, University of Tasmania, Hobart, Australia ** Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia CARTILAGE SIGNAL INTENSITY ON MRI: ASSOCIATION WITH BODY MASS INDEX, CARTILAGE DEFECTS AND TYPE II COLLAGEN BREAKDOWN
32	*Tummala S., **Dam E.B., *Nielsen M. * eScience Center, University of Copenhagen, Copenhagen, Denmark ** BiomedIQ, Rødovre, Denmark DIAGNOSIS OF OA BY AUTOMATIC QUANTIFICATION OF INCONGRUITY FROM KNEE MRI
34	*Lowitz T., *Zerfaß P., *Engelke K., *Museyko O., **Laredo J.-D., **Bousson V., *Kalender W.A. * Institute of Medical Physics, University of Erlangen-Nürnberg, Germany ** Service de Radiologie Ostéo-Articulaire, Hôpital Lariboisière, Paris, France QUANTITATIVE CT FOR KNEE OSTEOARTHRITIS

DOES ANKLE CARTILAGE ADAPT TO STRONG ALTERATIONS IN LOADING ENVIROMENT AFTER TRANSPLANTATION TO THE KNEE (VAN NEES ROTATIONPLASTY)?

*Maschek S., *Eckstein F., *Wirth W., **Gradl G., **Kirchhoff C., ***Wörtler K., **von Eisenhart-Rothe R.

*Institute of Anatomy and Musculoskeletal Research, Paracelsus Medical University, Salzburg, Austria & Chondrometrics GmbH, Ainring, Germany
**Clinic for Orthopaedics and Traumatology, Technical University, Munich, Germany
***Clinic for Radiology, Technical University, Munich, Germany

INTRODUCTION: Healthy articular cartilage is able to transfer high loads across diarthrodial joints, without suffering damage. As for other tissues with mechanical function such as muscle or bone, it is widely assumed that the emergence and maintenance of articular cartilage is guided by functional adaptation to mechanical stimuli (e.g. Wolff's law). However, evidence that cartilage thickness adapts to (changes in) the loading environment remains controversial [1-3].

OBJECTIVE: To study whether human ankle cartilage undergoes morphological changes due to strong alterations in the loading environment (after being transplanted to the site of the human knee - van Nees rotationplasty type A1), and develops a cartilage thickness similar to that in the contra-lateral knee.

METHODS: 12 participants (7 men, 5 women, age 17 to 61 years) were studied, in which the ankle of one limb had been transplanted to the site of the knee (rotationplasty type A1) between 8 and 18 years before this cross-sectional imaging study. Sagittal MR images (FLASH) of the transplanted ankle, contra-lateral ankle, and contra-lateral knee were obtained. Segmentation of the tibial and talar cartilage of the talocrural joint (TCJ), the talar and calcaneal cartilage of the subtalar joint (STJ), and the patella, trochlea, tibia, and weight-bearing femoral condyles of the knee joint (KJ) was performed using custom software (Chondrometrics GmbH, Ainring, Germany). The mean cartilage thickness (ThC.tAB) and size of the subchondral bone area (tAB) were computed in 3D using the same software. These were compared between transplanted and contra-lateral ankles, and with the knee (paired t-test with correction for comparisons of tests in 4 cartilage plates (required $p < 0.0125$ [$p<0.05/4$]).

RESULTS: The mean cartilage thickness (ThC.tAB.Me) and tABs tended to be lower (rather than greater) in the transplanted (TP) than in the contra-lateral (CL) ankle (Table 1). The differences reached significance in the STJ for ThC.tAB, and in the TCJ talus and STJ calcaneus for tAB. Values were significantly greater in the corresponding knee cartilage plates than in the transplanted TCJ and STJ.

Table 1: Mean cartilage thickness (ThC.tAB.Me) and subchondral bone area (tAB) in the transplanted (TP) talocrural joint (TCJ) and subtalar joint (STJ), in the contra-lateral (CL) TCJ and STJ, and in the CL knee joint (KJ): fem = femoral; § values from the medial and lateral sides averaged; # values added.

ThC.tAB.Me (µm)		TP ankle	CL ankle	[CL knee]
TCJ tibia	[KJ tibia§]	1.01± 0.15	1.08± 0.14)	[1.96± 0.36]*
TCJ talus	[KJ fem. condyle§]	1.00± 0.13	1.07± 0.15	[1.79± 0.28]*
STJ talus	[KJ patella]	0.96± 0.16	1.11± 0.19*	[2.30± 0.45]*
STJ calcaneus	[KJ fem. trochlea]	0.86± 0.13	0.97± 0.17*	[1.99± 0.24]*
tAB (cm^2)				
TCJ tibia	[KJ tibia#]	8.66± 1.35	9.06± 1.51	[22.0± 3.58]*
TCJ talus	[KJ fem. condyle#]	9.70± 1.70	11.33± 1.82*	[11.6± 1.69]*
STJ talus	[KJ patella]	5.57± 1.31	6.14± 1.24	[10.8± 1.63]*
STJ calcaneus	[KJ fem. trochlea]	4.92± 0.97	5.58± 1.06*	[22.0± 2.45]*

* significantly different from the TP ankle (paired t-test at $p<0.015$ [global sign. level = 0.05])

CONCLUSION: The findings suggest that the cartilage thickness and subchondral bone area of the human ankle (talocrural and subtalar joints) do not adapt, with an increase in thickness or area, to changes in mechanical loading environment, when being transplanted to the site of the knee (van Nees rotationsplasty).

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[3] Jones et al. 2003 Pediatr.Res 54:230; [4] Gratzke et al. 2007 Am J Sports Med 35:1346.

SPONSOR: None.
DISCLOSURE STATEMENT: see affiliations
CORRESPONDENCE ADDRESS: Dr-SusanneMaschek@web.de

AUTOMATIC SEGMENTATION OF BONE AND CARTILAGE FROM KNEE MRI

*Dam E.B., **Marques J.

* BiomedIQ, Copenhagen, Denmark
** BiomedIQ, Copenhagen, Denmark & University of Copenhagen, Denmark

INTRODUCTION: Osteoarthritis involves changes in bone shape and structure, articular cartilage shape and structure, meniscus, synovium, and ligaments. Magnetic resonance imaging allows more comprehensive inspection of bone and cartilage in multiple compartments compared to traditional radiography. For MRI to be available for large clinical trials with thousand(s) of participants and several visits, automation of the scoring seems desirable.

OBJECTIVE: We evaluated a method for fully automatic segmentation of bone and cartilage from knee MRI in terms of segmentation precision and accuracy.

METHODS: MRIs were acquired using a Turbo 3D T1 sequence from a 0.18T Esaote scanner (40° FA, TR 50ms, TE 16 ms, scan time 10 minutes, resolution 0.7mm x 0.7mm x 0.8mm). The sequence was optimized for cartilage visualization. Radiographs were acquired in a load-bearing semiflexed position using the SynaFlex and scoring by an experienced radiologist using the Kellgren and Lawrence grade.
The study included 145 left and right knees (51 with KLG 0, rest evenly KLG 1-3) from 22-79 years old subjects with 59% female. 31 representative knees were rescanned a week later to allow inter-scan precision validation.
All scans were manually segmented by a radiologist by slice-wise outlining. The Tibia bone and the medial tibial and femoral cartilages were segmented automatically using a computer-based voxel classification framework. The method was trained on 25 knees and evaluated on the rest.

RESULTS: All scans were successfully segmented and included in the statistics below. An example is seen in the figure.
Precision was measured as inter-scan coefficient of variation (CV). For the three compartments, CV on volume quantifications were 5.3%, 6.3%, and 10.0% for Tibia, tibial cartilage (MT.VC), and femoral cartilage (MF.VC), respectively.
Segmentation accuracy was measured as the Dice volume overlap. Dice were 97%, 81%, and 79%, for Tibia, tibial cartilage, and femoral cartilage, respectively.
For comparison, repeated manual radiologist segmentations gave precision of CV 7.3% and 6.8% and accuracy of Dice 86% and 86%, for tibial and femoral cartilages respectively.

CONCLUSION: The results demonstrate the feasibility of performing automatic segmentation of bone and cartilage in knee MRI with a performance similar to manual segmentation by a trained radiologist.

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CORRESPONDENCE ADDRESS: erikdam@diku.dk

CARTILAGE THICKNESS, DENUDED AREAS, AND BONE SIZE IN KNEES PRIOR TO TOTAL KNEE REPLACEMENT (TKR) – DATA FROM THE OSTEOARTHRITIS INITIATIVE

[1]Eckstein F., [2]Kwoh CK.., [3]Boudreau R., [2]Wang Z., [2]Hannon JM., [1]Cotofana S., [1]Hudelmaier M., [1]Wirth., [4]Guermazi A., [5]Nevitt M., [6]John M., [7]Hunter DJ., for the OAI investigators

[1]Paracelsus Medical University, Salzburg, Austria & Chondrometrics Gmbh, Ainring, Germany
[2] Div. of Rheumatology and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA
[3]Dept. of Epidemiology, Grad. School of Public Health, Univ. of Pittsburgh, PA; [4]BICL & Boston Univ., Boston, MA; [5]OAI Coordinating Center, UCSF, San Francisco, CA; [6]Novartis Pharma AG, Basel, Switzerland; [7] Royal North Shore Hospital & Northern Clinical School, Univ. Sydney, Australia

INTRODUCTION: Total knee replacement (TKR) has been proposed to represent an important clinical endpoint in knee OA. Imaging biomarkers capable of predicting relevant clinical endpoints may be valuable surrogate markers for testing the efficacy of DMOADs in clinical trials.

OBJECTIVE: To determine whether knees receiving a TKR show differences in cartilage thickness (ThC), denuded subchondral bone areas (dABs), and subchondral bone size (tABs) compared with control knees from matched controls who did not receive a TKR.

METHODS: Knees from OAI participants who received a TKR between baseline and 48 month follow-up were studied. These were compared with control knees with similar KL grade (central X-ray readings strata 0-1, 2-3, 4) from OAI participants with the same sex and age within 5 years who did not receive a TKR during this period. Quantitative cartilage measures were obtained from sagittal DESSwe images acquired at 3 Tesla in the OAI. The time point prior to the advent of the TKR (≤1 year) was used; segmentation of weight-bearing femorotibial cartilage was performed by 12 readers using Chondrometrics software. A cross-sectional comparison between TKR cases and control knees was carried out using a paired t-test with adjustment for multiple comparisons. A p-value of <0.0042 was considered significant (0.05/12), and a p-value <0.05 borderline significant.

RESULTS: 191 knees of 165 OAI participants received a TKR, of whom 155 had an MRI at the visit prior to surgery. Of these, 71 knees (25 men, 46 women, age 45 to 78 yrs, BMI 21.2 to 41.8, 4 KLG0, 1 KLG1, 20 KLG2, 44 KLG3, and 2 KLG4) could be adequately matched with 71 control knees (no TKR). ThC tended to be less in TKR cases than in controls, reaching borderline significance in the medial femur and lateral tibia. dABs in TKR cases were significantly greater than controls in the medial compartment, and reached borderline significance in the lateral compartment. tABs were not significantly different between cases and controls (p>0.16; data not shown).

Table 1: Mean cartilage thickness (ThC), denuded areas (dAB), and subchondral bone size (tAB) in knees prior to TKR (n= 71), compared with matched controls (n= 71)

		TKR Cases		Controls		Difference		
		Mean	SD	Mean	SD	(%)	Mean	p-value
ThC	Medial tibia (MT)	1.628	0.31	1.69	0.262	-3.7	-0.06	0.15
(mm)	Medial femur (cMF)	1.60	0.44	1.70	0.36	-7.5	-0.13	0.04 #
	Lateral tibia (LT)	1.75	0.46	1.92	0.36	-8.0	-0.16	0.01 #
	Lateral femur (cLF)	1.91	0.42	1.99	0.30	-3.6	-0.07	0.22
dAB	Medial tibia (MT)	12	15	4	8	214	8	0.0005§
(%)	Medial femur (cMF)	23	28	7	14	241	17	<.0001§
	Lateral tibia (LT)	9	17	4	9	152	5	0.03 #
	Lateral femur (cLF)	7	14	3	7	180	5	0.02 #

§ Significant after adjustment for multiple comparisons; # borderline significant

CONCLUSION: OA knees displayed greater dABs at the time point prior to TKR compared with matched controls (without TKR); differences were most prominent in the weight-bearing medial femur. Further longitudinal studies should investigate whether longitudinal changes in the above parameters in the year prior to TKR differ from those in control knees who do not receive TKR.

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DISCLOSURE: see affiliations
CORRESPONDENCE ADDRESS: felix.eckstein@pmu.ac.at

LONGITUDINAL WITHIN-GRADE SCORING OF CARTILAGE AND BONE MARROW LESIONS: VALIDITY ANALYSES FROM THE MOST STUDY

*,***Roemer F.W., ***Nevitt M.C, ****Felson D.T., ****Niu J., ***Lynch J.A., **,*****Crema M.D., **,*****Marra M.D.,******Lewis C.E., *******Torner J., **Guermazi A.

*Department of Radiology, Klinikum Augsburg, Augsburg, Germany, **Quantitative Imaging Center (QIC), Department of Radiology and ****Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, USA, ***Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA, *****Institute of Diagnostic Imaging (IDI), Ribeirão Preto, Ribeirão Preto, SP, Brazil, ******Department of Epidemiology, University of Alabama, Birmingham, AL, USA, *******Department of Epidemiology, University of Iowa, Iowa City, IA, USA

INTRODUCTION: Semiquantitative MRI scoring systems for knee OA, typically define longitudinal change in cartilage morphology and bone marrow lesions (BMLs) within a subregion in terms of at least one full grade change between time points. In order to increase the sensitivity to detect change, so-called within-grade changes were introduced to code longitudinal changes that do not fulfill the criteria of a full grade difference between time-points.

OBJECTIVE: To examine the validity provided by within-grade scoring of cartilage and BMLs in the WORMS system in comparison to full grade assessment using baseline and 30 months follow-up MRIs from the MOST study.

METHODS: The Multicenter Osteoarthritis (MOST) Study is a longitudinal observational study of subjects with knee OA or at risk of developing OA. The MRI protocol included axial and sagittal proton-density weighted fat-suppressed fast-spin echo and a coronal STIR sequence. All knees with available baseline and 30 months MRI and radiographic readings were included. MRIs were read according to the modified WORMS scoring system including within-grade assessment. The sensitivity and specificity of MRI-defined cartilage loss to detect increase in X-ray defined joint space narrowing was assessed using cartilage scores applying within-grades plus full grades vs. full grades only.
The ability of baseline knee malalignment and meniscal damage to predict compartment-specific structural progression was assessed using ordinal logistic regression adjusting for age, sex and body mass index. Progression was defined as cartilage loss and BML worsening considering half grade scoring only vs. full grade scoring only.

RESULTS: 1867 knees were analyzed. Sensitivity to detect increase in joint space narrowing for full grade changes only was 0.55 and specificity was 0.86. For scoring of within-grade plus full grades combined, sensitivity was 0.66 and specificity 0.81.
Any varus malalignment predicted both within-grade and full grade worsening of BMLs in the medial compartment (Within-grade scoring: moderate malalignment (mMA) adjusted odds ratio (aOR) (95% confidence interval-95% CI) 1.9 (1.5, 2.5) severe malalignment (sMA) aOR 3.3 95% CI (2.2, 5.0) Full grade scoring: mMA aOR 1.8, 95% CI (1.4, 2.3) sMA 2.3 95% CI (1.5, 3.7)). Malalignment similarly predicted half (and full) grade WORMS medial cartilage loss. Results were comparable for valgus malalignment predicting subsequent within-grade and full grade changes in lateral cartilage and BML worsening.
Severe meniscal damage predicted within-grade and full grade worsening of cartilage and BMLs in a comparable fashion.

CONCLUSION: Use of within-grade coding increases sensitivity for the detection of X-ray defined increase in joint space loss by only slightly decreasing specificity.
Both, half grade and full grade cartilage and BML changes are predicted by malalignment and meniscal damage. Half grade scoring will increase number of compartments and subregions showing change. Those changes seem to be relevant as reflected in their associations with both risk factors and outcomes.

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CORRESPONDENCE ADDRESS: froemer@bu.edu

THE ROLE OF MRI-DEFINED SYNOVITIS IN HAND OSTEOARTHRITIS

*Haugen IK, *Bøyesen P, *Slatkowsky-Christensen B, *Sesseng S, * ***van der Heijde D, *Kvien TK

* Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway
** Dept. of Radiology, Diakonhjemmet Hospital, Oslo, Norway
*** Dept. of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

INTRODUCTION: MRI-defined synovitis is associated with pain in knee osteoarthritis (OA). However, no previous studies have explored the association between MRI-defined synovitis and pain and radiographic severity in patients with hand OA.

OBJECTIVE: To explore the frequency of MRI-defined synovitis in joints with different levels of radiographic severity and examine whether synovitis is associated with pain in patients with hand OA.

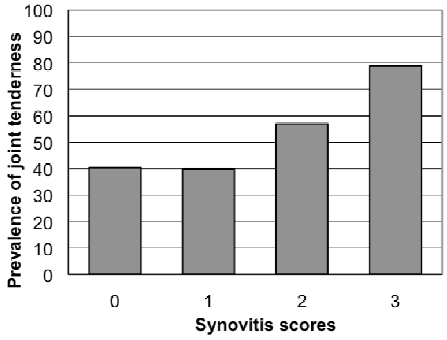
METHODS: We included 97 patients from the Oslo hand OA cohort (88 women, mean (SD) age 68.8 (5.6) years) with MRI (coronal/sagittal/axial pre- and post-gadolinium (Gd) T1w images and coronal/ axial STIR images), conventional posteroanterior radiographs and clinical joint examination of the dominant hand. One investigator (IKH) scored the distal (DIP) and proximal interphalangeal (PIP) joints according to the Oslo hand OA score for MRI (1). Synovitis was defined as "an area in the synovial compartment that shows post-Gd enhancement of a thickness greater than normal", and was graded on a 0-3 scale. Intra-reader reliability was good (weighted kappa=0.78). One investigator (IKH) scored the same DIP/PIP joints according to Kellgren-Lawrence (KL) (grade 0-4), and the intra-reader reliability was good (weighted kappa=0.86). KL grade (KLG) 3 and 4 were collapsed due to few joints in each category. One rheumatologist (BSC) assessed the same joints for tenderness upon palpation.

We calculated the prevalence of synovitis in joints with no (KLG=0), doubtful (KLG=1), mild (KLG=2) and moderate/severe OA (KLG=3-4). The odds ratio (OR) with 95% confidence intervals (CI) for increasing severity of synovitis in joints with KLG=1, KLG=2 and KLG=3-4 (KLG=0 as reference) was calculated by Generalized Estimating Equations (GEE) adjusted for age and sex. We calculated the prevalence of tenderness upon palpation in joints with no (grade=0), mild (grade=1), moderate (grade=2) and severe synovitis (grade=3). The OR (95% CI) for tenderness upon palpation in joints with moderate/severe synovitis (grade 2-3) compared with joints with no/mild synovitis (grade 0-1) was calculated by GEE adjusted for age and sex (corrected univariate analyses). We additionally adjusted for presence of structural MRI-features (osteophytes, joint space narrowing, erosions, sub-chondral collapse, bone marrow lesions and collateral ligament absence) in a multivariate GEE model.

RESULTS: Synovitis (grade 1-3) was frequently seen in joints with KLG=0 (58.7%) and KLG=1 (69.3%), but was most prevalent in joints with KLG=2 (74.2%) and KLG=3-4 (69.3%). Similarly, the prevalence of moderate/severe synovitis (grade 2-3) was 11.6% in KLG=0, 25.3% in KLG=1, 36.7% in KLG=2 and 28.8% in KLG=3-4. The OR (95% CI) for increasing severity of synovitis was 1.5 (1.0-2.3) in KLG=1, 2.4 (1.5-3.8) in KLG=2, and 1.5 (1.0-2.3) in KLG=3-4.

Tenderness upon palpation was most prevalent in joints with synovitis grade 2 and 3, while the prevalence was lower and similar in grade 0 and 1 (figure). The OR (95% CI) of tenderness upon palpation was 1.8 (1.3-2.6) in joints with synovitis grade 2-3 compared to joints with synovitis grade 0-1 in corrected univariate analyses (adjusted for age and sex). The association remained significant with OR 1.6 (1.1-2.5) in the multivariate model (adjusted for structural MRI features, age and sex).

Figure: Prevalence (%) of tenderness upon palpation in joints with different levels of MRI-defined synovitis (0=no, 1=mild, 2=moderate, 3=severe synovitis)



CONCLUSIONS: MRI-defined synovitis was most frequent in joints with mild radiographic hand OA, which may indicate a burn-out of inflammation in late disease. Synovitis was also associated with tenderness upon palpation, suggesting that inflammation may be a potential target for treatment of hand OA.

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SPONSOR: South-Eastern Norway Regional Health Authority
CORRESPONDENCE ADDRESS: haugen_ida@hotmail.com

ACTIVE SHAPE MODELLING OF BILATERAL KNEE OSTEOARTHRITIS IN THE OAI

Saunders F.R., Barr R.J, Reid D.M., Aspden R.M., Gregory J.S.
University of Aberdeen, Aberdeen, Scotland, UK

INTRODUCTION: Statistical shape modelling may be a useful tool for investigating the severity and progression of osteoarthritis. Studies so far have focused on individual joints, however this study is investigating whether a bilateral model of knee OA may be more beneficial.

OBJECTIVE: To determine the changes in osteoarthritis (OA) by active appearance modelling (AAM) of a bilateral model of the knees using radiographs from the Osteoarthritis Initiative.

METHODS: This model was based on an active shape model of a single knee used in previous studies, but extended to include both knees in a single model. A template of 186 points was applied to 156 baseline radiographs from the OAI using the AAM software to describe the shape of the knees. Here we describe the correlation (SPSS v18.0) between various measured parameters such as joint space narrowing and joint alignment in relation to shape and appearance models.

RESULTS: Hip-knee angle, medial joint space narrowing and joint alignment were highly correlated to both shape and appearance (Table). This was clearly shown by the model large changes observed in the distance between the knees, joint alignment, hip knee angle and medial joint space narrowing. Parameters such as symptomatic OA were linked to higher modes. In addition to the shape changes described above, appearance also showed sclerosis where there was evidence of joint space narrowing.

Variable	Shape mode 1 (r, (p))	Appearance mode 1 (r, (p))
Hip-knee angle (right)	0.558 (0.01)	0.565 (0.01)
Hip-knee angle (left)	0.507 (0.01)	0.523 (0.01)
Medial Joint space narrowing (right)	-0.348 (0.01)	-0.332 (0.01)
Medial Joint space narrowing (left)	0.367 (0.01)	0.370 (0.01)
Alignment (right)	-0.397 (0.01)	-0.391 (0.01)
Alignment (left)	-0.350 (0.01)	-0.346 (0.01)

CONCLUSION: The data shows that the new bilateral knee model shown here is a strong model which correlates common anatomical features of OA such as joint space narrowing with changes in shape and appearance.

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CORRESPONDENCE ADDRESS: Musculoskeletal Research, University of Aberdeen, 2.26 IMS, Foresterhill, Aberdeen, AB25 2ZD j.gregory@abdn.ac.uk 00 44 1224 437451

QUANTIFICATION OF TRABECULAR TIBIA BONE STRUCTURE RELATED TO THE PRESENCE OF OSTEOARTHRITIS

*,***Marques J., **Dam E.

* University of Copenhagen, Copenhagen, Denmark
** BiomedIQ, Rødovre, Denmark

INTRODUCTION: MRI has helped experts to diagnose OA by detecting early tissue changes. Current semiquantitative measures of the whole knee joint cover various structures within the joint, for example, the WORMS, the Knee Osteoarthritis Scoring System (KOSS) and the Boston-Leeds Osteoarthritis Knee Score (BLOKS). Focusing on bone quality, to the authors knowledge, only semi-automatic quantitative method exists for quantifying knee trabecular structure in MRI.

OBJECTIVE: We investigated the possibility of detecting OA by a fully automatic method analyzing the trabecular structure of the tibia bone in low-field MRI.

METHODS: The data consisted of 313 knees MRI from a community-based, non-treatment study with 159 subjects. The population characteristics were: age 56±16, BMI 26±4, 47% female, and 19% with radiographic OA (KLG>1). The KLG was determined from load-bearing radiographs in semi-flexed position using the SynaFlex (Synarc). MRI scans were acquired using a Turbo 3D T1 sequence from a 0.18T Esaote scanner (40° FA, TR 50ms, TE 16ms, scan time 10 minutes, resolution 0.7mm x 0.7mm x 0.8mm). Initially, the framework determines a region-of-interest (ROI) by segmenting the tibia bone using a voxel classification method. From the ROI, a generic set of 534 features is extracted by applying Gaussian derivatives at multiple scales. At next step, a machine learning approach applies partial least square feature extraction followed by linear discriminant analysis (LDA), using cross-validation with 300 repetitions. The first identifies the linear combination of the features that best discriminate the disease, and the second trains the classifier to recognize the trabecular bone of a knee with OA. For each knee, the bone structure marker estimates the classified probability of having OA.

RESULTS: The resulting marker was analyzed for the ability to separate OA (KLG>1) and healthy knees. The median area under the receiver-operator characteristics curve was 0.91 ($p<0.0001$). The figure shows the cross-sectional separation.

CONCLUSION: The investigation revealed that disease-related bone structure characteristics were reflected in the low-field MRI appearance. Even though the individual trabeculae are not visible, the outcome of our investigation demonstrated the possibility of analyze the intricate network of the trabecular bone as a whole and from this automatically quantify a bone structure marker strongly associated to the presence of OA.

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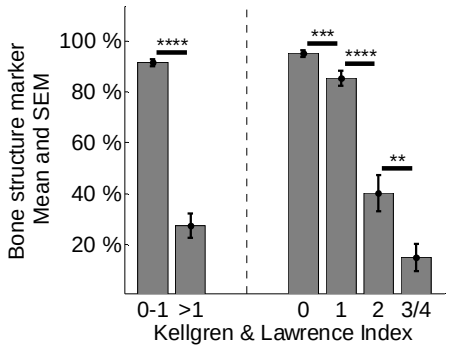
CORRESPONDENCE ADDRESS: jm@nordicbioscience.com



A MULTI-CENTER COMPARISON OF T2 RELAXATION TIMES CALCULATED CENTRALLY VERSUS THOSE GENERATED DIRECTLY BY THE MR SCANNER.

*Riek, J.K.

* VirtualScopics, Inc. Rochester, NY, USA

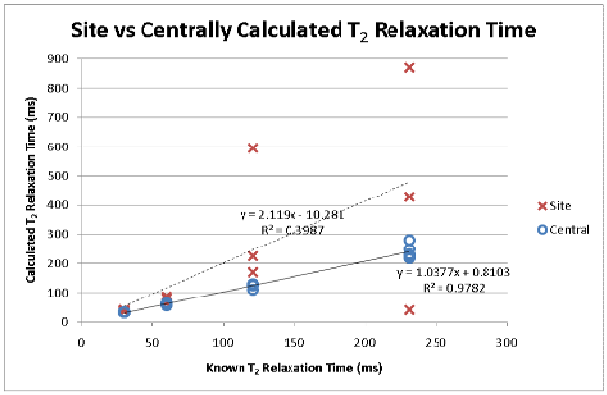
INTRODUCTION: T2 relaxation times in cartilage show differences according to variations in macromolecular concentration, collagen orientation and structure, and tissue hydration. Thus, T2 mapping has become a common method for analyzing the quality of cartilage tissue using magnetic resonance imaging (MRI). In a multi-center clinical trial, it is difficult to ensure that consistent T2 values are obtained across the different sites. Many scanners now provide T2 mapping sequences and the ability to generate a T2 map. These sequences and maps provide valuable information to the clinician, especially when looking at cartilage and cartilage repair tissue. This paper looks at the utility of these sequences and maps in the context of a multi-center clinical trial.

OBJECTIVE: The objective of this study was to examine the utility of imaging-site-generated T2 values via 1) the scan-rescan variability at a single site, 2) the inter-site variability across three imaging sites and 3) comparing the site measurements with centrally calculated measurements.

METHODS: Ten sets of four vials containing varying concentrations of copper sulfate ($CuSO_4$) (5mM, 10mM, 20mM and 40mM) were imaged in a GE 1.5T HDx magnet using a head coil to determine reference T2 values. Five single-slice, spin-echo series were collected (TR=2000ms, TE=12, 20, 40, 60, 80ms, thickness=1mm, matrix=256,256, FOV=17cm, NEX=2). Reference values of 30ms, 60ms, 121ms and 231ms were calculated using a linear regression on the natural log of the signal intensities. A different set of four vials was used for each magnet in this study. The different imaging parameters are shown in the table. For each sequence on the 3T magnets, a T2 map was also obtained directly from the scanner.

ID	Manufacturer	Model	Magnet	TR (ms)	TE (ms)
1	Philips	Achieva	3T	1050	13, 26, 39, 52, 65, 78, 91
2	Philips	Intera	3T	1050	13, 26, 39, 52, 65, 78, 91
3	Siemens	Verio	3T	1000	12, 23, 35, 47, 59, 70
4	GE	Signa HDxt	1.5T	800	8, 17, 25, 33, 42, 50, 58, 67
5	Siemens	Symphony	1.5T	3900	14,84

RESULTS: For the first objective, the T2 values from magnet 1 were calculated from five repeated scans. The average COV for the T2 values from the site T2 maps was 6.46%. For the centrally calculated T2 values, the average COV was 3.98%. For the second objective, the average T2 values were calculated from the site T2 maps for magnets 1-3. Results are shown in the graph. Average COV for the site values was 46.8%. For the centrally calculate T2 values, the average COV was 6.0%. For objective three, the centrally calculated T2 values for magnets 3 and 4 were added into the analysis. The average COV for the centrally calculated T2 values 5.0%. The Pearson correlation for site calculated values was R=0.63, and for the centrally calculated values, R=0.99.



CONCLUSION: From the results, it can be seen that there is a clear advantage to using centrally calculated T2 values, and that using T2 values generated from the scanner introduces substantial variability. The next step is to scan and analyze knees imaged on multiple magnets.

DICLOSURE STATEMENT: Jonathan Riek is the CTO of VirtualScopics, which provides consultative and central analysis services to several sponsors concerning T2 analysis.

CORRESPONDENCE ADDRESS: jon_riek@virtualscopics.com

IMPROVED ASSESSMENT BY QUANTITATIVE DIGITAL HISTOMORPHOMETRY OF HISTOPATHOLOGICAL CHANGES OF ARTICULAR CARTILAGE IN A SURGICAL MODEL OF POST-TRAUMATIC OSTEOARTHRITIS OF THE KNEE JOINT IN RATS

Rudolphi K, Aigner S, Berg-Scholl I, Bissinger T, Keiffer R, Wunschel, M

sanofi-aventis, TSU Aging, Musculoskeletal Cluster, Frankfurt-Main, Germany

INTRODUCTION: Surgically-induced knee joint instability in rats by transection of the Anterior Cruciate Ligament (ACLT), Partial Medial Meniscectomy (pMx) or a combination of both (ACLTpMx), is one of the most commonly used experimental animal models of post-traumatic osteoarthritis (Gerwin, N. et al. 2010, Osteoarthritis & Cartilage 18, S3: 24-34). However, little has been published on the temporal evolution of the histopathological changes (Hayami, T. et al. 2006, Bone 38:234-243).

OBJECTIVE: The goal of the study is to evaluate the development of the histopathological changes over time in a model of surgically-induced osteoarthritis of the knee joint in rats (ACLTpMx) and to compare the most frequently used subjective semi-quantitative scoring of joint damage with computerized quantitative digital histomorphometry.

METHODS: 88 male skeletally mature Lewis rats (12 weeks of age, n = 10-12 animals/group) were subjected to unilateral transection of the Anterior Cruciate Ligament plus 25% removal of the Medial Meniscus (ACLTpMx model) or sham operated. Three, 7, 28, 56 and 84 days following ACLTpMx the animals were sacrificed and 7µm Hematoxylin-Eosin- and Safranin-O-stained coronal paraffin sections were scored for the degree of joint damage by two observers in a blinded fashion using a modified Mankin-score consisting of 7 sub-scores (loss of chondrocytes, cartilage fibrillations and fissures, cartilage ulceration, loss of proteoglycan staining, synovitis and subchondral bone sclerosis). For quantitative histomorphometry digital images of the medial tibial plateau (MTP) were analyzed using the software Integrator VIS System Version Nr. 3.0.15.0 (http://www.visiopharm.com Denmark). The degree of cartilage destruction and subchondral bone sclerosis was quantified by measuring the following parameters: 1. Fibrillation Index (FI= the Euclidean length of the cartilage area divided by the surface curvature length), 2. the cartilage area, 3. the number of chondrocytes (total number and number/mm^2) and 4. the area of solid subchondral bone tissue.

RESULTS: The histopathological changes developed rapidly with increasing severity over time. Already 28 days after ACLTpMx moderate to severe signs of OA (chondrocyte loss, cartilage fibrillation and erosion as well as subchondral bone sclerosis) were observed. Only a mild synovitis developed. Chondrophytes were seen frequently but only very few classical mature osteophytes were observed, even at the latest time point of 84 days. Sham-operated animals did not develop significant OA pathology at any time point. The histomorphometric parameters showed a significant correlation with the respective Mankin-subscores. At the latest observation time point of 84 days post OA induction MTP cartilage area was 46±12% smaller and chondrocyte density 35±13% lower, whereas the area of sclerotic subchondral bone was 47±11% larger vs. an age-matched sham operated group.

CONCLUSION: The ACLTpMx model of OA in rats shows similar features as human knee OA regarding anatomical location and the specific histopathological morphology with the exception of osteophytosis. Quantitative digital histomorphometry of cartilage destruction and subchondral bone sclerosis offers a more objective and less time consuming assessment of OA histopathology in this experimental model than classical histopathological scoring, thus facilitating the preclinical pharmacological testing of potential DMOADs.

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CORRESPONDENCE ADDRESS: karl.rudolphi@sanofi-aventis.com; phone 0049-69-305-15299

AN INTEGRATIVE IMAGING APPROACH FOR EXAMINING BONE AND CARTILAGE TISSUES IN THE OSTEOARTHRITIC JOINT – A PILOT STUDY

*Stok, K.S., **Glanzmann, M., *Steiner, T., *,** Goldhahn, J., *Müller, R.

* Institute for Biomechanics, ETH Zürich, Switzerland
** Schulthess Clinic, Zürich, Switzerland

INTRODUCTION: Osteoarthritis (OA) is characterised in part, by architectural and structural alterations to the cartilage and bone matrices, and affects the quality of these materials and their arrangement, it is the aim of this work to relate material quality and structure (of bone and cartilage) to arthritis, with the goal of providing real targets for arthritis treatment. Conflicting reports of the spatial degeneration to the bone and cartilage tissues are exacerbated by the inability to image both tissues in one imaging system. In this pilot work an approach for integration of imaging data is explored.

OBJECTIVE: Micro-computed tomography (micro-CT) and magnetic resonance imaging (MRI) are used to examine the spatial relationships between cartilage and bone in the same human humeral head. Correlations between MRI and CT morphometry are used to draw conclusions for continued development of the approach for a larger study population.

METHODS: A humeral head was harvested during surgery from an elderly patient undergoing replacement of the joint. Consent from the patient and the local ethics committee was received. Gross observation showed pitting, delamination and full thickness loss of cartilage tissue. After surgery, the sample was scanned using micro-CT (μCT 80, Scanco Medical, CH) at an isotropic voxel size of 30 μm, followed by MRI (Achieva, 3.0 Tesla, Philipps, Andover, Massachusetts, USA). The sample was immersed in Fombolin oil to enhance cartilage contrast, and scanned at 0.15 mm in-plane (0.3 mm out-of-plane) resolution using a T1 enhanced Gradient Echo Sequence, with water selective excitation.
Following scanning the samples were dissected and prepared for paraffin histology, and subsequently stained with hematoxylin and eosin. Two-dimensional cartilage thickness from histology was calculated.
CT and MRI data were registered, and the four quarters of the humeral head were digitally extracted as regions of interest for subsequent analysis. Quantitative bone and cartilage morphometric analysis was performed for standard measures: bone volume density (BV/TV), trabecular thickness (Tb.Th), trabecular spacing (Tb.Sp), and cartilage thickness (Cg.Th). Correlation plots for the morphometric parameters were drawn as pilot data for a planned larger study.

RESULTS: Our results show that the cartilage thickness measured from histology slides was 0.73 to 0.97 mm, while that measured from MRI was 1.23 to 2.07 mm (S.D. 0.45 mm). A correlation between the two methods will be followed-up for presentation. Plotting Cg.Th against Tb.Th shows an inverse correlation, where the thicker cartilage lies across a thinner trabeculae, while a direct correlation appears to exist with Tb.Sp. No correlation was found for BV/TV and Cg.Th. Visual inspection of the data supports this where thinner cartilage overlies densified bone structures, and thus begs the question how best to divide the humeral head for the most suitable volume of interest definition. Also seen visually is the loss of curvature in the bone contours. Methods for measuring this will be explored, as it also appears to be co-registered with the worst cartilage changes.

CONCLUSION: Literature shows that the healthy humeral head has an average thickness between 0.77 and 1.11 mm with the thickest part being the central portion. Since MRI has an in-plane resolution of 0.15 mm and out-of-plane resolution of 0.3 mm, it is fair to assume that the partial volume effect would overestimate this value. Next steps will involve registering the histology slides to the MRI data to calculate a direct correlation between the methods (a necessary result for the integrated approach), and also explore the best definition for the spatial division (volumes of interest) of the samples.
This pilot study shows a promising approach for the integration of data from multiple technologies to draw conclusions about the relationships between cartilage and bone. This study will be completed with a further 46 humeral heads, including the identification of joint specific changes in the gene expression profile in human humeral cartilage and bone, and the correlation of this with bone and cartilage structural changes measured using this integrated imaging approach.

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CORRESPONDENCE ADDRESS: kas@ethz.ch

SIZE AND POSITION OF THE HEALTHY MENISCUS, AND ITS CORRELATION WITH SEX, HEIGHT, WEIGHT, BONE SIZE, AND AGE

*Bloecker K., *Wirth W., *Hudelmaier M., **Burgkart R., ***Frobell R., *Eckstein F.

* Institute of Anatomy and Musculoskeletal Res., Paracelsus Medical University, Salzburg , Austria
**Clinic for Orthopaedics and Traumatology, Technical University Munich, Germany
*** Department of Orthopaedics, Clinical Sciences Lund, Lund University, Lund, Sweden

INTRODUCTION: Symptomatic knee osteoarthritis is known to be more common in women than in men. Also, it is suspected that meniscus extrusion increases the peak loads in the knee, which in turn increase the incidence of knee OA. Recently, an MR imaging-based method for quantitative analysis of meniscus size, shape and position (extrusion) has been introduced, which can be applied in vivo [1]. Since men are, however, larger (and heavier) than women, a comparison of size-related morphometric meniscus measures between both sexes is not easily made.

OBJECTIVE: 1) To test whether meniscus size, shape or position differ between men and women who are without symptoms, signs and risk factors of knee OA; 2) To examine to what extent the size of the normal meniscus correlates with body height, weight, and bone size, in men and women. 3) To identify whether a relative measure of meniscus size can be derived for a direct comparison between sexes.

METHODS: Knees of the healthy reference cohort of the Osteoarthritis Initiative (47 men; 70 women) without radiographic signs, symptoms or risk factors for OA were studied. 3-D multi-planar reconstructed coronal DESSwe MR images were used. Segmentation of the tibial plateaus and menisci was performed in the medial and lateral femoro-tibial compartment, and 3-D measures of meniscal size and position were computed [1]. Differences in these measures between men and women (non-paired t-test) and Pearson correlation coefficients with body height, weight, ipsi-compartimental, contra-compartimental, and total tibial plateau size were calculated. Finally, the ratio between total meniscus surface and the ipsi-compartmental tibial bone size was compared between men and women

RESULTS: The total tibial plateau area was 26% greater in men (22.8cm^2) than in women (18.0cm^2). The total medial meniscal surface area (17.8cm^2 in men, 14.7cm^2 in women; +18%; $p<0.001$), and the total lateral meniscal surface area (18.5cm^2 in men, 14.5cm^2 in women; +22%; $p<0.001$) were also significantly different between both sexes.
Ipsi-compartmental tibial bone size was more strongly correlated with medial/lateral meniscus size in men (r=0.71/0.67) and women (r=0.63/0.68) than the contra-compartmental or total tibial bone size, body height or body weight. No significant correlation was observed with age.
The ratio between the total meniscus surface areas and the ipsi-compartmental tibial bone size was similar between men and women (medial meniscus: 1.52±0.16 in men and 1.55±0.16 in women; p=0.37; lateral meniscus: 1.69±0.19 in men and 1.71±0.16 in women; p=0.57). The within-sex, inter-subject variability for the above ratio was considerably smaller than that for total meniscus surface area without normalization (CV%: medial meniscus 10.3% vs. 14.8% in men / 10.5% vs. 13.3% in women; lateral meniscus 11.1% vs. 14.0% in men and 9.5% vs. 12.0% in women).
Tibial coverage was similar in men and women (50% medially; 58% laterally). However, medial meniscal extrusion was significantly greater in healthy women (1.82±1.03mm) than in healthy men (1.19mm±1.26mm; $p<0.01$).

CONCLUSION: The ratio between meniscus surface area and (ipsi-compartmental) tibial bone area provides a useful measure for comparing meniscus size across different cohorts with mixed sexes, for instance when testing whether knees with OA display meniscus hypertrophy [1,2]. Although tibial plateau coverage by the meniscus is similar in healthy men and women, medial meniscus extrusion was greater in women. This may provide potential clues as to why women are at greater risk of symptomatic knee OA than men.

REFERENCES: [1] Wirth W et al.. Magn Reson Med 2010; 63 1162-71; [2] Jung KA et al.. Rheumatol Int 2010; 30 1325-33
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CORRESPONDENCE ADDRESS: katja.bloecker@pmu.ac.at

FEASIBILITY OF BONE DENSITY EVALUATION USING PLAIN DIGITAL RADIOGRAPHY

* & ** Kinds M.B., * Marijnissen A.C.A., ** Vincken K.L., ** Bartels L.W., ** Viergever M.A.,
*** de Jong H.W.A.M., *Lafeber F.P.J.G.

* Rheumatology & Clinical Immunology, University Medical Center Utrecht, the Netherlands
** Image Sciences Institute, University Medical Center Utrecht, the Netherlands
*** Radiology, University Medical Center Utrecht, the Netherlands

INTRODUCTION: For the evaluation of subchondral bone density (BD) changes due to OA, Dual Energy X-ray Absorptiometry (DEXA) is the most validated method. The need for DEXA might be reduced if the quantitative measurement of clinically relevant BD changes on radiographs is proved feasible, since radiographs are commonly acquired to evaluate structural changes due to OA. Precision of BD evaluation might be influenced by variations in acquisition settings that commonly occur in clinical practice and by post-processing (PP) that was introduced with the transition from conventional film-screen radiography to digital radiography.

OBJECTIVE: To evaluate the effects of PP and acquisition settings on the precision and with that feasibility of BD measurement using plain digital radiography.

METHODS: A bone density standard (BDS) was created consisting of eight cups with hydroxyapatite (HA: range 1.0-5.75 g/cm^2). Digital radiographs of the BDS were taken (Philips Digital Diagnost), with variations in the acquisition and PP settings. Tube voltage (in kilovolt: kV), exposure (in milliampere seconds: mAs), tube added filtering, and BDS position in the field-of-view were systematically varied and the default clinical PP was compared with minimal PP (at minimal strength). An aluminum step wedge served as an internal reference to express gray values of the BDS in mm aluminum equivalents (mmAl), by use of custom made software. In all cases a human (cadaver) knee joint was added to simulate clinical conditions. The relation (R^2) between the BD values normalized to the reference wedge (in mmAl equivalents) and actual BD (HA in g/cm^2), with variations in acquisition and PP settings was evaluated with linear regression analyses. Precision of BD measurement of the BDS was calculated in early OA (Cohort Hip & Cohort Knee: CHECK) to evaluate the relevance for clinical (research) practice.

RESULTS: The BDS was validated by DEXA scanning and the relation between actual HA (g/cm^2) and DEXA values was strongly linear: R^2=0.99. In general for digital radiographs a strong correlation between actual BD and BD in mmAl was found for all settings. The correlation improved by changing PP from clinical (R^2=0.96) to minimal (R^2=0.98). Higher kV improved the correlation further. Even, for clinical PP mean SD was 0.97 mmAl, much smaller than the change of 2.51 mmAl clinically observed during two-year follow-up in early OA which implies the feasibility of BD measurements using plain digital radiography.

CONCLUSION: Accurate bone density measurement using digital radiography is feasible in a clinically relevant range, which removes the need for additional DEXA scans since plain radiographs are acquired for to evaluate structural changes due to osteoarthritis. Care should be taken in changing post-processing and acquisition settings, which can have profound effect on outcome.

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CORRESPONDENCE ADDRESS: M.B.Kinds@umcutrecht.nl.

SIDE DIFFERENCES OF THIGH MUSCLE CROSS SECTIONAL AREAS IN KNEES WITH THE SAME RADIOGRAPHIC OA (KL) GRADE, BUT UNILATERAL FREQUENT PAIN

*Sattler M., *Dannhauer T., *Hudelmaier M., **Sänger A.M., ***Hunter DJ., ****Kwoh K., *Eckstein F., for the OAI investigators

* Paracelsus Medical University, Salzburg , Austria & Chondrometrics GmbH, Ainring, Germany
** Organismic Biology, Natural Science Faculty, Salzburg University, Salzburg, Austria
*** Royal North Shore Hospital & Northern Clinical School, University of Sydney, Sydney, Australia.
**** Division of Rheum. and Clinical Immunology, Univ. of Pittsburgh and Pittsburgh VAHS, PA

INTRODUCTION: It has been reported that thigh muscle status, specifically anatomical cross sectional areas (ACSAs) and maximal force, may play a role in the onset and progression of knee OA. It is, however, less clear whether changes in ACSAs and muscle force are associated with OA "per se", or with knee pain (that is associated with knee OA). As many, but not all knees with radiographic OA (rOA) are painful, we aim to take a first step in disentangling the above relationships by studying whether the pain status in knees with OA is associated with differences in thigh muscle status.

OBJECTIVE: 1) To determine whether ACSAs of the thigh extensors, flexor, and adductors display significant side-differences (same person) between the knee with frequent pain (i.e. painful knees) vs. those without pain (i.e. painless knees) with the same rOA grade (i.e. calculated KLG2 or 3, from OARSI atlas graded osteophyte and JSN status); 2) to analyze whether extensor and flexor muscle forces show significant side-differences in painful vs. painless rOA knees, and 3) to examine the correlation between force and ACSAs in painful vs. painless rOA knees.

METHODS: A between-knee, within-person design was used to study knees with frequent pain (most days of the month within the past 12 months; P01SxKOA=2) versus knees without pain P01SxKOA =0), in participants with the same rOA grade (P01OAGRD: KLG2 or 3) in both knees. All cases satisfying these criteria (that did not show a change in pain frequency >1 grade within the next 12 months) were drawn from the 4796 Osteoarthritis Initiative (OAI) participants (public-use data sets 0/1.2.2): 31 women, 17 men (n=48; age 45-78 years). Public use MRI data (0.E.1.: T1-weighted SE sequence) and custom software were used to determine the ACSAs of the extensors, flexors and adductors in the axial image that was located at 35% of the femoral length (from distal to proximal; estimated based on body height) and in the two adjacent images (0.5 cm proximal and 0.5cm distal). The vastus medialis (VMO) MSCA was determined in a slice located at 31% (distal to proximal). Maximal isometric extensor (V00_R/L_EmaxF) and flexor forces (V00_R/L_FmaxF) were taken from the OAI data base. These were measured using an isometric chair (Metitur Oy, Jyvaskyla, Finland). A paired t-test was used to compare between painful and contra-lateral painless knees within participants.

RESULTS: Painful knees showed significantly lower extensor ACSAs (49.6 vs. 52.6 cm^2; -6.2%; p=0.00003), VMO ACSAs (16.5 vs. 17.6 cm^2; -7.8%; p=0.0007) and maximal extensor muscle forces (331 vs. 364 N; -15,4%; p=0.003) compared with contra-lateral painless knees. In contrast, there were no significant differences in flexor and adductor ACSAs or flexor forces (all p>0.39). Results were similar in men and women, and in KLG2 and KLG3 knees. The maximal force per unit ACSA tended to be lower in painful vs. painless knees (6.55 vs. 6.87 N/cm^2, p=0.058 for the extensors, and 4.39 vs. 4.48 N/cm^2, p=0.57 for the flexors) but the differences did not reach statistical significance. The correlations between extensor force vs. extensor ACSA were r=0.64 in painful and r= 0.66 in painless knees, those between flexor force vs. flexor ACSA r=0.44 in painful and r= 0.52 in painless knees, and those between extensor and flexor force 0.69 in painful and 0.79 in painless knees. Again, the correlations were similar in men and women and in KLG2 and KLG3 knees.

CONCLUSION: Knees with rOA and frequent knee pain demonstrate reduced extensor muscle ACSAs and force compared to contra-lateral rOA knees without knee pain, but no differences in flexor ACSAs and force, or adductor ACSAs. Further longitudinal studies are needed to determine whether muscle status is "cause or consequence" of knee pain. Nevertheless, the current findings provide support to quadriceps strengthening programs for knee pain in rOA.

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DISCLOSURE STATEMENT: see affiliations
CORRESPONDENCE ADDRESS: martina.sattler@pmu.ac.at

SIGNIFICANT INFLUENCE ON LOAD RESPONSE OF KNEE CARTILAGE T2 BY MENISCUS DISORDER –A LOADING MRI STUDY

*Nishii T., *Tamura S., ** Shiomi T., ***Yamazaki Y., ***Murase K., ****Tanaka H., *Yoshikawa H., **Sugano N.

* Department of Orthopaedic Medical Engineering, ** Department of Orthoaedic Surgery,
*** Department of Medical Physics and Engineering, and **** Department of Radiology,
at Osaka University, Osaka, Japan

INTRODUCTION: Disorder of the meniscus may lead to abnormal load distribution in response to load-bearing, resulting in high prevalence of osteoarthritis progression. Non-invasive evaluation of intra-articular biomechanical condition after meniscus injury is important to estimate risk of subsequent progression of osteoarthritis. We previously showed that responsiveness of cartilage T2 value to compressive loading during MRI is a potent index of pressure distribution on the cartilage, reflecitng dynamic changes in the collagenous architecture or water influx or efflux.

OBJECTIVE: Difference of load response of cartilage T2 was compared between patients with and without (w/wo) meniscus disorder using loading MRI system, to estimate change of abnormal pressure distribution associated with meniscus disorder.

METHODS: Nineteen patients who were scheduled for arthroscopic surgery due to ACL injury and/or meniscus injury underwent MRI on a 3.0 T scanner. There were 3 men and 16 women and the mean age was 30 years (18 to 47). During MRI, patients were laid on a custom-made loading apparatus which had a pulley system linked to a sliding foot plate, and 50% of the body weight was applied via the foot plate when loading (Fig 1). On unloading and loading conditions, sagittal T2 maps of the medial and lateral femoro-tibial (FT) joints were obtained from multi- spin echo sequence with fat-suppression (TR, 1500 ms; 8 echoes between 10.0 ms and 80.0 ms; FOV, 12 cm; matrix, 384 × 256; slice thickness, 3 mm). On each of medial and lateral mid-sagittal image, the cartilages at the weight-bearing ranging anterior and posterior margins of the meniscus were divided into 3 sections with equal length, and each section was further divided into deep and superficial layers with equal thickness using a custom-made software (Fig 2). Change of T2 values by loading in each ROI was compared between knees w/wo meniscus tears at each medial and lateral FT joint, using Mann-Whitney U test.

RESULTS: Meniscus tears were found in 8 knees at the medial FT joint and in 9 knees at the lateral FT joint by arthroscopy. On unloading condition, there was no significant difference of cartilage T2 at each ROI between knees w/wo meniscus tears at each medial and lateral joint. By loading, T2 was likely to decease at each zone, as compared with unloading condition. At the medial FT joint, there was no significant difference of T2 change by loading at each ROI between knees w/wo medial meniscus tear. At the lateral FT joint, however, there was significantly difference of T2 change at the PS of the tibial cartilage between knees w/wo lateral meniscus tear. (+6.1 % vs -2.4 %, $p<0.05$, Fig 3).

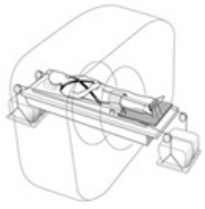

Fig 1. loading apparatus

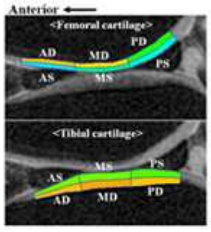

Fig 2. Definition of ROIs

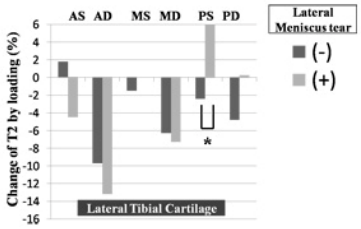

Fig 3. T2 change by loading on the lateral tibial cartlage

CONCLUSION: Assuming that decrease of T2 value by loading was correlated with applied pressure load onto the cartilage, lateral meniscus disorder might result in shift of stress concentration to the anterior part of lateral tibial condyle. T2 assessment using loading MRI may be useful in estimating risk of subsequent OA progression and determination of indication for meniscus surgery.

SPONSOR: none
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CORRESPONDENCE ADDRESS: nishii@ort.med.osaka-u.ac.jp

CARTILAGE SIGNAL INTENSITY ON MRI: ASSOCIATION WITH BODY MASS INDEX, CARTILAGE DEFECTS AND TYPE II COLLAGEN BREAKDOWN

*Stannus O.P., *Jones,G., * **Ding C.

* Menzies Research Institute, University of Tasmania, Hobart, Australia
** Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

INTRODUCTION: MRI has enabled the observation of many abnormal features of OA. However, the ability of MRI to detect early osteoarthritic changes is limited.

OBJECTIVE: Our aim was to develop a semi-automatic computer program to assess cartilage signal intensity on T1-weighted MRI images, and then examine whether signal intensity is associated with 1) body mass index (BMI), 2) cartilage defects, and 3) type II collagen breakdown in young to middle-aged adults.

METHOD: A total of 50 subjects (mean age 41, range 29-57; 64% female) were randomly selected from the community. MRI scans of right knees were performed (sagittal T1-weighted fat saturation 3D gradient recall acquisition in the steady state; flip angle 55°; repetition time 58ms; echo time 12ms; 512x512 matrix with 0.31x0.31mm resolution; 60 partitions at 1.5mm thickness). Image segmentation was performed semi-automatically using custom software written in MATLAB, and measures of mean signal intensity for different regions of cartilage were obtained. Urinary levels of C-terminal crosslinking telopeptide of type II collagen (U-CTX-II) were measured. Cartilage defects were scored using a 5-point scale. Multivariable linear regression was used to test associations.

RESULTS: Cartilage signal intensity varied by site (mean (SD) for femur: 120.1 (8.4); medial tibia: 94.5 (9.8); lateral tibia: 95.9 (11.6); patella: 123.4 (10.7)). After adjustment for confounders, BMI was negatively associated with mean signal intensity of cartilage in the medial femoral (β=-0.82 per kg/m², p=0.005), lateral femoral (β=-0.69 per kg/m², p=0.020), whole femoral (β=-0.60 per kg/m², p=0.034) and lateral tibial (β=-0.80 per kg/m², p=0.027) sites. Cartilage defects were associated with same-region mean intensity in the lateral tibia (β=-10.22 per grade, p=0.017), and patella (β=-6.06 per grade, p=0.002). After excluding cases with cartilage defects, CTX-II was negatively associated with mean signal intensity in the medial femoral (β=-2.46 per pg/ml, p=0.010), lateral femoral (β=-2.13 per pg/ml, p=0.036), whole femoral (β=-2.44 per pg/ml, p=0.010) and patellar (β=-2.77 per pg/ml, p=0.031) sites.

CONCLUSION: Reduced cartilage signal intensity on MRI is associated with early osteoarthritic changes and thus may be used as a marker of early osteoarthritis.

SPONSOR: University of Tasmania Rising Star Program
DICLOSURE STATEMENT: none.
CORRESPONDENCE ADDRESS: ostannus@utas.edu.au

DIAGNOSIS OF OA BY AUTOMATIC QUANTIFICATION OF INCONGRUITY FROM KNEE MRI

*Tummala S., **Dam E.B., *Nielsen M.

* eScience Center, University of Copenhagen, Copenhagen, Denmark
** BiomedIQ, Rødovre, Denmark

INTRODUCTION: Biomechanical factors play a vital role in the pathogenesis of OA. Incongruity may be an important factor that is responsible for the initiation and progression of OA in the synovial joints.

OBJECTIVE: We investigated whether medial tibio-femoral incongruity computed automatically from MRI could be appropriate as a diagnostic marker of OA.

METHODS: The study population consisted of 159 subjects with 48% female. The age and BMI of the subjects were 21-82 years and 18-38 (kg/m^2) respectively. Radiographs were acquired to grade the severity of OA by the KLG. The MRI scans were acquired using an Esoate C-span scanner at 0.18T (40^0 flip angle, 50 ms repetition time and 16 ms echo time). The medial FT cartilage compartments were segmented automatically using a voxel classification approach.
Contact area (CA) of the tibio-femoral compartment was estimated by employing the voxel width (0.7mm) as threshold. Further, in the contact region, the point-by-point incongruity (dimensionless number) was quantified over CA as the inverse mean of the distance between local normal vectors scaled by signed curvature along local principal knee motion. The precision of incongruity was quantified on 30 scan-rescan pairs as Root mean squared coefficient of variation (RMS CV). The ability of incongruity to separate healthy from OA was quantified as area under ROC curve (AUC). The population was randomly split into train subpopulation and validation subpopulation. The parameters in the quantification (curvature scale and iteration number in mean curvature flow) were optimized for best AUC on train subpopulation and then tested on validation subpopulation. The process was repeated 100 times and the resulting median scores on the validation subpopulation were reported.

RESULTS: The precision of the incongruity measure was 7.7%. The incongruity map for a healthy knee was shown below (blue is good and red is bad). The ability of the incongruity to separate healthy (KL 0) and early OA (KL 1) was significant with AUC 0.64 ($p < 0.01$). The ability of the incongruity to separate KL (0-1) and KL > 1 was significant with AUC 0.71 ($p < 0.0001$) and the corresponding cross-sectional separation was also shown in the figure.

CONCLUSION: We present a method to quantify the medial tibio-femoral joint congruity automatically from MRI. From the quantifications, we conclude that the incongruity might separate healthy from early OA with statistical significance. In general, the healthy knees were less incongruent than OA knees in the medial tibio-femoral compartment.

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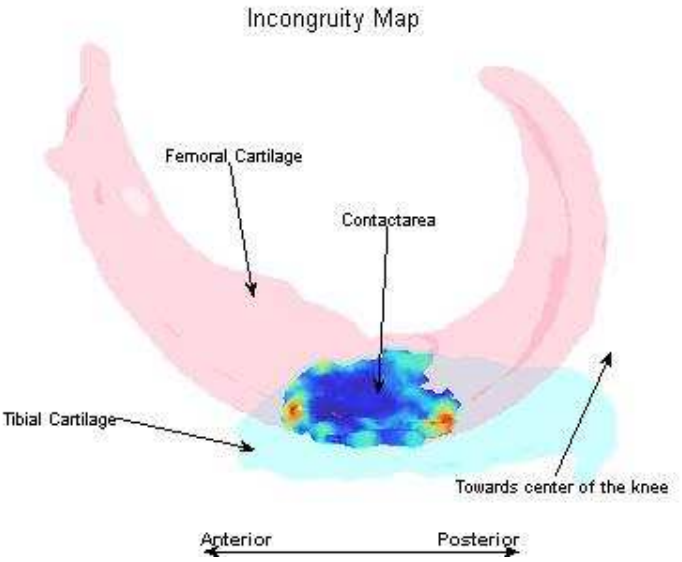
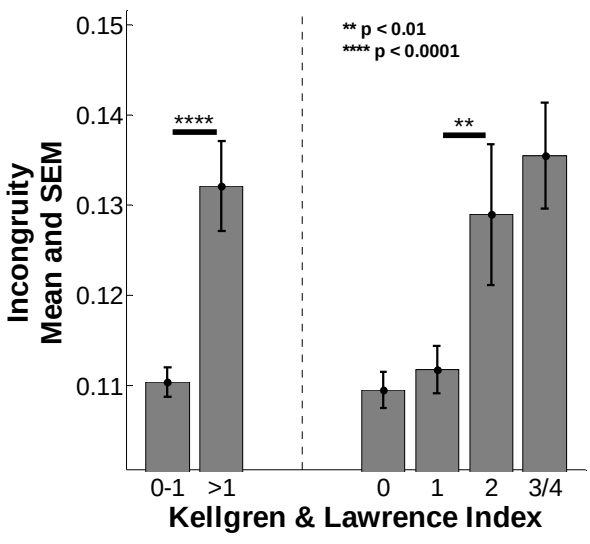
CORRESPONDENCE ADDRESS: stu@nordicbioscience.com





QUANTITATIVE CT FOR KNEE OSTEOARTHRITIS

*Lowitz T., *Zerfaß P., *Engelke K., *Museyko O., **Laredo J.-D., **Bousson V., *Kalender W.A.

* Institute of Medical Physics, University of Erlangen-Nürnberg, Germany
** Service de Radiologie Ostéo-Articulaire, Hôpital Lariboisière, Paris, France

INTRODUCTION: As changes in subchondral bone structure are a major factor in OA progression, quantifying them would strongly improve the understanding of the pathogenesis of the disease. QCT is a promising tool to analyze changes in bone density and structure.

OBJECTIVE: 1) Our goal is to segment femur and tibia in the knee environment, as well as the growth plates in both bones that will further be used to automatically define an anatomic coordinate system and volumes of interest (VOIs) that differentiate between medial and lateral bone side, as well as regions of different distances from the joint gap.
2) We further calculate several parameters within these VOIs that quantify the bone state.
3) Finally we evaluate the reproducibility of our method.

METHODS: In order to evaluate the precision of our analysis results, we used CT-datasets of 20 ex-vivo knees, which have been scanned twice (with repositioning). The images were acquired on a Siemens SOMATOM Sensation 64 scanner with a slice thickness of 0.5 mm, a tube voltage of 120 kV and a tube current of 212 mA. The CT images were reconstructed with a reconstruction increment of 0.3 mm and a field of view of 13 cm, leading to a voxel size of 0.254 x 0.254 x 0.3 mm³. To obtain BMD values, a calibration with the Siemens Osteo phantom was performed. Subsequently, the images were segmented and the respective parameters calculated. These are BMD, BMC, volume, the texture parameters global and local homogeneity, global and local anisotropy, entropy and fractal dimension in every VOI, as well as joint gap volume, minimum and average joint gap distance. To quantify the reproducibility of the results, the root mean square deviation of the coefficient of variation (CV(RMSD)) of all parameters was calculated.

RESULTS: The results of the precision analysis of the BMD values of all VOIs are presented in Table1(Tibia) and Table2(Femur). The VOIs go from near to far according to distance from joint gap and are namely cortical, extended cortical, subchondral epiphyseal, mid-epiphyseal and juxtaphyseal VOIs. They are each divided into a medial, lateral and total region.

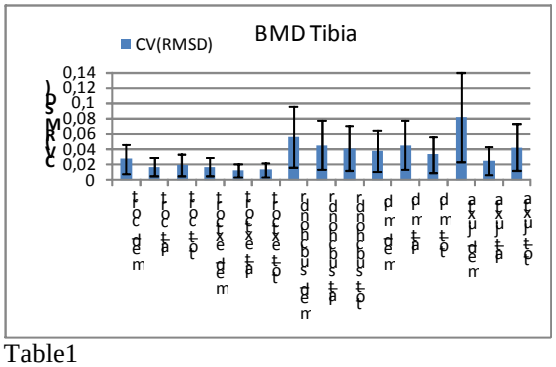


Table1

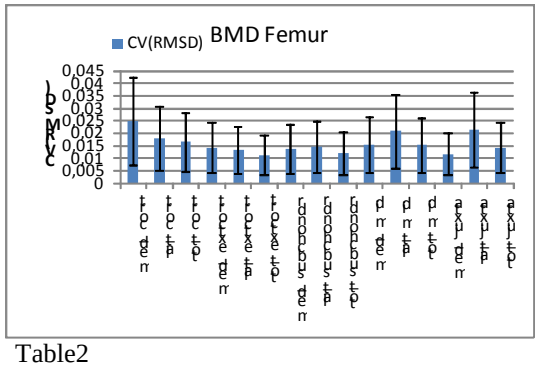


Table2

CONCLUSION: A semi-automatic software application was built, that is capable of segmenting the relevant bone structures in the knee, automatically places VOIs in important bone regions and calculates various parameters that further needs to be evaluated. As can be seen from the tables, the BMD precision of the femur VOIs is already pretty good with a CV(RMSD) of no more than 2,5 %. Improvement is yet needed on the results of some VOIs of the tibia.

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CORRESPONDENCE ADDRESS: Torsten.Lowitz@imp.uni-erlangen.de

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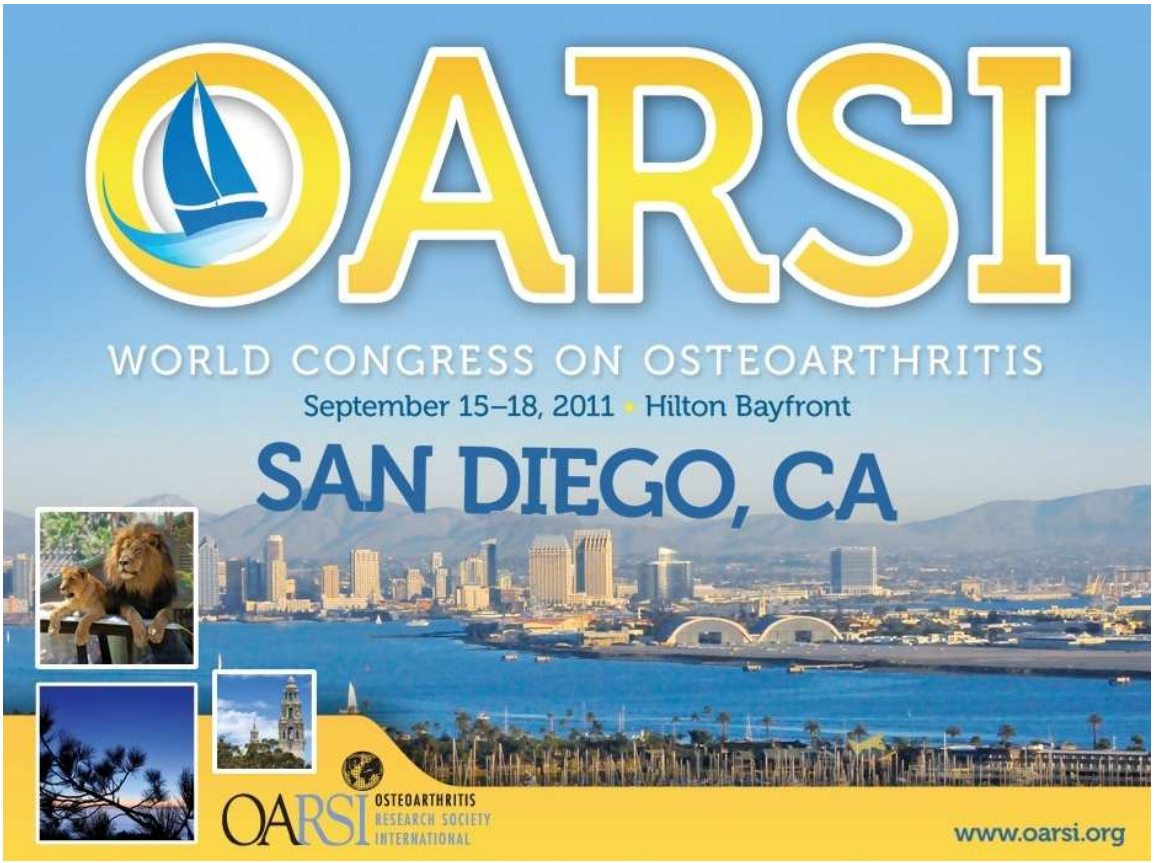

6th International Workshop on Osteoarthritis Imaging combined with the
OARSI OA Biomarkers Workshop III - Imaging Biomarker Validation and Qualification

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